REVIEW PAPER

TRAUMA & RECONSTRUCTIVE UROLOGY

Robot-assisted laparoscopic ureteral reconstruction: a systematic review of literature

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Introduction To review the literature, as well as to analyze and compare available data on robot-assisted laparoscopic (RAL) surgery versus open surgery, carried out in ureteral reconstructions in terms of different surgical characteristics.

Materials and methods Eligible studies, published between 1997 and July 2016, were retrieved through MEDLINE by applying predetermined inclusion and exclusion criteria with the English language restriction. Publications on RAL surgeries, carried out in different ureteral reconstructions and of any study design, including case series and comparative studies, were included. The study was performed in accordance with the PRISMA statement.

Results A total of 12 retrospective studies (case series and comparative studies) met the systematic review selection criteria involving 245 RAL and 76 open ureteral surgery cases. Main indications for ureter reconstruction were strictures, tumors and injuries. The individual results of comparative studies revealed that the EBL was statistically significantly lower for RAL than for open surgery. As for operation time, length of hospital stay and follow-up time, the data was contradictory.

The rate of recurrent stricture in RAL and open groups was similar:-9.0%. The meta-analysis of three comparative studies confirmed that patients lose statistically significantly less blood in RAL, compared to open surgery.

Conclusions The analysis of limited data available shows that robot-assisted laparoscopic ureteral reconstruction is a safe and effective minimally invasive technique with high cure rates similar to those of the conventional open approach and, with favorable safety profile. Future well-designed randomized controlled trials are required to strengthen our findings.

Key Words: laparoscopic surgery ‹› robotic surgery ‹› systematic review ‹› ureteral reconstruction ‹› ureteral trauma

INTRODUCTION

The known consequences of the open laparotomy procedure, including blood loss, postoperative pain, leading to increased narcotic requirements, ileus and lengthy hospital stay has compelled medical scientists to invent less invasive surgical techniques, such as laparoscopy, and more recently – robot-assisted laparoscopic (RAL) surgery. The latter is becoming increasingly popular due to its minimally invasive nature, increased dexterity of intracorporeal suturing and improved visualization. The Da Vinci Surgical System® (Intuitive Surgical, USA) allows surgeons to accomplish progressively complex procedures with a shorter learning curve and better efficacy [1]. Robotic assistance provides a big workspace, clear operative field, magnified (×10) 3D depth perception, handy instrumentation, tremor filtration, motion scaling and a comfortable operation set-up [2, 3].

The improved intracorporeal suturing makes ureteral surgery a logical extension, based on the experience with anastomoses in a prostatectomy operation [4, 5]. RAL is currently used in numerous urologic procedures, including ureteral reconstruction, leading to

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a decreased morbidity and better clinical outcomes when compared to open surgery [6, 7]. On the other hand, existing studies of robotic ureteral surgery, mainly case series, have been limited to small cohorts of patients and restricted follow-up, that do not allow to decisively conclude on the significant advantages of RAL ureteral reconstruction over the open approach [7–12]. The aim of this study is to review the literature, as well as to analyze and compare available data on RAL surgery versus open surgery carried out in ureteral reconstructions in terms of different surgical characteristics, such as the estimated blood loss, operation time, length of hospital stay, follow-up time, as well as the rate of stricture recurrence.

MATERIAL AND METHODS

The study was performed in accordance with the PRISMA statement [13]. The eligible studies, published between 1997 and 2016, were retrieved through MEDLINE – PubMed. The search has been conducted in May-July, 2016 with the English language restriction. Studies were selected by applying predetermined inclusion and exclusion criteria. Two independent reviewers were blinded to one another's abstracted articles. We included publications on RAL surgeries carried out in different ureteral reconstructions and of any type of study design, including mostly case series and comparative studies.

PubMed search strategy

The following keywords with the English language restriction were used for the article search: Robot* AND distal ureter* AND re-implantation, Robot* AND distal ureter* AND re-implantation, Robot* AND lower ureter* AND re-implantation, Robot* AND lower ureter* AND re-implantation, Robot* AND distal ureter* AND reconstruction, Robot* AND distal ureter* AND injury, Robot* AND lower ureter* AND reconstruction, Robot* AND lower ureter* AND injury, Da Vinci AND distal ureter* AND re-implantation, Da Vinci AND distal ureter* AND re-implantation, Da Vinci AND lower ureter* AND re-implantation, Da Vinci AND lower ureter* AND re-implantation, Da Vinci AND distal ureter* AND reconstruction, Da Vinci AND distal ureter* AND injury, Da Vinci AND lower ureter* AND reconstruction, Da Vinci AND lower ureter* AND injury.

