Minimally invasive approach for endometrial cancer: robotic assisted *vs.* straight stick laparoscopy

Oded Raban[1,2,3], Yasir Ahmad Bukhari[1,2,3], Walter Henri Gotlieb[1,2,3]

[1]Division of Gynecologic Oncology, Jewish General Hospital, McGill University, Montreal, Quebec, Canada; [2]Segal Cancer Center, Lady Davis Institute of Medical Research, Montreal, Quebec, Canada; [3]Department of Obstetrics and Gynecology, McGill University, Montreal, Quebec, Canada

Contributions: (I) Conception and design: WH Gotlieb, O Raban; (II) Administrative support: All authors; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: O Raban, YA Bukhari; (V) Data analysis and interpretation: All authors; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Walter Henri Gotlieb. Division of Gynecologic Oncology, Jewish General Hospital, McGill University, Segal Cancer Center, Lady Davis Institute of Medical Research, Department of Obstetrics and Gynecology, McGill University, 3755 Cote Ste. Catherine Road, Montreal, QC H3T 1E2, Canada. Email: walter.gotlieb@mcgill.ca.

Abstract: The introduction of laparoscopic surgery in the early 1990's presented an improved alternative to laparotomy, slowly shifting the surgical treatment for Endometrial Cancer (EC) toward minimally invasive surgery (MIS), with equivalent oncologic outcome and reduced perioperative morbidity. Robotic assisted surgery (RAS) introduced multiple technical improvements to straight stick laparoscopy (LS), associated with improved perioperative outcome including reduced blood loss, fewer conversions to laparotomy and shorter hospital stay, whereas other perioperative outcomes appear similar. Due to its technical advantages, adaptation of RAS involves a shorter learning curve than LS and offers improved ergonomics compared to straight stick instrumentation. The advantages of RAS are more pronounced in patients with increased body mass index (BMI). Both LS and RAS have been shown to be safe in elderly patients and although available data shows benefit compared to laparotomy, it does not suggest superiority of one MIS approach over the other. Even though RAS and LS have comparable oncologic outcomes, the integration of RAS facilitated the shift toward MIS, where LS had failed to significantly reduce the rate of laparotomy. This shift to MIS was associated with reduced postoperative length of stay and complication rates, offsetting the increased costs involved with RAS. By introducing a computer interface, RAS is allowing augmented reality and digital analysis, leading surgery towards precision surgery and a high-tech future.

Keywords: Endometrial cancer; uterine cancer; minimally invasive surgery; laparoscopy; robotic assisted surgery

Received: 04 January 2021; Accepted: 12 April 2021; Published: 25 March 2022.
doi: 10.21037/gpm-21-1
View this article at: http://dx.doi.org/10.21037/gpm-21-1

Introduction

The standard of care treatment for Endometrial Cancer includes total hysterectomy, bilateral salpingo-oophorectomy and lymph node assessment. Staging procedure via straight stick laparoscopy has been described in the early 1990's (1) and has 20 years later been established as the gold standard, improving patients' quality of life, reducing perioperative complications, with comparable oncologic outcomes (2-6). Despite its proven benefits, the adoption of minimally invasive surgery (MIS) has been slow, and laparotomy remained the dominant approach (7,8). Robotic-assisted laparoscopy was introduced when the Da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA, USA) was approved by the FDA for gynecologic surgery in 2005. Among the technical advantages of robotic assisted surgery (RAS) over straight stick laparoscopic surgery (LS) are 7 degrees of movement, smaller instruments, improved three-dimensional immersion vision with no fulcrum effect, neutralization of tremor, and control of the camera by the primary surgeon. Potential disadvantages of robotic assisted surgery include lack of haptics and the high acquisition cost. The Laparoscopic Approach to Cervical Cancer (LACC) trial, an international multi-center randomized trial, unexpectedly reported a worse oncologic outcome for the patients with cervical cancer who underwent MIS, and challenged our perception of the safety of MIS, and refocused all of us on the importance of safe oncologic principles in surgery. In this article, we aim to review the advantages and shortcomings of robotic assisted laparoscopy compared to straight stick laparoscopy and the impact of MIS on the treatment of endometrial cancer patients.

Procedure and perioperative outcome

Duration of procedure

Robotic assisted surgery requires a particular setup of the operative room as well as additional time required for the docking process, whereas the technical advantages including better visualization and intuitive manipulation are expected to facilitate and accelerate complex procedures. Therefore, the overall effect of RAS on operative times compared to LS was questioned. In a meta-analysis by Ind *et al.* including 36 studies and 8,075 patients, studies have shown variable findings, with some retrospective studies reporting longer operating time for RAS by 18.4 min, while a randomized control trial (RCT) found RAS to have a shorter operating time (9). Overall, the total operating theater time was similar (retrospective studies) or even shorter (RCT).

