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## Robotic Versus Laparoscopic Adrenalectomy: A Systematic Review and Meta-analysis.

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## Abstract

### Context

Over the last decade, robot-assisted adrenalectomy has been included in the surgical armamentarium for the management of adrenal masses.

### Objective

To critically analyze the available evidence of studies comparing laparoscopic and robotic adrenalectomy.

### Evidence acquisition

A systematic literature review was performed in August 2013 using PubMed, Scopus, and Web of Science electronic search engines. Article selection proceeded according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-analysis criteria.

### Evidence synthesis

Nine studies were selected for the analysis including 600 patients who underwent minimally invasive adrenalectomy (277 robot assisted and 323 laparoscopic). Only one of the studies was a randomized clinical trial (RCT) but of low quality according to the Jadad scale. However, the methodological quality of included nonrandomized studies was relatively high. Body mass index was higher for the laparoscopic group (weighted mean difference [WMD]: -2.37; 95% confidence interval [CI], -3.01 to -1.74;  $p < 0.00001$ ). A transperitoneal approach was mostly used for both techniques (72.5% of robotic cases and 75.5% of laparoscopic cases;  $p = 0.27$ ). There was no significant difference between the two groups in terms of conversion rate (odds ratio [OR]: 0.82; 95% CI, 0.39–1.75;  $p = 0.61$ ) and operative time (WMD: 5.88; 95% CI, -6.02 to 17.79;  $p = 0.33$ ). There was a significantly longer hospital stay in the conventional laparoscopic group (WMD: -0.43; 95% CI, -0.56 to -0.30;  $p < 0.00001$ ), as well as a higher estimated blood loss (WMD: -18.21; 95% CI, -29.11 to -7.32;  $p = 0.001$ ). There was also no statistically significant difference in terms of postoperative complication rate (OR: 0.04; 95% CI, -0.07 to -0.00;  $p = 0.05$ ) between groups. Most of the postoperative complications were minor (80% for the robotic group and 68% for the conventional laparoscopic group). Limitations of the present analysis are the limited sample size and including only one low-quality RCT.

### Conclusions

Robot-assisted adrenalectomy can be performed safely and effectively with operative time and conversion rates similar to laparoscopic adrenalectomy. In addition, it can provide potential advantages of a shorter

hospital stay, less blood loss, and lower occurrence of postoperative complications. These findings seem to support the use of robotics for the minimally invasive surgical management of adrenal masses.

## Keywords

- Adrenalectomy;
  - Comparative;
  - Meta-analysis;
  - Laparoscopic;
  - Robotic
- 

## 1. Introduction

Laparoscopic adrenalectomy was first reported in 1992. Since then it has largely replaced the open approach as the standard of care for adrenal removal, given well-known advantages such as less postoperative pain, minor blood loss, and better cosmetic appearance [1]. Nevertheless, laparoscopy is recognized as associated with a steep learning curve [2]. In 1999, Piazza et al. [3] and Hubens et al. [4] described the first robotic adrenalectomy cases using the AESOP 2000, which was the commercially available robotic platform in Europe at that time.

With the introduction of the da Vinci system (Intuitive Surgical, Sunnyvale, CA, USA), several series of robotic adrenalectomy have been reported, showing the safety and feasibility of the procedure as well as potential advantages over laparoscopy, given the unique features of the currently available robotic system, such as three-dimensional vision and the EndoWrist technique [5].

Robotic surgery in urology has been mainly used to date for procedures involving reconstruction such as radical prostatectomy and partial nephrectomy, whereas its use for extirpative procedures such as nephrectomy and adrenalectomy has been limited, mainly because of cost issues [6].

The aim of this study was to review systematically the available evidence comparing the surgical outcomes of robot-assisted adrenalectomy with those of conventional laparoscopic adrenalectomy.

## 2. Evidence acquisition

### 2.1. Literature search and study selection

A systematic literature review was performed in August 2013 using the PubMed, Scopus, and Web of Science databases to identify relevant studies. Searches were restricted to publications in English. Two

separate searches were done by applying a free-text protocol with the following search terms: *robotic adrenalectomy* and *robot-assisted adrenalectomy*.

