The Modern Surgical Strategy for Endometrial Cancer: Laparoscopic Surgery

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Abstract Surgical staging and management through laparotomy has been the "gold standard" for treatment of endometrial cancer. However, recent advances in laparoscopic surgical techniques and instrumentation have meant that all surgical procedures for the treatment of endometrial cancer can now be performed using laparoscopy, which has naturally led to an increase in its use for treating this condition. Indeed, laparoscopic surgery is now the preferred alternative to laparotomy for the surgical management of endometrial cancer. Laparoscopic surgery is associated with improved outcomes, less complications, and improved quality of life, without compromising survival of patients. This review provides an update on the role of laparoscopic surgery for the surgical management of endometrial cancer with particular emphasis on feasibility, safety, and efficacy, based on the results of randomized, controlled trials comparing laparoscopy and laparotomy for surgical staging of endometrial cancer.

Keywords Endometrial cancer · Laparoscopy · Laparotomy · Staging operation · Surgical management

Introduction

Endometrial cancer is the sixth most common female cancer and the second most common gynecologic cancer worldwide [1, 2]. It is the most common gynecologic cancer in developed western countries [3, 4], and the number of patients in these countries is increasing [5]. In eastern countries, the incidence also is increasing rapidly [5], and

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it will likely become the most common gynecologic cancer in the near future [6–9].

Approximately 75 % of endometrial cancers are diagnosed at an early stage in which the disease is confined to the uterus [10]. The cure and survival rate is very high in these patients after surgical management, with or without adjuvant therapy. Surgical management is the mainstay of treatment for patients with endometrial cancer. Contemporary standard surgical management for endometrial cancer includes total hysterectomy, bilateral salpingo-oophorectomy, and pelvic and/or paraaortic lymphadenectomy through laparotomy. However, a recent trend in the surgical management of endometrial cancer is the use of laparoscopic surgery. Laparoscopic surgery has been shown to have several benefits over a conventional abdominal approach in the surgical management of benign disease, including less postoperative pain, improved cosmesis, less blood loss, shorter recovery time, and shorter length of hospital stay without increasing perioperative complications [11]. Indeed, whilst endometrial cancer is the first gynecologic cancer to be treated laparoscopically, a laparoscopic approach also is being used for the surgical management of malignant disease. Following the first report on the use of laparoscopic surgery for endometrial cancer by Childers et al. [12], the feasibility, safety, and efficacy of laparoscopic surgery in the surgical management of endometrial cancer has been reported in numerous retrospective studies [13-25], prospective nonrandomized studies [26–29], or randomized, controlled trials (RCTs) [30-42, 43., 44., 45.]. With advances in surgical technique and instrumentation, laparoscopic surgery recently has become widely used for the surgical management of endometrial cancer, with an increasing role being noted for treatment of the disease.

This review provides an update on the role of laparoscopic surgery for the surgical management of endometrial cancer with particular emphasis on feasibility, safety, and efficacy based on the results of randomized, controlled trials



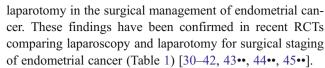
comparing laparoscopy and laparotomy for surgical staging of endometrial cancer.

