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Original Article

Endostar and chemoradiotherapy for advanced cervical cancer: comparing efficacy and prognosis

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Abstract: Objective: To investigate the efficacy of endostar combined with simultaneous chemoradiotherapy versus conventional treatment methods for locally advanced cervical cancer (LACC) and assess the prognosis of these patients. Methods: A retrospective analysis was conducted on the medical records of 182 LACC patients treated at Shaanxi Provincial Cancer Hospital between January 2017 and February 2021. Of these, 88 patients underwent conventional synchronous chemoradiotherapy (control group), while 94 patients received endostar combined with synchronous chemoradiotherapy (combined group). Treatment efficacy, adverse reactions, and tumor marker levels before and after treatment were compared. The 1-year and 3-year survival rates of the two groups were analyzed. Risk factors for 3-year mortality were identified through Cox regression analysis, and the prognostic predictive value of independent factors was assessed using ROC curve analysis. Results: The objective remission rate (ORR) in the combined group (74.47%) was significantly higher than that in the control group (54.55%, $P<0.005$). Adverse reactions, including gastrointestinal symptoms, bone marrow suppression, liver and kidney function abnormalities, and skin damage, showed no significant differences between the groups ($P>0.05$). Post-treatment levels of squamous cell carcinoma antigen (SCC-Ag), carbohydrate antigen 125 (CA125), and carcinoembryonic antigen (CEA) were significantly lower in the combined group ($P<0.05$). The 1-year and 3-year survival rates were notably higher in the combined group ($P<0.05$). Cox regression analysis identified FIGO stage, histologic grade, and post-treatment SCC-Ag levels as independent risk factors for 3-year mortality, while endostar combined with chemoradiotherapy was an independent protective factor. ROC curve analysis demonstrated AUC values of 0.614 (FIGO stage), 0.625 (histologic grade), 0.622 (treatment modality), and 0.662 (post-treatment SCC-Ag). Conclusion: Endostar combined with synchronous chemoradiotherapy for LACC significantly improves short-term treatment efficacy and long-term survival outcomes compared to chemoradiotherapy alone. This approach is safe and does not increase adverse effects, highlighting its potential as a superior treatment strategy.

Keywords: Endostar, simultaneous chemoradiotherapy, locally advanced cervical cancer, prognosis

Introduction

Cervical cancer is one of the most prevalent malignancies of the female reproductive system, originating in the cervical region of the uterus [1]. Globally, approximately 600,000 women are diagnosed with cervical cancer annually, with more than 300,000 succumbing to the disease [2]. This condition poses a significant public health challenge, particularly in low- and middle-income countries, where it often ranks as the first or second leading cause of cancer-related morbidity and mortality among women [3]. Overall, cervical cancer is the fourth most common cancer affecting women worldwide [4].

Locally advanced cervical cancer (LACC) is characterized by tumor invasion beyond the cervix without distant metastasis, typically with a tumor size of ≥4 cm [5]. LACC presents significant clinical challenges, including difficulties in achieving local control, limitations in surgical management, and a high risk of recurrence and metastasis following treatment, contributing to its poor prognosis [6]. Identifying effective

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treatment strategies for LACC remains a critical area of research in cervical cancer management.

Concurrent chemoradiotherapy combines the advantages of radiotherapy and chemotherapy, leveraging the local control achieved through radiotherapy alongside the systemic effects of chemotherapy. This combination enhances both local control rates and overall survival outcomes in tumor management [7]. Despite its benefits, concurrent chemoradiotherapy is associated with notable limitations and side effects. The intensified treatment burden can lead to severe adverse effects such as bone marrow suppression, gastrointestinal reactions, radiation cystitis, and proctitis [8, 9]. Moreover, while concurrent chemoradiotherapy effectively improves local control, its efficacy in preventing distant metastases remains limited, leaving patients vulnerable to recurrence and metastasis post-treatment [10].

Recent advancements in medical research have introduced novel therapeutic options, including innovative drugs like endostar, a promising anti-angiogenic agent. The primary component of endostar, recombinant human endostatin, functions by inhibiting tumor angiogenesis and disrupting the tumor's nutrient supply, ultimately suppressing tumor growth and metastasis [11, 12]. Endostar has demonstrated significant clinical efficacy in treating various solid tumors, including lung, liver, and gastric cancers, particularly when combined with chemotherapy or radiotherapy. These combinations have shown improved therapeutic outcomes and safety profiles [13]. However, while endostar has shown potential in treating cervical cancer, specific research focusing on its use, particularly in combination with concurrent chemoradiotherapy for LACC remains limited. Additional studies are essential to better understand its role and optimize its application in this context. Building on this background, the present study aimed to evaluate the efficacy and safety of combining endostar with concurrent chemoradiotherapy in the treatment of LACC and to assess its impact on patient prognosis.

Methods

This retrospective study analyzed the medical record database of Shaanxi Provincial Cancer Hospital from January 2017 to February 2021. Approval for the study was obtained from the Medical Ethics Committee of the hospital. A total of 182 patients diagnosed with LACC were included, all of whom had received either conventional concurrent chemoradiotherapy or endostar combined with concurrent chemoradiotherapy during the study period. The diagnosis of LACC was confirmed based on pathological biopsy criteria [14]. Inclusion criteria were age ≥18 years, FIGO stage II B-III [15], an expected survival time of at least 3 months, and availability of complete clinical medical records. However, patients were excluded if they could not tolerate chemoradiotherapy, were allergic to the drugs used, had distant metastasis, had other malignant tumors or blood system diseases, had abnormal liver or kidney function, or had a history of chemoradiotherapy. After applying these criteria, 88 patients who underwent conventional concurrent chemoradiotherapy were designated as the control group, while 94 patients treated with endostar combined with concurrent chemoradiotherapy comprised the combined group.

