



Contents lists available at ScienceDirect

## Taiwanese Journal of Obstetrics &amp; Gynecology

journal homepage: [www.tjog-online.com](http://www.tjog-online.com)

## Original Article

## Comparisons of survivals and toxicities between young and elderly patients with cervical cancer treated with definitive radiotherapy or concurrent chemoradiotherapy

Weiping Wang, Xiaoliang Liu, Qingyu Meng, Fuquan Zhang<sup>\*,1</sup>, Ke Hu<sup>\*\*,1</sup>

Department of Radiation Oncology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences &amp; Peking Union Medical College, Beijing, China

## ARTICLE INFO

Article history:  
Accepted 21 August 2018Keywords:  
Uterine cervical neoplasms  
Age groups  
Aged  
Radiotherapy  
Chemotherapy

## ABSTRACT

**Objective:** To compare the survivals and toxicities of young and elderly patients with cervical cancer treated with definitive radiotherapy or concurrent chemoradiotherapy (CCRT).**Materials and methods:** Patients with cervical cancer treated with radiotherapy or CCRT between January 2010 and December 2015 in our institute were reviewed. A dose of 50.4 Gy in 28 fractions was delivered to the pelvis with intensity modulated radiation therapy. In addition, a dose of 30–36 Gy in 5–7 fractions was prescribed to point A with brachytherapy. Weekly cisplatin was the first-line regimen of concurrent chemotherapy. Comparisons were made between patients in the young group (<60 years) and those in the elderly group (≥70 years) with multivariate analysis and propensity score matching.**Results:** There were 991 patients in the young group and 70 patients in the elderly group. The median follow-up period was 30.2 months. In multivariate analysis, age was an independent factor of overall survival (OS, hazard ratio, HR 1.99,  $p = 0.014$ ), but it was not significant in predicting disease-free survival (DFS, HR 1.41,  $p = 0.179$ ) and cancer-specific survival (CSS, HR 1.38,  $p = 0.332$ ). After propensity score matching, 64 pairs of patients were selected. The 3-year OS, DFS, and CSS rates in the young and elderly groups were 86.5% and 73.9% ( $p = 0.280$ ), 74.6% and 75.4% ( $p = 0.744$ ), and 87.9% and 81.7% ( $p = 0.967$ ), respectively. Significant differences between the young and elderly groups were observed in grade 3 and above chronic toxicities (2.9% and 8.6%,  $p = 0.027$ ) and grade 3 and above chronic gastrointestinal toxicities (2.4% and 8.6%,  $p = 0.009$ ).**Conclusion:** After definitive radiotherapy or CCRT, the DFS and CSS of elderly patients with cervical cancer were similar to those in young patients. Elderly patients experienced more chronic toxicities than did young patients.© 2019 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).<sup>\*</sup> Corresponding author. Department of Radiation Oncology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, No. 1 Shuaifuyuan Wangfujing, Dongcheng District, 100730, Beijing, China. Fax: +86 010 69155482.<sup>\*\*</sup> Corresponding author. Department of Radiation Oncology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, No. 1 Shuaifuyuan Wangfujing, Dongcheng District, 100730, Beijing, China. Fax: +86 010 69155482.E-mail addresses: [zhangfuquan3@sina.com](mailto:zhangfuquan3@sina.com) (F. Zhang), [huke8000@163.com](mailto:huke8000@163.com) (K. Hu).<sup>1</sup> Fuquan Zhang and Ke Hu contributed equally to this work.

## Introduction

Cervical cancer is one of the most common cancers in China. In 2015, it was estimated that there were 98.9 thousand new cases and 30.5 thousand deaths from cervical cancer [1]. With the use of the human papillomavirus (HPV) vaccine, the incidence of cervical cancer decreased in developed countries in the past decades. However, the incidence did not decrease significantly in elderly women [2].

In most large retrospective studies, the treatment outcomes of elderly cervical cancer patients are worse than those of patients who are younger [3–5]. It worth noting that elderly patients were likely to have more advanced disease and receive less aggressive treatment [3–7]. The worse survival of elderly patients potentially

was mainly the result of more advanced disease and less aggressive treatment rather than age itself. After definitive radiotherapy alone, elderly patients had an equivalent survival to young patients [8,9]. At present, concurrent chemoradiotherapy (CCRT) is the standard treatment for locally advanced cervical cancer. In a previous study, we found that elderly patients could benefit from concurrent chemotherapy [10]. However, it is an inconclusive issue whether the survival of elderly patients is equivalent to that of young patients in the era of CCRT, and the literature on this issue is limited [11,12]. In the present study, we compared the treatment outcomes and toxicities of patients treated with definitive radiotherapy or CCRT between young and elderly patients.

