

Robotic Versus Laparoscopic Adrenalectomy: Systemic Review

Emad Rezkallah^{1*}, Wael Elsaify¹, Andrew Elsaify² and Grace Lim¹

¹General Surgery Department, James Cook University Hospital, South Tees NHS Foundation Trust,
England.

²Andrew Elsaify, Medical School, Misr University for Science and Technology, Egypt.

Authors' contributions

This work was carried out in collaboration among all authors. Author ER designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors WE and AE managed the analyses of the study. Author GL managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Minimal invasive surgery has become the standard for most surgical procedures now. Many studies have tried to compare robotic versus laparoscopic to adrenalectomy.

Objectives: The aim of this study is to review most of the available studies comparing robotic to laparoscopic adrenalectomy to evaluate which procedure provides the superior clinical outcomes.

Methods: A systematic literature search of ScienceDirect and PubMed databases. The perioperative clinical outcomes were collected by two independent reviewers. We used Random-effects (DerSimonian-Laird) models to get the pooled effect estimates.

Results: 18 studies were eligible in our study. 10 of them were prospective and 8 were retrospective. A total of 1376 patients underwent adrenalectomy, 592 (43.02%) were treated with RA and 784 (56.9%) with the LA technique. There were no significant differences between both groups regarding the conversion rate (Odds ratio: 0.70, 95% CI 0.31-1.57, P= 0.65), intraoperative complications (OR: 2.18, 95% CI 0.49- 9.71, P= 0.28), post-operative complications (OR: 0.83, 95% CI: 0.55-1.24, P= 0.49), and mortality (OR: 0.42, 95% CI: 0.07-2.72, P= 0.98). However, robotic adrenalectomy was associated with longer operative times (MD: 9.89 min, 95% CI: -2.79 to 22.58), shorter hospital stay (MD: -0.33, 95% CI: -0.46 to -0.21) with less blood loss (MD: -25.34, 95% CI: -

*Corresponding author: E-mail: emad.mofid@yahoo.com;

36.77 to -13.91).

Conclusions: We proved that robotic adrenalectomy has equal safety and feasibility with similar clinical outcomes when compared with laparoscopic approach. However, better well-designed studies are required to determine the role and cost-effectiveness of robotic adrenal surgery.

Keywords: Adrenalectomy; robotic; laparoscopic; studies; outcomes.

1. INTRODUCTION

Over the last few decades, mini-invasive adrenalectomy has been introduced as an alternative to the conventional open technique. Laparoscopic adrenalectomy was first introduced into the clinical practice in 1992 by Gagner [1]. Several subsequent studies have proven the safety and feasibility of laparoscopic surgery when compared with the open procedure including decreased hospital stay, faster recovery, decreased pain and narcotic use, and fewer peri- and post-operative complications [2]. Minimally invasive adrenalectomy is now considered the standard treatment for benign small adrenal masses (<8 cm) [3]. In selected cases, Laparoscopic adrenalectomy (LA) has also been utilized in the management of small (<5 cm) malignant adrenal carcinomas [4]. Alternative approaches, such as lateral retro-peritoneal or posterior retro-peritoneal adrenalectomy (PRA), have been developed to eliminate the need for mobilization of adjacent structures and to reduce the risk of associated complications [5,6]. Recently, laparoscopic PRA (LPRA) has demonstrated better surgical outcomes compared with Laparotomic adrenalectomy (LTA) despite disadvantages such as the small working space and cardiovascular compromise due to higher insufflation pressures in PRA [7,8]. However, laparoscopic adrenalectomy does have certain drawbacks, namely the loss of three-dimensional vision, the unstable camera platform and the rigid instrumentation.

Recently, mini-invasive robotic adrenalectomy has been introduced as an alternative technique to conventional laparoscopic surgery to overcome the drawbacks of laparoscopic surgery [9]. Robotic equipment offers seven degrees of freedom allowing for delicate movements in limited working spaces. In addition, its 3D optics provides better resolution and depth perception to the surgeon. Finally, its design maximizes the surgeon's comfort during the operation [10]. In addition, robotic adrenalectomy has showed advantages in certain circumstances, especially in the posterior retro-peritoneal approach where

space is limited, when dealing with anatomic variants and in case of cortical sparing adrenalectomy because it can achieve a safe resection while reducing post-operative steroid dependence [11]. However, robotic adrenalectomy has not yet proved significant improvements in terms of estimated blood loss, conversion rate, perioperative complications or overall cost, while operative times remain higher than laparoscopic surgery [12,13].

Till now, there is no universal agreement regarding the best surgical approach for adrenalectomy. We aimed in this study to review the available data regarding both techniques to help to identify the superior one of them.