Selection criteria

Inclusion criteria:

1. Original study describing RAL ureteral reconstructions carried out in different conditions.
2. Patients follow-up longer than 3 months.
3. English language articles.

Exclusion criteria:

1. Sample size less than 10 subjects.
2. The same cohort of patients (duplicates in different editions).

The following characteristics were considered for observations/review:

A. Demographical: the number and the age of patients; indications for the ureteral surgery; the lesion side; time of repair; and the presence of a nephrostomy/stent before surgery.
B. Perioperative: intraoperative complications; the volume of blood loss; need for a blood transfusion; conversion to open surgery; duration of the operation; length of stay at the hospital.
C. Postoperative: postoperative complications; mean follow-up time; complications/recurrence at follow-up.

Data collection process

A data extraction table was created in Microsoft Excel (Microsoft Office 2010, USA) and refined accordingly. Two study authors independently extracted the data from selected studies. Discrepancies and disagreements have been resolved through source article verification and consensus among the study authors.

Data items

All study-collected data for case series (RAL cases) was summarized descriptively. As for comparative studies (RAL vs open intervention) the data was summarized descriptively both by individual and pooled estimates. Descriptive statistics for the continuous variables included the number of patients (n), mean, standard deviation (SD), median, and interquartile range (IQR). Categorical variables included counts and percentages. The primary endpoints for the meta-analysis were raw mean differences (d) between RAL and open surgery with respect to estimated blood loss (EBL, mL), operation time (OT in minutes), Length of hospital stay (LOS in days) and follow-up time (FUT in months). Additional endpoints such as the number of complications, as well as indications were counted for individual studies. Recurrence rates were calculated for the comparative studies for RAL versus open groups and Fisher's exact test was used to detect the significance level of the difference.
For the purpose of deriving SD out of IQR (in those cases where SD was not reported), all continuous primary endpoints were assumed to be drawn from the normally distributed random variables of the original data. Thus assuming the normally distrib-

uted primary endpoint, SD can be approximated by dividing IQR by 1.35 [14].
All statistical analyses were performed, by using SAS (version 9.3, SAS Institute Inc, USA) statistical software.

Summary measures

The principal summary measure for comparative meta-analysis is a d between RAL and open interventions, where positive difference favors the open intervention and negative difference favors the RAL intervention. 95% Confidence interval (CI) of mean difference, associated p-value, as well as I2 (%) as a measure of statistical heterogeneity between studies (with, I2 = 0% indicating no heterogeneity; and the larger the value for I2, the larger the heterogeneity) are presented.

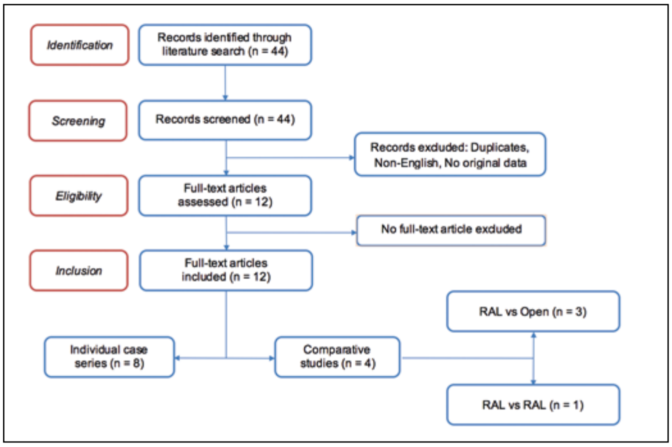

Figure 1. *Flowchart of study selection for systematic review and meta-analysis.*

Synthesis of results

The random effect model was employed to pool the effects of three comparative studies [15]. The inverse variance method was used to weight the individual study effects.
Due to small samples in the selected studies, d has a slight bias tending to overestimate the absolute value of delta (δ). This bias was removed by a simple correction that yields an unbiased estimate of δ, with the unbiased estimate, sometimes called Hedges' g [15]. To convert from d to Hedges' g we used a correction factor. The approach of a random effects analysis was to decompose the observed variance into its two component parts, within-studies and between-studies also known as tau squared (τ2) and then use both parts when assigning the weights. The goal was to take account of both sources of variances.

