The role of postoperative radiotherapy in patients with vulvar squamous carcinoma: findings based on the SEER database

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Abstract

Introduction: The role of postoperative radiotherapy in treating squamous cell carcinoma of the vulva remains controversial. This study evaluated the effect of radiotherapy on the survival of patients with postoperative squamous cell carcinoma of the vulva.

Methods Clinical and prognostic information on patients diagnosed with vulvar squamous cell carcinoma from 2010 to 2015 was collected from the Surveillance, Epidemiology, and Prognosis (SEER) database. A propensity score matching (PSM) approach was used to balance the differences in clinicopathological characteristics between groups. The impact of postoperative radiotherapy on overall survival (OS) and disease-specific survival (DSS) was assessed.

Results The study included 3629 patients with squamous cell carcinoma of the vulva, of whom 767 (21.1%) underwent postoperative radiotherapy. After propensity score matching, multivariate analysis showed that Age, M stage, tumor size, and lymph node surgery were independent prognostic factors affecting patient survival. Postoperative radiotherapy improved patients' overall survival and disease-specific survival. Further subgroup survival analysis showed that overall survival was significantly improved among patients who received radiotherapy in patients with Grade III, IV, AJCC stage III, N1, lymph node metastasis, large tumor diameter, and those who received chemotherapy.

Conclusion: Postoperative radiotherapy may provide a survival benefit for patients with squamous cell carcinoma of the vulva, especially for AJCC stage III, lymph node metastases, large tumor diameter, and those receiving postoperative chemotherapy.

Introduction:

Vulvar cancer is a rare gynecologic malignancy, accounting for 5% of gynecologic malignancies, and it is most common in older women (Tan et al. 2019). Over the past decade, the overall incidence of vulvar cancer has increased by an average of 4.6% every five years(Zapardiel et al. 2020). According to reports, there were 6120 new vulvar cancer cases in the United States in 2020 and 1350 deaths(Michalski et al. 2021). The most common pathological type of vulvar cancer is vulvar squamous cell carcinoma, followed by melanoma. Vulvar bleeding, pain, and sexual dysfunction are the main clinical symptoms of the disease, which seriously affect the quality of life and physical and mental health of patients.

Surgery is the primary method of treatment for vulvar cancer. Compared to radical vulvectomy, partial radical vulvectomy has become the procedure of choice in recent years due to fewer postoperative complications(Dellinger et al. 2017; Ghoniem et al. 2020; He et al. 2021). The main reasons currently affecting the prognosis of patients with vulvar cancer are postoperative complications and a high rate of local recurrence. Although postoperative radiotherapy is thought to enhance the control of postoperative tumors, the role of postoperative radiotherapy is not fully understood due to the low incidence of vulvar cancer and limited clinical studies in large samples.

This study explored the impact of postoperative radiotherapy on the prognosis of patients with vulvar squamous cell carcinoma using data from the SEER database. To minimize selection bias in the included sample, propensity score matching was performed to balance the distribution of baseline clinicopathological variables between the two cohort populations.

Materials And Methods:

Patient data for this study were obtained from the National Cancer Institute's SEER database between 2010 and 2015. The SEER database is a sizeable cancer-related database in the United States (Doll et al. 2018; Zhao et al. 2019), containing information on the incidence, treatment, and prognosis of cancer patients collected by multiple institutions since 1973. We used SEER*Stat software (version 8.3.9) to extract eligible cases from the database.

For patients with pathologically confirmed vulvar cancer from 2010 to 2015, the primary vulvar site cases were obtained using the "primary site" variable. The histological subtype of vulvar cancer was determined using the variable "ICD-0-3 Hist/Behav, malignant". We extracted demographic variables, including age at diagnosis, race, primary site, histological type, tumor grade, tumor size, surgery, radiotherapy, chemotherapy, lymph node status, marital status, cause of death, survival (from diagnosis to end or last follow-up), TNM staging, and AJCC staging (7th edition).

