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Comparison of Surgical Techniques in Living Donor Nephrectomy: A Systematic Review and Bayesian Network Meta-Analysis

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: The aim of this study was to compare and evaluate surgical techniques used for living donor nephrectomy (LDN).

Material/Methods: We performed a meta-analysis to compare 4 surgical techniques: open LDN (OLDN), laparoscopic LDN (LLDN), hand-assisted LLDN (HALLDN), and robot-assisted LLDN (RLDN).

Results: No significant differences were found among these surgical techniques in terms of BMI, donor postoperative complications, 1-year graft survival, and DGF. Compared to the OLDN, the other 3 surgical techniques preferred to harvest the left kidney. When the right kidney was chosen as a donor, OLDN was the first-choice surgical technique. EBL was significantly lower in the HALLDN, LLDN, and RLDN groups when compared to the OLDN group. However, operative time and WIT were significantly shorter in the OLDN group. The RLDN group had an increased rate of donor intraoperative complications and a significantly lower VAS on day 1. The OLDN group required more morphine intake than the LLDN group. The length of hospital stay was significantly longer and AR was significantly higher in the OLDN group than in the LLDN and HALLDN groups.

Conclusions: There are no significant differences in donor postoperative complications, recipient DGF, and graft survival among the 4 surgical techniques. OLDN reduces WIT and operation time, but increases EBL and AR. RLDN and LLDN reduce the length of hospital stay, morphine intake, and VAS, and thus accelerate recovery. However, RLDN is associated with increased intraoperative complications.

MeSH Keywords: **Hand-Assisted Laparoscopy • Laparoscopy • Living Donors • Robotics**

Full-text PDF: https://www.annalsoftransplantation.com/abstract/index/idArt/926677

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Background

Kidney transplantation remains the treatment of choice for patients with end-stage kidney failure. Kidneys for transplantation are obtained either from a deceased donor or a living donor. The relative shortage of deceased donor kidneys has led to long waiting times for a kidney transplant, so living donor kidney transplantation is a more realistic option for patients. Living donor kidneys not only expand the donor pool, but offer better graft function and have longer graft survival than kidneys from deceased donors [1]. However, since living kidney donors are healthy individuals, it is of the utmost importance that the safety of donors is ensured so they can resume their normal activities as soon as possible [2].

The first open living donor nephrectomy (OLDN) was reported by Murray et al. in 1954, and since then has been a standard procedure for live kidney donation for many years [3]. However, postoperative pain, scarring, and other discomforts and complications associated with large flank incisions were found in many donors undergoing OLDN surgery. To solve these problems, laparoscopic living donor nephrectomy (LLDN) was introduced in 1995 by Ratner and colleagues to replace the OLDN approach [4]. Compared to the OLDN approach, LLDN is associated with less postoperative pain, shorter hospital stay, better cosmetic results, and quicker recovery [5]. Several technical modifications of laparoscopic surgery have been made, including hand-assisted laparoscopic surgery, robot-assisted laparoscopic surgery, retroperitoneoscopic access, laparoscopic single-site surgery, and natural orifice transluminal endoscopic surgery. The first hand-assisted laparoscopic living donor nephrectomy (HALLDN) was performed in 1998 [6]. HALLDN makes surgical dissection more efficient because of the multiple ways that hands and instruments can be used, significantly increasing the technical capability and resulting in a faster procedure and a shorter operative time. This helps surgeons feel the consistency of kidney tissues and take full advantage of the OLDN approach [7]. In 2002, Horgan [8] first reported robot-assisted laparoscopic living donor nephrectomy (RLDN). Compared to the standard laparoscopic surgery, this robotic system provides 3-dimensional vision with increased precision, thus enhancing the ability of surgeons to perform complex tasks in a laparoscopic environment [9]. Each of these laparoscopic surgery modifications has its own specific technical advantages.

Many studies have used the standard pairwise meta-analyses to compare surgical techniques available in living donor nephrectomy (LDN) for kidney transplantation. However, an insurmountable limitation of these meta-analyses is that only 2 surgical approaches can be directly compared. Surgeons face huge challenges in selecting the best surgical strategy. To address this important issue, we performed a network meta-analysis (NMA), which allows simultaneous comparisons of all surgical approaches in LDN. Another advantage of using NMA is that it enables the integration of both direct and indirect evidence from clinical trials and allows indirect comparisons of a variety of treatments that have not previously been directly compared in head-to-head studies. To guide the selection of surgical procedures for LDN, we systematically reviewed and summarized the NMA results of different surgical techniques.

Material and Methods

Literature search strategy

This study was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines. PubMed, EMBASE, and Cochrane Library databases were searched without any language restrictions. The following searching keywords were used in combination: living donor, nephrectomy, kidney transplantation, laparoscopy, robotics, and hand-assisted laparoscopy. All abstracts, clinical studies, and citations were reviewed. To try to collect more clinical trials, a manual search was also done to identify additional publications of relevant studies. The latest literature search date for this study was July 22, 2020. The literature search was done independently by 2 authors (B.F. and K.S.).

Data extraction and quality assessment

Two authors (Q.X. and S.C.) independently extracted the following data from collected studies: first author, publication year, country, study design, mean age and standard deviation, sex, inclusion and exclusion criteria, total number of patients, and number of subjects undergoing each type of surgical method. Any disagreements between the reviewers occurring during analysis of outcomes of interest were resolved through discussion with the other authors (J. L. and J.X.). If the continuity data were provided as median and range, we estimated the mean difference (MD) and standard deviation (SD) based on the formula of Hozo et al. [10]. Study quality was evaluated using the Cochrane risk of bias assessment tool for random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. Studies were judged as low risk of bias, high risk of bias, or unclear risk of bias. Review Manager software version 5.3 was used to plot the quality assessment.

Inclusion criteria

Articles were included only if they satisfied the following criteria: (1) adults undergoing nephrectomy for live organ donation; (2) surgical techniques involved: OLDN, including mini-open approach, transperitoneal approach, and extraperitoneal

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Table 1. The results of the ranking probabilities for all interventions.

Outcomes	Ranks			
	1st	2nd	3dr	4th
AR	OLDN P=0.99	LLDN P=0.53	HALLDN P=0.53	NA
DGF	OLDN P=0.45	LLDN P=0.49	HALLDN P=0.39	RLDN P=0.47
1-year Graft survival	OLDN P=0.6	HALLDN P=0.35	LLDN P=0.36	RLDN P=0.29
Donor intraoperative complications	RLDN P=0.99	LLDN P=0.64	HALLDN P=0.38	OLDN P=0.45
Donor intraoperative complications (III–IV)	RLDN P=0.98	LLDN P=0.48	OLDN P=0.37	HALLDN P=0.79
Donor postoperative complications	RLDN P=0.5	HALLDN P=0.39	LLDN P=0.36	OLDN P=0.59
Donor postoperative complications (I–II)	RLDN P=0.4	HALLDN P=0.35	LLDN P=0.35	OLDN P=0.37
Donor postoperative complications (III–IV)	RLDN P=0.73	LLDN P=0.64	HALLDN P=0.49	OLDN P=0.58
Left nephrectomy	RLDN P=0.83	LLDN P=0.59	HALLDN P=0.60	OLDN P=0.98
Right nephrectomy	OLDN P=0.98	HALLDN P=0.57	LLDN P=0.57	RLDN P=0.83
BMI	OLDN P=0.82	HALLDN P=0.51	LLDN P=0.48	RLDN P=0.52
Donor length of hospital stay	OLDN p=0.99	RLDN P=0.42	LLDN P=0.46	HALLDN P=0.35
EBL	OLDN p=1	HALLDN P=0.47	LLDN P=0.47	RLDN P=0.42
Morphia intake	OLDN p=0.85	HALLDN P=0.51	LLDN P=0.51	RLDN P=0.51
Operative time	RLDN P=0.86	LLDN P=0.85	HALLDN P=0.99	OLDN P=1
VAS	OLDN p=0.92	HALLDN P=0.67	LLDN P=0.71	RLDN P=0.97
WIT	RLDN P=0.93	LLDN P=0.93	HALLDN P=0.99	OLDN P=1

OLDN – open living donor nephrectomy; LLDN – laparoscopic living donor nephrectomy; HALLDN – hand-assisted laparoscopic living donor nephrectomy; RLDN – robot-assisted laparoscopic living donor nephrectomy; NA – not available; BMI – body mass index; WIT – warm ischemia time; EBL – estimated blood loss; DGF – delayed graft function; AR – acute rejection; VAS – visual analogue scale.

approach; LLDN, including conventional laparoscopic surgery, standard laparoscopic surgery, laparoendoscopic single-site surgery, and retroperitoneoscopic surgery; RLDN, including robotic-assisted retroperitoneoscopic surgery, and robotic-assisted laparoscopic surgery; and HALLDN, including hand-assisted retroperitoneoscopic surgery and hand-assisted laparoscopic surgery; (3) comparative studies evaluating 2 or more surgical techniques (OLDN, LLDN, RALLDN and/or HALLDN); and (4) studies that had at least 1 of the outcomes of interest of our study (see below).

Exclusion criteria

Articles were not included if they met the following criteria: (1) studies that did not meet the inclusion criteria; (2) children and patients undergoing nephrectomy for cancer or a benign kidney disease; and (3) a publication that was an abstract, case report, review, editorial, or letter, or that reported incomplete data, duplicate data, or experiments on non-human animals.

Outcomes of interest

The outcomes of the study include the side of nephrectomy (right or left kidney), body mass index (BMI), warm ischemia time (WIT), estimated blood loss (EBL), operation time, intraoperative and postoperative donor complications, visual analogue scale (VAS), morphine intake on day 1, length of hospital stay, delayed graft function (DGF), acute rejection (AR), and 1-year graft survival.

