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Robot-assisted versus conventional laparoscopic surgery in the treatment of advanced stage endometriosis: a meta-analysis

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Summary

Objective: To evaluate the safety and efficacy of robot-assisted laparoscopy (RAL) versus conventional laparoscopy (CL) in the treatment of advanced stage endometriosis. *Materials and Methods:* Utilizing electronic databases (PubMed, Embase, and Elsevier), a systematic literature review was performed between 2008 and 2015 to compare the RAL surgery with CL surgery (CLS) in the treatment of advanced stage endometriosis. According to meta-analysis criteria, two comparative clinical trials were selected. Outcome measures including length of operation, blood loss, operative complications, and the length of hospitalization, were estimated by the RevMan 5.1 software. *Results:* In the meta-analysis, there were no significant differences in blood loss, complication, and hospital stay between RAL and CL surgeries in the treatment of advanced stage endometriosis. However, RAL surgery required a higher mean operating time than CL surgery (WMD: 73.85, 95% CI: 56.77−90.94; $p < 0$ .00001). Comparative studies demonstrated that RAL displayed no outstanding advantages. *Conclusions:* As a new minimally invasive method, RAL technology is safe and efficient alternative to CL in the treatment of advanced stage endometriosis. The latent benefits of RAL technology for the treatment of advanced stage endometriosis remain uncertain.

Key words: Robot-assisted; Laparoscopy; Endometriosis; Advanced stage endometriosis; Conventional laparoscopy.

Introduction

Endometriosis, a chronic and recurrent disease characterized by the dystopic location and proliferation of endometrial tissues outside the uterine cavity, is one of the most common gynecological disorders, and affects approximately 6–20% of reproductive-age women [1]. Currently, laparoscopic surgery is considered the gold standard for diagnosis and treatment of endometriosis [2]. With the proper techniques and skills, laparoscopy as an ideal tool can relieve pain and remove all visible focus of lesions of endometriosis. However, for advanced endometriosis (stages III and IV), the pelvic extension adhesion needs to be decomposed and restore normal anatomy. In this case, laparoscopic surgery might be technically difficult and requires specialists with high laparoscopic techniques [3]. Due to these limitations, many complex endometriosis surgical procedures are still done as an open procedure. However, with the advent of the da Vinci robotic system, robot-assisted surgery in gynecology has overcome certain limits of conventional laparoscopy (CL), such as complex sutures and deep infiltrating endometriosis dissection [4]. In the infiltrating endometriosis (bowel, bladder, and urethral endometriosis), numerous clinical trials reported robot-assisted laparoscopy (RAL) has superior advantages [5-8] and offered excellent outcomes with no doubt. However fewer publications reported the comparison of the treatment of advanced stage endometriosis, respectively, by RAL and CL. The aim of this paper was to perform a systematic review in order to evaluate the safety and efficacy of RAL versus CL in the treatment of advanced stage endometriosis.

Materials and Methods

Search strategy

The authors searched electronic databases (PubMed, Embase, and Elsevier) for relevant studies. All articles comparing CL with RAL in the treatment of advanced stage endometriosis between 2008 and 2015 have been reviewed. Some search terms, such as "robotic", "laparoscopic", "endometriosis" "severe endometriosis" "advanced stage endometriosis", and "laparoscopic endometriosis", were used. The "related articles" offered by databases were explored to broaden the search, and all abstracts, studies, and citations were reviewed as well. A manual search was also carried out to identify trials for possible inclusion as a supplement. Studies in English language were considered for inclusion. The latest date for this search was on Mar 30th, 2015.