Article selection proceeded according to the search strategy based on Preferred Reporting Items for Systematic Reviews and Meta-analysis criteria ([www.prisma-statement.org](http://www.prisma-statement.org)) (Fig. 1). Only studies comparing robot-assisted and laparoscopic techniques were included for further screening. Cited references from the selected articles retrieved in the search were also assessed for significant papers. Conference abstracts were not included because they were not deemed to be methodologically appropriate. Two independent reviewers completed this process, and all disagreements were resolved by their consensus.

## 2.2. Study quality assessment

The level of evidence was rated for each included study according to the criteria provided by the Oxford Center for Evidence-Based Medicine [7]. The methodological quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS) for non-randomized controlled trials (RCTs) [8] and the Jadad scale for RCTs [9].

## 2.3. Data extraction and outcomes of interest

Two reviewers reviewed the full texts of the included studies. Preoperative demographic characteristics as well as perioperative and postoperative outcomes between the two procedures were compared. Data were extracted from each eligible study: age, gender, body mass index (BMI), side, past history of abdominal surgery, tumor size, operative time, estimated blood loss, length of hospital stay, conversion (defined as a procedure not completed using a technique different from the one initially planned and used), and complication rates.

Postoperative complications were reported during the hospital stay and within 30 d after surgery, and they were classified according to the Clavien-Dindo grading system [10].

## 2.4. Statistical analysis

A meta-analysis was performed to assess the outcomes of robot-assisted adrenalectomy when compared with laparoscopy. Odds ratio (OR) or risk ratio was used for binary variables, and mean difference or standardized mean difference was used for the continuous parameters.

For studies presenting continuous data as means and range, standard deviations were calculated using the methodology described by Hozo and associates [11]. Pooled estimates were calculated with the fixed-

effect model (Mantel-Haenszel method) [12] if no significant heterogeneity was detected; otherwise, the random-effect model (DerSimonian-Laird method) was used [13].

The pooled effects were determined by the  $z$  test;  $p < 0.05$  was considered statistically significant. The Cochrane chi-square test and inconsistency ( $I^2$ ) were used to evaluate the heterogeneity among studies. Data analysis was performed with Review Manager software (RevMan v.5.1, Cochrane Collaboration, Oxford, UK).

## 2.5. Description of included studies and quality assessment

Nine studies were selected for the analysis including 600 patients who underwent an adrenalectomy procedure for an adrenal mass. Overall, 277 robot-assisted cases (46%) and 323 laparoscopic cases (54%) were included.

All except one of the included studies were observational retrospective comparative studies. Five of them compared consecutive series of patients (level of evidence [LE]: 3a) [14], [15], [16], [17] and [18], and two performed a retrospective nonconsecutive study (LE: 3b) [19] and [20]. Only one of the studies was an RCT (LE: 2b) [21].

The da Vinci system was used in all included studies. One study using the Zeus platform was excluded from the analysis [22].

The methodological quality of included studies was relatively high for the nonrandomized studies, whereas the only RCT was found to be of low quality (Table 1).

## 3. Evidence synthesis

### 3.1. Patient demographics and perioperative outcomes

Table 2 presents the demographics of the studies. There was no significant difference between the two groups for any of the demographic parameters, except for the BMI, which was higher for the laparoscopic group (weighted mean difference [WMD]:  $-2.37$ ; 95% confidence interval [CI],  $-3.01$  to  $-1.74$ ];  $p < 0.00001$ ). The transperitoneal approach was mostly used for both techniques (72.5% of robotic cases and 75.5% of laparoscopic cases; OR: 1.20; 95% CI, 0.87–1.67;  $p = 0.27$ ).

length, conversion, and postoperative complications rates.

There was no significant difference between the two groups in terms of conversion rate (OR: 0.82; 95% CI, 0.39–1.75;  $p = 0.61$ ) ( Fig. 2) and operative time (WMD: 5.88; 95% CI, -6.02 to 17.79;  $p = 0.33$ ) ( Fig. 3).

There was a significantly longer hospital stay in the conventional laparoscopic group (WMD: -0.43; 95% CI, -0.56 to -0.30;  $p < 0.00001$ ) ( Fig. 4) and higher estimated blood loss in this same group (WMD: -18.21; 95% CI, -29.11 to -7.32;  $p = 0.001$ ) ( Fig. 5).