## Patients and methods

### Patients

We reviewed the database of patients with cervical cancer treated with definitive radiotherapy in our institute from January 2010 to December 2015. The inclusion criteria were as follows: biopsy-confirmed cervical cancer, FIGO stage IB–IVA, and treated with definitive radiotherapy or CCRT. To compare the treatment outcomes between young and elderly patients, patients aged less than 60 years (young group) and those aged 70 years and older (elderly group) were selected. This study was approved by the Institutional Review Board of Peking Union Medical College Hospital.

Before treatment, patients completed a physical examination, a gynecological examination, routine laboratory tests, pelvic magnetic resonance imaging (MRI) or computed tomography (CT), and chest and abdomen CT.

### Treatment

All patients were scheduled to receive definitive intensity modulated radiation therapy (IMRT) and intracavitary brachytherapy (ICBT).

The gross tumor volume (GTV) and clinical target volume (CTV) were delineated on the CT slices. The GTV was defined as the regional metastatic lymph nodes (MLNs). And, the CTV covered the primary tumor, the GTV, the cervix, uterus, parametrium, upper part of the vaginal and regional lymph node regions, including the common iliac, internal iliac, external iliac, obturator, presacral, with/without para-aortic lymph node regions. Planning gross tumor volume (PGTV) was defined as the GTV plus a margin of 5 mm. The planning clinical target volume (PCTV) was generated with a margin of 6–10 mm added to the CTV. A dose of 50.4 Gy in 28 fractions was delivered to the PCTV with IMRT. And, the PGTV was simultaneously boosted to 59–61 Gy in 28 fractions. A dose of 30–36 Gy in 5–7 fractions was prescribed to point A with high dose rate ICBT.

The first-line regimen of concurrent chemotherapy was weekly cisplatin. For patients with renal dysfunction, weekly paclitaxel was given. The detailed treatment approach was described previously [10,13].

### Patient follow-up and toxicity evaluation

After treatment, follow-up examinations were performed every 3 months in the first 2 years, every 6 months in years 3–5, and once a year thereafter. Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 was used to evaluate toxicities.

### Statistics

The endpoints were overall survival (OS), disease-free survival (DFS), and cancer-specific survival (CSS). The baseline characteristics, failure pattern, and toxicities between the young group and the elderly group were compared with the chi-square test, continuity correction, and the Fisher exact test, as appropriate. OS, DFS, and CSS were calculated with the Kaplan–Meier method and compared between two groups with the log-rank method. Multivariate analysis was performed to compare survivals between the young group and the elderly group while adjusting the effects of other possible factors. The Cox proportional hazard model was used in univariate and multivariate analysis. As the baseline characteristics were significantly different between the young and elderly groups, a propensity score matching was conducted with a ratio of 1:1. The matching covariates included histology [grouped to squamous cell carcinoma (SCC), adenocarcinoma (AC), and adenosquamous cell carcinoma (ASC)], FIGO stage (grouped to stage I, stage II, and stage III–IVA), tumor size (grouped to < 4 cm and ≥ 4 cm), para-aortic metastatic lymph nodes (MLNs), pelvic MLNs, pretreatment hemoglobin (HGB, grouped to < 110 g/L, ≥ 110 g/L, and unknown), equivalent dose in 2 Gy per fraction (EQD2) of point A (grouped to < 85 Gy and ≥ 85 Gy), and concurrent chemotherapy. OS, DFS, and CSS were estimated with the Kaplan–Meier method, and compared between the young group and the elderly group with the log-rank method before and after matching. The cumulative dose of point A was converted to EQD2 ( $\alpha/\beta = 10$ ). All statistical analyses were performed with SPSS (version 22.0; SPSS, Inc., Chicago, IL, USA). A two-sided *p*-value < 0.05 was considered to be statistically significant.

