RESEARCH ARTICLE

Long Term Outcomes of Patients with Endometrial Carcinoma Treated with Radiation - Siriraj Hospital Experience

Jiraporn Setakornnukul[1], Janjira Petsuksiri[1]*, Sirentra Wanglikitkoon[2], Malee Warnnissorn[3], Kullathorn Thephamongkhol[1], Yaowalak Chansilp[1], Vutisiri Veerasarn[1]

Abstract

Background: To evaluate treatment outcomes of patients with stage I-III endometrial cancer treated with postoperative radiation. Materials and Methods: A retrospective review of 166 endometrial cancer patients, undergoing surgery and postoperative radiotherapy at Siriraj Hospital from 2005-2008 was performed. Pathology was reviewed. Results of treatment were reported with 5-year loco-regional recurrence free survival (LRRFS), 5-year overall survival (OS), patterns of failure and toxicity, and according to stage and risk groups. Results: Median follow up time was 62.8 months. Pathological changes were found in 36.3% of the patients after central reviews, leading to 19% changes in risk groups. Most of the patients (83.7%) received pelvic radiation (PRT) and vaginal brachytherapy (VBT). Five-year LRRFS and OS of all patients were 94.9% and 85.5%, respectively. There was no recurrence or death in low and low-intermediate risk groups. For the high-intermediate risk group, 5-year LRRFS and OS were 96.2% and 90.8%, respectively, and for the high risk group 90.5% and 71%. Late grade 3 and 5 gastrointestinal toxicity was found in 3% and 1.2% of patients, respectively. All of them received PRT 5,000 cGy in 25 fractions. Conclusions: Low and intermediate risk patients had good results with surgery and adjuvant radiation therapy. For high risk patients, postoperative radiation therapy alone appeared to be inadequate as the most common pattern of failure was distant metastasis.

Keywords: Endometrial carcinoma - radiation therapy - survival - central pathological review - FIGO 2009

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Introduction

Endometrial cancer is the third most common gynecologic malignancy in Thailand (2.12% of all new cancer patients in year 2008) (Ratanawichitrasin, 2008). Primary therapy of endometrial cancer is total abdominal hysterectomy (TAH) and bilateral salpingo-oophorectomy (BSO) with peritoneal washing. Lymph node dissection (LND) was performed variously, based upon the surgeons' decisions. Recently, there are several changes and controversies regarding staging system and treatments for endometrial carcinoma patients. FIGO staging in endometrial cancer has been revised from FIGO 1988 to FIGO 2009 system. Despite this revision, the adjuvant treatments are based on the prior FIGO stages, grading of the tumors and stratifying as risk groups (Table 1) (Perez, 2004). Furthermore, emerging data of vaginal brachytherapy (VBT) alone in high intermediate risk (HIR) group from PORTEC 2 has a high impact upon clinical practice (Nout et al., 2011).

The primary objective of this study is to evaluate treatment outcomes, especially for 5-year loco-regional recurrence free survival (LRRFS) of patients with stage I-III endometrial cancer, treated with adjuvant radiation therapy. Also, the 5-year overall survival (OS), 5-year disease free survival (DFS) and 5-year cancer specific survival (CSS) will be reported. As the trend of adjuvant treatment in the intermediate risk group is moving to VBT alone, therefore the secondary objectives are to review the patterns of failure and side effects from PRT and VBT in our patients. In addition, we will report the treatment outcomes according to the accurate grading and staging of the diseases after central pathology reviews. Finally, we will report the outcomes of the patients based on the new FIGO 2009 staging system (Creasman, 2009) to determine whether the 2009 system is more capable of classifying the patients with different stages more accurately than the 1988 FIGO staging system.