Data extraction

Two of the present authors (Shao-Hui Chen, Zhao-Ai Li) reviewed relevant articles and extracted the specific studies on comparing CL with RAL. If disagreements about inclusion existed, a third reviewer (Xiu-Ping Du) was asked to assess the articles involved until obtaining a consensus. The quality of each study was

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evaluated by using the Newcastle-Ottawa Scale (NOS) [9]. Four studies were performed by the criteria as follows: patient selection, comparability of CL and RAL groups, and exposure. Evaluating studies grades based on an ordinal star scoring scale: higher scores represented studies with higher quality. Maximum of one star for each numbered item within the selection and exposure categories in one study and a maximum of two stars for the comparability of the two groups. Obtaining six or more stars were considered to be of much higher quality.

Inclusion criteria

In the meta-analysis, all selected studies had to abide by the following criteria: (1) all contained the comparison of outcomes of RAL (da Vinci system) and CL for advanced stage endometriosis, which should include the length of operation, blood loss, operative complications, and length of hospital stay; (2) the basic data (age, history of abdominal surgery, pre-existing complication conditions) in both groups were not statistically different; (3) patients covered in the study were all on endometriosis stage III or IV (American Society for Reproductive Medicine criteria).

Exclusion criteria

Some research reported only as letters, editorials, and expert opinions were excluded. Studies without original data, case reports or studies lacking conventional laparoscopy as control group were not considered either. The studies were excluded if the patients employed by the study were found to have stage I or II endometriosis or that required bladder, ureter, or bowel resection (including disk excision). In addition, these studies that did not clearly provide the outcomes and basic data of patients, or just compared with traditional open operation and single port laparoscopic surgery, or only reported RAL surgeries were all excluded.

Statistical analysis

The meta-analysis was performed by the present three authors using the Review Manager v. 5.1 software for the four primary outcome parameters (length of operation, blood loss, operative complications, and the length of hospitalization), and the statistical package of which was used to analyze the odds ratios (OR) for dichotomous variables and weighted mean difference (WMDs) for continuous variables. Heterogeneity was evaluated by F and I^2. The authors considered heterogeneity to be present if the I^2 statistic was > 50% and the threshold of significance was considered at $p < 0.05$.

Results

The four studies [10-13] were selected from the search on RAL versus CL on treatment of advanced stage endometriosis (Figure 1). The studies were all retrospective, non-randomized controlled comparisons. The characteristics of these studies were summarized and the quality of studies was assessed. A total of 684 patients in enrolled searches: 218 in the RAL group and 466 in the CL group.

Characteristics of included studies

All studies involved RAL and CL surgery for advanced stage endometriosis. First author and year of publication, patients characteristics (age, body mass index, previous abdominal surgeries, and outcome assessment), study design, and the quality assessment of studies in the included studies are shown in Table 1. All surgical operators in all studies possessed skilled techniques and were not influenced by the training curve when using the device.

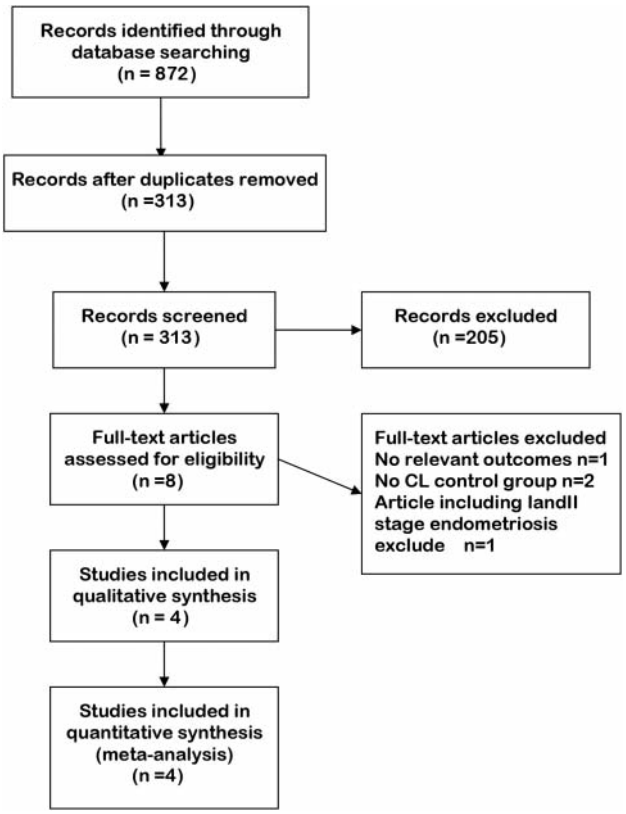

Figure 1. — Flow diagram of studies identified in the meta-analysis.