Since the distribution of patients in the SEER database is not randomized, selection bias of baseline characteristics may affect the final results. To reduce the effects of data bias and confounding variables, propensity score matching (PSM) was used to adjust for potential baseline confounders (Badhiwala et al. 2021; Liang et al. 2021). In calculating the propensity score, a logistic regression model was used simultaneously. The following baseline covariates were considered: tumor grade, tumor size, T-stage, N-stage, M-stage, and marital status. Based on the score calculated by the nearest neighbor 1:1 matching algorithm, patients receiving postoperative radiotherapy are matched with other patients.

The primary and secondary endpoints were overall survival (OS) and disease-specific survival (DSS). Categorical variables were analyzed using the chi-square test. The Kaplan-Meier method was used to produce survival curves and the two-stage test to analyze the differences between the survival outcomes of the two curves. Univariate and multivariate Cox scale risk models were used to identify risk factors affecting OS and DSS. A Cox proportional risk model was used in the subgroup analysis to determine the population of patients who might benefit from radiotherapy. It is considered statistically significant when the bilateral p-value is less than 0.05. The above statistical analysis was calculated using SPSS software (version 24.0) and R software (version 4.0.2).

Results:

This study included 3629 patients with vulvar squamous cell carcinoma who underwent surgery between 2010 and 2015 and were diagnosed with vulvar cancer, 767 (21.1%) of whom received radiotherapy.

Table 1 shows the demographic and clinicopathological characteristics between the group receiving postoperative radiotherapy and those not receiving postoperative radiotherapy. Before propensity score matching (PSM), there were significant differences in race, tumor cell grading, disease stage, tumor size, chemotherapy status, lymph node metastasis, and distribution of lymph node surgery between the two groups. After balancing the baseline characteristics of these two groups of PSM patients, there were 401 patients in each group. All features were balanced between the cohorts using matched propensity scores (Table 1).

Before PSM, 5-year OS and DSS were significantly higher in the no-radiotherapy group (OS: 67.9%; DSS: 86.2%) than in the radiotherapy group (OS: 48.6%; DSS: 62.0%, both P<0. 001)。 The K-M survival analysis of the radiotherapy group versus the no-radiation group after PSM suggested that the model was a non-equivalent proportional regression model, After Two-stage test, OS and DSS were higher in the radiotherapy group than in the no radiotherapy group (p=0.025, p=0.026) (Figure 1).

Multivariate analysis showed a non-significant effect of postoperative radiotherapy on patients' OS (HR 1.181, 95% CI 0.696-1.029, p-value 0.095) and DSS (HR 1.027, 95% CI 0.752-1.259, p-value 0.837). AJCC staging (HR 0.187, 95% CI 1.465-19.334, p=0.011) was a significant factor affecting patients' DSS; M staging (HR 0.294, 95% CI 1.534-7.522, p=0.002) was a significant factor affecting patients' OS. Age (HR 0.312, 95% CI 2.082-4.922, p<0.001; HR 0.242, 95% CI 2.206-7.715, p<0.001), tumor size (HR 0.933, 95% CI 1.035-1.109, p<0.001; HR 0.931, 95% CI 1.026- 1.122, p=0.002), and lymphadenectomy (HR 1.749, 95% CI 0.441-0.740, p<0.001; HR 1.540, 95% CI 0.451-0.934, p=0.02) were independent influences on patients' OS and DSS (Table 2).

Subgroup analysis showed a significant benefit of postoperative radiotherapy in improving OS (p=0.037, p=0.022) in patients with Grade III and IV stages. Postoperative radiotherapy improved OS in patients with AJCC stage I and N1 (P=0.037, P=0.013). For patients with lymph node metastases, postoperative radiotherapy significantly improved OS (p=0.011). Postoperative radiotherapy had better OS for adjuvant chemotherapy patients (p=0.031) (Figure 2).

Discussion:

Owing to the low incidence of vulvar squamous cell carcinoma, it is challenging to study the prognostic impact of postoperative radiotherapy on patients with vulvar squamous cell carcinoma using large randomized controlled trials (Mahner et al. 2015). In recent years, oncologic radiotherapy techniques have developed rapidly. Their role in treating patients with vulvar cancer has received increasing attention (Rao et al. 2017a); however, the effect of postoperative radiotherapy on the survival of patients with squamous cell carcinoma of the vulva is unclear. To obtain data with strong relevance to current clinical practice, this study used clinically relevant data from the SEER database of patients with vulvar cancer from 2010 to 2015. A retrospective analysis revealed a significant survival benefit of postoperative radiotherapy for patients with vulvar squamous cell carcinoma.

