

# Perioperative Events and Complications in Minimally Invasive Live Donor Nephrectomy: A Systematic Review and Meta-Analysis

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**Background.** Minimally invasive live donor nephrectomy has become a fully implemented and accepted procedure. Donors have to be well educated about all risks and details during the informed consent process. For this to be successful, more information regarding short-term outcome is necessary. **Methods.** A literature search was performed; all studies discussing short-term complications after minimally invasive live donor nephrectomy were included. Outcomes evaluated were intraoperative and postoperative complications, conversions, operative and warm ischemia times, blood loss, length of hospital stay, pain score, convalescence, quality of life, and costs. **Results.** One hundred ninety articles were included in the systematic review, 41 in the meta-analysis. Conversion rate was 1.1%. Intraoperative complication rate was 2.3%, mainly bleeding (1.5%). Postoperative complications occurred in 7.3% of donors, including infectious complications (2.6%), of which mainly wound infection (1.6%) and bleeding (1.0%). Reported mortality rate was 0.01%. All minimally invasive techniques were comparable with regard to complication or conversion rate. **Conclusions.** The used techniques for minimally invasive live donor nephrectomy are safe and associated with low complication rates and minimal risk of mortality. These data may be helpful to develop a standardized, donor-tailored informed consent procedure for live donor nephrectomy.

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Live donor nephrectomy is considered to be a safe, low-risk procedure, fully implemented in many transplant centers worldwide. There are many different surgical techniques for this procedure, and preference differs between centers.<sup>1,2</sup> Although the traditional open technique is still used, minimally invasive procedures should be recommended as the criterion standard, because morbidity is reduced and quality of life improved.<sup>3–5</sup> Modifications to the laparoscopic technique

have been introduced, including the retroperitoneoscopic approach (retroperitoneoscopic donor nephrectomy), hand-assistance (hand-assisted laparoscopic donor nephrectomy/hand-assisted retroperitoneoscopic donor nephrectomy), and robot-assisted approach as well as the single incision laparoscopic donor nephrectomy (laparoendoscopic single-site surgery [LESS]). More recently, the first cases of natural orifice transluminal endoscopic surgery live donor nephrectomy have been reported, with transvaginal kidney extraction.<sup>6–8</sup> With the introduction of these techniques, a great number of studies, including randomized controlled trials (RCTs), have been performed to assess their value, safety and efficacy. Still, there does not seem to be 1 technique that evidently stands out from the rest, and preferences vary among surgeons and centers (as seen in a recent survey among kidney transplant surgeons, Kortram et al, unpublished). Overall, complication rates are low and mortality occurs only sporadically.<sup>9,10</sup> However, if a healthy donor is not well informed and experiences complications related to the procedure anger and distress may occur, negatively affecting the outcome for this patient as well as the living donation program. Therefore, donors must be well educated during the informed consent process. A key condition for the successful employment of donor education and informed consent is the availability of a complete overview of the specific details and risks of the operative techniques.

Little research has been performed regarding the specific contents of the informed consent procedure, and there are no well-designed studies on how donors experience the informed consent and the educational process.<sup>11</sup> Available evidence is quite subjective, and if anything, suggests that some

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donors report feeling misinformed, in a single incidence to such a degree that the donor felt the transplant team had withheld the truth about possible complications, long-term results and recipient outcome.<sup>12</sup> On the other hand, providing more information does not necessarily improve donors' comprehension of details and risks of the procedure.<sup>13-15</sup>

The current project has 2 major objectives. First, to provide a systematic review of all available evidence on informed consent including all information regarding short term outcome of minimally invasive live donor nephrectomy focusing on the incidence of individual complications. Second, to conduct a meta-analysis comparing the different procedures for live donor nephrectomy and complications. By creating a clear overview of the incidence of complications and (serious) adverse events, evidence-based information can be provided to potential donors, thereby further optimizing our educational and informed consent process for the live donor nephrectomy.

## MATERIALS AND METHODS

All aspects of the Cochrane Handbook for Interventional Systematic Reviews were followed, and the study was written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement<sup>16</sup> for Randomized Controlled Trials and the Meta-analysis of Observations Studies in Epidemiology guidelines<sup>17</sup> for observational studies. The initial review protocol was registered in the PROSPERO database with number CRD4201404170 ([www.crd.york.ac.uk/PROSPERO/](http://www.crd.york.ac.uk/PROSPERO/)).