2. MATERIALS AND METHODS

2.1 Literature Search and Study Selection

In this study, we aimed to compare the clinical outcomes of laparoscopic and robotic adrenalectomy, and to determine the differences that could affect these outcomes.

A systematic search was performed using ScienceDirect, SpringerLink and PubMed databases to identify all published studies comparing laparoscopic and robotic adrenalectomy from 2000 to 2020 (End-of-search date on March 31, 2021). Two reviewers worked independently to collect and select the data from each study. This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2009) [14].

Inclusion criteria include studies that were: (1) reported in humans, (2) published in English, (3) including more than 3 patients ($n > 3$), (4) and compare characteristics and perioperative outcomes of patients who have been treated with robotic vs. laparoscopic adrenalectomy. Exclusion criteria include studies that were: (1) carried on animals, (2) reviews and meta-analyses, (3) studies in which the outcomes of interest were not reported or were impossible to

calculate for both techniques, (4) and studies with overlapping data. (Fig.1).

2.2 Outcomes of Interest

Two reviewers, blind to each other, worked independently to review the eligible studies and performed the data extraction and analysis. General agreement was reached by consensus. Particularly, the following data were extracted: first author, year of publication, country of enrollment, study interval, study design, number of patients who received LA or Robotic adrenalectomy (RA), patient demographics (age, preoperative Body Mass Index (BMI), tumor size). The outcomes of interest which have been assessed and compared in this study include: operative time, estimated blood loss, conversion rate to laparoscopy/laparotomy, intraoperative and postoperative complications, mortality and length of hospital stay.

2.3 Statistical Analysis and Quality Assessment

Data analysis was performed to identify clinical outcomes of robotic adrenalectomy when compared with traditional laparoscopic

adrenalectomy. Regarding categorical outcomes, the extracted data were categorized in 2×2 tables (namely the numbers of patients presenting with the outcome and those free of the outcome, separately for the laparoscopic and robotic groups). Odds ratio (ORs) was calculated for dichotomous outcomes, $OR > 1$ indicates that the outcome is more frequently present in the robotic group. Regarding the continuous outcomes, the mean, standard deviation and number of patients for both groups were obtained. All outcomes were reported with 95% confidence interval (95% CI). However, some studies reported the continuous data as medians and range; in this condition we applied the Hozo et al. method to roughly estimate the respective means and standard deviations [15]. Random-effects (DerSimonian-Laird) models were used to calculate pooled effect estimates. The Cochran chi-square test (Q) and inconsistency (I^2) were used to evaluate the heterogeneity among studies [16].

The quality of our included studies was evaluated by using the Newcastle-Ottawa Quality scale [17]. Studies achieving a score of 7 or more indicated a higher quality.

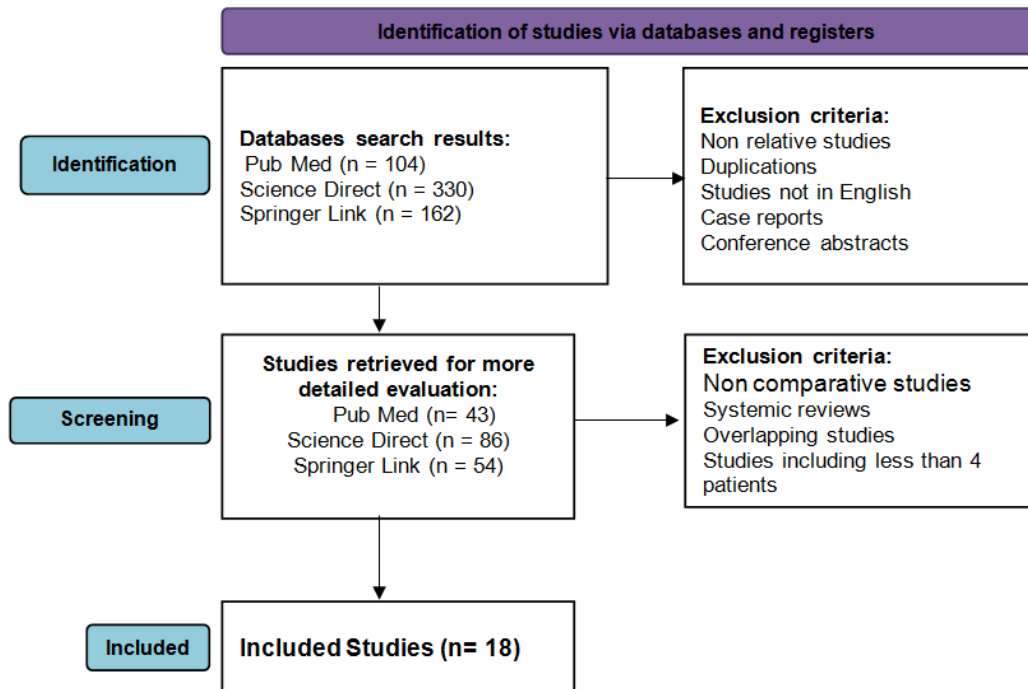


Fig. 1. Systemic literature search for eligible studies comparing robotic to laparoscopic adrenalectomy

