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Original article

Safety of total laparoscopic modified radical hysterectomy with or without lymphadenectomy for endometrial cancer

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ABSTRACT

Study objective: In order to reduce the risk of vaginal recurrence, we have chosen total laparoscopic modified radical hysterectomy instead of extrafascial hysterectomy in the treatment of endometrial cancer. The aim of this study was to assess the safety of this method.
Design: Retrospective study of gynecological patients.
Setting: Yokohama City University Medical Center, Yokohama, Japan.
Patients: Forty-nine patients who underwent total laparoscopic modified radical hysterectomy for the treatment of endometrial cancer at our hospital between December 2011 and September 2015.
Interventions: Total laparoscopic modified radical hysterectomy + bilateral salpingo-oophorectomy ($n = 20$), total laparoscopic modified radical hysterectomy + bilateral salpingo-oophorectomy + pelvic lymphadenectomy ($n = 18$), or total laparoscopic modified radical hysterectomy + bilateral salpingo-oophorectomy + pelvic and para-aortic lymphadenectomy ($n = 11$).
Measurements and Main Results: The surgical outcomes were analyzed and compared to previous reports. The median operative time was 204 minutes (range, 99–504 minutes) and the median intraoperative blood loss was 150 mL (range, 0–680 mL). No patients needed a blood transfusion, conversion to laparotomy, or reoperation. Intra- and postoperative complications were observed in three patients and nine patients, respectively. The amount of blood loss and the incidence of complications in our study were almost identical to previous reports of laparoscopic hysterectomy. The operative time in our study was equivalent to previous reports of total laparoscopic modified radical hysterectomy.
Conclusion: Total laparoscopic modified radical hysterectomy is safe and feasible for the treatment of early stage endometrial cancer. This procedure can be an alternative to total laparoscopic hysterectomy, especially when the uterus must be removed completely.

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Introduction

Endometrial cancer is the most common gynecological malignant neoplasm, and its standard treatment is surgical removal of the uterus. Total abdominal hysterectomy and bilateral salpingo-oophorectomy with or without bilateral pelvic/para-aortic lymphadenectomy has been the standard surgery for early stage endometrial cancer. However, recent advances in laparoscopic surgery have enabled it to be utilized for the treatment of early stage endometrial cancer as a less invasive surgical option than laparotomy. Most previous studies that compared laparoscopic surgery to laparotomy showed a comparable or significantly lower incidence of treatment-related morbidity, a shorter hospital stay, less blood loss, less pain, and a faster recovery with the laparoscopic approach.[1] For this reason, we have also adopted laparoscopic surgery for the treatment of early stage endometrial cancer. While extrafascial hysterectomy is usually recommended to remove the uterus thoroughly, we have chosen total laparoscopic modified radical hysterectomy (TLmRH; equivalent to Piver-

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Rutledge class II hysterectomy) as a highly effective procedure to reduce the risk of vaginal recurrence after surgery. We included the operated cases with or without lymphadenectomy in order to investigate the feasibility of these procedures comprehensively.

Aim

The aim of this study was to assess the safety of TLmRH, because very few studies describing this technique have been reported thus far.

Materials and Methods

We retrospectively reviewed the operated cases with endometrial cancer at the Department of Gynecology, Yokohama City University Medical Center, Yokohama, Japan between December 2011 and September 2015. General consent was obtained from all patients preoperatively, and the Yokohama City University Medical Center Institutional Ethics Committee approved this study. Preoperative histological diagnosis was made via uterine cavity curettage. The extent of muscle invasion was based on preoperative examination using enhanced magnetic resonance imaging. Metastases were evaluated with computed tomography (CT) scan. TLmRH + bilateral salpingo-oophorectomy (BSO) + pelvic lymphadenectomy (PLA) + para-aortic lymphadenectomy (PALA) was undertaken fundamentally for the patients with endometrial cancer. It has been reported that para-aortic lymph node metastasis was found to be 10–17% in the endometrial cancer when muscle invasion was > 50%.[2–4] It has also been reported that PALA is not necessary when cytological examination is negative and pelvic lymph node metastasis is not found by pelvic lymphadenectomy.[5] Based on these observations, PALA was excluded and TLmRH + BSO + PLA was undertaken for patients with Grade 1 endometrioid cancer when superficial muscle invasion was suspected to be < 50%. Because it has been reported that lymph node metastasis is seen in only 1–2% of endometrial cancer patients when muscle invasion is not found,[6,7] lymphadenectomy was excluded and TLmRH + BSO was undertaken for patients with Grade 1 endometrioid cancer with no obvious muscle invasion.

