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Comparison of laparoscopic and abdominal radical hysterectomy in early stage cervical cancer patients without adjuvant treatment: Ancillary analysis of a Korean Gynecologic Oncology Group Study (KGOG 1028)

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HIGHLIGHTS

- Laparoscopic radical hysterectomy showed lower rates of DFS, specifically pelvic and hematogenous recurrence.
- Laparoscopic radical hysterectomy was associated with lower rates of DFS but not OS.
- Inferior DFS in the laparoscopy group may be compensated due to better response to radiation therapy in pelvic recurrence

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ABSTRACT

Objective. We compared two groups of early stage cervical cancer patients treated with different surgical methods without adjuvant treatment using retrospective multicenter data previously collected for Korean Gynecologic Oncology Group (KGOG) study designed for developing prognostic models.

Method. We initially assessed data from the multi-institutional cohort with early stage (IB-IIA) cervical cancer patients treated with radical hysterectomy without adjuvant treatment between 2000 and 2008. Propensity score matching was performed to compare disease-free survival (DFS) and overall survival (OS) of patients with laparoscopic to abdominal radical hysterectomy. Additionally, survival comparison was performed in patients with tumor size <2 cm.

Results. After matching, 119 patients with laparoscopic radical hysterectomy were compared with 357 patients with abdominal radical hysterectomy (median follow-up of 63.9 months). Inferior DFS was observed in the laparoscopy group (HR 2.738 [95% CI 1.326–5.650], $p = 0.005$) with a significant difference in pelvic (HR 5.110 [95% CI 1.817–14.473], $p < 0.001$) and hematogenous recurrence (HR 3.171 [95% CI 1.059–9.494], $p = 0.03$), but OS was not significantly different between two groups ($p = 0.624$). In subgroup analysis in the patient with tumor size <2 cm (laparoscopy 62 vs. laparotomy 186, median follow-up of 69.1 months), laparoscopy was associated with lower rate of DFS (HR 12.987 [95% CI 1.451–116.244], $p = 0.003$), but no significant difference in OS was observed between groups. Regarding OS, number of events is lacking, and inferior DFS in the laparoscopy group may be compensated by better response to radiation therapy in pelvic recurrence.

Conclusions. In this analysis, laparoscopic radical hysterectomy was associated with lower rates of DFS but not OS in early stage cervical cancer patients without adjuvant treatment. Further larger scale studies are needed.

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1. Introduction

Cervical cancer is the fourth most frequent malignancy in women and the seventh most frequent malignancy overall worldwide [1]. In Korea, it is one of the common gynecologic cancers, representing 9.8% of newly diagnosed malignancies in women [2]. According to guidelines from the National Comprehensive Cancer Network and European Society of Gynecological Oncology, radical hysterectomy (either laparoscopy or laparotomy) is the standard treatment for International Federation of Gynecology and Obstetrics (FIGO) stage IA–IIA uterine cervical cancer patients [3].

In the past, a number of retrospective studies showed no significant differences in survival outcomes between surgical methods [4–6], with better surgical outcomes for laparoscopy including less blood loss and shorter hospital stay [7,8]. However, result of recent studies showed different perspectives. Epidemiologic study in the United States showed that minimally invasive radical hysterectomy was associated with shorter overall survival than open surgery among women with stage IA2 or IB1 cervical carcinoma [9]. Also, a recent phase 3, multicenter, prospective randomized trial, the Laparoscopic Approach to Cervical Cancer (LACC) Trial, concluded that laparoscopic radical hysterectomy in patients with cervical cancer was associated with lower rates of disease-free survival (DFS) and overall survival (OS) than open radical hysterectomy [10]. However, more information for low-risk early stage cervical cancer patients (tumor size, <2 cm; no lymphovascular invasion; depth of invasion, <10 mm; and no lymph-node involvement) is needed.

Previously, we analyzed retrospective data from a Korean Gynecologic Oncology Group (KGOG)-affiliated multi-institutional cohort to develop a prognostic model for early stage cervical cancer patients. To obtain additional information regarding survival outcomes of the two surgical methods, we assessed data from the KGOG 1028 study. In this trial, after propensity score matching, DFS (specifically, for lymphatic, hematogenous, and pelvic recurrence) and OS were compared between early stage cervical cancer patients who were treated with laparoscopic radical hysterectomy or abdominal radical hysterectomy without adjuvant treatment. Additional analysis was performed in low-risk early stage cervical cancer patients with tumor size <2 cm.