Feasibility of Laparoscopic Surgery

With recent advances in surgical instrumentation and technique, all surgical procedures for the management of endometrial cancer can now be performed using laparoscopy. However, in the largest randomized, controlled trial (Gynecologic Oncology Group (GOG), LAP 2 trial) comparing laparoscopy with laparotomy for surgical staging of endometrial cancer, the rate of conversion to laparotomy after initially being assigned to laparoscopic surgery was 25.8 % [44••]. The main reason for conversion to laparotomy was obesity (approximately 60 % of cases), and the conversion rate for morbidly obese women was 57 % [44...]. Lack of surgical experience in using a laparoscopic technique for cancer treatment may be one key reason for such a high conversion rate; only 8 % of surgical staging procedures for endometrial cancer were performed using laparoscopic surgery during the GOG LAP2 trial in the United States (1996-2005) [46•]. The results of eight RCTs comparing laparoscopy and laparotomy for surgical staging of endometrial cancer are shown in Table 1 [30-42, 43., 44., 45.]. The main reasons for conversion to laparotomy after initial assignment to laparoscopic surgery in these RCTs are shown in Table 2 [30-42, 43., 44., 45.]. Excluding the GOG LAP2 trial, the conversion rate in RCTs ranged from 0 % to 10.8 %. In experienced surgeons' retrospective or prospective series, the conversion rate is approximately 5 % [14, 17, 23, 26, 47]. In series where experienced surgeons performed consecutive laparoscopic surgery for all patients with earlystage endometrial cancer, regardless of age, body mass index, uterine size, or history of prior surgery, the conversion rate was only 3-5 % [46•, 48], and only 7 % for morbidly obese patients [46•]. This indicates that laparoscopic surgery is feasible for the vast majority of patients with early-stage endometrial cancer; however, surgeon's experience in using the laparoscopic technique is critical to achieve good outcomes.

Perioperative Outcomes and Complications of Laparoscopic Surgery

Many retrospective studies [13–25], prospective non-randomized studies [26–29], and meta-analyses [49•, 50–52, 53•] published during the last decade have suggested that laparoscopic surgery has an improved outcomes profile in terms of estimated blood loss and transfusion requirements, recovery of bowel movement, postoperative hospital stay, and perioperative complications compared with



The following discussion of outcomes and complications of laparoscopic surgery compared with laparotomy is based on the results of the eight RCTs presented in Table 1. It can be seen that the operating time for laparoscopic surgery was similar to or slightly longer than that of laparotomy for surgical staging of endometrial cancer. However, operating time depended on the surgeon's experience with laparoscopic surgery. Estimated blood loss was significantly less for laparoscopic surgery in all RCTs, and transfusion requirement also was less frequent for laparoscopic surgery in most studies. The time interval to the recovery of bowel movement was reported in only one RCT, and it was significantly shorter in the laparoscopic surgery group. Postoperative hospital stay was significantly shorter for the laparoscopic surgery group in all RCTs. These results demonstrate the overall faster recovery of patients who undergo laparoscopic surgery compared with laparotomy. Other studies have reported less need for pain medication and quicker resumption of daily activities in patients who undergo laparoscopic surgery [42]. Intraoperative complication rates were similar between laparoscopic surgery and laparotomy in all RCTs, but postoperative complication rates were lower for the laparoscopic surgery group in most studies. The number of lymph nodes retrieved was similar between laparoscopic surgery and laparotomy in most studies. Therefore, laparoscopic surgery for surgical staging of endometrial cancer is associated with less blood loss and transfusion, faster recovery of bowel movement, less use of pain medication and quicker resumption of daily activities, shorter postoperative hospital stay, and less frequent postoperative complications compared with laparotomy. Operating time of laparoscopic surgery is similar to or slightly longer than that of laparotomy.

Quality of Life after Laparoscopic Surgery

Only four RCTs have reported quality of life (QOL) data for patients undergoing either laparoscopic or laparotomy [36, 37, 39, 42, 43••]. Zullo et al. performed QOL assessments at baseline, at 1, 2, and 6 months, and then annually for 7 years after surgery [36, 37]. Laparoscopic surgery was associated with a significantly better QOL for the first 3 years after surgery, after which time no difference was noted.

