International Journal of Clinical Oncology (2024) 29:1380–1390
https://doi.org/10.1007/s10147-024-02560-w

ORIGINAL ARTICLE

Prognostic significance of adjuvant chemotherapy in stage I–II endometrial carcinoma patients who underwent lymphadenectomy

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Received: 17 February 2024 / Accepted: 22 May 2024 / Published online: 19 June 2024

Abstract

Background Endometrial carcinoma, the most common gynecologic carcinoma, has an excellent prognosis post-surgery when diagnosed early. The role of postoperative adjuvant chemotherapy in stages I–II endometrial carcinoma remains controversial. This study assesses the efficacy of adjuvant chemotherapy in improving prognosis for these patients.

Methods A retrospective analysis was conducted on 1223 stage I–II endometrial carcinoma patients who underwent surgical treatment including total hysterectomy, bilateral salpingo-oophorectomy, and lymph-node biopsy or dissection across four Jikei University School of Medicine-affiliated facilities between 2001 and 2018. Patients were divided into low intermediate risk (LIR) and high intermediate risk (HIR) groups based on recurrence risk. Propensity score matching adjusted for various covariates was used to compare progression-free survival (PFS) and overall survival (OS) between patients who received adjuvant chemotherapy and those who did not.

Results The study included 443 eligible patients, with 288 in the LIR group and 155 in the HIR group. Post propensity score matching, no significant difference in PFS or OS was observed between the observation and adjuvant chemotherapy groups within both risk categories. Notably, the 5-year OS for LIR was 97.6% in the observation group and 96.7% in the chemotherapy group; for HIR, the 5-year OS was similarly high with no significant difference.

Conclusions The findings suggest that postoperative adjuvant chemotherapy does not significantly contribute to the improvement of recurrence or prognosis in patients with stage I–II endometrial carcinoma who are categorized outside the low-risk group and have no lymph-node metastasis.

Keywords Endometrial carcinoma · Adjuvant chemotherapy · Staging · Lymph-node excision

Introduction

Endometrial carcinoma is the most common gynecologic malignancy [1, 2]. In Japan, the number of patients has increased in recent years, reaching approximately 17,880 in 2019. The percentage of each surgical stage according to FIGO 2008 for endometrial carcinoma in Japan is as follows: stage IA, 57.1%; stage IB, 15.4%; and stage II, 5.7%, whereas early-stage carcinoma confined within the uterus accounts for 78.4% of all patients. The 5-year survival rate is 95.3% for stage IA, 88.8% for stage IB, and 87.6% for stage II, which has an excellent prognosis [3]. The standard treatment for endometrial carcinoma is surgery, which includes total hysterectomy and bilateral salpingo-oophorectomy, whereas staging laparotomy includes biopsy or dissection of the regional lymph nodes of the pelvic and para-aortic retroperitoneal lymph nodes, omentectomy, and ascites cytology

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or peritoneal washing cytology. Regarding the therapeutic significance of staging laparotomy, there are no reports of a clear prognostic improvement in stage I–II patients [4, 5]. A randomized phase III trial is ongoing to determine the prognostic benefit of retroperitoneal lymph-node dissection. However, if metastases are detected by retroperitoneal lymph-node biopsy or dissection, even if the disease is confined to the uterus, the disease is considered stage III, and the 5-year survival rate decreases to 71.4%. Therefore, an accurate diagnosis of the disease stage is important. In Japan, > 90% of the hospitals perform retroperitoneal lymph-node biopsy or dissection, albeit with some conditions [6].

Postoperative adjuvant therapy is determined by classifying risk of postoperative recurrence into low, intermediate, and high categories based on the stage and pathologic factors, which includes histologic type, differentiation, myometrial invasion, vascular invasion, and cervical stromal invasion [7–9]. For the low-risk group, the prognosis with surgery alone is excellent, so postoperative adjuvant therapy is not recommended [10–12]. For the high-risk group, however, chemotherapy and radiation therapy are recommended [13–16]. The need for adjuvant therapy for the intermediate-risk group is controversial and adjuvant therapy is administered on an individualized basis. A Japanese report indicated that approximately 70% of patients in the intermediate-risk group receive adjuvant chemotherapy [17]. Several randomized trials have examined the benefit of postoperative adjuvant therapy for patients in the intermediate-risk group, however, the benefit of postoperative adjuvant therapy for surgery alone has not been evaluated [15, 16, 18]. Furthermore, because most studies included stage III–IV patients, the contribution of adjuvant therapy to prognosis is unclear for stage I–II patients, excluding the low-risk group. In the present study, we examined the efficacy of postoperative adjuvant chemotherapy for surgery alone in stage I–II patients, excluding the low-risk group, who were accurately diagnosed and staged by performing pelvic and para-aortic lymph-node biopsy or dissection as a staging laparotomy.