Lymph node assessment and sentinel lymph node mapping

RAS and LS had a higher rate of lymphadenectomy compared to laparotomy for staging in high risk EC, while the median number of lymph nodes extracted or the number of positive nodes did not differ (10). The number of pelvic or paraaortic lymph nodes obtained using RAS and LS was found to be similar in a meta-analysis comparing the two approaches (9). These studies were relevant as benchmarks, although today the value of the number of nodes resected has lost its relevance in view of the introduction of the more targeted sentinel node mapping.

In recent years, sentinel lymph node (SLN) sampling was shown to be a good alternative to lymphadenectomy in endometrial cancer demonstrating good detection rate with high negative predictive value and reduced morbidity (11). Sentinel lymph node procedure in the SENTI-ENDO study was performed by either open or laparoscopic approach and used dual mapping with technetium and patent blue. Detection rate of any SLN for laparoscopic cases was 90% with 65% bilateral mapping (12). In the more recent FIRES study, SLN mapping using indocyanine green (ICG) during RAS, showed successful mapping of 86% with bilateral mapping 52% (13). Sentinel lymph node mapping using ICG was studied in high-risk endometrial cancer undergoing both LS (14) and RAS (14,15) with positive node detection sensitivity of 96% and 98% respectively. A recent Australian study comparing LS and RAS for SLN mapping reported a slightly higher overall detection rate for laparoscopy (97% *vs.* 88%), with similar bilateral mapping rate (16). The small number of robotic cases (n=33) could explain these findings, given that the learning curve for robotic SLN mapping using indocyanine green was reported to reach a plateau after 27–40 cases (17,18).

Perioperative complications

Numerous studies have compared perioperative outcome between MIS approaches. Average blood loss associated with RAS was reported by Ind *et al.* to be reduced by 57.7 mL compared to LS, however this difference was not clinically significant, and transfusion rate and hemoglobin levels did not differ between the groups (9). No significant difference was found for adverse outcomes, including re-interventions, re-admissions, post-operative complications or major post-operative complications. However, robotic assisted surgery had fewer total complications compared to laparoscopy (RR =0.82).

The rate of conversion of laparoscopy to laparotomy has varied considerably from no conversion (19) to 25.8% (5). Evaluating factors that affect the rate of conversion to laparotomy in LS, morbid obesity [odds ratio (OR), 4.51], suboptimal pelvic examination or enlarged uterus during preoperative evaluation, para-aortic lymphadenectomy, uterine size 250 g or greater, and the presence of extrauterine disease were found to be independent predictors for conversion to laparotomy (20). In a multicenter study, Palomba *et al.* reported a conversion rate of 13.9% of 512 patients undergoing laparoscopy for EC. After Adjusting for stage and other confounding factors, conversion did not significantly affect recurrence rate or overall survival (21).

Thanks to its technical advantages, including better ergonomics and more intuitive manipulation, robotic surgery was expected to allow more complicated procedures

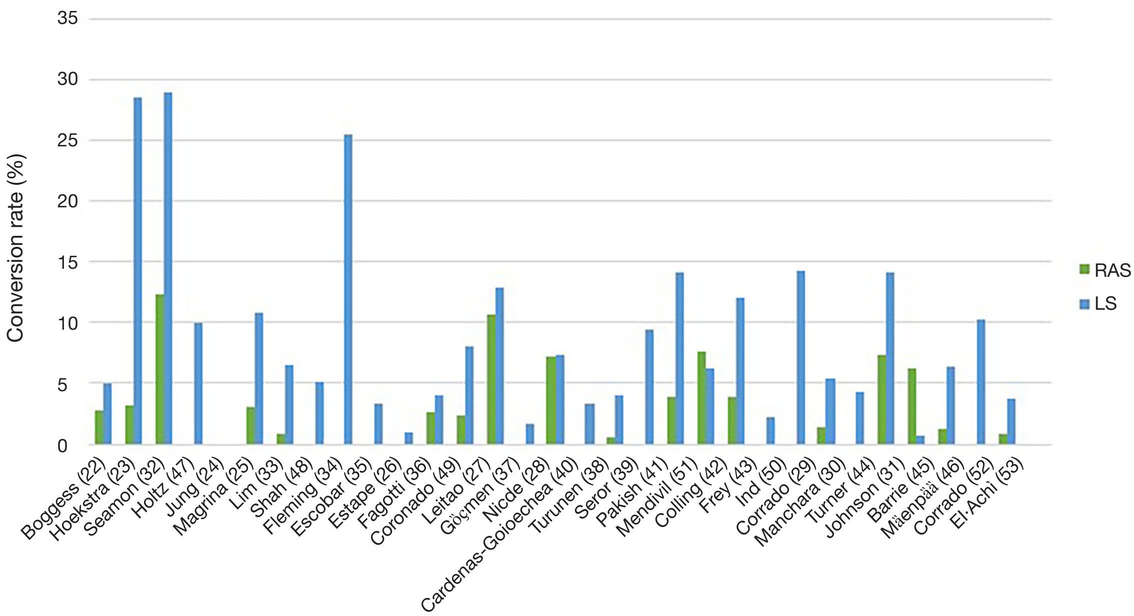

Figure 1 Comparison of conversion rate to laparotomy between LS and RAS. Studies (22-31) reported comparative clinical outcomes between LS, RAS and laparotomy; studies (32-46) reported comparative outcomes between different MIS approaches; studies (47-50) described conversion rates as part of cost-effective analysis; studies (51-53) reported outcomes for morbidly obese patients. RAS, robotic assisted surgery; LS, laparoscopic surgery; MIS, minimally invasive surgery.