### Results

A total of 1061 patients were included in this study, with 991 patients in the young group and 70 patients in the elderly group. The baseline characteristics of patients in the two groups are shown in Table 1. More patients in the young group had a large primary tumor (66.4% and 41.4%, *p* < 0.001) and pelvic MLNs (32.2% and 8.6%, *p* < 0.001), compared with the elderly group. The EQD2 of point A was less than 85 Gy in 11 patients (15.7%) in the elderly group and 29 patients (2.9%) in the young group (*p* < 0.001). Concurrent chemotherapy was conducted in 92.5% of patients in the young group and 44.3% of patients in the elderly group (*p* < 0.001). The median treatment durations in the young and elderly groups were 53 and 50 days, respectively. And, the treatment durations were 8 weeks or longer in 26.5% of patients in the young group and 20.0% of patients in the elderly group (*p* = 0.229).

The median follow-up period was 30.2 months (range, 1.9–93.0 months) for the total cohort. For patients in the young group and the elderly group, the median follow-up periods were 30.7 months and 28.9 months, respectively. During follow-up, 256 patients (24.1%) had treatment failure, including 108 patients (10.2%) with pelvic failure, 116 patients (10.9%) with distant failure, and 32 patients (3.0%) with concurrent pelvic and distant failure. In the young and elderly groups, there were 242 patients (24.4%) and 14 patients (20.0%) who had treatment failure (*p* = 0.404).

A total of 179 patients (16.9%) died during follow-up, with 161 patients (16.2%) in the young group and 18 patients (25.7%) in the elderly group (*p* = 0.041). There were 165 patients (15.6%) with cancer-specific death, including 153 patients (15.4%) in the young group and 12 patients (17.1%) in the elderly group (*p* = 0.704). Fourteen patients (1.3%) died of noncancer causes, with eight patients (0.8%) in the young group and six patients (8.6%) in the elderly group (*p* < 0.001).

**Table 1**  
The baseline characteristics of patients in the young and elderly groups.

	Before matching			After matching		
	Young group (n = 991)	Elderly group (n = 70)	P	Young group (n = 64)	Elderly group (n = 64)	P
Age (years)						
Median	49 (range, 23–59)	74 (range, 70–88)		48 (range, 23–59)	74 (range, 70–88)	
Histology						
SCC	888 (89.6%)	65 (92.9%)	0.656	58 (90.6%)	60 (93.8%)	0.510
AC	80 (8.1%)	4 (5.7%)		6 (9.4%)	4 (6.3%)	
ASC	23 (2.3%)	1 (1.4%)		0	0	
FIGO stage						
IB	118 (11.9%)	7 (10.0%)	0.907	6 (9.4%)	6 (9.4%)	0.747
IIA	67 (6.8%)	11 (15.7%)		6 (9.4%)	10 (15.6%)	
IIB	607 (61.3%)	36 (51.4%)		38 (59.4%)	34 (53.1%)	
IIIA	30 (3.0%)	5 (7.1%)		2 (3.1%)	4 (6.3%)	
IIIB	161 (16.2%)	9 (12.9%)		11 (17.2%)	8 (12.5%)	
IVA	8 (0.8%)	2 (2.9%)		1 (1.6%)	2 (3.1%)	
FIGO stage						
IB–IIIA	822 (82.9%)	59 (84.3%)	0.773	52 (81.3%)	54 (84.4%)	0.639
IIIB–IVA	169 (17.1%)	11 (15.7%)		12 (18.8%)	10 (15.6%)	
Tumor size						
<4 cm	333 (33.6%)	41 (58.6%)	<0.001	34 (53.1%)	35 (54.7%)	0.859
≥4 cm	658 (66.4%)	29 (41.4%)		30 (46.9%)	29 (45.3%)	
Para-aortic MLNs						
Yes	70 (7.1%)	2 (2.9%)	0.269	1 (1.6%)	2 (3.1%)	1.000
No	921 (92.9%)	68 (97.1%)		63 (98.4%)	62 (96.9%)	
Pelvic MLNs						
Yes	319 (32.2%)	6 (8.6%)	<0.001	7 (10.9%)	5 (7.8%)	0.544
No	672 (67.8%)	64 (91.4%)		57 (89.1%)	59 (92.2%)	
HGB						
≥110 g/L	739 (74.6%)	57 (81.4%)	0.014	49 (76.6%)	53 (82.8%)	0.629
<110 g/L	197 (19.9%)	5 (7.1%)		8 (12.5%)	5 (7.8%)	
Unknown	55 (5.5%)	8 (11.4%)		7 (10.9%)	6 (9.4%)	
EQD2 of point A						
<85Gy	29 (2.9%)	11 (15.7%)	<0.001	7 (10.9%)	8 (12.5%)	0.783
≥85Gy	962 (97.1%)	59 (84.3%)		57 (89.1%)	56 (87.5%)	
Concurrent chemotherapy						
Yes	917 (92.5%)	31 (44.3%)	<0.001	30 (46.9%)	31 (48.4%)	0.860
No	74 (7.5%)	39 (55.7%)		34 (53.1%)	33 (51.6%)	
Treatment duration (days)						
Median	53 (range, 20–117)	50 (range, 15–73)		53 (range, 44–94)	50 (range, 15–73)	
<8 weeks	728 (73.5%)	56 (80.0%)	0.229	49 (76.6%)	53 (82.8%)	0.380
≥8 weeks	263 (26.5%)	14 (20.0%)		15 (23.4%)	11 (17.2%)	