Patients and methods

Study population

Between 2001 and 2018, 1,971 patients who underwent surgery as initial treatment for pathologically diagnosed endometrial carcinoma at four facilities affiliated with The Jikei University School of Medicine were reviewed to identify eligible patients. The patients were diagnosed as stage I–II by staging laparotomy, including total hysterectomy, bilateral salpingo-oophorectomy, and biopsy or dissection of the pelvic and para-aortic lymph nodes. Any method of hysterectomy was considered acceptable. For patients who did not undergo para-aortic lymph-node biopsy or dissection, a preoperative CT scan confirmed the absence of obvious para-aortic lymph- node enlargement. Cases of minimally invasive surgery were excluded because laparoscopic surgery and robot-assisted surgery are not covered by insurance in Japan for stages IB and II, and resulting in a small number of such cases. Patients with histological types other than endometrioid, serous, clear cell, or mucinous carcinoma were excluded as well as carcinosarcoma, mixed carcinoma, synchronous tumor, low-risk group for postoperative recurrence, and patients with insufficient data (Fig. 1). The diagnosis of stage was done according to FIGO 2008 [19]. The risk of postoperative recurrence was classified according to the risk classification of the Japanese Society of Gynecologic Oncology [9] (Fig. 2).

Methods

The follow-up period, age, histological type, surgical method, histopathological diagnosis (ascites cytology, myometrial invasion, vascular invasion, cervical stromal invasion), surgical stage, postoperative adjuvant chemotherapy, recurrence, and prognosis were retrospectively extracted from the medical records. Recurrence was assessed based on imaging or histological diagnosis. Patients were classified into two groups: a low intermediated risk (LIR) and a high Intermediate risk (HIR) group. LIR was defined as an intermediate-risk group for recurrence in stage I–II, and HIR was defined as a high-risk group for recurrence in stage I–II. We summarized the clinicopathological characteristics of the observation and adjuvant chemotherapy groups in LIR and HIR. For each group, progression-free survival (PFS) and overall survival (OS) with and without adjuvant chemotherapy were evaluated. This study was approved by The Jikei University School of Medicine IRB [IRB No. 33–203 (10,820)].

Statistical analysis

The observation and adjuvant chemotherapy groups were compared using t tests for continuous variables and a Fisher's exact test for categorical variables. Survival analyses were done using propensity score matching to reduce bias from confounding factors and estimate the effects of postoperative adjuvant chemotherapy. Propensity scores were estimated with a multiple logistic model using age, histology, extent of lymph-node dissection, ascites cytology, myometrial invasion, vascular invasion, cervical stromal invasion, and surgical stage as covariates to match patients receiving adjuvant chemotherapy with those observed. The patients were matched by one-to-one nearest neighbor matching with a predefined caliper width of 0.2. To ensure that the two groups were comparable, we examined