## Literature Search Strategy

A comprehensive search was performed with the help of a biomedical information specialist on September 24, 2014, and updated on March 8, 2016, in Embase, Medline OvidSP, Web-of-Science, PubMed, CENTRAL, and Google Scholar (Figure 1). No date limits were used. Search strings for each database are provided in Appendix 1, no other limits were applied during the search. During screening, only articles written in English were included to prevent any misinterpretations of data. All references were screened by 2 independent reviewers (K.K., F.J.M.F.D.). If any discrepancies occurred, a third investigator was consulted (J.N.M.I.). Study selection was accomplished through 2 phases. During the first phase, titles and abstracts were reviewed for relevance, and full-text articles were obtained. Published abstracts were included if they contained detailed information regarding complications. During the second phase, full-text articles were reviewed. Case reports, commentaries, and letters were excluded. Survey studies and studies describing results from national databases were excluded to prevent double inclusion of donors. Studies mentioning short-term complications after minimally invasive live donor nephrectomy were eligible for inclusion. If a full text article corresponding to a published meeting abstract was available, the abstract was disregarded. The same strategy was used for preliminary results of which definitive results were also available. If data was unclear or pooled for different techniques or indications, the authors were contacted to provide source data. Authors were also contacted when study cohorts of 2 or more publications seemed to overlap. If no response

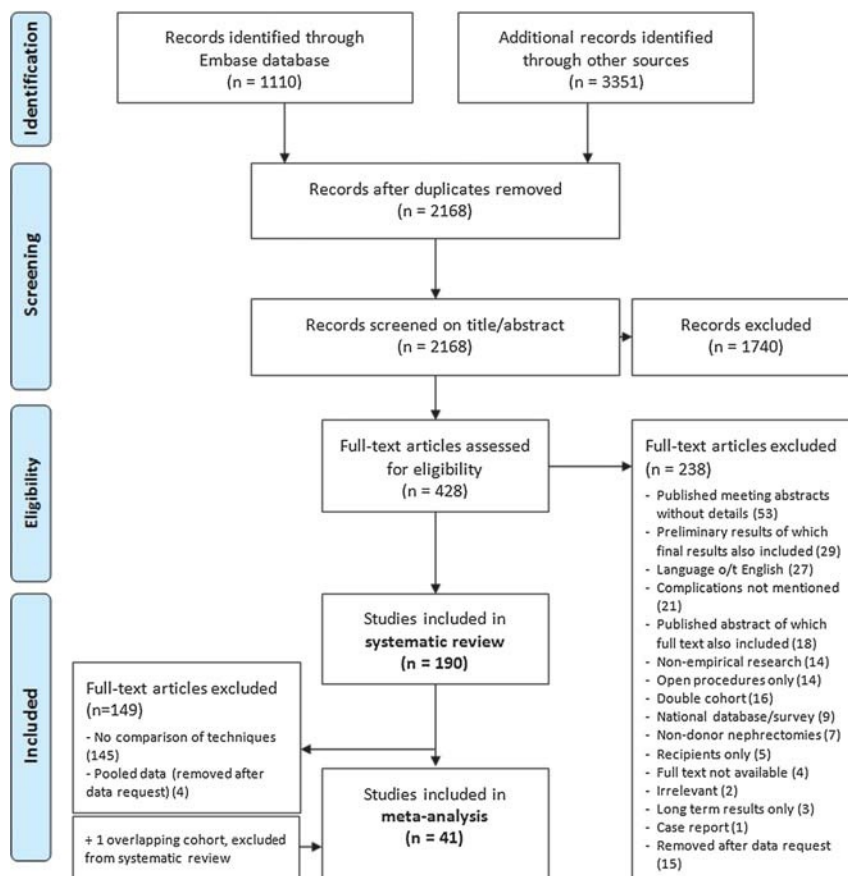


FIGURE 1. Flowchart of literature search.

was obtained after 2 reminders, articles were excluded if data were pooled for different nephrectomy indications, or if the classic open technique was included in their cohort. In some articles, with evident overlapping cohorts, inclusion was based on a number of criteria. Preferably, the most recent publication or the largest cohort of patients was included. However, in some cases, a dated publication contained more details, and it was therefore decided to include the article with the greatest evidential value. If operative techniques were pooled, articles were included in the systematic review but not in the meta-analysis. Systematic reviews and meta-analyses were carefully screened for already published/background information but were not included in the data analysis process. All references of included full text articles were manually scrutinized to ensure that no relevant articles were missed.

All articles were used for the systematic review part of this project; only those that compared (or mentioned, within 1 cohort) 2 or more different minimally invasive live donor nephrectomy techniques were included in the meta-analysis.

### Data Extraction and Critical Appraisal

Data extraction was performed by 2 authors (K.K., F.J.M. F.D.). Again, if any discrepancies occurred, consensus was reached after consulting a third investigator (J.N.M.I.). Data were collected on study design, population, operative technique, procedural details, and complications. A list of all possible complications was created before the start of data extraction, and if complications came up that were not included, these were added to the checklist. All intraoperative and postoperative complications and conversions were scored, as well as mortality. Conversions from LESS to multiport laparoscopy or a hand-assisted procedure or from pure laparoscopy/retroperitoneoscopy to hand-assisted were not scored in this analysis. If an article only described specific complications, all other complications were scored as “unknown.” If however the description of complications was detailed (for instance split to minor and major) but some “common” complications were not listed in an article, it was assumed these did not occur in that specific population and were scored as “zero.” Less frequently mentioned complications like (but not limited to) testicular pain and thigh numbness were scored as unknown. Mortality was scored as “none” or the number of fatalities, when this was literally stated. It was scored as “none assumed” when for instance “no (other) major complications occurred,” or when no donors were missing in follow-up data. All other cases were scored as “unknown.” A number of other outcome measures were scored, namely, operative time, estimated blood loss, warm ischemia time, length of stay, readmissions, length of convalescence, pain score, analgesic requirement, quality of life, and costs.