Several previous studies have reported the role of radiotherapy in treating patients with vulvar cancer

(Raspagliesi et al. 2006). Ignatov T et al. recruited 257 patients with squamous cell carcinoma of the vulva, divided the enrolled patients into lymph node metastasis positive and negative groups, and found that adjuvant radiotherapy improved the prognosis of lymph node-positive patients (Ignatov et al. 2016). Meanwhile, Macit Arvas et al. studied 107 postoperative vulvar cancer patients with long-term follow-up. They found that postoperative radiotherapy improved the 5-year overall survival rate of patients with positive surgical margins from 29–67.6%, and mortality was significantly reduced in patients with vulvar cancer who received postoperative radiotherapy (Arvas et al. 2018). In a recent clinical study, adjuvant radiation therapy significantly reduced the risk of local recurrence in patients with HPV-positive vulvar cancer compared with patients with HPV-negative vulvar squamous cell carcinoma, significantly improved overall survival, and enhanced the quality of life of patients (Woelber et al. 2022).

The above study analyzed the effects of postoperative radiotherapy on survival outcomes or disease recurrence in patients with vulvar cancer from the perspective of different subgroups of the population. The present study utilizes the multicenter, large sample platform of the SEER database. It uses PSM to balance the clinical characteristics of the two samples, which can be closer to a randomized controlled study and make the results more reliable. According to the inclusion criteria, 3629 patients with vulvar squamous cell carcinoma were enrolled in this study. The effect of postoperative radiotherapy on OS and DSS was analyzed by 1:1 PSM matching according to whether they received postoperative radiotherapy. The results showed that postoperative radiotherapy significantly improved OS and DSS in patients with vulvar squamous cell carcinoma, which is consistent with previously reported findings, suggesting that radiotherapy can be an important complementary treatment for patients with vulvar squamous cell carcinoma after surgery.

Concerning prognostic factors of vulvar cancer, VULCAN retrospectively analyzed the clinicopathological characteristics and prognosis of 1727 patients with vulvar cancer (Zapardiel et al. 2020). Multivariate analysis suggested that tumor stage, tumor size, and lymph node status were independent prognostic factors affecting patients' OS. In addition, the French Society of Radiation Oncology clearly states that the main factors affecting the postoperative prognosis of patients with vulvar cancer include lymph node involvement, tumor stage, and patient age (Chargari et al. 2022). Our cohort was analyzed by multivariate COX regression after PSM analysis, and lymph node surgery was also an independent factor affecting patients' OS and DSS; however, postoperative radiotherapy was not an independent influencing factor in patients with vulvar squamous cell carcinoma.

To further clarify the subgroup population of vulvar cancer benefiting from postoperative radiotherapy and to guide personalized clinical treatment, we conducted a subgroup survival analysis, which showed that among patients receiving radiotherapy, patients with Grade III, IV, AJCC stage III, N1, lymph node metastasis, large tumor diameter, and those receiving chemotherapy had significantly improved OS. A recent study analyzing factors associated with overall survival and disease recurrence in patients with vulvar cancer pointed out that the size of the primary lesion is a vital reference indicator of overall survival (Salani et al. 2017). Tumor diameter is closely related to lymph node metastasis. When the lesion diameter was less than 2 cm, the lymph node metastasis rate was about 23%, while when the lesion

diameter was more significant than 2 cm, the lymph node metastasis rate was as high as 47% (Viswanathan et al. 2013). Adjuvant radiotherapy has been shown to significantly prolong the overall survival of patients with advanced disease (Chargari et al. 2022; Miljanović-Špika et al. 2021). In a retrospective analysis of 54 vulvar cancers by S C Han 1 et al, adjuvant radiotherapy was found to significantly improve disease-specific survival (P = 0.03) and overall survival (P = 0.04) in patients with locally advanced vulvar cancer(Han et al. 2000). In this study, survival analysis of the PSM-matched cohort showed a significant improvement in overall survival after postoperative radiotherapy in patients with advanced (stage III, IV, M1) vulvar cancer, which may be associated with better control of disease recurrence with adjuvant radiotherapy.