Table 1
Characteristics of the patients and surgical results.

	All	Breakdown of surgical procedure		
		TLmRH	TLmRH+PLA	TLmRH+PLA+PALA
	($n = 49$)	($n = 20$)	($n = 18$)	($n = 11$)
Age (y)	57.0 (39–77)	56.5 (39–73)	55.0 (46–70)	61.0 (46–77)
BMI (kg/m^2)	23.7 (17.7–39.4)	23.8 (17.7–39.4)	22.9 (18.3–32.9)	23.9 (18.1–30.8)
No. of nulliparous	13 (26.5)	6 (30.0)	3 (16.7)	4 (36.4)
No. of patients with any abdominal surgical history	12 (24.5)	7 (35.0)	4 (22.2)	1 (9.1)
Histological diagnosis (postoperative)				
G1	33	18	13	2
G2	10	2	5	3
G3	3	0	0	3
Others	3	0	0	3
FIGO staging 2008 (postoperative)				
1A	44	20	16	8
1B	2	0	1	1
2	1	0	0	1
3C1	2	0	1	1
Operative time (min)	204 (99–504)	143 (99–211)	214.5 (165–274)	435 (328–504)
Estimated blood loss (mL)	150 (0–680)	100 (0–325)	200 (0–680)	200 (50–520)
No. of intraoperative transfusions	0	0	0	0
Weight of uterus (g)	140 (85–375)	155 (85–325)	145 (85–375)	100 (85–180)
Length of cervical cuff (mm)	20.0 (10.0–27.5)	20.5 (13.5–27.5)	19.5 (10–25)	19.0 (15–25)
Time to make cervical cuff (min)	15.0 (3–30)	15.0 (3–30)	12.5 (8–21)	18.0 (12–26)
No. of dissected pelvic lymph nodes	29 (7–56)	—	28 (15–47)	33 (7–56)
No. of dissected para-aortic lymph nodes	37 (14–57)	—	—	37 (14–57)
Time to remove all drains (d)	3 (2–10)	2 (2–7)	3 (2–10)	4 (2–7)
Postoperative Hb value (g/dL)	10.4 (8.4–11.8)	10.8 (8.4–11.8)	10.3 (8.7–11.3)	10.8 (8.9–11.4)
Postoperative CRP value (mg/dL)	1.609 (0.131–10.577)	1.092 (0.194–2.414)	1.675 (0.131–10.577)	3.837 (1.686–7.117)
Time to walk (d)	1 (1–2)	1 (1–2)	1 (1–2)	1 (1–2)
Time to passage of flatus (d)	1 (0–3)	1 (1–2)	1 (1–3)	1 (0–1)
Time to hospital stay after surgery (d)	6 (3–14)	6 (3–9)	6 (4–14)	6 (5–9)
Complications				
Overall (No. of patients)	10 (20.4)	2 (10.0)	7 (38.9)	1 (9.1)
Intraoperative (No. of patients)	3 (6.1)	1 (5.0)	1 (5.6)	1 (9.1)
Bladder injury	1 (2.0)	1 (5.0)	0	0
Ureter injury	1 (2.0)	0	0	1 (9.1)
Nerve injury	1 (2.0)	0	1 (5.6)	0
Postoperative (No. of patients)	9 (18.4)	1 (5.0)	7 (38.9)	1 (9.1)
Ureter–vagina fistula	1 (2.0)	0	1 (5.6)	0
Urinary dysfunction requiring intervention	2 (4.1)	1 (5.0)	1 (5.6)	0
Neurological disorder requiring intervention	1 (2.0)	0	1 (5.6)	0
Lymphedema requiring intervention	1 (2.0)	0	1 (5.6)	0
Pelvic infection requiring intervention	1 (2.0)	0	1 (5.6)	0
Chylous ascites	1 (2.0)	0	0	1 (9.1)
Atelectasis	1 (2.0)	0	1 (5.6)	0
Vein thrombosis	1 (2.0)	0	1 (5.6)	0