The level of evidence of each article included in the meta-analysis was established using the Grades of Recommendation, Assessment, Development and Evaluation tool.<sup>18</sup> The Grades of Recommendation, Assessment, Development and Evaluation approach defines the quality of a body of evidence by consideration of risk of bias (methodological quality), directness of evidence, heterogeneity, precision of effect estimates and risk of publication bias (Figure S1, SDC, <http://links.lww.com/TP/B308>).

### Statistical Analysis

For the systematic review, individual complications were presented as absolute values and percentages. Continuous factors were provided in means and range.

A meta-analysis was performed using Review Manager version 5.3 (The Nordic Cochrane Center, Copenhagen, Denmark). Random effects models were used to account for possible clinical heterogeneity. Results were presented in forest plots with risk ratios (RR). Overall effects were determined using the Z-test, and results were presented in RRs. Ninety-five percent confidence intervals (CI) of these values were given, and *P* values less than 0.05 were considered statistically significant. Heterogeneity between studies was assessed by 3 methods. First, a Tau<sup>2</sup> test and a  $\chi^2$  test were conducted for statistical heterogeneity, with *P* less than 0.1 being considered statistically significant. In addition, I<sup>2</sup> statistics were used to assess clinical heterogeneity, using a cut-off point of 35%. The number of donors in each study group weighted group means. Sensitivity analyses were performed for all outcome measures per comparison, first isolating only randomized trials, then excluding all retrospective studies. Studies with substantially more weight than others were also left out to assess different effects.

## RESULTS

Of 2168 unique articles identified in the search, 205 fell within the scope of our predetermined search. However, there were substantial issues with 20 of these publications, that is, evidently overlapping cohorts, no specification of complications (ie, only overall percentages or grades) or pooled data for different nephrectomy indications. Five authors provided us with source data, and the other articles were excluded according to the criteria stated in the methods section. A total of 190 articles remained for the systematic review.<sup>19–208</sup> There were a great number of publications that addressed 2 or more operative techniques but pooled complications. Two authors provided us with source data, and the other articles were excluded from the meta-analysis part of this review. Forty-one remained for inclusion in the meta-analysis. Figure S1 (SDC, <http://links.lww.com/TP/B308>) depicts the flowchart of the literature search.

The included articles originated from transplant centers worldwide. A table providing an overview of the number of included articles per country is included as Table S1 (SDC, <http://links.lww.com/TP/B308>).

### Part 1—Systematic Review of Complications After Minimally Invasive Live Donor Nephrectomy

The studies comprised a total of 32,038 live donor nephrectomies. Table 1 shows the distribution of these donors over the different techniques.

For this part of the review, complications were not divided over the different operative techniques. The purpose was to provide an overview of which complications occur and in which frequency.

#### Conversion

Conversion to a traditional open technique was mentioned in 160 articles (84%). The overall conversion rate was 1.1% (Table 2). The reason for conversion could not be determined in all cases; reasons were provided in 288 of a total of

**TABLE 1.**  
Distribution of 32 038 live donors over the different operative techniques<sup>a</sup>

Procedure	N (%)
Laparoscopic	18 374 (57.4)
Hand-assisted laparoscopic	8112 (25.3)
Retroperitoneoscopic	1107 (3.7)
Hand-assisted retroperitoneoscopic	1300 (3.8)
Single-port laparoscopic (LESS)	1214 (3.8)
Robot-assisted laparoscopic	417 (1.3)
Mini-open	1436 (4.5)
NOTES	78 (0.2)

<sup>a</sup> Although we know the exact numbers for each of the procedures, results are, unfortunately, not always split over the different operative techniques

NOTES, natural orifice transluminal endoscopic surgery

316 conversions (91%). Elective conversions for adhesions, vascular anomalies or failure to progress were scored, although these were not considered to be complications. Conversions for bleeding or injury to other organs were also scored as intraoperative complications.

