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ORIGINAL ARTICLE

A meta-analysis of mini-open versus standard open and laparoscopic living donor nephrectomy

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Summary

Mini-open donor nephrectomy (MODN) potentially combines advantages of standard open (SODN) and laparoscopic techniques (LDN). This article is a comparison of these techniques. A literature search was performed for studies comparing MODN with SODN or LDN. Nine studies met our selection criteria. Of the 1038 patients, 433 (42%) underwent MODN, 389 (37%) SODN and 216 (21%) LDN. *MODN* versus *SODN:* Operative time ($P = 0.17$), warm ischemia time ($P = 0.20$) and blood loss ($P = 0.30$) were not significantly different. Hospital stay and time to return to work were shorter for MODN by 1.67 days ($P < 0.001$) and 5 weeks ($P = 0.03$). Analgesia requirement and overall complications were less in the MODN group ($P < 0.001$) and ($P = 0.03$). Ureteric complications ($P = 0.21$) and 1-year graft survival ($P = 0.28$) were not significantly different. *MODN* versus *LDN:* Operative and warm ischemia times were significantly shorter for the MODN by 55 min ($P = 0.005$) and 147 s ($P < 0.001$). Analgesia requirement was greater for the MODN group by 9.62 mEq morphine ($P = 0.04$). No significant differences were found for blood loss ($P = 0.8$), hospital stay ($P = 0.35$), donor complications ($P = 0.40$) or ureteric complications ($P = 0.83$). MODN appears to provide advantages for the donor in comparison to SODN and also has a shorter operative time when compared with the LDN.

Introduction

Donor nephrectomy for living donor kidney transplantation has been performed for years using the traditional, standard open (SODN) approach. In 1995, Ratner *et al.* [1] reported the first laparoscopic donor nephrectomy (LDN). Since then, other methods have been developed including mini-open donor nephrectomy (MODN).

Donor nephrectomy is an unusual procedure as it is performed on healthy individuals with the sole purpose of benefiting others. As such, it is vital that any technique implemented must be safe and acceptable to the donor. The living donor pool is crucial as deceased donor organs do not meet the current level of recipient need [2] and pose problems with delay to transplantation [2,3].

Laparoscopy was introduced to reduce postoperative pain, hospital stay, length of time to return to work and increase patient satisfaction [4–6]. However, this technique has developed concerns including the possible adverse effects of the pneumoperitoneum on the blood supply to the cortex of the kidney, the cost implications to the surgical center and the need for laparoscopically trained surgeons. In response, the MODN technique has been developed with the hope of maintaining the advantages of laparoscopy whilst eliminating some of the problems.

There is a limited amount of literature available evaluating MODN and only one randomized controlled trial (RCT) [7]. It is important that this new method is properly compared with the well-established techniques of SODN and LDN to ensure that it does indeed provide advantages without any adverse effects to either donor or recipient.

This study aims to use meta-analytic techniques to compare MODN with both SODN and LDN with regards to operative and postoperative parameters for the donor and recipient graft function.

Methods

Study selection

A Medline and Cochrane database search was performed for studies between 1980 and September 2007. Mesh search headings used were: 'mini incision', minimal incision', 'mini-open', 'laparoscopy', 'nephrectomy', 'renal', 'transplant', 'donor outcomes', 'recipient outcomes', 'met-analysis' and 'comparative study'. The above terms, and their combinations were also searched as text-words. All abstracts, studies, and citations scanned were reviewed. References of the articles acquired were also searched manually for further relevant studies. The latest eligible study for the above search period was 29th of July 2006.

Data extraction

Two reviewers (DA and TN) both reviewed the selected studies and independently extracted the year of publication, first author, study design, study population characteristics, inclusion and exclusion criteria, and number of subjects undergoing each type of operation. Where discrepancies arose, papers were re-examined and consensus was reached by discussion.

Inclusion criteria

Studies were included only if they fulfilled the following criteria: (i) they were comparative studies comparing MODN to SODN or LDN and (ii) they included at least one outcome of interest to our study.

MODN was defined as a procedure using an incision of <15 cm in length (Table 1) anterior to the eleventh or twelfth rib without rib resection and using a retroperitoneal approach. SODN was defined as a retroperitoneal procedure performed via a long flank incision with the patient in the lateral decubitus position. Rib resection was performed in some cases as necessary. LDN used a non-hand-assisted transperitoneal approach with kidney extraction via either a pfannensteil or right upper quadrant incision of around 6–8 cm depending on the side of kidney being removed. Kidney retrieval was achieved using an Endocatch bag.