Kornblith et al. reported quality of life (QOL) data for the first 802 patients of the GOG LAP2 study [43••]. Assessments were performed at baseline, at 1, 3, and 6 weeks, and 6 months after surgery. Laparoscopic surgery was associated with significantly higher Functional Assessment of Cancer Therapy-General (FACT-G) scores, better physical



Table 1 Results of randomized, controlled trials comparing laparoscopy and laparotomy for surgical staging of endometrial cancer

Author	Year	Surgery mode	7	n	Age (yr)	В	MI	OP Hx	Me	ed Dz	Operating time	Estimated blood loss		ransfusior
Fram et al. [30]	2002	Laparo	scopy	29	61.2	2	5.7	nr	nr		136.2	145.5	1	
		Laparo		32	60.6		6.2	nr	nr		101.9	501.6	2	
T 1 [22]	2005	P value		(2	ns	n		22 (26 5 0/)	20	(41.2.0/)	<0.05	<0.05		*
Tozzi et al. [32]	2005	Laparo:		63 59	67 (35–88) 66 (36–89)		1.3 (20.2–43.6) 2.1 (20–51.3)	23 (36.5 %) 21 (35.4 %)		(41.2 %)	176.4* 166.1*	229.2* 594.2*		* 1*
		P value	-	33	ns	n	` /	ns	ns	(30.9 /0)	ns	0		.01
Zorlu et al. [34]	2005	Laparo		26	56.6 (40-7		4.4	nr	nr		155	nr	n	
		Laparo	-	26	54.9 (36-7	7) 2	6.2	nr	nr		144	nr	n	r
	•	P value		0.4	ns	n					ns	5 0 (3 0 0)	~ `	
Malzoni et al. [35]	2009	Laparo:		81 78	60 (39–81) 63 (43–84)		8 (19–37) 9 (17–39)	nr	nr		136 (118–181) 123 (111–198)	`	′	
		P value		70	ns (43–64)	n		nr	nr		<0.01	145 (60–2 <0.01	255) n	I
Zullo et al. [36]	2009	Laparos		40	62.1		9.9	15	nr		196.7	173.9	0	
. ,		Laparo		38	61.5	3	1.8	14	nr		135.3	282.5	1	
		P value			ns	n	S	ns			< 0.05	< 0.05		
Janda et al. [39]	2010	Laparo		190	62.8	n		nr	nr		138	nr	n	
		Laparo		142	62.7	n	r	nr	nr		109 0	nr	n	r
Mourits et al. [42]	2010	Laparos		185	ns 62 (40–89)	2	9 (17–55)	55 (29.7)	10	7 (57.8)	115 (35–267)	100 (10-1	1500) n	r
would et al. [42]	2010	Laparo		94	63 (39–86)		8 (19–48)	23 (24.5)		(61.7)	71 (31.239)	200 (50–2		
		P value	-		, ,		,	, ,		,	< 0.001	< 0.001	,	
Walker et	2012	Laparo			63	2		nr	nr		204	nr		43 (9)
al. [45••]		Laparo	-	902	63	2		nr	nr		130	nr		6 (7)
		P value			ns	n	S				<0.001		0	.28
Author	LND)	LNs		Convers to laparo		Intraoperative complication			Operative mortality		Hospital stay	DFS	OS
Fram et al. [30]	16		21.3		2		0	3		0	nr	2.3	nr	nr
	17		21.9				2	4		0	nr	5.5	nr	nr
			ns									< 0.05		
Tozzi et al. [32]	52 (8	34 %)	28.6	(18-61) 5		3 (4.7 %)	15 (23.8	%)	0	2*	8.6*	82.7 %	87.4 %
	`	33.5 %)		(16-54			9 (15.2 %)	28 (47.4	- 1	0	2.4*	11.7*	86.5 %	91.6 %
	., (,,,,	20	(10 0	•)		0.08	0.01	, 0)	Ü	0.02	< 0.001	0.38	0.33
7	26		10.2	(0. 21)	0					0				
Zorlu et al. [34]	26			(9-31)			0	0		0	nr	4.1	nr	nr
	26			(9–38)			0	5		0	nr	8.2	nr	nr
			ns									ns		
Malzoni et al. [35]	81			(16–39	/		1	8		0	nr	2.1 (1-5)		
	78		22.2	(17–38	3)		2	11		0	nr	5.1 (1-7)	88.5 %	91.1 %
												< 0.01	0.28	0.31
Zullo et al. [36]	40		11.5		5		3 (7.5)	11 (27.5)		0	nr	3	80.0 %	82.5 %
	38		10.7				4 (10.5)	18 (47.4))	0	nr	6.9	81.6 %	84.2 %
							ns	< 0.05				< 0.05	0.51	0.54
Janda et al. [39]	77 (4	10.5)	nr		8		14 (7.4)	15 (7.9)		nr	nr	nr	nr	nr
> [6>]	96 (6		nr				8 (5.6)	27 (19)		nr	nr	nr	nr	nr
) o (111				0.53	2, (1)		***	***	-11	111	***
Mourite et al [40]	***		42.00		20 (10 0	`		22 (11 0)	**			2 (1 25)	***	
Mourits et al. [42]	nr		nr		20 (10.8)	5 (2.7)**	22 (11.9)		nr	nr	2 (1–25)	nr	nr
	nr		nr				4 (4.3)** 0.49	10 (10.6)	**	nr	nr	5 (3-32) <0.001	nr	nr
Walker et	1585	(98)	18		434 (25.	8)	160 (10)	240 (14)		10 (<1)	nr	3	86.3 %	89.8 %
Walkerer	1000	()			.5. (25.	~,	` /							
al. [45••]	868	(99)	17				69 (8)	[9] (7) (1)		× (1)	nr			
	868	(99)	17 0.18				69 (8) 0.11	191 (21) <0.001		8 (1) 0.4	nr	4	88.4 %	% 89.8 % ns