3. RESULTS

From our systematic literature review we identified 18 studies which were eligible in our study. 10 of them were prospective [12,18,19,20, 13,21,22,23,24,25] and 8 were retrospective [26,27,28,29,30,31,32,33]. Seven of these studies were conducted in USA, 5 in Korea, two in Italy, one in Taiwan, one in France, one in China and one was share between Italy and France. A total of 1376 patients underwent adrenalectomy, 592 (43.02%) were treated with RA and 784 (56.9%) with the LA technique. The Da Vinci robotic surgery system was used in all studies except the study by Wu et al. which involved the Zeus AESOP 2000® system [18]. Table 1 shows the characteristics of the eligible studies.

There was no significant difference between the two groups regarding the age, sex or tumor size, except for the body mass index which was higher in the laparoscopic group (WMD: -0.75 kg, 95% CI, -1.51 to 0.00, $p = 0.00001$). (Fig. 2). The other two studies reported the median only for the BMI, and were not included in data analysis.

3.1 Conversion Rate

Nine studies reported the rate of conversion to either laparoscopy or laparotomy; there was no significant difference between both robotic (3.3%) and laparoscopic (4.75%) groups (Odds ratio: 0.70, 95% CI 0.31-1.57, $P=0.65$) (Fig. 3).

3.2 Intraoperative Complications

Four studies reported the rate of intra operative complications, which was slightly higher in the robotic group (10.98%) than the laparoscopic group (4.95%) (OR: 2.18, 95% CI 0.49- 9.71, $P=0.28$) (Fig. 4).

3.3 Post-Operative Complication

Thirteen studies have reported the rate of postoperative complications. No significant difference was found between robotic (10.94%) and laparoscopic (13.04%) groups, (OR: 0.83, 95% CI: 0.55-1.24, $P=0.49$) (Fig. 5).

3.4 Mortality

Three studies reported the operative related mortality rate, no significant difference was found between both the robotic (0%) and the

laparoscopic (2%) groups (OR: 0.42, 95% CI: 0.07-2.72, $P= 0.98$) (Fig. 6).

3.5 Operative Time

17 studies reported the operative time, which was higher in the robotic group (159.11min) than the laparoscopic (146.19min) group (MD: 9.89 min, 95% CI: -2.79 to 22.58) (Fig. 7).

3.6 Length of Hospital Stay

Data from 15 studies used to report the length of hospital stay which was significantly shorter in the robotic (3.472 days) and the laparoscopic (4.16 days) groups (MD: -0.33, 95% CI: -0.46 to -0.21) (Fig. 8).

3.7 Estimated Blood Loss

Data from twelve studies were used to determine the estimated blood loss, which was less in the robotic (66.675 ml) than the laparoscopic (93.15ml) group (MD: -25.34, 95% CI: -36.77 to -13.91) (Fig. 9)

4. DISCUSSION

Minimally invasive surgery is now considered the standard for many surgical operations thanks to better clinical outcomes, lower perioperative morbidity and mortality, shorter hospitalization and better cosmetic results [34]. Adrenal surgery has also undergone rapid advances since the implementation of laparoscopy in 1992 and robotic technology in 1999⁽¹⁾. However, there is no consensus regarding the true benefit of robotic surgery over conventional laparoscopy in management of adrenal pathology [35].

We systematically reviewed all available literature on the topic and identified 18 eligible studies which were published during the period from 2000 to 2020. We performed a meta-analysis of these studies including 1376 patients. Ma et al. and Morino et al. published the only 2 randomized clinical trials (RCT) comparing RA to LA [23,24]. We did not found significant differences in the demographics and pre-operative characteristics except for BMI which was lower in the robotic group. Other meta-analyses also documented similar results [36,37]. This finding could be due to a bias in patients' selection because surgeons tend to choose patients who are generally fitter to facilitate robotic procedures. However, 3 of our studies reported higher BMI with the robotic group than the laparoscopic group [21,25,30].