Outcomes of interest

The following outcome data was extracted from the studies:

1 *Donor operative parameters.* Operative time (min), warm ischemic time (s), and estimated blood loss (ml).
2 *Donor postoperative parameters.* Total in-patient analgesia requirement (milligram equivalent of morphine), hospital stay (days) and time to return to work (weeks).
3 *Donor adverse events.* Donor complications were split into (i) overall number of complications, (ii) intra-operative complications occurring during surgery such as organ or vessel injury, and (iii) postoperative complications. Postoperative complications were further split into in-patient and long-term complications defined as complications occurring posthospital discharge. A complication was defined as any event causing patient morbidity. More specifically, rates of bleeding, blood transfusion, re-operation and incisional hernias/wound bulging were extracted. The available data were insufficient for the purpose of comparing for more specific donor complications or rates of re-admission.
4 *Recipient and graft parameters.* One-year recipient and graft survival rates, delayed graft function and ureteric leaks, strictures and total complications.

Statistical analysis

The meta-analysis was performed in line with recommendations from the Cochrane Collaboration and the Quality of Reporting of Meta-analyses guidelines [8,9]. Statistical analysis of dichotomous variables was carried out using odds ratio (OR) as the summary statistic, while continuous variables such as operative time or length of stay, were analyzed using the weighted mean difference (WMD), both were reported with 95% confidence intervals (CI). Odds ratios represent the odds of an adverse event occurring in the mini-incision group compared with the control group while WMDs summarizes the differences between the two groups with respect to continuous variables, accounting for sample size. For studies that presented continuous data as means and range values, the standard deviations (SD) were calculated using statistical algorithms [10]. An odds ratio of <1 favors the MODN group and the point estimate of the odds ratio is considered to be statistically significant at the $P < 0.05$ level if the 95% CI does not include the value 1. In the tabulation of the results, squares indicate the point estimates of the treatment effect (OR, WMD) with 95% CI indicated by horizontal bars. The diamond represents the summary estimate from the pooled studies with 95% CI.

The Mantel–Haenszel method was used to combine the odds ratios for the outcomes of interest using a 'random effect' meta-analytic technique. In a random effect model, it is assumed that there is variation between studies and the calculated odds ratio, thus the latter has a more conservative value [11,12]. The random effect model is preferable when meta-analytic techniques are used in

Table 1. Characteristics of included studies.

Authors *et al.* (year)	Study type	Cases			Incision length (cm)		Donor age (mean years)			Conversion* (%)	% Right kidney: MODN/control	Exclusion criteria: MODN†	Exclusion criteria: control†	Matching‡	Study quality (star rating)
		MODN	LDN	SODN	MODN	SODN	MODN	LDN	SODN						
Kok (2006) [66]	R	60		86	10.5 (8–15)§	20 (8–30)§	53.5		49	0	55/45	A E	–	1 3 4 5 6 8	*****
Neipp (2004) [54]	P	69		127	6–10¶	–	48		48	–	36/42	–	–	1 2 3 6 8 9 10	*******
Schnitzbaur (2006) [68]	R	34		36	8–10¶	–	49		49	–	50/14	–	–	1 2 3	**
Yang (2002) [65]	P RCG	45		13	8.6**	21.8**	34		39	–	8/15	–	–	1 2 3	*****
Kok (2006) [56]	P	51	49		10–12¶		47.5	48.5		4	53/49	A G I	A G I	1 3 4 5 6 8 10	*******
Kok (2006) [7]	RCT	50	50		10.5 (8–15)§		48	49		0	38/40	D F G H	D F G H	1 2 3 4 5 8 10	N/A
Kumar (2003) [67]	R	25/50	25/50	25	7–10¶	16–22¶	–	–	–	–	–	–	–	–	***
Lewis (2004) [63]	P	20	20	20	10–15¶	–	43	43	45	0	25/15/15	–	–	1 2 3 8	*******
Morrissey (2004) [64]	P	29	22	82	8–10¶	12–20¶	39.3	41.3	41.2	–	–	A	A B C	1 2 10	***

MODN, mini-open donor nephrectomy; LDN, laparoscopic donor nephrectomy; SODN, standard open donor nephrectomy; R, retrospective; RCG, retrospective control group; P, prospective; RCT, randomized controlled trial.

*Conversion of LDN to SODN.

†Exclusion criteria (exclusion criteria used by primary papers for patient exclusion from an operative technique): A = patient choice, B = right nephrectomies necessary, C = laparoscopic team not available to perform procedure, D = other intra-abdominal pathology requiring concomitant surgery, E = surgeons preference for procedure, F = abnormal renal anatomy, G = previous adrenal/renal surgery, H = language spoken, I = maximum vessel length required.

‡Matching: 1 = age, 2 = gender, 3 = weight/body mass index, 4 = American Association of Anesthesiologists fitness grade, 5 = number of renal arteries, 6 = number of renal veins, 7 = operating surgeon/team, 8 = side of nephrectomy, 9 = renal function, 10 = related/unrelated – donor/recipient.