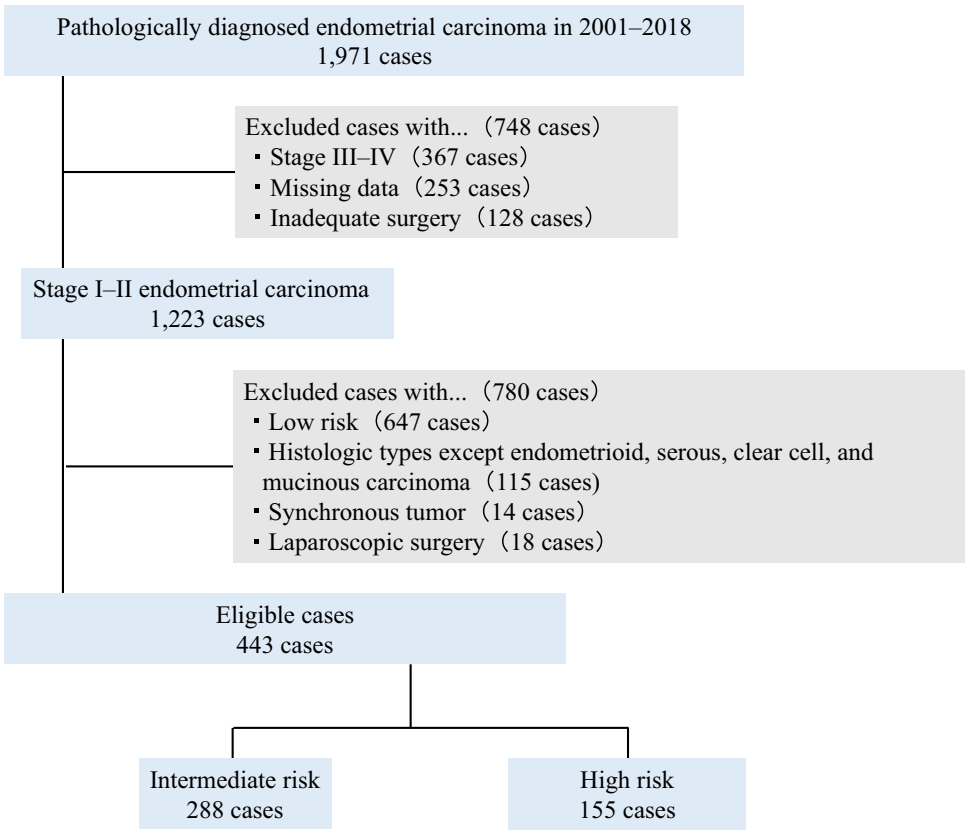

Fig. 1 Outline of cohort selection

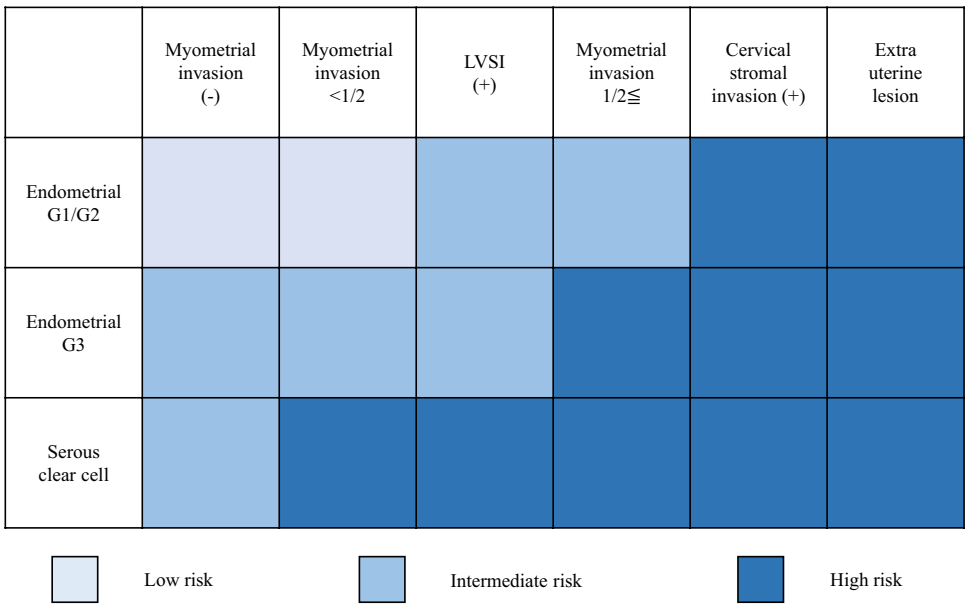

Fig. 2 Recurrence risk classification of the Japanese Society of Gynecologic Oncology. *LVSI* lymphovascular space invasion, *G* grade

LVSI, lymphovascular space invasion; G, grade.

the balance of covariate distribution using standardized mean differences. The PFS and OS of the two groups were compared using the Kaplan–Meier survival curve. The log-rank test was used to assess differences between the two groups in terms of PFS and OS. The Cox proportional hazards model was used to examine independent

prognostic factors and hazard ratios and corresponding 95% confidence intervals were calculated. OS was defined as the period from the date of the first surgery to the date of the last confirmed survival from any cause. PFS was defined as the period from the date of the first surgery to the date of disease progression, or the date of the last confirmed survival without progression. Two-tailed p values were calculated and p values < 0.05 were considered statistically significant. All statistical analyses were performed using EZR software (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria) [20].

Results

Patient characteristics

Of the 1223 stage I–II patients who underwent total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph-node biopsy or dissection as staging laparotomy, 443 patients (LIR group: 288 patients, HIR group: 155 patients) were considered eligible for this study (Table 1).

LIR

Patient characteristics before and after propensity score matching are listed in Table 1. Of the 288 patients before propensity score matching, 153 were in the observation group and 135 were in the adjuvant chemotherapy group. The median follow-up period was 1820 days (60.6 months) and 2143 days (71.4 months). The median age was 64 years and 60 years, respectively. For the adjuvant chemotherapy group, there were significantly more patients with positive ascites cytology ($P = 0.040$) and positive vascular invasion ($P = 0.001$); however, no significant differences were evident for other histopathological factors. The number of recurrences was 18 and 13 patients, and the number of deaths was 5 and 5 patients, respectively.

Because of propensity score matching, we were able to match 101 patients in the observation group and 101 patients in the adjuvant chemotherapy group on a one-to-one basis. The median follow-up period was 1,827 days (60.9 months) and 1,902 days (63.4 months), whereas the median age was 59 years and 61 years, respectively. A matched cohort was created with no significant difference in histopathological factors between the two groups. The number of recurrences was 14 and 11 patients, and the number of deaths was 4 and 3 patients, respectively.

HIR

Patient characteristics before and after propensity score matching are listed in Table 2. Of the 155 patients before propensity score matching, 50 were in the observation group and 105 were in the adjuvant chemotherapy group. The median follow-up period was 1854 days (61.8 months) and 1895 days (63.2 months). The median age was 63 years and 61 years, respectively. For the adjuvant chemotherapy group, significantly more patients with Type 2 histology ($P = 0.021$), para-aortic to pelvic lymph-node dissection ($P < 0.001$), $\geq 1/2$ muscle layer involvement ($P < 0.001$), positive vascular invasion ($P < 0.001$), and FIGO classification stage IB ($P = 0.01$) were observed. The number of recurrences was 7 and 10 patients, whereas the number of deaths was 7 and 5 patients, respectively.