Meta-analysis results

The results summarized from four studies [10-13] indicated that the length of operation in the robotic group is longer compared to the conventional laparoscopic one. The authors used the analysis of the pooled data to compare the length of operation between the two groups (WMD: 73.85, 95% CI: 56.77−90.94; $p < 0$ .00001) (Figure 2.1). However, three studies [11-13] reported that the median length of hospital stay was not significantly different in the RAL group compared to the CL group (WMD: 0.00, 95% CI: -0.05−0.05; $p = 1.00$) (Figure 2.2). For operative complications, the present analysis of the pooled data indicated that the estimated operative complications were not different in the two groups (OR: 0.79, 95% CI: 0.10−6.12; $p = 0.82$) (Figure 2.3). The blood loss of the RAL group was less than that of the CL group, but there was no statistical significance (WMD: -5.64, 95% CI: -30.88−19.60; $p = 0.66$) (Figure 2.4).

The literature by Weavil *et al.* [14] was excluded from meta-analysis because the outcome data were not displayed completely. However, Sirota *et al.* [11] compared RAL with

Table 1. — *Characteristics of included studies in this meta-analysis.*

		Chu C.M., *et al.* [11]	Sirato I., *et al.* [12]	Sirota *et al.*, [13]	Camran *et al.*, [14]
Year		2011	2013	2014	2015
Study design		Retrospective	Retrospective	Retrospective	Retrospective
Study quality (Newcastle-Ottawa Scale)		****	*******	*******	*******
Patients	Total	121	25	118	420
	Robotic	25	14	32	147
	Laparoscopic	96	11	86	273
Age	Robotic	NA	42.5 (36-45)	39 (33.5-44)	30 (21-38)
(median, ± SD/range)	Laparoscopic	NA	40 (32-50)	38 (31-44)	31 (19-42)
BMI	Robotic	30.4	>30 kg/m^2	27.36 (23.9-34.09)	23 (19-32)
(median, ± SD/range)	Laparoscopic	24.8		24.53 (22.27-26.96)	23 (19-29)
Previous surgery	Robotic	NA	NA	22	36
	Laparoscopic	NA	NA	53	108
Operative time	Robotic	238 (120-630)	282.5 (224-342)	250.5 (176-328.5)	196 (185-209)
(median, ± SD/range)	Laparoscopic	190 (71-674)	174 (130-270)	173.5 (123-237)	135 (115-156)
		$p = 0.05$	$p = 0.0255$	$p = 0.0005$	$p < 0.001$
Estimated bloss loss,	Robotic	NA	100 (50-200)	100 (50-200)	40
ml, mean	Laparoscopic	NA	100 (10-200)	100 (50-200)	25
		NE	$p = 0.6606$	$p = 0.8755$	$p = 0.86$
Intraoperative	Robotic	NA	0	1	0
complication	Laparoscopic	NA	0	0	0
		NE	NE	$p = 0.2712$	NE
Postoperative	Robotic	NA	1	5	0
complication	Laparoscopic	NA	3	10	0
		NE	$p = 0.2878$	$p = 0.6570$	NE
Duration of hospitalization	Robotic	NA	1 (0-1)	1 (0-2)	1 (0-2)
(median, ± SD/range)	Laparoscopic	NA	1 (0-2)	1 (0-2)	1 (0-1)
		NE	$p = 0.8626$	$p = 0.5582$	$p < 0.001$

NA: not available; NE: not estimable. *score.