Table 1. The characteristics of the eligible studies

Study	Study period	Country	Type of study	N of patients		Age (Years)		Sex of patients		BMI (kg/m ²)		Tumor size	
				Rob	Lap	Rob	Lap	Rob	Lap	Rob	Lap	Rob	Lap
Agcaoglu 2012	2000 - 2011	USA	Prospective	24	38	52.4	52.5	28	34	27.1 ± 0.8	30.2 ± 0.9	6.5	6.2
Aksoy 2013	2003 - 2012	USA	Prospective	42	57	54.2	51.3	25	64	35.4 ± 1	38.8 ± 0.8	4	4.3
Aliyev 2013	2000 and 2012	USA	Retrospective	25	40	50.9	51.3	27	38	27.6 ± 1.5	28.7 ± 1.1	5.5	4.4
Brunaud 2006	Nov 96- Nov 05	France	Prospective	50	59	49.6	50.1	42	66	(28.75± 5.75)	28.75± 5.25)	2.8	3.4
Colvin 2017	2000 - 2014	USA	Retrospective	20	16	49.9	50.7	18	18	33.2± 1.60	32.6± 1.79	1.7	1.3
Dickson 2013	Jan 09 -June 2011	USA	Prospective	23	23	52.3	52	20	26	31.6 ± 6.1	30.0 ± 6	3.8	2.8
Karabulut 2012	2008 - 2011	USA	Prospective	50	50	53	53	35	65	30 ± 1	32 ± 1	3.9	3.1
Kook 2016	Mar 05 - Apr 16	Korea	Retrospective	29	34	53.1	51.4	28	35	25.9± 3.8	25.2±3.5	3.3	3.6
L F Brandao 2014	Jan 04 -Oct 2013	Korea	Retrospective	30	46	62	54.5	37	39	29.5	29	3	4
M Piccoli 2020	Jan 6 - Dec 19	Italy	retrospective	76	84	57.2	57.9	70	90	(29.6± 5.6)	(28.65± 7.35)	4.03	5.1
Ma 2019	Mar 16 - Apr 19	China	Prospective	70	70	44	50	76	64	(21.8± 1.1)	(22.9± 1.1)	4.6	4
Morino 2004	Mar 02 - Dec 02	Italy	Prospective	10	10	38.7	40.3	9	11	22.2 (23.55± 3.15)	25.8 (25.2± 2.15)	3.3	3.1
Pineda-Solis 2012		USA	Retrospective	30	30	54	53	27	33	32.7	33.6	3.2	3.88
Rafaelli 2013	Jan 99 - Dec 12	Italy, France	Prospective	13	11	42.8	41.2	4	20	30.2 ± 6.5	27.9 ± 4.6		
Sheng-Qiang Fu 2020	Mar 16 - Jan 19	Korea	Retrospective	19	32	44	47.53	26	25	26.64 ± 3.82	25.83 ± 4.45	8	7.65
W Kim 2019	Jan 14 - Dec 17	Korea	Retrospective	61	169	46.5	50.1	85	145	24.8 ± 3.5	24.8 ± 3.9	3.7	3.4
Wu 2007	Jan 03 - Feb 05	Taiwan	Prospective	5	7	58.2	56.3	4	8	23.5 ± 1.8	23.2 ± 1.8	5.1	4.7
You 2013	Oct 09 - May 12	Korea	Prospective	15	8	45.5	53	10	13	(23.55± 2.64)	(24.39± 2.98)	2.57	2.8

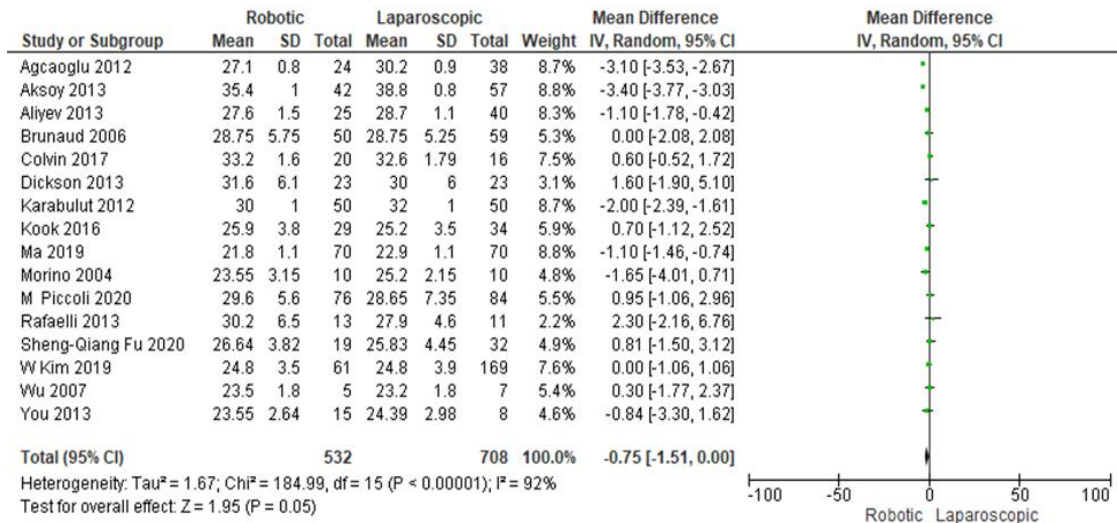


Fig. 2. Forest plot representing analysis of Body Mass Index; CI = confidence interval; MD = mean difference; SD = standard deviation; W = Weight