Because of propensity score matching, 35 patients were matched in the observation group with 35 patients in the adjuvant chemotherapy group on a one-to-one basis. The median follow-up period was 1,713 days (57.1 months) and 1000 days (33.3 months), whereas the median age was 66 years and 63 years, respectively. A matched cohort was created with no significant differences in histopathological factors between the two groups. The number of recurrences was five and three patients, and the number of deaths was five and two patients, respectively.

Overall survival and progression-free survival

LIR

Before propensity score matching, the 5-year PFS for the observation and adjuvant chemotherapy groups was 86.3% and 89.5%, respectively, and the 10-year PFS was 84.6% and 89.5%, with no significant difference ($P = 0.375$). Furthermore, the 5-year OS was 97.5% and 95.7%, whereas the 10-year OS was 93.7% and 95.7%, respectively, with no significant difference ($P = 0.90$). In the subgroup analysis of PFS, adjuvant chemotherapy was associated with an improvement in PFS in the LVSI-positive subgroup. Still, no difference was observed between the adjuvant chemotherapy group and the observation group in other subgroups. In addition, in the subgroup analysis of OS, no difference was observed between the two groups in any subgroup (Supplementary Table 1). After adjusting the patient characteristics by propensity score matching, the 5-year PFS of the observation group and the adjuvant chemotherapy group was 81.4% and 87.8%, respectively, the 10-year PFS was 81.4% and 87.8% ($P = 0.455$), the 5-year OS was 97.6% and 96.7%, and the 10-year OS was 92.0% and 96.7%, respectively, with no significant difference between the two groups ($P = 0.605$)

Table 1 Patient characteristics before and after propensity score matching in LIR

Characteristics	Before propensity score matching, *n* (%)					After propensity score matching, *n* (%)				
	All patients (*n* = 288)	Observation (*n* = 153)	Chemotherapy (*n* = 135)	*p*-value	SMD	All patients (*n* = 202)	Observation (*n* = 101)	Chemotherapy (*n* = 101)	*p*-value	SMD
Follow-up period (days)										
Median (range)	1861 (59–5363)	1820 (96–4859)	2143 (59–5363)			1832 (59–5363)	1827 (96–4859)	1902 (59–5363)		
Age (years)				0.002	0.372				0.343	0.134
Median (range)	61 (30–82)	64 (39–82)	60 (30–82)			60 (39–82)	59 (39–79)	61 (43–82)		
Histology type				0.351	0.115				1.000	0.023
Type 1	212 (73.6)	109 (71.2)	103 (76.3)			151 (74.8)	76 (75.2)	75 (74.3)		
Type 2	76 (26.4)	44 (28.8)	32 (23.7)			51 (25.2)	25 (24.8)	26 (25.7)		
Lymphadenectomy				0.278	0.14				0.771	0.062
PLN	173 (60.1)	87 (56.9)	86 (63.7)			127 (62.9)	65 (64.4)	62 (61.4)		
PLN-PAN	115 (39.9)	66 (43.1)	49 (36.3)			75 (37.1)	36 (35.6)	39 (38.6)		
Peritoneal cytology				0.040	0.254				1.000	< 0.001
Negative	229 (79.5)	129 (84.3)	100 (74.1)			160 (79.2)	80 (79.2)	80 (79.2)		
Positive	59 (20.5)	24 (15.7)	35 (25.9)			42 (20.8)	21 (20.8)	21 (20.8)		
Myometrial invasion				0.548	0.081				1.000	0.02
< 1/2	117 (40.6)	65 (42.5)	52 (38.5)			85 (42.1)	43 (42.6)	42 (41.6)		
1/2≦	171 (59.4)	88 (57.5)	83 (61.5)			117 (57.9)	58 (57.4)	59 (58.4)		
LVSI				0.001	0.406				0.770	0.062
Negative	189 (65.6)	114 (74.5)	75 (54.7)			129 (63.9)	66 (65.3)	63 (62.4)		
Positive	99 (34.4)	39 (25.5)	60 (44.4)			73 (36.1)	35 (34.7)	38 (37.6)		
Cervical stromal invasion				-	-				-	-
Negative	288 (100.0)	153 (100.0)	135 (100.0)			202 (100.0)	101 (100.0)	101 (100.0)		
Positive	0	0	0			0	0	0		
FIGO stage				0.472	0.094				1.000	0.02
IA	118 (41.0)	66 (43.1)	52 (38.5)			85 (42.1)	43 (42.6)	42 (41.6)		
IB	170 (59.0)	87 (56.9)	83 (61.5)			117 (57.9)	58 (57.4)	59 (58.4)		
Recurrence	31 (10.8)	18 (11.8)	13 (9.6)			25 (12.4)	14 (13.9)	11 (10.9)		
Death	10 (3.5)	5 (3.3)	5 (3.7)			7 (3.5)	4 (4.0)	3 (3.0)		