2. Material and methods

2.1. Patients

After obtaining approval from the local institutional review board, medical records of patients with early stage cervical cancer from January 2000 to December 2008 from nine KGOG-affiliated institutions were retrospectively reviewed. All medical records were collected according to the protocol and case report forms approved by each institutional review board, which waived the requirement for informed consent. The inclusion criteria were as follows: patients with pathologically confirmed cervical cancer, a clinical diagnosis of FIGO stage (2014) IB-IIA disease [11], and who had undergone radical hysterectomy (type II or III) with pelvic and/or para-aortic lymphadenectomy. Patients treated with neoadjuvant chemotherapy before surgery, those with previous radiation therapy, those with cervical cancer incidentally found after simple hysterectomy, and those with rare cell types (mostly adenosquamous carcinoma and other types with neuroendocrine small cell carcinoma and clear cell carcinoma) were excluded. Patients with insufficient data were also excluded from analysis. Patients who had adjuvant treatment to surgery due to lymph node metastasis, parametrial involvement, and resection margin positive were additionally excluded. Analysis was performed with 738 patients who satisfied the eligibility criteria (laparoscopy 133, laparotomy 605) as shown in Fig. 1.

2.2. Clinical management

Patients were staged according to the FIGO staging system (2014) according to physical examination, chest X-ray, intravenous

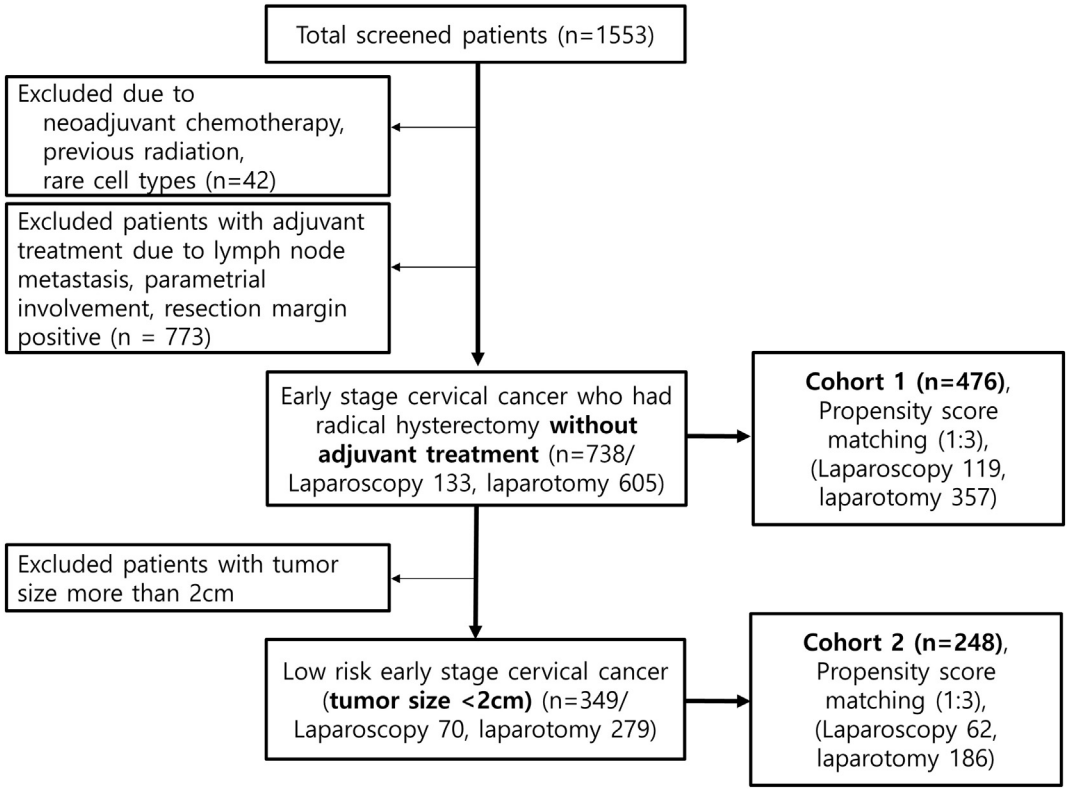

Fig. 1. Flowchart of patients included in the analysis.

Table 1
Characteristics of early stage cervical cancer cohort without adjuvant treatment ($n = 738$) and after matching (cohort 1, $n = 476$).