### Complications

Table 2 provides an overview of all encountered complications and their incidence. There were many different definitions for intraoperative bleeding. Some authors regard it as a complication only if total blood loss exceeded 500 mL, whereas others set the limit at 300 mL. Some studies only listed bleeding as a complication when an additional intervention (ie, extra clip, suture or even conversion) was necessary and some authors did not specify at all. The need for blood transfusion was stated in 168 articles. Injury to other organs was stated in most articles; however, the action taken to repair this remained unclear in the majority thereof. Table 3 sums up the postoperative complications. The reported complications vary between studies. Although some authors report every adverse event from nausea to severe complications requiring surgical reintervention, others only mention specific types of or major complications.

### Mortality

Mortality within 30 days is very rare after live donor nephrectomy. Of the 190 included studies, mortality was reported in 65 (34%, N = 16 604 nephrectomies). In 77 additional articles (8512 nephrectomies), it was assumed that no mortality occurred based on complication rates and follow up. In the remaining 46 articles (24%, 6922 nephrectomies), the occurrence of mortality could not be reliably deduced. In the remaining population of 27 816, only 3 deaths were reported, adding up to an overall reported mortality rate after live donor nephrectomy of 0.01%.

### Surgical Reinterventions

A total of 165 surgical reinterventions were reported (0.6%). However, as with mortality, not every article clearly stated it; in 27 articles, reinterventions were not mentioned (N = 3.522 procedures). In addition, 4% of studies (N = 6, 12 cases) that did mention reoperations did not specify the indication therefor, and some other studies provided indications for some, but not all reinterventions (N = 14 cases). Whether reoperation was done via laparoscopy or

laparotomy was unclear in the majority of studies. Most reoperations were due to bleeding or to evacuate a hematoma (N = 61, 37%). Small bowel obstruction due to internal or port-side hernia, or entrapment in a suture was the reason for reintervention in 26 cases (16%). Other indications for reintervention were wound infection or dehiscence (9), bowel injury (7), fascial dehiscence (7), splenectomy (5), appendectomy (4), orchidectomy due to torsion or ischemia (3), chylous ascites (3), pancreatic injury (2), retrieval of corpus alienum (2), abscess drainage (1), bladder injury (1), ovariectomy (1), perforated duodenal ulcer (1), vocal cord injury (1). In addition, 5 laparotomies were performed due to abdominal pain, but no abnormalities were encountered during surgery.

### Other Outcome Measures

Intraoperative parameters were described in nearly all articles. Unfortunately, operative time, warm ischemia time, blood loss, length of stay, and duration of convalescence were provided in means and medians, as was the visual analog scale for postoperative pain. Because the majority of data was given in means (80%), those in medians were disregarded. Table 3 provides an overview of these extra parameters. Convalescence was defined differently in the included articles, ranging from return to daily activities to full physical function. These definitions were combined. Analgesic use, although described with fair regularity, was documented in many different ways, regarding drugs, dosage or days or even hours of use. Overall costs were not often reported, but if so, these varied enormously. The broad spectrum of inclusion dates and countries may very well account for this.

### Part 2—Meta-Analysis

Forty-one articles were included in the meta-analysis. Comparisons were made between pure laparoscopic and retroperitoneoscopic procedures and hand-assisted procedures, laparoscopic procedures and retroperitoneoscopic procedures, multiport and single-port procedures, and all of these together versus mini-open donor nephrectomy. Two retrospective, small-populated studies comparing the robotic technique with any of the other techniques were found in our search and 1 RCT. Unfortunately, complications in the RCT were only mentioned in Clavien-Dindo scales, and the individual complications could not be determined.<sup>209</sup> This technique was therefore left out of the meta-analysis.

The main finding was that there were only few significant differences between the minimally invasive techniques.

### Hand Assistance

Nineteen articles compared laparoscopic and/or retroperitoneoscopic procedures with and without hand assistance, 3 RCTs,<sup>30,64,99</sup> 4 prospective,<sup>43,65,69,208</sup> and 11 retrospective studies.<sup>38,41,54,92,116,117,139,151,152,177,179</sup> A total of 777 procedures were performed with hand assistance, and 1465 without hand assistance, but because not all studies mentioned every outcome, total numbers vary per outcome measure. Conversion rate (1.5% vs 2.1%), and overall intraoperative (6.2% versus 5.7%) and postoperative (9.9% vs 10.3%) complication rates and surgical reinterventions (0.6% vs 0.7%) were comparable between the 2 groups. The only difference, although not statistically significant, found between these 2 techniques was intraoperative bleeding

**TABLE 2.**  
**Conversions, intraoperative and postoperative complications, reinterventions and mortality after minimally invasive live donorn nephrectomy**