LIR low intermediate risk, *PLN* pelvic lymphadenectomy, *PAN* para-aortic lymphadenectomy, *LVSI* lymphovascular space invasion, *FIGO* International Federation of Gynecology and Obstetrics, *SMD* standardized mean difference

P values were calculated by the Fisher's exact test

Table 2 Patient characteristics before and after propensity score matching in HIR

Characteristics	Before propensity score matching, *n* (%)					After propensity score matching, *n* (%)				
	All patients (*n* = 155)	Observation (*n* = 50)	Chemotherapy (*n* = 105)	*p*-value	SMD	All patients (*n* = 70)	Observation (*n* = 35)	Chemotherapy (*n* = 35)	*p*-value	SMD
Follow-up period (days)										
Median (range)	1884 (12–4465)	1854 (12–4067)	1895 (14–4465)			1164 (12–4445)	1713 (12–4067)	1000 (14–4445)		
Age (years)				0.084	0.289				0.438	0.187
Median (range)	62 (32–86)	63 (41–86)	61 (32–80)			64 (32–86)	66 (41–86)	63 (32–80)		
Histology type				0.021	0.427				1.000	0.058
Type 1	59 (38.1)	26 (52.0)	33 (31.4)			31 (44.3)	15 (42.9)	16 (45.7)		
Type 2	96 (61.9)	24 (48.0)	72 (68.6)			39 (55.7)	20 (57.1)	19 (54.3)		
Lymphadenectomy				< 0.001	0.781				1.000	0.064
PLN	87 (56.1)	40 (80.0)	47 (44.8)			51 (72.9)	25 (71.4)	26 (74.3)		
PLN-PAN	68 (43.9)	10 (20.0)	58 (55.2)			19 (27.1)	10 (28.6)	9 (25.7)		
Peritoneal cytology				0.105	0.356				1.000	< 0.001
Negative	143 (92.3)	49 (98.0)	94 (89.5)			68 (97.1)	34 (97.1)	34 (97.1)		
Positive	12 (7.7)	1 (2.0)	11 (10.5)			2 (2.9)	1 (2.9)	1 (2.9)		
Myometrial invasion				< 0.001	0.834				1.000	0.057
< 1/2	65 (41.9)	34 (68.0)	31 (29.5)			37 (52.9)	19 (54.3)	18 (51.4)		
1/2≦	90 (58.1)	16 (32.0)	74 (70.5)			33 (47.1)	16 (45.7)	17 (48.6)		
LVSI				< 0.001	0.759				1.000	0.062
Negative	88 (56.8)	40 (80.0)	48 (45.7)			49 (70.0)	25 (71.4)	24 (68.6)		
Positive	67 (43.2)	10 (20.0)	57 (54.3)			21 (30.0)	10 (28.6)	11 (31.4)		
Cervical stromal invasion				0.229	0.231				1.000	< 0.001
Negative	74 (47.7)	20 (40.0)	54 (51.4)			34 (48.6)	17 (48.6)	17 (48.6)		
Positive	81 (52.3)	30 (60.0)	51 (48.6)			36 (51.4)	18 (51.4)	18 (51.4)		
FIGO Stage				0.01	0.541				1.000	< 0.001
IA	24 (15.5)	12 (24.0)	12 (11.4)			16 (22.9)	8 (22.9)	8 (22.9)		
IB	51 (32.9)	9 (18.0)	42 (40.0)			18 (25.7)	9 (25.7)	9 (25.7)		
II	80 (51.6)	29 (58.0)	51 (48.6)			36 (51.4)	18 (51.4)	18 (51.4)		
Recurrence	17 (11.0)	7 (14.0)	10 (9.5)			8 (11.4)	5 (14.3)	3 (8.6)		
Death	12 (7.7)	7 (14.0)	5 (4.8)			7 (10.0)	5 (14.3)	2 (5.7)		

HIR high intermediate risk, *PLN* pelvic lymphadenectomy, *PAN* para-aortic lymphadenectomy, *LVSI* lymphovascular space invasion, *FIGO* International Federation of Gynecology and Obstetrics, *SMD* standardized mean difference

P values were calculated by the Fisher's exact test

(Fig. 3). No difference in the improvement of PFS and OS was observed in all subgroups between the two groups (Supplementary Table 2).