^{*}Data were reported only in preliminary report



^{**}Major complications

Table 2 Cases that were convereted to laparotomy after assinged to laparoscopic surgery in randomized, controlled trials

Author	Year	Cases in laparoscopy group, n	Converted cases, n (%)	Reasons of conversion		
Fram et al. [30]	2002	29	2 (6.9)	1-improper bowel preparation		
				1-thick omental adhesion		
Tozzi et al. [32]	2005	63	5 (7.9)	4-intraperitoneal disease		
				1-small bowel injury during adheisolysis		
Zorlu et al. [34]	2005	26	0	_		
Malzoni et al. [35]	2009	81	0	_		
Zullo et al. [36]	2009	40	5 (12.5)	3-anesthesiologist indication for the impossibility to maintain a Trendelenburg's position during surgical internvention		
				1-extrauterine spread		
				1-severe adhesion		
Obermair et al. [40]	2012	404	24 (5.9)	15-anatomical reasons that prevneted completion of TLH		
				7-intraoperative complication		
				2-technical reasons		
Mourits et al. [42]	2010	185	20 (10.8)	9-inadequate exposure		
				9-uterus too large		
				1-bleeding		
				2-technical problems		
				5-obesity or anaesthetic complications to obesity		
				3-additional pathology		
				1-other reason		
				Some patients had more than one reason for conversion		
Walker et al. [45••]	2012	1682	434 (25.8)	246 (56.7)—poor exposure		
				69 (43.1)—cancer requiring laparotomy for resection		
				49 (11.3)—excessive bleeding		
				10 (2.3)—equiment failure		
				70 (16.1)—other cuase		

functioning, better body image, less pain (including its effect on QOL), and an earlier resumption of normal activities and return to work at 6 weeks after surgery compared with laparotomic surgery. However, the difference in body image and return to work between laparoscopic and laparotomic surgery groups was modest at 6 weeks after surgery, and differences in QOL parameters were not significant at 6 months after surgery except for body image where laparoscopic surgery showed a significant benefit.

Janda et al. compared the QOL results of 361 patients undergoing either laparoscopy or laparotomy for stage I endometrial cancer [39]. QOL assessments were performed at baseline, at 1 and 4 weeks (early), and 3 and 6 months (late) after surgery. Laparoscopic surgery was associated with a significantly greater improvement in QOL from baseline compared with that of laparotomic surgery in all

subscales of FACT-G except emotional and social well being in the early phase of recovery. Improvement in QOL up to 6 months after surgery continued to favor laparoscopic surgery, except for the emotional and social well being subscale of FACT-G and the visual analogue scale of the EuroQOL five dimensions (EuroQOL-VAS).