Materials and Methods

After received the IRB's approval, the patients' data,

*[1]Division of Radiation Oncology, [3]Department of Pathology, Siriraj Hospital, Faculty of Medicine, Mahidol University, Bangkok, [2]Udon Thani Cancer Hospital, Muang Udon Thani, Thailand *For correspondence: janjira.pet@mahidol.ac.th*

Table 1. Risk Groups Classification (adapt from Perez, 2004)

FIGO 1988	FIGO 2009	Grade 1	Grade 2	Grade 3	UPSC**CCC***
IA		Low	Low	Low-Intermediate	High
IB	IA	Low	Low-Intermediate	High-Intermediate	High
IC	IB	High-Intermediate	High-Intermediate	High	High
IIA, MI<50%		Low-Intermediate	Low-Intermediate	High-Intermediate	High
IIA, MI≥50%		High-Intermediate	High-Intermediate	High	High
IIB	II	High	High	High	High
III	III	High	High	High	High
IV	IV	High	High	High	High

* Myometrial invasion; ** Uterine papillary serous carcinoma; *** Clear cell carcinoma

treatment information and outcomes were reviewed. We enrolled patients aged more than 18 years old, who underwent curative surgery at least TAH and adjuvant radiotherapy with pathological stage I-III endometrioid or non-endometrioid carcinoma endometrial cancer from January 2005-July 2008. Exclusion criteria were patients treated with definite radiation or salvage radiation and patients who previously received any therapy before surgery. These patients were classified into risk groups (with FIGO 1988 staging system) as in Table 1 (Perez, 2004).

Adjuvant radiation therapy was indicated in postoperative patients with stage and grading of the tumor higher than stage IA G2 or IB G1 (FIGO, 1988). Radiation therapy techniques followed the standard institution's practice guideline of 2002, in which most of patients were considered to receive PRT and VBT. Some patients received VBT alone, based on physicians' decisions. PRT was utilized with conventional AP/PA technique with a total dose of 46-50 Gy in 1.8-2 Gy/fraction. For the brachytherapy treatment, either vaginal ovoids or vaginal cylinders were used with high dose rate afterloading system with Iridium (Ir) 192 source. A total dose of 15 Gy in 3 fractions was prescribed at 5 mm from the vaginal surface for patients who received both PRT and VBT. For VBT alone, a dose of 21 Gy in 3 fractions was used. After complete treatment, physical and pelvic exams were done routinely. CT scan of abdomen was performed only in patients who suspected of recurrent or metastatic disease. For patients who loss to follow up, the information was obtained by phone calls or civil registration. Acute and late side effects were assessed by the grading system of the European Organization for Research and Treatment of Cancer and Radiation Therapy Oncology Group (EORTC-RTOG) for radiation toxicity effects (Cox et al., 1995).

Central pathology reviewed was performed by the gynecologic oncology pathologist at our institute. Inter-observer agreement between the general pathologists (prior pathology reports) and gynecologic oncology pathologist was evaluated by using Kappa (κ) statistics. The κ value can be interpreted as good if 0.61-0.80, moderate if 0.41-0.6 and fair if the value 0.21-0.40 (Altman, 1991).

Statistical analyses

For sample size calculation, we use 3% locoregional recurrent rate from our pilot data with 3% allowable error and 5% type I error. The sample size was equal to 126. LRRFS, OS, DFS and CCS were defined according to the FDA survival definitions starting at the first date of radiotherapy (Georgopoulou et al., 2007). The Kaplan-Meier method was used for these survivals. Time-to-event analyses were done with log-rank tests and Cox proportional hazards regression models, which are reported with Hazard Ratio (HR), 95% confidence interval (CI) and p value.

Results

From January 2005-July 2008, 189 patients were included in this study. 22 patients were excluded as in the exclusion criteria. After pathology review 1, one patient was excluded as the final pathology confirmed primary cervical cancer. Ultimately, 166 patients remained for the analysis. The median follow up time was 62.8 months (1-92 months). Fourteen patients (8.4%) were loss to follow up.

The patients 'mean age was 59.6 years old (28.2-93.7). Most of the patients were in postmenopausal status (74.1%) Most of the patients were in stage I disease (68.6%). The most common pathology was endometrioid adenocarcinoma (86.2%). The pathology, risk groups and staging of the patients are shown in Table 2.

