Archives of Gynecology and Obstetrics (2019) 300:683–691
https://doi.org/10.1007/s00404-019-05225-6

GYNECOLOGIC ONCOLOGY

Lymphadenectomy and prognosis for elderly females with stage I endometrioid endometrial cancer

Ling Zhao[1] · Ling Li[1] · Yaping Ye[1] · Xiling Han[2] · Xueshu Fu[1] · Yanjun Yu[1] · Jiali Luo[2,3]

Received: 4 March 2019 / Accepted: 19 June 2019 / Published online: 29 June 2019

Abstract

Purpose The potential therapeutic benefits of lymphadenectomy in endometrial cancer (EC) patients are still ambiguous. Therefore, a population-based retrospective analysis was conducted to determine the association between lymphadenectomy and survival in elderly female patients with stage I endometrioid EC.

Methods The Surveillance, Epidemiology, and End Results (SEER) program database was retrospectively analyzed, and data of 63,372 female patients with early-stage type I EC from 1988 to 2013 were collected. The main patient and tumor characteristics included marital status, age, ethnicity, time of diagnosis, tumor grade, radiotherapy, and lymphadenectomy status. Kaplan–Meier and Cox proportional hazard regression analyses were performed to determine the association between lymph node dissection and the overall survival (OS) and cancer-specific survival in women older than 50 years with stage I endometrioid EC.

Results The majority (83.7%) of the patients who met the inclusion criteria for the study were older than 50 years. In both grade 1 and 2 patients aged over 50 years, lymph node conservation was associated with a higher mortality risk compared to lymphadenectomy (all $P < 0.005$). Multivariate analysis indicated that lymphadenectomy was an independent predictor of improved OS in early-stage type 1 EC patients, with hazard ratios of 0.893 and 0.827 for the grade 1 and grade 2 patients, respectively ($P < 0.0001$).

Conclusions Lymphadenectomy could improve long-term OS in women older than 50 years with grade 1 and 2 endometrioid EC.

Keywords Lymphadenectomy · Prognosis · Elderly · Endometrioid endometrial cancer

Abbreviations

CI	Confidence interval
EC	Endometrial cancer
HR	Hazard ratio
ICD-O-3	International Classification of Diseases for Oncology, 3rd ed
LND	Lymph node dissection
OR	Odds ratio
OS	Overall survival
SEER	Surveillance, Epidemiology, and End Results

Introduction

Endometrial cancer (EC) is one of the three most prevalent malignancies in the female reproductive tract, and it usually occurs in menopausal women. The overall mortality due to uterine corpus cancers increased by almost 2% annually from 2011 to 2015 [1]. The lymph node is an important factor in the staging of most cancers, including EC, and it is also an indicator of cancer progression and metastasis. The International Federation of Gynecology and Obstetrics (FIGO) revised the EC staging system in 1988 to guide the surgical dissection and evaluation of lymph nodes [2]. Furthermore, the National Comprehensive Cancer Network's Clinical Practice Guidelines in Oncology has recommended

✉ Jiali Luo
luojiali418@hotmail.com

[1] Department of Gynecologic Oncology, Dalian Medical University, Dalian, Liaoning, China

[2] Department of Obstetrics and Gynecology, Clinical Medical College of Yangzhou University, Northern Jiangsu People's Hospital, Yangzhou 225001, Jiangsu, China

[3] Department of Obstetrics and Gynecology, Northern Jiangsu People's Hospital, Yangzhou, Jiangsu, China

pelvic and para-aortic lymph node dissection (LND) for EC patients, instead of nodal sampling [3].

Studies on the correlation between early EC prognosis and lymphadenectomy have yielded ambiguous results, with some retrospective studies indicating a survival benefit of LND, and the others showing that systematic lymphadenectomy may not be necessary for grade 1 lesions or minor myometrial invasion (< 5 mm) [4]. Besides, it has been reported that lymphadenectomy could increase the chances of survival in women at intermediate or high risk of endometrioid EC [4], while other studies did not find any significant correlation between lymphadenectomy and survival in women with early-stage EC [5, 6]. These inconsistencies could be the result of selective patient enrollment. In fact, several studies have shown advanced age to be an independent predictive factor of poor prognosis for EC [7, 8]. However, the older patients are often underrepresented in clinical studies even though they are at higher risk of EC, and it is unclear whether lymphadenectomy is helpful for this population. Therefore, the aim of this retrospective study was to determine the correlation between lymphadenectomy and prognosis in women with early-stage endometrioid EC, especially for those aged ≥ 50 years, according to the trends in the mortality rate of all EC types.

Methods

Study population

Endometrial cancer cases were identified through the Surveillance, Epidemiology and End Results (SEER) program of the National Cancer Institute, which included data of 27.8% of the US population from 11 states and 7 areas, and represented the different demographical groups. The information was accessed from the SEER database, and the requirement for informed consent was exempted by the University of Southern California Institutional Review Board. Data were extracted from the SEER18 Regs Research Data as well as Hurricane Katrina Impacted Louisiana Cases (1973–2013) using SEER*STat 8.3.5 [9]. The inclusion criteria for the SEER 18 registries included: microscopically confirmed EC [International Classification of Diseases for Oncology, 3rd ed. (ICD-O-3), primary site tumors (C54.0–C54.9 Corpus Uteri, NOS)], no concurrent diseases, and female gender. Data of stage I EC cases with or without pelvic lymphadenectomy at the time of hysterectomy from 1988 and 2013 were analyzed, and the cases between 1982 and 1988 were excluded due to incomplete information regarding surgery and staging.