to be completed using MIS and reduce the need for conversion to laparotomy. Studies comparing conversion rates to laparotomy for LS and RAS are presented in *Figure 1*. In a randomized controlled trial, Mäenpää *et al.* 10% conversions were observed in LS *vs.* none in the RAS group. On the other hand, a population-based study, including 4,034 Laparoscopic surgeries and 6,313 robotic assisted cases showed a similar conversion rate (54). In a meta-analysis by Ind *et al.* RAS had fewer conversions compared to LS (115 *vs.* 274) with a relative risk of 0.41 (9).

Several studies, including a meta-analysis, reported a shorter hospital stay following RAS *vs.* LS (9), however, it was suggested that variability in management protocols among surgeons contributed to this difference. A large retrospective study comparing surgical approach in 3,712 patients with EC, reported that the mean length of stay was similar between RAS and LS, while it was 2.3 days longer for laparotomy. Robotic assisted procedures were associated with fewer early readmissions, but no difference in overall readmission rate (55). In a recent study reporting the initial experience with RAS in New south Wales, Australia, hospital stay was shorter for RAS compared to LS (1.3 *vs.* 1.8 days) (56).

Studies have shown that the use of opioids analgesics is reduced in RAS compared to laparotomy (57) and LS (58), however, others failed to show a difference (44). No differences could be demonstrated between the two groups for pain scores or post-operative analgesia usage in a meta-analysis (9). Herniation through trocar incisions has been shown to be associated with higher BMI, though similar rates were found for LS and RAS (59). MIS for EC is involved with a low post-operative mortality rate, which was shown to be similar between LS and RAS in a meta-analysis by Behbehani *et al.* (60).

Quality of life

Quality of life (QoL) assessment is a complementary measure in evaluating the outcome of a surgical approach. Several randomised trials showed an advantage LS over laparotomy in QoL measures (3,61). In the GOG LAP2 trial, analysis of postoperative QoL showed an advantage for LS in several parameters including physical functioning, less pain, and earlier resumption of physical activity and return to work (4). In contrast, the overall adjusted QoL did not meet the minimally important difference (MID) between the two surgical arms over 6 weeks. Studies that evaluated immediate QoL following RAS have reported a return to baseline 3–5 weeks post surgery (62,63) which suggests an advantage over LS, although it may originate from different analysis methods. Ferguson *et al.* conducted a multi-center study evaluating QoL and sexual health post RAS, LS, and laparotomy using a series of validated questioners (64). MIS was associated with improved QoL at 3 months and functional well-being at 6 months compared to laparotomy. No difference was found between laparoscopy and RAS. Surgical approach did not have a significant effect on sexual health, although all patients met criteria for sexual dysfunction.

Oncologic outcome and survival

The impact of MIS approach on recurrence and survival in EC has been studied extensively. The LAP2 study included 2,182 patients, of which 31.4% had stage IB and above, and had similar recurrence rates between LS and laparotomy (11.4 *vs.* 10.2) and similar 5-year overall survival (OS, 89.8%) (5). These findings were further supported by the Laparoscopic Approach to Cancer of the Endometrium (65) randomized study which demonstrated a similar 4.5 DFS (0.3% difference favoring laparoscopy) and OS between LS and laparotomy in 760 patients (2).

In addition to these randomized controlled studies, some studies have presented discrepant findings. Song *et al.* compared RAS *vs.* laparotomy in 179 patients with high-intermediate risk EC (66), and found a recurrence rate of 5.9% and a 5-year DFS of 91.8% in the RAS group whereas surprisingly none of the laparotomy group patients recurred. Similar results were found with a HR of 0.9 comparing MIS to open approach in high-risk EC (67), and in a retrospective analysis of the National Cancer Database (68). On the other hand, Monterossi *et al.* reported an increase in recurrence rate after laparotomy compared to MIS in patients with type II endometrial cancer (31.7% *vs.* 17.7%) (69). In addition, an observational study including 419 patients with high-intermediate risk EC who underwent staging including pelvic and paraaortic lymphadenectomy found that LS was associated with improved overall survival compared to open surgery on multivariate analysis, but recurrence rate and recurrence free survival (RFS) were similar (70).

