

Treatment paradigms and survival outcomes in esophageal adenocarcinoma with liver metastasis: a retrospective cohort study using the SEER database

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Background: Esophageal adenocarcinoma with liver metastasis (EACLM) at the time of diagnosis has a poor prognosis and few therapeutic options. The best treatment options and prognostic factors for EACLM patients are unclear. The present study sought to explore the optimal treatment modalities for and the prognosis of these patients.

Methods: Patients diagnosed with EACLM at the time of diagnosis were identified from the Surveillance, Epidemiology and End Results (SEER) database between 2010 and 2015. The last follow-up date was December 31, 2018. Treatment patterns were divided into four groups: local therapy (surgery/radiation), systemic therapy [chemotherapy (CT)], combination therapy (surgery/radiation + CT), and no treatment. The Kaplan-Meier (K-M) method and log-rank test were used for overall survival (OS) and disease-specific survival (DSS). Univariable and multivariable Cox regression were performed to identify the prognostic factors. Propensity score-matching (PSM) analyses were performed for sensitive analyses.

Results: A total of 925 patients diagnosed with EACLM were included in the study. The median OS was 12, 10, 3, and 2 months for combination therapy, systemic therapy, local therapy, and no treatment, respectively (P<0.001). After PSM, the patients who received systemic treatment had a better OS (median 9 *vs.* 2 months; P<0.001) and DSS (median 9 *vs.* 3 months; P<0.001) than those who received no treatment. Compared to systemic therapy, combination therapy did not increase patients' OS (median 13 *vs.* 12 months, P=0.069) but did improve their DSS (median 19 *vs.* 13 months, P=0.048).

Conclusions: EACLM patients might benefit the most from systemic therapy and combination therapy. For patients who are well-tolerated, combination therapy should be considered as a preferable option.

Keywords: Esophageal adenocarcinoma (EAC); liver metastasis; prognostic factor; treatment; survival

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Introduction

Esophageal cancer (EC) is one of the most common cancers worldwide (1). In 2020, 604,100 new cases of EC were

reported, and EC was ranked as the 6th leading cause of death from cancer (1). Esophageal squamous cell carcinoma (ESCC) and esophageal adenocarcinoma (EAC) are the

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two major histological types of EC (2). During the last few decades, the incidence of EAC has been rising rapidly, and it has become the most common esophageal malignancy in Western countries (3,4). According to a previous study, liver metastasis occurs in approximately 20% of EAC cases, and the liver is the most common organ of metastasis (5). With a median overall survival (OS) of 8–10 months and a 5-year OS rate <5%, the prognosis of EC patients is extremely poor (6).

Patients with esophageal adenocarcinoma with liver metastasis (EACLM) are classified as stage IVB under the tumor, node, metastasis (TNM) classification system, and are considered suitable for palliative therapy, such as chemotherapy (CT), palliative radiation therapy (RT), and salvage surgery (7-9). Systemic therapy can provide palliation of symptoms, improved survival, and enhanced quality of life in patients with locally advanced or metastatic esophageal or esophagogastric junction (EGJ) cancers (10-12). Radiation alone rarely cures EC, the combination of radiotherapy and concurrent CT has led to long-term survival approximately 25% of patients (13). Despite the increase in perioperative risks, the estimated 5-year survival of 25% has been reported in selected patients for salvage esophagectomy (2). However, the prognostic value of different treatment modalities for EACLM patients is not clear, with only a small number of retrospective case series have been described in the worldwide literature (7,14,15). Further, there is also a relative lack of knowledge about the prognostic factors for EACLM. Thus, the effects of optional treatment modalities on patients' survival based on a largescale cohort study urgently needed to be investigated.

This study sought to compare the OS and DSS of EACLM patients who were divided into the following groups: local therapy (surgery/radiation), systemic therapy (CT), combination therapy (surgery/radiation + CT), and no treatment using the Surveillance, Epidemiology and End Results (SEER) database. PSM analyses were performed to minimize the differences between the groups at baseline. We present the following article in accordance with the STROBE reporting checklist (available at https://jgo. amegroups.com/article/view/10.21037/jgo-22-420/rc).

Methods

Data source

of last contact, treatment, and recurrence are updated to maintain accurate surveillance information. Patients were followed through the death date or the last follow-up

followed through the death date or the last follow-up date (December 31, 2018). The SEER database is an authoritative, public source of information on cancer incidence, mortality, prevalence, lifetime risk statistics, and survival in the United States (US) (16). We used SEER-Stat software (version 8.3.9) to access the database in this study. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). All data were extracted from the public database and did not involve personally identifiable information, so informed consent was not required.

were obtained from the SEER database from 2010 to 2015. Follow-up data are obtained through active and passive

methods. Data fields concerning patient vital status, date

Inclusion and exclusion criteria

According to the SEER database coding manual, all patients with histologic type, 8140/3, as coded by the International Classification of Diseases for Oncology (ICD-O-3), were included in the study. Patients were excluded from the study if they met any of the following exclusion criteria: (I) were not diagnosed at the first screening; (II) did not have liveronly metastases; (III) had missing treatment information; and (IV) had <1 month of follow-up (these patients were excluded to limit the immortal time bias) (17).

Study variables

Data and information were collected from the SEER database using SEER-Stat software for the following variables: age, gender, race, marital status, year of diagnosis, primary tumor site, T stage, N stage, tumor grade, treatment patterns, and survival time. Patients were divided into the following 4 groups based on age at diagnosis: 30-55, 56-65, 66-70, and >70 years old. Patients were divided into the following groups based on race: white, black, and other. Patients were divided into the following 4 groups based on marital status: separated/divorced, married, unmarried/single, and widowed/other. Patients were divided into the following 4 groups based on the distance from the incisors to the primary tumor site: 15-24 cm (C150-C153), 25-32 cm (C154), 33-40 cm (C155), and other (C158-159) (18). T stage and N stage were determined according to the American Joint Committee on Cancer (AJCC) (7th edition) staging system using the

The current study was a retrospective cohort study, and data about all the patients and their relevant information

available clinical and pathologic data on tumor invasion, and lymph nodes status, respectively. Grade was defined by the following codes: well-differentiated (grade I), moderately differentiated (grade II), poorly differentiated or undifferentiated (grade III and grade IV), and unknown grade (other). Patients were divided into the following four groups based on treatment patterns: local therapy (surgery/ radiation), systemic therapy (CT), combination therapy (surgery/radiation + CT), and no treatment.

Statistical analysis

Baseline

The baseline demographic and clinical characteristics are described as the medians with interquartile ranges (IQRs) for the continuous variables, and as the percentages for the categorical variables. The different groups (alive *vs.* dead) were compared using logistic regression models for all variables.

Univariate and multivariate regression analyses

For the univariate and multivariate regression analysis, the Cox regression model was used to assess the hazard ratios (HRs) and 95% confidence intervals (CIs). The proportional hazards assumption was met. OS was used as the primary endpoint and defined as the time from diagnosis of EACLM to death from any cause. DSS was used as the secondary endpoint and referred to the period between diagnosis of EACLM and death due to EACLM. All the variables were included in the multivariate analysis to predict the independent prognosis factors, and the OS and DSS curves were examined using the Kaplan-Meier (K-M) method and compared using the log-rank test.

Propensity score-matching (PSM) analyses

PSM analyses were performed for sensitivity analysis. We used a PSM method to minimize the differences between the groups at baseline. A logistic regression model was conducted to evaluate the propensity score based on the following variables: age, gender, race, marital status, primary tumor site, T stage, N stage, and histological grade. A 1:1 PSM was implemented between patients with systemic therapy or no therapy, and their prognoses were also compared. We then further compared patients who underwent combination therapy and systemic therapy using a matching ratio of 1:2 to compare their prognoses. We used the nearest-neighbor matching algorithm based on the R package MatchIt and chose the caliper value at 10% of the standard deviation of the propensity score value as converted by the logit model. The standardized mean differences (SMD) before and after matching are illuminated in Figures S1,S2. The balance between datum line covariates in both the matched and unmatched cohorts was scanned by standardized differences, and <10% was adequately credible (19). After matching, the balance of variables between two groups was evaluated by the χ^2 test and love-plot; a P value >0.05 for the χ^2 tests or plots within two dashed vertical lines in the love-plot were considered balanced. R (version 4.0.5; https://www.r-project.org/) was used for the statistical analysis. A two-sided P<0.05 was considered statistically significant.

Results

Patient characteristics

A total of 952 patients from 2010 to 2015 were identified as the study cohort from the SEER database. All the patients were confirmed to have EACLM at the time of the initial diagnosis. A flowchart of patient selection is presented in Figure 1. The median age of all patients at diagnosis was 63.0 (range, 30-97) years. Among these patients, the proportion of men was much greater (87.0%) than that of women (13.0%). Most patients (93.0%) were white; 4.0% were black, and 3.0% were other. Among the patients with EACLM, 24 (3%) of the 952 patients underwent surgery, 17 (2%) received RT, and 710 (75%) received CT. In relation to the various combination therapies, 26 (3%) of the 952 patients received combination therapy, 5 (1%) received local therapy, 685 (72%) received systemic therapy, and 236 (25%) did not received any treatment. Table 1 shows the baseline characteristics of all the patients extracted from the SEER database.

Survival analyses and prognostic factors

The median follow-up time of all 952 EACLM patients was 10.9 (range, 1–83) months. To investigate the relationship between treatment modality and prognosis, K-M survival analyses were conducted. The EACLM patients treated with CT had a better prognosis than those who were not treated with CT (P<0.001). Additionally, we found that the OS of patients who underwent surgery was longer than that of those who did not undergo surgery (P=0.005). However, there was no statistically significant different in the radiated patients compared to the non-radiated patients



Figure 1 Flowchart of selection of patients with EC and liver metastasis at 1st diagnosis used in the SEER database. EC, esophageal cancer; SEER, Surveillance, Epidemiology and End Results.

(P=0.271; see *Figure 2A-2C*). Similar results were also found in relation to DSS (see *Figure 2D-2F*). We further examined the effect of the treatment combinations on the OS and DSS of patients with EACLM. The median OS was 12, 10, 3, and 2 months for patients treated with combination therapy, systemic therapy, local therapy, and no therapy, respectively (see *Figure 3A*). Similar results were found for DSS. The median DSS was 19, 11, 3, and 3 months for patients treated with combination therapy, systemic therapy, local therapy, and no therapy, respectively (see *Figure 3B*).

In the univariate analyses, older age $(71-97 \ vs. \ 30-55$: HR =1.343, 95% CI: 1.119–1.611, P=0.002), year of diagnosis (2015 vs. 2010: HR =0.755, 95% CI: 0.597–0.954, P=0.019), T stage (T2 vs. T1: HR =0.640, 95% CI: 0.449– 0.913, P=0.014; and T3 vs. T1: HR =0.798, 95% CI: 0.649– 0.980, P=0.031), surgery (HR =0.528, 95% CI: 0.334–0.833, P=0.006), CT (HR =0.361, 95% CI: 0.310–0.420, P<0.001) were associated with OS. In the multivariate analyses, gender (HR =1.242, 95% CI: 1.055–1.535, P=0.045), T stage (T2 vs. T1: HR =0.583, 95% CI: 0.402–0.845, P=0.004; T3 vs. T1: HR =0.731, 95% CI: 0.586–0.912, P=0.006; and T4 vs. T1: HR =0.778, 95% CI: 0.292–0.407, P<0.001) were independent prognostic factors for OS (see *Figure 4A*).

In relation to DSS, we also observed that factors such as older age (71–97 *vs.* 30–55: HR =1.341, 95% CI: 1.101– 1.633, P=0.004), year of diagnosis (2015 *vs.* 2010: HR =0.755, 95% CI: 0.586–0.973, P=0.03), surgery (HR =0.522, 95% CI: 0.317–0.858, P=0.01), CT (HR =0.377, 95% CI: 0.319–0.445, P<0.001) were significant prognostic factors. The multivariate analysis of DSS indicated that marital status (married *vs.* divorced/separated: HR =0.778, 95% CI: 0.613–0.989, P=0.04), T stage (T2 *vs.* T1: HR =0.626, 95% CI: 0.421–0.930, P=0.02; T3 *vs.* T1: HR =0.779, 95% CI: 0.614–0.989, P=0.041), and CT (HR =0.360, 95% CI: 0.300–0.431, P<0.001) had significant predictive power compared to the other available factors (see *Figure 4B*).

PSM analyses

To better balance the patients in the systemic treatment group and the no therapy group, we performed a 1:1 PSM analysis for variables to decrease the selection bias and further compared their OS and DSS using the Cox regression model. The PSM analysis generated 224 matched pairs with similar baseline characteristics (see *Table 2* and Figure S1). The results showed that patients who received systemic treatment demonstrated a better OS and DSS than those who did not received any therapy (9 *vs.* 2 months, P<0.001 and 9 *vs.* 3 months, P<0.001; see *Figure 5*).