It has been confirmed that lymph node status, including whether the lymph nodes are metastatic and the number of positive lymph nodes, affects the recurrence of vulvar cancer and the prognosis of patients (Te Grootenhuis et al. 2016; Van der Zee et al. 2008). Meanwhile, the International Federation of Obstetrics and Gynecology guidelines recommend adjuvant radiotherapy as a necessary treatment for lymph node-positive vulvar cancer patients. For patients with lymph node-positive vulvar cancer, adjuvant radiotherapy was associated with a lower risk of local recurrence (25.5% vs. 15.8%) (Woelber et al. 2022). A recent AGO-CaRE 1 study found that adjuvant radiotherapy significantly improved progression-free survival in lymph node-positive vulvar cancer (Mahner et al. 2015).

A study using the National Cancer Database to assess the prognostic impact of radiotherapy on patients with vulvar cancer noted that radiotherapy was significantly associated with higher overall survival than radiotherapy alone (Rao et al. 2017b). A subgroup survival analysis revealed that patients who received radiotherapy were substantially more likely to survive than those who received postoperative radiotherapy alone. This may be related to the fact that some chemotherapeutic drugs such as fluorouracil and cisplatin (Moore et al. 2012), in addition to their anti-tumor effects, also act as radiosensitizers, resulting in a 15%-20% reduction in the dose of radiotherapy, thus reducing the incidence of acute local radiotherapy reactions in patients and improving their tolerability (Blake 2003; Olawaiye et al. 2021; van Triest et al. 2021).

Whether the degree of pathological differentiation of squamous cells affects the prognosis of patients with vulvar cancer treated with postoperative radiotherapy is poorly reported. Further studies are needed to elucidate the mechanisms involved.

Our study has some limitations: first, it is a retrospective study with some selection bias, and PSM minimized the influence of confounding factors on the results. Secondly, the SEER database does not contain indicators of specific radiotherapy methods, radiotherapy sites, and radiotherapy regimens, which also affect patient prognosis.

In conclusion, analysis of vulvar cancer data from the SEER database showed that postoperative radiotherapy improved overall and disease-specific survival in patients with vulvar squamous cell carcinoma. Age, tumor size, and lymph node surgery are independent prognostic factors that affect the survival of patients with vulvar cancer. Postoperative radiotherapy improves survival outcomes in

patients with Grade III, IV, AJCC stage III, N1, lymph node metastases, large tumor diameter, and those receiving chemotherapy.

Declarations:

Authors' Contributions

Li Wang conducted the statistical analysis and drafted the article. Tao Wang is responsible for downloading and organizing the data. Jing Sun was responsible for the design and guidance of the whole experiment. All authors contributed to manuscript revision, read, and approved the submitted version.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

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Tables:

Table1 Patient information based on their baseline features before and after 1:1 PSM in surgery plus radiotherapy and radiotherapy groups.

Characteristic	Before PSM			After PSM		
	PROT(-) No(%)	PROT(+) No(%)	P-value	PROT(-) No(%)	PROT(+) No(%)	P-value
All patients	2862	767		401	401	
Age(years)						
≤49	459(12.6)	104(2.9)	0.054	43(5.4)	44(5.5)	0.051
50-69	1200(33.1)	356(9.8)		143(17.8)	175(21.8)	
≥70	1203(33.1)	307(8.5)		215(26.8)	182(22.7)	
Race						
White	2548(70.2)	600(18.2)	0.011	344(42.9)	344(42.9)	0.729
Black	234(6.4)	70(1.9)		40(5.0)	36(4.5)	
Other	80(2.2)	37(1.0)		17(2.1)	21(2.6)	
Marital statues						
Married	1077(29.7)	298(8.2)	0.536	125(15.6)	149(18.6)	0.074
Other	1785(49.2)	469(12.9)		276(34.4)	252(31.4)	
Grade						
I	972(26.8)	128(3.5)	0.001	85(10.6)	60(7.5)	0.163
II	1032(28.4)	366(10.1)		187(23.3)	195(24.3)	
III	296(8.2)	204(5.6)		91(11.3)	110(13.7)	
IV	18(0.5)	7(0.2)		4(0.5)	5(0.6)	
Unknown	544(15.0)	62(1.7)		34(4.2)	31(3.9)	
AJCC stage						
I	2568(70.8)	219(6.0)	0.001	166(20.7)	181(22.6)	0.499
II	86(2.4)	70(1.9)		36(4.5)	38(4.7)	
III	161(4.4)	399(11.0)		161(20.1)	154(19.2)	
IV	47(1.3)	79(2.2)		38(4.7)	28(3.5)	
T						