There was also a trend favoring robot-assisted surgery for postoperative complications, but the  $p$  value did not reach statistical significance (OR: -0.04; 95% CI, -0.07 to -0.00;  $p = 0.05$ ) ( Fig. 6). Most of the postoperative complications were minor (Clavien grade 1 and 2) in both groups (80% for the robotic group and 68% for the conventional laparoscopic group). There were two cases of Clavien grade 3 in the robotic group, and two cases of grade 4 and three cases of grade 5 occurred in the laparoscopic group.

### 3.2. Critical analysis

With the advent of the da Vinci system, robotic surgery has rapidly increased in popularity worldwide, initially for radical prostatectomy and later also for a wide range of procedures, especially those requiring advanced laparoscopic reconstructive skills, such as partial nephrectomy and pyeloplasty. Well-described advantages of robot-assisted over conventional laparoscopy include stereoscopic vision, filtration of tremor, and 7 degrees of freedom [6]. Our institution reported its initial experience with robotic adrenalectomy in the porcine model in 2000 [23] and 2 yr later in the clinical setting [2].

Since then, the feasibility and safety of minimally invasive adrenalectomy using the robot-assisted technique has been widely demonstrated by several series from different centers [5]. We systematically reviewed the outcomes of robotic and laparoscopic adrenalectomy, and performed a meta-analysis of nine eligible studies published between 2004 and 2013 including 600 patients. Only one RCT of low quality was identified. The authors did not describe the method of randomization and also did not report how the study was powered [21].

We observed no significant difference between the two techniques in terms of baseline characteristics, except for BMI, which was significantly lower in the robotic group ( $p < 0.00001$ ). This can be regarded as a selection bias, and it is intuitively explained by the fact that surgeons initially tried to avoid obese patients early in their robotic experience. In a landmark analysis of the American College of Surgeons-National Surgical Quality Improvement Project data set of >1600 adrenalectomy patients, Kazaure et al. examined the impact of obesity on 30-d outcomes of adrenalectomy [24]. Obesity represented an independent risk factor that needs to be considered in surgical decisions regarding adrenalectomy. Only a few reports have specifically addressed the use of robotic adrenalectomy in obese patients. Brunaud et al. pointed out that the robotic approach offered advantages in obese patients as well and that they did

not encounter any technical difficulty in their patients with a mean BMI of 30 kg/m<sup>2</sup> (maximum of 44 kg/m<sup>2</sup> in their series) [17]. In contrast, Aksoy et al. reported no significant difference in perioperative outcomes between robot-assisted surgery and laparoscopy in obese patients undergoing adrenalectomy [16]. These authors experienced difficulty using the same robotic trocar configurations in obese patients due to the need for retraction of the spleen and liver compared with normal-weight individuals.

Overall, we found no statistically significant difference in the operative time between the two techniques (WMD: 5.88; 95% CI, -6.02 to 17.79;  $p = 0.33$ ). The slight difference in terms of time can be related to the necessity of robot setup and docking time for the robotic procedure. However, this is likely to have a lesser impact on the overall operative time as the surgical experience with the use of the robot progresses. Brunaud et al. analyzed operative time according to the learning curve [17]. When considering only the first 20 procedures, they observed a significant difference between the groups favoring laparoscopy, whereas this difference was no longer detectable for the following 20 procedures. Agcaoglu et al. reported a significant improvement in operative time after the 10th procedure in the robot-assisted group [15]. In all the studies included in this review, the laparoscopic groups represented a more mature learning curve in comparison with robotic adrenalectomy. This fact may have biased some of the outcomes favoring laparoscopy. In the Karabulut et al. study, 28 cases were performed by two groups of staff (OR time =  $142 \pm 12$  min) and 22 cases were done by one group of staff and one fellow (OR time:  $201 \pm 12$  min); the difference in operative time was significantly different ( $p = 0.002$ ) [18]. Agcaoglu et al. also reported the presence of a fellow or a resident in almost 50% of surgeries in both groups, but this fact did not affect the operative time significantly [14].