Data are expressed as median (range) or *n* (%).
BMI = body mass index; PALA = para-aortic lymphadenectomy, PLA = pelvic lymphadenectomy; TLmRH = total laparoscopic modified radical hysterectomy.

Table 2
Comparison with the previous reports of laparoscopic hysterectomy.

Study	*n*	Surgical procedure (%)	Operative time (min)	Blood loss (mL)	Hospital stay after surgery (d)	Complications (%)	Transfusion (%)	Conversion to laparotomy (%)	Reoperation (%)	Death (%)
Our study	49	TLmRH 40.8 TLmRH+PLA 36.7 TLmRH+PLA+ PALA 22.4	204 (99–504)	150 (0–680)	6 (3–14)	Intraoperative 6.1 Bladder 2.0, ureter 2.0, nerve 2.0 Postoperative 18.4 Urinary fistula 2.0, urinary dysfunction 4.1, neurological disorder 2.0, lymphedema 2.0, pelvic infection 2.0, chylous ascites 2.0, atelectasis 2.0, pulmonary embolism 2.0	0	0	0	0
Walker et al[8] (LAP2 study)	1630	TLH/LAVH/RH 1.4 TLH/LAVH/RH+ PLA 6.8 TLH/LAVH/RH+PLA +PALA 91.5	204 [160–252]	NR	3 [2–4]	Intraoperative 10 Bladder 1, ureter 1, intestinal 2, artery 2, vein 3, others 2 Postoperative 14 Urinary tract infection 2, fever 3, pelvic cellulitis 1, abscess 1, venous thrombophebitis 1, pulmonary embolus 1, bowel obstruction 1, ileus 4, pneumonia 1, wound infection 3, urinary tract fistula 1, bowel fisula 1, congestive heart disease 1, arrhythmia 1	9	25.8	3	<1
Kyrgiou et al[9]	99	LH 54.5 LH+PLA 45.5	105 [60–150]	NR	4 (2–35)	Overall 21 Ileus 2, deep venous thrombosis 2, pulmonary embolism 1, minor wound dehiscensce 10, other significant morbidity 9	4	27	NR	NR
Boosz et al[10]	107	TLH 28.0 TLH+PLA 36.4 TLH+PLA+ PALA 35.5	190.6 ± 83.2	NR	NR	Intraoperative 5.6 Bladder 2.8, ureter 0.9, intestinal 0.9, vagina 0.9 Postoperative 10.3 No detailed data	NR	NR	0.9	NR
Farthing et al[11]	191	TLH 96.9 TLH+PLA 3.1	75 (25–300)	100 (5–2000)	2 (1–13)	Intraoperative 4.19 Visceral 1.57, vagina 1.04, vascular 0.52%, pulmonary 1.04 Postoperative 6.80 Wound infection 1.04, cardiac causes 0.52, any bleeding 2.61, pulmonary 1.57, visceral 1.04, metabolic 0.52	1.57	1.04	NR	0
Wright et al[12]	1027	TLH/LAVH 44.2 TLH/LAVH+ PLA 55.8	NR	NR	NR	Overall 9.8 Intraoperative 4.0 Bladder 1.0, ureter 0.7, intestinal 0.5, vascular 0.1, others 3.1 Postoperative Wound complication 1.5, abscess 0.3, bowel obstruction 1.0, venous thromboembolism 0.4, cardiopulmonary arrest 0.1, respiratory failure 3.2, renal failure 1.2, stroke 0.2, bacteremia 0.3, shock 0.7, pneumonia 0.3	3.2	NR	0.8	0.2