Characteristics	All patients (n = 738)		*P*-value	Cohort 1, after matching (n = 476)		*P*-value
	Laparoscopy ($n = 133$)	Laparotomy ($n = 605$)		Laparoscopy ($n = 119$)	Laparotomy ($n = 357$)	
Age, years, mean	45.2 ± 10.8	48.9 ± 11.2	0.001	45.6 ± 10.8	46.2 ± 10.5	0.628
FIGO Stage (%)			>0.999			>0.999
IB1	129 (97.0)	559 (92.4)		116 (97.5)	348 (97.5)	
IB2	0	0		0	0	
IIA1	4 (3.0)	46 (7.6)		3 (2.5)	9 (2.5)	
Histology (%)			0.155			0.599
Squamous cell carcinoma	91 (68.4)	453 (74.9)		82 (68.9)	257 (72.0)	
Adenocarcinoma	42 (31.6)	152 (25.1)		37 (31.1)	100 (28.0)	
Lymphovascular Space Invasion (%)			0.968			0.893
Negative	104 (81.2)	461 (81.9)		97 (81.5)	287 (80.4)	
Positive	24 (18.8)	102 (18.1)		22 (18.5)	70 (19.6)	
Invasion depth, (%)			0.039			0.721
Inner 1/3	65 (53.7)	321 (54.8)		65 (54.6)	210 (58.8)	
Middle 1/3	48 (39.7)	183 (31.2)		46 (38.7)	126 (35.3)	
Deep 1/3	8 (6.6)	82 (14.0)		8 (6.7)	21 (5.9)	
Lymph node metastasis (%)						
Negative	133 (100.0)	605 (100.0)		119 (100.0)	357 (100.0)	
Pelvic LN positive	0	0		0	0	
Paraaortic LN positive	0	0		0	0	
Parametrial involvement (%)						
Negative	133 (100.0)	605 (100.0)		119 (100.0)	357 (100.0)	
Positive	0	0		0	0	
Resection margin (%)						
Negative	134 (100.0)	605 (100.0)		119 (100.0)	357 (100.0)	
Positive	0	0		0	0	
Tumor size, cm, mean	1.8 ± 1.2	2.0 ± 1.3	0.210	1.8 ± 1.2	1.8 ± 1.1	0.789
Serum SCC level, ng/mL, mean	1.3 ± 1.7	1.3 ± 1.7	0.933	1.3 ± 1.7	1.1 ± 1.3	0.242
Recurrence type						
Pelvic	9 (6.8)	11 (1.8)	0.004	9 (7.5)	6 (1.7)	0.004
Lymphatic	1 (0.8)	7 (1.2)	>0.999	1 (0.8)	4 (1.1)	>0.999
Hematogenous	6 (4.5)	10 (1.7)	0.085	6 (5.0)	7 (2.0)	0.144

FIGO, International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; LN, lymph node; CIN, cervical intraepithelial neoplasia.

pyelography, and abdominopelvic computed tomography (CT) and/or magnetic resonance imaging (MRI) findings. Patients were treated and followed according to the guidelines at each institution. Tumor size was determined by clinical palpation or inspection; and in cases without clinical data, size was measured using CT or MRI. The surgical records of radical hysterectomy with pelvic lymphadenectomy, with or without para-aortic lymphadenectomy, were reviewed by investigators to determine the appropriateness of the surgical procedure as practice guidelines [12]. Pathological reports including histology, depth of invasion (divided into thirds), lymphovascular space invasion (LVSI), numbers of resected lymph nodes and positive nodes, parametrial involvement, and invasion of the resection margin were reviewed. Lymph node recurrence was defined as any lymph node >1 cm in diameter along the short axis on CT. All patients were examined regularly by physical examination and/or radiographic imaging work-ups at 3–6-month intervals after treatment. For imaging study during surveillance, chest radiography and abdominopelvic MRI or abdominopelvic CT scan were performed every 6 months for the first 3 years, and every 12 months thereafter or if indicated based on symptoms or examination findings suspicious for recurrence. Treatment response in patients with clinically visible tumors was determined by radiographic findings and assessed according to the revised Response Evaluation Criteria in Solid Tumors (RECIST, version 1.1) [13]. When lymphatic recurrence was suspected, needle biopsy was often performed. Hematogenous recurrence was defined as distant recurrence regardless of concurrent lymphatic recurrences. Pelvic recurrence was defined as recurrence in the pelvic area limited to the area below the pelvic brim. DFS was defined as the time interval from surgery to the first evidence of any recurrence or last follow-up. DFS to lymphatic recurrence or hematogenous recurrence was defined as the time interval from surgery to the first evidence of lymphatic or hematogenous recurrence, respectively. OS was described as the time interval from diagnosis to date of death or last follow-up.