Statistical analysis

For each outcome of interest, a network plot was drawn using STATA 14.0 software. The consistency test of all the surgical techniques was performed to assess their interest outcomes. In the network plot, nodes represent surgical techniques and connecting lines represent the evidence of direct comparison between the 2 groups of surgical techniques. The area of the nodes represents the cumulative number of enrolled patients for each intervention, and the width of the lines is proportional to the number of trials that have compared paired

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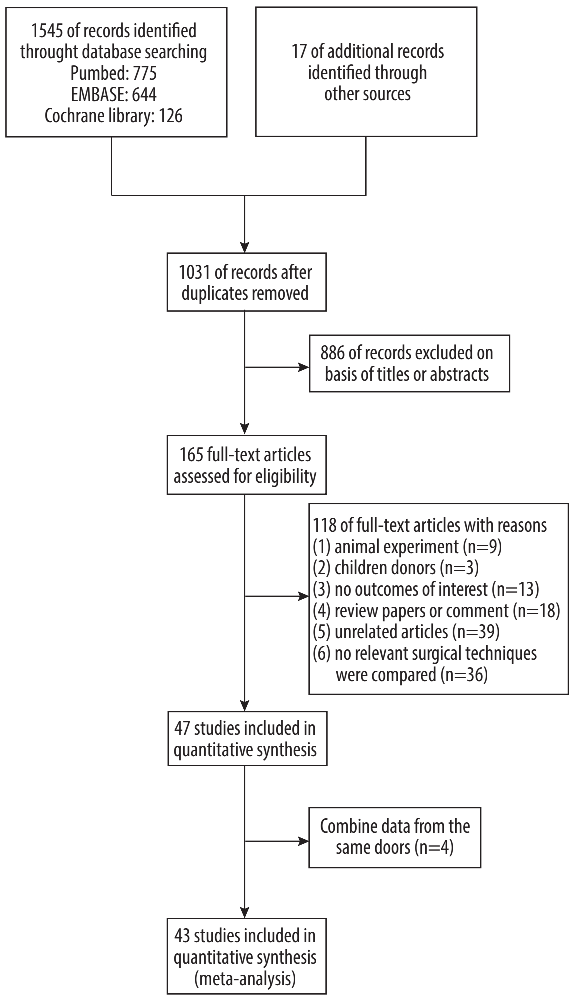

Figure 1. Flow diagram of study selection for inclusion.

surgical treatments. In the consistency analysis, *P*>0.05 indicates a consistency between direct and indirect estimates in a specific closed loop. Otherwise, a node-splitting approach was used to assess the origin of the inconsistency between direct and indirect evidence in the network.

We used a Bayesian approach utilizing the "GEMTC" package to analyze data by a random-effects or fixed-effects model using the Markov chain Monte Carlo chain. Three parallel chains were simultaneously run with different initial values. A total of 20 000 interactions were performed for each chain, and the first 5000 were used for a "burn-in" cycle to eliminate the impact of initial values. For binary data, odd ratios (OR) with 95% credible intervals (CrI) were estimated for the comparisons. When the 95% CrI of OR did not contain the value 1, it was regarded as indicating a statistically significant difference between 2 groups. For continuous outcomes, the MD with 95% CrI was calculated. If the 95% CrI of MD did not contain the value 0, it was considered to be significantly different. The ranking probability of each type of surgery technique for each outcome of interest was calculated. Cumulative ranking was estimated based on the surface under the cumulative ranking curve (SUCRA) to evaluate the ranking probabilities of each type of surgery technique. The results of ranking probabilities are shown in Table 1.

Results

Literature search and study characteristics

A total of 1545 publications were retrieved using the aforementioned search criteria. An additional 17 records were obtained from other sources, including the reference lists of the retrieved articles. After removing redundant ones, 1031 publications were further reviewed. Extensive screening identified 47 publications, as shown in Figure 1 [11–57]. Hamidi 2009 [13] and Oyen 2005 [14], Nicholson 2010 [16] and Nicholson 2011 [17], Simforoosh 2005 [18] and Simforoosh 2012 [19], and Waller 2001 [20] and Waller 2002 [21] reported the same donor datasets, so we combined their outcomes of interest into 4 studies. Finally, 43 studies were included. Among these included studies, 31 were non-RCTs (25 retrospective and 6 prospective) and 12 were RCTs.

The characteristics of the included studies are summarized in Table 2, including the surgical techniques compared and patient demographics in individual studies. A total of 6772 patients were included in the selected studies. Thirty-four studies were two-arm trials and 9 were three-arm trials involving different types of surgeries for kidney transplantation. Of all patients, 2003 were treated with OLDN, 2710 with LLDN, 1809 with HALLDN, and 250 with RALLDN. A wide geographic distribution of patients was seen, with patients mainly from North America, South America, Europe, Oceania, and Asia. The network plots of comparisons between different surgical approaches with their corresponding sample sizes are shown in Figure 2, in which the cumulative number of enrolled patients for each intervention and the number of trials comparing each pair of treatments are indicated by the node area and the line width, respectively.

Risk of bias in included studies

The risk of bias in the included studies was evaluated by use of the Cochrane Collaboration's risk of bias assessment tool. When evaluating selection bias, we found that 10 of the included studies reported sufficient details to evaluate sequence generation and allocation concealment. Of the included studies, only 2 mentioned the use of blinding of participants and personnel and/or blinding of outcome assessment, but none of them reported incomplete outcome data or no selective

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Table 2. Characteristics of studies included in the meta-analysis.

ID	First author, year	Country	Study type	Surgical technique	Sex (Male/ Female)	Age Mean(SD)	Total donors	Per group donors	Outcomes of interest
1	Brook 2005 [11]	UK	RCT	LLDN *vs.* OLDN	NA	57 *vs.* 50	60	40 *vs.* 20	(1)(3)(7)(8)
2	Brook 2010 [12]	Australia	Retrospective	LLDN *vs.* OLDN	(196/119) *vs.* (659/500)	45.1 *vs.* 46.8	1474	315 *vs.*1159	(6)(7)(8)
3	Hamidi 2009 [13]; Oyen 2005 [14]	Norway	RCT	LLDN *vs.* OLDN	(28/35) *vs.* (26/33)	46(13) *vs.* 45(12.75)	122	63 *vs.* 59	(1)(2)(3)(5)(9)(10)(11)(13)
4	Kok 2006 [15]	Netherlands	RCT	LLDN *vs.* OLDN	(29/21) *vs.* (24/26)	49(14.25) *vs.* 48.5(13.5)	100	50 *vs.* 50	(1)(2)(3)(4)(5)(7)(8)(9)(10)(11)(12)
5	Nicholson 2010 [16]; Nicholson 2011 [17]	UK	RCT	LLDN *vs.* OLDN	(20/36) *vs.* (14/14)	47(12) *vs.* 45(11)	84	56 *vs.* 28	(1)(2)(3)(4)(5)(6)(7)(8)(9)(10)(11)(12)(13)
6	Simforoosh 2005 [18]; Simforoosh 2012 [19]	Iran	RCT	LLDN *vs.* OLDN	(86/14) *vs.* (92/8)	27.8(3.9) *vs.* 29.2(5.2)	200	100 *vs.* 100	(1)(2)(3)(5)(6)(7)(9)(10)(11)
7	Waller 2001 [20]; Waller 2002 [21]	UK	Retrospective	LLDN *vs.* OLDN	(8/12) *vs.* (12/22)	44(13) *vs.* 44(9)	54	20 *vs.* 34	(1)(5)(6)(7)(8)(9)(13)
8	Wolf 2001 [22]	USA	RCT	HALLDN *vs.* OLDN	(12/11) *vs.* (14/13)	38(11) *vs.* 41(12)	50	23 *vs.* 27	(2)(3)(4)(5)(7)(9)(11)(13)
9	Yadav 2016 [23]	USA	Prospective	LLDN *vs.* OLDN	(14/36) *vs.* (9/41)	45.5(11) *vs.* 45(12.75)	100	50 *vs.* 50	(1)(2)(3)(4)(5)(7)(9)
10	Bhattu 2015 [24]	India	RCT	RLDN *vs.* LLDN	(2/13) *vs.* (7/23)	46.47(11.21) *vs.* 45.33(9.37)	45	15 *vs.* 30	(1)(2)(3)(5)(8)(9)(11)(12)
11	Cohen 2015 [25]	USA	Retrospective	RLDN *vs.* HALLDN	NA	37.7 *vs.* 41	120	100 *vs.* 20	(1)(5)(9)(10)(11)
12	Geffner 2011 [26]	USA	Retrospective	RLDN *vs.* LLDN	NA	44.5(11.7) *vs.* 43.6(11.2)	70	35 *vs.* 35	(2)(3)(4)(5)(8)(9)(10)(11)
13	Janki 2017 [27]	Netherlands	Retrospective	RLDN *vs.* LLDN *vs.* HALLDN	NA	53(14.25) *vs.* 49.3(12.5) *vs.* 55(15.5)	184	59 *vs.* 61 *vs.* 64	(2)(3)(4)(5)(8)(9)(10)(11)
14	Liu 2012 [28]	USA	Retrospective	RLDN *vs.* LLDN	NA	34.8(8.94) *vs.* 40.7(8.94)	25	5 *vs.* 20	(2)(3)(4)(5)(6)(9)(13)
15	Luke 2018 [29]	Canada	Prospective	RLDN *vs.* LLDN	(9/5) *vs.* (7/18)	51(6.81) *vs.* 50(10.5)	39	14 *vs.* 25	(1)(2)(3)(4)(5)(9)(11)(13)
16	Yang 2018 [30]	USA	Retrospective	RLDN *vs.* LLDN	(12/10) *vs.* (44/29)	38.2(11.4) *vs.* 39.4(11.3)	95	22 *vs.* 73	(1)(2)(3)(4)(5)(6)(8)(9)(11)
17	Bargman 2006 [31]	Indiana	RCT	HALLDN *vs.* LLDN	NA	NA	40	20 *vs.* 20	(1)(3)(4)(5)(9)(11)(13)
18	Branco 2008 [32]	Brazil	Retrospective	HALLDN *vs.* LLDN	(32/35) *vs.* (44/45)	38(9.2) *vs.* 38.9(10.4)	156	67 *vs.* 89	(1)(3)(4)(5)(9)(10)(11)
19	Buell 2004 [33]	USA	Retrospective	HALLDN *vs.* LLDN	(15/16) *vs.* (10/18)	41.1(11.5) *vs.* 44.5(8.5)	59	31 *vs.* 28	(2)(3)(4)(5)(6)(7)(9)(10)
20	Choi 2014 [34]	Korea	Retrospective	HALLDN *vs.* LLDN	(19/61) *vs.* (10/61)	38.7(9.6) *vs.* 38.3(10.7)	160	80 *vs.* 80	(1)(2)(3)(4)(5)(6)(7)(9)(10)(11)(12)

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Table 2 continued. Characteristics of studies included in the meta-analysis.