To determine if the combination therapy was superior to systemic therapy, we conducted a PSM analysis to assemble cohorts of patients with similar baseline characteristics and thereby reduced the possible bias in estimating treatment effects. Following 2:1 matching by propensity score, 24 patients in the combination therapy group were matched to 48 patients in the systemic therapy group. The baseline characteristics were well balanced between the two groups in both cohorts (see *Table 3* and Figure S2). The results demonstrated that combination therapy did not improve the OS rate compared to systemic therapy (13 vs. 12 months,

 Table 1 Clinical characteristics of patients with EACLM

Variables	No. of patients [%]	P value
Age (years)		0.504
30–55	259 [27]	
56–65	314 [33]	
66–70	133 [14]	
71–97	246 [26]	
Sex		0.149
Female	124 [13]	
Male	828 [87]	
Race		1.000
Black	40 [4]	
White	886 [93]	
Other	26 [3]	
Marital status		0.896
Married	546 [57]	
Divorced/separated	115 [12]	
Single/unmarried	173 [18]	
Widowed/other	118 [12]	
Year of diagnosis		<0.001*
2010	155 [16]	
2011	148 [16]	
2012	160 [17]	
2013	141 [15]	
2014	162 [17]	
2015	186 [20]	
Tumor location (cm)		0.280
15–24	25 [3]	
25–32	30 [3]	
33–40	771 [81]	
Other	126 [13]	
T stage		0.164
T1	218 [23]	
T2	43 [5]	
Т3	186 [20]	
T4	140 [15]	
Тх	365 [38]	

Table	1	(continued)
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Variables	No. of patients [%]	P value
N stage		0.598
NO	261 [27]	
N1	453 [48]	
N2	69 [7]	
N3	44 [5]	
Nx	125 [13]	
Grade		0.02*
I	26 [3]	
II	314 [33]	
III + IV	464 [49]	
Other	148 [16]	
Treatment		<0.001*
Combination therapy	26 [3]	
Local therapy	5 [1]	
Systemic therapy	685 [72]	
None	236 [25]	
Surgery		0.057
Yes	24 [3]	
No	928 [97]	
СТ		<0.001*
Yes	710 [75]	
No	242 [25]	
Radiation		1.000
Yes	17 [2]	
No	935 [98]	

*, statistically significant. Percentages were calculated after excluding missing cases from the denominator. EACLM, esophageal adenocarcinoma with liver metastasis; CT, chemotherapy.

P=0.069; see *Figure 6A*). However, patients who received combination therapy had better DSS than those who received systemic therapy (19 *vs.* 13 months, P=0.048; see *Figure 6B*).

Discussion

Table 1 (continued)

The liver is the most common metastatic organ in patients



Figure 2 K-M OS and DSS analyses stratified by different treatments. (A-C) K-M curve of OS by CT, surgery, and radiation in the total study population; (D-F) K-M curve of DSS by CT, surgery, and radiation in the total study population. OS, overall survival; DSS, disease-specific survival; K-M, Kaplan-Meier; CT, chemotherapy.



Figure 3 K-M OS and DSS analyses stratified by different treatment groups. (A) K-M curve of OS by different treatment groups in the total study population; (B) K-M curve of DSS by different treatment groups in the total study population. OS, overall survival; DSS, disease-specific survival; K-M, Kaplan-Meier.