Data analysis of the Danish population between 2005 and 2015 has shown an improved OS since the introduction of robotic assisted surgery (HR of 1.22). Following the incorporation of RAS in the management of EC, laparotomy procedures were associated with decreased OS compared to RAS and LS, whereas no significance difference between MIS approaches was reported (71). In a retrospective study by Cardenas-Goicoechea *et al.* including 415 women, no significant difference was found between RAS and LS in recurrence rate (14.8% *vs.* 12.1%), 3-year disease free survival (DFS, 83.3% *vs.* 88.4%) and 3-year OS (93.3% *vs.* 93.6%) (40). Comparison of single port laparoscopy to LS and RAS did not find difference in progression free survival (PFS) or OS (72). A more recent study summarizing 10 years of robotic experience in a single institution, did not find differences in 5-year DFS or OS between MIS to laparotomy as well as between RAS and LS (73).

Port site recurrence has always been evaluated following MIS in gynecologic oncology (74). The LAP2 study reported a presumed trocar recurrence rate of 0.24% (5), and Barraez *et al.* have reported a low rate for port site metastasis (0.9%) in 438 patients undergoing RAS for EC (75).

General effect on rate of MIS surgery

When examining the impact of robotic surgery on the surgical management of endometrial cancer, a broader view can be used by examining the effect of introducing RAS on the rate of MIS. While laparoscopic approach has been available for almost three decades, the rate of LS increased very gradually, benefitting around 15% of eligible cases (76,77). Early reports have shown that by introducing RAS practice into the care of endometrial cancer, the overall MIS rate was increased by 34.2–81% and was associated with shortened hospital stay and reduced complication rates (50,78).

Database analysis of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) showed that although MIS was associated with increased operating times, it decreased hospital stay by 2.4 days and was associated with a significant decrease in postoperative complications (8). In a follow-up study based on the ACS-NSQIP database by Casarin *et al.*, laparotomy increased odds ratios for major complications (OR=2.4), perioperative complications and perioperative death (OR=3.8). Between 2008 and 2014 an increase in overall MIS rate from 24.2% to 71.4% was accompanied by a decrease in 30-day morbidity (79). An updated analysis published in 2018 distinguished between MIS approaches. The implementation of RAS in the United States has resulted in an absolute 47.3% increase in RAS for endometrial cancer between 2008 and 2015 (9.48%

to 56.82%), while the rate of open surgery has declined by 42.37% (70.45% to 28.08%) and a 4.28% absolute reduction in LS was observed (18.11 to 13.83%) (80). These trends were associated with reduced rate of perioperative morbidity without significant increase in cost compared to open surgery. The effect of RAS on surgical management of EC was not limited to the United States and Canada. In a recent Danish nationwide prospective cohort study including 5,654 with early-stage EC, the introduction of robotic surgery has resulted in a significant increase in the rate of MIS from 3% to 95% and was associated with a reduction in severe complication rate (81).

Special considerations

Obesity

The management of EC is further challenged by the fact that up to 80% of patient are obese and 19% to 36% are morbidly obese and have a higher rate of associated co-morbidities.

Obesity has been associated with increased perioperative morbidity including venous thromboembolism and surgical wound complications, mainly after open surgical staging (82,83). Challenges associated with surgical staging using MIS approach in obese patients include reduced exposure in addition to difficult ventilation and possible cardiovascular compromise, secondary to increased abdominal pressure combined with steep Trendelenburg position. Several observational studies evaluating the laparoscopic approach for obese patients did not show a difference in surgical outcomes or perioperative complications when compared to non-obese patients (84-86).

Robotic surgery has been shown to be safe in surgical staging of obese patients with endometrial cancer. Retrospective studies evaluating RAS showed that increasing BMI did not affect conversion rate, lymph node dissection rate or yield (87) or postoperative complications (87,88). Compared to laparotomy, RAS had a lower rate of postoperative complications (17.7% *vs.* 44%) and shorter length of stay (2 *vs.* 4 days) in patients with BMI >35 kg/m^2 (89). Evaluating MIS approach in obese and morbidly obese patients, RAS was associated with shorter operative time, decreased blood loss, and shorter hospital stay compared to LS (90). *Table 1* (51-53,89-99) summarizes studies comparing RAS with open surgery and/or LS. In a comparative study evaluating 1,087 morbidly obese EC patients, open surgery was associated with increased blood transfusion rate and longer hospital stay compared to LS and RAS (99). In a multi-institutional study comparing RAS and LS including 655 obese and extremely obese patients, a lower conversion rate and reduction in hospital length of stay were reported in the RAS arm. Estimated blood loss was higher and operating time was longer in the RAS group, which could possibly be explained by a higher rate of pelvic lymphadenectomy in the RAS group compared to the LS group (43% *vs.* 19.7%) (52). A meta-analysis including 10,800 obese patients showed slightly higher conversion rates for LS compared to RAS in patients with BMI ≥30 (6.5% *vs.* 5.5%) or BMI ≥40 (7% *vs.* 3.8%). The most common cause for conversion was insufficient exposure, however, the 31% conversion in LS were due to intolerance of Trendelenburg position *vs.* 6% of RAS (100).