§Median and range.

¶Range.

**Mean.

surgical research as for a given surgical technique each center has its own patient selection criteria. Yate's correction was used for those studies that contained a zero in one cell for the number of events of interest in one of the two groups [13,14].

The quality of the studies was assessed by using the Newcastle–Ottawa Scale (NOS) with some modifications to match the needs of this study [15]. The quality of the studies was evaluated by examining three factors: method of patient selection, comparability of the study groups and number of outcomes reported. A star rating of zero to nine was allocated to each study based on these parameters. The NOS is not validated for RCTs; accordingly, it was applied only to nonrandomized studies. On the whole, RCTs provide the highest quality methodology; accordingly, unless there was any doubt, randomized trials were included as high-quality studies.

Heterogeneity was assessed by two methods. First, graphical exploration with funnel plots was used to evaluate publication bias [12,16]. Sensitivity analysis was undertaken using studies of high quality and those reporting on more than 50 patients in the MODN group. Heterogeneity was analyzed using a Chi-squared test.

Analysis was conducted by using Review Manager Version 4.2 (The Cochrane Collaboration, Software Update, Oxford).

Results

Eligible studies

The literature search found over 150 potential papers of which 52, published between 1994 and 2007, fitted selection criteria. Several had to be omitted because of the lack of a comparative group [17–26], or because on further inspection, the article did not clearly include patients who underwent MODN. [27–37]. Two papers were excluded because the control groups were drawn from results in the literature from other institutions [38,39]. Three papers had to be excluded because the references did not correspond to the journal articles cited and despite thorough database searches no similar articles could be found [40–42]. Studies were excluded that compared different forms of mini-incision nephrectomy without open or laparoscopic control [43], that contained unusable data [44–47] or that were not confined to nephrectomy solely for kidney donation [48,49]. Two cited articles were excluded as they were letters in response to another paper [50,51]. In papers with case overlap the ones with the best methodology and larger numbers of patients were used [7,52–57]. For example, both references [7] and [56] are based on patients from the same institutions for the same time period. Where possible, the RCT has been used for data collection except in the instances where it did not report an outcome when the alternative was used, in no situation was data from both studies combined. Five studies were excluded because they used a gasless laparoscopic technique [58–62]. No studies were excluded based on language alone.

Study characteristics and matching criteria

Nine studies finally fulfilled the inclusion criteria and they are summarized in Table 1. In total, 1038 patients were analyzed of which 433 (42%) underwent MODN, 389 (37%) SODN and 216 (21%) LDN.

The incidence of conversion to open procedure was poorly reported in the LDN group. Overall, it was 1.6% from all studies reporting it. Left kidneys were predominantly retrieved by all techniques while 40%, 36% and 39% of patients donated their right kidney in MODN, SODN and LDN groups respectively for studies including this parameter.

The studies included one RCT [7], four prospective comparisons [54,56,63,64] and one study with prospective data collection in the MODN group but with a retrospective control group [65]. The other three studies were all retrospective [66–68].

In all but two of the included studies, MODN was performed via a flank incision, in the remainder an anterior approach was used [54,68]. All cases of MODN were performed retroperitoneally. SODN was performed via a flank incision in all cases using a retroperitoneal approach. In four studies, rib resection was required [63–65,67] but in one study [64] in only 30% of the patients. LDN was performed via a transperitoneal, nonhand-assisted technique in all cases.

MODN versus SODN

Intra-operative parameters

Operative time was not significantly different between the groups (WMD: 8.52 min; 95% CI: −3.52, 20.57 min; $P = 0.17$), neither was warm ischemic time (WMD: −8.19 s; 95% CI: −20.68, 4.29 s; $P = 0.20$), estimated blood loss (WMD; −231.13 ml; 95% CI: −667.2, 205.01 ml; $P = 0.30$), or intra-operative complications (OR: 0.91; 95% CI: 0.02, 41.62; $P = 0.96$).

Postoperative parameters

Hospital stay (Fig. 1) and time to return to work were significantly shorter for the MODN group by 1.67 days (95% CI: −2.35, −0.99 days; $P < 0.001$) and 5 weeks (95% CI: −9.38, −0.62 weeks; $P = 0.03$) respectively. The amount of inpatient analgesia used was significantly less in the MODN group by 96 mEq of morphine (95% CI: −149.81, −42.19 mEq; $P < 0.001$). Total postoperative complica-