2.3. Statistical analysis

We used summary statistics to describe the data. Median (range) or mean (standard deviation) were used for continuous variables. The Mann-Whitney test was used for comparing median values, and Student's *t*-test for comparing mean values was used after the Shapiro-Wilks test to confirm normal distributions. We presented categorical variables as frequency (percentage). We used Fisher's exact test or the χ^2 test for analyzing the distributions of characteristics according to surgical method. Analyses of survival curves were performed by the Kaplan–Meier method, and comparisons were made by the log-rank test, with calculation of a hazard ratio (HR), an accompanying 95% confidence interval (CI), and a *P* value. All *P* values were two-sided, and we considered P values <0.05 to be statistically significant. Statistical analyses were performed using R 3.3.2 (Vienna, Austria; http://www.R-project.org/).

In the cohort used for comparisons between two different surgical groups, propensity score matching was performed to reduce bias in further investigations. Patients treated with laparoscopy were nearest-neighbor 1:3 matched with the closest propensity patients who were treated with laparotomy according to variables of age, FIGO stage, histology, and risk factors such as LVSI, depth of invasion, and tumor size (performed with R using the MatchIt package).

3. Results

3.1. Characteristics of early stage cervical cancer patients who had surgical treatment without adjuvant treatment (cohort 1)

Among a total of 1553 patients for whom we collected KGOG 1028 data, 42 met the exclusion criteria (i.e., neoadjuvant chemotherapy, previous radiation, and rare cell type) (Fig. 1), leaving 1511 early stage (IB1, IB2, IIA1) cervical cancer patients initially enrolled for analysis.