	No. Articles	No. Nephrectomies	No. events	%
Conversion (ALL)	160	28376	316	1.1
Emergent	149	27694	189	0.7
Bleeding	145	27694	185	0.7
Injury other organs	149		4 <sup>a</sup>	0.01
Intraoperative Complications (ALL)	173	27776	612	2.2
Bleeding	175	27776	391	1.5
Injury other organs	153	2644026	221	0.8
Spleen	151	26440264	97	0.4
Bowel	153	40	49	0.2
Bladder	151	26440	12	0.05
Liver	151		14	0.05
Adrenal gland	151		22	0.08
Other	151		27 <sup>b</sup>	0.1
Postoperative Complications (ALL)	187	30970	2174	7.0
Bleeding (ALL)	176	30443	290	1.0
Requiring transfusion	175	29443	128	0.4
Requiring intervention	173	29878	60	0.2
Injury to other organs (ALL)	170	28562	26	0.09
Bowel	170	28562	14	0.05
Spleen	167	28074	6	0.02
Bladder	167	28074	3	0.01
Pancreas	167	28074	3	0.01
Infectious complications (ALL)	163	26729	697	2.6
Wound infection	158	25650	405	1.6
Abscess	152	25910	19	0.07
Urinary tract infection	141	23573	105	0.4
Pneumonia	153	25808	148	0.6
Thoracic Empyema	104	19845	1	0.01
Infectious—other <sup>c</sup>	111	19785	12	0.06
Fever e causa ignota	55	11095	71	0.6
Cardiopulmonary complications				
Cardiovascular	148	25431	18	0.07
Cerebrovascular	149	25475	1	0.004
Pneumothorax	150	25842	36	0.1
Pulmonary—other <sup>d</sup>	113	20436	71	0.3
Thromboembolic complications	146	23574	39	0.2
Gastro-intestinal complications				
Ileus	138	24958	187	0.7
Small bowel obstruction	58	13854	30	0.2
Chylous ascites	78	17564	81	0.5
GI—bleed	88	16022	5	0.03
GI—other <sup>e</sup>	62	12399	115	0.9
Other complications				
Fascial defect	121	22532	3692	0.2
Testicular swelling/pain/epididymitis	63	14390	32	0.6
Thigh numbness	51	11235	95	0.3
Pain	61	12062	24	0.8
Remnant kidney function disorder	41	8681	100	0.3
Urinary retention	100	19537	2	0.5
Drug reaction	38	7065	194	0.03
Other general complications <sup>f</sup>	101	20030		1.6
Mortality	142	25116	3	0.01
Surgical reinterventions	163	28516	165	0.6

<sup>a</sup> Injury to other organs included spleen (2), bowel (1), mesentery (1).

<sup>b</sup> Other organs/structures include: pancreas (4), gallbladder (1), diaphragm (18), mesentery (4).

<sup>c</sup> Other infectious complications included sepsis (3), pyelonephritis (1), phlebitis (8).

<sup>d</sup> Other pulmonary complications included atelectasis (35), respiratory distress (13), pulmonary edema (8), pleural effusion (10), hypoxia (5).

<sup>e</sup> Other GI complications included gastroenteritis (58), pancreatitis (11), constipation (13), liver function disorder (24), appendicitis (4), cholecystitis (2), gastric ulcer (3).

<sup>f</sup> Other general complications included: Seroma (68), neuropathy/neurapraxia (23), subcutaneous emphysema (18), ocular complications (16), rhabdomyolysis (12), skin complications (16), electrolyte disorder (8), urethral injury (12), headache (4), ear hematoma (1), parotitis (1), depression (5), vertigo (1).

**TABLE 3.****Overview of additional intraoperative and postoperative parameters during and after minimally invasive live donor nephrectomy**

Parameter	Population (n)	Value
Intraoperative parameters		
Operative time: mean (range), min	22594	194.3 (78-320)
Warm ischemia time: mean (range), min	18544	3.7 (0.7-8.7)
Blood loss: mean (range), mL	17489	147 (15-545)
Postoperative parameters		
Length of stay: mean (range), d	22898	3.8 (0.6-13)
Pain (VAS score): mean (range)		
Day 1	1004	4.1 (0.37-8)
Discharge	757	2.2 (2-5)
Outpatient clinic <sup>a</sup>	488	1.3 (0.8-1.25)
Readmissions	3084	95 (3.1%)
Duration of convalescence: mean (range), d	2363	24.1 (4-60)
Postoperative Quality of Life (SF36): mean (range) <sup>b, c</sup>	787	68.2 (34.5-90.5)

<sup>a</sup> Values are reported at a time interval of 14 to 30 days postoperatively.

<sup>b</sup> Quality of life was assessed at a time interval of 1 to 6 months. The majority of studies assessed this between 4 and 6 weeks, 1 study at 3 months and 1 at 6 months postoperatively.

<sup>c</sup> One additional study used the The World Health Organization Quality of Life instead of the SF36 (n = 50 donors), reporting a mean value of 72.8 (range, 69.4-76.2).