ID	First author, year	Country	Study type	Surgical technique	Sex (Male/ Female)	Age Mean(SD)	Total donors	Per group donors	Outcomes of interest
21	Dols 2014 [35]	Netherlands	RCT	HALLDN *vs.* LLDN	(43/52) *vs.* (49/46)	52.8(11.8) *vs.* 52.4(11.7)	190	95 *vs.* 95	(2)(3)(4)(5)(8)(9)(10)(11)(12)(13)
22	EL-Galley 2004 [36]	USA	RCT	HALLDN *vs.* LLDN *vs.* OLDN	NA	NA	100	17 *vs.* 28 *vs.* 55	(2)(3)(4)(5)(9)(11)
23	Gershbein 2002 [37]	USA	Retrospective	HALLDN *vs.* LLDN	(9/20) *vs.* (3/12)	40.2(11.75) *vs.* 38.9(10.47)	44	29 *vs.* 15	(3)(4)(5)(7)(8)(9)(10)(11)(13)
24	Gjertsen 2006 [38]	Sweden	Prospective	HALLDN *vs.* LLDN *vs.* OLDN	(4/7) *vs.* (6/9) *vs.* (10/15)	54(8.21) *vs.* 50(9.36) *vs.* 50(16.5)	51	11 *vs.* 15 *vs.* 25	(5)(10)(11)
25	Greco 2009 [39]	Germany	Retrospective	HALLDN *vs.* OLDN	NA	44(13) *vs.* 40(14)	82	45 *vs.* 37	(3)(5)(7)(8)
26	Hirose 2018 [40]	Japan	Retrospective	HALLDN *vs.* LLDN	(40/70) *vs.* (84/210)	52.2(11) *vs.* 53.9(10.5)	404	110 *vs.* 294	(1)(2)(3)(4)(5)(6)(7)(8)(10)(11)
27	Hofker 2012 [41]	Netherlands	RCT	HALLDN *vs.* OLDN	(10/15) *vs.* (14/11)	51(8.5) *vs.* 52(12.75)	50	25 *vs.* 25	(1)(2)(3)(5)(6)(9)(11)(12)(13)
28	Klop 2014 [42]	Netherlands	RCT	HALLDN *vs.* LLDN	(12/8) *vs.* (5/15)	47(14) *vs.* 49(12.75)	40	20 *vs.* 20	(1)(2)(3)(4)(5)(8)(9)(10)(11)(12)(13)
29	Kocak 2007 [43]	USA	Retrospective	HALLDN *vs.* LLDN	(151/167) *vs.* (209/273)	41(10) *vs.* 39(10)	800	318 *vs.* 482	(1)(6)(9)(10)(11)
30	Lai 2010 [44]	Tai wan	Prospective	HALLDN *vs.* LLDN	(17/35) *vs.* (16/29)	42(11.9) *vs.* 44.8(12.1)	97	52 *vs.* 45	(1)(2)(3)(5)(6)(8)(9)
31	Lucas 2013 [45]	Indiana	Retrospective	HALLDN *vs.* LLDN	NA	41.4(11.33) *vs.* 37.5(11.7)	268	116 *vs.* 152	(1)(3)(5)(7)(9)(10)(11)
32	Mateo 2003 [46]	USA	Prospective	HALLDN *vs.* LLDN	(9/9) *vs.* (17/12)	37.8(11.4) *vs.* 38.7(12.7)	47	18 *vs.* 29	(1)(2)(3)(4)(5)(6)(9)(11)
33	Minnee 2008 [47]	Netherlands	Retrospective	HALLDN *vs.* OLDN	(90/78) *vs.* (19/25)	46.7(12.5) *vs.* 44.7(10.6)	202	158 *vs.* 44	(1)(3)(5)(7)(8)(9)(10)(11)
34	Mjogen 2010 [48]	Norway	Retrospective	HALLDN *vs.* LLDN	NA	NA	305	203 *vs.* 102	(1)(3)(5)(9)(10)(11)(13)
35	Percegona 2008 [49]	Brazil	Retrospective	HALLDN *vs.* LLDN	NA	NA	55	21 *vs.* 34	(3)(4)(5)(9)
36	Ruiz-Deya 2001 [50]	USA	Retrospective	HALLDN *vs.* LLDN *vs.* OLDN	(13/10) *vs.* (7/4) *vs.* (10/9)	NA	53	23 *vs.* 11 *vs.* 19	(3)(5)(7)(9)
37	Ruszat 2006 [51]	Switzerland	Retrospective	HALLDN *vs.* LLDN *vs.* OLDN	(6/27) *vs.* (24/51) *vs.* (24/45)	50(13) *vs.* 51.88 (10.26) *vs.* 53(11)	177	33 *vs.* 75 *vs.* 69	(1)(2)(3)(4)(5)(9)(10)(11)
38	Salazar 2005 [52]	USA	Retrospective	HALLDN *vs.* LLDN *vs.* OLDN	(13/11) *vs.* (4/7) *vs.* (10/5)	44(10) *vs.* 39(10) *vs.* 41(8)	50	24 *vs.* 11 *vs.* 15	(1)(2)(5)(9)(10)
39	Stifelman 2001 [53]	USA	Retrospective	HALLDN *vs.* OLDN	(30/30) *vs.* (13/18)	41.6(10.6) *vs.* 42.4(9.5)	91	60 *vs.* 31	(1)(2)(4)(5)(6)(7)(9)(11)

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Table 2 continued. Characteristics of studies included in the meta-analysis.

ID	First author, year	Country	Study type	Surgical technique	Sex (Male/Female)	Age Mean(SD)	Total donors	Per group donors	Outcomes of interest
40	Sundqvist 2004 [54]	Sweden	Prospective	HALLDN *vs.* LLDN *vs.* OLDN	(6/5) *vs.* (8/6) *vs.* (2/9)	48(7.9) *vs.* 53.5(8.5) *vs.* 45(7.92)	36	11 *vs.* 14 *vs.* 11	(2)(3)(4)(5)(9)(13)
41	Ungbhakorn 2012 [55]	Thailand	Retrospective	HALLDN *vs.* LLDN *vs.* OLDN	(11/12) *vs.* (29/53) *vs.* (34/61)	36(8) *vs.* 38(10) *vs.* 38(10)	200	23 *vs.* 82 *vs.* 95	(1)(3)(4)(5)(9)(11)
42	Velidedeoglu 2002 [56]	USA	Retrospective	HALLDN *vs.* LLDN *vs.* OLDN	(23/37) *vs.* (13/27) *vs.* (30/20)	43.6 *vs.* 44.3 *vs.* 43.2	150	60 *vs.* 40 *vs.* 50	(9)(10)(11)
43	Wadstrom 2003 [57]	Sweden	Retrospective	HALLDN *vs.* LLDN	(15/17) *vs.* (2/9)	47.88(7.04) *vs.* 52(10.21)	43	32 *vs.* 11	(1)(2)(3)(4)(5)(9)

RCT – randomized controlled trail; OLDN – open living donor nephrectomy; LLDN – laparoscopic living donor nephrectomy; HALLDN – hand-assisted laparoscopic living donor nephrectomy; RLDN – robot-assisted laparoscopic living donor nephrectomy; NA – not available. Outcomes of interest: (1) nephrectomy side (right or left nephrectomy); (2) body mass index (BMI); (3) warm ischemia time (WIT); (4) estimated blood loss (EBL); (5) operation time; (6) delayed graft function (DGF); (7) acute rejection(AR); (8) 1-year graft survival; (9) donor length of hospital stay; (10) donor intraoperative complications; (11) donor postoperative complications; (12) visual analogue scale (VAS) on day 1; (13) Morphine intake on day 1.

outcome reporting; therefore, the attrition bias of the included studies was evaluated as low risk. Other sources of bias were identified as unclear risk in all articles, because there were too few available details to make a decision (Figure 3).

Consistency analysis

We used node-splitting models and heat plots for direct and indirect comparisons to evaluate the consistency of outcomes of interest. The data showed that all *P* values were >0.05, indicating that there was no evidence of a significant inconsistency in the network (Figure 4).

Outcomes of interest

The results of all pairwise comparisons of the different surgical techniques for the outcomes of interest are displayed in Table 3. Table 1 shows the results of the ranking probabilities for all interventions based on the SUCRA value for each outcome of interest.

Donor demographics

There was no significant difference in BMI among the OLDN, HALLDN, LLDN, and RLDN groups. Compared with the OLDN group, the other 3 groups preferred to harvest the left kidney. When we chose the right kidney as a donor, OLDN was the first choice for treatment compared to HALLDN, LLDN, and RLDN; however, there was no significant difference in selecting the side of nephrectomy among the HALLDN, LLDN, and RLDN groups.

Donor operative parameters

EBL was significantly lower in the HALLDN, LLDN, and RLDN groups when compared to the OLDN group. OLDN ranked first for high probability of EBL. However, operative time and WIT were significantly shorter in the OLDN group compared to the other 3 groups. Compared to the LLDN and RLDN groups, the HALLDN group had a shorter operative time and WIT. HALLDN and OLDN ranked third and fourth, respectively, with high probabilities for operation time and WIT. The rate of intraoperative complications was higher in the RLDN group, but there was no significant difference in the postoperative complications. RLDN ranked first for donor intraoperative complications. We performed a subgroup analysis of intraoperative and postoperative complications according to the Clavien scale. In terms of the donor intraoperative complication, most of the reported data were Clavien scale III and IV. The rate of intraoperative complications (III-IV) was higher in the RLDN group, but there was no significant difference in the postoperative complications (I–II and III–IV). The RLDN group had a significantly lower VAS on day 1 when compared to the OLDN, HALLDN, and LLDN groups. The OLDN group required more morphine intake than the LLDN group. The length of hospital stay was significantly longer in the OLDN group. OLDN ranked first for probabilities for the VAS on day 1, morphine intake, and duration of hospital stay.