Assigning weights under the random effects model

The weight under the random effect model for each study is calculated as follows:
Where: is the within-study variance for study (i) plus the between-studies variance, τ2. That is,
the weighted mean is then computed as:
i.e., the sum of the products (effect size multiplied by weight) divided by the sum of the weights.
The statistical analysis data are summarized in forest plots for better visualization.

RESULTS

Individual Studies

A total of 44 articles was screened. After removing repeated studies and applying inclusion and exclusion criteria, 12 articles were included into the systematic review [2, 4–7, 16–22]. Figure 1 shows the flow diagram. In addition, Table 1 and Table 2 report the main characteristics of the studies included. All selected studies had a retrospective nature. From them, eight were case series [2, 4, 5, 16–20] and four had comparative study design comparing RAL and open approaches (two articles) [7, 21], two different RAL techniques (one article) [6], as well as RAL, laparoscopic and open surgeries (one article) [22]. Review and analysis of the last article data were performed only in RAL and open groups [22]. Overall, data comprised 245 RAL and 76 open ureteral surgery cases (85 laparoscopic cases were omitted).
In case series, the main indications for the surgery included strictures (n = 27; 14.2%), tumors (n = 40; 21.1%) and injuries (n = 14; 7.4%). In the article authored by Fifer et al., tabulation of indications for 55 patients (28.9%) was not presented [16]. On the other hand, for comparative studies, the main indications for the surgery included strictures (n = 72; 55%), tumors (n = 55; 17.1%) and injuries (n = 31; 14%). Indications in each study are presented in Table 2.
In a series of 190 RAL, the calculated median of EBL was 98.2 mL (IQR: 50–123 mL), OT – 245.8 mins (IQR: 208.9–276.5 mins), LOS – 2.5 days (IQR: 2.4 –3.92 days), and FUT – 14.35 months (IQR: 9.9–19.25 months).
The individual results of comparative studies revealed, that EBL was reported to be statistically significantly lower for RAL than for open surgery (Figure 2).
OT was statistically significantly shorter for RAL than for open (270 ±182.8 vs. 306.6 ±48.4 mins, $p < 0.05$) in the report of Kozinn et al. [7]. Similar results were reported in the study by Elsamra et al.

Table 1. *Summary of selected publications [2, 4–7, 16–22]*

Ref	Author, year	Number of cases	Mean age, years	EBL, mL	OT, min	LOS, days	FUT, months	Complications, N (%)
17	Slater, 2015	14	39	40	286	2.3	20.7	1 (7.1%)
5	Wason, 2015	13	46	123	282	2.5	9.8	6 (46.2%)
13	Fifer, 2014	55	52	50	221	1.6	6	5 (9.1%)
19	Elsamra, 2014	RAL 20	60	100	236	2	16	2 (10%)[#]
		Open 25	56	300	257	5	58	5 (20%)[#]
18	Isac, 2013	RAL 25	49	100	279	3	11.6	2 (8%)
		Open 41	40	150	200	5	44.5	3 (7.3%)
14	Lee, 2013	10	52.9	102.5	211.7	2.8	28.5	2 (20%)
15	Musch, 2013	16	63.5	NR	260	7.5	10.2	14 (87.5%)
7	Kozinn, 2012	RAL 10	49.3	30.6	306.6	2.4	24	0 (0%)
		Open 10	53.7	327.5	270	5.1	30	1 (10%)
6	Eandi, 2010	RAL* 11	67.4	200	326	4.7	15.2	3 (27.3%)
		RAL** 4	73.5	200	311	4.7	30.5	1 (25%)
2	Hemal, 2010	44	NR	98.2	137.9	2.4	13.5	2 (4.5%)
4	Schimpf, 2009	11	65.2	82	189	2.4	12	3 (27.3%)
16	Patil, 2008	12	41.3	48	208	4.3	15.5	0 (0%)