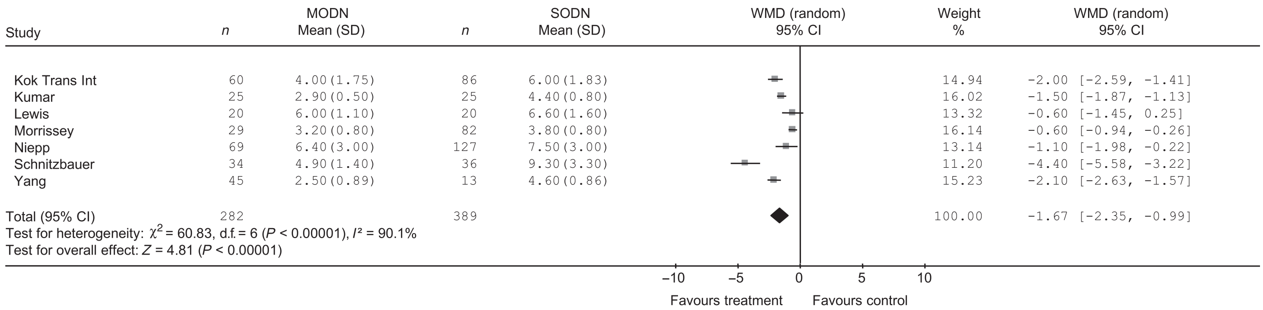

Figure 1 Forrest plot of MODN versus SODN for hospital stay. WMD, weighted mean difference; CI, confidence interval; SD, standard deviations. Test for heterogeneity, Chi-squared test with its degrees of freedom (d.f.) and *P*-value. Inconsistency among results: I^2. Test for overall effect: *Z*-statistic with *P*-value.

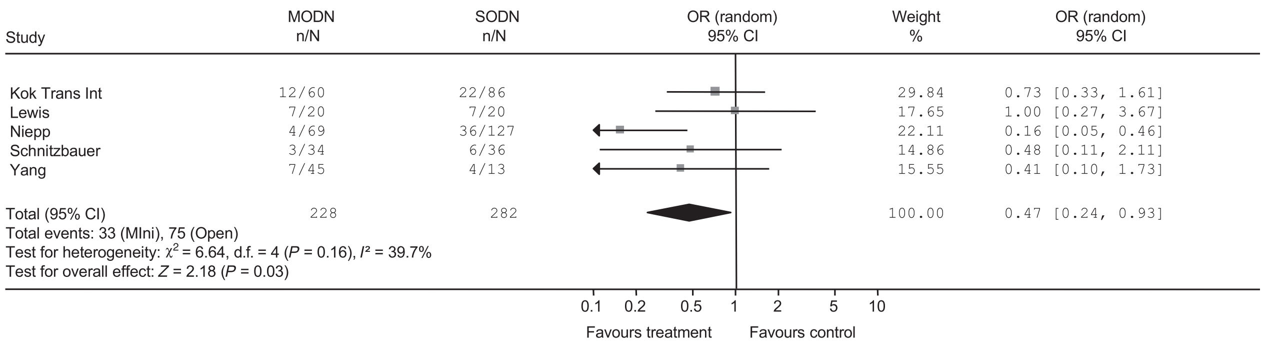

Figure 2 Forrest plot of MODN versus SODN for total donor complications. OR, odds ratio; CI, confidence interval; SD, standard deviations. Test for heterogeneity, Chi-squared test with its degrees of freedom (d.f.) and *P*-value. Inconsistency among results: I^2. Test for overall effect: *Z*-statistic with *P*-value.

tions were significantly fewer in the MODN group (OR: 0.47; 95% CI: 0.24, 0.93; $P = 0.03$) (Fig. 2) as was the frequency of incisional hernia and wound bulging (OR: 0.26; 95% CI: 0.08, 0.87; $P = 0.03$). When they were broken down into early and late complications, there were no significant differences. There was no difference in the rates of bleeding, transfusion, or re-operation (Table 2).

Recipient parameters

Limited data were available to perform good meta-analytic comparisons for these parameters but there were no differences in rates of total ureteric complications or ureteric strictures. Data were available from only one study for rates of ureteric leak, delayed graft function, and 1-year recipient survival. However, the data available suggest no significant differences in these parameters (Table 2).

MODN versus LDN

Intra-operative parameters

Mini-open donor nephrectomy had a significantly shorter operative time (Fig. 3) by 55 min when compared with LDN (95% CI: −93.46, −16.36 min; $P = 0.005$) and a significantly shorter warm ischemic time by 147 s (95% CI: −205.10, −88.23 s; $P < 0.001$). The difference in blood loss between the procedures was insignificant (WMD: 27.16 ml; 95% CI: −188.37, 242.68 ml; $P = 0.80$) as were the rates of intra-operative complications (OR: 0.47; 95% CI: 0.11, 1.99; $P = 0.30$).