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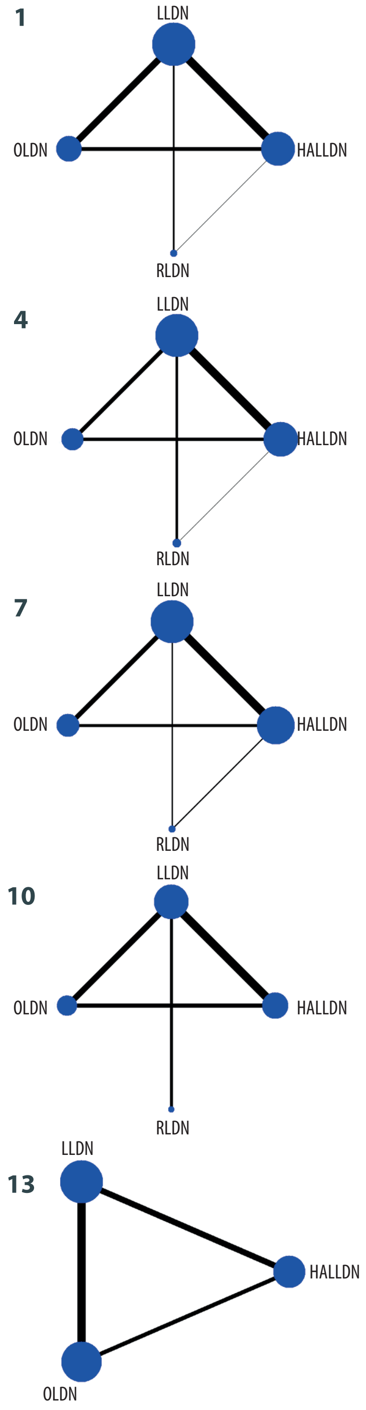

Figure 2. Network plots for different outcomes of interest of different surgical approaches. The area of the nodes represents the cumulative number of enrolled patients for each intervention and the width of the lines represents the number of trials comparing each pair of treatments. OLDN, open living donor nephrectomy; LLDN, laparoscopic living donor nephrectomy; HALLDN, hand-assisted laparoscopic living donor nephrectomy; RLDN, robot-assisted laparoscopic living donor nephrectomy. (**1**) Right nephrectomy; (**2**) left nephrectomy; (**3**) body mass index (BMI); (**4**) warm ischemia time; (**5**) estimated blood loss; (**6**) operation time; (**7**) donor intraoperative complications; (**8**) donor postoperative complications; (**9**) visual analogue scale (VAS) on day 1; (**10**) Morphine intake on day 1; (**11**) donor length of hospital stay; (**12**) delayed graft function; (**13**) acute rejection; and (**14**) 1-year graft survival.

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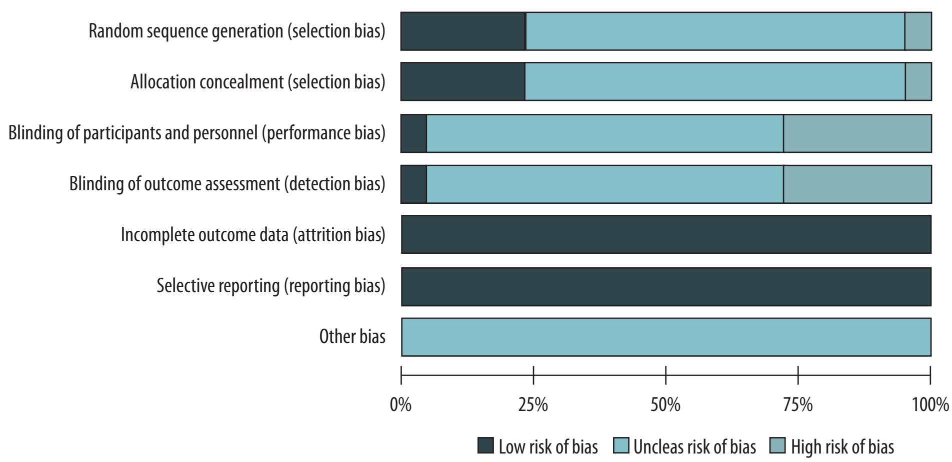

Figure 3. Assessment of study quality using the Cochrane Collaboration's risk of bias tool.

Recipient parameters

There were no significant differences in 1-year graft survival and DGF among the 4 surgical methods. The OLDN group had a significantly higher AR when compared to the LLDN and HALLDN groups; it ranked first for AR with a high probability. There was no significant difference in AR between the HALLDN and LLDN groups.

Discussion

LDN is a unique surgical procedure because healthy people take surgical risks for the benefits of patients. It is very important to choose the best surgical approach to obtain a living donor kidney. There are 2 major issues to keep in mind: (1) donor mortality and morbidity risks could be minimized by carefully selecting safe surgical techniques, which are negatively associated with the surgical skills and experience of the transplant center and operating surgeons; and (2) maintain the optimal function of the donor kidney to ensure the recipient gets the best results after kidney transplantation [58].

In this meta-analysis, we found that there was no significant difference in BMI among the donors enrolled for LDN with different surgical techniques. The left kidney was preferable in LDN, especially when using the RLDN approach. Left kidney donor nephrectomy is technically easier to perform due to a longer renal vein, which provides implantation advantages. In addition, using the transperitoneal approach in right kidney RLDN is more difficult because the presence of the liver complicates the dissection [59,60].

WIT and operation time in the LLDN and RLDN groups were longer than those in the HALLDN and OLDN groups, but there were no significant differences in WIT and operation time between the RLDN and LLDN groups. This is most likely due to the rapid extraction of the kidney through the hand port after vascular ligation in the manual-assisted approach, while the LLDN and RLDN approaches require a bag removal and incision [61]. Our data show that EBL was significantly lower in the HALLDN, LLDN, and RLDN groups compared to the OLDN group, which may be due to the use of finer instruments, magnified view, and multi-angle vision in the laparoscopic surgery [62]. The included studies used the VAS to assess pain on the first day after surgery. We found that the RLDN group had the lowest VAS score among all 4 interventions. Moreover, the OLDN group required more morphine intake than the LLDN group, indicating that RLDN and LLDN reduce donor postoperative pain. RLDN ranked last in VAS and morphine intake. One possible reason for the reduced pain in the robotic surgery is the robotic arms, which rotate around the port site and move at a fixed remote center; therefore, there is less leverage and pressure around the port, resulting in less trauma to the abdominal tissue around the port [24]. Accordingly, relief of pain leads to an earlier recovery. Therefore, we further analyzed the length of hospital stay and found that the OLDN group had a significantly longer hospital stay than the other 3 groups. However, the rate of intraoperative complications was higher in the RLDN group, but there was no significant difference in postoperative complications among all groups. Intraoperative complications were mainly attributable to vascular injury in addition to other causes, such as instrument failure, improper use, and visceral injury [25–27]. The presence of intraoperative complications reflects a less experienced surgeon but is expected to diminish as the surgeon gains experience and develops surgical expertise. Using cadavers for training can

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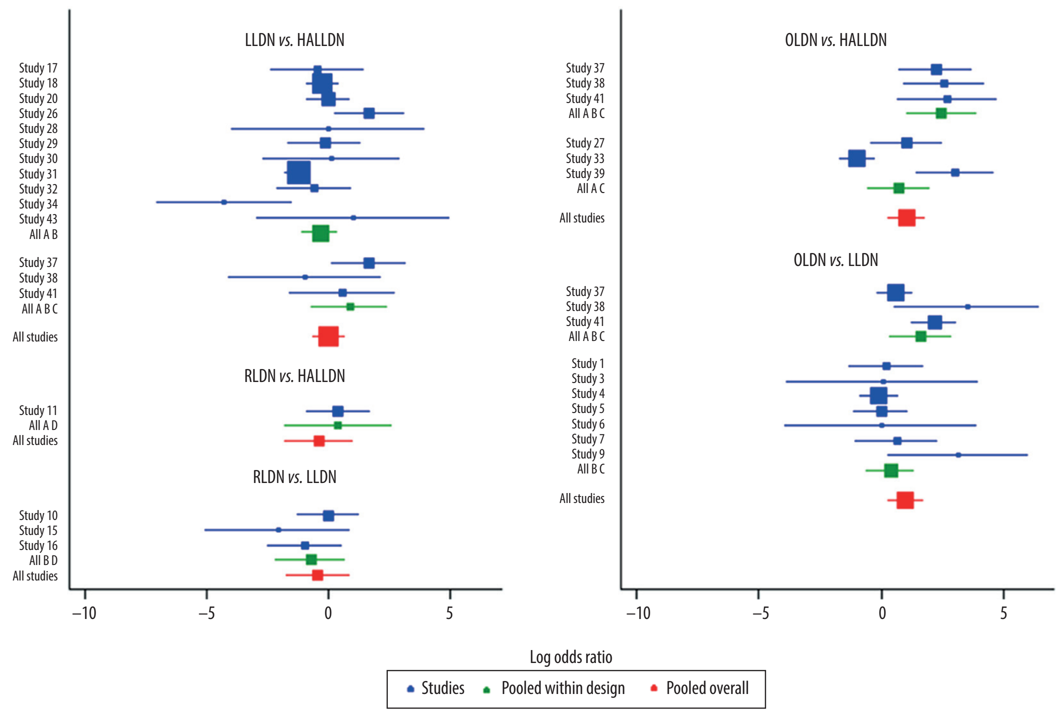
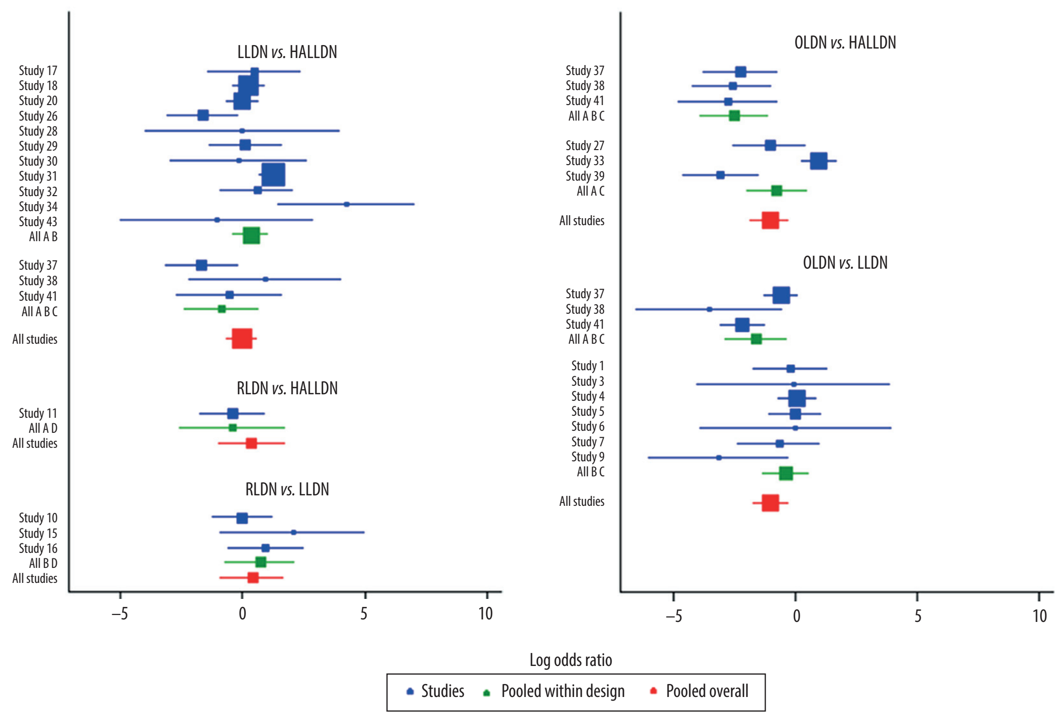
1