Treatment plan

Patients in the control group underwent concurrent radiotherapy using a 23-EX Varian linear accelerator with 15 MV X-rays for external beam radiation therapy, combined with a high-dose-rate Ir-192 radiation source. The treatment area included the pelvic tissues, with the central pelvic region receiving a total dose of 40 Gy, administered in 20 fractions of 2 Gy each over four weeks. Additionally, point A received 6 Gy per fraction, with a total dose ranging from 18 to 30 Gy, while the lateral pelvic tissues outside the uterine cavity received a dose ranging from 4 to 16 Gy, with a maximum of 2 Gy per fraction. Internal pelvic irradiation was paused at the start of external irradiation, with the maximum dose for external irradiation limited to 14-15 units. The lower border of the treatment area was defined by the lower edge of the obturator foramen, and the outer border was set 2 cm from the pelvic sidewall. On the first day of radiotherapy, patients were administered 20 mg/m^2 of cisplatin (Dalian Meilun Biotechnology, China, batch number: MB1055) intravenously once a week for four weeks. Patients in the observation group received

combination therapy, which included additional endostar (Xiansheng Medzyn Biopharmaceutical Co., Ltd., China, batch number: 2017-01075). Endostar was administered as a daily intravenous infusion at a dosage of 7.5 mg/m^2 for four weeks, starting on the first day of radiotherapy.

Observation indicators

Key observational indicators included the following: Clinical response was assessed according to the RECIST criteria of the World Health Organization, categorizing patient outcomes into complete remission (CR), partial remission (PR), stable disease (SD), and progression (PD) [16]. The objective remission rate (ORR) was calculated as the sum of CR and PR. CR was defined as no detectable tumor lesions post-treatment via imaging and other relevant examinations. PR indicated a reduction of at least 30% in tumor volume compared to pre-treatment. SD was characterized by a tumor volume reduction of less than 30% or an increase of no more than 25%. PD was defined as a tumor volume increase of over 25% or the appearance of new lesions. All patients were followed for 3 years, with 1-year and 3-year survival rates recorded for both groups. Kaplan-Meier (K-M) curves were used to compare survival outcomes between the two groups. Secondary observational indicators, including treatment-related adverse reactions, such as gastrointestinal reactions, bone marrow suppression, skin lesions, and peripheral neuropathy, were recorded for both groups. Changes in tumor marker levels, specifically squamous cell carcinoma antigen (SCC-Ag), cancer antigen 125 (CA125), and carcinoembryonic antigen (CEA), were measured and compared before and after treatment between the two groups. Independent factors affecting patient prognosis were analyzed using univariate and multivariate analyses, and the prognostic predictive value of these independent factors was evaluated using ROC curves.

Statistical methods

Data were statistically analyzed using SPSS 20.0 software (IBM Corporation). The sample size calculation refers to the predictive model calculation formula, which is N = EPV × X/P, where the number of events per variable (EPV) should be at least 10; X is the number of predictive factors to be included in the model, with this study predicting 6-8; P is the incidence rate of the outcome event, with previous studies reporting the 3-year mortality rate for LACC ranging from 22.2% to 48.6% [17, 18]. The calculation shows that at least 123 patients are needed, and ultimately, we collected 182 cases based on actual collection. Microsoft Excel software was used for analysis and table generation. Measurement data were presented as mean ± standard deviation (mean ± SD), and an independent samples t-test was used to compare means between groups. Categorical data were compared using the chi-square test. Rank data were analyzed using the rank sum test and expressed as Z-values. K-M survival analysis was conducted to evaluate patient survival at 1 year and 3 years post-treatment, employing the log-rank test for comparison. Univariate and multivariate analyses were performed using the Cox regression model to assess prognostic factors, and the prognostic predictive value was evaluated using ROC curves. A *p*-value of less than 0.05 was considered statistically significant.

Results

General information of the two groups of patients

The general information of all patients is shown in **Table 1**. There were no statistical differences between the two groups in age, tumor diameter, FIGO stage, smoking history, pathological type, and histological grade (P>0.05).

Comparison of treatment efficacy between the two groups

The therapeutic efficacy of the combined group was significantly better than that of the control group (rank sum test, P<0.001). The ORR of the combined group was 74.47%, which was significantly higher than that of the control group (54.55%, P<0.005), as shown in **Table 2**.

Comparison of adverse reactions between the two groups

The adverse reactions of the two groups are summarized in **Table 3**. There were no statistical differences in the incidence of gastrointestinal reactions, bone marrow suppression, abnormal liver and kidney function, and skin damage between the two groups (P>0.05). Specifically, both groups had grade 3 adverse

Table 1. General information of the two groups of patients

	Control group (n = 88)	Combined group (n = 94)	χ^2	P
Age			0.266	0.606
≤50 years	51 (57.95)	58 (61.70)		
>50 years	37 (42.05)	36 (38.30)		
Tumor diameter			0.691	0.406
≥4 cm and ≤5 cm	48 (54.55)	57 (60.64)		
≥5 cm	40 (45.45)	37 (39.36)		
FIGO installments			0.266	0.606
II	37 (42.05)	36 (38.30)		
III	51 (57.95)	58 (61.70)		
Smoking history			0.66	0.417
Yes	18 (20.45)	24 (25.53)		
No	70 (79.55)	70 (74.47)		
Pathological type			1.206	0.547
Squamous cell carcinoma	69 (78.41)	79 (84.04)		
Adenocarcinoma	13 (14.77)	9 (9.57)		
Adenosquamous cell carcinoma	6 (6.82)	6 (6.38)		
Histological grading			0.632	0.729
Highly differentiated	13 (14.77)	11 (11.70)		
Moderately differentiated	60 (68.18)	69 (73.40)		
Poorly differentiated	15 (17.05)	14 (14.89)		
Lymph node metastasis			0.660	0.417
Yes	18 (20.45)	24 (25.53)		
No	70 (79.55)	70 (74.47)		
Whether menopause			0.792	0.374
Yes	47 (53.41)	44 (46.81)		
No	41 (46.59)	50 (53.19)		

FIGO: Federation International of Gynecology and Obstetrics.