The demographical data included age at the time of diagnosis, year of diagnosis, ethnicity, and marital status, and clinical data included tumor staging, histological subtyping, grading, and surgery. The patients were broadly classified as grade 1/2 endometrioid EC [10]. In addition, the 8140-3, 8262-3, 8380-3, 8382-3, and 8383-3 histological types were also identified using the ICD-O-3 Site/Histology Validation List and the World Health Organization Histological Classification [11]. Tumor staging was based on the 7th Surgical-Pathological Staging Classification Scheme on Cancer by the American Joint Committee. Furthermore, based on the surgical interventions, the patients were also divided into the hysterectomy and non-hysterectomy, as well as the lymphadenectomy and conserved lymph nodes groups.

Outcomes and statistical analysis

The primary outcomes were the characteristics and trends of lymphadenectomy among the stage I type I EC patients, and the secondary outcome was the survival of the grade 1 and 2 endometrioid EC patients older than 50 years who underwent lymphadenectomy. In addition, the lymphadenectomy and lymph nodes conservation groups were also compared. Ordinal and categorical variables were analyzed by the Chi-square test, and the significant risk factors of lymphadenectomy were determined by multivariate analysis using the binary logistic regression test. All case characteristics, along with tumor-related factors in this model, were incorporated into the final model. The Kaplan–Meier method was used to plot survival curves of patient groups of different lymph node status, whereas the hazard ratios (HRs) and corresponding 95% confidence intervals (95% CIs) were estimated using the Cox proportional hazards regression model.

Results

The case selection method is outlined in Fig. 1, and the characteristics of the patients are summarized in Table 1. Of the total 202,551 EC patients identified in the SEER database, 63,372 had stage I type 1 EC, including 40,055 (63.2%) grade 1 and 23,317 (36.8%) grade 2, with known pelvic lymph node status and had undergone the hysterectomy. In addition, 32,915 (51.9%) women had conserved lymph nodes, while 30,457 (48.1%) underwent lymphadenectomy. Trend analysis indicated that the mortality risk was remarkably increased in patients aged 50 years or older (Fig. 2a). Furthermore, the incidence of EC was 0.470‰ among those aged 50–54 years, and it increased to 0.726‰ (95% CI 0.714–0.739‰) in the 55–59 years age group and 1.019‰ (95% CI 1.002–1.037‰) among those aged 65–69 years (risk difference 0.293‰, 95% CI 0.288–0.298‰). The mortality rate also increased in an age-dependent manner, and it was higher than 0.50‰ among patients aged between 50–59 years and ≥ 85 years. During the study period, the