T1	2724(75.1)	582(16.0)	0.001	318(39.7)	325(40.5)	0.276
T2	114(3.1)	147(4.1)		61(7.6)	65(8.1)	
T3	22(0.6)	36(1.0)		20(2.5)	10(1.2)	
T4	2(0.1)	2(0.1)		2(0.2)	1(0.1)	
N						
N0	2672(73.6)	312(8.6)	0.001	217(27.1)	225(28.1)	0.932
N1	106(2.9)	232(6.4)		103(12.8)	97(12.1)	
N2	72(2.0)	202(5.6)		71(8.9)	68(8.5)	
N3	12(0.3)	21(0.6)		10(1.2)	11(1.4)	
M						
M0	2839(78.2)	732(20.2)	0.001	386(48.1)	391(48.8)	0.311
M1	23(0.6)	35(1.0)		15(1.9)	10(1.2)	
Tumor size（cm）						
≤0.3(25%)	837(23.1)	83(2.3)	0.001	34(4.2)	38(4.7)	0.881
0.3–1.7(50%)	821(22.6)	108(3.0)		69(8.6)	62(7.7)	
1.7–3.5(75%)	702(19.3)	232(6.4)		116(14.5)	120(15.0)	
3.5	502(13.8)	344(9.5)		182(22.7)	181(22.6)	
Chemotherapy						
Yes	2827(77.9)	411(11.3)	0.001	366(45.6)	349(43.5)	0.054
No	35(1.0)	356(9.8)		35(4.4)	52(6.5)	
LN metastasis						
Yes	2673(73.7)	313(8.6)	0.001	217(27.1)	225(28.1)	0.571
No	189(5.2)	454(12.5)		184(22.9)	176(21.9)	
Surgery to LN						
No	1454(40.1)	232(6.4)	0.001	134(16.7)	134(16.7)	0.934
lymph node biopsy	270(7.4)	75(2.1)		37(4.6)	40(5.0)	

lymphadenectomy	1138(31.4)	460(12.7)	230(28.7)	227(28.3)

PORT, postoperative radiotherapy; PSM; propensity score matching;LN, Lymph nodes.

Table2 Univariate and multivariate Cox regression analyses of different variables considered for OS for patients with carcinoma of vulva

Characteristic	Univariate		Multivariate		Landmark	
	HR(95%CI)	P-value	HR(95%CI)	P-value	HR(95%CI)	P-value
Age(years)		0.001				
≤49	1		1		1	
50-69	1.439(0.950-2.179)	0.086	1.519(0.987-2.339)	0.057	0.714(0.899-2.1818)	0.136
≥70	3.705(2.496-5.501)	0.001	3.710(2.435-5.652)	0.001	0.312(2.082-4.922)	0.001
Race		0.055		0.098		
White	1		1		1	
Black	0.694(0.493-0.976)	0.036	1.033(0.723-1.476)	0.858	1.015(0.676-1.438)	0.941
Other	0.732(0.456-1.173)	0.195	0.591(0.365-0.958)	0.033	1.596(0.381-1.031)	0.066
Marital statues	1.279(1.050-1.558)	0.014	1.944(0.722-5.511)	0.183		
Grade		0.042		0.31		
I	1		1		1	
II	1.129(0.871-1.462)	0.359	0.982(0.753-1.281)	0.892	1.051(0.720-1.257)	0.726
III	1.371(1.035-1.815)	0.028	1.057(0.787-1.419)	0.713	0.944(0.779-1.438)	0.715
IV	0.892(0.326-2.436)	0.823	1.051(0.380-2.906)	0.924	0.963(0.374-2.878)	0.942
Unknown	0.795(0.522-1.212)	0.286	0.660(0.425-1.026)	0.065	1.501(0.421-1.053)	0.082
AJCC stage						
I	1		1		1	
II	1.727(1.244-2.397)	0.001	1.249(0.770-2.025)	0.367	0.794(0.763-2.074)	0.366
III	2.044(1.656-2.523)	0.001	1.489(0.680-3.263)	0.319	0.623(0.723-3.557)	0.245