Table 2. Treatment efficacy

	CR	PR	SD	PD	ORR
Control group (n = 88)	16 (18.18)	32 (36.36)	19 (21.59)	21 (23.86)	48 (54.55)
Combined group (n = 94)	38 (40.43)	32 (34.04)	12 (12.77)	12 (12.77)	70 (74.47)
Z/χ^2				3.488	7.912
P				<0.001	0.005

CR: Complete Response, PR: Partial Response, SD: Stable Disease, PD: Progressive Disease, ORR: Objective Response Rate.

reactions in gastrointestinal reactions. As for bone marrow suppression, there were 5 cases and 2 cases of grade 3 and 4 reactions in the control group. In the combined group, there were 9 cases of grade 3 and 2 cases of grade 4 bone marrow suppression reactions. There was 1 case of grade 3 liver and kidney function abnormalities in the control group, and none in the combined group, but 2 cases in the combined group had grade 3 reactions of skin damage.

Comparison of changes in tumor markers between the two groups

Comparing the changes in the levels of tumor markers SCC-Ag, CA125, and CEA between the two groups, it was found that there was no statistical difference in the levels of SCC-Ag, CA125, and CEA between the two groups before treatment (P>0.05), while the levels of SCC-Ag, CA125 and CEA in the combined group were significantly lower than those in the con-

Table 3. Adverse reactions

	Control group (n = 88)					Combined group (n = 94)					P
	Grade 1	Grade 2	Grade 3	Grade 4	Total	Grade 1	Grade 2	Grade 3	Grade 4	Total	
Gastrointestinal reactions	30	8	1	0	39	35	13	0	0	48	0.363
Myelosuppression	43	16	5	2	66	46	22	9	2	79	0.130
Abnormalities in liver and kidney function	19	5	1	0	25	24	9	0	0	33	0.333
Skin lesion	14	6	0	0	20	22	7	2	0	31	0.124

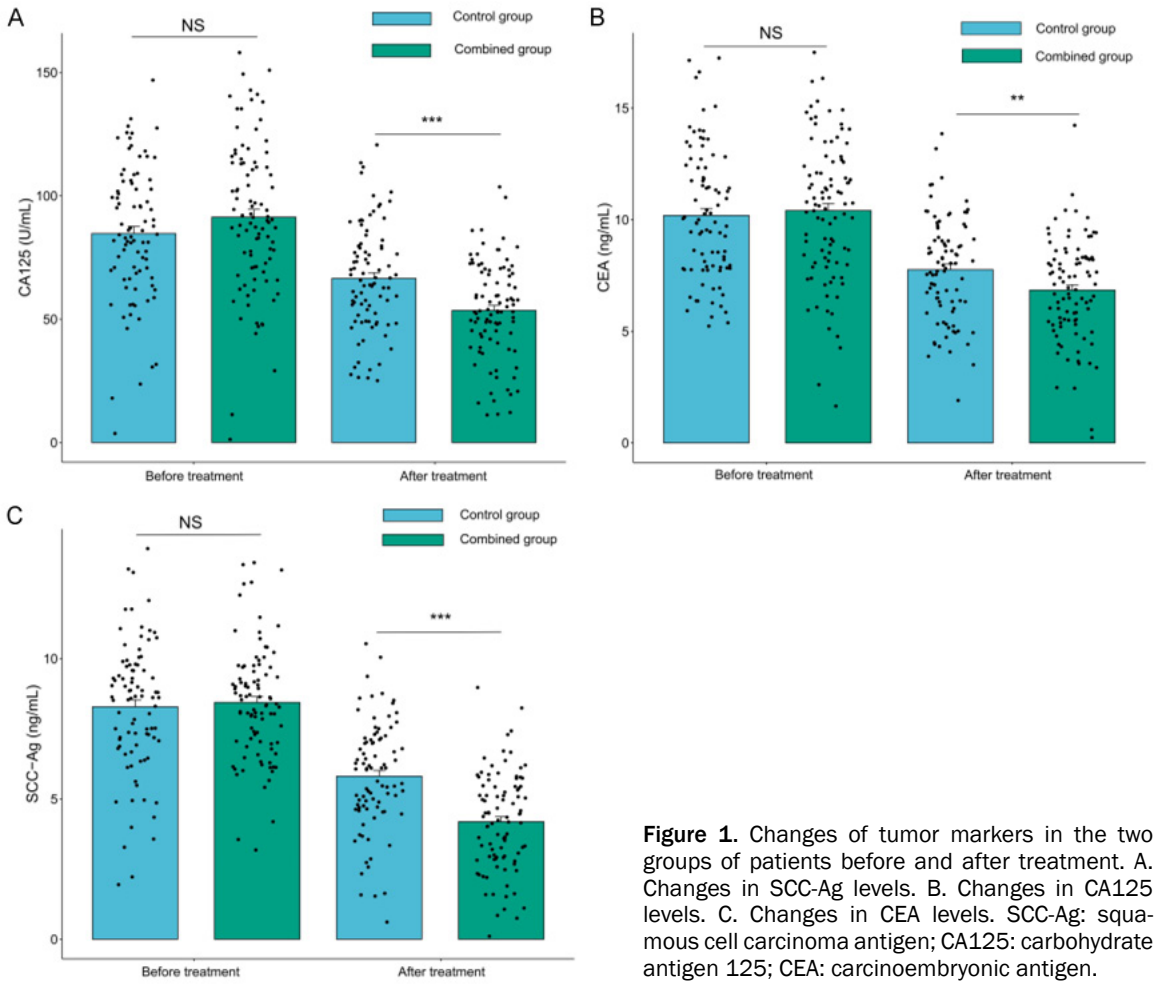

Figure 1. Changes of tumor markers in the two groups of patients before and after treatment. A. Changes in SCC-Ag levels. B. Changes in CA125 levels. C. Changes in CEA levels. SCC-Ag: squamous cell carcinoma antigen; CA125: carbohydrate antigen 125; CEA: carcinoembryonic antigen.

trol group after treatment (P<0.05). See **Figure 1**.