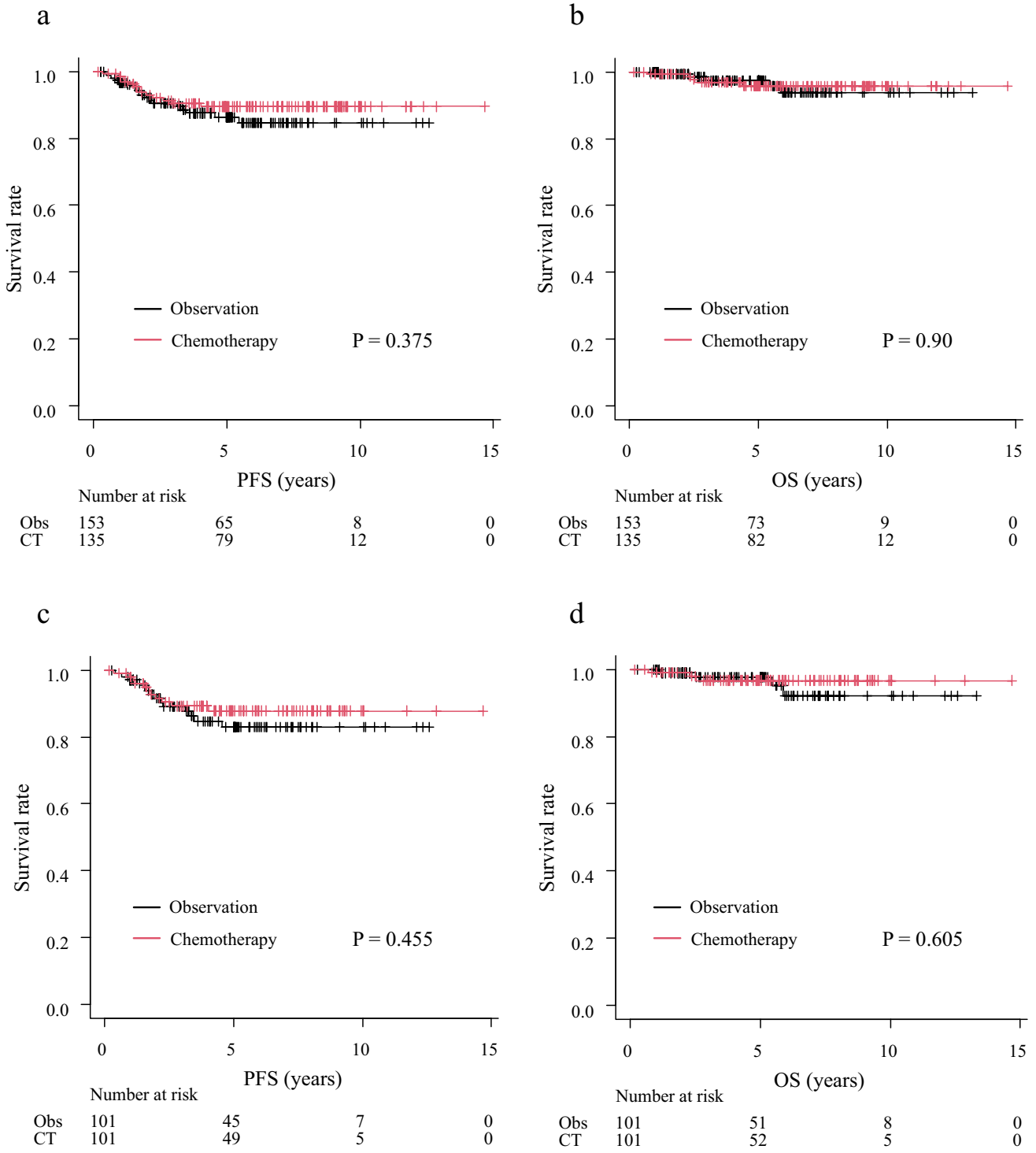

Fig. 3 Kaplan–Meier curves of PFS and OS in the observation group and chemotherapy group in LIR. **A**–**B** Before propensity score matching. **C**–**D** After propensity score matching. *LIR* low intermediate risk, *PFS* progression-free interval, *OS* overall survival, *Obs* observation, *CT* chemotherapy. *P* values were calculated by the log-rank test

HIR

Before propensity score matching, the 5-year PFS of the observation and adjuvant chemotherapy groups was 84.9% and 90.0%, respectively, whereas the 10-year PFS was 84.9% and 87.8%, with no significant difference ($P=0.326$). The 5-year OS was 89.1% and 95.0%, and the 10-year OS was 79.3% and 93.2%, respectively, which were significantly longer in the adjuvant chemotherapy group ($P=0.039$). In the subgroup analysis of PFS, adjuvant chemotherapy was associated with an improvement in PFS in the LVSI-positive subgroup. Still, no difference was observed between the adjuvant chemotherapy group and the observation group in other subgroups. In addition, in the subgroup analysis of OS, adjuvant chemotherapy was associated with improved OS in patients undergoing pelvic lymph-node dissection, with negative peritoneal cytology, and positive LVSI (Supplementary Table 3). After the patient characteristics were adjusted by propensity score matching, the 5-year PFS was 83.9% and 93.1%, respectively, the 10-year PFS was 83.9% and 81.5% ($P=0.505$), the 5-year OS was 84.1% and 91.9%, and the 10-year OS was 84.1% and 91.9%, respectively, with no significant differences between the two groups ($P=0.314$) (Fig. 4). No difference in the improvement of PFS and OS was observed in all subgroups between the two groups (Supplementary Table 4).