Elderly patients

Surgical intervention in older patients is affected by the fact that they tend to be frailer and have more comorbidities. For these reasons, this population is expected to benefit greatly from the advantages of MIS. However, surgeons and anesthesiologists refrained from performing MIS in these patients due to fear from complications associated with deep Trendelenburg position. Straight stick laparoscopy was shown to be feasible, however, in patients older than 65 years it was associated with longer operating time and higher rate of transfusion compared to laparotomy in addition to a high conversion rate to laparotomy (22.4%) (101). In a retrospective analysis of patients from Gynecologic Oncology Group LAP2, benefits of LS over laparotomy were more evident in patients over the age of 60, and included reduced rate of postoperative pneumonia, thromboembolism and ileus in addition to shorter hospital stay (102).

RAS was associated with reduced perioperative complications, reduced blood loss and shortened hospital stay when compared to laparotomy (103-106). Several studies have reported MIS outcomes in elderly patients (*Table 2*) (103-116). Focusing on the effect of age in robotic assisted surgery, studies have reported that perioperative complication rate associated with lymphadenectomy procedure was not significantly altered when a cut-off age of 70 or 75 years was used (116,117). A Healthcare Cost and Utilization Project National Inpatient Sample (HCUP-NIS) database analysis found that age >65 was associated with similar intraoperative complication rate, but higher rates of perioperative (8.3% *vs.* 5.2%), medical complications

Table 1 Comparison of robotic surgery to laparoscopy and/or laparotomy for the treatment of endometrial cancer

Study	Surgical approach	BMI criteria (kg/m^2)	N	Operative time (min)	EBL (mL)	Conversion to open surgery (%)	Post-op complications (%)		Hospital stay (d)
							Wound related	Other	
Bernardini *et al.* (89)	OS/RS	>35	41/45	165/270$^{\#}$	300/200$^{\#}$	–/8.9	19.5/4.4$^{\#}$	44/17.7^,$^{\#}$	4/2$^{\#}$
Borgfeldt *et al.* (91)	OS/RS	≥35	28/79	193/201	427/100$^{\#}$	NR	NR		6.1/2.4$^{\#}$
Fornalik (92)	OS/RS	≥40	35/76	126/203$^{\#}$	500/150$^{\#}$	–/0	3/1.3	29/15	5/1$^{\#}$
Hinshaw *et al.* (93)	OS/RS	≥35	80/56	200/212	338/150$^{\#}$	–/5.4	7/2	28/9$^{\#}$	4/1$^{\#}$
		≥40	52/31	225/210	488/235$^{\#}$		4/2	17/4$^{\#}$	4/1$^{\#}$
Leitao *et al.* (94)	OS/MIS	≥40	299/125	170/191$^{\#}$	250/125$^{\#}$	10.5^{LS}/3.4^{RS}	27/6$^{\#}$	36/15^,$^{\#}$	5/1$^{\#}$
Nevadunsky *et al.* (95)	OS/RS	≥30	43/66	134/204$^{\#}$	193/83$^{\#}$	–/9.7	20/0$^{\#}$	4/4	3.8/1.3$^{\#}$
Seamon *et al.* (96)	OS/RS	≥30	191/109	143/228$^{\#}$	394/109$^{\#}$	–/15.6	17/2$^{\#}$	27/11$^{\#}$	4/2$^{\#}$
Subramaniam *et al.* (97)	OS/RS	≥30	104/73	246/138$^{\#}$	409/96$^{\#}$	–/11	20.2/4.1$^{\#}$	29.8/9.6$^{\#}$	5.1/2.7$^{\#}$
Tang *et al.* (98)	OS/RS	≥30	110/129	128/188$^{\#}$	292/160$^{\#}$	–/10.9	32.7/13.9$^{\#}$; 0/6$^{\dagger,\#}$	36.4/13.2$^{\#}$	4.1/1.5$^{\#}$
Chan *et al.* (99)	OS/LS/RS	≥40	567/98/422	NR	NR	NR	23/13/8$^{\#}$		4/1/1$^{\#}$
Corrado *et al.* (52)	LS/RS	30–34.9	232/130	115/176$^{\#}$	50/100$^{\#}$	2.2/1.5	5.2/6.2 (E)*	2.2/3.8 (L)*	3/3
		35–39.9	98/61	121/170$^{\#}$	50/100	6.1/0$^{\#}$	4.1/6.6	5.1/0	3/3
		40–49.9	62/44	110/142$^{\#}$	50/80$^{\#}$	1.6/0	4.8/6.8	3.2/2.3	3/3
		≥50	14/14	157/170	50/75	0/0	21.4/14.3	0/7.1	4/3
El-Achi *et al.* (53)	LS/RS	≥40	33/31	196/215	98/44$^{\#}$	0/0	NR		1/1
Gehrig *et al.* (90)	LS/RS	30–39.9	25/36	215/189**,$^{\#}$	150/50**,$^{\#}$	7/0	24/13.9		1.3/1.0**,$^{\#}$
		≥40	7/13			14/0	14.2/7.6		
Mendivil *et al.* (51)	OS/LS/RS	>40	24/16/13	81/109/167$^{\#}$	250/175/100$^{\#}$	–/6.3/7.7	16.6/6.3/15.3		4/2/2$^{\#}$