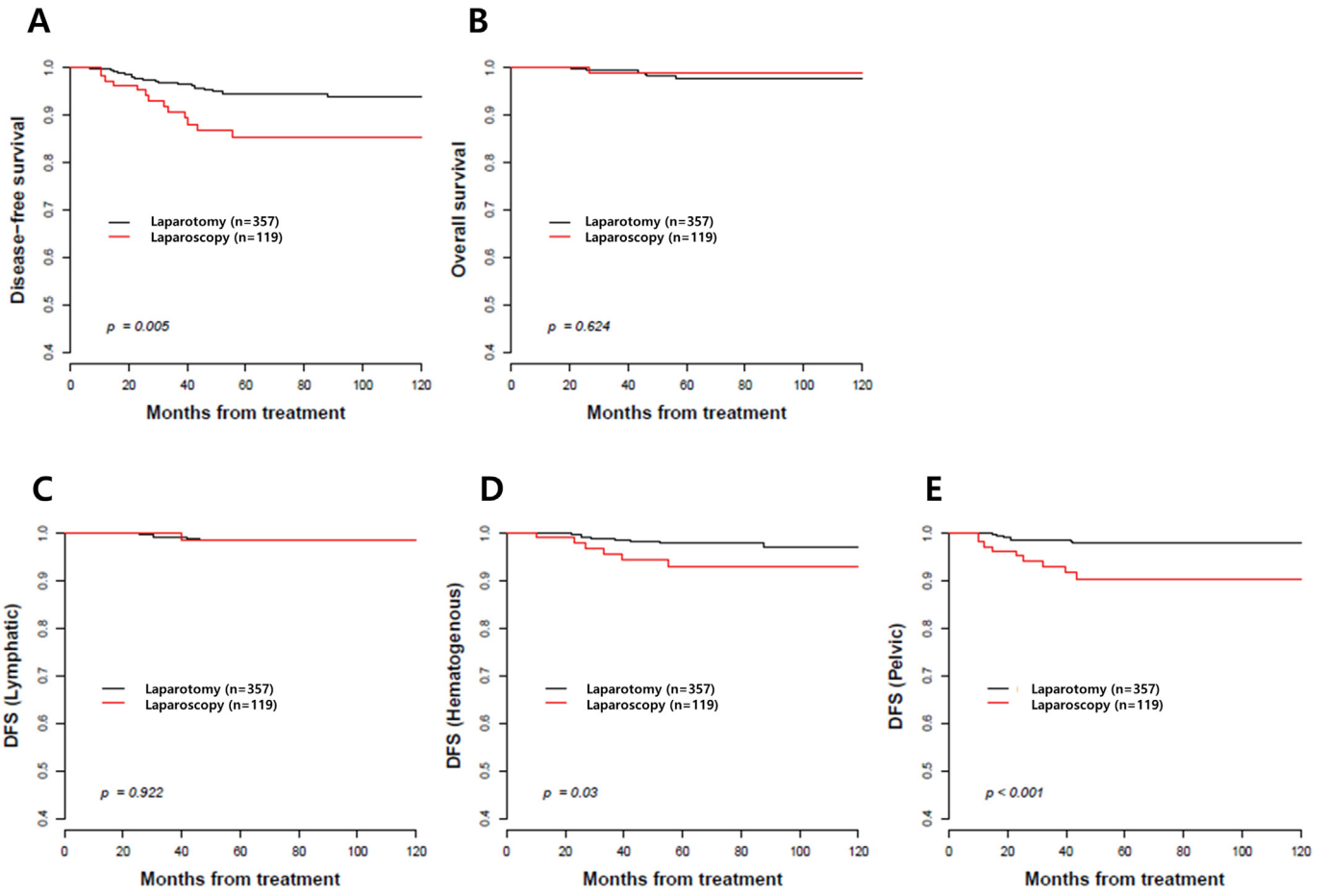

Fig. 2. Kaplan-Meier curves of (A) DFS, (B) OS, (C) lymphatic recurrence, (D) hematogenous recurrence, and (E) pelvic recurrence in early stage cervical cancer patients without adjuvant treatment after propensity score matching. OS, overall survival; DFS, disease-free survival.

Additionally, 773 patients who had adjuvant treatment to surgery due to lymph node metastasis, parametrial involvement, and resection margin positive were excluded. We used data of 738 patients (laparoscopy 133, laparotomy 605) of early stage cervical cancer without adjuvant treatment to surgery for analysis. After a median follow-up period of 63.6 months (range, 3.0–183.3 months), 33 patients experienced recurrences, and there were 13 deaths. In comparisons of patients who underwent laparoscopic radical hysterectomy ($n = 133$) or abdominal radical hysterectomy ($n = 605$) in patients without adjuvant treatment, age, and depth of invasion, showed significant differences between groups (Table 1). Propensity score matching was performed to reduce bias when comparing the two groups of patients, and matching was successful with no significant differences between the two groups for all matched variables (S1). After propensity score matching, a total of 476 patients was analyzed for survival comparisons, with no significant differences between the two groups for any of the matched variables (cohort 1, median follow-up period of 63.9 months [range, 3.0–183.3 months], median age; 45 years [range 22–77], 119 patients with laparoscopy vs. 357 patients with laparotomy) (Table 1).

3.2. Survival outcomes after propensity score matching

A total of 33 recurrences were observed in low-risk patients. The types of recurrence differed between groups. In the laparoscopy group (total 16 recurrences, 13.3%), 9 cases with pelvic recurrence (7.5% of laparoscopy patients), 6 hematogenous recurrences (5.0%), and 1 lymphatic recurrence (0.8%) were observed (Table 1). In the laparotomy group (total 17 recurrences, 4.8%), hematogenous recurrence was seen in 7 cases (2.0% of laparotomy patients), pelvic recurrence in 6 patients (1.7%), and lymphatic recurrence observed in 4 patients (1.1%). We observed 6 deaths in patients treated with laparoscopy and 1 in patients treated with laparotomy.

The results of survival analysis of patients after propensity score matching with Kaplan-Meier curves are shown in Fig. 2. Patients treated with laparoscopy showed inferior DFS (median DFS, 53.6 vs. 67.5 months; HR 2.738 [95% CI 1.326–5.650], $p = 0.005$, Fig. 2-A), although there was no significant difference in OS between the two groups (HR 0.592 [95% CI 0.071–4.922], $p = 0.624$, Fig. 2-B). In analyses of each type of recurrence, significant differences between groups were observed for pelvic recurrence (HR 5.110 [95% CI 1.817–14.473], $p < 0.001$, Fig. 2-E) and hematogenous recurrence (HR 3.171 [95% CI 1.059–9.494], $p = 0.03$, Fig. 2-D) but not for lymphatic recurrence (HR 0.897 [95% CI 0.100–8.027], $p = 0.922$, Fig. 2-C).

3.3. Survival outcomes of low-risk early stage cervical cancer patients with tumor size <2 cm (cohort 2)

For comparisons in low-risk patients, we excluded patients with tumor size <2 cm (Fig. 1). There were 349 low-risk early stage cervical cancer patients (70 laparoscopy, 279 laparotomy, Table 2), and 1:3 propensity score matching was performed (S2). A total of 248 patients were analyzed for survival comparisons, with no significant differences between the two groups for any of the matched (cohort 2, median follow-up period of 69.1 months [range, 3.0–173.3 months], median age; 45 years [range 24–77], 62 patients with laparoscopy vs. 186 patients with laparotomy) (Table 2).

A total of 7 recurrences was observed in low-risk patients with tumor size <2 cm. In the laparoscopy group (total 6 recurrences, 9.6%),

Table 2
Characteristics of low-risk early stage cervical cancer cohort (<tumor size 2 cm) without adjuvant treatment ($n = 349$), and after matching (cohort 2, $n = 248$).