Discussion

In this study, we examined patients with endometrial carcinoma with a pathological diagnosis of stage I–II after undergoing total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and para-aortic lymph-node biopsy or dissection. We determined the effectiveness of postoperative adjuvant chemotherapy by comparing the prognosis of the observation and adjuvant chemotherapy groups using propensity score matching. After classifying the eligible patients into LIR and HIR, no significant difference in PFS and OS between the two was observed in LIR after propensity score matching. Similarly, no significant difference in PFS and OS was observed in HIR. The results indicate that postoperative adjuvant chemotherapy does not contribute to recurrence or prognosis in stage I–II patients, who are histopathologically diagnosed as having no lymph-node metastasis.

For the intermediate-risk group in stages I–II, which we defined as LIR, there were significantly more patients with positive ascites cytology and positive vascular invasion in the adjuvant chemotherapy group compared with that in the observation group before propensity score matching. There were no significant differences in PFS and OS between the observation and adjuvant chemotherapy groups. Even after adjusting for patient characteristics by propensity score matching, there was no significant difference in PFS and OS between the observation and adjuvant chemotherapy groups. The 5-year OS was 97.6% in the observation group and 96.7% in the adjuvant chemotherapy group, which represents an excellent prognosis and indicates that there is no benefit of adjuvant chemotherapy for LIR.

For the high-risk group in stages I–II, which we defined as HIR, there were significantly more patients with para-aortic lymph-node biopsy or dissection, positive ascites cytology, and positive vascular invasion in the adjuvant chemotherapy group compared with that in the observation group before propensity score matching. There was no significant difference in PFS, however, OS was significantly longer in the adjuvant chemotherapy group. This suggests that some patients with HIR may benefit from adjuvant chemotherapy. Results of the OS subgroup analysis showed the efficacy of adjuvant chemotherapy in cases with pelvic lymph-node dissection, negative ascites cytology, and positive LVSI. However, after propensity score matching, no difference was observed between the groups in any subgroup, and no significant differences in PFS or OS were observed. This means that the differences between groups before propensity score matching were merely because cases with factors favoring the effectiveness of adjuvant chemotherapy happened to be more common in the chemotherapy group, and when covariates were adjusted by propensity score matching, the differences between groups disappeared. Of course, the disappearance of OS differences after propensity score matching may be due to the small number of cases. However, from this additional analysis, we support the former interpretation. The 5-year OS for both groups was 84.1% and 91.9%, respectively, similar to the previously reported baseline risk for HIR [21]. However, both OS and PFS tended to be lower in the observation group. Although no statistically significant difference was observed, a cautious approach is necessary when evaluating the effectiveness of adjuvant chemotherapy as in LIR. In addition to total hysterectomy and bilateral salpingo-oophorectomy, however, retroperitoneal lymph-node biopsy or dissection and preoperative imaging diagnosis may be used to sufficiently diagnose advanced-stage disease. If this condition is met, postoperative adjuvant chemotherapy may not be necessary for stage I–II patients.

When administering postoperative adjuvant therapy, the potential for adverse events caused by adjuvant therapy should be considered. Adverse events of CTCAE Grade 3 or higher have been reported to be 4.7–35% for postoperative chemotherapy, such as blood toxicity and nausea, and 1.6–16% for postoperative radiotherapy, which includes intestinal obstruction and enteritis [15, 16]. Adjuvant therapy should be administered only to those patients who need it, by identifying the populations for whom postoperative therapy has little prognostic benefit. The LIR in the present study presents a population that is

