

ORIGINAL ARTICLE

Clinicopathological factors influencing the prognosis of cervical cancer

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Summary

Purpose: This research was designed to analyze the clinicopathological factors affecting the prognosis of cervical cancer.

Methods: The clinical and follow-up data of 79 patients with cervical cancer were retrospectively analyzed by univariate and multivariate analysis. The 5-year overall survival rate was 74% for all patients.

Results: Univariate analysis showed that the 5-year survival rate of patients with clinical stage I-IIA cervical cancer was higher than that of IIB-IV. The 5-year survival rates were higher in patients without parametrial invasion than those

with parametrial invasion; higher in patients without vascular invasion than those with vascular invasion; and higher in patients without lymph node metastasis than those with lymph node metastasis. Multivariate analysis showed that vascular invasion, lymph node metastasis, and clinical stage were independent predictors of overall survival.

Conclusion: Vascular invasion, lymph node metastasis, and clinical stage are independent predictors for the prognosis of cervical cancer.

Key words: cervical cancer, lymph node metastasis, prognostic factors, survival

Introduction

In clinical oncology, the three major gynecological malignancies are cervical cancer, endometrial cancer, and ovarian cancer [1-5]. Currently, cervical cancer has the highest incidence among gynecological malignancies, and it is the second leading cause of death among gynecological malignancies [6-8]. Studies have suggested that the prognosis of cervical cancer is related to multiple factors, but no consensus has been reached regarding these factors, especially for pathological factors [9-13]. We retrospectively analyzed the clinical data of 79 patients with cervical cancer admitted to our hospital, which was combined with the existing literature, in order to further investigate the clinical and pathological factors influencing the prognosis of these cases.

Methods

The research was approved by the Ethics Committees of the Central Hospital of Binzhou. The requirement of informed consent from patients was waived because of the retrospective nature of the research, since it was not a prospective study.

Between January 2010 and January 2014, 79 patients with stage I-IV cervical cancer were admitted and treated at our hospital; the diagnosis of all cases was confirmed by pathology. Based on the latest version of cervical cancer staging criteria, patients were classified into stage I-IIA or stage IIB-IV; tumor diameter < 4 cm or ≥ 4 cm; and three levels of tumor cell differentiation (i.e. well-, moderately- and poorly differentiated) according to the imaging and postoperative or post-biopsy pathological results.

Treatment plans for the 79 patients with cervical cancer were realized according to their clinical stage, tumor size, and wishes [14-26]: 62 patients underwent

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surgical treatment, of which 46 underwent radical hysterectomy and pelvic lymphadenectomy. Five patients underwent radical hysterectomy and pelvic lymphadenectomy with intraoperative retention of ovaries. Six patients underwent total hysterectomy. Five patients who wished to preserve fertility underwent cervical conization. Among the 62 patients who underwent surgical treatment, 23 patients received postoperative chemotherapy, and 24 received postoperative radiotherapy. Among the 17 patients who did not receive surgical treatment, 13 patients received radiotherapy alone, 4 received chemotherapy alone, and 2 received combined chemoradiotherapy.

At discharge, patient's place of living and addresses were recorded, and they were put on follow-up through local primary hospital, outpatient clinics, or at-home visits. Due to the large impact our hospital has in treating gynecological malignancies, local primary hospitals were willing to assist us in conducting post-discharge follow-up work for our patients.

Statistics

Data are presented as means and standard deviations for variables with normal distribution. For data with a non-normal distribution, results are expressed as medians and ranges. Survival rates were analyzed using the Kaplan-Meier method. Univariate analyses were performed to identify prognostic variables related to overall survival and to identify prognostic variables related to prognosis. Univariate variables with probability values <0.05 were selected for inclusion in the multivariate Cox proportional hazard regression model. $P < 0.05$ was considered statistically significant. SPSS 14.0 (SPSS Inc., Chicago, IL, USA) Microsoft Windows version was used for all statistical analyses.

Results

The clinical and pathological data of the 79 patients with stage I-IV cervical cancer are shown in Table 1.