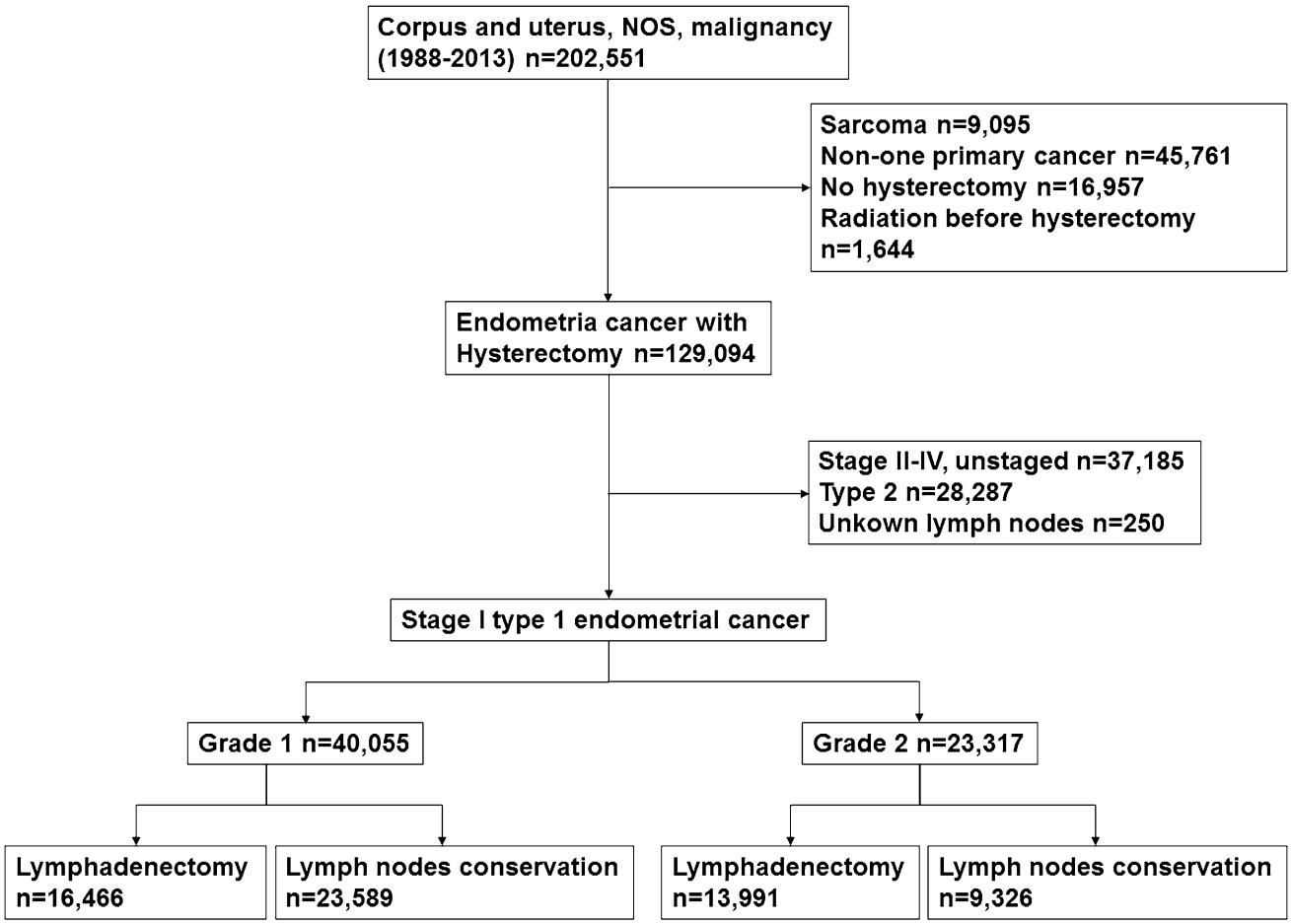

Fig. 1 Selection methods. NOS, not otherwise; type 1, grade 1 and 2 endometrioid types

mortality rates increased in 2009 to 0.349‰ (APC − 0.11, 95% CI − 0.5 to 0.3; Fig. 2b).

The majority of patients with stage I type I EC were older than 50 years (53,015/63,372, 83.7%), of which 26,159 (41.3%) patients had received LND. There was no significant correlation between marital status and lymphadenectomy ($P = 0.067$). Multivariate analysis indicated that age > 50 [odds ratio (OR) 1.311, 95% CI 1.251–1.373, $P < 0.001$], grade 2 tumors (OR 2.285, 95% CI 2.207–2.367, $P < 0.001$), and tumor size of > 6.1 cm (OR 2.285, 95% CI 2.207–2.367, $P < 0.001$) were significant risk factors of lymphadenectomy (Table 1). Furthermore, older women (> 50 years), who underwent lymphadenectomy and had larger (≥ 2 cm) and higher grade tumors, were more likely to undergo total hysterectomy and more likely to receive surgery without radiotherapy (all $P < 0.001$; Table 2). More women underwent lymphadenectomy between 2008–2013 compared to those who received LND between 1988 and 1992. Univariate analysis showed significant differences between the cause-specific and overall survival (OS) rates in stage I grade 2 endometrioid EC cases. However, lymphadenectomy in the early-stage grade 2 EC was not significantly correlated with cancer-specific survival ($P = 0.517$; Fig. 3a), while LND was markedly correlated with OS ($P < 0.001$; Fig. 3b). Lymphadenectomy in stage I grade 1 EC patients was associated with improved OS ($P = 0.001$; Fig. 3c) but worse cancer-specific survival ($P = 0.002$; Fig. 3d).

Multivariate analysis showed that lymphadenectomy was an independent predictive factor of reduced mortality risk in type 1 stage I grade 1 EC patients aged over 50 years, regardless of the demographical and clinical characteristics (HR 0.893, 95% CI 0.827–0.964, $P < 0.001$; Table 3). However, lymphadenectomy and lymph nodes conservation were associated with similar mortality risks in the entire EC cohort (HR 1.143, 95% CI 0.952–1.372, $P = 0.259$; Table 3). Finally, the OS (HR 0.827, 95% CI 0.766–0.893, $P < 0.001$; Table 4) and cancer-specific survival (HR 0.599, 95% CI 0.527–0.680, $P = 0.944$; Table 4) rates were similar in the grade 1 and 2 EC groups.

Table 1 Characteristics of patients diagnosed with stage I type 1 EC in 1988–2013

	All subjects	Lymphadenectomy	Lymph nodes conservation	*P*	OR (95% CI)	*P* value
Patients (*n*)	63,372	30,457 (48.1)	32,915 (51.9)			
Age (years)				< 0.001		
< 50	10,357	4298 (41.5)	6024 (58.5)		1.000 (ref)	
> 50	53,015	26,159 (49.3)	26,856 (50.7)		1.311 (1.251–1.373)	< 0.001
Race				< 0.001		
White	54,758	25,926 (47.3)	28,832 (52.7)		1	
Black	3232	1720 (53.2)	1512 (46.8)		1.094 (1.014–1.180)	0.02
Others	5025	2633 (52.4)	2392 (47.6)		1.203 (1.131–1.279)	< 0.001
Unknown	357	178 (49.9)	179 (50.1)		0.984 (0.792–1.223)	0.885
Marital status				0.067		
Single	9966	4822 (48.4)	5144 (51.6)		1.000 (ref)	
Married	35,647	17,191 (48.2)	18,456 (51.8)		1.082 (1.032–1.135)	0.001
Others	15,286	7317 (47.9)	7969 (52.1)		1.013 (0.959–1.069)	0.653
Unknown	2473	1127 (45.6)	1346 (54.4)		0.887 (0.808–0.973)	0.011
Year of diagnosis				< 0.001		
1988–1992	4468	996 (22.3)	3472 (77.7)		1.000 (ref)	< 0.001
1993–1997	6259	1839 (29.4)	4420 (70.6)		1.450 (1.323–1.588)	< 0.001
1998–2002	11,412	4719 (41.4)	6693 (58.6)		2.579 (2.376–2.799)	< 0.001
2003–2007	16,687	8854 (53.1)	7833 (46.9)		4.267 (3.942–4.619)	< 0.001
2008–2013	24,546	14,049 (57.2)	10,497 (42.8)		2.285 (2.207–2.367)	< 0.001
Tumor size (cm)				< 0.001		
≤ 2.0	10,871	4838 (44.5)	6033 (55.5)		1.000 (ref)	
2.1–4.0	13,063	7700 (58.9)	5363 (41.1)		1.680 (1.593–1.772)	< 0.001
4.1–6.0	5554	3498 (63.0)	2056 (37.0)		1.886 (1.761–2.020)	< 0.001
≥ 6.1	2331	1461 (65.5)	770 (34.5)		2.078 (1.883–2.294)	< 0.001
Unknown	31,653	12,960 (40.9)	18,693 (59.1)		1.042 (0.994 – 1.091)	0.085
Grade				< 0.001		
Grade 1	40,055	16,466 (41.1)	23,589 (58.9)		1.000 (ref)	
Grade 2	23,317	13,991 (60.0)	9326 (40.0)		2.285 (2.207 – 2.367)	< 0.001