Abbreviations: AC = adenocarcinoma; ASC = adenosquamous cell carcinoma; EQD2 = equivalent dose in 2 Gy per fraction; MLNs = metastatic lymph nodes; SCC = squamous cell carcinoma.

The 3-year OS, DFS, and CSS rates in the young and elderly groups were 82.8% and 71.9% ( $p = 0.030$ ), 73.9% and 73.4% ( $p = 0.453$ ), and 83.3% and 78.9% ( $p = 0.567$ ), respectively.

#### Univariate and multivariate analysis

In univariate analysis (Table 2), age was a significant prognostic factor of OS (HR 1.71, 95% CI: 1.05–2.78,  $p = 0.032$ ). However, it was

not significantly associated with DFS (HR 1.19, 95% CI: 0.75–1.88,  $p = 0.455$ ) and CSS (HR 1.19, 95% CI: 0.66–2.14,  $p = 0.568$ ). Age and other significant factors in univariate analysis were included in multivariate analysis. As shown in Table 3, age remained significant in predicting OS (HR 1.99, 95% CI: 1.15–3.43,  $p = 0.014$ ) after multivariate analysis. And, it was still not significant in predicting DFS (HR 1.41, 95% CI: 0.86–2.32,  $p = 0.179$ ) and CSS (HR 1.38, 95% CI: 0.72–2.62,  $p = 0.332$ ).

**Table 2**  
Results of univariate analysis of cervical cancer patients treated with definitive radiotherapy or concurrent chemoradiotherapy.

Variables	OS		DFS		CSS	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Age (<60 vs. ≥ 70)	1.71 (1.05–2.78)	0.032	1.19 (0.75–1.88)	0.455	1.19 (0.66–2.14)	0.568
Histology (SCC vs. non-SCC)	2.26 (1.53–3.32)	<0.001	2.08 (1.51–2.87)	<0.001	2.26 (1.52–3.38)	<0.001
FIGO stage (IB–IIIA vs. IIIB–IVA)	3.06 (2.26–4.14)	<0.001	2.39 (1.84–3.10)	<0.001	3.26 (2.38–4.45)	<0.001
Tumor size (<4 cm vs. ≥ 4 cm)	2.76 (1.87–4.07)	<0.001	2.42 (1.79–3.27)	<0.001	2.85 (1.90–4.27)	<0.001
Para-aortic MLNs (No vs. Yes)	5.40 (3.76–7.77)	<0.001	4.86 (3.56–6.64)	<0.001	5.54 (3.81–8.06)	<0.001
Pelvic MLNs (No vs. Yes)	2.85 (2.12–3.82)	<0.001	2.68 (2.11–3.41)	<0.001	3.02 (2.22–4.09)	<0.001
HGB (<110 g/L vs. ≥ 110 g/L)	1.84 (1.32–2.57)	<0.001	1.62 (1.22–2.15)	0.001	1.85 (1.31–2.61)	0.001
EQD2 of point A (<85 Gy vs. ≥85 Gy)	2.58 (1.50–4.46)	0.001	2.14 (1.31–3.50)	0.002	2.59 (1.47–4.57)	0.001
Concurrent chemotherapy (No vs. Yes)	0.54 (0.37–0.78)	0.001	0.64 (0.16–0.89)	0.009	0.61 (0.41–0.93)	0.020

Abbreviations: CI = confidence interval; CSS = cancer-specific survival; DFS = disease-free survival; EQD2 = equivalent dose in 2 Gy per fraction; HR = hazard ratio; MLNs = metastatic lymph nodes; non-SCC = non-squamous cell carcinoma; OS = overall survival; SCC = squamous cell carcinoma.