All patients underwent TAH (100%) with BSO (99.4%). Median numbers of pelvic lymph node dissection/sampling and para-aortic lymph node sampling were 14 nodes (range 0-40 nodes) and 3 nodes (range 0-17 nodes), respectively. After subgroup analysis between patients who had more than or equal to 12 nodes and those with fewer than 12 nodes dissected, according to the median number of lymph nodes on the MRC/ASTEC trial (Kitchener et al., 2009), 5-yr OS of those were 79.5% (≥12 nodes) and 89.6% (<12 nodes), respectively, HR 0.56 and 95%CI 0.17-1.86, p value=0.34.

For radiotherapy, 99.4% of the patients completed radiation treatment. Most of the patients received both PRT and VBT (83.7%). PRT mean dose was 50.4 Gy (26-66 Gy) at 1.8-2 Gy/fraction. Only 1 patient stopped radiation treatment at 26 Gy due to systemic metastasis. The others were treated with total doses range from 46 to 66 Gy. Vaginal ovoids were mostly used for VBT (91.4%) with mean total doses of 15 Gy with 5-7 Gy/fraction. For chemotherapy, only 7 patients (4.2%) received 2-6 cycles of adjuvant chemotherapy (Table 3).

Table 2. Pathology, Risk Groups and Staging (total 166 patients)

Characteristics		Number of patient (%)	
Pathology (central reviewed)			
Endometrioid			
Grade 1		57 (34.1%)	
Grade 2		63 (37.7%)	
Grade 3		24 (14.4%)	
Non-endometrioid			
Clear cell carcinoma		4 (2.4%)	
Uterine papillary serous carcinoma		18 (10.8%)	
Squamous cell carcinoma		1 (0.6%)	
Risk groups*			
Low risk		15 (9%)	
Low-intermediate risk (LIR)		25 (15%)	
High- intermediate risk (HIR)		57 (34%)	
High risk		69 (42%)	
FIGO staging system 1988		FIGO staging system 2009	
IA	4 (3%)	IA	56 (33.7%)
IB	46 (28%)	IB	58 (34.9%)
IC	50 (30%)		
IIA	5 (3%)	II	21 (12.7%)
IIB	20 (12%)		
IIIA	27 (16%)	IIIA	17 (10.3%)
IIIB	2 (1%)	IIIB	2 (1.2%)
IIIC	12 (7%)	IIIC1	11 (6.6%)
		IIIC2	1 (0.6%)

*Classified with FIGO 2009 and Grading of tumors

Table 3. Treatment by Surgery, Radiation, and Chemotherapy

Treatments	No. of patients (%) (total of 166 patients)
Surgery	
TAH	166 (100%)
BSO	165 (99.4%)
Pelvic node surgery (median node=14)	
Lymphadenectomy (median node=16)	70 (42.2%)
Sampling (median node=11)	67 (40.3%)
No pelvic node surgery	29 (17.5%)
Numbers of pelvic node harvested	
< 12	87 (52.4%)
≥ 12	79 (47.6%)
Para-aortic node surgery (median node=3)	
Lymphadenectomy (median node=4.5)	12 (7.2%)
Sampling (median node=3)	82 (49.4%)
No Para-aortic node surgery	72 (43.4%)
Peritoneal washing	129 (77.7%)
Omentectomy	77 (46.4%)
Radiotherapy	
Complete radiation treatment	165 (99.4%)
Radiation techniques	
VBT	12 (7.2%)
PRT	15 (9%)
VBT and PRT	139 (83.7%)
Chemotherapy	7 (4.2%)
Stage III Endometrioid adenocarcinoma	4 (57.1%)
Uterine papillary serous carcinoma	1 (14.3%)
Clear cell carcinoma	2 (28.6%)

*Abbreviations: TAH=Total Abdominal Hysterectomy, BSO=Bilateral Salpingo -Oophorectomy, VBT=Vaginal Brachytherapy, PRT= Pelvic Radiotherapy