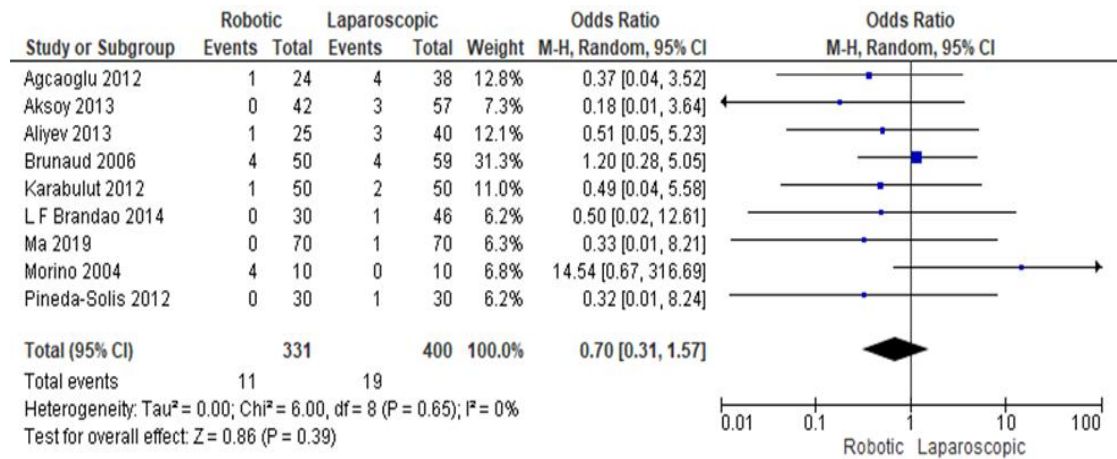


Fig. 3. Forest plot representing analysis of conversion rate; CI = confidence interval; OR = Odds Ratio; W = Weight

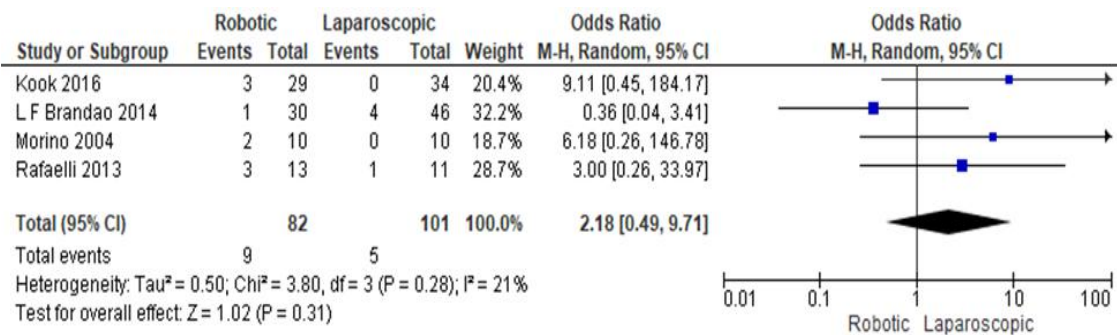


Fig. 4. Forest plot representing analysis of intra-operative complication rate; CI = confidence interval; RD = Risk Difference; SD = standard deviation; W = Weight