Characteristics	All patients (n = 349)		*P*-value	Cohort 2, after matching (n = 248)		*P*-value
	Laparoscopy ($n = 70$)	Laparotomy ($n = 279$)		Laparoscopy ($n = 62$)	Laparotomy ($n = 186$)	
Age, years, mean	45.4 ± 10.8	49.0 ± 10.7	0.013	46.3 ± 10.7	46.6 ± 9.4	0.839
FIGO Stage (%)			0.026			0.434
IB1	70 (100.0)	267 (95.7)		62 (100.0)	181 (97.3)	
IB2	0	0		0	0	
IIA1	0	12 (4.3)		0	5 (2.7)	
Histology (%)			0.463			0.872
Squamous cell carcinoma	48 (68.6)	206 (73.8)		43 (69.4)	133 (71.5)	
Adenocarcinoma	22 (31.4)	73 (26.2)		19 (30.6)	53 (28.5)	
Lymphovascular Space Invasion (%)			0.801			0.804
Negative	59 (86.8)	220 (84.6)		55 (88.7)	169 (90.9)	
Positive	9 (13.2)	40 (15.4)		7 (11.3)	17 (9.1)	
Invasion depth (%)			0.039			0.381
Inner 1/3	45 (71.4)	208 (77.0)		45 (72.6)	147 (79.0)	
Middle 1/3	18 (28.6)	49 (18.1)		17 (27.4)	39 (21.0)	
Deep 1/3	0	13 (4.8)		0	0	
Lymph node metastasis (%)						
Negative	70 (100.0)	279 (100.0)		62 (100.0)	186 (100.0)	
Pelvic LN positive	0	0		0	0	
Paraaortic LN positive	0	0		0	0	
Parametrial involvement (%)						
Negative	70 (100.0)	279 (100.0)		62 (100.0)	186 (100.0)	
Positive	0	0		0	0	
Resection margin (%)						
Negative	70 (100.0)	279 (100.0)		62 (100.0)	186 (100.0)	
Positive	0	0		0	0	
Tumor size, cm, mean	1.0 ± 0.5	0.9 ± 0.6	0.443	1.0 ± 0.5	0.9 ± 0.6	0.509
Serum SCC level, ng/mL, mean	1.0 ± 0.5	1.0 ± 1.6	0.582	1.0 ± 0.5	1.1 ± 1.9	0.529
Recurrence type						
Pelvic	3 (4.3)	3 (1.1)	0.182	3 (4.8)	1 (0.5)	0.081
Lymphatic	1 (1.4)	1 (0.4)	0.861	1 (1.6)	0	0.563
Hematogenous	1 (0.4)	1 (0.4)	0.193	2 (3.2)	0	0.101

FIGO, International Federation of Gynecology and Obstetrics; SCC, squamous cell carcinoma; LN, lymph node; CIN, cervical intraepithelial neoplasia.

3 cases with pelvic recurrence (4.8% of laparoscopy patients), 2 hematogenous recurrences (3.2%), and 1 lymphatic recurrence (1.6%) were observed (Table 2). In the laparotomy group, only 1 pelvic recurrence (0.5%) was observed. We observed 1 death with laparotomy in this patients group.

Kaplan-Meier curves for DFS and OS comparing the two surgical groups are shown in Fig. 3. Patients treated with laparoscopy showed inferior DFS (HR 12.987 [95% CI 1.451–116.244], $p = 0.003$, Fig. 3-A), although there was no significant difference in OS between the two groups ($p = 0.562$, HR not calculated, Fig. 3-B). Significant differences between groups were observed for pelvic recurrence ($p = 0.016$, HR not calculated, Fig. 3-E) and hematogenous recurrence ($p = 0.011$, HR not calculated, Fig. 3-D) but not for lymphatic recurrence ($p = 0.064$, HR not calculated, Fig. 3-C).

4. Discussion

Our results demonstrated a significant difference in DFS between patients treated with laparoscopic radical hysterectomy and abdominal radical hysterectomy in early stage cervical cancer patients without adjuvant treatment and additionally, with less than tumor size 2 cm. Inferior DFS was shown in the laparoscopy group, but there was no significant difference for OS. We compared survival outcomes according to surgical method in early stage cervical cancer patients without adjuvant treatment and with tumor size <2 cm using retrospective data from a KGOG-affiliated multi-institutional cohort, which was designed for developing a prognostic model for early stage cervical cancer patients.