OS, open surgery; RS, robotic assisted surgery; BMI, body mass index; MIS, minimally invasive surgery; LS, straight stick laparoscopy; y, years; min, minutes; EBL, estimated blood loss; ml, millilitres; d, days; NR, not reported; ^, overall complications rate; $^{\#}P<0.05$; †, vaginal cuff wound complications; *, complications reported as early (E) *vs.* late (L); **, all BMI categories were reported together.

(12.3% *vs.* 6.7%) and longer hospital stay (110) after laparotomy. Among patients above the age of 80 undergoing RAS, a multi-institutional study found no difference in operative outcomes such as operative time, conversion rate or blood loss compared to younger patients. The rate of intraoperative complications did not differ, although there was a higher rate of postoperative complications (33% *vs.* 13%) (112). Lau *et al.* reported a similar minor complications rate for patients older than 80 years compared to patients younger than 80, and they resumed activities quicker than younger patients (115). Perioperative complication rate including vascular, urinary and transfusion rate were lower

Table 2 Outcome for elderly patients

Study	Surgical approach	Age group (y)	N	EBL (mL)	Intra-op complications (%)	Post-op complications (%)			Hospital stay (d)
						Minor	Major	Overall	
Scribner *et al.* (107)	OS/LS	65≤	45/67	336/298	0/7.5	NR	NR	57.9/12$^{\#}$	5.6/3$^{\#}$
Bijen *et al.* (108)	OS/LS	70≤	23/38	NR	4.3/5.3	NR	NR	17.4/23.7	NR
Bogani *et al.* (109)	OS/LS	75≤	66/59	175/100$^{\#}$	2/3	NS	NR	3/14	6/2$^{\#}$
Lavoue *et al.* (104)	OS/RS	70≤	50/113	334/75$^{\#}$	10/6	60/17$^{\#}$	6/4	NR	8/3.1$^{\#}$
Doo *et al.* (103)	OS/RS	65≤	47/26	235/131$^{\#}$	14.9/3.8	29.8/3.8$^{s,\#}$	29.8/19.2^{m}	NR	4.4/2.2$^{\#}$
Guy *et al.* (110)	OS/RS	65≤	5,914/1,228	NR	4.1/5.9$^{\#}$	20.5/8.3$^{s\#}$	23.3/12.3$^{m,\#}$	NR	5.1/2$^{\#}$
Backes *et al.* (105)	OS/RS	70≤	93/89	300/75$^{\#}$	NR	NR	NR	94/24†	4/1$^{\#}$
Bourgin *et al.* (111)	OS/LS/RS	75≤	26/27/16	NR	7.6/0/0	19.2/3.7/6.2	3.8/3.7/0	NR	10.7/7.2/4.5$^{\#}$
Lindfors *et al.* (106)	OS/RS	70≤	137/141	381/47$^{\#}$	1/4	22/10	5/6	NR	6.3/2.5$^{\#}$
Lowe *et al.* (112)	RS	<80/80≤	395/27	50/50	5.1/7.4	NR	NR	13/33$^{\#}$	1/1
Siesto *et al.* (113)	LS	≤65/65<	60/48	100/100	1.7/4.2	NR	NR	23.4/25	2/2
Frey *et al.* (114)	LS	<65/65≤	36/31	166/165	NR	NR	NR	12/0	1.7/3$^{\#}$
	RS	<65/65≤	25/17	218/147	NR	NR	NR	2.8/5.6	3.5/1.8
Doo *et al.* (103)	RS	<65/65≤	72/26	83/131	2.8/3.8	2.8/3.8	2.8/19.2$^{\#}$	NR	1.3/2.2$^{\#}$
Guy *et al.* (110)	RS	<65/65≤	1,574/1,228	NR	6.8/5.9	5.2/8.3$^{\#}$	6.7/12.3$^{\#}$	NR	1.7/2$^{\#}$
Zeng *et al.* (115)	RS	<70/70-80/80<	197/75/31	78/69/88	0.5/0/3	16/12/19	0/1/10$^{\#}$	NR	1.6/1.4/5.2$^{\#}$
Bourgin *et al.* (111)	LS	<75/75≤	127/27	NR	14.9/0$^{\#}$	11.8/3.7	3.1/3.7	NR	5.2/7.2$^{\#}$
	RS	<75/75≤	75/16	NR	5.3/0	8/6.2	2.6/0	NR	3.7/4.5
Hotton *et al.* (116)	RS	<70/70≤	86/62	NR	2.3/3.2	NS	NS	10.5/12.9	6.5/6.5