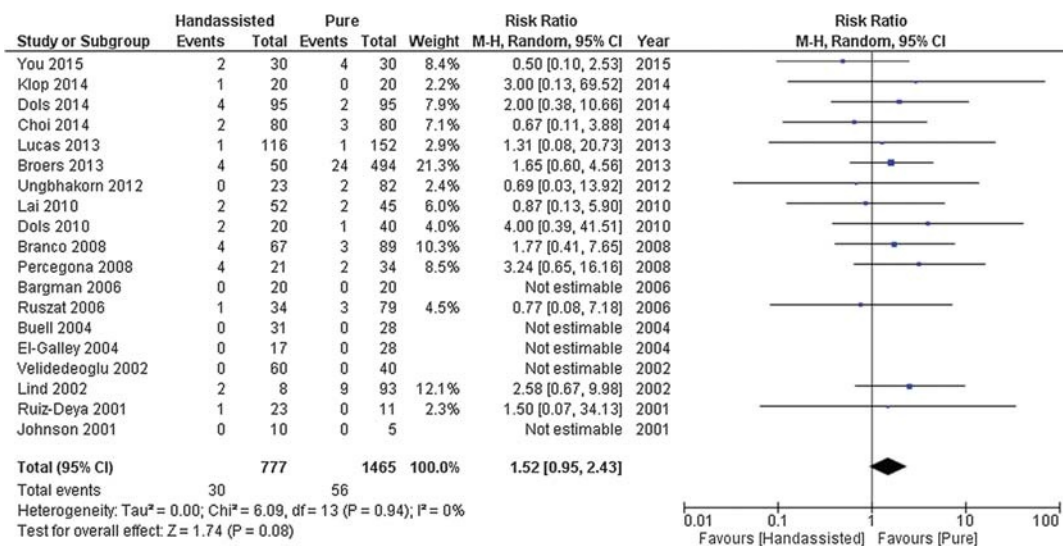
(defined as every bleeding mentioned by the author that exceeded “normal expected blood loss”), which was more frequently encountered after hand-assisted procedures (4.0 vs 3.9%; RR, 1.52; 95% CI, 0.95-2.43;  $P = 0.08$ ) (Figure 2).

### Laparoscopic Versus Retroperitoneoscopic Donor Nephrectomy

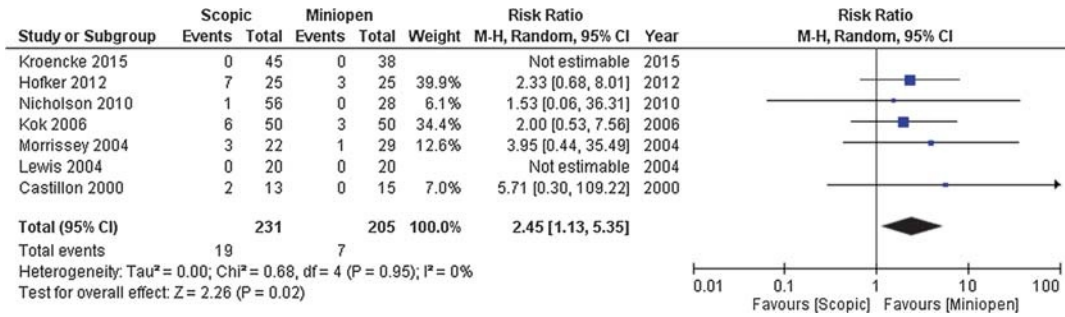
Seven articles compared laparoscopic with retroperitoneoscopic techniques, 2 RCTs,<sup>64,99</sup> 2 prospective,<sup>65,132</sup> and 3 retrospective studies.<sup>41,152,163</sup> A total of 311 procedures were retroperitoneoscopic, 1159 laparoscopic. Conversion (1.6 vs 2.0%), overall intraoperative (4.5 versus 5.6%) and postoperative complications (9.6 vs 12.2%) were again comparable between techniques. None of the individual intraoperative or postoperative complications showed statistically significant differences.

### Multiport Versus Single-Port Donor Nephrectomy

Ten studies were identified comparing single-port with multiport procedures, 3 RCTs,<sup>27,107,149</sup> 1 prospective study,<sup>194</sup> and 6 retrospective series.<sup>20,31,47,144,183,205</sup> In total, 764 single port procedures were compared with 1214 laparoscopic procedures. Conversions were rare in these studies; only 2 occurred (0.1%), both in multiport donor nephrectomies, of which 1 was elective and 1 emergent due to bleeding. Intraoperative (0.9% in both groups) and postoperative (6.5% vs 5.2%) complications were again comparable, as were re-interventions (0.1% vs 0.9%). Postoperative pain was slightly more often described after LESS donor nephrectomies (2.7% vs 0.8%; RR, 3.56; 95% CI, 0.90-14.11;  $P = 0.07$ ), other pulmonary complications (ie, pleural effusion, atelectasis, respiratory distress, pulmonary edema, or hypoxia) were more frequently reported after LESS donor nephrectomy (1.5% vs 0%; RR, 7.51;  $P = 0.03$ ; 95% CI, 1.25-44.94).