In our study, we sought to provide additional information to previous studies. A recent phase 3, multicenter, prospective randomized trial, known as the LACC Trial, concluded that minimally invasive radical hysterectomy was associated with lower rates of DFS and OS in cervical cancer patients [10]. Before the LACC trial, most retrospective studies comparing outcomes between laparoscopy and laparotomy in cervical cancer showed no significant differences in survival. A meta-analysis of 22 studies by Cao et al. [14] and a meta-analysis of 12 studies by Wang et al. [8] comparing surgical methods showed no significant differences in DFS and OS rates between laparoscopy and laparotomy. Regarding intraoperative and short-term postoperative outcomes, another meta-analysis suggested that robotic radical hysterectomy is superior to the abdominal approach, with less blood loss, shorter hospital stay, less febrile morbidity, and fewer wound-related complications [15]. These previous retrospective studies had main limitations including lack of information or short follow-up times. The LACC trial has strengths including its design as a prospective, randomized trial that included a large number of centers worldwide, and we intended to provide more information to previous studies.

We observed a lower rate of DFS in the laparoscopy group, but OS did not differ significantly between groups. Reasons for inferior DFS in patients treated by the laparoscopic approach may include increased tumor spillage due to use of a uterine manipulator or exposure of tumor cells by intracorporeal colpotomy [16] or tumor cell growth and spread by use of insufflation gas (CO_2) in laparoscopy [17]. However, it is difficult to explain how differences in DFS did not lead to differences in OS. The main reason may be related to small number of patients for differences in OS to be shown (only seven deaths in cohort 1, and one death in cohort 2 were observed). In cohort 1, six deaths in laparoscopy group and only one death in laparotomy group were shown. Although statistical significance was not shown, it may be meaningful difference in small number of cohort, and it is assumed that significant difference of OS would be shown in larger number of cohort. Also, there was a difference in pattern of recurrence between surgical groups. Pelvic recurrence was more frequent in the laparoscopy group than in the laparotomy group. For patients who did not have previous radiotherapy, better response to salvage therapy can be expected in patients with pelvic recurrence. *Re*-irradiation historically had been associated with unacceptable toxicity and limited benefit, although