**Table 3**

Results of multivariate analysis of cervical cancer patients treated with definitive radiotherapy or concurrent chemoradiotherapy.

Variables	OS		DFS		CSS	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	p
Age (<60 vs. ≥ 70)	1.99 (1.15–3.43)	0.014	1.41 (0.86–2.32)	0.179	1.38 (0.72–2.62)	0.332
Histology (SCC vs. non-SCC)	2.74 (1.85–4.08)	<0.001	2.28 (1.65–3.16)	<0.001	2.71 (1.80–4.08)	<0.001
FIGO stage (IB–IIIA vs. IIIB–IVA)	2.52 (1.84–3.44)	<0.001	1.96 (1.50–2.57)	<0.001	2.66 (1.93–3.68)	<0.001
Tumor size (<4 cm vs. ≥4 cm)	2.30 (1.54–3.44)	<0.001	2.00 (1.47–2.73)	<0.001	2.23 (1.47–3.39)	<0.001
Para-aortic MLNs (No vs. Yes)	2.44 (1.63–3.67)	<0.001	2.38 (1.68–3.37)	<0.001	2.43 (1.60–3.70)	<0.001
Pelvic MLNs (No vs. Yes)	2.16 (1.55–3.02)	<0.001	2.08 (1.59–2.72)	<0.001	2.20 (1.56–3.11)	<0.001
HGB (<110 g/L vs. ≥ 110 g/L)	1.24 (0.99–1.55)	0.062	1.15 (0.95–1.40)	0.147	1.18 (0.93–1.50)	0.163
EQD2 of point A (<85 Gy vs. ≥85 Gy)	3.23 (1.83–5.69)	<0.001	2.53 (1.53–4.20)	<0.001	3.52 (1.96–6.32)	<0.001
Concurrent chemotherapy (No vs. Yes)	0.61 (0.41–0.92)	0.017	0.68 (0.48–0.97)	0.032	0.64 (0.41–0.99)	0.046

Abbreviations: CI = confidence interval; CSS = cancer-specific survival; DFS = disease-free survival; EQD2 = equivalent dose in 2 Gy per fraction; HR = hazard ratio; MLNs = metastatic lymph nodes; non-SCC = non-squamous cell carcinoma; OS = overall survival; SCC = squamous cell carcinoma.

### Propensity score matching

After propensity score matching, 64 patients were selected. As shown in Table 1, all baseline characteristics were not significantly different between the young and elderly groups after matching.

After matching, the median follow-up period was 33.2 months (range, 3.0–84.1 months). The 3-year OS, DFS, and CSS rates in the young and elderly groups were 86.5% and 73.9% ( $p = 0.280$ , Fig. 1A), 74.6% and 75.4% ( $p = 0.744$ , Figs. 1B), and 87.9% and 81.7% ( $p = 0.967$ , Fig. 1C), respectively.

For patients treated with definitive radiotherapy, the 3-year OS, DFS and CSS rates in the young and elderly groups were 78.5% and 63.7% ( $p = 0.347$ ), 69.7% and 66.1% ( $p = 0.721$ ), 80.8% and 74.5% ( $p = 0.970$ ), respectively. For patients treated with concurrent chemoradiotherapy, the 3-year OS, DFS and CSS rates in the young and elderly groups were 96.2% and 86.7% ( $p = 0.612$ ), 78.7% and 86.6% ( $p = 0.986$ ), 96.2% and 90.3% ( $p = 0.962$ ), respectively.