The results of the univariate analysis are shown in Table 2, where it can be seen that the 5-year survival rate of patients with clinical stage I-IIA cervical cancer is higher than those with clinical stage IIB-IV. The 5-year survival rate of patients without parametrial infiltration was higher than those with parametrial invasion. The 5-year survival rate of the patients without vascular invasion was higher than those with vascular invasion. The 5-year survival rate of patients without lymph node metastasis was higher than those with lymph node metastasis.

Factors screened from the univariate analysis, including clinical stage, parametrial invasion, vascular invasion and lymph node metastasis, were included in the multivariate Cox regression model for analysis. The results in Table 3 indicate that vascular invasion, lymph node metastasis, and clinical stage reached statistical significance.

Table 1. Clinical and pathological data of the 79 patients (n=79)

Data	n	%
Age, years, median (range)	51 (35-71)	
BMI, kg/m ² , median (range)	20 (17-28)	
FIGO stage		
I-IIA	38	48.1
IIB-IV	41	51.9
Tumor histology		
Squamous	67	84.8
Adenocarcinoma	10	12.7
Adenosquamous	2	2.5
Tumor grade		
G1	27	34.2
G2	38	48.1
G3	14	17.7
Parametrial infiltration		
No	51	64.6
Yes	28	35.4
Vascular invasion		
No	48	60.8
Yes	31	39.2
Lymph node metastasis		
No	57	72.1
Yes	22	27.9
Medical comorbidities		
Type 2 diabetes mellitus	1	1.3
Hypertension	4	5.1
Hyperlipidemia	11	13.9
Liver cirrhosis	1	1.3
Ischemic heart disease	2	2.5
Atrial fibrillation	1	1.3

BMI: body mass index, FIGO: International Federation of Gynecology and Obstetrics

Discussion

Cervical cancer is the second most common malignancy after breast cancer among malignant tumors in women. The World Health Organization (WHO) reported that there were more than 500,000 new cases of cervical cancer in 2005, and about 260,000 deaths among women due to cervical cancer, of which 95% were from developing countries [1-4]. There are still unresolved controversies in domestic and foreign studies on the prognostic factors of cervical cancer, especially in terms of pathological factors [8-14]. Therefore, exploring the prognostic factors of cervical cancer, improving early detection rate, and developing effective treatment measures to improve survival rate are of utmost importance.

Table 2. Univariate analysis of overall survival (n=79)

Variables	Five-year survival (%)	p value
FIGO stage		0.024
I-IIA	81	
IIB-IV	47	
Parametrial infiltration		0.001
No	87	
Yes	59	
Vascular invasion		0.010
No	79	
Yes	54	
Lymph node metastasis		0.001
No	91	
Yes	58	
Tumor grade		0.009
G1	87	
G2	74	
G3	49	

FIGO: International Federation of Gynecology and Obstetrics

Table 3. Multivariate analysis of overall survival (n=79)

Variables	Adjusted hazard ratio	95%CI	p value
Vascular invasion		1.55-3.50	0.025
No	1.00		
Yes	2.01		
FIGO stage		1.55-2.88	0.011
I-IIA	1.00		
IIB-IV	2.69		
Lymph node metastasis		1.33-2.10	0.041
No	1.00		
Yes	1.58		

FIGO: International Federation of Gynecology and Obstetrics

In this study, we found that advanced clinical stage, vascular invasion, parametrial invasion, and lymph node metastasis were high-risk factors influencing the prognosis of cervical cancer. However, prognosis had no significant correlation with age, cervical myometrial invasion, tumor size, and histological grade. In addition, multivariate analysis showed that only clinical stage, vascular invasion, and lymph node metastasis were associated with prognosis. This suggests that advanced clinical stage, vascular invasion, and lymph node metastasis were independent predictors of overall survival.