Mourits et al. also compared QOL results between laparoscopy and laparotomy as a secondary outcome of their study [42]. Assessments were performed at baseline, and at 6 weeks, 3 months, and 6 months after surgery. The response rate from the 283 study participants to the QOL questionnaire was 90.1 %. Laparoscopic surgery was associated with a significantly higher physical functioning subscale of the SF-36 at 6 weeks and a significantly higher rolephysical subscale at 3 months after surgery. However, laparoscopic surgery was associated with a significantly lower



vitality subscale of the mental dimension at 3 months after surgery. There was no difference in other subscales between the two surgery groups.

These RCTs demonstrate that laparoscopic surgery is associated with an improved QOL compared with laparotomy after surgical staging for endometrial cancer, especially in the early phase of recovery. This benefit is, however, subdued in the late phase of recovery.

Survival Outcomes After Laparoscopic Surgery

There is no evidence that laparoscopic surgery compromises the survival of patients with endometrial cancer. Retrospective [13–25] or prospective, nonrandomized studies [26–29] have shown comparable survival outcomes for laparoscopic surgery and laparotomy. Four RCTs reported the long-term survival outcomes after laparoscopic surgery compared with laparotomy in patients with endometrial cancer (Table 1) [33, 35, 36, 45••]. Laparoscopic surgery had similar survival outcomes compared with laparotomy in these RCTs. The GOG LAP2 trial was designed to confirm the noninferiority of recurrence-free interval, defined as a hazard ratio of 1.4, for laparoscopy relative to laparotomy with sufficient statistical power [45...]. This trial confirmed the equivalence of survival outcomes between laparoscopy and laparotomy for surgical management of endometrial cancer. The estimated 5-year recurrence rate was 13.68 % for the laparoscopy group and 11.61 % for the laparotomy group. The estimated 5-year overall survival was 89.8 % for both surgery groups. The pattern of recurrence was not different between the two groups. Trocar site recurrence occurred in only 4 of 1,696 patients (0.24 %) in the laparoscopy group. Because three of the four patients with trocar site recurrence had stage III-IV disease, the risk of trocar site recurrence after laparoscopic surgery in patients with stage I-II disease appears negligible. It can be concluded that laparoscopic surgery has equivalent survival outcomes compared with laparotomy after stating operation of endometrial cancer.

Conclusions

Surgical management is the main stay for the treatment of endometrial cancer. Surgical staging through laparotomy has been the "gold standard" surgical management for endometrial cancer. However, with recent advances in laparoscopic surgical techniques and instruments, all surgical procedures for the treatment of endometrial cancer can be performed using laparoscopy, and the use of laparoscopic surgery for the surgical management of endometrial cancer is continuously increasing. Current literature shows that laparoscopic surgery is the preferred alternative to

laparotomic surgery for the surgical management of endometrial cancer. Laparoscopic surgery is feasible in the vast majority of patients with endometrial cancer if the surgery is performed by an experienced surgeon. Laparoscopic surgery is associated with favorable operative outcomes, including less blood loss and need for transfusion, less use of pain medication, faster recovery of bowel movement, shorter postoperative hospital stay, less frequent perioperative complications, earlier return to work, and faster resumption of daily activities. The lymph node yield is similar between laparoscopic surgery and laparotomic surgery. The OOL of patients in the early phase of recovery after surgery is significantly improved in patients who undergo laparoscopic surgery. The disease-free and overall survival rates after either laparoscopic or laparotomic surgery are comparable. Surgeon's training and experience are important factors in achieving optimal outcomes when using a laparoscopic approach.

Disclosures No potential conflicts of interest relevant to this article were reported.

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