Kuoppala et al[13]	40	LH 10 LH+PLA 87.5	145 ± 32	171 ± 145	2.7 ± 1.1	Intraoperative 0 Postoperative 37.5 Urosepsis 2.5, lower urinary tract 2.5, vaginal cuff ellulitis 10, port-site wound 2.5, lymphedema 12.5. Pelvic lymphcyst 2.5, port-site hernia 2.5, ileus 2.5	2.5	2.5	NR	NR
Mourits et al[1]	185	TLH 100	115 (35–267)	100 (10–1500)	2 (1–25)	Overall: major 14.6, minor 13.0 Intraoperative: major 2.7, minor 8.1 Bowel 2.2, ureter 1.1, bladder 1.1, hemorrhage 3.2 Postoperative: major 11.9, minor 9.7 Infection 38.0°C 2.2, hematoma 0.5, wound dehiscence 1.1, wound infection 1.6, ileus 1.6, urinary tract infection 7.0, urinary retention 2.2	3.2	10.8	NR	1.6

Data are expressed as median (range), median [interquartile range], or mean ± standard deviation.
LAVH = laparoscopic assisted vaginal hysterectomy; LH = laparoscopic hysterectomy (details unknown); NR = not reported; PALA = para-aortic lymphadenectomy; PLA = pelvic lymphadenectomy; RH = robotic hysterectomy; TLH = total laparoscopic hysterectomy; TLmRH = total laparoscopic modified radical hysterectomy.

In cases where PALA was performed, this procedure was undertaken through the retroperitoneal cavity, followed by TLmRH and PLA. When PLA and/or PALA was excluded, we diagnosed the stage of patients clinically using preoperative CT scan.

The surgical procedure for TLmRH, equivalent to Piver–Rutledge class II hysterectomy, was as follows: patients were under endotracheal general anesthesia in a modified dorso-lithotomy position. To prevent the scattering of cancer cells to the vagina, a cervical cuff was made to cover the external os of the uterus transvaginally prior to the laparoscopic surgery. We used a five-port technique without intrauterine manipulation. The initial 12-mm umbilical port was inserted and the abdomen was insufflated with carbon dioxide (10 mmHg). Three additional 5-mm trocars were inserted in the right, left, and medial part of the lower abdomen at the level of the anterior superior iliac spine. Another 5 mm trocar was inserted under the left costal arch to retract the uterus with grasping forceps. After collecting peritoneal washings for cytologic examination, the bilateral tubes were coagulated with bipolar forceps to prevent scattering of cancer cells to the peritoneal cavity. After opening the vesicouterine peritoneum, the round ligament was cut with an ENSEAL tissue sealer (Ethicon Endo-Surgery, Cincinnati, OH, USA). The uterine arteries and the ureters were identified and the uterine arteries were ligated and cut. The vesicouterine, infundibulopelvic, and uterosacral ligaments were transected. The paracolpium was ligated and resected, then circumferential colpotomy was performed on the rim of the Vagi-pipe (Hakko, Chikuma, Japan). The uterus and adnexa were removed through the vagina and the vaginal vault was sutured laparoscopically. The operation was completed by placing a drain on the pouch of Douglas.

We analyzed the characteristics and surgical outcomes of our patients and compared them to previously reported results.

Results

Forty-nine patients who underwent TLmRH were included; of these, 20 underwent TLmRH + BSO, 18 underwent TLmRH + BSO + PLA, and 11 underwent TLmRH + BSO + PLA + PALA. The characteristics of the patients and surgical results are summarized in Table 1. The median age was 57 years (range, 39–77 years), the median body mass index was 23.7 kg/m^2 (range, 17.7–39.4 kg/m^2), and 24.5% of our patients had previous abdominal surgery. The postoperative histological diagnosis of the majority of patients was Grade 1 or 2 endometrioid carcinoma (43 cases, 88%). The staging of the majority of patients was FIGO 1A (90%). The median operative time was 204 minutes (range, 99–504 minutes), and the median intraoperative blood loss was 150 mL (range, 0–680 mL). None of the patients needed a blood transfusion, conversion to laparotomy, or reoperation. The mean length of vaginal wall that was removed with the uterus was 20.0 mm (range, 10.0–27.5 mm).