Postoperative parameters

There was no significant difference in any of the postoperative parameters including length of hospital stay and time to return to work (Table 3). Total quantity of analgesia used was significantly less in the LDN group by 9.6 mEq of morphine (95% CI: 0.36, 18.87 mEq; $P = 0.04$). Donor complication rates were not significantly different for the two techniques, either overall or whilst in hospital. Similarly no significant differences were seen in rates of bleeding, re-operation or transfusion (Table 3).

Recipient parameters

Rates of total ureteric complications and strictures were not significantly different between the two groups (OR: 0.90; 95% CI: 0.36, 2.25; $P = 0.83$) and (OR: 1.17; 95% CI: 0.49, 2.82; $P = 0.72$) respectively. Delayed graft

Table 2. Comparison of MODN versus SODN.

Outcome of interest	No. studies	No. patients	Outcome by group % (MODN, SODN)	OR/WMD*	95% CI	*P*-value	HG χ^2	HG *P*-value
Donor operative parameters								
Operative time (min)	4	452	–	8.52*	−3.52, 20.57	0.17	11.04	**0.01**
Warm ischemic time (s)	4	382	–	−8.19*	−20.68, 4.29	0.20	4.08	0.25
Operative blood loss (ml)	2	186	–	−231.13*	−667.28, 205.01	0.30	2.25	0.13
Donor postoperative parameters								
Hospital stay (days)	7	671	–	−1.67*	−2.35, −0.99	**<0.001**	60.83	**<0.001**
Time to return to work (weeks)	1	40	–	−5.00*	−9.38, −0.62	**0.03**	–	–
Total in-patient analgesia (mEq of morphine)	1	40	–	−96.00*	−149.81, −42.19	**<0.001**	–	–
Donor adverse events								
Overall complications	5	510	14.5, 26.5	0.47	0.24, 0.93	**0.03**	6.64	0.16
Bleeding	4	452	3.3, 2.2	1.35	0.38, 4.74	0.64	3.23	0.36
No. patients requiring re-operation	3	306	1.6, 2.2	0.74	0.18, 3.09	0.68	0.79	0.67
No. patients requiring transfusion	4	452	1.6, 1.1	1.31	0.29, 5.86	0.73	1.29	0.73
Total intra-operative complications	2	204	4.8, 3.0	0.91	0.02, 41.62	0.96	5.26	**0.02**
In-hospital postoperative complications	5	510	11.0, 12.1	0.76	0.42, 1.39	0.38	1.68	0.79
Long-term postoperative complications	3	412	1.8, 15.3	0.20	0.02, 1.55	0.12	4.56	0.10
Incisional hernias/wound bulging	4	493	1.7, 7.6	0.26	0.08, 0.87	**0.03**	2.27	0.52
Graft/recipient complications								
Total/unspecified ureteric complications	2	236	7.9, 4.1	2.03	0.67, 6.12	0.21	0.08	0.78
Ureteric stricture	2	236	1.1, 1.4	0.99	0.11, 9.21	1.00	0.91	0.34
Ureteric leak	1	196	8.7, 3.2	2.93	0.80, 10.76	0.11	–	–
Delayed graft function	1	111	3.4, 2.4	1.43	0.12, 16.37	0.77	–	–
1-year graft survival (%)	2	236	100, 97.3	5.06	0.27, 95.47	0.28	–	–
1-year recipient survival (%)	1	196	100, 99.2	1.65	0.07, 41.00	0.76	–	–

OR, odds ratio; WMD*, weighted mean difference; HG, heterogeneity between studies; CI, confidence interval; MODN, mini-open donor nephrectomy; SODN, standard open donor nephrectomy.
Statistically significant results are shown in bold.

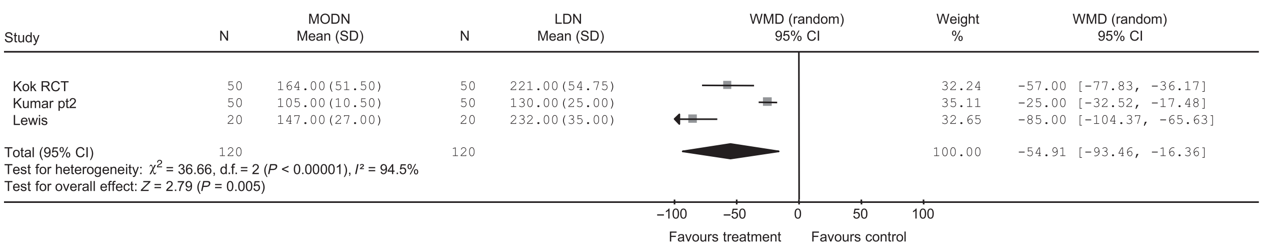

Figure 3 Forrest plot of MODN versus LDN for operative time. WMD, weighted mean difference; CI, confidence interval; SD, standard deviations. Test for heterogeneity, Chi-squared test with its degrees of freedom (d.f.) and *P*-value. Inconsistency among results: I^2. Test for overall effect: *Z*-statistic with *P*-value.

function, 1-year patient and graft survival rates were also similar between the two groups (Table 3).