Acceleration (in the section of the section	Δ	Charateristics	Unadjusted HR(95	%CI)	P value	Adjusted HR(95%CI)		P value
B 1282084-1103 1280827-1223 1980827-1233 1980827-12	~	Age category	1 033(0 860-1 228)		0.713	1 012(0 846-1 214)		0.880
7-79 1.340(11) 1 0.055 1.37(0.996-1.48) 0.055 0.055 Normality 1.1660.55-1.420 0.132 1.20(10.87-1.53) 0.055 0.055 Others within 0.5560.51-1.210 0.010 1.20(10.87-1.53) 0.015 0.005 Maria V. Disconsignated 0.5560.51-1.200 0.012 0.0055 0.007 0.005 Maria V. Disconsignated 0.5560.57-1.200 0.012 0.0055 0.007 0.012 Maria V. Disconsignated 0.5560.67-1.200 0.012 0.0055 0.000 0.012 2011 v. 2010 0.0310.66-1.060 0.013 1.20(0.95-1.30) 0.012 0.012 0.012 0.012 2014 v. 2010 0.0550.07-0.055 0.055 0.055 0.055 0.000 0.012 </th <th></th> <th>66~70 vs. 30~55</th> <th>1.052(0.844-1.311)</th> <th></th> <th>0.652</th> <th>0.984(0.783-1.235)</th> <th></th> <th>0.887</th>		66~70 vs. 30~55	1.052(0.844-1.311)		0.652	0.984(0.783-1.235)		0.887
Set: The Transle 1440.035-1.420 0.12 120.10.05-1.530 0.05 More vs., Illack 0.850.035-1.420 0.33 1.150.064-1.940 0.440 More vs., Illack 0.850.035-1.420 0.430 0.857.0-1.940 0.957 More vs., Illack 0.9570.05-1.200 0.440 0.957.0-1.940 0.957 StageVoldment vs., Disconsingenet 0.810.06-1.060 0.911 0.950.057-1.940 0.952 StageVoldment vs., Disconsingenet 0.831.06-1.600 0.911 0.950.057-1.910 0.952 StageVoldment vs., Disconsingenet 0.831.06-1.600 0.911 0.950.057-1.910 0.911 0.952 <		71~97 vs. 30~55	1.343(1.119-1.611)		0.002	1.217(0.996-1.488)		0.055
Product Construction Output		Sex Male vs. Female	1.168(0.954–1.429)	•	0.132	1.242(1.005-1.535)		0.045
Martiel Construction		Race Others vs. Black White vs. Black	0.856(0.512-1.432)		0.555	1.136(0.664-1.944)		0.641
Marcia vs. Disconsidynamical or Disconsidynamical vs. Disconsidynamical vs. Disconsidynamical vs. Disconsidynamical (Disconsidynamical (Discon		Marital	0.070(0.05-1.210)		0.45	1.009(0.715-1.420)		0.555
Bigeoli Lablerido, D. Developmenta 0.980(39-2):130 0.331 0.332 Diggooli 0.311 0.201(3-201) 0.312 0.332 2011 0.201 0.201(3-201) 0.312 0.332 0.332 2011 0.201 0.201(3-201) 0.312 0.332 0.332 0.332 2014 0.201 0.201(3-201) 0.331 0.320(3-201-323) 0.332 0.332 2015 0.2010 0.2530(3-71-0.232) 0.331 0.350(3-71-0.232) 0.331 0.350(3-71-0.232) 0.332 2015 0.2010 0.2530(3-71-0.232) 0.031 0.331 0.350(3-71-0.232) 0.041 0.331 2015 0.2010 0.290(3-71-353) 0.031 0.271(0-35-0.921) 0.041 0.049 2015 0.2010 0.290(3-71-0.232) 0.001 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921) 0.031 0.271(0-35-0.921)		Married vs. Divorced/separated	0.814(0.659-1.006)		0.057	0.769(0.617-0.958)	•••••	0.019
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Single/UnMarried vs. Divorced/separated	0.976(0.762-1.249)		0.845	0.965(0.749-1.243)		0.781
2017 2010 0.810/064-1.080 +++ 0.115 1.020(086-1.92) 0.032 0.032 2014 2010 0.840(084-1.61) +++ 0.131 0.980(037-1.62) 0.031 2014 0.021 0.850(037-1.62) +++ 0.031 0.980(037-1.62) 0.031 21-300 0.250(037-0.62) +++ 0.980(047-1.63) 0.031 0.980(047-1.63) 0.041 0.980(047-1.63)		Diagnosis	1.022(0.76-1.54)		0.072	0.002(0.04)=1.145)		0.502
312 3210 0.840(399-1.05) 0.940(399-1.26) 0.970(399-1.26) 3215 3210 0.359(397-1.25) 0.971 0.351(0.952-1.26) 0.971 25-32m N.15-26m 0.359(0.457-1.55) 0.971 0.971 0.971 0.971 25-32m N.15-26m 0.359(0.457-1.55) 0.971		2011 vs. 2010	0.831(0.66-1.046)	• — • — •	0.115	1.026(0.808-1.302)		0.832
$B = \frac{1}{2} $		2012 vs. 2010	0.863(0.689-1.08)		0.198	0.956(0.759-1.204)		0.702
215 x. 2010 0.750 (0.970-0.954) 0.019 0.838 (0.62-1.055) 0.13 22-32m v. 15-32m 0.460 (0.490-1.51) 0.637 (0.926 (0.45-1.62)) 0.049 (0.45-1.62) 0.049 (0.45-1.62)) Other v. 15-32m 0.980 (0.45-1.62) 0.989 (0.45-1.62) 0.989 (0.45-1.62) 0.999 (0.45-1.62) Other v. 15-32m 0.980 (0.45-1.62) 0.011 (0.271 (0.58-0.912) 0.014 (0.58-0.912) 0.056 (0.58-0.912) Other v. 15-32m 0.980 (0.45-1.62) 0.011 (0.271 (0.58-0.912) 0.015 (0.91-1.52) 0.015 (0.91-1.52) 0.015 (0.91-1.52) N1 v. N0 0.9710 (7.45-1.02) 0.049 (0.92-1.23) 0.910 (3.55-1.08) 0.930 (3.65-1.92) N1 v. N0 0.9710 (7.45-1.102) 0.049 (0.429-1.25) 0.357 (0.95-1.11) 0.270 (0.45-1.11) N1 v. N0 0.9710 (7.45-1.102) 0.311 (0.420-1.25) 0.321 (0.420-1.25) 0.321 (0.420-1.25) N1 v. N0 0.9710 (7.45-1.102) 0.321 (0.420-1.25) 0.321 (0.420-1.25) 0.321 (0.420-1.25) N1 v. N0 0.9710 (7.45-1.02) 0.321 (0.420-1.25) 0.321 (0.420-1.25) 0.321 (0.420-1.25) N1 v. N0 0.9220 (0.41-1.24) 0.321 (0.420-1.25) 0.321 (0.420-1.25) 0.321 (0.420-1.25) <		2013 vs. 2010 2014 vs. 2010	0.954(0.756-1.202)		0.887	1.032(0.819-1.3)		0.454
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		2015 vs. 2010	0.755(0.597-0.954)		0.019	0.833(0.656-1.058)		0.133
1		Primary site	0.055(0.100.1.5)					
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		25~32cm vs. 15~24cm 33~40cm vs. 15~24cm	0.856(0.489-1.5) 0.874(0.581-1.313)		0.587	0.808(0.45-1.45) 0.862(0.56-1.327)		0.474
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		Others vs. 15~24cm	0.989(0.637-1.534)		0.959	1.001(0.633-1.582)		0.998
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		AJCC T		i i			i i	
$ \begin{array}{c} \mathbf{B} \\ \mathbf{Characteristics} \\ \mathbf{Ac category } \\ Ac categor$		T2 vs. T1	0.64(0.449-0.913)		0.014	0.583(0.402-0.845)		0.004
Tw. T1 0.93(0.729-1.12) 0.99 0.9(0.738-1.09) 0.15 ALCCN 0.97(0.742-102) 0.99 0.9(0.738-1.09) 0.35 St v. N0 0.90(0.81-1.19) 0.99 0.18(90.916-1.285) 0.35 N v. N0 0.92(0.717-1.162) 0.93 1.16(0.0387-1.275) 0.35 Others v. I. 0.73(0.61-1.19) 0.35 0.577(0.69-1.11) 0.257 Others v. I. 0.71(0.455-1.20) 0.06 0.06(0.41-1.05) 0.257 Marcin V. I. 0.71(0.455-1.10) 0.027 0.080(0.40-1.10) 0.047 Marcin V. NO 0.577(0.61-1.241) 0.027 0.080(0.40-1.109) 0.137 Chemotherapy 0.57(0.61-1.241) 0.027 0.080(0.40-1.199) 0.147 VES v. NO 0.57(0.61-1.241) 0.027 0.080(0.40-1.199) 0.147 0.0417 VES v. NO 0.57(0.61-1.241) 0.027 0.080(0.40-1.99) 0.149 0.147 0.0417 0.0417 VES v. NO 0.57(0.61-1.241) 0.025 0.350 0.50 0.71 1.01.41 0.056 0.017 0.025 0.3450 0.0350 0.0361 0.0407 <		T4 vs. T1	0.835(0.667-1.044)		0.031	0.778(0.613-0.987)		0.038
AICC N NI v. NO 0.5710.742-1.022 0.689 1.6890.916-1.255 0.6710.742-1.022 0.335 NI v. NO 0.900.81-1.107 0.641 1.1620.359-1.571 0.335 0.3710.642-1.255 0.331 0.3710.642-1.255 0.331 0.3710.642-1.255 0.331 0.3710.642-1.255 0.331 0.3710.642-1.255 0.331 0.3710.642-1.255 0.331 0.3710.642-1.255 0.331 0.3710.641-1.251 0.238 II v. I. 1.12520.674-1.560 0.7610.641-1.241 0.771 0.464 1.3800.658-1.217 0.238 0.237 Others v. I. 0.7270.641-1.241 0.777 0.800.642-1.390 0.477 0.2400.442-1.390 0.477 Hadiation 0.5280.034-0.333 0.35 0.570.071 1.0 1.411 0.250.050.071 0.101.412.2.0 B Charaterizaria Insteaded HR0955C1 P value Adata test test 0.3450.0520.071 0.114.12.00 0.250.050.071 0.114.12.00 B Charaterizaria Insteade HR0956-1501 0.777 0.2350.150.071 0.711.0 1.411.00 0.777		Tx vs. T1	0.943(0.792-1.123)		0.509	0.91(0.758-1.093)		0.315
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $		AJCC N	0.871/0.742 1.022		0.080	1.090/0.01(.1.205)	<u> </u>	0.226
$ \begin{array}{c} \textbf{N} \\ N$		N1 vs. N0 N2 vs. N0	0.8/1(0.742 - 1.022) 0.9(0.681 - 1.19)		0.089	1.089(0.916-1.295)		0.336
Name 0.932(0,747-1.162) 0.57 0.877(0.694-1.11) 0.776 Grade 11 vs. 1 0.784(0.512-1.20) 0.264 0.786(0.598-1.217) 0.786 H14V vs. 1 0.73(0.455-1.168) 0.31 0.552(0.415-1.63) 0.557 Outs vs. 1 0.73(0.455-1.168) 0.052 0.552(0.415-1.63) 0.066 VES vs. NO 0.528(0.346-1.231) 0.066 0.668(0.403-1.109) 0.437 VES vs. NO 0.570(0.461-1.241) 0.050 0.531(0.42-1.369) 0.437 VES vs. NO 0.570(0.461-1.251) 0.066 0.668(0.403-1.109) 0.437 VES vs. NO 0.570(0.461-1.251) 0.066 0.648(0.42-1.369) 0.437 VES vs. NO 0.570(0.461-1.251) 0.066 1.048(0.82-1.369) 0.251 0.352 VES vs. NO 1.098(0.97-1.415) 0.066 1.114(0.639-0.228) 0.067 0.332 Make vs. Fenale 1.139(0.97-1.415) 0.066 1.134(0.639-0.228) 0.071 0.321 Sec 1.139(0.97-1.415) 0.026 0.238 1.137(0.471-1.38) 0.027		N3 vs. N0	1.042(0.745-1.457)	· · · · · · · · · · · · · · · · · · ·	0.81	1.327(0.923-1.907)	· · · · · · · · · · · · · · · · · · ·	0.127
$ \begin{array}{c} \mbox{Grade} & \mbox{Grade} $		N4 vs. N0	0.932(0.747-1.162)	• • •••	0.53	0.877(0.694-1.11)	••••	0.276
III-IV vs. 1 10250 074-156) 00000 00000 000000 00000			0 784(0 512-1 201)		0 264	0 786(0 508-1 217)		0.281
Others vs. 1 0.71(0.455-1.108) 0.131 0.632(0.413-1.03) 0.067 YES vs. NO 0.258(0.334-0.833) 0.006 0.668(0.403-1.109) 0.119 Radiation 0.257(0.461-1.241) 0.27 0.813(0.462-1.366) 0.437 Chemotherapy 0.35(0.31-0.42) 0.35 0.50 0.71 1.0 1.41 Obsci 0.55 0.50 0.71 1.0 1.41 0.025 0.35 0.50 0.71 1.0 1.41 0.025 0.35 0.50 0.71 1.0 1.41 0.025 0.35 0.50 0.71 1.0 1.41 0.025 0.35 0.50 0.71 1.0 1.41 0.025 0.35 0.50 0.71 1.0 1.41 0.010 0.25 0.35 0.50 0.71 1.0 1.41 0.010 0.35 0.50 0.71 1.0 1.01 0.025 0.35 0.50 0.71 1.0 0.41 0.35 0.35 0.35 0.50 0.71 0.35 0.35		III+IV vs. I	1.025(0.674-1.56)		0.204	1.071(0.694-1.654)		0.231
Surgery VES vs. NO 0.528(0.334-0.833) 0.005 0.668(0.403-1.109) 1 0.119 VES vs. NO 0.757(0.461-1.241) 0.27 0.803(0.462-1.396) 0.437 Chemotherapy VES vs. NO 0.36(0.31-0.42) 0.27 0.803(0.462-1.396) 0.437 Chemotherapy VES vs. NO 0.36(0.31-0.42) 0.27 0.401824-1.233) 0.25 0.350.050.0.71 1.01.41 2.0 B Charateristics Marcetary vs. 30-55 1.045(0.852-1.527) 0.696 1.044(0.854-1.233) 0.887 Sec. 1.341(1.101-1.633) 0.004 1.134(0.854-1.234) 0.887 Sec. 1.341(0.97-1.415) 0.238 1.233(0.982-1.548) 0.071 Marital 0.887(0.641-1.384) 0.238(0.641-1.384) 0.668 1.154(0.632-0.82) 0.665 Marital 0.887(0.641-1.384) 0.887(0.641-1.384) 0.885 0.778(0.613-0.989) 0.64 Single/UMArried vs. Diveced/separatel 0.817(0.641-1.144) 0.885 0.778(0.613-0.989) 0.64 Single/UMArried vs. Diveced/separatel 0.817(0.641-1.164) 0.836 0.871(0.641-1.144) <th></th> <th>Others vs. I</th> <th>0.71(0.455-1.108)</th> <th>· · · · · · · · · · · · · · · · · · ·</th> <th>0.131</th> <th>0.652(0.413-1.03)</th> <th>i i i i i i i i i i i i i i i i i i i</th> <th>0.067</th>		Others vs. I	0.71(0.455-1.108)	· · · · · · · · · · · · · · · · · · ·	0.131	0.652(0.413-1.03)	i i i i i i i i i i i i i i i i i i i	0.067
Relativition 0.757(0.461-1.241) 0.27 0.803(0.462-1.396) 0.437 VES vs. NO 0.361(0.31-0.42) 0.350 0.50 0.71 1.0 1.41 0.350(0.322-0.407) 0.25 0.350 0.50 0.71 1.0 1.41 2.0 B Charateristics Marcial United HR/95% CD) P value Adjusted HR/95% CD) P value B Charateristics Unadiusted HR/95% CD) P value Adjusted HR/95% CD) P value B Charateristics 1.045(0.822-1.327) 0.071 0.0717 0.972(0.759-1.245) 0.887 Sec 1.045(0.822-1.327) 0.004 0.213(0.976-1.245) 0.887 0.822 Mare vs. Female 1.139(0.917-1.415) 0.238 1.213(0.976-1.928) 0.668 0.881 0.887 Maried vs. Formale 0.817(0.649-1.029) 0.065 1.154(0.639-2.082) 0.668 0.668 Maried vs. Divecediseparated 0.210(736-1.373) 0.668 1.154(0.639-2.082) 0.668 Nige/Charled vs. Divecediseparated 0.210(736-1.373) 0.676 0.371(0.641-1.144) 0.445 0.210 0.930(96-1.161) 0.210 0.871(0.641-1.144) 0.445 0.980(0.678-1.161) 0.981 <td< th=""><th></th><th>Surgery YES vs. NO</th><th>0.528(0.334-0.833)</th><th></th><th>0.006</th><th>0.668(0.403-1.109)</th><th>→</th><th>0.119</th></td<>		Surgery YES vs. NO	0.528(0.334-0.833)		0.006	0.668(0.403-1.109)	→	0.119
Chemotherapy VLS vs. NO 0.361(0.31-0.42)		Radiation YES vs. NO	0.757(0.461-1.241)		0.27	0.803(0.462-1.396)	⊢	0.437
B Charateristics Age category So-65 vs. 30-55 Co-70 vs		Chemotherapy YES vs. NO	0 361(0 31-0 42)	→	< 0.001	0 345(0 292-0 407)	▲	< 0.001
B Charateristics Age category S-6-6 vs, 30-55 Unadiusted HR/95%CD P value Adjusted HR/95%CD P value B Charateristics Age category S-6-6 vs, 30-55 1.038(0.861-1.251) 0.696 1014(0.834-1.233) 0.887 G-70 vs, 30-55 1.134(1.01-1.633) 0.096 1014(0.834-1.233) 0.0887 Male vs, Remale 1.139(0.917-1.415) 0.238 1.233(0.982-1.548) 0.081 Male vs, Remale 0.880.5-1.551) 0.666 1.154(0.639-2.022) 0.663 White vs, Black 0.880.0-1.531) 0.668 1.083(0.78-1.589) 0.668 Married vs, Diverced/separated 0.817(0.649-1.029) 0.085 0.770(0.613-0.989) 0.641 Niedweid Others vs, Black 0.833(0.65-1.068) 0.19 103(0.07-1.298) 0.995 Vidoweid Others vs, Diverced/separated 0.0360(0.57-1.224) 0.418 0.837(0.63-1.016) 0.992 2011 vs, 2010 0.843(0.65-1.016) 0.149 1005(0.77-1.289) 0.995 2011 vs, 2010 0.843(0.66-1.016) 0.370 0.317(0.641-1.184) 0.512 2014 vs, 2010 0.935(0.67-1.029) 0.418 0.848(0.63-1.161) 0.418 2012 vs, 2010 0.942(0.675-1.353) 0.418 0.848(0.33-1.657) 0.926 2014 vs, 2010 <td< th=""><th></th><th>125 13.110</th><th>0.501(0.51-0.42)</th><th></th><th>< 0.001</th><th>0.545(0.252-0.407)</th><th></th><th>1</th></td<>		125 13.110	0.501(0.51-0.42)		< 0.001	0.545(0.252-0.407)		1
B Characteristics Acc category Acc category				0.35 0.50 0.71 1.0 1.41		0.25 0	0.35 0.50 0.71 1.0 1.41 2	.0
Age category Joss(0.861-1.251) 0.696 1.014(0.834-1.233) 0.887 66-70 vr. 30-55 1.045(0.821-1.37) 0.717 0.972(0.759-1.245) 0.822 71,7-97 vr. 30-55 1.34(1.101-1.633) 0.004 1.213(0.976-1.507) 0.881 Sc Male vs. Female 1.139(0.917-1.415) 0.238 1.233(0.982-1.548) 0.0711 Chens vs. Black 0.880.5-1.551) 0.666 1.154(0.639-2.082) 0.6684 Marrial 0.817(0.649-1.029) 0.685 0.780.613-0.989) 0.04 Single/UnMarried vs. Divorced/separated 0.817(0.649-1.039) 0.885 0.0776 0.871(0.611-0.989) 0.04 Single/UnMarried vs. Divorced/separated 0.2377(0.23776 0.871(0.611-1.84) 0.376 Diagnosis Diagnosis 0.149 1.003(0.76-1.298) 0.981 201 vs. 2010 0.833(0.65-1.068) 0.149 1.003(0.76-1.181) 0.512 201 vs. 2010 0.936(0.77-1.24) 0.350 0.817(0.611-0.181) 0.512 201 vs. 2010 0.936(0.77-1.24) 0.350 0.817(0.611-0.181) 0.512 <t< th=""><th></th><th></th><th></th><th></th><th></th><th></th><th></th><th></th></t<>								
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	В	Charateristics	Unadjusted HR(959	%CI)	P value	Adjusted HR(95%C	I)	P value
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	В	Charateristics Age category	Unadjusted HR(959	%CI)	P value	Adjusted HR(95%C	D	P value