### Toxicities

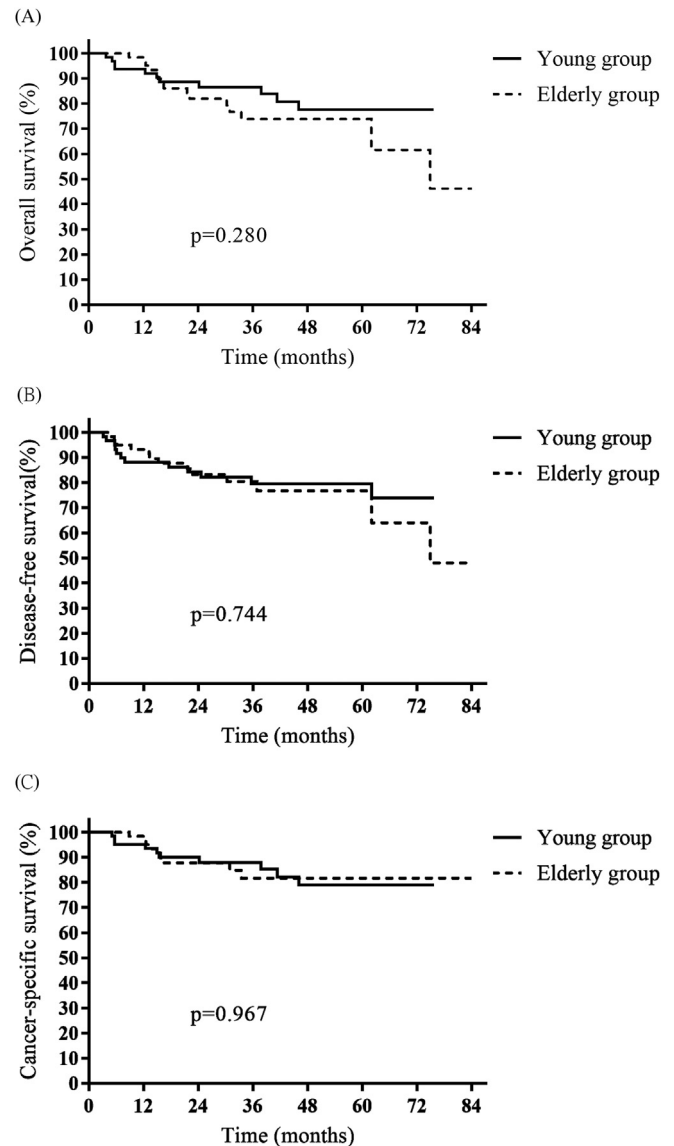
Grade 3–4 acute hematological toxicity rates were 46.0% (456/991) and 32.9% (23/70,  $p = 0.033$ ) in young and elderly groups, respectively. In young and elderly groups, Grade 3–4 hematological toxicity rates were 49.0% (449/917) and 58.1% (18/31,  $p = 0.319$ ) for patients treated with CCRT, and 9.5% (7/74) and 12.8% (5/39,  $p = 0.581$ ) for patients treated with radiotherapy.

A total of 35 patients (3.3%) developed grade 3 or greater chronic toxicities, with 29 patients (2.9%) in the young group and 6 patients (8.6%) in the elderly group ( $p = 0.027$ ). In the young group and the elderly group, the incidences of ≥ grade 3 chronic gastrointestinal toxicities were 2.4% and 8.6% ( $p = 0.009$ ), respectively. And, incidences of grade 3 or greater chronic genitourinary toxicities were 1.0% and 0% ( $p = 1.000$ ), respectively. Of the six patients with grade 3 or greater chronic toxicities in the elderly group, four patients developed grade 3–4 enteritis, one patient had grade 3 intestinal obstruction, and one patient died of treatment-related rectum hemorrhoid. In the young group, one patient died of acute renal failure during treatment, and one patient died of chronic bowel obstruction. The incidences of grade 5 toxicities were 0.2% and 1.4% in the young and elderly groups ( $p = 0.185$ ), respectively. The details of grade 3 and greater chronic toxicities in the young and elderly groups are shown in Table 4.

### Discussion

A study from Taiwan reviewed 138 elderly cervical cancer patients (≥75 years of age) and 334 young patients (<60 years of age) who underwent definitive radiotherapy or CCRT. The median follow-up period for survivors was 60.6 months. With propensity

score matching based on FIGO stage, histology, lymph node status, and treatment methods, a cohort of 99 pairs of patients was selected for comparison. The 5-year OS rates in young and elderly patients were 71.5% and 49.2% ( $p < 0.001$ ), respectively. But, there



**Fig. 1.** The overall survival (A), disease-free survival (B), and cancer-specific survival (C) of 64 pairs of patients with cervical cancer in the young group (<60 years old) and elderly group (≥70 years old) after propensity score matching.