A low conversion rate was reported in all studies for both techniques (4.4% conversion rate for the robotic group and 7.1% for the laparoscopic group; OR: 0.82; 95% CI, 0.39-1.75;  $p = 0.61$ ). In the Brunaud et al. study, all four robot conversions were to the laparoscopic approach [17]. Morino et al. reported five conversions in the laparoscopic group including four to hand-assisted laparoscopy and one to open surgery [21]. Two studies had no conversions in both groups [15] and [20]. Aliyev et al., who compared both techniques only for pheochromocytomas surgeries, reported one case (3.9%) of conversion for the robotic group that was related to the adherence of tumor to surrounding strictures. The laparoscopic group presented three cases of conversion (7.5%) due to bleeding from tumor, bleeding from accessory renal vein, and difficulty with the dissection plane [25].

Morino et al. reported four cases of conversion in the robotic group (40%), three of them among the first five cases. The authors noted a statistically significant decrease in the conversion rate with increasing surgical experience [21].

The robotic approach provided significantly shorter hospitalization, which resulted in about a half-day less than for laparoscopy (WMD: -0.43 d;  $p < 0.0001$ ). This could be regarded as a cost-saving feature. However, it should also be recognized that hospital stay can be influenced by a variety of factors other than the actual surgical procedure.

The other significant outcome in favor of robotic surgery was the lower estimated blood loss, with a difference between groups reaching statistical significance ( $p = 0.001$ ); seven of the nine studies reported less bleeding for robotics [14], [15], [16], [17], [18] and [19]. However, the detected difference of about

25 ml is not clinically relevant. Thus it can be concluded that both techniques are quite safe and associated with minimal blood loss.

There was a higher complication rate in the laparoscopic group (6.8% vs 3.6%), but it did not achieve significant statistical difference (OR: 0.04; 95% CI, -0.07 to -0.00;  $p = 0.05$ ). There were more severe complications in the laparoscopic group, according to the Clavien grading system, including three deaths (Clavien grade 5), two resulting from respiratory failure due to severe pulmonary hypertension [16] and [18] and one from cardiac arrest [25]. You et al. reported two grade 4 complications in the laparoscopic group (acute kidney failure and cerebral infarction) requiring intensive care unit treatment [20]. In the robot-assisted group, there was one grade 3 complication in two studies [16] and [17]. In his RCT study, Morino et al. demonstrated that robot-assisted surgery is comparable with conventional laparoscopy in terms of postoperative morbidity and mortality [21].

The role of minimally invasive surgery for the management of malignant adrenal disease has been debated and remains a key issue. In a multicenter study, Greco et al. demonstrated that laparoscopic surgery for malignant adrenal tumors should be performed only in high-volume centers with at least  $\geq 10$  adrenalectomies per year [26]. We did not specifically analyze and compare oncologic outcomes from the studies included in the present meta-analysis because only two of them partially reported on these outcomes. Agcoaglu et al. followed three patients with adrenocortical carcinoma (one from the robotic group and two from the laparoscopic group). The patient in the robotic group died after 18 mo of follow-up presenting multifocal recurrence. The other two patients, from the laparoscopic arm, remained alive after 9 mo and 49 mo, respectively, of follow-up (one with no recurrence, and the second underwent resection and chemotherapy for recurrence after 6 mo) [14]. Aliyev et al. reported a median follow-up of 12 mo for pheochromocytoma patients. Only one patient with a succinate dehydrogenase complex subunit B mutation developed systemic recurrence associated with elevated metanephrine levels, without local recurrence, at 5 mo. Follow-up for plasma metanephrine levels was similar between the two groups [25].

We must acknowledge that, in general, meta-analyses carry limitations. Most of the studies included in this review were retrospective nonrandomized comparisons, with an inherent potential risk of selection bias. Ideally, meta-analysis of RCTs would provide more reliable comparisons and enable stronger recommendations. However, due to the increased complexity to implement this type of study design, especially those comparing surgical techniques, they are few in the literature. Only one RCT was identified and included in the present meta-analysis, and it was of low quality [21].

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 ( $I^2 = 96\%$ ,  $88\%$ , and  $90\%$ , 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 for the robotic group, the variety of treated diseases (benign, malignant, functioning, and nonfunctioning adrenal masses). It can be argued that the sample used for the present analysis is limited, so that some of the differences between the two study groups might have remained undetected or underestimated. Similarly, differences detected in some of the parameters might have not reached a

statistical significance, given the small number of cases. However, clinical significance, besides the statistical significance itself, should always be taken into account when analyzing surgical outcomes.