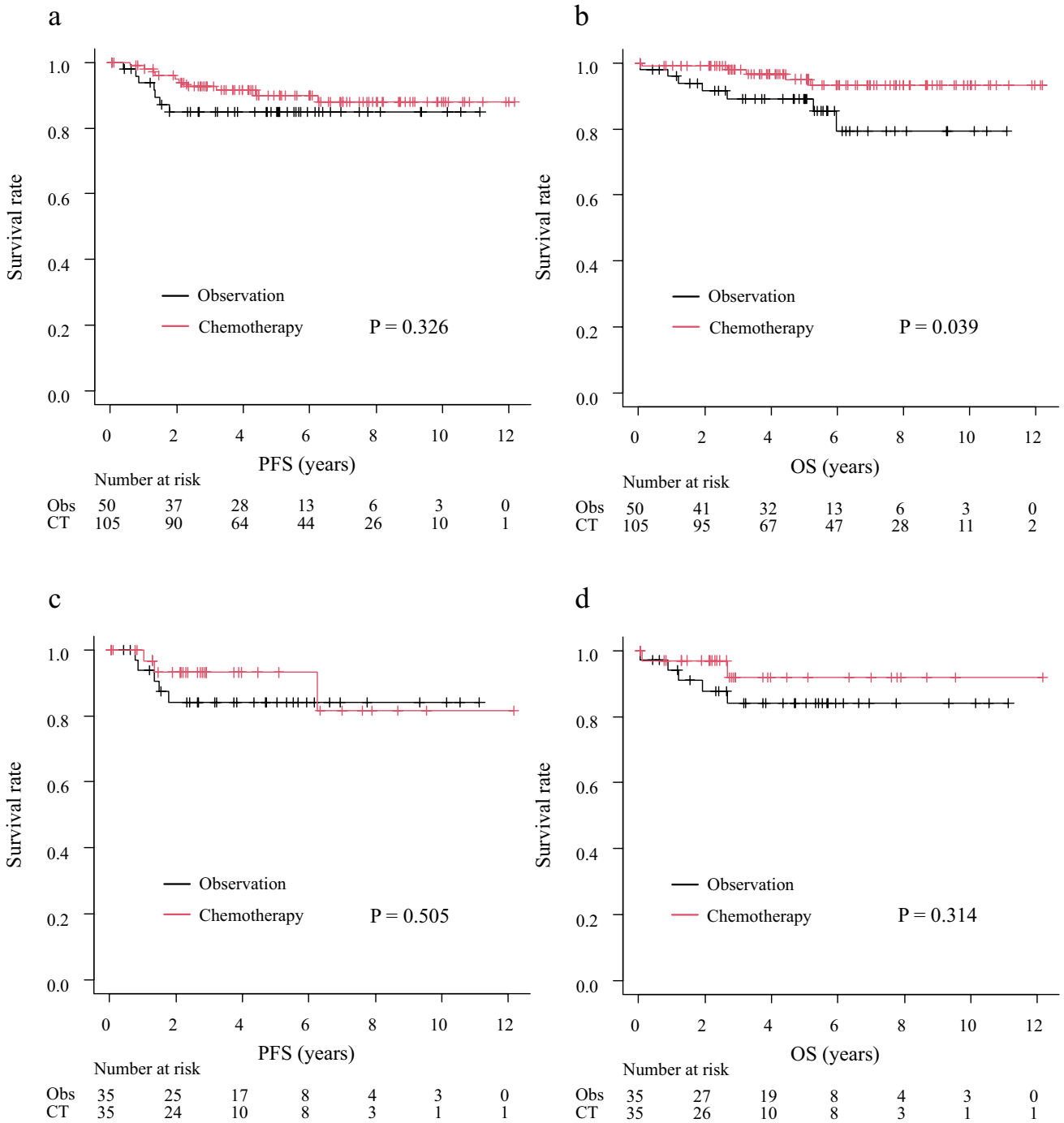

Fig. 4 Kaplan–Meier curves of PFS and OS in the observation group and chemotherapy group in HIR. **A**–**B** Before propensity score matching. **C**–**D** After propensity score matching. *HIR* high intermediate risk, *PFS* progression-free interval, *OS* overall survival, *Obs* observation, *CT* chemotherapy. *P* values were calculated by the log-rank test

expected to have a prognosis similar to that of the low-risk group without adjuvant therapy and is considered eligible to avoid unnecessary adverse events. In addition, patients who underwent minimally invasive surgery by laparoscopic or robot-assisted surgery were excluded from this study because of the small number of eligible patients; however, it is necessary to determine whether the results of this study can be applied to patients who undergo minimally invasive surgery. It has been reported that there is no difference in the outcome of early-stage endometrial carcinoma depending on the surgical technique [22–25]. If there is no difference in surgical outcomes, we believe

that the results of this study can be applied to minimally invasive surgical patients.

There are several limitations to this study. For example, although this study adjusted for patient characteristics using propensity score matching, it was a retrospective study. To conduct a more accurate examination, prospective studies are essential. As a prospective study examining the efficacy of adjuvant chemotherapy in similar subjects, the ENGOT-EN2 / DGCG trial is currently undergoing in Europe. This study is a phase II randomized trial of postoperative chemotherapy or no further treatment for patients with node-negative stage I–II intermediate or high-risk endometrial carcinoma. The results of this study are awaited with interest. Furthermore, this study has not been able to evaluate molecular classifications due to the large number of cases and the high cost of testing. In recent years, molecular classification has been regarded as important for determining the staging and treatment of endometrial cancer, and p53 mutation-positive endometrial carcinoma has already been recognized as a poor prognostic factor. By considering molecular classification in addition to histopathological factors as risk factors, it is possible to more thoroughly assess the effectiveness of postoperative adjuvant therapy. This is a task for the future. The careless use of chemotherapy as adjuvant therapy should be avoided, as it is not expected to significantly improve patient prognosis. The results of this study indicate that the efficacy of adjuvant chemotherapy for intermediate- and high-risk groups in stages I–II should be determined.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10147-024-02560-w.

Acknowledgements We gratefully acknowledge the cooperation of the participating hospitals affiliated with the Department of Obstetrics and Gynecology in The Jikei University School of Medicine and the gynecologic doctors.

Author contributions Conceptualization: J.S., M.T. Data curation: J.S., Y.K., M.K., K.T. Formal analysis: J.S., H.M. Methodology: M.T. Project administration: J.S., H.T. Supervision: A.O. Writing — original draft: J.S. Writing — review and edition: H.T., H.M., M.S., H.T., K.Y., A.O.

Declarations

Conflict of interest The authors have no conflicts of interest, sources of financial support, corporate involvement, or patent holdings to disclose concerning this study.

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