Sec Male vs. Female 1.390.917-1.415) 4 0.238 1.233(0.982-1.548) 0.071 Race 0.880.5-1.55) 0.666 1.154(0.639-2.082) 0.635 0.635 Waite vs. Black 0.928(0.644-1.338) 0.668 1.083(0.738-1.58) 0.668 Marrital Marrital 0.1000.778(0.613-0.989) 0.04 0.041 Single/UnMarried vs. Divorced/separated 0.102(0.781-1.331) 0.885 0.778(0.613-0.989) 0.04 Widowed/Others vs. Divorced/separated 1.020(0.781-1.331) 0.886 0.0876 0.778(0.613-0.989) 0.04 Diagnosis 0.104(0.761-1.381) 0.881 0.030(0.761-1.28) 0.0378 Diagnosis 0.120,0781-1.230 0.876 0.871(0.641-1.184) 0.652 201 vs. 2010 0.942(0.669-1.161) 0.448 0.86(0.662-1.116) 0.227 2014 vs. 2010 0.960(0.894-1.661) 0.448 0.660(662-1.116) 0.227 2015 vs. 2010 0.960(0.894-1.661) 0.421 0.484(0.674-1.165) 0.493 Others vs. 15-2.4cm 0.996(0.491-610)	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55	Unadjusted HR(959 1.038(0.861–1.251) 1.045(0.823–1.327)	%CD	P value 0.696 0.717	Adjusted HR(95% C)	D.	P value 0.887 0.822
Race 1 0.66 $1.154(0.639-2.02)$ 0.635 White vs. Black $0.928(0.644-1.338)$ 0.688 $1.083(0.738-1.589)$ 0.635 Marital $0.817(0.649-1.029)$ 0.685 $0.778(0.613-0.989)$ 0.04 Single/UnMarited vs. Divorced/separated $0.202/0.781-1.331)$ 0.885 $0.1710(.641-1.84)$ 0.045 Widowed/Other vs. Divorced/separated $0.224(0.733-1.373)$ 0.885 $0.1710(.641-1.84)$ 0.045 Diagnosis $0.210(2.52.010)$ $0.833(0.65-1.068)$ 0.149 $1.003(0.776-1.298)$ 0.981 2011 vs. 2010 $0.940(693-1.161)$ 0.149 $0.036(0.652-1.161)$ 0.127 0.227 2014 vs. 2010 $0.960(98-1.161)$ 0.148 $0.88(0.652-1.16)$ 0.227 2014 vs. 2010 $0.960(9.49-1.661)$ 0.756 $1.096(0.857-1.401)$ 0.425 0.225 2013 vs. 2010 $0.960(9.49-1.661)$ 0.621 $0.84(0.55-1.358)$ 0.025 0.021 $0.84(0.57-1.401)$ 0.425 27-32cm vs. 15-24cm $0.960(0.49-1.652)$ 0.621 $0.83(0.41-1.56)$ 0.926 $0.101(0.613-1.655)$ 0.025	В	Charateristics - Age category - 56-65 vs. 30-55 - 66-70 vs. 30-55 - 71-97 vs. 30-55 -	Unadiusted HR(959 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633)	*CI)	P value 0.696 0.717 0.004	Adjusted HR(95% C) 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507)		P value 0.887 0.822 0.081
Others vs. Black $0.88(0.5-1.51)$ 0.66 $1.54(0.639-2.082)$ 0.638 Marital 0.688 $0.880(0.78-1.589)$ 0.668 Marital $0.880(0.78-1.589)$ 0.648 Marital $0.880(0.78-1.589)$ 0.648 Marital $0.280(0.54-1.038)$ 0.688 $0.780(6.13-0.989)$ 0.044 Single/UnMarried vs. Divorced/separated $1.020(781-1.331)$ 0.885 $0.1780(6.13-0.989)$ 0.04 Diagnosis $0.240(.66-1.076)$ 0.149 $0.030(.776-1.298)$ 0.981 2011 vs. 2010 $0.8420(.66-1.076)$ 0.169 $0.920(.16-1.181)$ 0.512 2013 vs. 2010 $0.960(.987-1.401)$ 0.418 $0.860(.687-1.401)$ 0.425 $2014 vs. 2010$ $0.956(0.797-1.224)$ 0.756 $1.960(.857-1.401)$ 0.457 $25-32cm$ $0.996(0.497-1.661)$ 0.749 $0.83(0.41-1.65)$ 0.926 $1.011(0.613-1.65)$ 0.927 Diagnosis $0.996(0.497-1.025)$ 0.725 $0.936(0.737-1.62,0)$ 0.926 0.926 $0.910(.637-1.62,0)$ 0.926 Di as $0.996(0.797-1.218)$ $0.996(0.798-1.17)$	В	Charateristics Age category - 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female	Unadiusted HR(959 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415)	%CD	P value 0.696 0.717 0.004 0.238	Adjusted HR(95% C) 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548)		P value 0.887 0.822 0.081 0.071
$\begin{tabular}{ c c c c c c c c c c c c c c c c c c c$	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race	Unadjusted HR(959 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415)	€CD	P value 0.696 0.717 0.004 0.238	Adiusted HR(95%Cl 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548)		P value 0.887 0.822 0.081 0.071
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black	Unadiusted HR(959 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415) 0.88(0.5–1.551) 0.029(0.644,1.328)	ECI)	P value 0.696 0.717 0.004 0.238 0.66	Adjusted HR(95% Cl 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.082(0.738–1.580)		P value 0.887 0.822 0.081 0.071 ■ 0.635 0.684
Single/UnMarried vs. Divorced/separated 1.02(0.781-1.33) Widowed/Others vs. Divorced/separated 1.024(0.763-1.373) Diagnosis 2011 vs. 2010 0.843(0.66-1.076) 2012 vs. 2010 0.942(0.66-1.076) 2013 vs. 2010 0.95(0.698-1.161) 2014 vs. 2010 0.95(0.698-1.161) 2014 vs. 2010 0.95(0.698-1.161) 2015 vs. 2010 0.95(0.698-1.161) 2015 vs. 2010 0.95(0.698-1.161) 2015 vs. 2010 0.95(0.698-1.161) 2015 vs. 2010 0.95(0.698-1.161) 2016 vs. 15-24cm 0.99(0.494-1.661) 33-40cm vs. 15-24cm 0.888(0.471-1.005) Ta vs. 15-24cm 0.888(0.471-1.005) Ta vs. T1 0.888(0.691-1.121) 71 vs. T1 0.888(0.691-1.121) 72 vs. N0 0.995(0.707-1.276) 73 vs. T1 0.888(0.691-1.121) 74 vs. N0 0.951(0.642-1.367) 75 vs. N0 0.952(0.317-0.858) 75 vs. N0 0	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black Wharital	Unadjusted HR(955 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415) 0.88(0.5–1.551) 0.928(0.644–1.338)	€CD	P value 0.696 0.717 0.004 0.238 0.66 0.688	Adjusted HR(95% Cl 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589)		P value 0.887 0.822 0.081 0.071 ■ 0.635 0.684
Windowed Olinets Vs. Divorced/separated 10/40/-05-1/5/3) 0.3/6 0.3/10.05/1-1.18) 0.5/6 2011 vs. 2010 0.842(0.66-1.076) 0.149 10/03(0.776-1.28) 0.5/1 2013 vs. 2010 0.90(0.698-1.161) 0.418 0.86(0.662-1.116) 0.257 2014 vs. 2010 0.93(0.075-1.224) 0.756 1.99(0.877-1.401) 0.462 2015 vs. 2010 0.95(0.866-0.973) 0.03 0.317(0.631-1.057) 0.125 Primary site 0.524/cm 0.99(0.494-1.661) 0.749 0.33(0.441-1.56) 0.493 25-32cm vs. 15-24cm 0.996(0.494-1.610) 0.621 0.948(0.571-1.358) 0.493 Others vs. 15-24cm 0.88(0.471-1.005) 0.621 0.948(0.571-1.358) 0.997 72 vs. T1 0.88(0.691-1.121) 0.301 0.522(0.421-0.93) 0.021 T3 vs. T1 0.84(0.676-1.055) 0.136 0.779(0.614-0.989) 0.041 T4 vs. T1 0.88(0.671-1.210) 0.311 0.322(0.677-1.062) 0.134 T4 vs. T1 0.88(0.674-1.466) 0.719 0.332(0.677-1.062) 0.134 N1 vs. N0 0.881(0.741-1.046) 0.722 0.943(0.773-1.1	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black Married vs. Divorced/separated	Unadiusted HR(959 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415) 0.88(0.5–1.551) 0.928(0.644–1.338) 0.817(0.649–1.029)	€CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085	Adjusted HR(95% Cl 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04
2011 vs. 2010 0.833(0.65-1.068) 0.149 1.003(0.776-1.298) 0.981 2012 vs. 2010 0.842(0.66-1.076) 0.169 0.92(0.716-1.181) 0.512 2014 vs. 2010 0.93(0.757-1.274) 0.169 0.92(0.716-1.181) 0.465 2015 vs. 2010 0.93(0.757-1.274) 0.03 0.03 (0.37(0.631-1.057) 0.125 2014 vs. 2010 0.96(0.494-1.661) 0.756 1.096(0.857-1.401) 0.465 25-32cm vs. 15-24cm 0.990(0.494-1.661) 0.749 0.83(0.441-1.56) 0.493 0.04 mvs. 15-24cm 0.990(0.632-1.363) 0.926 1.011(0.613-1.665) 0.967 ALCC T 1.023(0.633-1.653) 0.926 1.011(0.613-1.665) 0.967 T2 vs. T1 0.688(0.471-1.005) 0.053 0.626(0.421-0.93) 0.021 T3 vs. T1 0.88(0.671-1.121) 0.301 0.822(0.637-1.062) 0.114 Tx vs. T1 0.966(0.798-1.17) 0.725 0.943(0.773-1.151) 0.564 AJCC N N1 vs. N0 0.881(0.741-1.046) 0.732 1.1540(.796-1.732) 0.26 N1 vs. N0 0.837(0.524-1.367) 0.732 1.020(0.873-1.652) 0.261	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 50-70 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black Marital Married vs. Divorced/separated Single/UnMarried vs. Divorced/separated	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331)	ECD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885	Adjusted HR(95% Cf 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336)		P value 0.887 0.822 0.081 0.071 → 0.635 0.684 0.04 0.905
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$\begin{array}{c c c c c c c c c c c c c c c c c c c $	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black White vs. Black Marital Marrital vs. Divorced/separated Single/UMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010	Unadiusted HR(955 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415) 0.988(0.541–1.338) 0.9810(0.649–1.029) 1.020(781–1.331) 1.024(0.763–1.373) 0.833(0.65–1.068)	ECD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.876 0.149	Adjusted HR(95% Cl 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 0.778(0.613–0.989) 0.871(0.641–1.184) 1.003(0.776–1.298)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black White vs. Black Marital Marrital Marrital vs. Divorced/separated Single/UnMarritod vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010	Unadjusted HR(955 1.038(0.861–1.251) 1.045(0.823–1.327) 1.341(1.101–1.633) 1.139(0.917–1.415) 0.98(0.5–1.551) 0.98(0.644–1.338) 0.817(0.649–1.029) 1.02(0.781–1.331) 1.024(0.763–1.373) 0.833(0.65–1.068) 0.842(0.66–1.076) 0.842(0.66–1.076)	ECD)	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.885 0.885 0.876	Adjusted HR(95% Cl 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.288) 0.92(0.716–1.184)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.512
Primary site $25-32cm$ $0.906(0.494-1.661)$ 0.749 $0.83(0.441-1.56)$ 0.562 $33-40cm$ vs. $15-24cm$ $0.894(0.572-1.396)$ 0.621 $0.348(0.53-1.358)$ 0.493 Others vs. $15-24cm$ $1.023(0.633-1.653)$ 0.926 $1.01(0.613-1.665)$ 0.493 T2 vs. T1 $0.884(0.676-1.055)$ 0.053 $0.626(0.421-0.93)$ 0.021 T3 vs. T1 $0.844(0.676-1.055)$ 0.136 $0.779(0.614-0.989)$ 0.041 T4 vs. T1 $0.88(0.691-1.121)$ 0.301 $0.822(0.677-1.062)$ 0.134 Tx vs. T1 $0.966(0.798-1.17)$ 0.722 $0.943(0.773-1.151)$ 0.564 AJCC NN1 vs. N0 $0.881(0.741-1.046)$ 0.712 0.732 $1.020(0.873-1.655)$ 0.266 N1 vs. N0 $0.9397(0.482-1.367)$ 0.732 $1.020(0.873-1.655)$ 0.26 N3 vs. N0 $0.9397(0.482-1.367)$ 0.732 $1.054(0.79-1.732)$ 0.49 N4 vs. N0 $0.837(0.524-1.336)$ 0.917 $0.606(0.58-1.708)$ 0.126 Grade $0.777(0.485-1.23)$ 0.917 $0.660(0.58-1.708)$ 0.103 Radiation $0.777(0.457-1.318)$ 0.349 $0.877(0.483-1.59)$ 0.665 YES vs. NO $0.777(0.457-1.318)$ 0.349 $0.877(0.483-1.59)$ 0.665 Chember argyYES vs. NO $0.377(0.415-1.438)$ 0.349 $0.877(0.483-1.59)$ 0.665	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black Maried vs. Divorced/separated White vs. Black Married vs. Divorced/separated Single/UmMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.020(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.66-1.076) 0.963(0.757-1.224)	ECD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.876 0.149 0.169 0.148 0.769	Adiusted HR(95% Cf 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.512 0.257 0.465
2 - 32-cm vs. 15 - 24-cm 0.960(0.494-1.661) 0.749 0.83(0.41-1.56) 0.621 33-40cm vs. 15 - 24-cm 0.984(0.572-1.366) 0.621 AJCCT 0.757(0.614-0.989) 0.621 T 2 vs. T1 0.648(0.471-1.05) 0.053 0.626(0.421-0.93) 0.021 T 3 vs. T1 0.844(0.676-1.055) 0.053 0.626(0.421-0.93) 0.041 T 2 vs. T1 0.848(0.671-1.121) 0.301 0.822(0.637-1.062) 0.0134 T x vs. T1 0.966(0.798-1.17) 0.725 0.943(0.773-1.151) 0.564 AJCC N N1 vs. N0 0.881(0.741-1.046) 0.149 1.085(0.9-1.307) 0.391 N2 vs. N0 0.937(0.421-1.367) 0.732 1.1202(0.873-1.655) 0.265 N3 vs. N0 0.937(0.421-1.367) 0.732 1.154(0.796-1.732) 0.49 N4 vs. N0 0.872(0.684-1.113) 0.271 0.818(0.632-1.058) 0.126 Grade II vs. I 0.952(0.41-1.23) 0.455 0.835(0.518-1.348) 0.462 II vs. I 0.522(0.317-0.858) 0.126 Grade II vs. I 0.522(0.317-0.858) 0.101 0.63(0.361-1.998) 0.103 Radiation YES vs. NO 0.377(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 Chemotherapy YES vs. NO 0.377(0.319-0.445) 0.455 0.03(0.3-0.431) 0.455 0.03(0.3-0.431) 0.455 0.437(0.483-1.59) 0.665 Chemotherapy	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 58 Male vs. Female Race Others vs. Black Mairei vs. Black Maritei vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2015 vs. 2010	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.66-1.076) 0.9(0.698-1.161) 0.96(0.757-1.224)		P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.885 0.885 0.885 0.885 0.866 0.149 0.169 0.418 0.750 0.03	Adjusted HR(95% Cf 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.920(716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.425
D-bold in V. 15-24cm 0.021 0.012 1.0500 0.021 0.012 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0100 0.021 0.021 0.0200 0.021 0.021 0.0200 0.021 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.021 0.0200 0.0200 0.0	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 71–97 vs. 30–55 Sex Male vs. Female Race Others vs. Black White vs. Black Maritel Married vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2015 vs. 2010 2015 vs. 2010	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.943(0.65-1.061) 0.906.058-1.161) 0.9063(0.757-1.224) 0.755(0.586-0.973)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.876 0.169 0.169 0.418 0.756 0.035	Adjusted HR(95% Cf 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 1.096(0.857–1.401) 0.817(0.631–1.057)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.125
AJCC T 0.688(0.471-1.005) 0.053 0.626(0.421-0.93) 0.02 T3 vs. T1 0.844(0.676-1.055) 0.136 0.779(0.614-0.989) 0.041 T4 vs. T1 0.884(0.691-1.121) 0.301 0.822(0.637-1.062) 0.134 Tx vs. T1 0.966(0.798-1.17) 0.725 0.943(0.773-1.151) 0.564 AJCC N 0.95(0.707-1.276) 0.149 1.085(0.9-1.307) 0.391 N2 vs. N0 0.937(0.642-1.367) 0.735 1.154(0.769-1.732) 0.49 N4 vs. N0 0.87(0.524-1.36) 0.775 0.735 0.136(0.632-1.058) 0.126 Grade 0.114 1.025(0.646-1.626) 0.917 1.06(0.658-1.708) 0.126 II vs. I 0.270(0.645-1.233) 0.265 0.835(0.518-1.348) 0.462 UH-IV vs. I 0.020(0.645-1.233) 0.265 0.63(0.361-1.098) 0.810 YES vs. NO 0.522(0.317-0.858) 0.01 0.63(0.361-1.098) 0.103 Radiation 0.377(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.457-1.318) 0.349 0.36(0.3-0.431) 0.001 </th <th>В</th> <th>Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black Marital Marrided vs. Divorced/separated Single/UnMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2014 vs. 2010 2014 vs. 2010 2015 v</th> <th>Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.943(0.757-1.224) 0.755(0.586-0.973) 0.964(0.494-1.661) 0.964(0.494-1.661) 0.964(0.494-1.661) 0.964(0.494-1.331) 0.964(0.494-1.334) 0.964(0.494-1.344) 0.964(0.4</th> <th>ECD</th> <th>P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.885 0.885 0.885 0.885 0.876 0.149 0.169 0.418 0.418 0.756 0.03 0.756 0.63</th> <th>Adjusted HR(95% CI 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 0.778(0.613–0.989) 0.770(6.614–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.846(0.51–1.55)</th> <th></th> <th>P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.465</th>	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black White vs. Black Marital Marrided vs. Divorced/separated Single/UnMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2014 vs. 2010 2014 vs. 2010 2015 v	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.943(0.757-1.224) 0.755(0.586-0.973) 0.964(0.494-1.661) 0.964(0.494-1.661) 0.964(0.494-1.661) 0.964(0.494-1.331) 0.964(0.494-1.334) 0.964(0.494-1.344) 0.964(0.4	ECD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.885 0.885 0.885 0.885 0.876 0.149 0.169 0.418 0.418 0.756 0.03 0.756 0.63	Adjusted HR(95% CI 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 0.778(0.613–0.989) 0.770(6.614–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.846(0.51–1.55)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.465