Test of consistency: chi²(4)=7.37, P=0.117

2



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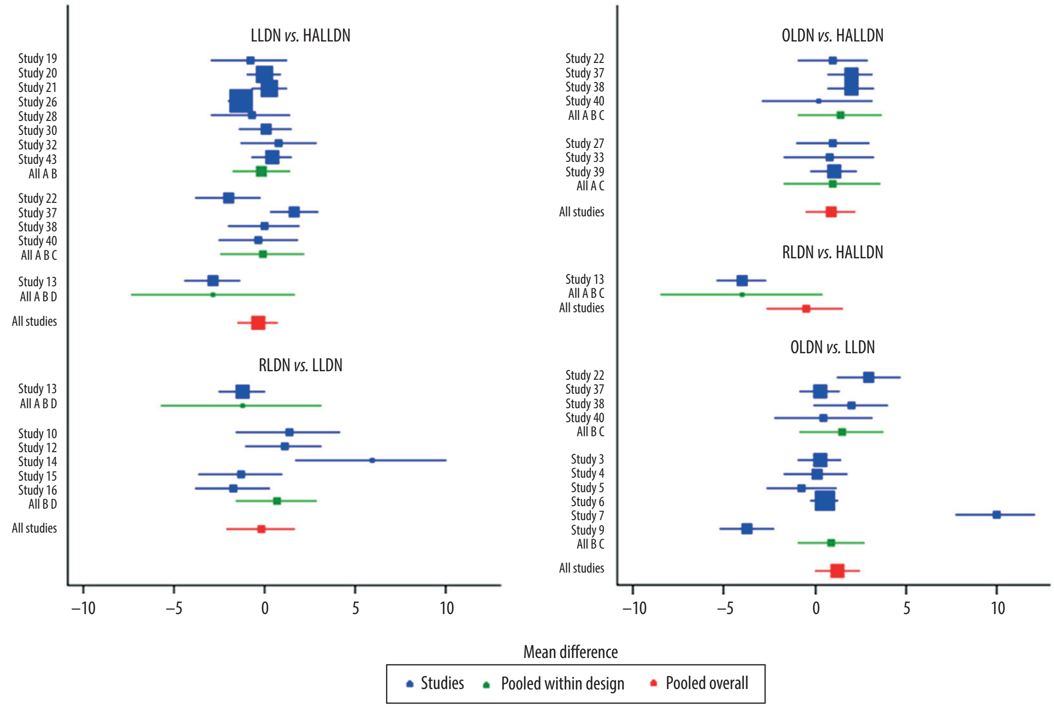
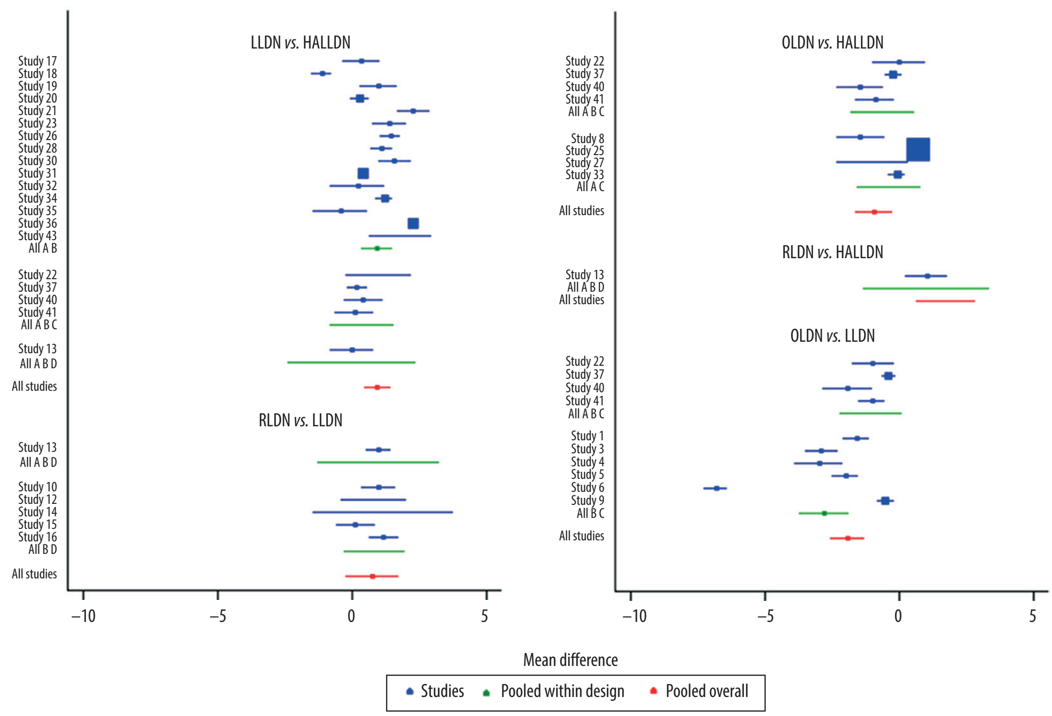


Test of consistency: chi²(5)=3.35, P=0.646

4



Test of consistency: chi²(5)=7.10, P=0.213

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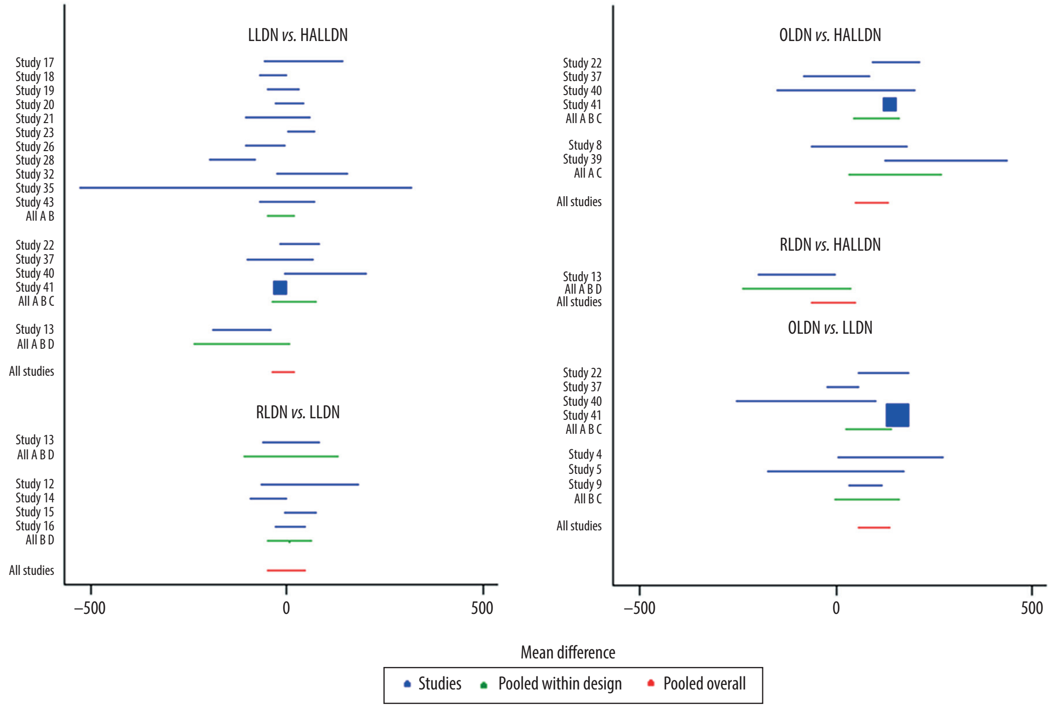
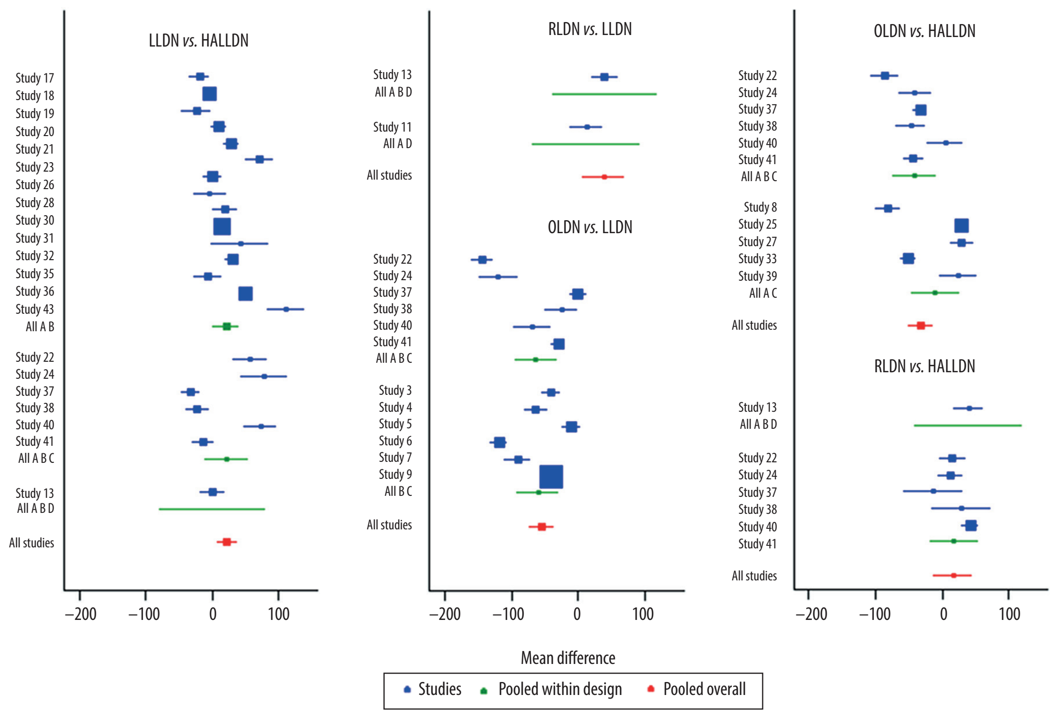