Tumor marker levels in patients with different treatment efficacies

Further, we compared the tumor marker levels between patients with or without objective remission after treatment and found that the SCC-Ag, CA125, and CEA levels of patients with objective remission were significantly higher than those without (P<0.05), as shown in **Figure 2**.

Comparison of 1- and 3-year survival between the two groups

By counting the 1-year and 3-year survival status of the two groups, it was found that there were 70 cases of 1-year survival and 41 cases of 3-year survival in the control group, and 85 cases of 1-year survival and 66 cases of 3-year survival in the combined group. K-M curve showed that the 1-year and 3-year survival rates of the combined group were significantly higher than those of the control group (P<0.05). See **Figure 3**.

Comparison of 1-year and 3-year survival rates between patients with different treatment efficacies

The 1-year and 3-year survival rates in patients with or without objective remission after treatment were then compared. The K-M curve showed that the 1-year and 3-year survival rates of patients with objective remission were significantly higher than those of patients without (P<0.05), as shown in **Figure 4**.

Univariate analysis of factors affecting patients' 3-year prognosis

The 107 patients who survived for 3 years were included in the survival group, and the 75 patients who died were included in the death

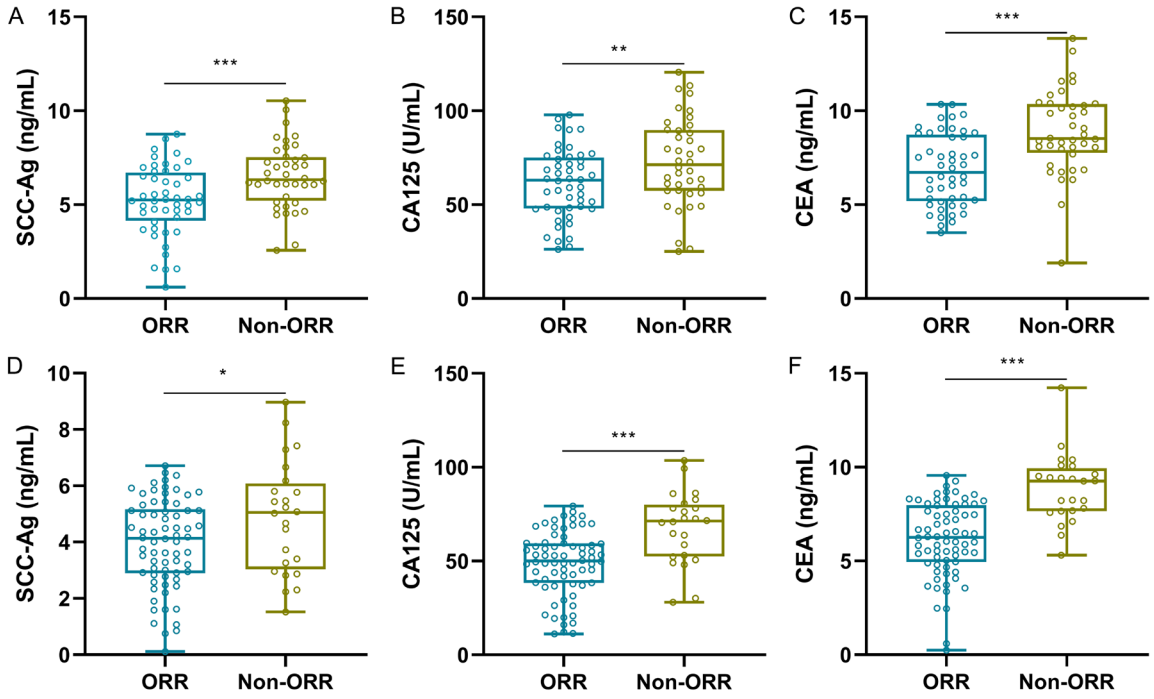

Figure 2. Tumor marker levels between patients with different efficacy. A. Comparison of SCC-Ag levels between patients in the control group with or without objective remission after treatment (t = 3.446, P<0.001). B. Comparison of CA125 levels between patients in the control group with or without objective remission after treatment (t = 2.612, P = 0.011). C. Comparison of CEA levels between patients in the control group with or without objective remission after treatment (t = 4.569, P<0.001). D. Comparison of SCC-Ag levels between patients in the combined group with or without objective remission after treatment (t = 2.285, P = 0.025). E. Comparison of CA125 levels between patients in the combined group with or without objective remission after treatment (t = 4.582, P<0.001). F. Comparison of CEA levels between patients in the combined group with or without objective remission after treatment (t = 5.945, P<0.001). ORR: objective remission rate; SCC-Ag: squamous cell carcinoma antigen; CA125: carbohydrate antigen 125; CEA: carcinoembryonic antigen. *P<0.05; **P<0.01; ***P<0.001.