T2 vs. Ti 0.688(0.471-1.005) 0.053 0.022(0.421-0.33) 0.021 T3 vs. Ti 0.844(0.676-1.055) 0.136 0.797(0.614-0.989) 0.041 T4 vs. Ti 0.88(0.691-1.121) 0.301 0.822(0.637-1.062) 0.134 Tx vs. Ti 0.966(0.798-1.17) 0.725 0.943(0.773-1.151) 0.564 AJCC N 0.149 1.085(0.9-1.307) 0.391 0.321 N2 vs. N0 0.950(0.707-1.276) 0.732 1.202(0.873-1.655) 0.26 N3 vs. N0 0.937(0.642-1.367) 0.732 1.154(0.769-1.732) 0.49 N4 vs. N0 0.87(0.642-1.367) 0.455 0.835(0.518-1.348) 0.462 II vs. I 1.025(0.646-1.626) 0.917 1.06(0.658-1.708) 0.812 Others vs. I 0.770(0.457-1.318) 0.455 0.63(0.361-1.998) 0.462 YES vs. NO 0.777(0.457-1.31	В	Charateristics Age category 56–65 vs, 30–55 66–70 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black Married vs. Black Married vs. Black Married vs. Divorced/separated Single/UmMarried vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2015 vs. 2010 25–32cm vs. 15–24cm 33–40cm vs. 15–24cm	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 0.024(0.763-1.373) 0.833(0.65-1.068) 0.963(0.757-1.224) 0.755(0.586-0.973) 0.906(0.494-1.661) 0.894(0.572-1.365)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.876 0.149 0.169 0.419 0.756 0.03 0.756 0.03	Adiusted HR(95% CC 1.014(0.834–1.233) 0.072(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.665)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.493 0.964
13 vs. 11 0.840(05)(6-1.053) 0.136 0.179(0.5)(4-0589) 0.041 T4 vs. T1 0.966(0.798-1.17) 0.301 0.822(0.677-1.062) 0.134 Tx vs. T1 0.966(0.798-1.17) 0.725 0.943(0.773-1.151) 0.564 NI vs. N0 0.881(0.741-1.046) 0.149 1.085(0.9-1.307) 0.391 N2 vs. N0 0.937(0.482-1.367) 0.732 1.1260(0.79-1.722) 0.49 N4 vs. N0 0.872(0.684-1.13) 0.271 0.818(0.632-1.058) 0.126 Grade 0.171 1.025(0.464-1.626) 0.917 1.06(0.658-1.708) 0.422 II vs. I 0.252(0.317-0.858) 0.261 0.917 1.06(0.658-1.708) 0.812 Others vs. I 0.777(0.457-1.318) 0.49 0.477(0.483-1.59) 0.103 Radiation YES vs. NO 0.377(0.457-1.318) 0.349 0.877(0.483-1.59) 0.103 YES vs. NO 0.377(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black Mairei ds. Divorced/separated Single/UnMarried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Diagnosis 2011 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2014 vs. 2010 2015 vs. 2010 25–32em vs. 15–24cm 33–40cm vs. 15–24cm	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.8342(0.66-1.076) 0.963(0.757-1.224) 0.755(0.386-0.973) 0.906(0.494-1.661) 0.894(0.572-1.396) 1.023(0.6633-1.653)	ECD	P value 0.696 0.717 0.004 0.238 0.668 0.688 0.688 0.685 0.885 0.885 0.876 0.149 0.169 0.418 0.756 0.031 0.031 0.031 0.031 0.031 0.031 0.031 0.032 0.035 0.041 0.035 0.041 0.035 0.041 0.035 0.041 0.041 0.045 0.041 0.045 0.041 0.045 0.041 0.045 0.041 0.045 0.055 0.175 0.041 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.045 0.175 0.041 0.045 0.175 0.045 0.175 0.045 0.149 0.041 0.041 0.045 0.041 0.045	Adiusted HR(95% Cf 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.788–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.281) 0.92(0.716–1.281) 0.92(0.161–1.181) 0.84(0.662–1.116) 1.094(0.857–1.401) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.665)		P value 0.887 0.822 0.081 0.071 0.0635 0.6684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.125 0.562 0.493 0.967
Tx vs. T1 0.966(0.798-1.17) 0.725 0.943(0.773-1.151) 0.564 AJCC N 0.725 0.943(0.773-1.151) 0.564 N1 vs. N0 0.881(0.741-1.046) 0.149 1.085(0.9-1.307) 0.391 N2 vs. N0 0.957(0.642-1.367) 0.732 1.202(0.873-1.655) 0.26 M4 vs. N0 0.872(0.684-1.113) 0.271 0.818(0.632-1.058) 0.126 Grade 0.114 0.251 0.835(0.518-1.348) 0.462 II vs. I 1.025(0.466-1.623) 0.263 0.692(0.419-1.14) 0.812 Others vs. I 0.757(0.465-1.233) 0.261 0.01 0.630.361-1.098) 0.103 Radiation YES vs. NO 0.777(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.319-0.445) 0.349 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 58-20 Male vs. Female Race Others vs. Black Mariet vs. Biack Mariet vs. Divorced/separated Single/UnMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 23-40cm vs. 15-24cm 33-40cm vs. 15-24cm AUCC T T2 vs. T1	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.940(0.66-1.076) 0.906(0.894-1.61) 0.963(0.757-1.224) 0.906(0.494-1.661) 0.9906(0.494-1.661) 0.894(0.6772-1.396) 1.023(0.633-1.653) 0.688(0.471-1.005) 0.9044(0.671.055) 0.904(0.471.055	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.885 0.876 0.169 0.169 0.418 0.756 0.041 0.0756 0.041 0.021 0.021 0.021 0.021 0.021 0.021 0.033 0.033	Adjusted HR(95% Cf 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.848(0.531–1.58) 1.011(0.613–1.665) 0.628(0.421–0.93) 0.672(0.421–0.93)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.517 0.465 0.125 0.465 0.125 0.465 0.125 0.463 0.967 0.967 0.02 0.01
AJCC N NI vs. N0 0.881(0.741-1.046) 0.149 1.085(0.9-1.307) 1.202(0.873-1.655) 0.26 N3 vs. N0 0.937(0.642-1.367) 0.872(0.684-1.113) 0.271 0.818(0.321-1.38) 0.271 0.455 0.835(0.518-1.348) 0.470 0.455 0.812 0.464-1.626) 0.951(0.646-1.626) 0.917 0.952(0.317-0.858) 0.263 0.692(0.419-1.14) 0.148 Surgery 0.101 YES vs. NO 0.522(0.317-0.858) 0.777(0.457-1.318) 0.349 0.817(0.483-1.59) 0.665 Chemotherapy YES vs. NO YES vs. NO 0.377(0.457-1.318)	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 71-97 vs. 30-55 Sex Male vs. Female Race Others vs. Black Marited vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 25-32cm vs. 15-24cm 33-40cm vs. 15-24cm AJCC T T2 vs. T1 T3 vs. T1	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.675-1.224) 0.906.098-1.161) 0.906(0.494-1.661) 0.906(0.494-1.661) 0.906(0.494-1.653) 0.894(0.672-1.396) 1.023(0.633-1.653) 0.884(0.671-1.005) 0.848(0.671-1.025) 0.884(0.671-1.025) 0.884(0.671-1.025) 0.884(0.671-1.025) 0.884(0.671-1.025) 0.884(0.671-1.21)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.885 0.885 0.885 0.876 0.149 0.149 0.418 0.756 0.0418 0.756 0.041 0.621 0.621 0.621 0.621 0.621 0.621 0.621 0.633 0.301	Adjusted HR(95% Cf 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.181) 1.096(0.857-1.401) 0.84(0.631-1.165) 0.848(0.531-1.65) 0.848(0.531-1.55) 0.626(0.421-0.93) 0.772(0.614-0.989) 0.720(0.614-0.989) 0.720(0.612-0.55) 0.626(0.421-0.93) 0.732(0.617-1.062) 0.822(0.637-1.062) 0.82(0.637-1.062		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.465 0.125 0.562 0.967 0.02 0.041 0.031
N1 vs. N0 0.081(0.741-1.086) 0.149 1.083(0.9-1.307) 0.391 N2 vs. N0 0.95(0.707-1.276) 0.735 1.154(0.769-1.732) 0.49 N4 vs. N0 0.937(0.642-1.367) 0.735 1.154(0.769-1.732) 0.49 N4 vs. N0 0.872(0.684-1.113) 0.271 0.818(0.632-1.058) 0.126 Grade 0.455 0.835(0.518-1.348) 0.462 0.812 II + vs. I 0.837(0.524-1.336) 0.917 1.06(0.658-1.708) 0.412 Others vs. I 0.757(0.465-1.233) 0.263 0.692(0.419-1.14) 0.812 Others vs. I 0.522(0.317-0.858) 0.01 0.63(0.361-1.098) 0.103 Radiation 725 vs. NO 0.777(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.419-1.41) 0.349 0.37(0.483-1.59) 0.665 Chemotherapy YES vs. NO 0.377(0.419-1.41) 0.349 0.36(0.3-0.431) 0.001	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black White vs. Black White vs. Black Married vs. Divorced/separated Single/UmMarried vs. Divorced/separated Diagnosis 2011 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 25–32cm vs. 15–24cm Others vs. 15–24cm AJCCT T 2 vs. T1 T 2 vs. T1 T 4 vs. T1 T 4 vs. T1	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.66-1.076) 0.963(0.757-1.224) 0.755(0.586-0.973) 0.906(0.494-1.661) 0.894(0.572-1.396) 0.844(0.675-1.055) 0.844(0.675-1.055) 0.844(0.675-1.055) 0.868(0.691-1.721) 0.966(0.798-1.17)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.885 0.885 0.885 0.885 0.149 0.169 0.149 0.69 0.149 0.621 0.926 0.926 0.925	Adiusted HR(95% CC 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.053(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.181) 0.861(0.652-1.401) 0.817(0.631-1.657) 0.83(0.441-1.56) 0.848(0.53-1.358) 1.011(0.613-1.665) 0.628(0.421-0.93) 0.779(0.614-0.989) 0.822(0.637-1.062) 0.842(0.53-1.151)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.951 0.512 0.257 0.465 0.425 0.463 0.125 0.562 0.493 0.967 0.02 0.02 0.041 0.134 0.544
N3 vs. N0 0.937(0.642-1.367) 0.735 1.154(0.769-1.732) 0.49 N4 vs. N0 0.872(0.684-1.113) 0.271 0.818(0.632-1.058) 0.126 Grade II vs. I 0.837(0.524-1.336) 0.455 0.835(0.518-1.348) 0.462 II H4V vs. I 0.025(0.646-1.626) 0.917 1.06(0.658-1.708) 0.812 Others vs. I 0.757(0.465-1.233) 0.265 0.992(0.419-1.14) 0.148 Surgery YES vs. NO 0.777(0.457-1.318) 0.01 0.63(0.361-1.098) 0.103 Radiation YES vs. NO 0.777(0.457-1.318) 0.349 0.877(0.483-1.59) 0.6655 Chemotherapy YES vs. NO 0.377(0.319-0.445) 0.349 0.877(0.483-1.59) 0.6655	В	Charateristics Age category 56–65 vs, 30–55 66–70 vs, 30–55 71–97 vs, 30–55 Sex Male vs. Female Race Others vs. Black Married vs. Black Married vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2014 vs. 2010 2015 vs. 2010 2015 vs. 15–24cm 33–40cm vs. 15–24cm AJCC T T2 vs. T1 T3 vs. T1 T4 vs. T1 T4 vs. T1 T4 vs. T1 T4 vs. T1 T4 vs. T1	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.020(781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.833(0.65-1.068) 0.963(0.757-1.224) 0.963(0.757-1.224) 0.906(0.494-1.661) 0.844(0.572-1.396) 1.023(0.633-1.653) 0.688(0.471-1.005) 0.844(0.675-1.055) 0.88(0.691-1.21) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.968(0.784-1.17) 0.988(0.784-1.17) 0.988(0.784-1.17) 0.988(0.784-1.17) 0.988(0.784-1.17) 0.988(0.784-1.17) 0.988(0.784-1.140)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.876 0.149 0.169 0.418 0.756 0.031 0.021 0.023 0.0749 0.621 0.926 0.053 0.136 0.301 0.725 0.301 0.725 0.025 0.025 0.021 0.025 0.021 0.025 0.021 0.025 0.025 0.021 0.025 0.035 0.036 0.035 0.036	Adiusted HR(95% CC 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.652–1.116) 1.096(0.652–1.116) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.057) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.655) 0.626(0.421–0.93) 0.779(0.614–0.989) 0.822(0.637–1.062) 0.943(0.773–1.151)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.125 0.562 0.493 0.967 0.967 0.967 0.921 0.941 0.134 0.544 0.904 0.905 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.455 0.562 0.991 0.967 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.257 0.455 0.125 0.257 0.455 0.257 0.455 0.125 0.257 0.455 0.552
N4 vs. N0 0.872(0.684-1.113) 0.271 0.818(0.632-1.058) 0.126 Grade 0.126 0.126 0.126 0.126 0.126 II vs. I 0.837(0.524-1.336) 0.455 0.835(0.518-1.348) 0.462 Ultvs. I 0.250(0.464-1.626) 0.917 1.06(0.658-1.708) 0.126 Others vs. I 0.757(0.465-1.233) 0.263 0.692(0.419-1.14) 0.148 Surgery 0.10 0.63(0.361-1.098) 0.103 0.103 Radiation 0.177(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.319-0.445) 0.349 0.37(0.483-1.59) 0.665 YES vs. NO 0.377(0.481-1.59) 0.665 0.001 0.36(0.3-0.431) 0.001	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 Sex Male vs. Female Race Others vs. Black Maried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2013 vs. 2010 2015 vs. 2010 2017 vs. 2010 2018 vs. 15-24cm 33-40cm vs. 15-24cm AUCC T 73 vs. T1 74 vs. T1 74 vs. T1 74 vs. T1 74 vs. T1 74 vs. T1 74 vs. T0 72 vs. N0	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.66-1.076) 0.906(0.794-1.61) 0.996(0.0494-1.651) 0.996(0.494-1.651) 0.894(0.572-1.396) 1.023(0.653-1.653) 0.688(0.471-1.005) 0.88(0.691-1.121) 0.966(0.798-1.17) 0.881(0.741-1.046) 0.950(0.771-2.75) 0.88(0.771-1.246) 0.950(0.771-2.75) 0.88(0.771-1.246) 0.950(0.771-2.75) 0.88(0.771-1.246) 0.950(0.771-2.75) 0.88(0.771-1.246) 0.950(0.771-2.75) 0.950(0.771-2.75) 0.580(0.771-2.75) 0.580(0.771-1.246) 0.950(0.771-2.75) 0.580(0.771-2.75) 0.590(0.771-2.75)	ECD	P value 0.696 0.717 0.004 0.238 0.688 0.885 0.885 0.885 0.876 0.149 0.169 0.418 0.756 0.418 0.756 0.031 0.032 0.053 0.136 0.301 0.725 0.432	Adiusted HR(95% CC 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.86(0.662–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.665) 0.626(0.421–0.939) 0.779(0.614–0.989) 0.822(0.637–1.651) 0.943(0.773–1.151) 1.085(0.9–1.37) 1.202(0.877–1.655)		P value 0.887 0.822 0.081 0.071 0.684 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.493 0.967 0.967 0.02 0.041 0.391 0.264 0.391 0.264
Grane II vs. I 0.837(0.524–1.336) 0.455 0.835(0.518–1.348) 0.462 III +IV vs. I 1.025(0.646–1.626) 0.917 1.06(0.658–1.708) 0.812 Others vs. I 0.757(0.465–1.233) 0.263 0.692(0.419–1.14) 0.148 Surgery YES vs. NO 0.522(0.317–0.858) 0.01 0.63(0.361–1.098) 0.103 Radiation YES vs. NO 0.777(0.457–1.318) 0.349 0.877(0.483–1.59) 0.665 Chemotherapy YES vs. NO 0.377(0.319–0.445) <0.001 0.36(0.3–0.431) <0.001	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 58- Male vs. Female Race Others vs. Black Mariet Vs. Biack Mariet Vs. Biack Mariet Vs. Biack Mariet Vs. Divorced/separated Single/UnMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 213 vs. 2010 25-32 cm vs. 15-24 cm 33-40 cm vs. 15-24 cm 33-40 cm vs. 15-24 cm AJCC T 72 vs. T1 73 vs. T1 74 vs. T1 74 vs. T1 74 vs. T1 74 vs. T1 74 vs. T1 75	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.843(0.65-1.068) 0.942(0.66-1.076) 0.906(0.894-1.61) 0.963(0.757-1.224) 0.9906(0.494-1.661) 0.9906(0.494-1.661) 0.894(0.677-1.396) 1.023(0.633-1.653) 0.688(0.671-1.21) 0.966(0.798-1.17) 0.881(0.714-1.046) 0.957(0.624-1.367)		P value 0.696 0.717 0.004 0.238 0.68 0.885 0.885 0.885 0.885 0.885 0.876 0.149 0.149 0.149 0.621 0.621 0.621 0.621 0.621 0.025 0.301 0.301 0.301 0.301 0.325	Adjusted HR(95% C) 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.181) 0.86(0.662-1.116) 1.096(0.857-1.401) 0.817(0.631-1.057) 0.83(0.441-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.824(0.431-1.56) 0.822(0.637-1.062) 0.943(0.773-1.151) 1.085(0.9-1.732)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.517 0.465 0.125 0.465 0.125 0.465 0.125 0.465 0.125 0.463 0.967 0.02 0.041 0.391 0.264 0.391 0.29