**FIGURE 2.** Forest plot analysis for intraoperative bleeding during laparoscopic donor nephrectomy with or without hand-assistance.



**FIGURE 3.** Forest plot analysis for intraoperative complications compared between mini-open and laparoscopic donor nephrectomies.

**Mini-Open Versus Laparoscopic Donor Nephrectomy**

All articles comparing the mini-open technique with either 1 of the endoscopic techniques (ie, laparoperitoneoscopic, retroperitoneoscopic, with or without hand assistance) with the exception of single port donor nephrectomies were included in this comparison. There was 1 study that compared retroperitoneoscopic procedures to mini-open procedures, and 7 additional studies were identified comparing mini-open donor nephrectomies to laparoscopic ones. A total of 323 mini-open procedures were compared with 288 endoscopic procedures. This group comprised 3 RCTs<sup>85,133,210</sup> and 5 prospective studies.<sup>50,115,128,195,198</sup> Intraoperative complications were more frequently seen in laparoscopic procedures (8.2% vs 3.4%; RR, 2.45; 95% CI, 1.13-5.35; P = 0.02) (0.99-1.08; P= 0.1) (Figure 3).

This difference was mostly based on intraoperative organ damage, which demonstrated a trend in favor of open procedures (0% vs 2.8%; RR, 5.18; 95% CI, 0.91-29.35; P = 0.06) (Figure S2, SDC, <http://links.lww.com/TP/B308>). When sensitivity analysis was performed and only RCTs were included, the significant difference/trend disappeared (P = 0.09 and 0.1, respectively).

Overall postoperative complication rate was comparable, but nonetheless much higher than described for the other techniques (17% vs 23%). The design of the included studies, only RCTs and prospective series, might account for this finding. The incidence of pneumonia was significantly higher after open procedures (6.3% vs 3.3%; RR, 2.48; 95% CI, 1.05-5.87; P = 0.04) (Figure 4).

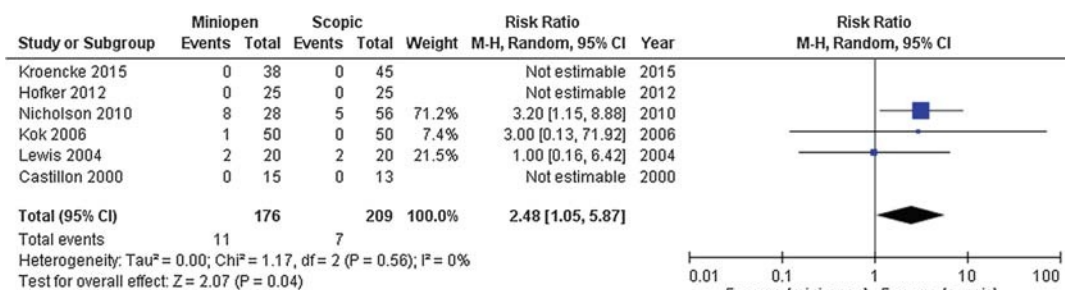
However, when performing sensitivity analysis, this difference was largely based on 1 study. When this group was left out of the forest plot analysis, results were quite comparable between procedures (2.0% vs 1.3%; RR, 1.32; P = 0.73 for pneumonia). Pneumothorax was not more often seen after either procedure; 0.6% for mini-open procedures (n = 1) and

1% for scopic procedures (n = 2). The surgical re-intervention rate was comparable 0.6% for mini-open procedures versus 1.8% for scopic ones, but this difference was not statistically significant.

All in all, none of the used minimally invasive techniques for live donor nephrectomy stand out from the rest.

**DISCUSSION**

Our study is, to the best of our knowledge, the first to extensively score all complications after minimally invasive live donor nephrectomies and compare outcomes of all different techniques. A great number of minimally invasive live donor nephrectomies were included from different countries all over the world. There was no significant heterogeneity encountered in the included studies. Short-term complication rates were comparable between different techniques currently used for live donor nephrectomy, and not one of the techniques stood out from the rest. In the included studies, the pure laparoscopic approach was used in the majority of cases (57.4%). This may not be an adequate portrait of the current situation, in which the hand-assisted approach is favored in many cases.<sup>1</sup> It is possible that some authors did indeed use hand assistance, but did not explicitly mention this in their article. No statistically significant differences were found in this meta-analysis comparing laparoscopic donor nephrectomies with and without hand assistance. The overall postoperative complication rate found in the systematic review part of our study (7.0%) is lower than the complication rates found in some of the meta-analyses (12.2% for retroperitoneoscopic techniques when compared with laparoscopic techniques and 23% for laparoscopic procedures when compared with mini-open procedures, which, in turn, had 17% complications). This may imply under reporting of complications in the systematic review part, which mainly consisted of retrospective case series. Complications were mentioned, but were



**FIGURE 4.** Forest plot analysis of the incidence of postoperative pneumonia, compared between mini-open and laparoscopic live donor nephrectomies.

not always the main outcome measure of the study. In the meta-analyses, only those studies that compared 2 or more techniques were included, and the focus was on complications in most studies. Conversions (316 overall) were described in a total of 160 articles. Unfortunately, complications were not specified for converted and nonconverted donors in most studies, so whether the conversion itself had any negative influence on the postoperative course or convalescence period remains unknown.