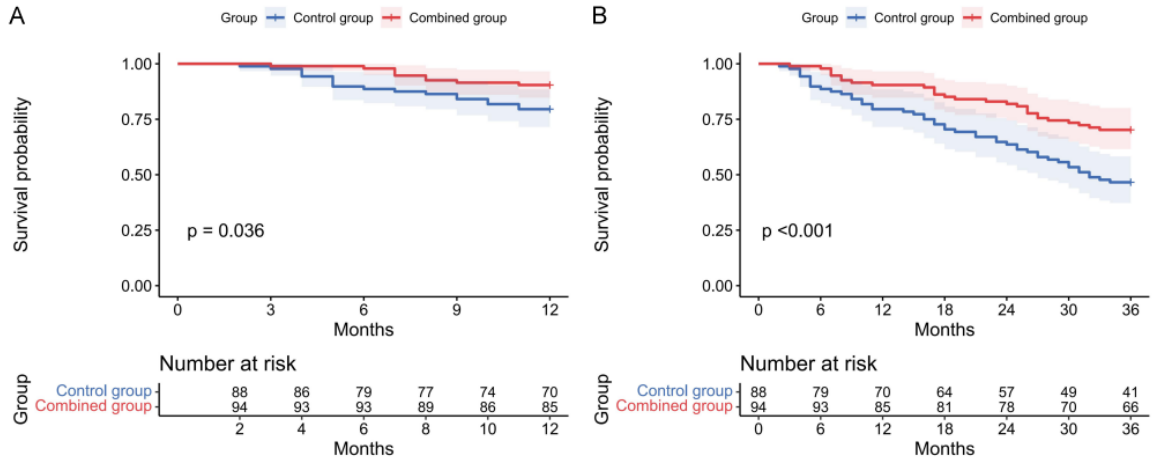

Figure 3. Comparison of 1- and 3-year survival between the two groups. A. K-M curves for 1-year survival. B. K-M curves for 3-year survival.

group. Univariate analysis found that age, pathological type, smoking history, menopause status, lymph node metastasis, and post-treatment CEA were not associated with death within 3 years (P>0.05), whereas the tumor diameter, FIGO stage, histological grading, treatment

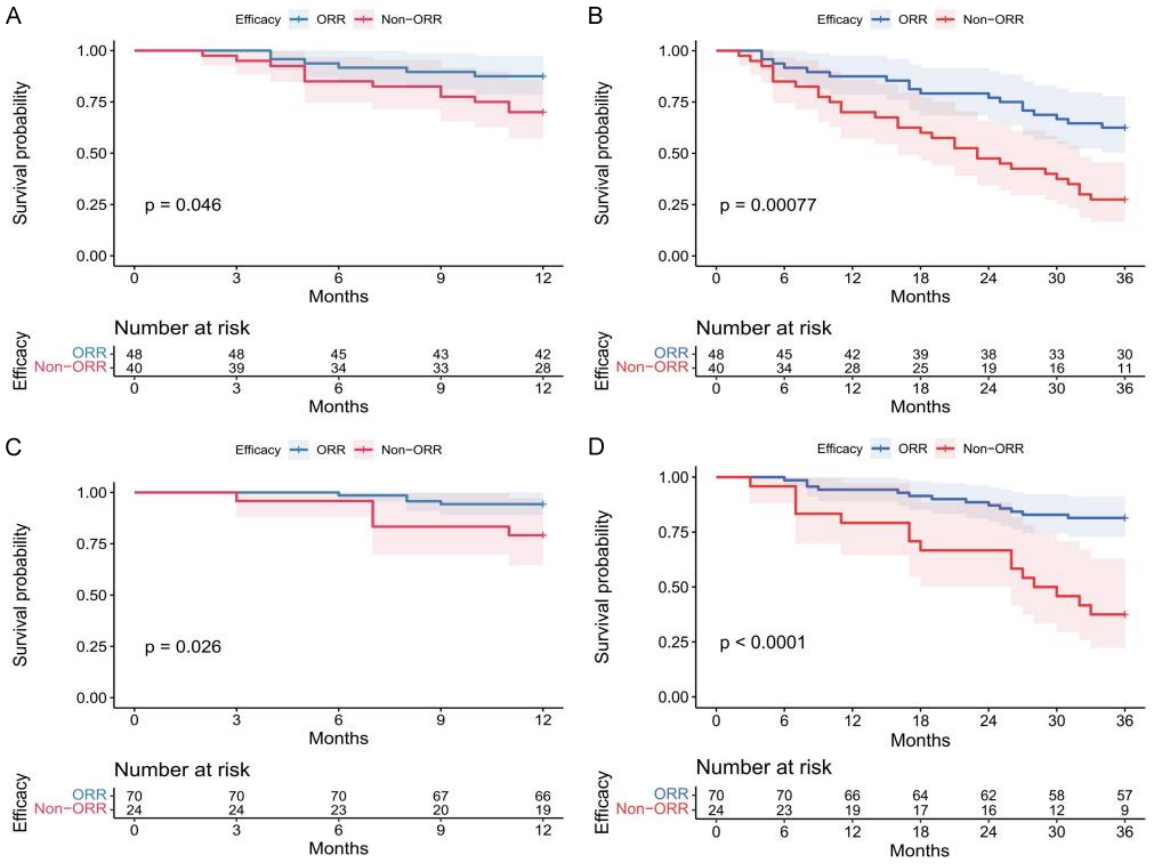

Figure 4. K-M curves of 1-year and 3-year survival of patients with different efficacy. A. K-M curves of 1-year survival of patients in the control group with or without objective remission. B. K-M curves of 3-year survival of patients in the control group with or without objective remission. C. K-M curves of 1-year survival of patients in the combined group with or without objective remission. D. K-M curves of 3-year survival of patients in the combined group with or without objective remission. ORR: objective remission rate.

regimens, post-treatment SCC-Ag, and post-treatment CA125 may be influential factors for 3-year mortality (P<0.05), as shown in **Figure 5**.

Multifactorial analysis of factors affecting patients' 3-year prognosis

After multivariate Cox analysis, tumor diameter and post-treatment CA125 were not found to be independent factors (P>0.05), whereas a FIGO stage of IIA (OR = 1.865, 95% CI = 1.110-3.133, P = 0.018), lower histologic grade (OR = 2.191, 95% CI = 1.418-3.385, P<0.001), and higher post-treatment SCC-Ag (OR = 1.135, 95% CI = 1.005-1.282, P = 0.041) were independent risk factors for patient death within 3 years. Treatment modality of endostar combined with simultaneous chemoradiotherapy (OR = 0.579, 95% CI = 0.347-0.966, P = 0.037) was an independent protective factor. See **Figure 6**.