EBL – mean estimated blood loss, FUT – mean follow-up time, LAP – laparoscopy, LOS – mean length of hospital stay, NR – not reported, OT – mean operation time, RAL – robot-assisted laparoscopy
* Nephroureterectomy, ** Distal ureterectomy with ureteral re-implantation
[#] Only Clavien-Dindo Grade IIIa or greater complications presented

Table 2. *Indications for ureter surgery*

Ref	Author, year	Number of cases	Indications, N (%)				
			Injuries	Stricture	Tumors	Other	Unknown
17	Slater, 2015	14	9 (64.3%)	2 (14.3%)	0 (0%)	3 (21.4%)	0 (0%)
5	Wason, 2015	13	0 (0%)	0 (0%)	0 (0%)	13 (100%)	0 (0%)
13	Fifer, 2014	55	0 (0%)	0 (0%)	0 (0%)	0 (0%)	55 (100%)
19	Elsamra, 2014	RAL 20	7 (35%)	2 (10%)	6 (30%)	5 (25%)	0 (0%)
		Open 25	10 (40%)	2 (8%)	9 (36%)	4 (16%)	0 (0%)
18	Isac, 2013	RAL 25	5 (20%)	16 (64%)	0 (0%)	4 (16%)	0 (0%)
		Open 41	9 (22%)	32 (78%)	0 (0%)	0 (0%)	0 (0%)
14	Lee, 2013	10	2 (20%)	0 (0%)	2 (20%)	6 (60%)	0 (0%)
15	Musch, 2013	16	0 (0%)	6 (37.5%)	6 (37.5%)	4 (25%)	0 (0%)
7	Kozinn, 2012	RAL 10	0 (0%)	10 (100%)	0 (0%)	0 (0%)	0 (0%)
		Open 10	0 (0%)	10 (100%)	0 (0%)	0 (0%)	0 (0%)
6	Eandi, 2010	RAL* 11	0 (0%)	0 (0%)	11 (100%)	0 (0%)	0 (0%)
		RAL** 4	0 (0%)	0 (0%)	4 (100%)	0 (0%)	0 (0%)
2	Hemal, 2010	44	2 (4.5%)	8 (18.2%)	10 (22.7%)	24 (54.5%)	0 (0%)
4	Schimpf, 2009	11	1 (9.1%)	1 (9.1%)	7 (63.6%)	2 (18.2%)	0 (0%)
16	Patil, 2008	12	0 (0%)	10 (83.3%)	0 (0%)	2 (16.7%)	0 (0%)

RAL – robot-assisted laparoscopy
* Nephroureterectomy, ** Distal ureterectomy with ureteral re-implantation

[22]. However, Isac et al reported, that OT was statistically significantly longer for RAL than for open (279 ±66.7 vs. 200 ±82.2 mins, p <0.01) [21].
LOS was statistically significantly shorter for RAL than for open (2 ±1.48 vs. 5 ±2.96 days, p <0.05) in the report of Elsamra et al. [22]. Similar results were also reported by Isac et al. [21]. However, Kozinn et al in their publication reported, that LOS was statistically significantly longer for RAL than for open (5.1 ±2.6 vs. 2.4 ±1.2 days, p = 0.01).
As for FUT, a notable statistical difference in favor of RAL was reported in the publications by Elsamra et al (3.68 ±4.17 vs. 13.34 ±18.57 months, p <0.05) and Isac et al. (11.6 ±8.4 vs. 44.5 ±35.6 months, p <0.01).

Complications

The intraoperative complications were presented only in one article: external iliac vein injury during a sharp dissection in one patient, and persistent hematuria in another [4]. The postoperative complications were not reported in a uniform approach across the studies. In seven articles, Clavien-Dindo classification of surgical complications was used for reporting, in the other five non-classified complications were listed. Elsamra et al presented only complications of Grade IIIa per Clavien-Dindo classification or greater [22]. Overall 15 (4.7%) grade IIIa or greater complications were reported in all articles combined. One conversion to open surgery happened out of all 245 RAL cases; this patient had massive peritoneal adhesions after a previous pancreatectomy [18]. The rate of complications per study is presented in Table 1.
Calculation of rates of recurrent strictures during the follow-up period was completed with the use of data from two comparative studies (45 patients in RAL group and 66 in open group) [21, 22]. The stricture recurrence rate in RAL group was 8.9% (4 cases) and in open group was 9.1% (6 cases). Difference between groups was not statistically significant (p >0.05).