Besides the surgical outcomes, cost remains an important drawback associated with robotic surgery, and this issue remains to be further scrutinized. Brunaud et al. calculated that the robotic adrenalectomy procedure was 2.3 times more costly in their experience than laparoscopy. They also calculated that a way to reach cost equivalence would be to increase da Vinci use, which means that capital and maintenance costs can become affordable at centers performing high-volume robotic surgery [17].

#### 4. Conclusions

Systematic review and a meta-analysis of current evidence show that robot-assisted adrenalectomy can be performed safely and effectively with operative time and complication rates similar to laparoscopic adrenalectomy. In addition it can provide the potential advantage of a shorter hospital stay and less blood loss. These findings seem to support the use of robotic surgery for the minimally invasive surgical management of adrenal masses. However, they should be confirmed in well-designed prospective RCTs with adequate power and follow-up.

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Study concept and design: Brandao, Autorino.

Acquisition of data: Brandao, Laydner, Ouzaid.

Analysis and interpretation of data: Brandao, Autorino, Laydner.

Drafting of the manuscript: Brandao, Autorino.

Critical revision of the manuscript for important intellectual content: Haber, De Sio, Perdonà, Stein, Porpiglia.

Statistical analysis: Brandao, Autorino, Laydner.

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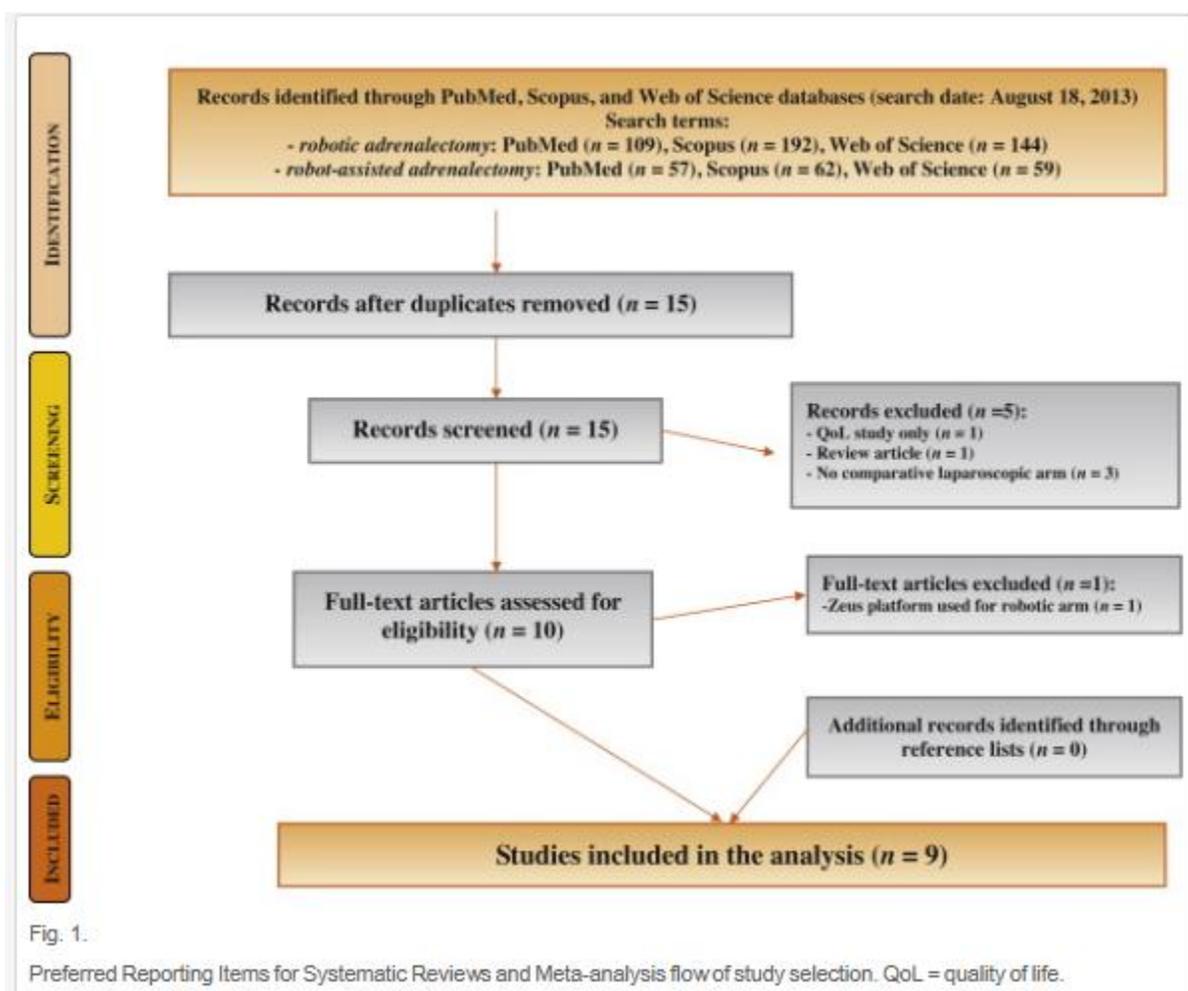