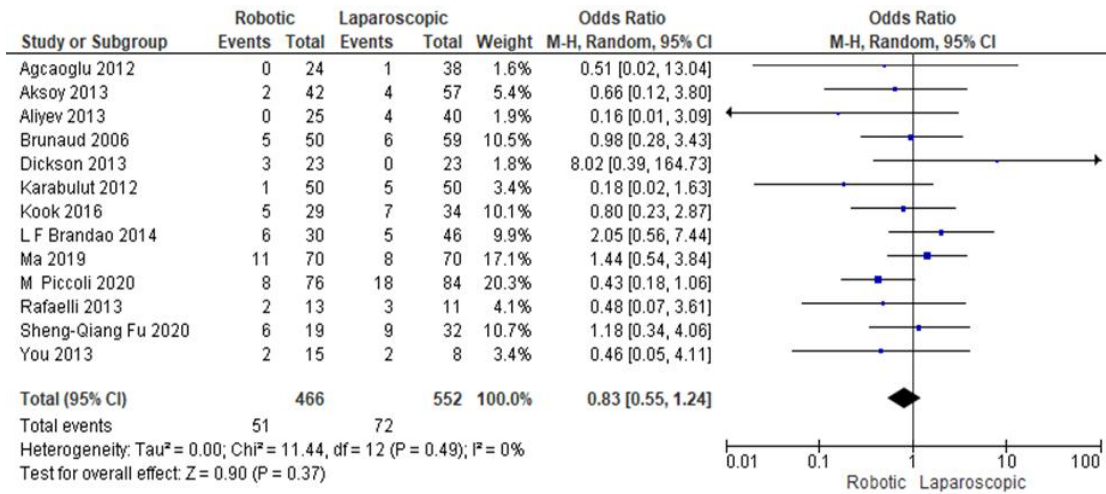


Fig. 5. Forest plot representing analysis of postoperative complication rate; CI = confidence interval; RD = Risk Difference

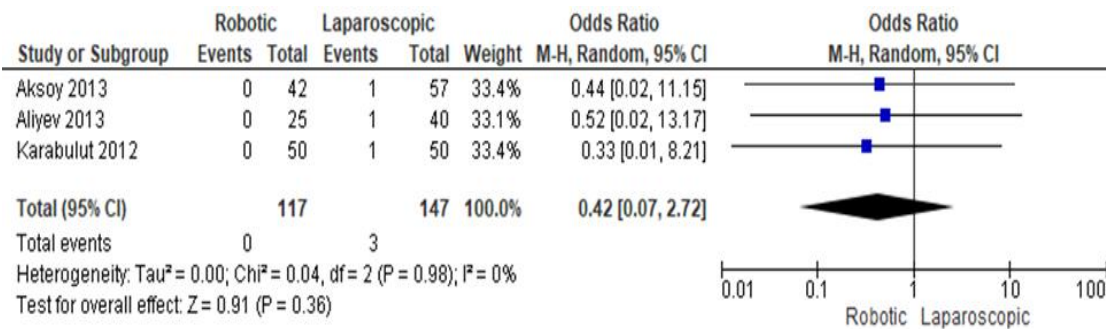


Fig. 6. Forest plot representing analysis of mortality rate; CI = confidence interval; RD = Risk Difference; SD = standard deviation; W = Weight

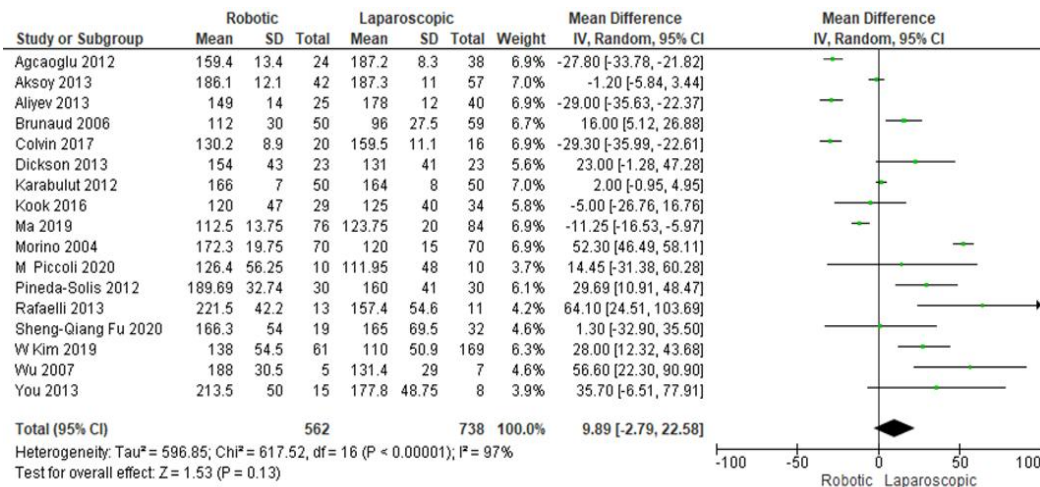


Fig. 7. Forest plot representing analysis of operative time; CI = confidence interval; RD = Risk Difference; SD = standard deviation; W = Weight