IV	3.640(2.664-4.974)	0.001	1.671(0.606-4.603)	0.321	0.485(0.737-5.752)	0.167
T						
T1	1		1		1	
T2	1.548(1.223-1.958)	0.001	1.239(0.867-1.771)	0.24	0.725(0.959-1.981)	0.082
T3	2.243(1.493-3.368)	0.001	1.305(0.506-3.366)	0.582	0.859(0.446-3.031)	0.757
T4	2.819(0.904-8.787)	0.074	0.357(0.093-1.375)	0.314	3.143(0.082-1.234)	0.097
N						
N0	1		1		1	
N1	1.542(1.236-1.923)	0.001	0.629(0.216-1.835)	0.396	0.787(0.577-2.781)	0.554
N2	2.416(1.909-3.057)	0.001	0.906(0.325-2.524)	0.85	0.552(0.844-3.883)	0.127
N3	4.045(2.464-6.638)	0.001	1.994(0.722-5.511)	0.183	0.526(0.678-5.318)	0.221
M	3.410(2.219-5.240)	0.001	3.340(1.508-7.401)	0.003	0.294(1.534-7.522)	0.002
Tumor size(cm)	1.084(1.055-1.113)	0.001	1.073(1.038-1.109)	0.001	0.933(1.035-1.109)	0.001
Radiotherapy	0.898(0.748-1.078)	0.249	0.904(0.750-1.090)	0.29	1.181(0.696-1.029)	0.095
Chemotherapy	0.904(0.667-1.226)	0.517	0.946(0.676-1.324)	0.746	1.031(0.689-1.364)	0.859
LN metastasis	1.914(1.592-2.301)	0.001	1.994(0.722-5.511)	0.183	0.475(0.757-5.850)	0.153
Surgery to LN		0.82		0.001		
NO	1		1		1	
lymph node biopsy	0.944(0.666-1.337)	0.746	0.674(0.459-0.989)	0.044	1.466(0.464-1.001)	0.051
lymphadenectomyy	1.040(0.853-1.269)	0.699	0.575(0.444-0.743)	0.001	1.749(0.441-0.740)	0.001

CI, confidence interval; HR, hazard ratio; DSS, disease specific survival; PORT, postoperative radiotherapy.

Table3 Univariate and multivariate Cox regression analyses of different variables considered for DSS for patients with carcinoma of vulva

Characteristic	Univariate		Multivariate		Landmark	
	HR(95%CI)	P-value	HR(95%CI)	P-value	HR(95%CI)	P-value
Age(years)						
≤49	1		1		1	
50-69	1.806(0.981-3.323)	0.058	1.954(1.034-3.695)	0.039	0.531(0.993-3.577)	0.052
≥70	4.344(2.416-7.810)	0.001	4.411(2.365-8.230)	0.001	0.242(2.206-7.715)	0.001
Race						
White	1		1		1	
Black	1.558(0.801-3.033)	0.192	0.561(0.301-1.046)	0.069	1.763(0.303-1.059)	0.075
Other	0.576(0.238-1.389)	0.219	0.487(0.246-0.963)	0.039	1.935(0.260-1.025)	0.058
Marital statues	1.197(0.921-1.556)	0.179	0.976(0.742-1.285)	0.865	0.993(0.758-1.336)	0.963
Grade						
I	1		1		1	
II	1.190(0.666-2.125)	0.557	1.012(0.700-1.462)	0.949	0.991(0.691-1.473)	0.964
III	1.502(0.892-2.528)	0.126	1.019(0.681-1.527)	0.925	0.947(0.698-1.595)	0.798
IV	1.769(1.029-3.041)	0.039	0.879(0.209-3.692)	0.86	1.141(0.208-3.689)	0.857
Unknown	0.999(0.230-4.347)	0.999	0.684(0.372-1.259)	0.223	1.399(0.386-1.323)	0.284
AJCC stage						
I	1		1		1	
II	1.824(1.126-2.955)	0.015	1.315(0.678-2.554)	0.418	0.778(0.658-2.507)	0.461
III	2.787(2.069-3.754)	0.001	1.986(0.764-5.167)	0.159	0.519(0.738-5.015)	0.181
IV	5.842(3.926-		4.746(1.311-	0.018	0.187(1.465-	0.011