Table 1.

Characteristics and quality assessment of the included studies

Study	Level of evidence	Study design	Quality assessment tool	Quality score
Agcaoglu et al. [14]	2b	CS	NOS	7 of 9
Agcaoglu et al. [15]	2b			7 of 9
Aksoy et al. [16]	2b			7 of 9
Aliyev et al. [25]	2b			7 of 9
Brunaud et al. [17]	2b			7 of 9
Karabulut et al. [18]	2b			7 of 9
Pineda-Solís et al. [19]	3b	NCR		6 of 9
You et al. [20]	3b			6 of 9
Morino et al. [21]	2a	RCT	Jadad <sup>*</sup>	2 of 5 points

CS = consecutive observational study; NCR = nonconsecutive retrospective study; NOS = Newcastle-Ottawa Scale for observational studies; RCT = randomized controlled trial.

\* Jadad Quality Scale for RCT studies (range of score quality: 0-2 = low, 3-5 = high).

Table 2.

Demographics

	Robotic adrenalectomy	Laparoscopic adrenalectomy
No. of cases	277	323
Age, yr	50.0 ± 5.0	50.9 ± 4.0
BMI, kg/m <sup>2</sup>	28.1 ± 4.0	30.1 ± 4.36
Previous abdominal surgery, <i>n</i> (%)	69 (24.9)	60 (18.5)
Tumor size, cm	3.86 ± 1.32	3.78 ± 1.06
Left side, <i>n</i> (%)	164 (59.2)	174 (53.8)
Pathology, <i>n</i> (%) <sup>*</sup>		
Adenoma	152 (54.8)	159 (49.2)
Pheochromocytoma <sup>**</sup>	82 (29.6)	116 (35.9)
Adrenocortical	6 (2.1)	13 (4.0)
Other	33 (11.9)	31 (9.5)

BMI = body mass index.

Values expressed as mean plus or minus standard deviation unless otherwise specified.

Table 3.  
Outcomes

Study	Cases, <i>n</i>		OT, min		EBL, ml		Conversions, <i>n</i>		LHS, d	
	Robotic	Lap	Robotic	Lap	Robotic	Lap	Robotic	Lap	Robotic	Lap
Agcaoglu et al. [14]	24	38	159.4 ± 13.4	187.2 ± 8.3	83.6 ± 59.4	166.6 ± 51.2	1	4	1.4 ± 0.2	1.9 ± 0.2
Agcaoglu et al. [15]	31	31	163.2 ± 10.1	165.7 ± 9.5	25.3 ± 10.3	35.6 ± 9.9	NA	NA	1	1
Aksoy et al. [16]	42	57	186.1 ± 12.1	187.3 ± 11	50.3 ± 24.3	76.6 ± 21.3	0	3	1.3 ± 0.1	1.6 ± 0.1
Aliyev et al. [25]	25	40	149 ± 14	178 ± 12	36 ± 12	43 ± 10	1	3	1.2 ± 0.1	1.7 ± 0.1
Brunaud et al. [17]	50	59	189 ± 43.7	159 ± 33	49	71	4	4	6.3	6.9
Karabulut et al. [18]	50	50	166 ± 7.0	164 ± 8.0	41 ± 10	41 ± 20	1	2	1.1 ± 0.3	1.5 ± 0.3
Morino et al. [21]	10	10	169 ± 19.7	115.3 ± 15	NA	NA	4 <sup>r</sup>	0	5.7 ± 1.2	5.4 ± 1.2
Pineda-Solís et al. [19]	30	30	189.6 ± 32.7	160 ± 41	30.0 ± 5.0	55.0 ± 74	0	5 <sup>r</sup>	1.3 ± 0.5	1.9 ± 0.5
You et al. [20]	15	8	207.0 ± 50	183.1 ± 48.7	NA	NA	0	0	5.8 ± 0.7	6.7 ± 0.7