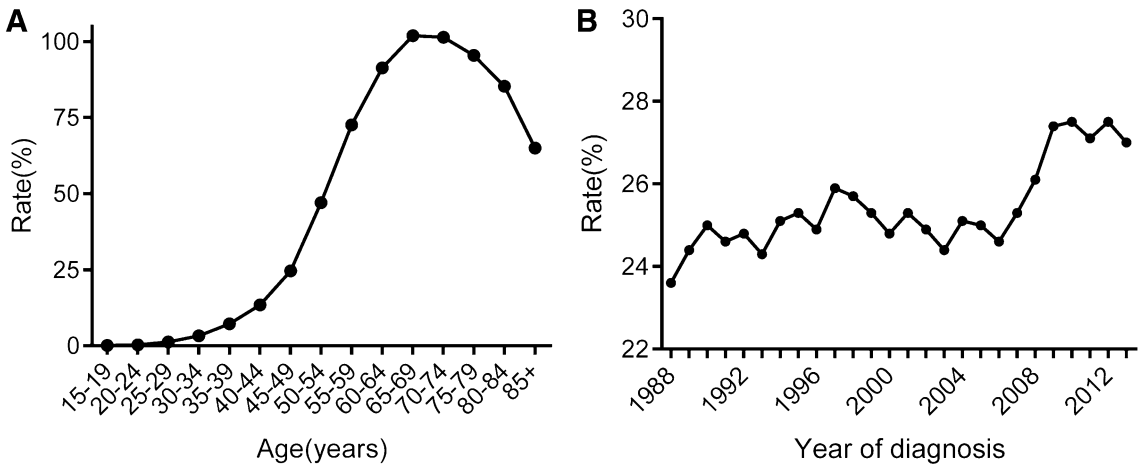

Fig. 2 Temporal trend in the mortality rates of endometrial cancer. Rates are per 100,000 and age adjusted to the 2000 US Std Population standard

Table 2 Characteristics in women aged older than 50 years with stage I endometrioid EC

	Lymphadenectomy	Lymph nodes conservation	*P* value
Age (years)	26,159 (49.3)	26,856 (50.7)	< 0.001
50–59	9735 (48.8)	10,201 (51.2)	
60–69	9764 (51.5)	9194 (48.5)	
70–79	5038 (48.4)	5361 (51.6)	
≥ 80	1622 (43.6)	2100 (56.4)	
Race			< 0.001
White	22,689 (48.6)	23,976 (51.4)	
Black	1399 (54.0)	1190 (46.0)	
Others	1920 (55.3)	1552 (44.7)	
Unknown	151 (52.2)	138 (47.8)	
Marital status			0.004
Single	3513 (50.3)	3477 (49.7)	
Married	14,790 (49.7)	14,964 (50.3)	
Others	6883 (48.5)	7313 (51.5)	
Unknown	973 (46.9)	1102 (53.1)	
Year of diagnosis			< 0.001
1988–1992	873 (22.7)	2976 (77.3)	
1993–1997	1559 (29.5)	3724 (70.5)	
1998–2002	3973 (42.3)	5418 (57.7)	
2003–2007	7491 (54.9)	6163 (45.1)	
2008–2013	12,263 (58.8)	8575 (41.2)	
Grade			< 0.001
Grade 1	13,810 (42.3)	18,825 (57.7)	
Grade 2	12,349 (60.6)	8031 (39.4)	
Tumor size (cm)			< 0.001
≤ 2.0	4237 (45.8)	5008 (54.2)	
2.1–4.0	6894 (59.9)	4620 (40.1)	
4.1–6.0	3016 (64.1)	1688 (35.9)	
≥ 6.1	1133 (67.2)	554 (32.8)	
Unknown	10,879 (42.1)	14,986 (57.9)	
Radiation			< 0.001
Yes	4653 (61.7)	2887 (38.3)	
No	21,506 (47.3)	23,969 (52.7)	
Surgery			< 0.001
Total hysterectomy	21,494 (45.7)	25,557 (54.3)	
Subtotal hysterectomy	153 (27.9)	396 (72.1)	
Others	4512 (83.3)	903 (16.7)	

Discussion

Through this study, it was mainly found that lymphadenectomy could significantly reduce long-term all-cause mortality in women older than 50 years with low-grade and early-stage EC, while EC-related mortality was markedly increased among the older female patients who had poor cancer-specific survival regardless of lymphadenectomy status, and lymphadenectomy could improve the long-term OS in both grade 1 and grade 2 stage 1 endometrioid EC patients older than 50 years.