III+IV vs.1 0.250(346-1.626) 0.913 0.933 0.933(0.316-1.3-6) 0.812 Others vs.1 0.757(0.465-1.233) 0.263 0.692(0.419-1.14) 0.148 Surgery 9 0.522(0.317-0.858) 0.01 0.63(0.361-1.098) 0.103 Radiation 9 0.777(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 Chemotherapy YES vs. NO 0.377(0.319-0.445) <0.001 0.36(0.3-0.431) <0.001	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black White vs. Black Married vs. Divorced/separated Single/UnMarried vs. Divorced/separated Married vs. Divorced/separated Diagnosis 2011 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2014 vs.	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1327) 1.341(1.101-1.633) 1.139(0.917-1.415) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 0.928(0.644-1.338) 0.833(0.65-1.068) 0.842(0.664-1.076) 0.963(0.757-1.224) 0.755(0.586-0.973) 0.906(0.494-1.661) 0.894(0.572-1.396) 0.884(0.671-1.205) 0.884(0.671-1.005) 0.884(0.671-1.005) 0.884(0.671-1.012) 0.966(0.798-1.17) 0.881(0.741-1.046) 0.937(0.642-1.367) 0.872(0.644-1.13)		P value 0.696 0.717 0.004 0.238 0.66 0.688 0.885 0.885 0.876 0.149 0.149 0.418 0.756 0.0418 0.756 0.030 0.621 0.621 0.621 0.621 0.621 0.621 0.621 0.621 0.621 0.621 0.621 0.63 0.301 0.725 0.149 0.321 0.301 0.725 0.149 0.321 0.325 0.321 0.325 0.321 0.325 0.355 0	Adjusted HR(95% C) 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.298) 0.92(0.716-1.184) 1.003(0.776-1.298) 0.92(0.716-1.184) 1.003(0.776-1.298) 0.92(0.716-1.184) 1.003(0.776-1.298) 0.92(0.716-1.184) 1.003(0.776-1.298) 0.92(0.613-0.57) 0.83(0.441-1.56) 0.626(0.421-0.93) 0.779(0.614-0.989) 1.011(0.613-1.665) 0.626(0.421-0.93) 0.779(0.614-0.989) 0.790(0.614-0.989) 0.790(0.614-0.989) 0.790(0.614-0.989) 0.790(0.614-0.989) 0.790(0.613-1.665) 0.626(0.421-0.93) 0.779(0.614-0.989) 0.790(0.714-0.989) 0.790(0.614-0.989		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.465 0.125 0.562 0.967 0.02 0.041 0.134 0.564 0.391 0.26 0.49 0.126
Others vs. I 0.757(0.465-1.233) 0.263 0.692(0.419-1.14) 0.148 Surgery 0.252(0.317-0.858) 0.01 0.63(0.361-1.098) 0.103 Radiation 0.277(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 Chemotherapy YES vs. NO 0.377(0.419-0.445) <0.001 0.36(0.3-0.431) <0.001	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 57 8 Male vs. Female Race Others vs. Black Married vs. Divorced/separated Widowed/Unfars vs. Divorced/separated Married vs. Divorced/separated Single/UmMarried vs. Divorced/separated Widowed/Uthers vs. Divorced/separated 2011 vs. 2010 2012 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2015 vs. 2010 2017 vs. 2010 2	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1327) 1.341(1.101-633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.020(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.064) 0.963(0.757-1.224) 0.963(0.757-1.224) 0.963(0.477-1.236) 0.906(0.494-1.661) 0.844(0.675-1.055) 0.844(0.675-1.055) 0.884(0.675-1.135) 0.8881(0.741-1.046) 0.95(0.707-1.276) 0.937(0.642-1.367) 0.872(0.684-1.133)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.885 0.885 0.876 0.149 0.621 0.926 0.0749 0.621 0.926 0.033 0.136 0.301 0.735 0.735 0.735 0.271	Adiusted HR(95% CC 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.940(0.652–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.665) 0.626(0.421–0.93) 0.779(0.614–0.989) 0.822(0.637–1.051) 1.083(0.973–1.151) 1.086(0.9–1.307) 1.202(0.873–1.655) 1.154(0.769–1.732) 0.818(0.632–1.058) 0.835(0.512–1.348)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.465 0.967 0.967 0.021 0.562 0.041 0.354 0.564 0.378 0.967 0.021 0.564 0.3564 0.326 0.463
Surgery YES vs. NO 0.522(0.317-0.858) 0.01 0.63(0.361-1.098) 0.103 Radiation YES vs. NO 0.777(0.457-1.318) 0.349 0.877(0.483-1.59) 0.665 Chemotherapy YES vs. NO 0.377(0.319-0.445) <0.001 0.36(0.3-0.431) <0.001	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black Maried vs. Black Maried vs. Black Maried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 2015 vs. 2010 25–32en vs. 15–24cm 33–40cm vs. 15–24cm 34 UCC T 72 vs. T1 73 vs. T1 74 vs. N0 72 vs. N0 74 vs. N0 74 vs. N0 75 vs. 15 75 vs. 15	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.31) 1.024(0.763-1.373) 0.831(0.654-1.333) 0.833(0.65-1.068) 0.963(0.757-1.224) 0.963(0.757-1.224) 0.963(0.757-1.224) 0.960(0.494-1.661) 0.996(0.494-1.661) 0.996(0.494-1.653) 0.688(0.471-1.005) 0.88(0.691-1.21) 0.966(0.798-1.17) 0.986(0.798-1.17) 0.981(0.741-1.046) 0.95(0.707-1.276) 0.937(0.642-1.367) 0.95(0.707-1.276) 0.937(0.642-1.367) 0.837(0.524-1.336) 0.837(0.524-1.336)		P value 0.696 0.717 0.004 0.238 0.68 0.688 0.885 0.885 0.885 0.876 0.149 0.149 0.418 0.756 0.031 0.023 0.0749 0.621 0.026 0.030 0.030 0.026 0.030 0.0749 0.621 0.026 0.030 0.030 0.0735 0.717 0.735 0.271	Adiusted HR(95% CC 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.281) 0.86(0.662–1.161) 1.086(0.662–1.161) 1.086(0.662–1.161) 0.83(0.441–1.56) 0.848(0.53–1.55) 1.011(0.613–1.665) 0.626(0.421–035) 0.622(0.637–1.057) 0.822(0.637–1.655) 1.154(0.769–1.732) 0.818(0.632–1.558) 1.154(0.769–1.738) 0.838(0.518–1.588) 0.838(0.518–1.588) 0.838(0.518–1.588)		P value 0.887 0.822 0.081 0.071 0.0635 0.6684 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.993 0.967 0.021 0.044 0.391 0.266 0.49 0.126 0.812
Radiation 1 0.349 0.877(0.483-1.59) 0.665 Chemotherapy 0.369 0.877(0.483-1.59) 0.665 YES vs. NO 0.377(0.419-0.445) 0.001 0.36(0.3-0.431) 0.001 </th <th>В</th> <th>Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 58- Male vs. Female Race Others vs. Black Mairei vs. Black Maritei vs. Black Maritei vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated 2011 vs. 2010 2013 vs. 2010 2015 vs. 2010 2017 vs. 2010 2018 vs. 15-24cm 2018 vs. 11 2018 vs. 11 2018 vs. 10 2018 vs. 10 2018</th> <th>Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.83(0.757-1.224) 0.906(0.494-1.61) 0.906(0.494-1.61) 0.906(0.494-1.61) 0.894(0.572-1.396) 1.023(0.633-1.653) 0.688(0.471-1.005) 0.884(0.671-0.55) 0.88(0.691-1.121) 0.956(0.798-1.17) 0.881(0.741-1.046) 0.957(0.0642-1.367) 0.937(0.642-1.367) 0.872(0.644-1.13) 0.837(0.524-1.336) 1.025(0.646-1.625) 0.757(0.465-1.233)</th> <th>ECD</th> <th>P value 0.696 0.717 0.004 0.238 0.66 0.688 0.885 0.885 0.876 0.169 0.169 0.418 0.756 0.169 0.418 0.756 0.021 0.0926 0.031 0.301 0.301 0.301 0.301 0.375 0.371 0.355 0.271 0.455 0.263</th> <th>Adjusted HR(95% C) 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.181) 0.86(0.662-1.116) 1.096(0.857-1.401) 0.817(0.631-1.057) 0.83(0.441-1.56) 0.484(0.53-1.358) 1.011(0.613-1.665) 0.622(0.421-0.939) 0.822(0.637-1.655) 1.154(0.769-1.732) 0.818(0.652-1.058) 0.83(0.518-1.348) 1.06(0.588-1.708) 0.652(0.419-1.14)</th> <th></th> <th>P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.1257 0.465 0.1257 0.465 0.1257 0.465 0.425 0.949 0.264 0.391 0.264 0.391 0.264 0.49 0.126 0.462 0.418</th>	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 58- Male vs. Female Race Others vs. Black Mairei vs. Black Maritei vs. Black Maritei vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated 2011 vs. 2010 2013 vs. 2010 2015 vs. 2010 2017 vs. 2010 2018 vs. 15-24cm 2018 vs. 11 2018 vs. 11 2018 vs. 10 2018	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.83(0.757-1.224) 0.906(0.494-1.61) 0.906(0.494-1.61) 0.906(0.494-1.61) 0.894(0.572-1.396) 1.023(0.633-1.653) 0.688(0.471-1.005) 0.884(0.671-0.55) 0.88(0.691-1.121) 0.956(0.798-1.17) 0.881(0.741-1.046) 0.957(0.0642-1.367) 0.937(0.642-1.367) 0.872(0.644-1.13) 0.837(0.524-1.336) 1.025(0.646-1.625) 0.757(0.465-1.233)	ECD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.885 0.885 0.876 0.169 0.169 0.418 0.756 0.169 0.418 0.756 0.021 0.0926 0.031 0.301 0.301 0.301 0.301 0.375 0.371 0.355 0.271 0.455 0.263	Adjusted HR(95% C) 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.181) 0.86(0.662-1.116) 1.096(0.857-1.401) 0.817(0.631-1.057) 0.83(0.441-1.56) 0.484(0.53-1.358) 1.011(0.613-1.665) 0.622(0.421-0.939) 0.822(0.637-1.655) 1.154(0.769-1.732) 0.818(0.652-1.058) 0.83(0.518-1.348) 1.06(0.588-1.708) 0.652(0.419-1.14)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.1257 0.465 0.1257 0.465 0.1257 0.465 0.425 0.949 0.264 0.391 0.264 0.391 0.264 0.49 0.126 0.462 0.418
Chemotherapy I <0.001	В	Charateristics Age category 56-65 vs. 30-55 66-70 vs. 30-55 Sex Male vs. Female Race Others vs. Black Maried vs. Black Maried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated Midowed/Others vs. Divorced/separated Diagnosis 2011 vs. 2010 2013 vs. 11 25-32em vs. 15-24cm 33-40cm vs. 15-24cm AUCC T 2 vs. T1 2 vs. N0 2 vs. N0 3 vs. N0 N	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.66-1.076) 0.906(0.494-1.661) 0.906(0.494-1.661) 0.906(0.494-1.661) 0.834(0.6572-1.396) 1.023(0.633-1.653) 0.688(0.471-1.005) 0.884(0.671-0.155) 0.88(0.691-1.121) 0.966(0.798-1.17) 0.950(0.770-1.276) 0.937(0.642-1.367) 0.957(0.054-1.336) 0.837(0.524-1.336) 0.522(0.317-0.858)		P value 0.696 0.717 0.004 0.238 0.688 0.885 0.885 0.885 0.876 0.149 0.149 0.418 0.756 0.149 0.621 0.0226 0.053 0.0301 0.725 0.149 0.735 0.735 0.717 0.455 0.917 0.455 0.917 0.917 0.9263 0.01	Adiusted HR(95% CC 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.288) 0.92(0.716-1.181) 0.86(0.662-1.116) 1.096(0.857-1.401) 0.87(0.631-1.057) 0.83(0.441-1.56) 0.848(0.53-1.358) 1.011(0.613-1.665) 0.626(0.421-0.939) 0.822(0.637-1.622) 0.943(0.773-1.151) 1.085(0.9-1.372) 1.154(0.769-1.732) 0.818(0.632-1.058) 0.83(0.518-1.348) 0.63(0.361-1.089) 0.63(0.361-1.089)		P value 0.887 0.822 0.081 0.0713 0.0614 0.0735 0.685 0.684 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.967 0.02 0.041 0.391 0.266 0.49 0.126 0.492 0.124 0.134
	В	Charateristics Age category 56–65 vs, 30–55 66–70 vs, 30–55 71–97 vs, 30–55 Sex Male vs. Female Race Others vs. Black Married vs. Divorced/separated Single/UmMarried vs. Divorced/separated Widowed/Others vs. Divorced/separated Widowed/Others vs. Divorced/separated 2011 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2016 vs. 15–24cm 33–40cm vs. 15–24cm 33–40cm vs. 15–24cm AJCC T T2 vs. T1 T3 vs. T1 T3 vs. T1 T3 vs. T1 T3 vs. T1 T3 vs. T1 T3 vs. T1 T4 vs. T1 T3 vs. T1 T4 vs. T1 T3 vs. T1 T4 vs. T1 T4 vs. T1 T3 vs. T1 T4 vs. T1	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.341(1.101-633) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.020(781-1.331) 1.024(0.763-1.373) 0.833(0.65-1.064) 0.963(0.757-1.224) 0.963(0.757-1.224) 0.963(0.477-1.224) 0.906(0.494-1.661) 0.844(0.675-1.234) 0.906(0.494-1.661) 0.844(0.675-1.234) 0.906(0.798-1.17) 0.8881(0.71-1.1055) 0.884(0.671-1.1055) 0.884(0.671-1.215) 0.884(0.671-1.227) 0.95(0.779-1.276) 0.957(0.642-1.365) 1.023(0.642-1.365) 0.837(0.524-1.364) 0.837(0.524-1.364) 0.757(0.465-1.233) 0.522(0.317-0.858) 0.777(0.457-1.318)	CD	P value 0.696 0.717 0.004 0.238 0.66 0.688 0.085 0.885 0.876 0.149 0.169 0.418 0.756 0.031 0.031 0.023 0.0749 0.621 0.926 0.053 0.136 0.301 0.732 0.735 0.271 0.455 0.917 0.263 0.917 0.263 0.917 0.263 0.917 0.263 0.917 0.263 0.917 0.926 0.917 0.926 0.926 0.927 0.926 0.927 0.926 0.927 0.926 0.927 0.926 0.927 0.926 0.927 0.927 0.926 0.927 0.926 0.927 0.926 0.927 0.927 0.926 0.927 0.926 0.927 0.937 0.917 0.926 0.917	Adiusted HR(95% CC 1.014(0.834–1.233) 0.972(0.759–1.245) 1.213(0.976–1.507) 1.233(0.982–1.548) 1.154(0.639–2.082) 1.083(0.738–1.589) 0.778(0.613–0.989) 1.017(0.774–1.336) 0.871(0.641–1.184) 1.003(0.776–1.298) 0.92(0.716–1.181) 0.840(0.652–1.116) 1.096(0.857–1.401) 0.817(0.631–1.057) 0.83(0.441–1.56) 0.848(0.53–1.358) 1.011(0.613–1.655) 0.626(0.421–0.93) 0.779(0.614–0.989) 0.822(0.637–1.052) 1.540(773–1.151) 1.085(0.9–1.307) 1.202(0.873–1.055) 1.154(0.769–1.732) 0.818(0.632–1.058) 0.830(0.518–1.348) 1.06(0.558–1.368) 0.632(0.518–1.348) 1.06(0.558–1.368) 0.632(0.518–1.348) 1.06(0.558–1.368) 0.632(0.518–1.348) 1.06(0.558–1.368) 0.632(0.518–1.348) 1.06(0.558–1.368) 0.632(0.518–1.348) 1.06(0.558–1.368) 0.632(0.419–1.14) 0.63(0.361–1.098) 0.877(0.483–1.59)		P value 0.887 0.822 0.081 0.071 0.635 0.684 0.905 0.378 0.981 0.512 0.257 0.462 0.493 0.967 0.021 0.312 0.562 0.431 0.564 0.391 0.564 0.49 0.134 0.564 0.49 0.134 0.564 0.492 0.148 0.103 0.665
0.35 0.50 0.71 1.0 1.41 0.35 0.50 0.71 1.0 1.41 2.0	В	Charateristics Age category 56–65 vs. 30–55 66–70 vs. 30–55 Sex Male vs. Female Race Others vs. Black Maried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Single/UnMarried vs. Divorced/separated Midowed/Others vs. Divorced/separated 2011 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2013 vs. 2010 2014 vs. 2010 2013 vs. 2010 2014 vs. 2010 2015 vs. 2010 2013 vs. 15–24cm 33–40cm vs. 15–24cm 34 UCC T 27 vs. T1 27 vs. T	Unadiusted HR(955 1.038(0.861-1.251) 1.045(0.823-1.327) 1.139(0.917-1.415) 0.88(0.5-1.551) 0.928(0.644-1.338) 0.817(0.649-1.029) 1.02(0.781-1.31) 1.024(0.763-1.373) 0.833(0.65-1.068) 0.842(0.66-1.076) 0.963(0.757-1.224) 0.963(0.757-1.224) 0.966(0.798-1.161) 0.964(0.572-1.396) 1.023(0.633-1.653) 0.688(0.471-1.005) 0.884(0.671-0.155) 0.88(0.691-1.121) 0.966(0.798-1.17) 0.95(0.707-1.276) 0.937(0.642-1.367) 0.95(0.707-1.276) 0.937(0.642-1.337) 0.832(0.654-1.622) 0.757(0.465-1.233) 0.522(0.317-0.8588) 0.777(0.457-1.318) 0.337(0.319.0.4455)	ECD	P value 0.696 0.717 0.004 0.238 0.668 0.688 0.885 0.885 0.876 0.149 0.169 0.418 0.756 0.149 0.621 0.026 0.033 0.0749 0.621 0.026 0.033 0.136 0.301 0.725 0.149 0.735 0.717 0.263 0.01 0.349 0.901	Adiusted HR(95% CC 1.014(0.834-1.233) 0.972(0.759-1.245) 1.213(0.976-1.507) 1.233(0.982-1.548) 1.154(0.639-2.082) 1.083(0.738-1.589) 0.778(0.613-0.989) 1.017(0.774-1.336) 0.871(0.641-1.184) 1.003(0.776-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.92(0.716-1.298) 0.83(0.441-1.56) 0.848(0.53-1.358) 1.011(0.613-1.665) 0.626(0.421-0.938) 0.822(0.637-1.622) 0.943(0.773-1.151) 1.08(0.9-1.372) 0.158(0.9-1.372) 0.158(0.9-1.372) 0.158(0.9-1.372) 0.158(0.9-1.372) 0.818(0.632-1.058) 0.835(0.518-1.348) 0.632(0.518-1.788) 0.632(0.419-1.14) 0.63(0.361-1.998) 0.877(0.483-1.59) 0.36(0.320-1.37)		P value 0.887 0.822 0.081 0.071 0.0634 0.04 0.905 0.378 0.981 0.512 0.257 0.465 0.125 0.562 0.967 0.021 0.044 0.391 0.266 0.492 0.126 0.482 0.103 0.6655