Predictive value of independent prognostic factors

The predictive value of the independent prognostic factors FIGO stage, histologic grading, treatment modality, and post-treatment SCC-Ag on patients' death at 3 years was tested by plotting ROC curves, and it was found that the AUCs of FIGO stage, histologic grading, treatment modality, and SCC-Ag after treatment were 0.614, 0.625, 0.622, and 0.662, respectively, as shown in **Figure 7**.

Discussion

In this study, we conducted a retrospective analysis to compare the efficacy and prognosis of endostar combined with concurrent chemoradiotherapy versus conventional concurrent chemoradiotherapy in patients with LACC. The results demonstrated that the group receiving

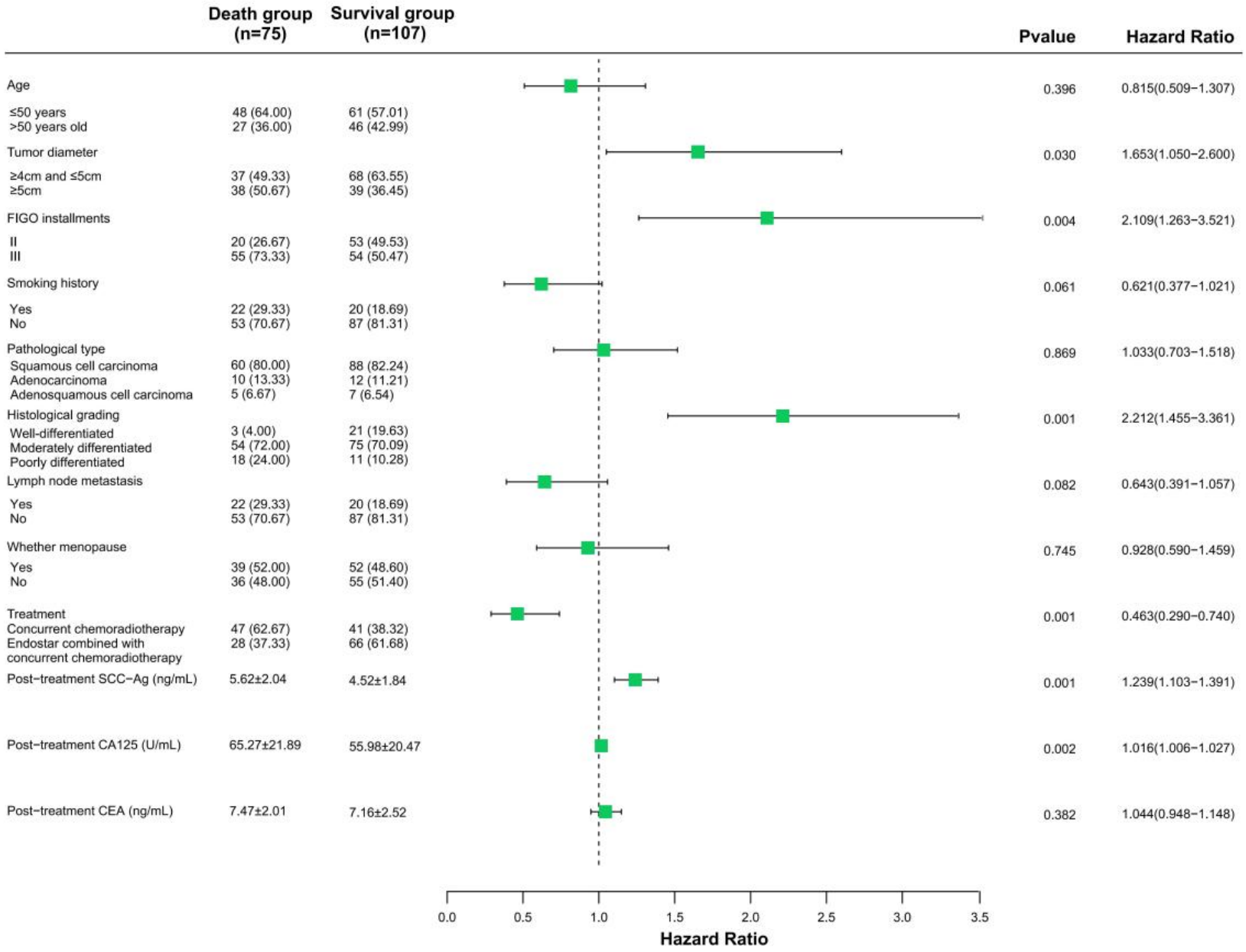
Death group (n=75)
Survival group (n=107)
Pvalue
Hazard Ratio
Age
0.396
0.815(0.509−1.307)
≤50 years
48 (64.00)
61 (57.01)
>50 years old
27 (36.00)
46 (42.99)
Tumor diameter
0.030
1.653(1.050−2.600)
≥4cm and ≤5cm
37 (49.33)
68 (63.55)
≥5cm
38 (50.67)
39 (36.45)
FIGO installments
0.004
2.109(1.263−3.521)
II
20 (26.67)
53 (49.53)
III
55 (73.33)
54 (50.47)
Smoking history
0.061
0.621(0.377−1.021)
Yes
22 (29.33)
20 (18.69)
No
53 (70.67)
87 (81.31)
Pathological type
0.869
1.033(0.703−1.518)
Squamous cell carcinoma
60 (80.00)
88 (82.24)
Adenocarcinoma
10 (13.33)
12 (11.21)
Adenosquamous cell carcinoma
5 (6.67)
7 (6.54)
Histological grading
0.001
2.212(1.455−3.361)
Well-differentiated
3 (4.00)
21 (19.63)
Moderately differentiated
54 (72.00)
75 (70.09)
Poorly differentiated
18 (24.00)
11 (10.28)
Lymph node metastasis
0.082
0.643(0.391−1.057)
Yes
22 (29.33)
20 (18.69)
No
53 (70.67)
87 (81.31)
Whether menopause
0.745
0.928(0.590−1.459)
Yes
39 (52.00)
52 (48.60)
No
36 (48.00)
55 (51.40)
Treatment
0.001
0.463(0.290−0.740)
Concurrent chemoradiotherapy
47 (62.67)
41 (38.32)
Endostar combined with concurrent chemoradiotherapy
28 (37.33)
66 (61.68)
Post−treatment SCC−Ag (ng/mL)
5.62±2.04
4.52±1.84
0.001
1.239(1.103−1.391)
Post−treatment CA125 (U/mL)
65.27±21.89
55.98±20.47
0.002
1.016(1.006−1.027)
Post−treatment CEA (ng/mL)
7.47±2.01
7.16±2.52
0.382
1.044(0.948−1.148)
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Hazard Ratio