Previous studies had reported about the factors regarding the application of lymphadenectomy for the EC. In this study, it was found that there were significant differences between patients who were treated by lymphadenectomy and lymph nodes conservation for the women aged older than 50 years with stage I type 1 EC or stage I endometrioid EC, including age, race, year of diagnosis, tumor size, grade, and others. The results also showed that marital status could affect the application of lymphadenectomy for the stage I type 1 EC but not the Stage I endometrioid EC. Besides, the application of radiation and the surgeries like hysterectomy could also significantly affect the application of lymphadenectomy. These findings showed that the application of lymphadenectomy was affected by many factors, and the corresponding factors should be considered and used to popularize lymphadenectomy to improve the treatment for EC patients in the clinic.

In the current study, it was found that age, race, and tumor size could significantly affect the cause-specific survival and OS for the women older than 50 years with stage I grade 1 endometrioid EC or with stage I grade 2 endometrioid EC in both the aspects of cause-specific survival and OS. Besides, the marital status could not affect the cause-specific survival for the women older than 50 years with stage I grade 1 endometrioid EC. Radiation could affect the cause-specific survival for women older than 50 years with stage I grade 1 or grade 2 endometrioid EC. While the hysterectomy could not affect both cause-specific survival and OS for women older than 50 years with stage I grade 1 or grade 2 endometrioid EC. These findings were consistent with previous studies, and they reflected that age, race, marital status, and tumor size were all factors about survival outcomes for patients with endometrioid EC [8, 12–14]. Besides, this finding showed that the treatment for EC had significantly improved in the past decades. This indicated that the development of medical technology played an important role in the improvement of health level around the world.

Previous studies had researched about the association between lymphadenectomy and OS among EC patients using SEER data. A recent large retrospective analysis found that systematic lymphadenectomy improved the disease-specific survival in women older than 80 years with high-grade lesions [15]. Trimble et al. reported that lymphadenectomy enhanced survival in stage I grade 3 patients, but not in stage I grade 1 and 2, or stage II EC patients [16]. In a retrospective analysis on 42,184 endometrial adenocarcinoma cases from 1988 to 2003, Smith et al. found that lymphadenectomy significantly increased both overall and cause-specific survival in EC patients of all grades, with over 11 lymphadenectomies in the entire cohort [17]. However, previous studies on the correlation between early EC prognosis and