Intraoperative complications were observed in three patients and included bladder, nerve, and ureter injury. The bladder injury occurred during the TLmRH procedure and was managed laparoscopically. The obturator nerve injury was observed during the PLA procedure and was fixed laparoscopically. The ureter injury occurred during the PALA procedure and required the indwelling of a urethral stent for 3 months after surgery. Postoperative complications were seen in nine patients (Table 1).

We compared these results to previous reports[1,8–13] that studied patients who underwent laparoscopic hysterectomy for endometrial cancer (Table 2). We found that the operative time was longer in our study (median, 204 minutes) than in others (75–204 minutes). The hospital stay after surgery also tended to be longer in our study (6 days) than in others (2–4 days). However, blood loss (150 mL vs. 100–171 mL), the incidence of intraoperative complications (6.1% vs. 0–10.8%), and the incidence of

Table 3
Comparison with the previous reports of TLmRH with or without pelvic lymphadenectomy.

	Present study	Terai et al[14]	Ditto et al[15] (cervical cancer)
	($n = 38$)	($n = 39$)	($n = 60$)
Age (y)	55.5 (39–73)	56.6 ± 10	46 (29–79)
BMI (kg/m^2)	23.5 (17.7–39.4)	22.5 ± 5.5	24.3 ± 2.9
No. of nulliparous	9 (23.7%)	9 (23.1%)	NR
Surgical procedure			
TLmRH	20 (52.6%)	15 (38.5%)	0
TLmRH+PLA	18 (47.4%)	24 (61.5%)	60 (100%)
Operative time (min)	192.5 (99–274)	321.1 ± 65.9	215.9 ± 61.6
Estimated blood loss (mL)	114 (0–680)	42.9 ± 76.3	50 (50–500)
Length of cervical cuff (mm)	20.0 (10.0–27.5)	12.0 ± 4.1	NR
No. of dissected pelvic lymph nodes	28 (15–47)	32.5	25.4 ± 10.0
Postoperative Hb value (g/dL)	10.4 (8.4–11.8)	11.5 ± 1.1	NR
Postoperative CRP value (mg/dL)	1.290 (0.131–10.577)	3.77 ± 2.7	NR
Time to passage of flatus (d)	1 (1–3)	1.6 ± 0.6	NR
Blood transfusion required	0	0 (autologous 1)	1 (2%)
Conversion of laparoscopy to laparotomy	0	0	NR

Data are expressed as median (range), median ± standard deviation, or mean ± standard deviation.
BMI = body mass index; NR = not reported; PLA = pelvic lymphadenectomy; TLmRH = total laparoscopic modified radical hysterectomy.

postoperative complications (18.4% vs. 6.8–37.5%) were almost identical to other reports.[1,8–13]

We also compared our results to previous reports[14,15] that studied patients who received TLmRH with or without PLA for endometrial cancer or cervical cancer (Table 3). We found that the estimated blood loss tended to be greater in our study than in others and the operative time was equivalent.

The patients were followed every 2–3 months for first 1–2 years and every 4–6 months thereafter for 5 years with bimanual examination, Papanicolaou smear of vaginal stump, ultrasonography, and serum CA125. Examination with CT scan is occasionally adopted. The median follow-up was 673 days (range, 97–1639 days). During the follow-up period, one patient of stage 1A, G1 who underwent TLmRH + BSO had peritoneal metastasis 4 months after the surgery. However, she obtained complete remission with chemotherapy. As of the latest follow-up, all patients were doing well and showed no signs of recurrence.