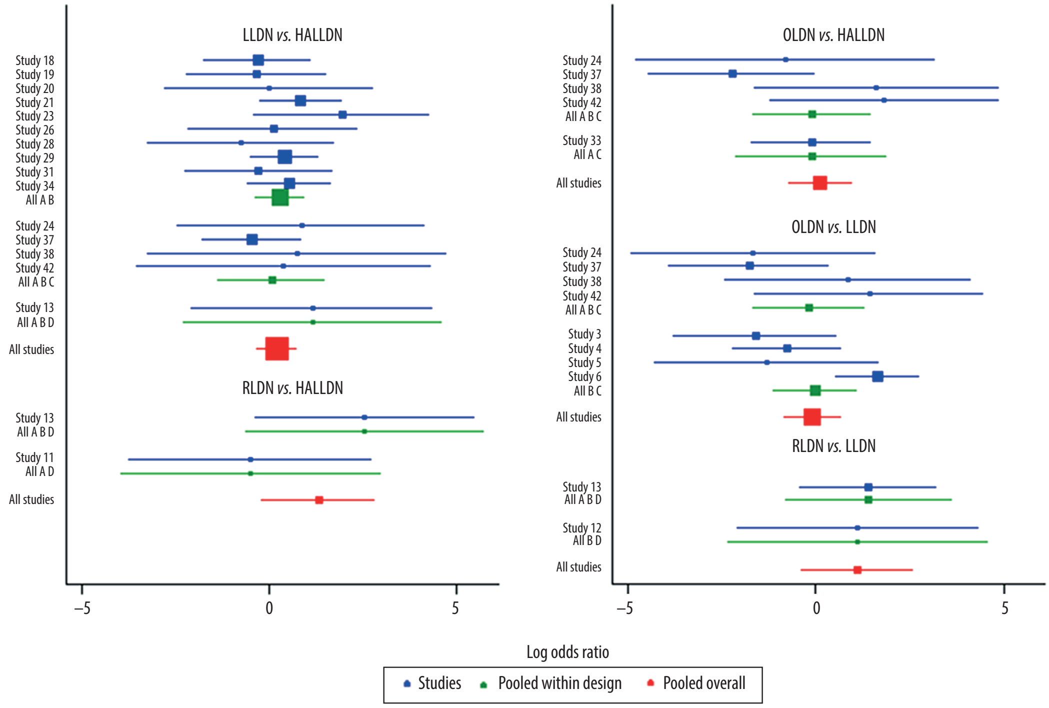
Test of consistency: chi²(5)=5.19, P=0.393

6



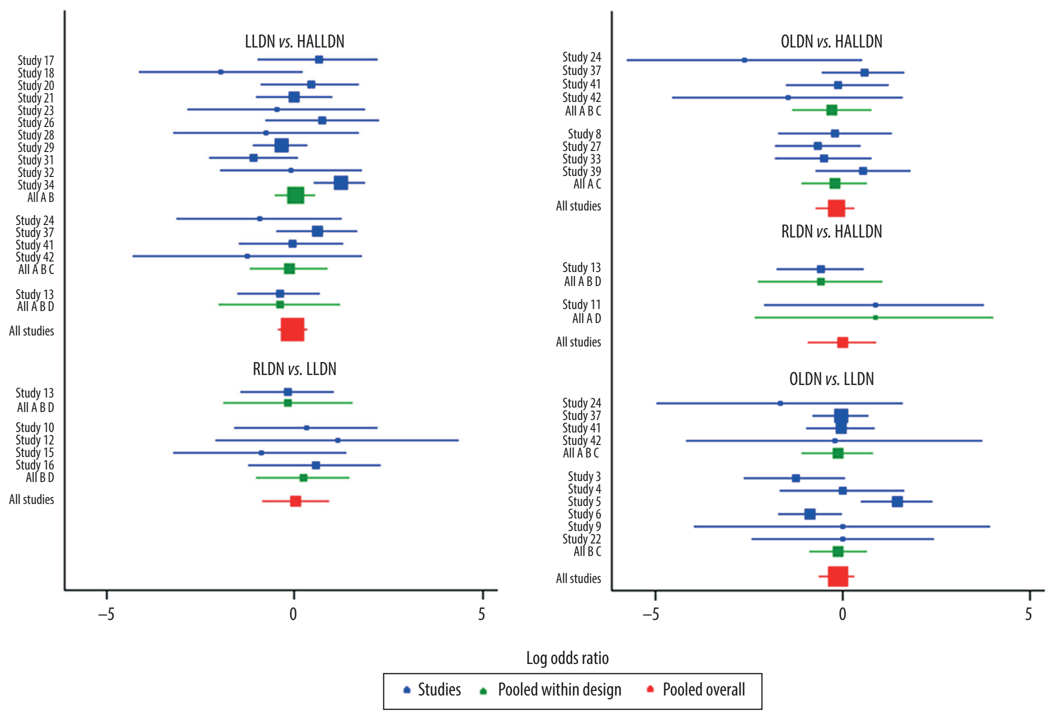
Test of consistency: chi²(6)=2.91, P=0.820

7



Test of consistency: chi²(6)=1.83, P=0.935

8



Test of consistency: chi²(6)=0.93, P=0.988

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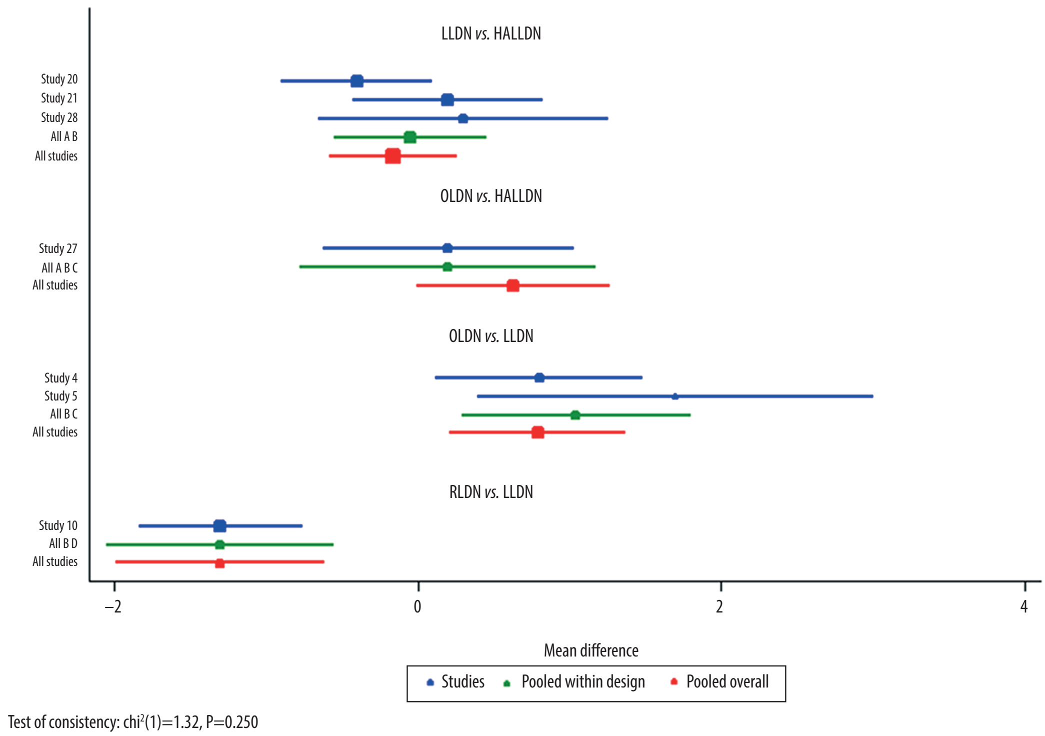
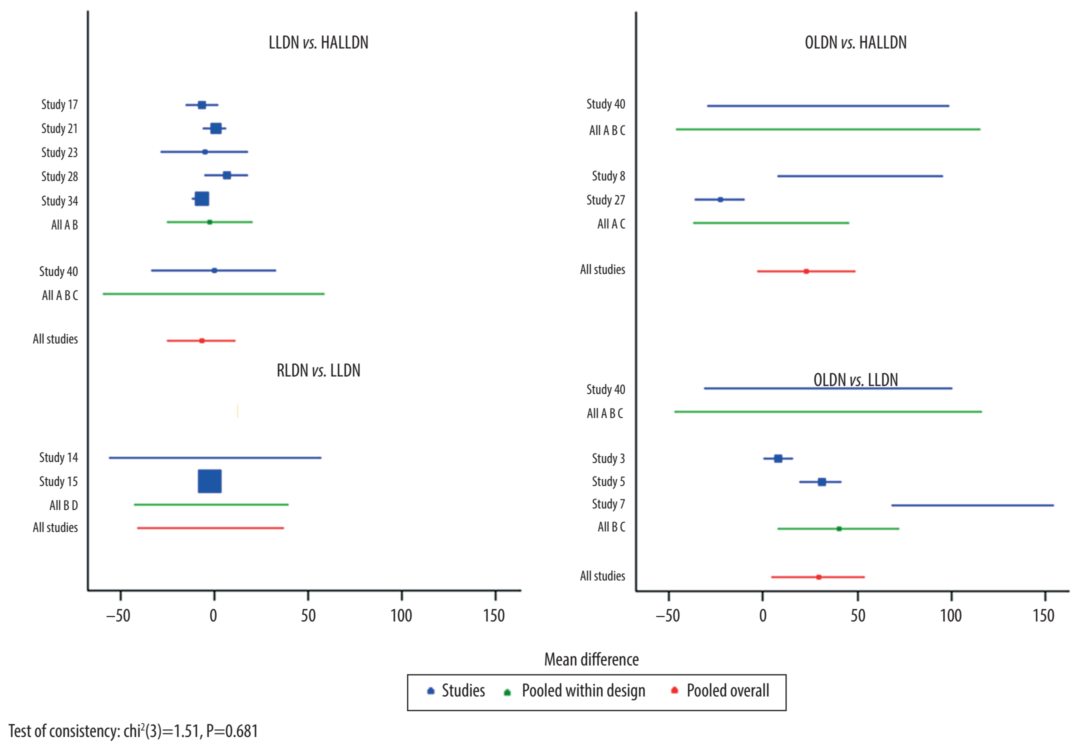
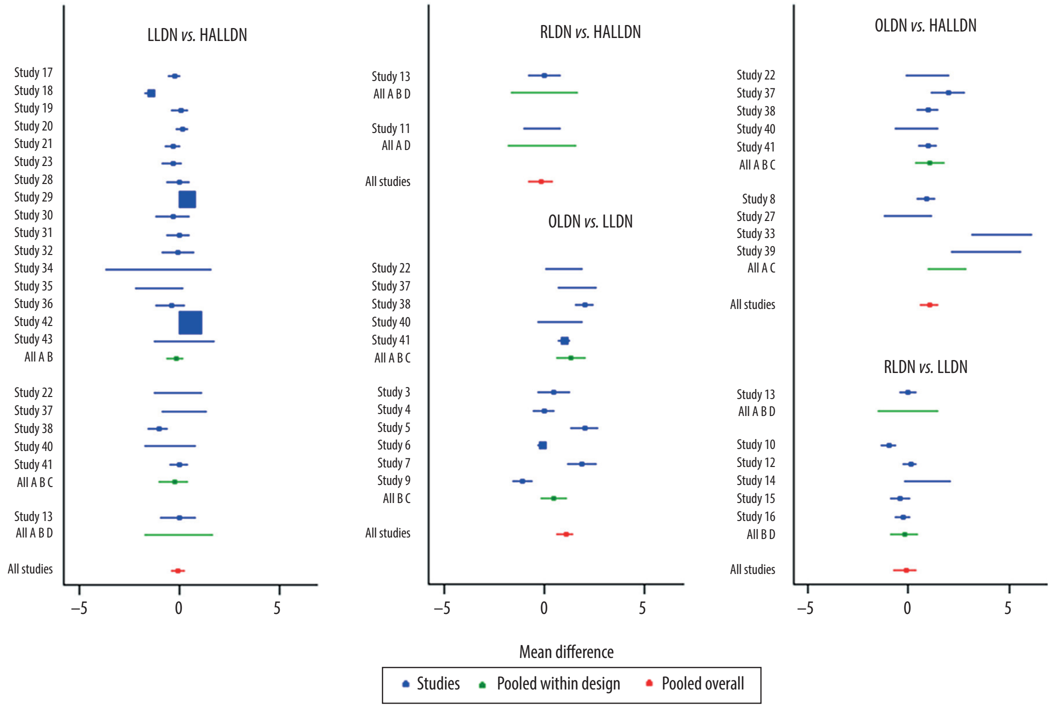