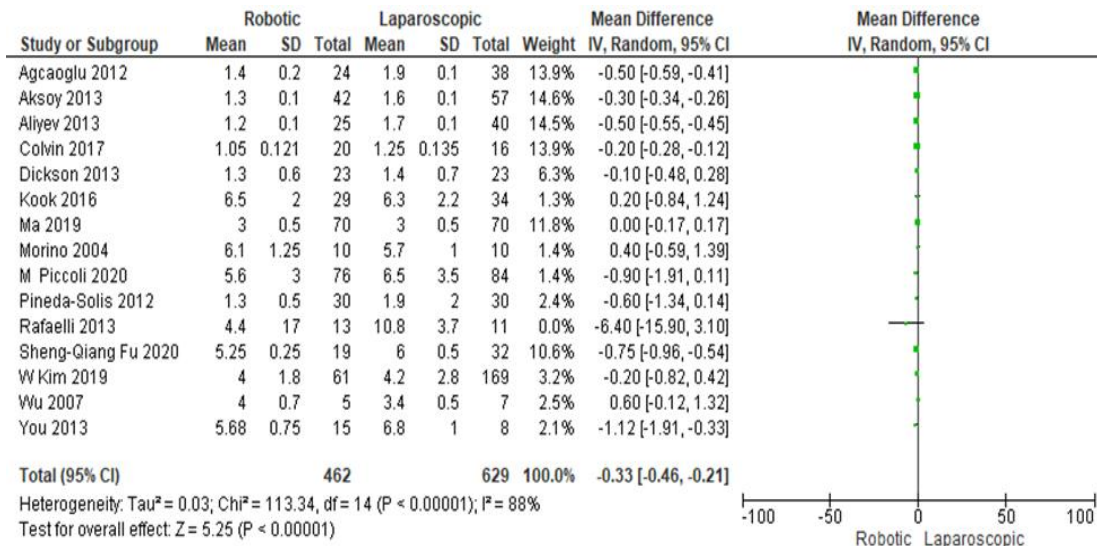


Fig. 8. Forest plot representing analysis of length of hospital stay; CI = confidence interval; RD = Risk Difference; SD = standard deviation; W = Weight

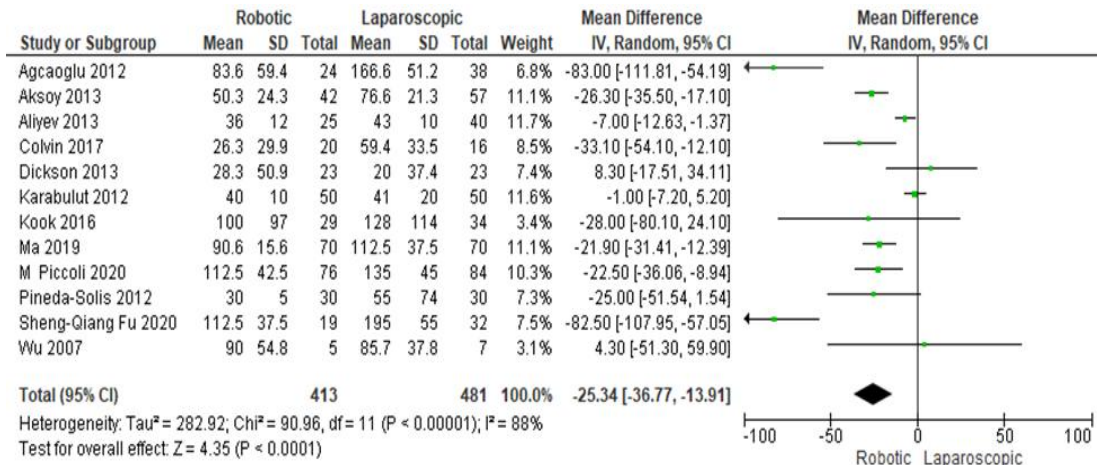


Fig. 9. Forest plot representing analysis of estimated blood loss; CI = confidence interval; RD = Risk Difference; SD = standard deviation; W = Weight

There was a significantly longer operative time in the robotic group than the laparoscopic group. Tang et al. also reported a significant difference in the operative time between the two techniques (WMD: 17.52 min, p = 0.01). This observation could be attributed to the robotic set up, the time needed to advance the robotic cart and connect the robotic arms to the robotic trocars in addition to the undocking times. In fact, the absence of a clearly defined start and end points of the operative time, and level of the experience of the operating surgeon had influenced the heterogeneity in our studies (97%, P= 0.00001).

However, one previous meta-analysis didn't report this difference in the operative time between both groups [37]. In addition three of our studies reported shorter operative time for the robotic than the laparoscopic technique [19,27,28]. In one study [23], when the docking time was excluded, the operative time was significantly lower in the robotic group (112.5 ±13.75m) than the laparoscopic group (123.75 ±20m). In addition, Agcaoglu et al. described the presence of a learning curve and reported a significant improvement in the operative time after the first 10 robotic procedures [19]. Brunaud

et al. [24] also observed no significant differences in operative time after the learning curve of 20 cases.