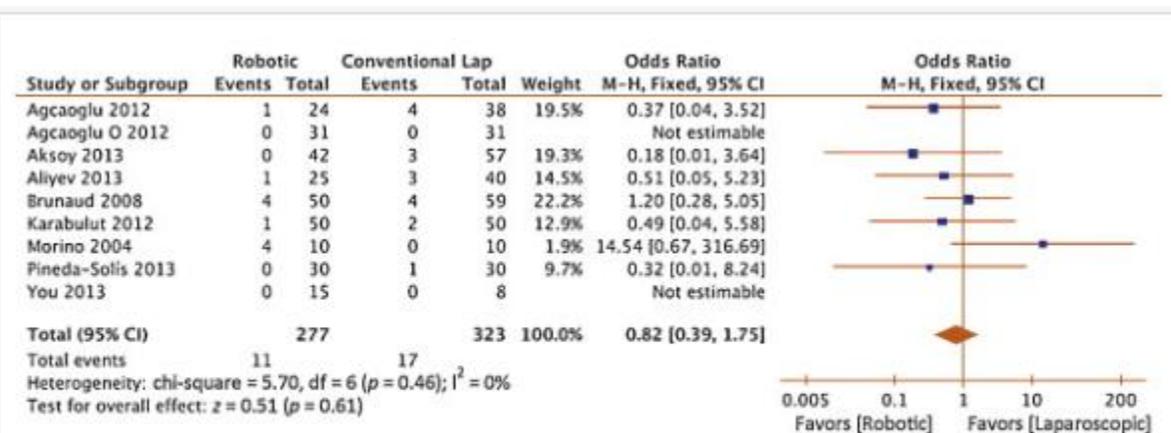


Fig. 2.

Forest plot representing analysis of conversion rate. CI = confidence interval; M-H = Mantel-Haenszel.

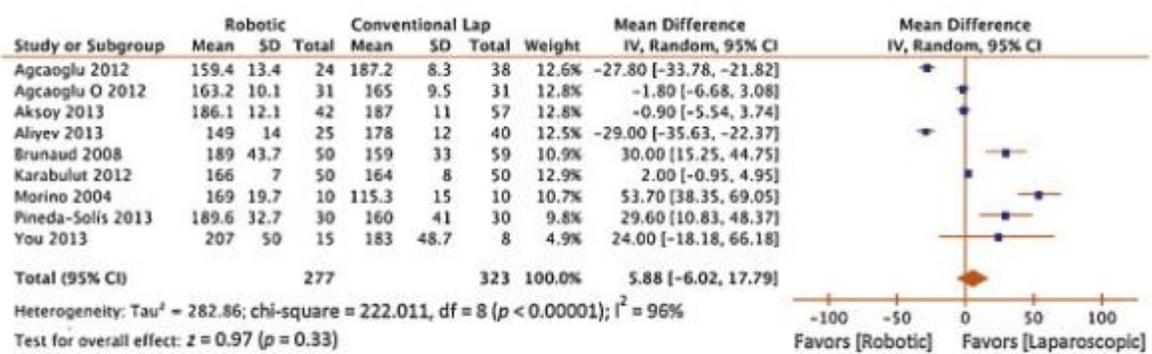


Fig. 3.

Forest plot representing analysis of operative time. CI = confidence interval; IV = inverse variance; SD = standard deviation.