**Table 4**  
Grade 3 or greater chronic toxicities in young and elderly groups.

Toxicities	Young group (n = 991)		Elderly group (n = 70)		P
	N	Percentage	N	Percentage	
gastrointestinal toxicities	24	2.4%	6	8.6%	0.009
genitourinary toxicities	10	1.0%	0	0%	1.000
Total	29	2.9%	6	8.6%	0.027

was no difference in CSS, local failure, and distant failure between the two groups [11]. A study from the US enrolled 69 nonelderly cervical cancer patients (<65 years of age) and 27 elderly patients ( $\geq 65$  years of age). Fewer elderly patients (56%) received concurrent chemotherapy, compared with the nonelderly patients (78%,  $p = 0.03$ ). The elderly patients had worse OS (nonelderly: 60.1%, elderly: 44.4%,  $p = 0.02$ ) and similar CSS (nonelderly: 61.6%, elderly: 70.8%,  $p = 0.38$ ). Moreover, age was not an independent factor of OS in multivariate analysis (HR 1.66, 95% CI 0.85–3.23,  $p = 0.13$ ) [12]. In the present study, young and elderly patients were defined as less than 60 years of age and 70 years of age and older. Patients in the elderly group had less advanced disease (fewer patients with large tumor and the pelvic MLNs) and less aggressive treatment (fewer patients with adequate dose to point A and concurrent chemotherapy). Multivariate analysis showed that age was an independent factor for OS, but it was not significant in predicting DFS and CSS. After propensity score matching, OS, DFS, and CSS were similar between the two groups. As patients in elderly group had more deaths due to noncancer causes, and the cancer-specific death was similar between the two groups, more deaths of noncancer causes might be the main reason for the worse OS in the elderly group before matching. The treatment outcomes of patients in the young group and the elderly group were similar.

As reported previously, elderly patients were always treated less aggressively [3,5–7]. Similarly, compared with young patients, less elderly cervical cancer patients received concurrent chemotherapy when they were treated with definitive radiotherapy [11,12]. The irradiation dose delivered was also lower in elderly patients [11]. In our study, there were also fewer patients in the elderly group receiving concurrent chemotherapy and adequate radiation dose. The main reason for less aggressive treatment was comorbidity and weakness of elderly patients, which may influence the tolerance of treatment. In the study from Taiwan, 79 pairs of patients were selected for complication comparisons, with treatment method, cervix dose, ICBT dose, and cumulative biological equivalent dose of point A being matched. After matching, the cumulative grade 2 and greater proctitis and grade 3 or greater proctitis in the young and elderly groups were 39.7% and 17.2% ( $p = 0.015$ ), 18.1% and 6.2% ( $p = 0.040$ ), respectively. The incidences of grade 2 proctitis were not significantly different between the two groups [11]. In the study from the US, there was no significant difference in complication rates between young and elderly patients ( $p = 0.61$ ) [12]. Similar to the study from Taiwan, our study demonstrated that more elderly patients developed grade 3 or greater gastrointestinal toxicities. And, the incidences of grade 3 or greater toxicities were not significantly different between the two groups. Although more patients in the elderly group developed chronic toxicities, the incidence of grade 3 or greater toxicities was just 8.6%. The acute hematological toxicity was not significantly different between young and elderly groups, no matter for patients treated with definitive radiotherapy or CCRT. These indicate that elderly patients could tolerate definitive radiotherapy or CCRT very well.

It was recommended that definitive radiotherapy of cervical cancer should be completed in 8 weeks. And, longer treatment duration may lead to poor survival [14]. In this study, the median

treatment duration in the elderly group (50 days) was slightly shorter than that in the young group (53 days). And, there were fewer patients treated for longer than 8 weeks in the elderly group (20.0%) than in the young group (26.5%), although it was not significant ( $p = 0.229$ ). Elderly patients did not have longer treatment duration. This also suggested the good tolerance of definitive radiotherapy or CCRT in elderly patients.

Despite the inclusion of a comparatively large number of patients, there are some limitations in the present study. First, as a retrospective study, our population may have some biases. A prospective study is needed to have a solid conclusion on the treatment of elderly patients. Second, the median follow-up period was just 30.2 months in the present study, which was not long enough. With a longer follow-up period, more patients in elderly group may die of noncancer specific reasons. And patients in elderly group may have significantly lower OS and DFS compared with patients in young group. Third, it is well known that comorbidity impacts the allocation of treatment and survival of elderly patients. However, our study lacks data on comorbidity. This may have influence on the results of the present study.