Synthesis of results – Meta-analysis

Three comparative studies were included in the meta-analysis of EBL, OT, LOS and FUT with a total of 131 cases (55 patients undergone RAL and 76 open intervention) [7, 21, 22]. The study by Kozinn et al was not included only in the analyses of FUT, because no measure of dispersion was reported [7].
Estimated Blood Loss (EBL): The EBL was significantly lower for RAL than for the open interventions. Pooled mean difference and its 95% CI along with statistical heterogeneity measure was -176 mL [-313; -40]; I2 = 99.5%, p = 0.011 (see Figure 2).

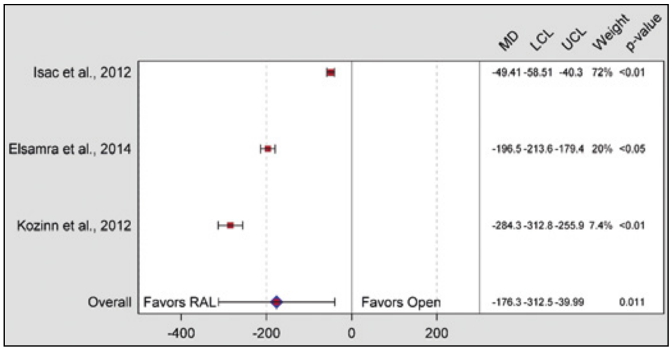

Figure 2. *Impact of Robot-Assisted Laparoscopy (RAL) vs. Open surgery on Estimated Blood Loss (mL).*
MD – Mean Difference, LCL – Lower Confidence Limit, UCL – Upper Confidence Limit

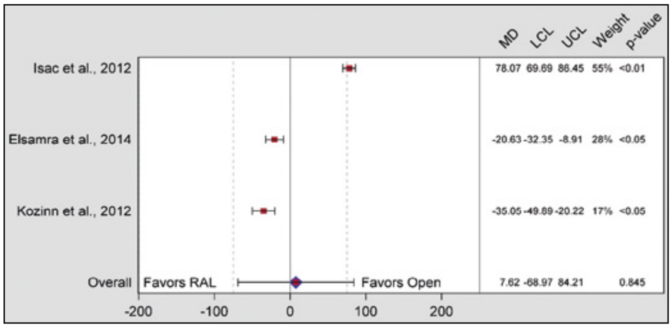

Figure 3. *Impact of robot-assisted laparoscopy (RAL) vs. Open surgery on operation time (min).*
MD – Mean Difference, LCL – Lower Confidence Limit, UCL – Upper Confidence Limit

In total, five patients needed a blood transfusion during the surgery, from which four were RAL patients and one from the open group.
Operation Time (OT): The OT was insignificantly longer for RAL than for the open interventions: 7.62 mins [-68.97; 84.21]; I2 = 99.3%, p = 0.845 (Figure 3).
Length Of hospital Stay (LOS): The LOS was insignificantly shorter for RAL than for the open interventions: -0.83 days [-3.7; 2.0]; I2 = 91.3%, p = 0.566 (Figure 4).
Follow-Up Time (FUT): The FUT was observed to be shorter but not statistically significant for RAL than for the open interventions: -13.8 months [-35.08; 4.31]; I2 = 98.2%, p = 0.134 (Figure 5).

DISCUSSION

The present systematic review collected all the available data on RAL ureteral surgeries, capturing the comparative and non-comparative (case series) publications in the peer-reviewed journals.