Large-sample clinical studies have shown that the 5-year overall survival rates for stage I and II cervical cancer were 89 and 79%, respectively

[27-30]. However, the treatments for advanced cervical cancer are still not satisfactory, and the 5-year survival rates were only 10-40% [27,28]. The results of this study showed that the 5-year survival rate of cervical cancer patients at stage I-IIA was higher than that at stage IIB-IV, suggesting that patients with advanced cervical cancer have poor prognosis. Multivariate analysis of this group of data showed that advanced clinical stage is an independent predictor affecting overall survival. More studies have shown that pelvic lymph node metastasis is an independent predictor of prognosis [31-33]. A comprehensive evaluation of 25 studies, which comprised of 6,500 cervical cancer patients, examined lymph node metastasis, clinical stage, tumor volume, and vascular invasion as potential prognostic factors [31-33]. The study by Zheng et al. [31] found that 91% of the literature considered lymph node metastasis as an independent risk factor for poor prognosis. Other studies have shown that pelvic lymph node metastasis is an important factor affecting the prognosis of cervical cancer [35]. Without the occurrence of pelvic lymph node metastasis after radical surgery, the patient's 5-year survival rate could be up to 90% [34-38]. However, once pelvic lymph node metastasis was present, their 5-year survival rate decreased to 50%. Similarly, our study showed that cervical cancer patients with pelvic lymph node metastasis had poor prognosis. Moreover, the multivariate analysis indicated that lymph node metastasis was an independent prognostic factor of overall survival.

In addition to lymph node metastasis, studies have found that vascular invasion is also an important factor associated with prognosis [35]. Large-sample clinical studies have shown that vascular invasion is an independent factor for poor prognosis in cervical cancer patients [34-38]. Our study also showed that cervical cancer patients with vascular invasion had poor prognosis, and multivariate analysis identified vascular invasion as an independent prognostic factor.

A study on 110 patients with early stage cervical cancer who received surgical intervention showed that parametrial invasion affected prognosis [35]. Our study also showed that patients with invasion of cervical cancer had poor prognosis. The 5-year survival rates of patient who were < 35-year-old and ≥35-year-old were 61 and 84%, respectively. This suggested that age had no significant effect on prognosis. Our results were also similar to other foreign studies. Some studies have shown that there was no significant correlation between histological grade and cervical cancer prognosis. Similar to other find-

ings [34-38], our results also showed the 5-year survival rates for patients with well, moderately, and poorly differentiated tumor cells were 92, 87, and 81%, respectively. The results of foreign and domestic studies are inconsistent as to whether myometrial invasion would affect the prognosis of cervical cancer. Our study showed that the 5-year survival rates of patients with tumor infiltration into the shallow and deep muscle layers were 80 and 75%, respectively, but our results were unable to determine the impact of myometrial invasion on prognosis. Current research results also differed on whether the diameter of cervical cancer would affect prognosis. The results of our study showed that the 5-year survival rates of patients with tumor diameter < 4 cm and \geq 4 cm were 81 and 75%, respectively, but they were unable to determine the impact of tumor size on prognosis.

In clinical oncology, follow-up care after discharge is very important [4-12]. However, the follow-up can be tedious, and is a challenge to clinician's patience. In our study, the follow-up rate of patients was as high as 100% due to our varied follow-up methods. If the patient's residential address was near our hospital, the patient was followed-up directly. If the patient lived in rural areas and commuting to our hospital was inconvenient, then we commissioned the local primary hospitals and gynecologists to follow-up the pa-

tient in accordance with the procedures developed by our hospital.

The limitations of this study are that it was a retrospective, single-center study and therefore had a lower level of evidence. In addition, the sample size was small (less than 100 cases) and follow-up time was relatively short.

In conclusion, vascular invasion, lymph node metastasis, and advanced clinical stage are independent predictors of cervical cancer prognosis. In clinical settings, patients with these aforementioned prognostic factors should be followed-up closely. This would enable immediate and effective treatment when tumor metastasis is detected, in order to improve the patient's long-term survival.

Authors' contributions

JG drafted this manuscript. JG and XW were mainly devoted on collecting and interpreting the data. YM and ZX revised it critically for important intellectual content. MK and YL were responsible for the conception and design of the study. All authors read and approved the final manuscript.

Conflict of interests

The authors declare no conflict of interests.

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