OS, open surgery; LS, straight stick laparoscopy; RS, robotic assisted surgery; y, years; min, minutes; EBL, estimated blood loss; d, days; NR, not reported; $^{\#}P<0.05$; s, surgical complications; m, medical complications; †, total complication events.

in LS and RAS compared to laparotomy in patients younger than 75 years, whereas in older patients, complication rate did not differ between the surgical approaches. This could be associated with less staging procedures in elderly patients (age >75) (111). Hospital stay was shorter for RAS and LS independent of age.

Ergonomics

Long operating hours is a keystone of gynecologic oncology surgeries. It leads to mental and physical strains on the surgeons, which have an accumulative effect, and at best cannot be beneficial for the patient undergoing surgery. One of the potential advantages of introducing robotic assisted surgery to the field of gynecologic oncology was alleviating the strain associated with prolonged surgery. A prospective French study of 88 robotic and 82 straight stick laparoscopy cases with a minimal duration of one hour evaluated 24 surgeons. The physical discomfort during LS was significantly higher, and the subjective pain score increased significantly during the procedure compared RAS. Concerning the mental demand, the overall workload and performance were significantly greater during the LS compared to the RAS. For young surgeons, the overall workload, effort, mental and physical demands were greater during LS, while for experienced surgeons only the physical demand was increased (118). In a review of ergonomics of gynecological surgeries, the prevalence of work-related musculoskeletal disorders (WMSD) was reported to be the lowest with RAS. The review also reported that RAS was characterized by more freedom, better motion scaling, tremor reduction and less need for arcing maneuvers. Finger pain and eye strain are more common with RAS than other approaches (119).

A survey of 236 of AAGL (American Association of Gynecologic Laparoscopists) affiliated surgeons asked about the physical demands of surgery and how they were affected by RAS, and showed that RAS helped decreasing surgeons' eye strain, but did not improve post-procedure neck stiffness or finger pain. Surgeons with high RAS volume noticed more pronounced effects, reporting fewer physical demands with RAS (120).

Learning curve

The adoption of any novel surgical approach is accompanied by a period of gaining experience in which a learning curve can be observed. The learning curve for performing surgical staging in EC using the laparoscopic approach was suggested to be between 25–30, mainly due to a high level of experience needed for laparoscopic lymphadenectomy (121-123). In vitro, surgeons who had little MIS experience showed faster improvement in performance of dexterity tasks using RAS compared to laparoscopy. Among experienced surgeons, however, the learning curve was similar between RAS and LS (124). Studies that have evaluated in-vivo learning curve for robotic surgery have reported that the progress curve plateaued after 9–20 cases (32,33,112,125-128), while a large series by Leitao *et al.* has reported further improvement until completion of 40 cases (27). Compared to laparoscopy, RAS was found to have a shorter learning curve when performing hysterectomy together with pelvic and para-aortic lymphadenectomy (33,126).

Cost effectiveness

Even though straight stick laparoscopy is associated with higher intra-operative instrument costs, it has been shown to reduce total healthcare associated costs when compared to laparotomy due to shorter hospital stays and lower complications rate (65). Since RAS is associated with a higher instrument cost due to the price of the platform, the maintenance, and its related accessories, its cost-effectiveness compared to LS has been questioned. Studies have evaluated cost-effectiveness by measuring just direct costs of surgery and perioperative complications, while others include indirect costs such as the need for rehabilitation, utilization of primary care services and time off the labor market.

It was hypothesized that robotic surgeries will decrease the treatment costs of EC as a result of shorter hospital stays and lower complication rates. A number of studies have shown comparable outcomes between laparoscopic surgeries and RAS with higher costs using RAS (38,54,129-132), and other studies have shown financial advantage to RAS over open surgery (133,134). An early study showed no benefit of RAS in obese women with EC (99), and a meta-analysis reported an increased total surgery cost of RAS by $1,869 (9). However, more recent studies showed improved treatment costs when utilizing RAS in elderly and obese women with EC and hyperplasia (83,94,106).