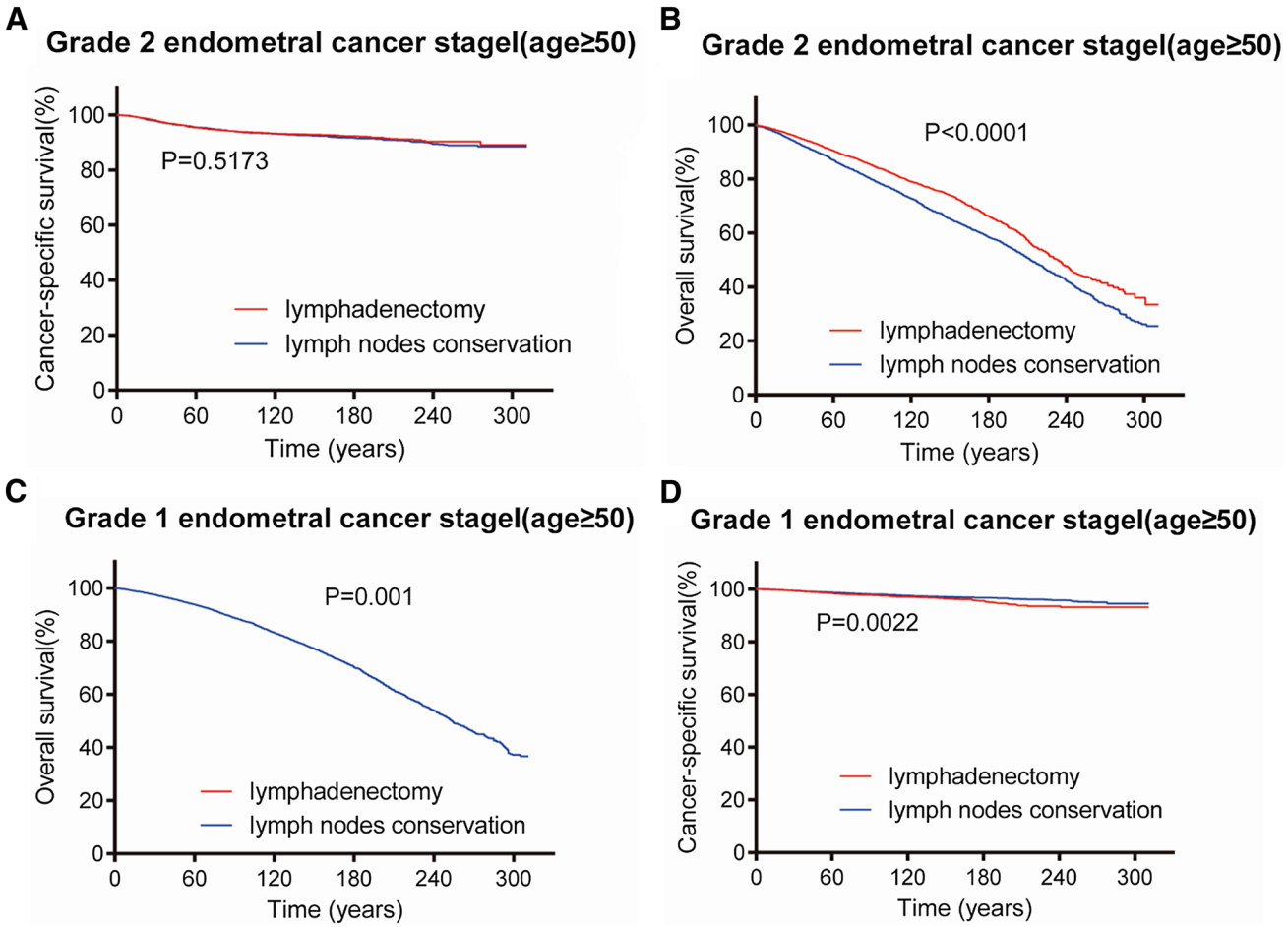

Fig. 3 Survival curves for women aged older than 50 years with stage I grade 1 and 2 endometrioid endometrial cancer. Log-rank test for *P* value. Survival curves were constructed for: cause-specific survival (**a**) and OS (**b**) for women aged older than 50 years with stage I grade 2 endometrioid cancer, and OS (**c**) and cause-specific survival (**d**) for women aged older than 50 years with stage I grade 1 endometrioid cancer

lymphadenectomy yielded ambiguous results. It found a similar OS between the lymph node conservation and lymphadenectomy groups [5, 18] by some reports. In the current study, the long-term OS was improved by lymphadenectomy for both the grade 1 and grade 2 stage 1 endometrioid EC female patients older than 50 years. This inconsistency might be caused by the sample size and the sample size in this study reached up to 60,000 cases, while the study of Panici et al. had just about 500 cases and the report on behalf of the ASTEC study group had just about 15,000 cases. It might also be caused by the time horizon for different studies and the research time horizon in the current study was from 1988 to 2013, and the cases were not evenly distributed in the research time horizon. Besides, this study also showed that different from OS, the cause-specific survival was similar between the lymph node conservation and lymphadenectomy groups. This difference indicated that lymphadenectomy improved the survival rates through improving the other factors for the survival but not just EC such as reducing the complications. The controversy about the clinical utility of LND in early-stage EC might be the result of the improvement in technology used for lymphadenectomy, and its risk of intraoperative complications might have been reduced in the past decades [4, 5, 19]. For example, the sentinel lymph node excision, which could significantly reduce the risk of intraoperative complications, was gradually widely used in clinic followed by lymphadenectomy.

There were several limitations in this study which should be addressed. First, only patients who underwent surgery were enrolled, which might have led to a bias towards elderly patients. Second, there was a possibility of functional status-associated selection bias for lymphadenectomy. Finally, women undergoing staging lymphadenectomy were linked to a higher probability of receiving adjuvant radiotherapy. In addition, the SEER database lacked information on the functional status, quality of life, comorbidities, additional adjuvant treatments like chemo- or hormonal therapy, and central pathological review. However, some of these factors

Table 3 Multivariate analysis for women older than 50 years with stage I grade 1 endometrioid EC

	Cause-specific survival		Overall survival	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (years)				
50–59	1		1	
60–69	1.588 (1.291–1.953)	< 0.001	2.179 (1.988–2.388)	< 0.001
70–79	2.288 (1.832–2.859)	< 0.001	5.877 (5.378–6.423)	< 0.001
≥ 80	5.796 (4.475–7.505)	< 0.001	14.831 (13.378–16.441)	< 0.001
Race				
White	1		1	
Black	1.826 (1.338–2.493)	< 0.001	1.326 (1.153–1.526)	< 0.001
Others	1.087 (0.774–1.525)	0.631	0.862 (0.746–0.996)	0.044
Unknown	0.447 (0.063–3.186)	0.422	0.423 (0.190–0.942)	0.035
Marital status				
Single	1		1	
Married	0.838 (0.651–1.080)	0.172	0.664 (0.605–0.730)	< 0.001
Others	1.030 (0.789–1.344)	0.829	0.909 (0.825–1.001)	0.052
Unknown	1.081 (0.691–1.691)	0.732	0.835 (0.700–0.995)	0.044
Year of diagnosis				
1988–1992	1		1	
1993–1997	1.054 (0.810–1.373)	0.694	0.993 (0.914–1.079)	0.868
1998–2002	0.893 (0.682–1.168)	0.407	0.882 (0.806–0.966)	0.007
2003–2007	0.866 (0.655–1.144)	0.311	0.793 (0.714–0.881)	< 0.001
2008–2013	0.711 (0.508–0.995)	0.046	0.640 (0.550–0.745)	< 0.001
Tumor size				
≤ 2.0	1		1	
2.1–4.0	1.332 (1.014–1.750)	0.4	1.156 (1.042–1.282)	0.006
4.1–6.0	1.618 (1.148–2.279)	0.006	1.507 (1.313–1.729)	< 0.001
≥ 6.1	2.139 (1.355–3.377)	0.001	1.667 (1.351–2.056)	< 0.001
Unknown	1.074 (0.849–1.360)	0.551	1.033 (0.949–1.124)	0.456
Radiation				
Yes	1		1	
No	0.540 (0.0.441–0.660)	< 0.001	0.951 (0.871–1.037)	0.254
Surgery				
Total hysterectomy	1		1	
Subtotal hysterectomy	0.869 (0.360–2.099)	0.755	1.228 (0.912–1.654)	0.177
Others	1.288 (1.008–1.646)	0.043	1.057 (0.956–1.169)	0.277
Lymphadenectomy				
No	1		1	
Yes	1.143 (0.952–1.372)	0.151	0.893 (0.827–0.964)	0.004