In summary, after definitive radiotherapy or CCRT, the DFS and CSS of elderly patients with cervical cancer were similar to those in young patients. Elderly patients could tolerate radiotherapy or CCRT very well, although the incidence of chronic toxicities in elderly patients were higher than that in young patients.

### Conflict of interest

The authors declare that they have no conflict of interest.

### Acknowledgement

This work was funded by the Ministry of Science and Technology of the People's Republic of China (grant number 2016YFC0105207).

### References

- [1] Chen W, Zheng R, Baade PD, Zhang S, Zeng H, Bray F, et al. Cancer statistics in China, 2015. *CA Cancer J Clin* 2016;66:115–32.
- [2] Skaznik-Wikiel ME, Sukumvanich P, Austin RM, Zorn KK, Krivak TC, Edwards RP, et al. Heavy cervical cancer burden in elderly women: how can we improve the situation? *Acta Cytol* 2012;56:388–93.
- [3] Nogueira-Rodrigues A, de Melo AC, Garces AH, Paulino E, Alves FV, Vilaca Mdo N, et al. Patterns of care and outcome of elderly women diagnosed with cervical cancer in the developing world. *Int J Gynecol Cancer* 2016;26:1246–51.
- [4] Sharma C, Deutsch I, Horowitz DP, Hershman DL, Lewin SN, Lu YS, et al. Patterns of care and treatment outcomes for elderly women with cervical cancer. *Cancer* 2012;118:3618–26.
- [5] Diver EJ, Hinchcliff EM, Gockley AA, Melamed A, Contrino L, Feldman S, et al. Assessment of treatment factors and clinical outcomes in cervical cancer in older women compared to women under 65 years old. *J Geriatr Oncol* 2018;9(5):516–9.
- [6] Pfaendler KS, Chang J, Ziogas A, Bristow RE, Penner KR. Disparities in adherence to national comprehensive cancer network treatment guidelines and survival for stage IB-IIA cervical cancer in California. *Obstet Gynecol* 2018;131:899–908.
- [7] Roque DR, Cronin B, Robison K, Lopes V, Rizack T, Dizon DS. The effects of age on treatment and outcomes in women with stages IB1-IIIB cervical cancer. *J Geriatr Oncol* 2013;4:374–81.
- [8] Sakurai H, Mitsuhashi N, Takahashi M, Yamakawa M, Akimoto T, Hayakawa K, et al. Radiation therapy for elderly patient with squamous cell carcinoma of the uterine cervix. *Gynecol Oncol* 2000;77:116–20.
- [9] Ikushima H, Takegawa Y, Osaki K, Furutani S, Yamashita K, Kawanaka T, et al. Radiation therapy for cervical cancer in the elderly. *Gynecol Oncol* 2007;107:339–43.
- [10] Wang W, Hou X, Yan J, Shen J, Lian X, Sun S, et al. Outcome and toxicity of radical radiotherapy or concurrent Chemoradiotherapy for elderly cervical cancer women. *BMC Cancer* 2017;17:510.
- [11] Wang YM, Wang CJ, Fang FM, Chen HC, Hsu HC, Huang YJ, et al. Differences in the outcomes and complications between elderly and younger uterine

- cervical cancer patients treated by definitive radiotherapy - a propensity score-matched study. *Gynecol Oncol* 2017;145:277–83.
- [12] Goodheart M, Jacobson G, Smith BJ, Zhou L. Chemoradiation for invasive cervical cancer in elderly patients: outcomes and morbidity. *Int J Gynecol Cancer* 2008;18:95–103.
- [13] Wang W, Meng Q, Hou X, Lian X, Yan J, Sun S, et al. Efficacy and toxicity of image-guided intensity-modulated radiation therapy combined with dose-escalated brachytherapy for stage IIB cervical cancer. *Oncotarget* 2017;8:102965–73.
- [14] Tanderup K, Fokdal LU, Sturdza A, Haie-Meder C, Mazon R, van Limbergen E, et al. Effect of tumor dose, volume and overall treatment time on local control after radiochemotherapy including MRI guided brachytherapy of locally advanced cervical cancer. *Radiother Oncol* 2016;120:441–6.