Figure 5. Forest plot of univariate analysis. FIGO: Federation International of Gynecology and Obstetrics; ORR: objective remission rate; SCC-Ag: squamous cell carcinoma antigen; CA125: carbohydrate antigen 125; CEA: carcinoembryonic antigen.

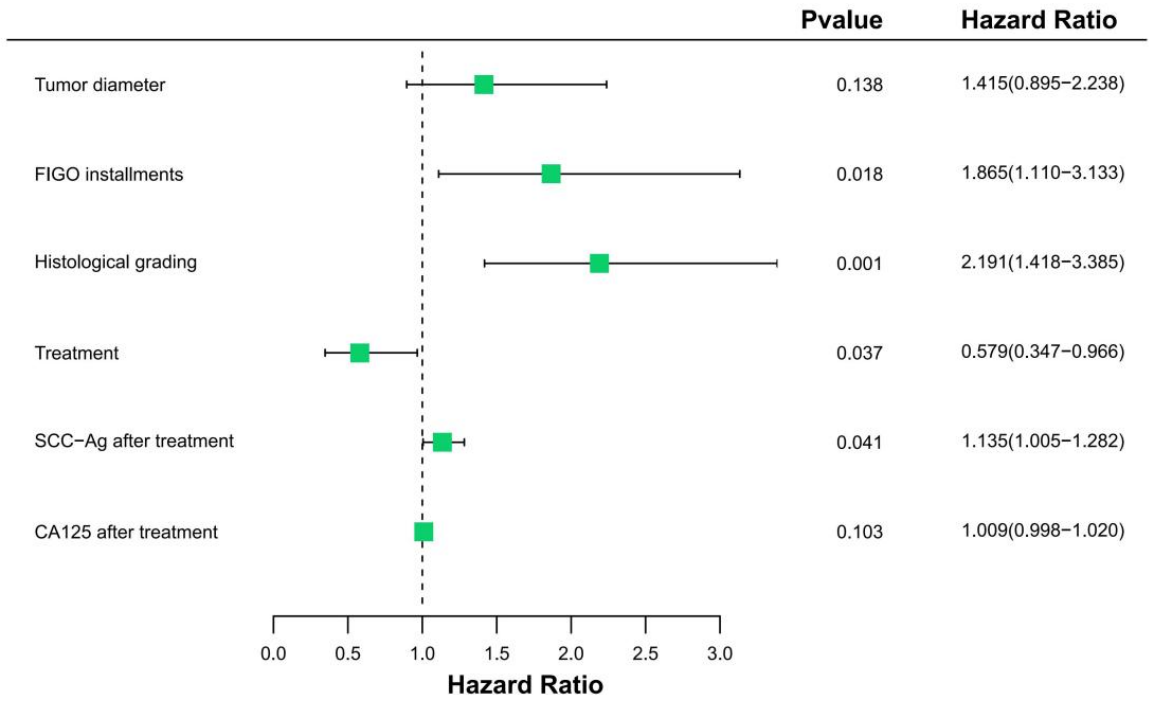

Figure 6. Forest plot of dy factor analysis. FIGO: Federation International of Gynecology and Obstetrics; SCC-Ag: squamous cell carcinoma antigen; CA125: carbohydrate antigen 125.

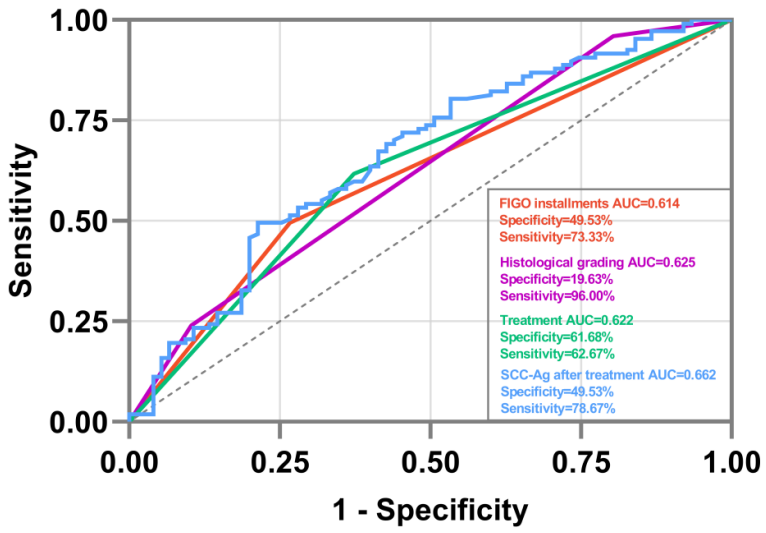

Figure 7. Predictive value of independent prognostic factors. FIGO: Federation International of Gynecology and Obstetrics; SCC-Ag: squamous cell carcinoma antigen.

endostar with concurrent chemoradiotherapy showed significantly better outcomes in terms of ORR, tumor marker levels, and 1-year and 3-year survival rates compared to the control group. Additionally, there was no significant difference in the incidence of adverse reactions between the two groups. These findings suggest that endostar combined with concurrent chemoradiotherapy holds high clinical value in the treatment of LACC.