Data are % unless otherwise specified

Cox proportional hazard regression models for multivariable analysis adjusted for collected covariates. All patient factors, tumor characteristics, and treatment patterns were entered in the final model

HR hazard ratio, *CI* confidence interval

should not be viewed as inherent limitations of the SEER database, since most patients might not have received any adjuvant treatment, and any "incomplete" clinical information likely indicates community practice. Nevertheless, reviewing the clinical outcome of lymphadenectomy in EC patients could help identify those at high preoperative risks who might instead benefit from adjuvant treatments.

In conclusion, lymphadenectomy can benefit grade 1 and 2 endometrioid EC patients aged over 50 years. With the global increase in the elderly and obese populations, more cases of EC are predicted for the near future, and it is vital to determine the optimum treatment for these patients.

Table 4 Multivariate analysis for women aged older than 50 years with stage I grade 2 endometrioid EC

	Cause-specific survival		Overall survival	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age (years)				
50–59	1		1	
60–69	1.598 (1.338–1.907)	< 0.001	2.220 (2.005–2.459)	< 0.001
70–79	2.473 (2.063–2.965)	< 0.001	5.191 (4.699–5.735)	< 0.001
≥ 80	3.835 (3.093–4.755)	< 0.001	11.602 (10.391–12.955)	< 0.001
Race				
White	1		1	
Black	1.800 (1.452–2.230)	< 0.001	1.446 (1.282–1.631)	< 0.001
Others	0.802 (0.588–1.094)	0.164	0.793 (0.683–0.922)	0.003
Unknown	0.351 (0.049–2.496)	0.295	0.318 (0.102–0.987)	0.047
Marital status				
Single	1		1	
Married	0.777 (0.640–0.944)	0.011	0.700 (0.635–0.771)	< 0.001
Others	0.954 (0.781–1.166)	0.647	0.945 (0.857–1.042)	0.26
Unknown	0.895 (0.608–1.317)	0.572	0.839 (0.691–1.019)	0.076
Year of diagnosis				
1988–1992	1		1	
1993–1997	1.051 (0.849–1.301)	0.649	0.971 (0.892–1.057)	0.495
1998–2002	0.963 (0.773–1.198)	0.734	0.894 (0.813–0.984)	0.022
2003–2007	0.890 (0.709–1.117)	0.314	0.880 (0.790–0.980)	0.02
2008–2013	1.036 (0.806–1.332)	0.782	0.906 (0.788–1.041)	0.165
Tumor size (cm)				
≤ 2.0	1		1	
2.1–4.0	1.667 (1.316–2.111)	< 0.001	1.295 (1.164–1.441)	< 0.001
4.1–6.0	2.032 (1.556–2.654)	< 0.001	1.574 (1.384–1.790)	< 0.001
≥ 6.1	2.596 (1.848–3.647)	< 0.001	1.546 (1.271–1.881)	< 0.001
Unknown	1.465 (1.175–1.827)	0.001	1.233 (1.120–1.357)	< 0.001
Radiation				
Yes	1		1	
No	0.578 (0.519–0.644)	< 0.001	0.926 (0.867–0.989)	0.022
Surgery				
Total hysterectomy	1		1	
Subtotal hysterectomy	1.227 (0.635–2.372)	0.543	1.167 (0.819–1.665)	0.393
Others	1.006 (0.827–1.224)	0.949	1.093 (0.994–1.202)	0.067
Lymphadenectomy				
No	1		1	
Yes	0.995 (0.858–1.153)	0.944	0.827 (0.766–0.893)	< 0.001

Cox proportional hazard regression models for multivariable analysis adjusted for collected covariates. All patient factors, tumor characteristics, and treatment patterns were entered in the final model

HR hazard ratio, *CI* confidence interval. Data are % unless otherwise specified

Funding There was no funding obtained for this study.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Author contributions LZ: conceptualization, project administration, manuscript writing. LL: data curation, investigation, methodology. YY: data curation, formal analysis, software. XH: formal analysis, methodology, software. XF: resources, validation. YY: project administration, validation. JL: conceptualization, supervision, manuscript reviewing and editing.

Ethics approval As the study consisted of the retrospective analysis of anonymized data according to the local ethics committee, a special approval is generally not required.