CL in the treatment of patients which was stratified by Basal Mass Index (BMI), and found no significant differences between the two groups in the normal and overweight categories. In Chu *et al.* [10] literature, there was no significant differences in estimated blood loss, length of hospitalization, complication rate, and conversions to laparotomy, but the length of operation was extended in RAL. The two conclusions were consistent with the outcomes of meta-analysis.

Discussion

Surgical procedures used to treat endometriosis include lyses of adhesions, excision or ablation of endometriosis' focus, removal of those organs affected, and restoring the pelvic anatomy [15]. LS is relatively safe and efficient for endometriosis treatment. However, if some patients with dense adhesions of deep and infiltrating endometriosis, self-borne risk factors such as obesity, experience of abdominal surgery, age, etc., the complication rates of the laparoscopic surgery will increase and the difficulty of the surgery will be correspondingly increasing [10, 16].

Robot-assisted system embracing numerous advantages such as three-dimensional imaging, tremor filtration, fixed instruments, and a comfortable operating floor for surgeons, has conquered most limits of conventional laparoscopy [17, 18]. Luciano *et al.* [19] compared the staging of endometriosis by traditional laparoscopy with that by RAL, and found that RAL improved the visualization of endometriosis lesions and its therapeutic effectiveness. During the course of complex and long-lasting gynaecological procedures, such as dissecting the deep retroperitoneal spaces, isolating the ureters or the bowel, as well as suturing excising nodule in rectovaginal septum, partial bladder resection or colorectal resection, RAL had particularly excellent outcomes [20-22]. However, it had similar results in the treatment of some gynecological benign diseases [23, 24] as CL.

In this meta-analysis, comparing RAL with CL, there was no significant difference in blood loss, operative complications, and the length of hospitalization. Those results demonstrated that RAL technology was safe and efficient, whereas, its operating room time was significantly longer than that of CL. In the systematic review, even operated by an experienced surgeon and operating room team, the length of operation by RAL surgery was still longer than CL. Some reasons, such as the time used for docking and undocking, removal of cyst wall pieces or endometriosis specimens, and