Figure 4 Univariate and multivariate Cox regression analyses of OS and DSS in EACLM patients. (A) Multivariate analysis for the OS of EACLM patients; (B) multivariate analysis for the DSS of EACLM patients. HR, hazard ratio; CI, confidence interval; AJCC, American Joint Committee on Cancer; OS, overall survival; DSS, disease-specific survival; EACLM, esophageal adenocarcinoma with liver metastasis.

Table 2 Baseline characteristics of patients who received no treatment and of patients who received systemic therapy before and after PSM

		Before PSM			After PSM	
Variables	No treatment (n=236)	Systemic therapy (n=685)	P value	No treatment (n=224)	Systemic therapy (n=224)	P value
Age (years), n [%]			<0.001*			0.577
30–55	37 [16]	213 [31]		37 [17]	46 [21]	
56–65	62 [26]	241 [35]		62 [28]	53 [24]	
66–70	38 [16]	93 [14]		37 [17]	41 [18]	
71–97	99 [42]	138 [20]		88 [39]	84 [38]	
Sex, n [%]			0.783			0.893
Female	33 [14]	89 [13]		31 [14]	33 [15]	
Male	203 [86]	596 [87]		193 [86]	191 [85]	
Race, n [%]			0.41			0.478
Black	13 [6]	26 [4]		10 [4]	14 [6]	
White	218 [92]	638 [93]		209 [93]	202 [90]	
Other	5 [2]	21 [3]		5 [2]	8 [4]	
Marital status, n [%]			<0.001*			0.924
Married	115 [49]	409 [60]		113 [50]	107 [48]	
Divorced/separated	30 [13]	83 [12]		30 [13]	29 [13]	
Single/unmarried	44 [19]	124 [18]		41 [18]	44 [20]	
Widowed/other	47 [20]	69 [10]		40 [18]	44 [20]	
Year of diagnosis, n [%]			0.053			0.264
2010	50 [21]	102 [15]		49 [22]	46 [21]	
2011	28 [12]	116 [17]		26 [12]	42 [19]	
2012	39 [17]	113 [16]		37 [17]	31 [14]	
2013	42 [18]	92 [13]		40 [18]	29 [13]	
2014	35 [15]	122 [18]		33 [15]	32 [14]	
2015	42 [18]	140 [20]		39 [17]	44 [20]	
Tumor location (cm), n [%]			0.205			0.677
15–24	10 [4]	14 [2]		9 [4]	5 [2]	
25–32	8 [3]	20 [3]		7 [3]	9 [4]	
33–40	183 [78]	565 [82]		174 [78]	173 [77]	
Other	35 [15]	86 13]		34 [15]	37 [17]	