Sensitivity analysis

Sensitivity analysis was conducted for (i) five studies with 50 or more cases of MODN and (ii) six high-quality studies with a score of five or more stars (Table 1). Sensitivity analysis was used to try to eliminate bias caused by the poorest quality studies. Although there is only one RCT and, hence only one study of the highest quality, we used the star rating system to establish the best quality studies of those available to us.

Table 3. Comparison of MODN versus LDN.

Outcome of interest	No. studies	No. patients	Outcome by group % (MODN, LDN)	OR/WMD*	95% CI	*P*-value	HG χ^2	HG *P*-value
Donor operative parameters								
Operative time (min)	3	240	–	−54.91*	−93.46, −16.36	**0.005**	36.66	**<0.001**
Warm ischemic time (s)	2	140	–	−146.66*	−205.10, −88.23	**<0.001**	3.21	0.07
Operative blood loss (ml)	2	140	–	27.16*	−188.37, 242.68	0.80	5.71	**0.02**
Donor postoperative parameters								
Hospital stay (days)	5	341	–	0.40*	−0.14, 0.94	0.15	33.75	**<0.001**
Time to return to work (weeks)	1	40	–	2.00*	−0.77, 4.77	0.16	–	–
Total in-patient analgesia (mEq of morphine)	2	140	–	9.62*	0.36, 18.87	**0.04**	0.15	0.70
Donor adverse events								
Overall complications	2	140	18.6, 24.3	0.70	0.30, 1.62	0.40	0.09	0.76
Bleeding	2	140	4.2, 4.3	0.96	0.18, 4.99	0.96	–	–
No. patients requiring re-operation	2	151	0, 1.4	0.24	0.01, 6.26	0.39	–	–
No. patients requiring transfusion	2	140	1.4, 1.4	1.00	0.10, 9.93	1.00	0.94	0.33
Total intra-operative complications	1	100	6.0, 12.0	0.47	0.11, 1.99	0.30	–	–
In-hospital postoperative complications	2	140	14.3, 15.7	0.88	0.32, 2.41	0.80	0.04	0.84
Long-term postoperative complications	–	–	–	–	–	–	–	–
Incisional hernias/wound bulging	2	140	2.8, 2.9	0.93	0.13, 6.53	0.94	0.84	0.36
Graft/recipient complications								
Total/unspecified ureteric complications	2	140	15.7, 17.1	0.90	0.36, 2.25	0.83	0.30	0.58
Ureteric stricture	2	140	19.7, 17.4	1.17	0.49, 2.82	0.72	0.58	0.44
Ureteric leak	–	–	–	–	–	–	–	–
Delayed graft function	3	191	1.0, 1.1	0.75	0.04, 12.70	0.84	–	–
1-year graft survival (%)	2	137	98.6, 98.5	1.01	0.10, 10.03	0.99	0.92	0.34
1-year recipient survival (%)	1	100	98, 96	2.04	0.18, 23.27	0.57	–	–

OR, odds ratio; WMD*, weighted mean difference; HG, heterogeneity between studies; CI, confidence interval; MODN, mini-open donor nephrectomy; LDN, laparoscopy donor nephrectomy.
Statistically significant results are shown in bold.

MODN versus SODN

Sensitivity analysis of high-quality studies showed that operative time was significantly different favoring SODN by 13 min (95% CI: 0.57, 25.82 min; $P = 0.04$). The duration of warm ischemic time became significantly shorter for the MODN group both when studies with more than 50 MODN cases (18.7 s; 95% CI: −33.48, −3.91 s; $P = 0.01$) and more than five stars were examined (17.6 s; 95% CI: −31.92, −3.25 s; $P = 0.02$). Postoperatively, long-term donor complications became significant in favor of MODN when studies with more then 50 patients in the MODN group (OR: 0.08; 95% CI: 0.02, 0.33; $P < 0.001$) and higher quality studies (OR: 0.08; 95% CI: 0.02, 0.33; $P < 0.001$) were examined. Although overall complication rates had favored MODN in the initial analysis, this failed to remain the case in any sensitivity analysis. All other parameters remained similar to the initial analysis. On the whole, the degree of heterogeneity fell or remained the same, except for overall donor complications, where heterogeneity became significant.