LLDN vs. HALLDN
Study 20
Study 21
Study 28
All A B
All studies
OLDN vs. HALLDN
Study 27
All A B C
All studies
OLDN vs. LLDN
Study 4
Study 5
All B C
All studies
RLDN vs. LLDN
Study 10
All B D
All studies
−2
0
2
4
Mean difference
Studies
Pooled within design
Pooled overall
Test of consistency: chi²(1)=1.32, P=0.250

10

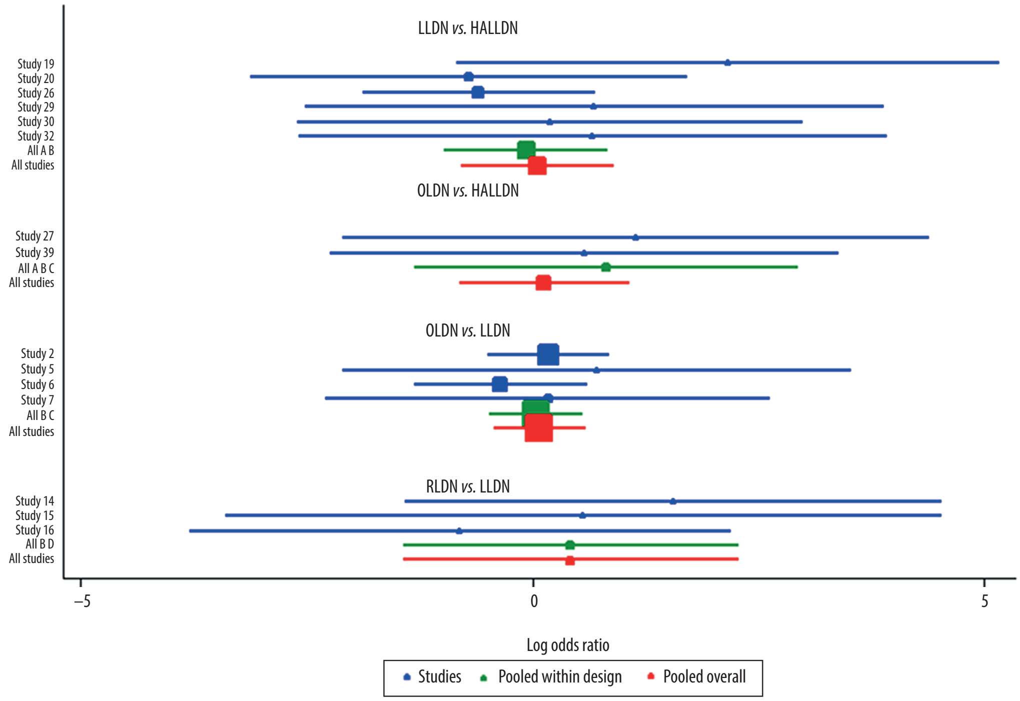

LLDN vs. HALLDN
Study 17
Study 21
Study 23
Study 28
Study 34
All A B
Study 40
All A B C
All studies
RLDN vs. LLDN
Study 14
Study 15
All B D
All studies
OLDN vs. HALLDN
Study 40
All A B C
Study 8
Study 27
All A C
All studies
OLDN vs. LLDN
Study 40
All A B C
Study 3
Study 5
Study 7
All B C
All studies
−50
0
50
100
150
Mean difference
Studies
Pooled within design
Pooled overall
Test of consistency: chi²(3)=1.51, P=0.681

11



Test of consistency: chi²(6)=7.49, P=0.278

12



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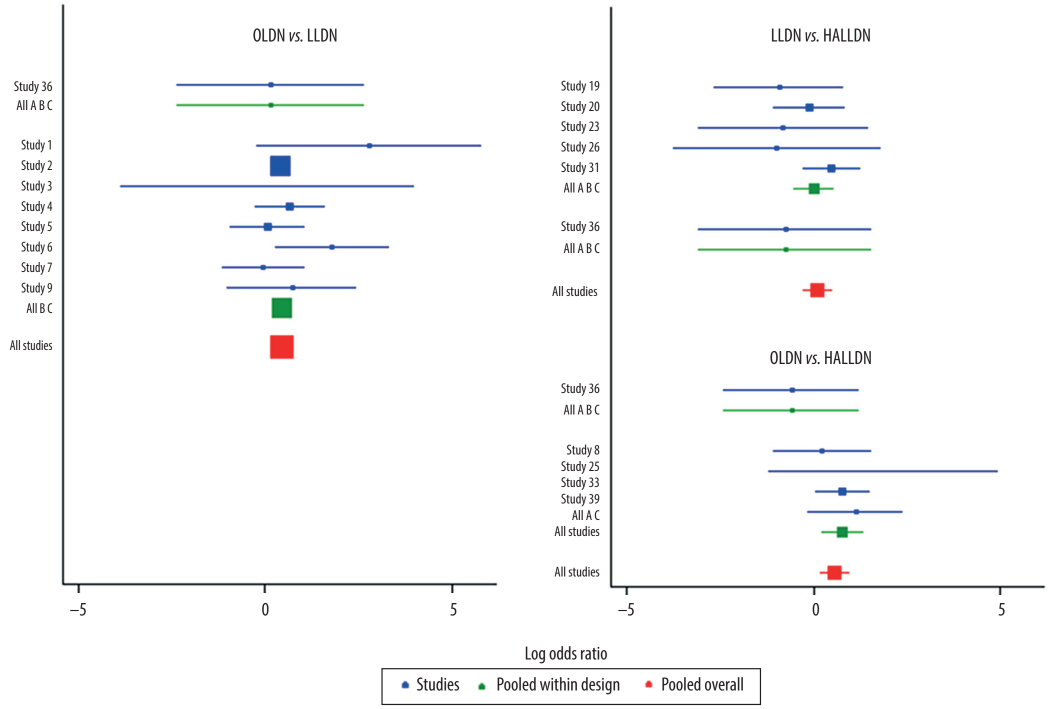
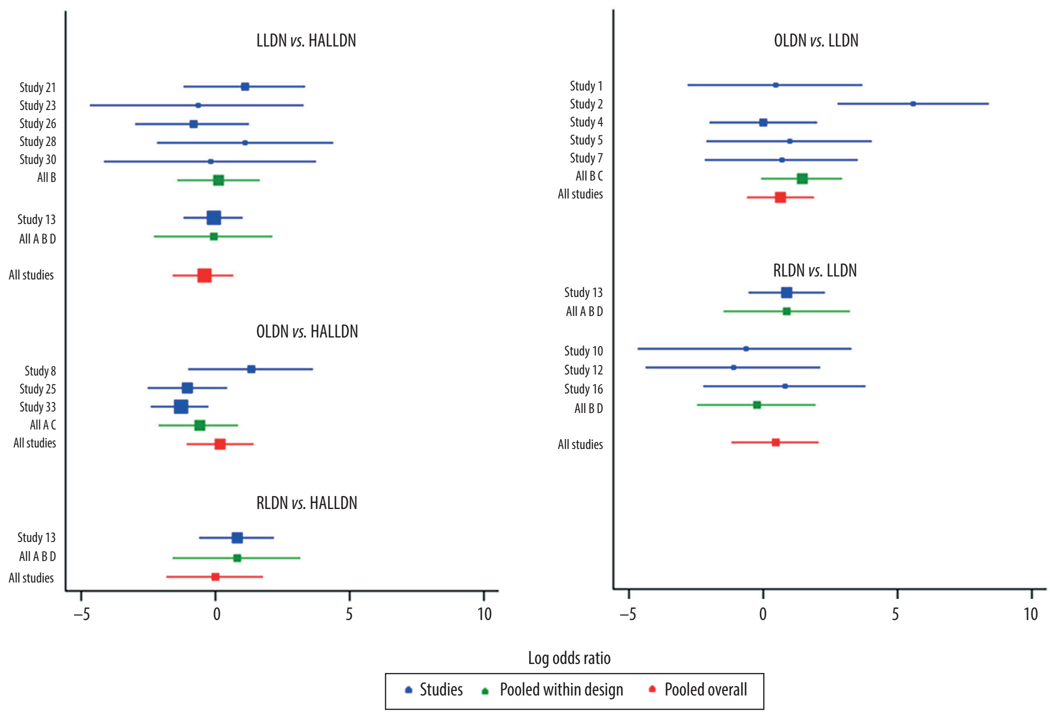
13