When analysing the economic impact of Robotic Assisted surgery for EC, one should take into account the overall effect of introducing RAS has on the rate of laparotomies performed. Leitao *et al.* reported a higher total amortized cost for RAS by $3,175 when compared to LS for newly diagnosed EC. However, a model incorporating the effect of the reduction in open surgery has neutralized the cost difference (132). A study that reviewed patient charts admitted to the gynecologic oncology ward one year before and 5 years following the introduction of RAS to a tertiary care hospital, showed better utilization of hospital resources with the introduction of RAS (79). More patients were admitted and operated on, while hospital stays were shorter resulting in a better turn-over and increased capacity. This turn-over helped adapting more complex cases in the inpatient ward, cases that required advanced medical care. Another benefit was the reduction in the cost of admission by almost a half with the introduction of RAS ($9,827 *vs.* $4,058) (135). An updated analysis reported that robotic assisted surgery was increased from 15% to 94%, and was associated with a $3.5 million saving during the course of 15 years (136). Korsholm *et al.* extracted data from a Danish national registry to study the long-term consequences of a nationwide introduction of RAS in treating early-stage EC and cost for evaluated for a period of 12 months before and after surgery. Records analysis of 4,133 patients showed that following the introduction of RAS the long-term health costs per patient increased by $7,309 (130). Of note, despite an increase in the rate of MIS from 22% to 72%, there was no reduction in bed days after adjusting for patients' characteristics and surgical year, which could explain the high relative cost. In their database analysis, Casarin *et al.* reported that RAS was associated with a 13.5% reduction in 30-day perioperative morbidity and similar 30-day (US $12,200 *vs.* 12,018) perioperative total cost compared to laparotomy (80).

Since many of the early studies regarding cost-effectiveness analysed the first years' experience with RAS, it was questioned whether further improvement of the technique would lower the associated costs of RAS. Avondstondt *et al.* have indeed reported a 15% reduction in cost of RAS mainly due to reduction in operative times (137). In addition to cost reduction associated with improved experience, increased competition in the field of computer assisted minimal invasive surgery is expected to reduce platform and instrument costs.

Future developments

The field of robotic assisted surgery was dominated by the da Vinci platforms. The gradual expiry of the patents together with development of competing platforms is expected to reshape the landscape of robotic assisted surgery, increase diversity and reduce costs (138,139). By introducing a computer interface into the operating theater, robotic assisted surgery is the stepping-stone towards high-tech surgery. Three-dimensional reconstruction techniques based on preoperative images are already being utilized for intraoperative navigation (140,141) and the use of augmented reality is bound to expand. Artificial intelligence using machine learning, allows the assessment and integration of large volume of data in order to develop surgical skills, improve surgical procedure planning and predict surgical outcomes (142-145). In addition, the possibility of remote control could serve as grounds for the development of tele-surgery (146).

Conclusions

Safety and oncologic outcomes remain the cornerstone of gynecologic oncology surgery. Following the LACC trial, the oncologic outcome of MIS approach for the management of cervix cancer was brought up for discussion, however, in endometrial cancer, MIS approach has been shown by numerous retrospective, prospective, as well as randomized trials to have major perioperative benefits compared to laparotomy, along with equivalent oncologic outcome. Because of the improved dexterity and vision, when compared to straight stick laparoscopy, robotic assisted surgery appears to be associated with reduced perioperative complications, lower conversion to laparotomy and reduced hospital stay, while accompanied by longer operative time and higher cost when directly compared to laparoscopy. The advantages of RAS are sustained in obese and elderly patients. It is fundamental to remember that both straight stick laparoscopy and Robotics are MIS approaches, just with different tools, and the overarching purpose is to allow as many the patients as possible to benefit from MIS rather than open surgery. In rare centers with high proportion of straight stick laparoscopy that are able to maintain a 70–80% rate of minimal invasive surgery for endometrial cancer, there is little added value at present to adopt robotics. Thus, the greatest impact of Robotic Assisted Surgery was to allow the shift toward MIS approach in centers where laparoscopy failed to considerably reduce the rate of laparotomy. In addition, the robotic platform with its stable controlled environment allows for integration of technological developments by incorporating the computer interface between the surgeon and the patient, leading to implementation of digital analysis and artificial intelligence in gynecologic surgery, that will lead to entire new paradigms in surgery.

Acknowledgments

Funding: Dr. Raban was supported by a grant from the Israel Cancer Research Fund. This work was supported in part by the Gloria's Girl Fund, and the Susan & Jonathan Wener Fund.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Federico Ferrari) for the series "Surgical Approaches for Gynecologic Cancers" published in *Gynecology and Pelvic Medicine*. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gpm.amegroups.com/article/view/10.21037/gpm-21-1/coif). The series "Surgical Approaches for Gynecologic Cancers" was commissioned by the editorial office without any funding or sponsorship. WHG serves as an unpaid editorial board member of Gynecology and Pelvic Medicine from June 2020 to May 2022. He reports personal fees from Minogue Medical and Intuitive Surgical, outside the submitted work. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/gpm-21-1
Cite this article as: Raban O, Bukhari YA, Gotlieb WH. Minimally invasive approach for endometrial cancer: robotic assisted *vs.* straight stick laparoscopy. Gynecol Pelvic Med 2022;5:8.