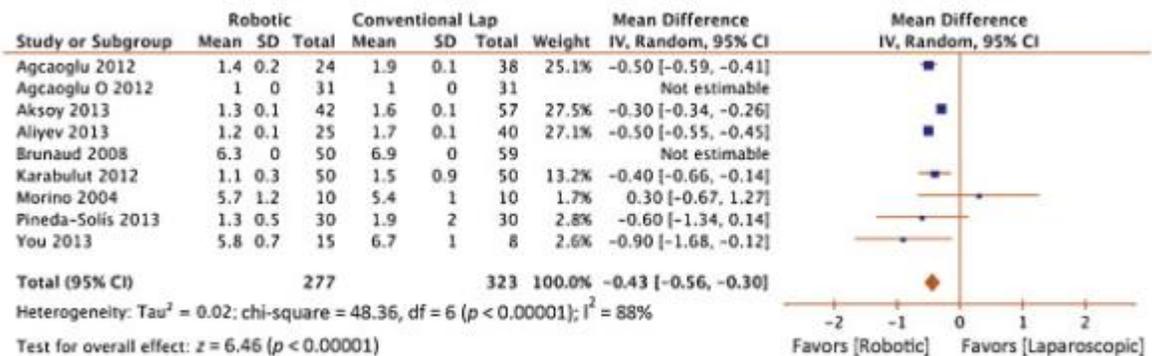


Fig. 4.

Forest plot representing analysis of hospital length of stay. CI = confidence interval; IV = inverse variance; SD = standard deviation.

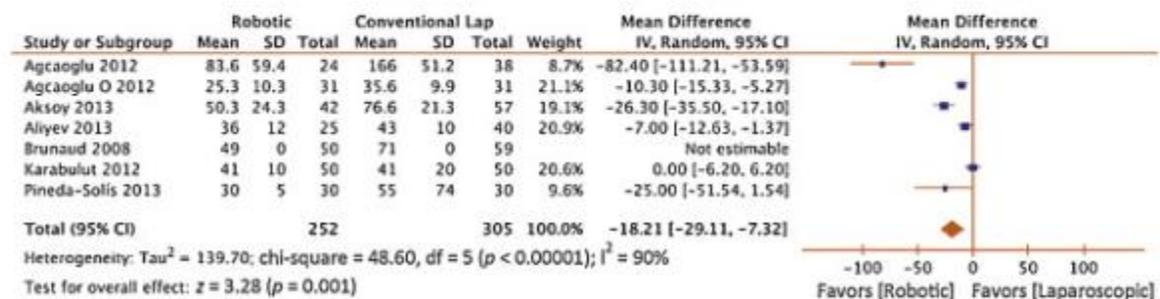


Fig. 5.

Forest plot representing analysis of estimated blood loss. CI = confidence interval; IV = inverse variance; SD = standard deviation.

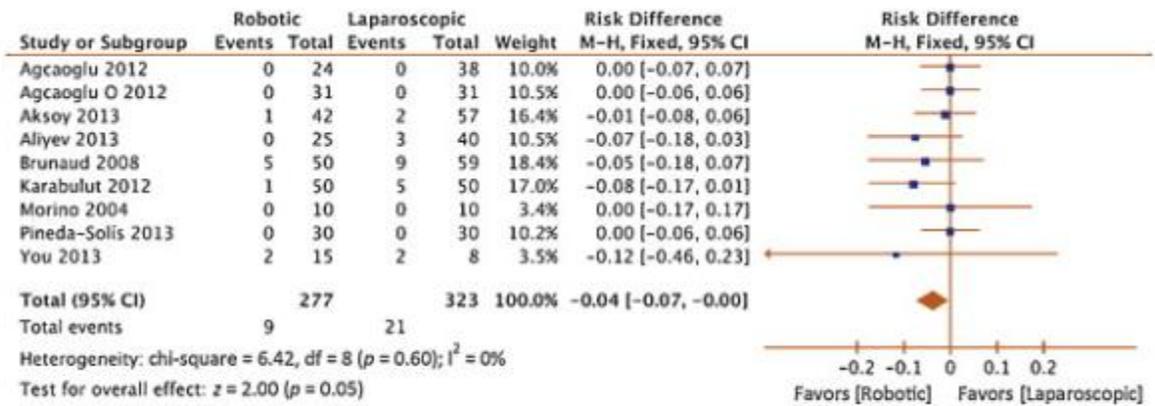


Fig. 6.

Forest plot representing analysis of complication rate. CI = confidence interval; M-H = Mantel-Haenszel; SD = standard deviation.