Test of consistency: chi²(3)=2.30, P=0.513

14



Test of consistency: chi²(3)=3.68, P=0.298

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Figure 4. The results of consistency analysis by node-splitting approach and the heat plots between the direct and indirect evidence comparisons among all outcomes of different surgical approaches. OLDN, open living donor nephrectomy; LLDN, laparoscopic living donor nephrectomy; HALLDN, hand-assisted laparoscopic living donor nephrectomy; RLDN, robot-assisted laparoscopic living donor nephrectomy. **1**) Right nephrectomy; (**2**) left nephrectomy; (**3**) body mass index (BMI); (**4**) warm ischemia time; (**5**) estimated blood loss; (**6**) operation time; (**7**) donor intraoperative complications; (**8**) donor postoperative complications; (**9**) visual analogue scale (VAS) on day 1; (**10**) Morphine intake on day 1; (**11**) donor length of hospital stay; (**12**) delayed graft function; (**13**) acute rejection; and (**14**) 1-year graft survival.

Table 3. The results of all pairwise comparisons of the different surgical techniques for the outcomes of interest.

		HALLDN	LLDN	RLDN
AR	OLDN	**0.55 (0.34, 0.93)**	**0.56 (0.35, 0.79)**	NA
	HALLDN	–	1.02 (0.56, 1.55)	NA
	LLDN	–	–	NA
BMI	OLDN	–0.89 (–2.43, 0.53)	–1.27 (–2.63, 0.05)	–1.43 (–3.64, 0.81)
	HALLDN	–	–0.37 (–1.61, 0.84)	–0.5 (–2.54, 1.52)
	LLDN	–	–	–0.15 (–2, 1.79)
DGF	OLDN	0.48 (0.07, 1.82)	0.86 (0.24, 2.42)	0.51 (0.01, 7.42)
	HALLDN	–	1.79 (0.57, 7.74)	1.02 (0.04, 25.4)
	LLDN	–	–	0.61 (0.02, 8.35)
Donor length of hospital stay	OLDN	**–1.08 (–1.56, –0.61)**	**–1.06 (–1.53, –0.61)**	**–1.06 (–1.86, –0.26)**
	HALLDN	–	0.02 (–0.31, 0.37)	0.02 (–0.68, 0.74)
	LLDN	–	–	–0.01 (–0.66, 0.69)
1-year Graft survival	OLDN	0.32 (0.01, 4.13)	0.17 (0.01, 1.86)	0.37 (0.00, 32.09)
	HALLDN	–	0.52 (0.03, 8.71)	1.15 (0.02, 109.09)
	LLDN	–	–	2.21 (0.04, 149.74)
Donor intraoperative complications	OLDN	0.97 (0.33, 1.48)	1.37 (0.53, 3.79)	**29.98 (1.88, 1021)**
	HALLDN	–	1.4 (0.67, 3.02)	**31.55 (2.07, 869.3)**
	LLDN	–	–	**22.5 (1.59, 630.1)**
Donor intraoperative complications (III–IV)	OLDN	1.56 (0.62, 3.95)	0.99 (0.42, 2.19)	**0.07 (0.00, 0.81)**
	HALLDN	–	0.64 (0.31, 1.20)	**0.05 (0.00, 0.46)**
	LLDN	–	–	**0.07 (0.00, 0.72)**
EBL	OLDN	**–91.57 (–137.48, –44)**	**–99.13 (–143.61, –53.89)**	**–96.47 (–166.5, –26.84)**
	HALLDN	–	–7.46 (–37.68, 23.84)	–4.69 (–65.95, 55.18)
	LLDN	–	–	2.6 (–52.57, 55.09)
Morphia intake	OLDN	–22.99 (–56.76, 4.22)	**–29.38 (–61.54, –3.74)**	–31.2 (–91.65, 22.68)
	HALLDN	–	–6.42 (–30.24, 16.08)	–8.5 (–60.57, 45.14)
	LLDN	–	–	–1.94 (–49.31, 46.91)

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Table 3 continued. The results of all pairwise comparisons of the different surgical techniques for the outcomes of interest.

		HALLDN	LLDN	RLDN
Operation time	OLDN	**31.57 (11.93, 51.23)**	**53.93 (35.01, 73.54)**	**70.08 (35.72, 105.92)**
	HALLDN	–	**22.37 (6.8, 38.09)**	**38.47 (6.38, 70.98)**
	LLDN	–	–	16.06 (–13.46, 46.82)
Donor postoperative complications	OLDN	1.31 (0.77, 2.37)	1.23 (0.7, 2.13)	1.39 (0.48, 4.43)
	HALLDN	–	0.93 (0.59, 1.44)	1.06 (0.4, 2.95)
	LLDN	–	–	1.15 (0.44, 3.07)
Donor postoperative complications (I–II)	OLDN	0.87 (0.47, 1.54)	0.93 (0.52, 1.64)	0.90 (0.29, 2.68)
	HALLDN	–	1.07 (0.70, 1.72)	1.03 (0.37, 2.84)
	LLDN	–	–	0.96 (0.36, 2.50)
Donor postoperative complications(III–IV)	OLDN	0.76 (0.12, 3.41)	0.32 (0.06, 1.33)	0.111 (0.00, 2.85)
	HALLDN	–	0.42 (0.09, 1.78)	0.15 (0.00, 3.78)
	LLDN	–	–	0.35 (0.01, 8.05)
VAS	OLDN	–0.65 (–1.69, 0.31)	–0.82 (–1.79, 0.02)	**–2.12 (–3.94, –0.63)**
	HALLDN	–	–0.19 (–0.99, 0.6)	**–1.46 (–3.18, –0.02)**
	LLDN	–	–	**–1.28 (–2.79, –0.04)**
WIT	OLDN	**0.95 (0.24, 1.7)**	**1.92 (1.22, 2.6)**	**2.69 (1.45, 3.95)**
	HALLDN	–	**0.97 (0.43, 1.48)**	**1.74 (0.59, 2.9)**
	LLDN	–	–	0.77 (–0.27, 1.85)
Left nephrectomy	OLDN	**3.61 (1.22, 11.23)**	**4.33 (1.57, 13.12)**	**11.14 (1.5, 106.7)**
	HALLDN	–	1.2 (0.5, 3.01)	3.09 (0.49, 25.5)
	LLDN	–	–	2.58 (0.45, 18.28)
Right nephrectomy	OLDN	**0.27 (0.08, 0.81)**	**0.23 (0.08, 0.66)**	**0.09 (0.01, 0.67)**
	HALLDN	–	0.86 (0.35, 2.13)	0.34 (0.04, 2.24)
	LLDN	–	–	0.39 (0.05, 2.36)

OLDN – open living donor nephrectomy; LLDN – laparoscopic living donor nephrectomy; HALLDN – hand-assisted laparoscopic living donor nephrectomy; RLDN – robot-assisted laparoscopic living donor nephrectomy; NA – not available; BMI – body mass index; WIT – warm ischemia time; EBL – estimated blood loss; DGF – delayed graft function; AR – acute rejection; VAS – visual analogue scale.

quickly improve the surgeon's surgical skills, and development of the surgical training model may also help improve the RLDN learning curve; for example, by using robot-assisted partial nephrectomy training models. In terms of recipient outcomes, the increase in WIT and operation time does not translate into the incidence of DGF or affect 1-year graft survival because the recipient DGF and graft survival were not different among the 4 surgical methods. Nevertheless, we found that the OLDN technique caused significantly higher AR compared to LLDN and HALLDN, but there was no significant difference in AR between the HALLDN and LLDN groups. We believe that this is related to a central bias effect, because we did not include information on immunosuppression in the meta-analysis, and they may have used a more active approach to immunosuppression than other centers.

To the best of our knowledge, this study is the first to use the NMA method to comparatively assess 4 surgical approaches in LDN. By including direct and indirect evidence, NMA improved the estimation precision of effects of treatments, and

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increased the analytical power when compared to a pairwise meta-analysis, which uses only direct evidence. However, several limitations should be noted in this study. First, a fundamental limitation of our study is the small number of randomized controlled trials eligible for inclusion, as well as the limited number of participants in each study. Second, the retrospective design inherently introduces a selection bias in the study population. Third, the immunosuppression factor was not included in this meta-analysis.

Conclusions

In summary, this NMA study found that there was no significant difference in donor postoperative complications, recipient DGF, and graft survival among the 4 surgical techniques. OLDN and HALLDN reduce WIT and operation time, but OLDN increases EBL and AR. RLDN and LLDN reduces the length of hospital stay, morphine intake, and VAS, and thus accelerate recovery. However, RLDN leads to increased intraoperative complications due to the learning curve. We performed a subgroup analysis of intraoperative complications according to the Clavien scale. The rate of intraoperative complications (III–IV) was higher in the RLDN group. Most intraoperative complications are due to uncontrolled bleeding due to intraoperative vascular injury or splenic tear, and surgeons can significantly reduce the incidence of such complications by training in the model. The expected benefits of individual patients should be considered when selecting a surgical method in LDN. Given the limitations of the included studies, more high-quality direct evidence and comparisons of multiple interventions are needed to support our findings.

Conflict of interest

None.

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