References

1. Siegel RL, Miller KD, Jemal A (2018) Cancer statistics, 2018. CA Cancer J Clin 68:7–30. https://doi.org/10.3322/caac.21442
2. Piver MS, Rose PG, Freedman MF (1988) Change in International Federation of Gynecology and Obstetrics staging. Am J Obstet Gynecol 158:678–679
3. Candiani GB, Belloni C, Maggi R, Colombo G, Frigoli A, Carinelli SG (1990) Evaluation of different surgical approaches in the treatment of endometrial cancer at FIGO stage I. Gynecol Oncol 37:6–8
4. Turan T, Kimyon Comert G, Turkmen O, Ureyen I, Fadiloglu E, Karalok A, Tasci T, Tulunay G, Basaran D (2018) Therapeutic value of lymphadenectomy and adjuvant radiotherapy in uterine corpus confined endometrioid-type cancer. J Chin Med Assoc 81:714–723. https://doi.org/10.1016/j.jcma.2017.05.014
5. Uccella S, Podratz KC, Aletti GD, Mariani A (2009) Re: Systematic pelvic lymphadenectomy vs no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 101:897–898 **(author reply 898–899)**. https://doi.org/10.1093/jnci/djp124
6. Benedetti Panici P, Basile S, Maneschi F, Alberto Lissoni A, Signorelli M, Scambia G, Angioli R, Tateo S, Mangili G, Katsaros D, Garozzo G, Campagnutta E, Donadello N, Greggi S, Melpignano M, Raspagliesi F, Ragni N, Cormio G, Grassi R, Franchi M, Giannarelli D, Fossati R, Torri V, Amoroso M, Croce C, Mangioni C (2008) Systematic pelvic lymphadenectomy vs. no lymphadenectomy in early-stage endometrial carcinoma: randomized clinical trial. J Natl Cancer Inst 100:1707–1716. https://doi.org/10.1093/jnci/djn397
7. Koual M, Ngo C, Girault A, Lecuru F, Bats AS (2018) Endometrial cancer in the elderly: does age influence surgical treatments, outcomes, and prognosis? Menopause 25:968–976. https://doi.org/10.1097/GME.0000000000001119
8. Benedetti Panici P, Basile S, Salerno MG, Di Donato V, Marchetti C, Perniola G, Palagiano A, Perutelli A, Maneschi F, Lissoni AA, Signorelli M, Scambia G, Tateo S, Mangili G, Katsaros D, Campagnutta E, Donadello N, Greggi S, Melpignano M, Raspagliesi F, Cormio G, Grassi R, Franchi M, Giannarelli D, Fossati R, Torri V, Croce C, Mangioni C (2014) Secondary analyses from a randomized clinical trial: age as the key prognostic factor in endometrial carcinoma. Am J Obstet Gynecol 210:363 e361–363 e310. https://doi.org/10.1016/j.ajog.2013.12.025
9. Surveillance, Epidemiology, and End Results (SEER) Program, SEER*Stat Database: Incidence - SEER 18 Regs Research Data + Hurricane Katrina Impacted Louisiana Cases, Nov 2015 Sub (1973-2013 varying) - Linked To County Attributes - Total U.S., 1969-2014 Counties, National Cancer Institute, DCCPS, Surveillance Research Program, released April 2016, based on the November 2015 submission. www.seer.cancer.gov
10. Matsuo K, Opper NR, Ciccone MA, Garcia J, Tierney KE, Baba T, Muderspach LI, Roman LD (2015) Time interval between endometrial biopsy and surgical staging for type I endometrial cancer: association between tumor characteristics and survival outcome. Obstet Gynecol 125:424–433. https://doi.org/10.1097/AOG.0000000000000636
11. Matsuo K, Machida H, Shoupe D, Melamed A, Muderspach LI, Roman LD, Wright JD (2016) Ovarian conservation and overall survival in young women with early-stage low-grade endometrial cancer. Obstet Gynecol 128:761–770. https://doi.org/10.1097/AOG.0000000000001647
12. Mahdi H, Munkarah AR, Ali-Fehmi R, Woessner J, Shah SN, Moslemi-Kebria M (2015) Tumor size is an independent predictor of lymph node metastasis and survival in early stage endometrioid endometrial cancer. Arch Gynecol Obstet 292:183–190. https://doi.org/10.1007/s00404-014-3609-6
13. Fleming ND, Lentz SE, Cass I, Li AJ, Karlan BY, Walsh CS (2011) Is older age a poor prognostic factor in stage I and II endometrioid endometrial adenocarcinoma? Gynecol Oncol 120:189–192. https://doi.org/10.1016/j.ygyno.2010.10.038
14. Milam M, Java J, Parker L, Metzinger D, Coleman R, Walker J (2013) Survival in early stage endometrioid endometrial cancer risk groups: a Gynecologic Oncology Group ancillary data study. Gynecol Oncol 130:e23. https://doi.org/10.1016/j.ygyno.2013.04.116
15. Lowery WJ, Gehrig PA, Ko E, Secord AA, Chino J, Havrilesky LJ (2012) Surgical staging for endometrial cancer in the elderly—is there a role for lymphadenectomy? Gynecol Oncol 126:12–15. https://doi.org/10.1016/j.ygyno.2012.05.003
16. Trimble EL, Kosary C, Park RC (1998) Lymph node sampling and survival in endometrial cancer. Gynecol Oncol 71:340–343. https://doi.org/10.1006/gyno.1998.5254
17. Smith DC, Macdonald OK, Lee CM, Gaffney DK (2008) Survival impact of lymph node dissection in endometrial adenocarcinoma: a surveillance, epidemiology, and end results analysis. Int J Gynecol Cancer 18:255–261. https://doi.org/10.1111/j.1525-1438.2007.01020.x
18. Kitchener H, Swart AM, Qian Q, Amos C, Parmar MK (2009) Efficacy of systematic pelvic lymphadenectomy in endometrial cancer (MRC ASTEC trial): a randomised study. Lancet 373:125–136. https://doi.org/10.1016/S0140-6736(08)61766-3
19. Bendifallah S, Koskas M, Ballester M, Genin AS, Darai E, Rouzier R (2012) The survival impact of systematic lymphadenectomy in endometrial cancer with the use of propensity score matching analysis. Am J Obstet Gynecol 206(500):e501–e511. https://doi.org/10.1016/j.ajog.2012.03.027