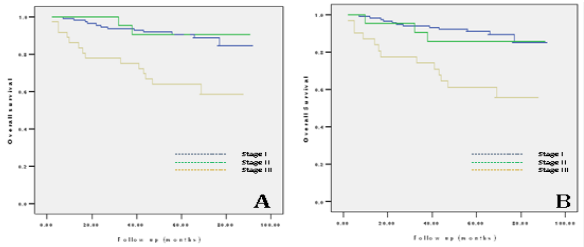

Figure 1. A Showed Survival Curves of Stage I, II and III According to FIGO 1988 Staging System and B Showed Survival Curves of Stage I, II and III According to FIGO 2009 Staging System

Treatment outcomes

5-yr OS were 100%, 100%, 90.6% (95%CI, 78.8%-96.0%) and 71.0% (95%CI, 58.7%-80.2%) in low risk, LIR, HIR and high risk groups, respectively. There was no disease recurrence in the low risk and LIR groups. 5-yr vaginal recurrent free survival, 5-yr pelvic recurrent free survival, and 5-yr LRRFS of HIR and high risk were 96.2% (95%CI, 85.7%-99.0%), 98.0% (95%CI, 86.9%-99.7%), 96.2% (95%CI, 85.7%-99.0%) and 91.9% (95%CI, 81.7%-96.6%), 96.7% (95%CI, 87.4%-99.2%), 90.5% (95%CI, 80.1%-95.6%), respectively. 5-yr distant metastatic free survivals were 93.8% (95%CI, 82.0%-98.0%) and 74.6% (95%CI, 61.9%-83.6%) for HIR and high risk, respectively. 5-yr DFS and 5-yr CSS of HIR and high risk were 88.6% (95%CI, 76.3%-94.8%), 94.6% (95%CI, 84.3%-98.2%) and 66.2% (95%CI, 53.6%-76.1%), 75.0% (95%CI, 62.9%-83.7%), respectively.

Patterns of failure and cause of death

Isolated vaginal recurrence was found in only 2 patients (1.2%) in HIR and high risk patients. For high risk group, the major pattern of failure was distant metastases (17/69 patients, 24.6%).

In this study, 16.86% of the patients (28/166 patients) died. Twenty patients (20/28 patients, 71%) died from endometrial cancer (18 patients died from cancer, 2 patients died from small bowel obstruction).

Side effects of treatment

There was no grade 3-5 acute GI/GU complications on this study. For late complications, 7 patients (4.2%) in our series developed grade 3-5 GI toxicity, which 5 patients were older than 60 years. Five patients (3%) had grade 3 GI toxicity. All of them underwent PRT and 4 patients received VBT. Grade 5 GI toxicity was developed in 2 patients (1.2%) and both of them die from complications of small bowel obstruction at 2 and 5 months after PRT and VBT. All patients who experienced grade 3-5 GI toxicities received conventional two opposing (AP/PA) beams with 50 Gy at 2Gy/fraction. There was no late grade 3-5 GU complication in this study.

Pathology review

66.4% (111/166 patients) of the pathology slides were available to review. Inter-observer agreement between the (prior) general pathologists and the gynecologic oncology pathologist was in good agreement (κ=0.61-0.80) for most factors and very good agreement (κ=0.81-1.00) for some factors.