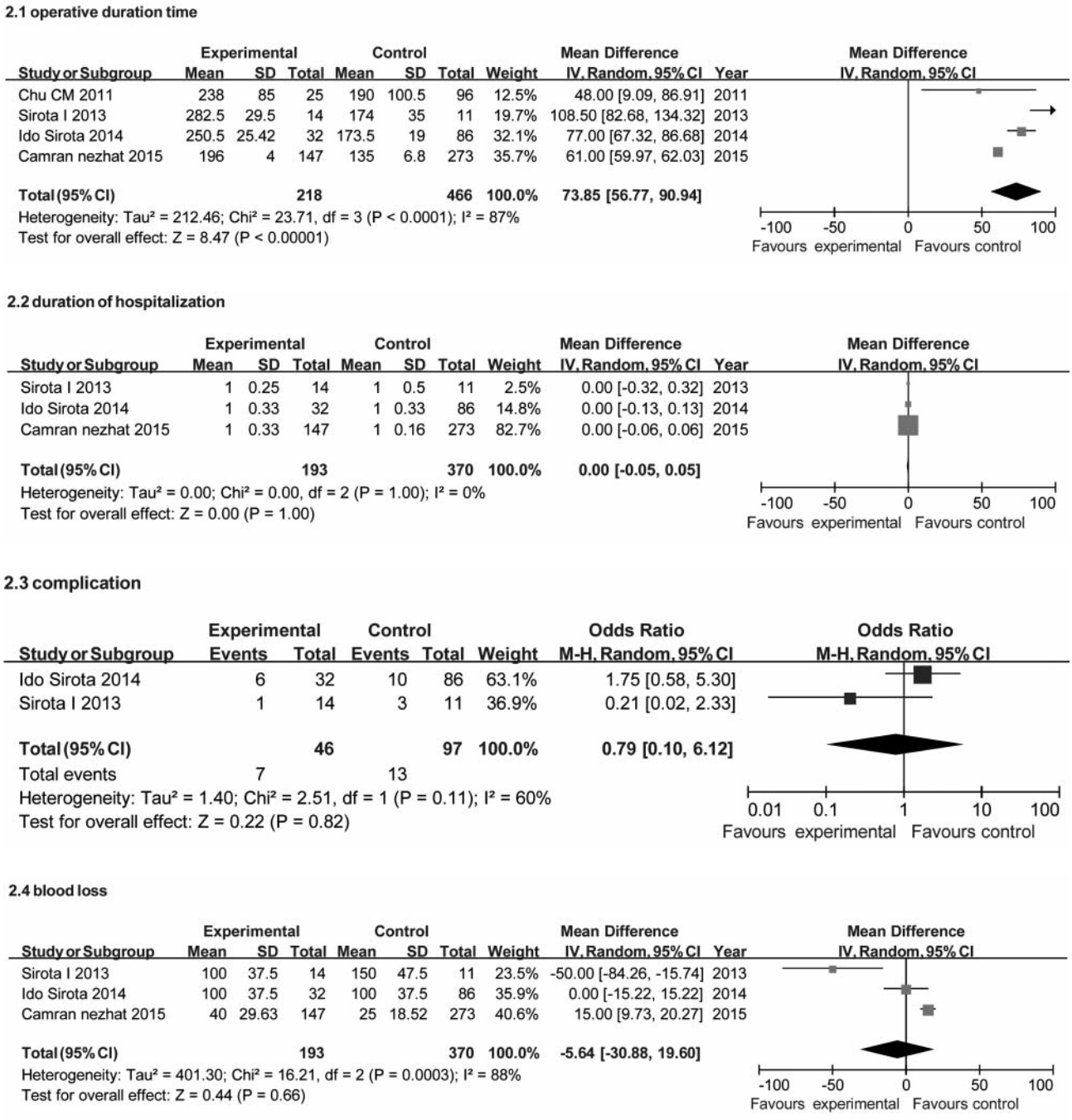

Figure 2. — (2.1) Forest plot for operative time comparing RAL with CL. (2.2) Forest plot for the duration of hospitalization comparing RAL with CL. (2.3) Forest plot for complication comparing RAL with CL. (2.4) Forest plot for blood loss comparing RAL with CL.

torpescence of robotic arms in manipulation, could be contributing factors to the extended operating room time. Meanwhile, if the patient was very thin and/or short, the operation space became narrow and led to collision of robotic arms. As a result, the operating room time would be prolonged as well. In addition, repositioning the bulky camera and replacing the assisting instruments also kept the operation an intricate and time-consuming process. Although this systematic review showed that RAL has no clinical advantages compared to CL, some authors [11, 25] have reported that obese patients might benefit from implementation of this new technology in the field of minimally-invasive surgery.

The meta-analysis had some limitations. The retrospective design and non- randomized controlled trials had been employed in the enrolled studies. The bias risk of this meta-analysis remained high. The number of the included patients was relatively small. Despite the present authors' efforts in the standardization of enrollment, the differences in patients and the differences in experience of surgeons between two groups could still not be removed. In addition, this meta-analysis only provided a short-term outcome in assessment of robotic assistance. They still need to observe its long-term outcome and enlarge the clinical data collection in order to further assess the value of robot-assisted laparoscopy.

In conclusion, in this meta-analysis, both RAL and CL provided excellent outcomes for the treatment of advanced stage endometriosis. However, the use of robotic surgical system is time-consuming and the overall cost remains high. In future, the long-term outcome studies and randomized trials should be conducted to further assess the value of robotic surgical system for treatment advanced stage endometriosis. With the development of minimally invasive techniques, the present limitations of the robotic surgical system will be overcome in the near future.

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