MODN versus LDN

On the whole, there was little change in the significant parameters with sensitivity analysis for the MODN versus LDN. However, the degree of blood loss became significantly greater for MODN when larger studies were reviewed (95% CI: 3.31, 276.69 ml; $P = 0.04$), but only by 140 ml. With studies gaining five or more stars hospital stay (95% CI: 0.64, 1.68 days; $P < 0.001$) became significant in favor of the LDN group by 1.16 days. Total quantity of analgesia fell out of significance when studies with more than 50 cases of MODN were examined. Heterogeneity remained the same or decreased with all sensitivity analyses.

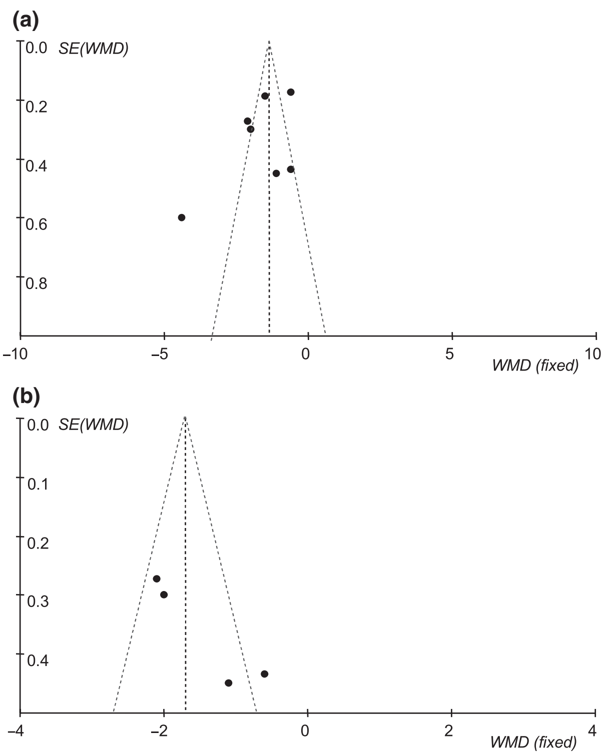

Figure 4 Funnel plots showing MODN versus SODN for hospital stay before (a) and after (b) sensitivity analysis of good quality studies. WMD, weighted mean difference. SE (effect estimate) versus effect estimate for each study under the outcome. Studies are marked by a dot. 95% CI lines.

Publication bias

Funnel plot analysis was used in an attempt to detect publication bias. Both the symmetry and distribution of the dots around the mid point are of significance when evaluating these plots. Evaluation was often limited because of the available numbers of studies. Where meaningful analysis was possible, publication bias was suggested for hospital stay, total donor complications and postoperative in hospital complications for MODN versus SODN and operative time for MODN versus LDN. Sensitivity analysis aimed to reduce this bias (Fig. 4).

Discussion

This study provides the first attempt to analyze the published literature comparing MODN with SODN and LDN techniques. MODN appears to combine benefits from both SODN and LDN. When compared with SODN, hospital stay and time to return to work were significantly shorter but with no prolongation of the operation or the warm ischemia time. Also, the incidence of incisional hernias and wound bulging appears less in the MODN group. There may also be a reduction in the rate of overall complications and the amount of postoperative analgesia required in the MODN group. Sensitivity analysis suggests that although immediate complications are similar, MODN may reduce long-term complications.

When compared with LDN, MODN provides consistently shorter operation and warm ischemic times but with a greater total quantity of analgesia required. It is noted that the warm ischemia time for LDN reported in these studies is greater than that seen elsewhere in the literature and this, along with a difference of only 150 s between MODN and LDN, throws doubt on either the reality or relevance of this finding. There is a suggestion arising out of sensitivity analysis that there may be more blood loss and longer hospital stay associated with the MODN. However, in all cases, the sensitivity analysis is based on only a few studies and the differences are relatively small, for example only a 140 ml blood loss, and may not be of real clinical significance.

Unfortunately, very limited data are available for the assessment of graft recipient parameters. This study suggests that there is no difference between techniques with regard to graft function; however, with present data, firm conclusions cannot be drawn. This is obviously a significant deficiency in the literature as although it is clearly important to provide a procedure that is acceptable for the donor, it is also vital that it does not have a negative effect on long-term graft survival and function.

It is important to recognize that, whilst the acceptability of a procedure and the outcomes for the patients concerned are of great interest, the choice to use a technique is often based on other factors. In this case economic implications are of interest. LDN is inherently expensive and MODN may provide a more economically viable alternative especially for developing countries where laparoscopic equipment may be unaffordable or not as readily available [56,64,67]. Similarly the apparently shorter time to return to work of MODN when compared with SODN has economic implications with less sick leave and greater productivity. The included studies were performed in different continents, America, Europe and Asia. The different socio-economic conditions of these continents may have had a direct effect on some of the donor outcomes. For example, depending on methods in place for healthcare funding, there may be a propensity for longer or shorter durations of hospital stay, this may account for the significant degree of heterogeneity seen with this variable (Tables 2 and 3). These differences need to be taken into account when the results of this meta-analysis are considered.