Table 4. Comparison Data from the Landmark Randomized Control Trials to Our Data

Author	Follow up (months)	Inclusion	TAH & BSO	5 yr LRR		5 yr OS	
				PRT	Observe	PRT	Observe
Adjuvant pelvic radiation +/- brachytherapy							
Aalders J et al., 1980 (Norwegian)	120	clinical stage I	No LND	1.90%	6.90%	90%	92%
				All VBT		All VBT	
Keys HM et al., 2004 (GOG 99)	68	IB, IC, IIA, IIB	LND	2%	7%	92%	86%
Creutzberg et al., 2000 (PORTEC1)	52	IB (G2-3) IC (G1-2)	No LND	4.20%	13.70%	81%	85%
Blake P et al., 2009 (ASTEC/EN5)	58	IA,IB (G3) IC IIA, IIB	No LND	3.20%	6.10%	84%	84%
				VBT≈53%		VBT≈53%	
Sorbe BG et al., 2012	62	I (G3, deep MI, or DNA aneuploidy)	No LND	1.50%	5%	89%	90%
				All VBT		All VBT	
Our study 2013	62.8	IBG3, ICG1-2	70% LND	3.50%	-	90.80%	-
				VBT 93%		VBT 93%	
Adjuvant brachytherapy							
Nout RA et al., 2010 (PORTEC 2)	45	IB (G3 &>60yr) IC (G1-2 &>60yr) IIA (no G3 &>1/2MI*)	No LND	PRT	VBT	PRT	VBT
				2.10%	5.10%	79.60%	84.80%

*Abbreviations: TAH: Total Abdominal Hysterectomy; BSO: Bilateral Oophorectomy; LRR: Loco-regional relapse; OS: Overall Survival; PRT: Pelvic Radiotherapy; VBT: Vaginal Brachytherapy; LND: Lymph Node Dissection; MI: Myometrial invasion

Cell type and grading were the most disagree upon issues between the general pathologists and the gynecologic oncology pathologist (31/111 patients; 28%). In this discordance, cell type change between endometriod and non-endometriod type was found in 35% of the specimens and endometriod grading change was found in 48% of the specimens.

In overall, pathology information had changed in 36.3% of the endometrial cancer patients (40/110 patients), leading to 19% (21/110 patients) changes in risk groups (5 patients under-risk and 16 patients over-risk with 89 unchanged-risk).

For under risk patients (5 patients), 3 patients had uterine papillary serous carcinoma (UPSC) on pathology review. They received only radiation therapy without additional chemotherapy. Eventually, 1 of these patients developed vaginal and distant recurrences.

For over risk patients (16 patients) who received both PRT and VBT, 6 patients should not receive any adjuvant treatment as the final pathology and staging were in low risk group.

Staging revision (FIGO 1988-FIGO 2009)

For FIGO staging revision (1988 to 2009), we used the reviewed-pathology reports for the analyses. We compared the outcomes of the patients according to the FIGO 1988 and 2009 systems. The 5-yr OS for stage IA and IB with FIGO 1988 were 100% and 98%, respectively while the 5-yr OS for stage IA with FIGO 2009 was 98.2%. The outcomes among stages are represented with hazard ratio (HR) as shown in Figure 1. The results confirmed that the revised FIGO 2009 staging system has a subtle higher prognostic value in determining the 5-yr survivals than the FIGO 1988.

Discussion

Treatments of endometrial cancer patients remain controversial, regarding role of lymphadenectomy, adjuvant radiation therapy and adjuvant chemotherapy. In this retrospective study, we reviewed surgery, pathology and adjuvant radiation treatment which were performed in our institute. We will discuss our results following the sequences of treatments.

Surgery

The major treatment for endometrial cancer is surgery, which TAH and BSO are mandatory. LND, however is the controversial issue. The prior studies demonstrated that aggressive lymphadenectomy didn't not improve the survival outcomes (Lutman et al., 2006; Benedetti el al., 2008; Kitchener et al., 2009; Dowdy et al., 2012). The median numbers of pelvic lymph node surgery was 14 nodes in our study, compared to 12 nodes in the ASTEC trial (Kitchener et al., 2009). Our analysis confirmed that high numbers of pelvic lymph node dissected didn't transfer into the survival benefits, which was similar to the prior studies. However, Chan et al reported that lymphadenectomy should be considered in high risk group (IC, grade 3, II-IV), as the subset analysis showed survival benefits over the non-lymphadenectomy group (Chan et al., 2007). Routine lymphadenectomy can be omitted; however, selective lymphadenectomy can be considered in high risk patients.