In this study, the ORR of the combination group (endostar with concurrent chemoradiotherapy) was found to be significantly higher than that of the control group (74.47% vs. 54.55%). This suggests that endostar, as an anti-angiogenic drug, can effectively enhance the efficacy of concurrent chemoradiotherapy by inhibiting tumor angiogenesis.

The anti-angiogenic mechanism disrupts the blood supply to tumors, making it difficult for them to grow and metastasize, thereby improving the local control rate and overall survival rate [19, 20]. It has been shown that many anti-angiogenic drugs exhibit good efficacy in various solid tumors [21]. For instance, Monk et al. [22] demonstrated that bevacizumab was effective and well-tolerated in patients with recurrent cervical cancer. In a basic study, Xu et al. [23] also found that endostar enhanced micro vessel density and serum VEGF-A expression in mice treated with chemoradiotherapy in a cervical cancer model, and the tumor volume in the combined treatment group was significantly less than that in the chemoradiotherapy-alone group, indicating the potential of endostar to improve the efficacy of chemoradiotherapy. VEGF is an important inducer of tumor angiogenesis and can regulate immune responses [24]. It reduces T-cell infiltration and activity by downregulating adhesion molecules and enhancing PD-1 expression, and it also inhibits the maturation and activation of dendritic cells, limiting antigen presentation. VEGF induces the expression of Fas ligand on tumor endothelial cells, mediating the apoptosis of effector T cells [25]. Therefore, anti-angiogenesis can improve the immunosuppressive tumor microenvironment.

In addition to the significant advantages in terms of efficacy in the group treated with endostar combined with simultaneous chemoradiotherapy, there was also no significant difference between the two groups in terms of adverse reactions. This suggests that the addition of endostar did not significantly increase the adverse effects of treatment and has a favorable safety profile. Antiangiogenic drugs may theoretically cause vascular-related side effects [26], but the results of this study showed that the use of endostar did not significantly increase the risk of adverse effects in patients, which provides a safety guarantee for its promotion in clinical applications. Chen et al. [27] mentioned that endostar is a naturally derived C-terminal fragment of type XVIII collagen. Compared with other anti-angiogenic drugs such as bevacizumab and anlotinib, it has a better simulation effect on endogenous endostatin in tumor suppression and fewer side effects. In the study by Liao et al. [28], it was found that the most common adverse reactions of endostar combined with chemotherapy were bone marrow suppression, gastrointestinal reactions, and liver function abnormalities, and compared with chemotherapy alone, it did not significantly increase the incidence of adverse reactions.

As an antiangiogenic drug, the main mechanism of action of endostar is to block the nutrient supply to tumors by inhibiting tumor angiogenesis [29, 30]. This mechanism of action may differ from the direct cytotoxicity induced by chemoradiotherapy and therefore may not significantly increase the side effects of chemoradiotherapy.

SCC-Ag, CA125, and CEA are commonly used tumor markers that reflect the presence and progression of tumors [31]. Previous studies have shown that a decrease in the levels of these markers is closely associated with an improved prognosis in patients [32]. In this study, the post-treatment levels of SCC-Ag, CA125, and CEA were significantly lower in the combination group than in the control group. The changes in the levels of these tumor markers reflected the reduction in tumor load, further supporting the effectiveness of endostar combined with simultaneous chemoradiotherapy in controlling tumors. In a study by Zhao et al. [33], it was found that endostar combined with chemoradiotherapy significantly reduced the levels of TK1, HE4, VEGF, and SCC-Ag in stage IIB-IVA cervical squamous cell carcinoma, which is consistent with our findings.

After comparing the survival rates of patients in the two groups, it was found that the 1-year and 3-year survival rates of the combination group were significantly higher than those of the control group. This indicates that the combination of endostar with simultaneous chemoradiotherapy not only improved short-term efficacy but also enhanced long-term prognosis. Improvement in survival rate is a crucial indicator of the effectiveness of tumor treatment, and the significant advantage observed in the combination group further underscores the clinical value of endostar. K-M curve analysis indicated that the survival curve of the combination group was significantly better than that of the control group, which verifies the effectiveness of combining endostar. Lu et al. [34] conducted a study to evaluate the efficacy of endostar combined with concurrent chemoradiotherapy for

the treatment of LACC. Their study found that the combination therapy group had significantly better distant metastasis-free survival rates at 1 year and 2 years compared to the group treated with chemoradiotherapy alone. The specific data were 92.7% versus 81.1% and 86.0% versus 65.1%, respectively, demonstrating a significant improvement effect of the combined treatment.

Multifactorial Cox analysis revealed that FIGO staging, histologic grading, and post-treatment SCC-Ag levels were independent risk factors for death at 3 years, while endostar combined with simultaneous chemoradiotherapy served as an independent protective factor. These results suggest that early FIGO staging, higher histologic grading, and lower post-treatment SCC-Ag levels are associated with a better prognosis, and endostar-combination therapy significantly reduces the risk of death in patients. Additionally, ROC curve analysis demonstrated that FIGO staging, histologic grading, treatment modality, and post-treatment SCC-Ag levels had high predictive value for prognosis, further emphasizing the importance of these factors in predicting the prognosis of patients with LACC.

Despite the valuable conclusions of this study, there are some limitations. Firstly, this study is a retrospective analysis, which introduces the possibility of selection bias. Although efforts were made to control for the balance of baseline information, it is not possible to completely exclude the influence of other potential confounders. Secondly, the relatively small sample size of this study may affect the statistical validity of the results. Future large-scale prospective studies are needed to further validate the efficacy and safety of endostar combined with simultaneous chemoradiotherapy in the treatment of LACC. In conclusion, endostar combined with simultaneous chemoradiotherapy for LACC increased the short-term efficacy and long-term prognosis compared with chemoradiotherapy alone, did not increase the adverse effects, and demonstrated a good safety profile.

Disclosure of conflict of interest

None.

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