If we would adhere to our national guideline, according to which only those complications with an incidence of greater than 1% or those with severe consequences have to be disclosed to patients undergoing any surgical procedure,<sup>211</sup> we would only be obliged to mention intraoperative and postoperative bleeding, conversion, wound infection (and possibly overall infectious complications), and ileus. In addition, the possibility of a reintervention and mortality should be mentioned, regardless of their incidence. However, is this really enough to ensure that a potential living kidney donor is optimally prepared and able to make a well-informed decision? Rare complications like damage to other organs, or cardiovascular events may or may not necessary have “severe consequences,” so should these be mentioned or not? Also, even though many other complications are also infrequent, and may not have significant medical consequences, they may be very relevant for donors. Prolonged pain, testicular complaints, neuropathies can be quite disconcerting to a donor who has no idea these adverse events are in fact quite “normal”.

## Limitations

This systematic review and meta-analysis has a number of significant limitations. None of the articles provided a complete overview of all complications, events and consequences. Some focused on intraoperative complications, others on specific postoperative complications. Conversion was mentioned in most, whereas mortality was actually mentioned in only 31% of the articles. The overall quality of reported data was quite low, and it was interesting to see the differences in portraying complications and adverse events.

Most studies are retrospective case series, some prospective and only 16 included studies were RTCs. The definition of complications in general, and especially individual complications, is bound to vary. Not every surgeon considers every adverse event to be a complication, and results are presented in that light. Overall, major complications were more often reported than minor complications, possibly leading to an underestimation of the latter. Even the definitions of frequently encountered and considered “standard” complications like bleeding or wound infection varies among authors. Some specify bleeding as the need for transfusion, or a specific amount of blood loss, but often (especially intraoperative) bleeding is not defined. When bowel or splenic injuries were encountered, it was often not stated whether resection was necessary. In addition, less frequently encountered complications like testicular complaints or thigh numbness were not mentioned in many articles, raising the question whether they did not occur, or were not reported. Overall complications rates varied greatly between different studies, and it is to be expected that complications are underreported.

Second, even though we have used all available channels to obtain as much unique data as possible, we were still dependent on the quality of published studies. Many studies included donor nephrectomies using different operative techniques, but pooled their complication data. We were able to obtain split data for a small number of these. In the majority of cases, data were no longer available or no response from the authors was received. For this reason, a number of studies could not be included in the meta-analysis, resulting in a smaller population for analysis. In addition, we had to exclude a number of studies presenting pooled data for different nephrectomy indications (other than kidney donation). Reversely, even though we applied strict exclusion criteria for overlapping cohorts, a small number of donors will inevitably have been analyzed in more than 1 included cohort.

Mortality after live donor nephrectomy is a catastrophic complication that is rarely reported. The largest cohort addressing donor mortality is reported by Segev et al,<sup>9</sup> who found 25 donor deaths within 90 days after 80 347 live donor nephrectomies (0.03%). These were United States donors, after conventional open donor nephrectomy as well as minimally invasive procedures, and donor death was established by checking the Social Security Death Master File. Cause of death was not reported, and even though a matched cohort of nonoperated adults demonstrated lower mortality rates, this mortality rate of 0.03% cannot, with entire certainty, be attributed to live donor nephrectomy alone. In our systematic review, a reported mortality rate of 0.01% was found. Whether this is an under or overestimate remains unclear. Based on the available literature, we do know that donor deaths still occur, and that vascular complications are often not published.<sup>212,213</sup> We therefore used strict criteria during data extraction. Mortality was scored when it was literally stated, or when the authors stated that “no complications” or no “major complications” occurred. In addition, if follow-up data were presented and none of the donors were missing, it was concluded that they had not died. Using these criteria, mortality was scored as inconclusive in 48 articles. If no deaths would have occurred in these populations, overall mortality rate would be 0.01%. Thus, we state that the actual mortality rate after live donor nephrectomy will be in the range of 0.01% to 0.1%.

Our article presents an extensive overview of different outcome measures, with emphasis on complication rates after minimally invasive live donor nephrectomy. Even though there is a risk of publication bias due to the number of included procedures, this overview will still provide quite a representable situation of current clinical practice. Based on these results, we may state that all used techniques for minimally invasive live donor nephrectomy are safe and associated with low risks of complications and an even lower risk of mortality. This allows the transplant surgeon to choose this technique with which he or she is most comfortable, and which best suits the intended donor. This form of tailor-made live donor nephrectomy fits perfectly into the current trend of shared elective surgical decision making.

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