Pathology review

Our study demonstrated that there were pathological changes in 36.3% of the patients, leading to 19% changes in risk groups. The prior study (PORTEC-2 trial) showed 14% changing of risk groups after central pathology review (Nout et al., 2010). Most of the pathological reviews by the gynecologic oncology pathologist were in concordance with the prior reports by the general pathologists in our study. However, this result should be interpreted cautiously. Although, there were only minority of patients who had pathological changes, these changes would relatively strongly alter the treatment decisions, such as under or over treatment, leading to inferior

treatment outcomes or unacceptable treatment side effects.

Therefore, we recommend a pathology review by an experienced gynecologic oncology pathologist, as it's crucial to determining the appropriate treatments and avoiding unnecessary side effects.

FIGO 1988 vs FIGO 2009

As the FIGO staging system was changed in 2009, our study attempts to evaluate whether this new staging system would be more capable to diverse the patients of each stage compared to the prior 1988 system (Creasman, 2009; AJCC 7th edition, 2010). Werner et al reported that FIGO 2009 system is more capable to separate survival outcomes between stage IA and IB compared to the 1988 system (5 yr OS for stage IA and IB; 94% and 97 % with FIGO 1988 and 96% and 87% with FIGO 2009). The authors also showed that there was no significant difference in survival among patients with stage IA, IB, and IIA according to FIGO 1988 system (Werner et al., 2012). Also, Tangjitgamol et al confirmed a better prognostic determination by using FIGO 2009 compared to the 1988 version (5-yr OS-94.9% (IA), 88% (IB) by FIGO 2009 and 100% (IA), 94.8% (IB), by FIGO 1988) (Tangjitgamol et al., 2013).

Our study showed that the overall survivals of stage IA, IB of FIGO 1988 (5-yr OS 100% and 98 %, respectively) were almost identical to stage IA of FIGO 2009 (5-yr OS 98.2%). In addition, our study also showed better survival differences between stage I and II by using the FIGO 2009 system (5 yr OS for stage I and II; 90.6% and 90.5 % with FIGO 1988 and 91% and 85.7% with FIGO 2009).

Treatment outcomes and pattern of failures according to risk groups

The results of treatment for low and LIR risk patients were excellent without any failure. For HIR group, our study showed 5-yr OS of 90.8%, with 3.5% loco-regional recurrence, and 5.3% distant metastasis. Our results were comparable with the results of postoperative radiation therapy studies (PORTEC-1, GOG-99, and the NORWEGIAN trial), in which the loco-regional recurrences were in the range of 1.9- 5% after adjuvant radiation therapy (Creutzberg et al., 2000; Scholten et al., 2005; Keys et al., 2004; Aalders et al., 1980) (Table 4).

As the trend is treating with VBT alone in the HIR patients, we compared our results with the results of PORTEC-2 trial. Our data showed that loco-regional failure, distant metastasis and 5-yr overall survival were 3.5%, 5.3% and 90.8% compared to 2.1%, 5.7% and 79.6% (PRT arm) and 5.1%, 8.3%, and 84.8% (VBT arm) in the PORTEC-2 trial. These data confirmed that our results were not inferior to the other studies. These results ensure the feasibility of changing our practice to VBT alone in HIR group. However, the outcomes of treating HIR patients with VBT alone should be verified and reported in the future.

For radiation therapy technique itself, the results from PORTEC-2 revealed that PRT provided identical overall survival to VBT in HIR patients (5-yr OS 86.2% VBT *vs* 82.1% PRT, p=0.66), although the incidence of 5 year loco-regional recurrence was slightly higher in the VBT alone arm (VBT 5.1% *vs* PRT 2.1%, p= 0.17). In contrast, Sorbe et al demonstrated that the incidence of 5 year loco-regional relapse rates was higher with VBT alone compared to PRT+VBT (5% after VBT alone *vs* 1.5% after PRT+VBT, p=0.013), without 5-year OS differences (90% *vs* 89%) (Sorbe et al., 2012) (Table 4). Our results showed that with PRT+VBT, there was 3.5 % loco-regional recurrence in the HIR group, which was in range of the results from PORTEC-2 and Sorbe et al.