	8.694)	0.001	17.184)		19.334)	
T						
T1	1		1		1	
T2	1.493(1.081-2.061)	0.015	1.274(0.805-2.014)	0.301	0.717(0.879-2.212)	0.157
T3	2.708(1.647-4.452)	0.001	0.741(0.225-2.439)	0.662	1.462(0.206-2.260)	0.533
T4	3.221(0.799-12.981)	0.1	0.300(0.059-1.529)	0.147	3.664(0.053-1.401)	0.119
N						
N0	1		1		1	
N1	1.988(1.474-2.682)	0.001	1.145(0.446-2.942)	0.779	0.872(0.446-2.939)	0.776
N2	3.215(2.351-4.395)	0.001	1.670(0.673-4.145)	0.269	0.609(0.663-4.058)	0.284
N3	6.598(3.693-11.786)	0.001	1.248(0.352-4.427)	0.731	0.868(0.322-4.110)	0.828
M	4.127(2.445-6.966)	0.001	2.139(0.797-5.742)	0.131	0.467(0.799-5.735)	0.13
Tumor size(cm)	1.095(1.058-1.134)	0.001	1.074(1.027-1.123)	0.002	0.931(1.026-1.122)	0.002
Radiotherapy	1.000(0.782-1.280)	0.997	1.008(0.784-1.297)	0.95	1.027(0.752-1.259)	0.837
Chemotherapy	1.121(0.770-1.632)	0.552	1.143(0.748-1.748)	0.537	0.856(0.762-1.788)	0.475
LN metastasis	2.548(1.978-3.281)	0.001	1.127(0.325-3.911)	0.851	0.868(0.322-4.110)	0.825
Surgery to LN						
NO	1		1		1	
lymph biopsy	1.461(0.955-2.236)	0.081	0.987(0.610-1.597)	0.957	0.979(0.625-1.665)	0.934
lymphadenectomy	1.258(0.951-1.663)	0.108	0.640(0.448-0.914)	0.014	1.540(0.451-0.934)	0.02

CI, confidence interval; OS, overall survival; HR, hazard ratio; PORT, postoperative radiotherapy.