Discussion

The present study revealed that TLmRH is a feasible and safe procedure for the treatment of early stage endometrial cancer. When we compared our results to those in previously reported studies of patients treated with total laparoscopic hysterectomy (TLH),[1,8–13] we tended to need more operating time. However, this is partly because our procedure also included the time needed to make the cervical cuff prior to the laparoscopic surgery and the time needed for the lymphadenectomies. The postoperative hospital stay also tended to be longer in this study. Although no study has compared the hospital stay length between Japan and Western countries, operated patients seem to have tendency to stay in the hospital longer in Japan compared to Western countries. For instance, in the studies that compare laparotomic and laparoscopic mRH, Terai et al[14] reported that mean days of hospital stay were 14.6 ± 12.6 and 9.3 ± 2.5, respectively, in a Japanese hospital. By contrast, Ditto et al[15] reported that median hospital stays were 6 days (3–14 days) and 4 days (3–11 days), respectively, in an Italian hospital. These differences may be the reason for the results, which showed longer postoperative hospital stay in this study. When we compared our cases to those previously treated with TLmRH, the estimated blood loss tended to be greater. The reason for this is uncertain; however, it does not seem to be remarkable. Aside from these observations, our results are comparable with previous studies.[14,15] In this study, transfusion, conversion to laparotomy, and reoperation were not observed. This may be due to improvements in technical equipment and the experience level of the surgeons.

Laparoscopic surgery has been increasingly utilized for patients with early stage endometrial cancer, consistent with the trend toward less invasive surgery. There have been many reports regarding laparoscopic surgery for early stage endometrial cancer. de la Orden et al[16] performed a systemic review of four randomized clinical trials and concluded that the safety and efficacy of laparoscopic surgery are equivalent to those of open surgery in the treatment of early stage endometrial cancer. They also reported that laparoscopic surgery appears to have certain advantages: more rapid recovery, less pain, less bleeding, and fewer complications. The numbers of lymph nodes resected were equivalent. The duration of surgery tended to be longer for laparoscopic surgery. Tozzi et al[17] reported that no difference was found between laparoscopic and open surgery in terms of overall, disease free, or cause-specific survival among patients with FIGO stage I to III endometrial cancer. Walker et al[8] compared laparotomy and laparoscopy for the surgical staging of endometrial cancer. In their report, laparoscopic surgery was associated with shorter hospital stays and fewer moderate-to-severe postoperative adverse events. Associated with this study, reports have also found that patients had a superior quality of life in the first 6 postoperative weeks,[18] comprehensive surgical staging can be performed with similar overall survival, and relatively small differences were observed in recurrence rates[19] in the patients with endometrial cancer treated with laparoscopy, compared with those treated with laparotomy.

TLH is the current standard procedure for removing the uterus laparoscopically. However, a risk of this procedure is the failure to accomplish the extrafascial procedure fully, resulting in a small part of the uterine cervix remaining. Han et al[20] compared laparotomic mRH and extrafascial hysterectomy in the treatment of stage I endometrial cancer and they could not see the statistical difference in recurrence rate and 5-year disease-free survival between them. However, they reported that further studies using larger sample sizes were needed because the different recurrence rate and 5-year disease-free survival that might show the superiority of mRH were observed in their small number of study population. Signorelli et al[21] also compared laparotomic mRH and extrafascial hysterectomy in the treatment of stage I endometrial cancer. They concluded that mRH did not improve locoregional control and survival compared to class I or extrafascial hysterectomy; however, mRH allows optional vaginal and pelvic control of disease with a

minimal increase in surgical morbidity in cases where an adequate vaginal cuff transection is not feasible with class I hysterectomy. Because TLmRH resects the uterus thoroughly with some length of vaginal wall, it may be a preferred option compared to extrafascial hysterectomy. For this reason, we adopted TLmRH for the treatment of early stage endometrial cancer. In this study, we obtained a median length of resected vaginal wall of 20 mm. The incidence of vaginal recurrence has been reported to be 3.1% in patients treated with total abdominal hysterectomy and BSO without vaginal brachytherapy.[22] TLmRH may help to reduce this rate, although further studies are needed to demonstrate the advantage of TLmRH over TLH.

In conclusion, TLmRH is safe and feasible for the treatment of early stage endometrial cancer. This procedure can be an alternative to TLH, especially in cases where the uterus must be removed completely.

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