Also of importance is the perceived cosmesis of each procedure. This was not directly addressed in this study but it may be that the single short incision of MODN has better cosmetic results than the long incision of SODN or the multiple incisions, including the kidney extraction incision, of LDN.

Many of the studies compared their initial experience with MODN. It has been demonstrated that a learning curve is present when new techniques are introduced [69–73] with operative time and warm ischemia time falling with experience. It may be expected that the same would apply to MODN and that with experience greater advantages of this technique may be seen. The heterogeneity seen with operative time may reflect different centers' experience with these techniques.

An inherent problem in this analysis is the variability of surgical techniques employed. Subtle differences in the techniques for LDN and SODN exist and are difficult to control for, however these tend to be relatively minor and are probably not of clinical significance. Most studies used a flank incision for MODN but two utilized an anterior vertical incision. Because of data limitations, these were analyzed together as MODN. We have no reason to believe that the position of the incision would greatly affect the outcome of the operation although there appears to be no data comparing these two approaches. The SODN were all performed via flank incisions but in some patients rib resection was required. It is easy to imagine that in patients requiring rib resection the amount of postoperative pain and hence analgesia use may be increased, possibly accounting for the degree of difference seen with this variable. Terms such as operative time and warm ischemic time were not always clearly defined and inequalities in definition may introduce a certain degree of error into the study.

Publication bias is inherent in this type of investigation. Every effort was made to reduce this and heterogeneity with sensitivity analysis. However, this often led to very small numbers of studies being combined, in some cases only leaving a single study, making meaningful meta-analysis impossible and representing only a summary of available literature. Heterogeneity was small for most of the dichotomous outcomes examined in this analysis, however, it was more marked for all of the continuous variables examined such as operative time, length of stay and blood loss. This may represent a much greater spread of results when a continuous variable is examined. In some cases, it is difficult to establish the reasons behind the degree of heterogeneity because of a lack of reporting within the original studies, it may represent variability in inclusion and exclusion criteria or the experience of different centers. For most variables, the heterogeneity failed to reach statistical significance, and where it did, heterogeneity was generally reduced when sensitivity analysis could be applied.

This meta-analysis, largely of nonrandomized studies, has several limitations. The role and strength of meta-analytic techniques in this setting has been a source of extensive debate. It should be taken into account that this study is limited by the quality and number of the papers available. The studies available were few, only one was a RCT and very few studies revealed their inclusion or exclusion criteria (Table 1). Many of the parameters of interest were investigated by only one or two studies hampering the extent of the meta-analysis; this was especially the case when MODN was compared with LDN. Publication, selection and reporting bias may all confound the results. Significant adverse outcomes may not be published in the literature and would therefore also be missing from any meta-analysis in this area. In this study, we have taken every care to exclude or take into account all of these factors. It is of interest that this meta-analysis has produced findings that conflict with those found in the only RCT comparing MODN to LDN. Kok *et al.* [7] found significantly shorter operating time and warm ischemic time as found in the meta-analysis, however, they also report greater blood loss, morphine requirement and hospital stay in the MODN group. Similar results were not found in the meta-analysis, although on sensitivity analysis some of these trends emerged. These differences may be accounted for in the methodological problems with meta-analysis as outlined and the hospital stay data may reflect socio-economic differences between countries that, when combined, clouds any difference between techniques. To this end, it may be argued that the results of the randomized trial are not applicable to populations outside that in which it was conducted. Although a greater volume of blood loss was seen in the MODN group, the only transfusion recorded is given in the laparoscopy group and it appears that three out of 50 patients in both groups had bleeding complications.

It is recognized that a meta-analysis of well-conducted RCTs is superior to that of retrospective data. Ideally, we would have performed sensitivity analysis using a group of RCTs, prospective studies and retrospective studies separately to attempt to delineate any errors introduced by combining these studies, however, the small number of studies available precluded this.

This study is by no means conclusive; however, it provides the most comprehensive analysis of the available data and highlights the possible advantages to the donor of MODN. It also serves to illustrate the need for more detailed studies especially in the form of RCTs and studies examining recipient outcomes.

Conclusion

Mini-open donor nephrectomy appears to provide post-operative advantages for the donor in comparison to

SODN and also has a shorter operative time when compared with the LDN. Further studies with larger series of patients who underwent MODN will be needed to confirm those results.

Authorship

DA, TGN: responsible for study design, data collection and analysis, and drafting the article. AWD, PPT, VEP: contributed to the design of the study, provided statistical support and advice, and contributed to drafting the article. VEP: guarantor.

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