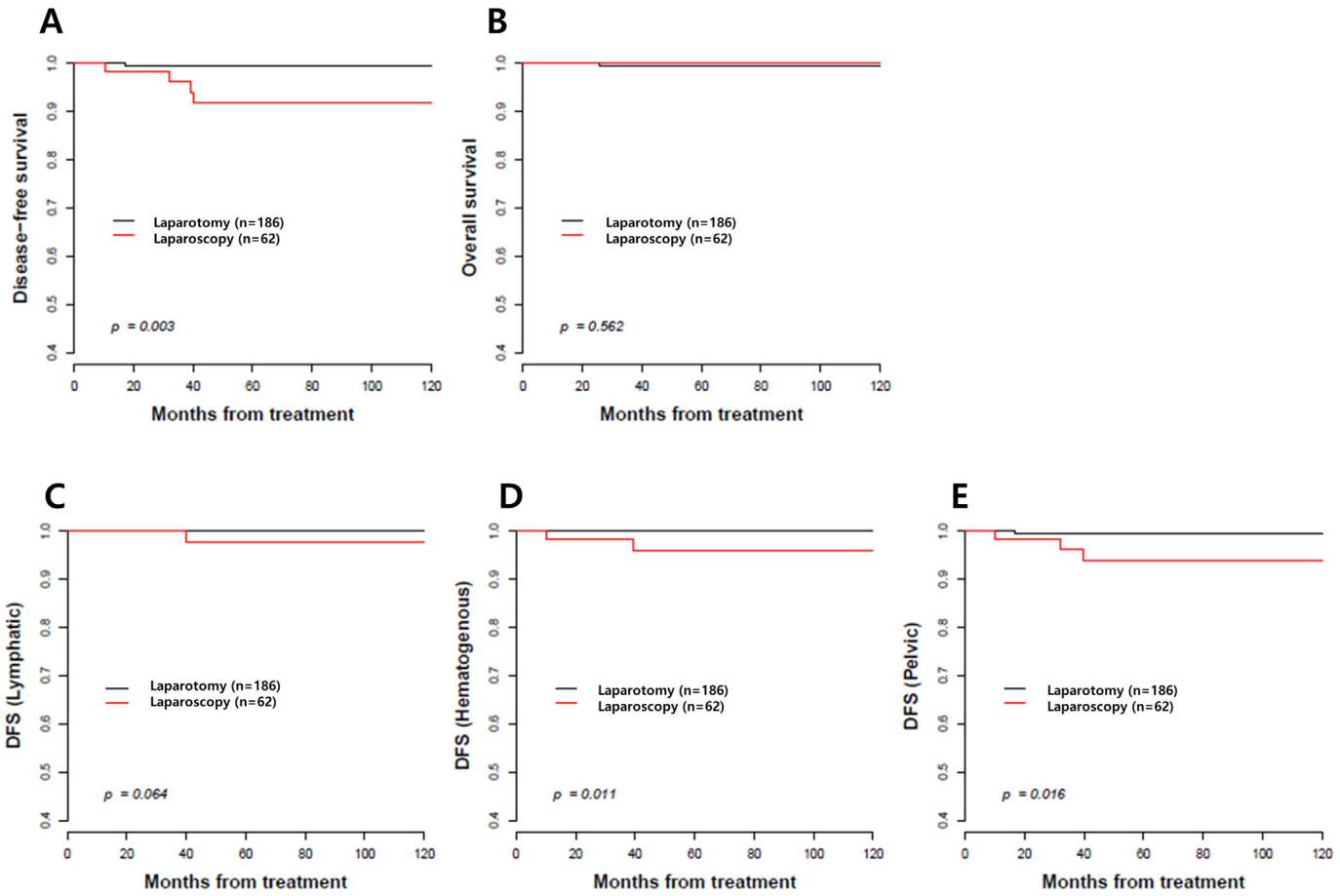

Fig. 3. Kaplan-Meier curves of (A) DFS, (B) OS, (C) lymphatic recurrence, (D) hematogenous recurrence, and (E) pelvic recurrence low risk early stage cervical cancer cohort (<tumor size 2 cm) without adjuvant treatment after matching. OS, overall survival; DFS, disease-free survival.

recent advances in radiotherapy are changing the treatment paradigm to provide new salvage treatments for recurrences of cervical and endometrial cancer [18]. Re-irradiation for pelvic recurrence of cancer improved symptoms of patients but the rate of late toxicity was high, and re-irradiation could be considered as a possible option for pelvic recurrence only in selected patients [19]. Considering that there were more cases of pelvic recurrence in the laparoscopy group, we hypothesize that the inferior DFS in the laparoscopy group compensated for OS due to better response to salvage therapy and better treatment outcomes in patients with pelvic recurrence. The mechanism underlying these observations should be elucidated in future studies.

The strength of our study is that we analyzed data of low-risk early stage cervical cancer patients. Results of adjuvant treatment to surgery could interfere with evaluation for outcomes of surgical treatment. Using patients group only with primary surgical treatment, outcomes of surgery could be more clearly determined. Also, our study used data with a relatively long follow-up period (median 63.9 months), and multicenter data with a wider range of population groups for better generalizability. However, there are a number of potential limitations in the current study. This study is based on data that were previously collected for a retrospective multicenter study. Therefore, our study may have biases including patient selection, random assignment, and incomplete data collection. Due to the retrospective nature, we inevitably used prior FIGO classification (2014) for cervical cancer [11], and we were unable to assess more information regarding surgical outcomes, including intraoperative or postoperative complications. Also, pathology was not centrally reviewed for analysis as we used previously interpreted result of each institution. In addition to limitations and biases associated with its retrospective nature, this study analyzed a small number of patients in surgical method comparisons. The KGOG 1028 study included data for early stage cervical cancer patients treated from 2000 to 2008, and laparoscopic radical hysterectomy was not popular during that period. We were able to perform analyses using only limited number of patients treated with laparoscopic surgery and compared these patients to the laparotomy group after propensity score matching. Finally, racial differences were not considered because patients treated at KGOG affiliated institutions are predominantly East Asian.

Despite these limitations, our results showed that low-risk early stage cervical cancer patients who underwent surgery without adjuvant treatment and with tumor size <2 cm, laparoscopic approach showed poorer outcomes for DFS, specifically for pelvic and hematogenous recurrence. These data provide additional information regarding surgical method comparisons in the treatment of early stage cervical cancer. However, further large scale studies should be elucidated in the future for specific subgroup of patients.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2019.06.023.

Declaration of Competing Interest

The authors report no conflict of interest.

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Author contribution

E Sun Paik: Data analysis and interpretation, manuscript writing, and final approval of manuscript.

Myong Cheol Lim: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

Moon-Hong Kim: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

Yun Hwan Kim: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

Eun Seop Song: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

Seok Ju Seong: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

Dong Hoon Suh: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

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Chulmin Lee: Provision of study materials or patients, collection and assembly of data, data analysis and interpretation, and final approval of manuscript.

Chel Hun Choi: Conception and design, provision of study materials of patients, collection and assembly of data, data analysis and interpretation, manuscript writing, and final approval of manuscript.

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