The existing studies on robotic ureteral surgery, pointing at advantages of RAL ureteral reconstruction over the open approach, especially in terms of patient safety, lack power due to the small number of patients, absence of randomization and the retrospective nature of studies [7–12].
Additionally, there were no cost-benefit analysis in the selected articles, comparing the use of the Da Vinci Surgical System® and open approaches. Considering similar cure rates of RAL and open procedures, as well as the lack of economic expediency analysis, the safety considerations and postoperative morbidity are becoming crucial factors to favor robotic approach over the other surgical procedures.
To address the aforementioned practical considerations, the systematic review and meta-analysis of EBL, OT, LOS and FUT were performed.
Among 5 patients who needed blood transfusion, 4 were from RAL group. However, pooled data analysis of EBL supported the results of all three comparative studies proving that patients lose blood statistically significantly less in RAL compared to open surgery. Though comparative studies showed longer duration of RAL surgeries, this meta-analysis did not support the statistical significance of this trend. No statistically significant differences of either LOS, or FUT in RAL and open interventions were revealed by this meta-analysis. However, the trends for the mentioned variables as well as for the recurrence rates were in favor of RAL.
The meta-analysis of the postoperative complications was not performed due to the high heterogeneity of data. Nevertheless, Elsamra et al [22] in their comparative study showed higher rates of complications by Clavien-Dindo severity system (grade ≥IIIa) [23] in open surgeries compared to RAL.

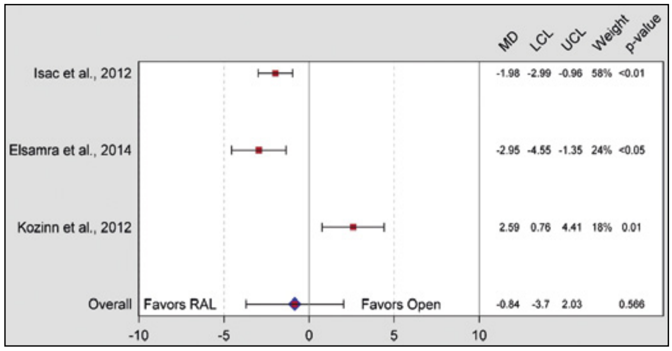

Figure 4. *Impact of Robot-Assisted Laparoscopy (RAL) vs. Open surgery on Length of Hospital Stay (days).*

MD – Mean Difference, LCL – Lower Confidence Limit, UCL – Upper Confidence Limit

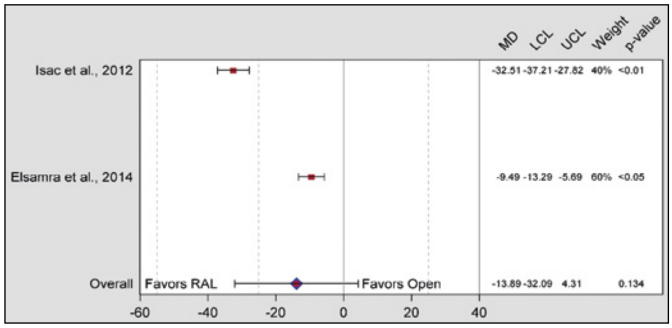

Figure 5. *Impact of Robot-Assisted Laparoscopy (RAL) vs. Open surgery on patients' Follow-Up Time (months).*

MD – Mean Difference, LCL – Lower Confidence Limit, UCL – Upper Confidence Limit

Limitations

There are several limitations known for this type of studies/meta-analyses. The internal validity of clinical trials might be affected by the selection bias (biased distribution of surgical groups), observer bias (not blinded outcome assessment), outcome reporting bias (choice of the outcome influenced by the results), etc. The main limitation of this type of study is that it is hard and sometimes impossible, due to the retrospective nature, to track the biases, impact levels and directions on the parameters of interest [24]. Another limitation is the inclusion of limited number of studies investigating the same research question. In this case only 12 articles out of 44 are selected, which are mainly investigating different aspects of RAL. Studies with negative/non-significant results, which are investigating the same topic, are less likely to get published and might not be brought to the attention of the investigators [25]. While leaving out of scope some unpublished studies of the same type, it eliminated the negative data from the data pool. In this way the pooled analysis is enhancing the likelihood of the overestimated positive results to be demonstrated [26].

CONCLUSIONS

The advances of medical technologies in the urological practice lead to the accumulation of increasing data on the efficacy and safety of RAL in ureteral surgery. The analysis of the limited data available shows that robot-assisted laparoscopic ureteral reconstruction is a safe, effective and minimally invasive technique with cure rates similar to those of the conventional open approach and with a favorable safety profile. However, given the inherent limitations, future well designed randomized controlled trials and comparative studies are required to strengthen our findings.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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