Since our late GI complications were 3% in grade 3 and 1.2% in grade 5 (treatment related death due to small bowel obstructions), we considered these complications seriously. In the GOG-99 randomized trial, 2 patients (1.1%) died from intestinal injury. Six patients (3.2%) had grade 3-4 GI obstruction, which could be from radiation, in the radiotherapy arm, whereas only 1 patient (0.5%) had grade 3 GI obstruction without grade 4-5 complications in the surgery alone arm. Similarly in PORTEC 2 study, there were 4 patients (2%) who developed grade 3 GI toxicity in PRT; however only 1 patient (<1%) had bowel obstruction in VBT due to adhesion or fibrosis. In brief, adjuvant PRT in endometrial cancer results in 2-3% of grade 3 GI toxicity and 1% of grade 5 GI toxicity. Some studies tried to find out predicting factors for GI toxicities after pelvic radiotherapy in gynecologic malignancy patients. Huscher et al. reported that age equal or more than 60 years, dose fraction equal or more than 180 cGy, and severe grade 3-4 acute GI toxicity predicted severe late GI toxicities. (Huscher et al., 2009) Another study showed that grade 3-4 late GI toxicities strongly correlated with previous abdominal surgery, smoking, and Diabetes Mellitus. (Iraha et al., 2007) In our study, all patients who developed grade 3-5 late GI toxicities underwent pelvic surgery followed by post-operative whole pelvic radiotherapy with 2 Gy/fraction. Five patients (72%) were older than 60 years old. Therefore, given an acceptable locoregional control with PRT+VBT with significant late GI side effects in our study, we considered treating our LIR and HIR patients with VBT alone. Yet, this new practice in our institute needs a close monitoring and follow up. Also, optimal radiation dose of VBT should be observed in these groups and it should wait the result from the ongoing PORTEC 4.

For high risk patients, the major pattern of failure was distant metastasis (5-yr distant metastatic rate 25.4%) with inferior 5-yr OS (71%) than other risk groups. As we included only high risk patients who received radiation therapy (7 patients, 4.2%), we couldn't compare the results between adjuvant chemotherapy and radiation therapy in this study. The studies of adjuvant chemotherapy versus adjuvant radiation therapy in high risk patients demonstrated pelvic relapse rates of 6.7-13% (RT) *vs* 7-18% (Chemotherapy) (Maggi et al., 2006; Randall et al., 2006; Susumu et al., 2008). Our study confirmed that in patients with high risk disease, adjuvant radiation therapy with PRT+VBT provided loco-regional control of 90.5% at 5 years in a similar range in the literatures. As distant metastasis is the major pattern of failure, there were multiple studies exploring the role of adjuvant chemotherapy in addition to radiation therapy. The results of these studies showed that adding chemotherapy tended to provide the survival benefits, especially for stage III,

IV diseases (Morrow et al., 1990; Greven et al., 2006; Kuoppala et al., 2008; Hogberg et al., 2010). There are ongoing trials exploring role of chemotherapy and/or radiation therapy in high risk patients in a randomized design, such as the PORTEC-3, GOG 249 and GOG 258; we have to await these results.

There were several limitations of our study including a retrospective manner, missing pathological specimens, not routinely performing CT/MRI imaging for follow up evaluation, and not comparing data from the patients who received surgery alone or adjuvant chemotherapy without radiation therapy. However, the results of our study did provide important data to assess and adjust our routine practices for patients with endometrial cancer.

In conclusion, FIGO 2009 system appears to be useful in differentiating the outcomes of different stages. Pathology review is essential and crucial to determine necessary adjuvant treatments and avoiding unnecessary treatment side effects. Our study showed that the intermediate risk endometrial cancer patients had good results after treating with surgery and adjuvant radiation therapy with external beam treatment and brachytherapy. For high risk patients, postoperative radiation therapy alone appeared to be inadequate, as the most common pattern of failure was distant metastasis.

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