Moreover, no significant difference was detected in the rate of conversion to laparoscopy/laparotomy between the robotic (3.3%) and the laparoscopic (4.75%) groups (OR: 0.70, 95% CI: 0.31 to 1.57, P= 0.65). Other studies have reported similar results [36,37,38]. The highest rate of conversion in the robotic group was reported by Morino et al. (40%) [24]. The main reasons of conversion were malposition of robotic trocars, prolonged operative time and difficulties to obtain accurate hemostasis. However, we strongly believe that that technological advances and new instruments development in addition to the increases experience in robotic surgery amongst surgeons will improve dissection, reducing operative time, bleeding and complications.

In addition, the length of hospital stay was shorter in the robotic group (3.472 days) than the laparoscopic group (4.16 days) by about a half-day (OR: -0.33, 95% CI: -0.46 to -0.21). Similar results were reported by L. Branda et al. and K. Tang et al. [36,37]. However, it should also be noted that hospital stay can be influenced by many factors other than the actual surgical procedure.

As regarding the estimated blood loss, it was found that EBL was lower in the robotic group (66.675ml) than the laparoscopic one (93.15 ml) (OR: -25.34, 95%CI:-36.77 to -13.91). L. Brandao et al. and K. Tang et al. [36,37] reported similar observation. However, the detected difference between both groups was about 25ml which is not clinically significant. Thus, it can be concluded that both techniques are quite safe and associated with minimal blood loss.

In terms of morbidity, there was no significant difference between RA and LA. Although the intra operative rate of complications was slightly higher in the robotic group (10.98%) than the laparoscopic group (4.95%) (OR: 2.18, 95%CI: 0.49 to 9.71), these results were obtained from 4 small sized studies. However, the rate of postoperative complication was insignificantly higher in the laparoscopic group (13%) than the robotic group (10.9%) (OR: 0.83, 95%CI: 0.55 to 1.24). L. Brandao et al. reported similar results [37]. However, the type of adrenal lesion and advanced cardiovascular and pulmonary diseases could be at fault for the disparity in complication rates, rather than the type of the

operation itself [39]. There was no difference in the operation related death between both groups; collectively 3 deaths occurred in the laparoscopic group due to cardiopulmonary complications postoperatively [20,22,26]. No mortality was documented in the RA group.

Increased costs represent the real drawbacks of the robotic procedures. Morino et al. reported higher cost of the robotic procedure without including the initial cost to buy the da Vinci system [24]. The use of disposable and semi-disposable robotic instruments and the longer operative time represented the main reasons for increased costs. Brunaud et al. calculated that RA was 2.3 times more expensive than LA [13]. However, the authors believe that capital and maintenance costs could be affordable at high-volume robotic surgery center reducing mean hospital stay and increasing the use of the robot by other surgical specialties. However, Cost was not evaluated statistically in this meta-analysis due to lack of reported data.

We must acknowledge that this meta-analysis carry limitations. This review included retrospective and prospective studies, two of them only were randomized controlled trials. The use of such retrospective studies was associated with slightly higher risk for selection bias with doubts in interpreting results. In addition, the authors have different surgical experience and this can influence the outcomes. Although the conversion and complication rates had low heterogeneity ($I^2 = 0\%$ and 0% , respectively), the operative time, hospital stay, and estimated blood loss had high heterogeneity ($I^2 = 97\%$, 88% , and 88% , respectively). Factors that could potentially explain the heterogeneity among the studies include surgeries conducted by several surgeons with different levels of experience, the shorter learning curve and the different types of the treated adrenal pathology.

In general, the advantages of robotic adrenalectomy over the conventional laparoscopic approach are still debatable. A large well designed, randomized controlled trials are required to investigate oncologic results in malignancies, perioperative hemodynamic, the learning curve for the surgeons and overall cost-effectiveness of the technique.

5. CONCLUSION

This present meta-analysis includes 1376 patients: 592 underwent to RA (cases group) and 784 treated with LA (controls group). Our aim

was to evaluate the demographic characteristics, operative parameters and clinical outcomes between RA and LA. RA is a safe and feasible technique with reduced blood loss and shorter hospital stay than LA. We found no significant differences in terms of intraoperative and postoperative complications, mortality, and conversion to laparotomy or laparoscopy/laparotomy. Laparoscopic approach seems to be a more rapid technique when comparing to RA, although recent studies [23, 27, 28] demonstrate a significant operative time reduction in RA with the learning curve improvement and the development of new surgical technology.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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