Figures

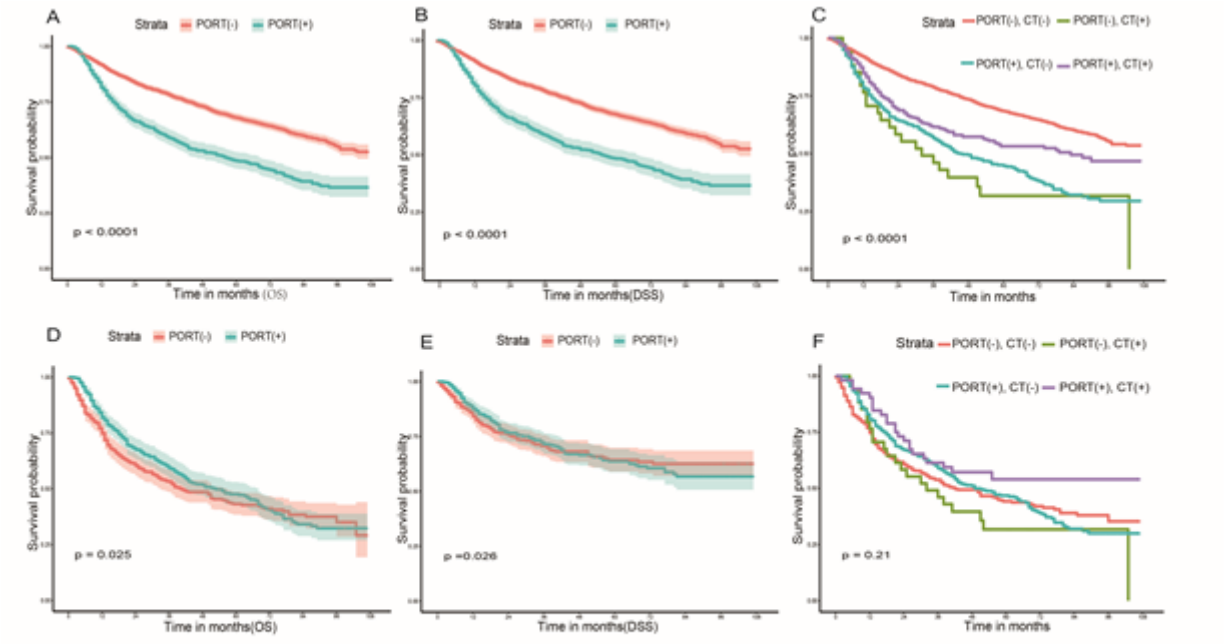

Figure 1

Comparison of OS (A) and DSS (B) in the PORT and non-PORT groups before PSM; Comparison of OS (D) and DSS (E) in the two groups after PSM; Compare the effect of radiotherapy combination on patient OS before and after PSM(C, F).

DSS, disease-specific survival; OS, overall survival; PORT, postoperative radiation therapy; PSM, propensity score matching.

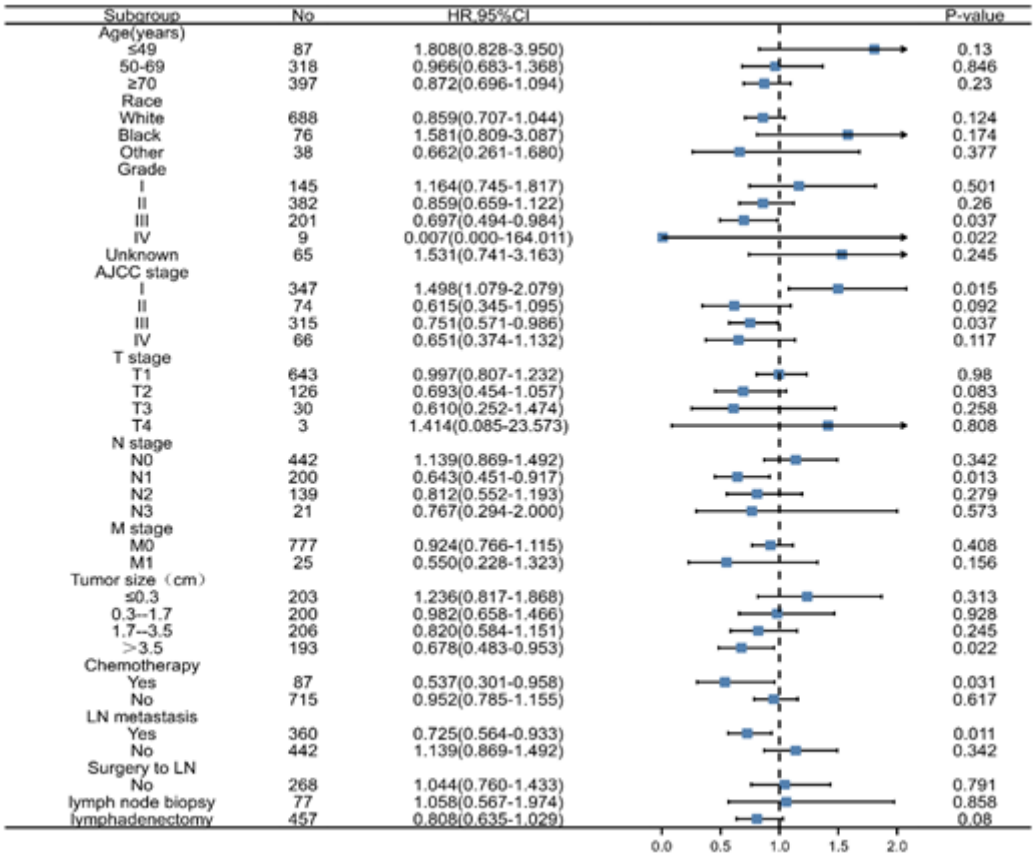

Figure 2

The forest plot of HRs comparing patients with postoperative vulvar cancer between the PORT group and no-PORT group according to different variables.