Table 2 (continued)

		Before PSM		After PSM		
Variables	No treatment (n=236)	Systemic therapy (n=685)	P value	No treatment (n=224)	Systemic therapy (n=224)	P value
T stage, n [%]			0.266			0.905
T1	58 [25]	153 [22]		56 [25]	49 [22]	
T2	10 [4]	32 [5]		10 [4]	9 [4]	
ТЗ	33 [14]	138 [20]		33 [15]	36 [16]	
T4	34 [14]	103 [15]		30 [13]	35 [16]	
Тх	101 [43]	259 [38]		95 [42]	95 [42]	
N stage, n [%]			<0.001*			0.516
N0	89 [38]	166 [21]		82 [37]	68 [30]	
N1	88 [37]	349 [54]		86 [38]	90 [40]	
N2	12 [5]	53 [8]		12 [5]	19 [8]	
N3	12 [5]	29 [4]		12 [5]	11 [5]	
Nx	35 [15]	88 [13]		32 [14]	36 [16]	
Grade, n [%]			0.185			0.810
I	9 [4]	16 [2]		9 [4]	11 [5]	
II	85 [36]	213 [31]		76 [34]	78 [35]	
III + IV	103 [44]	350 [51]		103 [46]	94 [42]	
Other	39 [17]	106 [15]		36 [16]	41 [18]	

Table 2 (continued)

*, statistically significant. Percentages were calculated after excluding missing cases from the denominator. PSM, propensity scorematching.

with EAC, and such patients have very poor outcomes (20). In this large cohort study, we explored the therapeutic modalities and survival outcomes of patients with EACLM. We found that while the use of systemic therapy was the highest, the use of local and combination therapy was very low. Additionally, we also found that a substantial proportion of the patients did not receive any treatment, which was most likely due to their nutritional insufficiency and performance status. Based on our findings, CT remains the main treatment modality for patients with EACLM. Regardless of whether the patients received surgery or radiotherapy, patients treated with CT had a better OS and DSS. Our findings are consistent with the current National Comprehensive Cancer Network guidelines that recommend systemic therapy for patients with metastatic EAC to palliate symptoms, improve survival, and enhance patients' quality of life (21).

Local therapy, including surgery or RT after effective systemic therapy, could reduce the tumor burden but their potential value in metastatic EC (mEC) remains controversial (9). Wu *et al.* analysed the OS of patients with mEC who were treated with local therapy, and found that patients who received preoperative RT had significantly better OS than patients who underwent primary surgery alone and postoperative RT (P<0.001) (9). In another study, Tanaka *et al.*, found that there was no difference in survival between patients who underwent surgery and those who did not undego surgery (P=0.1291) (6). In our study, the multivariate survival analysis indicated that either surgery or RT was associated with a survival benefit. Thus, we are of the view that simple local therapy is ineffective and should not be recommended to patients with EACLM.

In the era of personalized treatment, a comprehensive multidisciplinary approach is widely applied to determine



Figure 5 K-M OS and DSS analyses between the no treatment group and the systemic treatment group after PSM. (A) Comparison of the OS of the patients who received no treatment and those who received systemic treatment after PSM; (B) comparison of the DSS of the patients who received no treatment and those who received systemic treatment after PSM. OS, overall survival; DSS, disease-specific survival; K-M, Kaplan-Meier; PSM, propensity score-matching.

	В	efore PSM			After PSM	
Variables	Combination therapy (n=236)	Systemic therapy (n=685)	P value	Combination therapy (n=224)	Systemic therapy (n=224)	P value
Age (years), n [%]			0.863			0.946
30–55	9 [35]	213 [31]		8 [33]	14 [29]	
56–65	9 [35]	241 [35]		8 [33]	20 [42]	
66–70	2 [8]	93 [14]		2 [8]	4 [8]	
71–97	6 [23]	138 [20]		6 [25]	10 [21]	
Sex, n [%]			0.234			1.000
Female	1 [4]	89 [13]		1 [4]	3 [6]	
Male	25 [96]	596 [87]		23 [96]	45 [94]	
Race, n [%]			0.827			0.232
Black	0 [0]	26 [4]		0 [0]	3 [6]	
White	26 [100]	638 [93]		24 [100]	41 [85]	
Other	0 [0]	21 [3]		0 [0]	4 [8]	
Marital status, n [%]			0.464			0.490
Married	19 [73]	409 [60]		17 [71]	40 [83]	
Divorced/separated	1 [4]	83 [12]		1 [4]	1 [2]	
Single/unmarried	5 [19]	124 [18]		5 [21]	5 [10]	
Widowed/other	1 [4]	69 [10]		1 [4]	2 [4]	

Table 3 Baseline characteristics of patients who received combination therapy and of patients who received systemic therapy before and after PSM

Table 3 (continued)

Table 3 (continued)

_	B	efore PSM			After PSM	
Variables	Combination therapy (n=236)	Systemic therapy (n=685)	P value	Combination therapy (n=224)	Systemic therapy (n=224)	P value
Year of diagnosis, n [%]			0.428			0.992
2010	3 [12]	102 [15]		3 [12]	5 [10]	
2011	3 [12]	116 [17]		3 [12]	8 [17]	
2012	8 [31]	113 [16]		7 [27]	12 [25]	
2013	5 [19]	92 [13]		5 [21]	10 [21]	
2014	4 [15]	122 [18]		4 [17]	10 [21]	
2015	3 [12]	140 [20]		2 [8]	3 [6]	
Tumor location (cm), n [%]			0.280			0.677
15–24	1 [4]	14 [2]		1 [4]	2 [4]	
25–32	2 [8]	20 [3]				
33–40	20 [77]	565 [82]		20 [83]	40 [83]	
Other	3 [12]	86 [13]		3 [12]	6 [12]	
T stage, n [%]			<0.001*			0.016*
T1	6 [23]	153 [22]		6 [25]	13 [27]	
T2	0 [0]	32 [5]		0 [0]	2 [4]	
Т3	15 [58]	138 [20]		14 [58]	10 [21]	
T4	2 [8]	103 [15]		2 [8]	8 [17]	
Tx	3 [12]	259 [38]		2 [8]	15 [31]	
N stage, n [%]			<0.061			0.255
NO	3 [12]	166 [21]		3 [12]	13 [27]	
N1	15 [58]	349 [54]		13 [54]	20 [42]	
N2	4 [15]	53 [8]		4 [17]	6 [12]	
N3	3 [12]	29 [4]		3 [12]	2 [4]	
Nx	1 [4]	88 [13]		1 [4]	7 [15]	
Grade, n [%]			0.026*			0.002*
I	0 [0]	16 [2]				
II	16 [62]	213 [31]		15 [62]	10 [21]	
III + IV	8 [31]	350 [51]		7 [29]	24 [50]	
Other	2 [8]	106 [15]		2 [8]	14 [29]	

*, statistically significant. Percentages were calculated after excluding missing cases from the denominator. PSM, propensity scorematching.



Figure 6 K-M OS and DSS analyses between the combination treatment group and systemic treatment group after PSM. (A) Comparison of the OS of the patients who received combination treatment and those who received systemic treatment after PSM; (B) comparison of the DSS of the patients who received combination treatment and those who received systemic treatment after PSM. OS, overall survival; DSS, disease-specific survival; K-M, Kaplan-Meier; PSM, propensity score-matching.

the optimal treatment for patients with locally advanced primary EC; however, its role is not well defined for patients with mEC (22). Previous research has shown that the survival of stage IVB EC patients with distant metastasis treated with multimodality therapy was significantly better than that of patients treated with single-modality therapy or best supportive care alone (P<0.0001) (6). Shao et al. reported that there was no statistically significant difference between the CT group and chemoradiotherapy (CRT) group in terms of OS and cancer-specific survival (CSS) in mEC patients. Further, their subgroup analyses revealed that EAC patients who underwent CT had a favorable prognosis (8). In another study, Qiu et al. examined elderly stage IVB EAC patients with distant metastasis, and reported that compared to untreated patients, patients treated with surgery, RT, and CT had a better prognosis (OS and CSS: P<0.001) (20). Our PSM analyses showed that patients treated with systemic therapy had a much better prognosis in terms of OS and DSS than those who were untreated. Additionally, there was no significant difference in terms of OS between the patients who received combination therapy and systemic therapy. However, combination therapy had survival advantages in terms of the DSS of patients with EACLM. As local therapy (either surgery or RT) is inevitably accompanied by some treatment-associated complications (22,23), we suggest that combination therapy be considered for patients

with EACLM after a comprehensive assessment by a multidisciplinary team (24).

The prognostic factors for EACLM were investigated by Cox regression analyses. The results revealed that gender, T stage, and CT were powerful and independent prognostic factors for OS, while marital status, T stage, and CT were independent prognostic factors for DSS. According to Tang *et al.*, factors, including age, gender, grade at diagnosis, the number of metastatic organs at diagnosis, pathological type, local treatment, and CT, were independent predictors of CSS for patients with stage IV esophageal carcinoma (25). In line with a previous study (26), we found that married patients had better DSS than unmarried patients. A major reason for this is that married patients tend to choose positive treatment and demonstrate better compliance than unmarried patients, which may produce better survival advantages (27).

Our study revealed that age is not an independent prognostic factor for EACLM patients. Previous studies have drawn inconsistent conclusions about the relationship between age and prognostic risk in mEC patients (5,25). However, one such study did not distinguish between the histology types of EAC and ESCC, while another study did not indicate which type of organ metastasis was more likely to occur in younger patients. The identification of the prognostic factors associated with the patients would help in the prognostication and management of EACLM.

We undertook a comprehensive analysis of the treatment patterns and the survival outcomes of EACLM patients; however, this study still had some limitations. First, the data obtained from the SEER database lacked some important information, including information about the radiation dose, quality of life, and CT drug regimens, which may have led to an immortal time bias. Second, all the patients examined in this study were from the US; thus, the results do not represent the global population. Finally, as immune checkpoint inhibitors, such as programmed cell death protein 1, and programmed death-ligand 1, are currently being developed and examined, the prognosis of patients will certainly improve. Thus, it is necessary to provide updated information using such data.

Conclusions

This is a large-scale report on the treatment patterns and prognosis of patients with EACLM. CT-based combination therapy may be the most effective treatment strategy for such patients. The findings need to be externally validated in the future, but they may be useful in guiding clinical decision making, directing individualized treatment strategies, designing clinical trials, and ultimately improving patient prognosis.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-420/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-420/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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Supplementary





Figure S1 SMD in characteristics before and after PSM. SMD, standardized mean differences; PSM, propensity score-matching.

Figure S2 SMD in characteristics before and after PSM. SMD, standardized mean differences; PSM, propensity score-matching.