Systematic review and meta-analysis of the relation between body mass index and short-term donor outcome of laparoscopic donor nephrectomy

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In this era of organ donor shortage, live kidney donation has been proven to increase the donor pool; however, it is extremely important to make careful decisions in the selection of possible live donors. A body mass index (BMI) above 35 is generally considered as a relative contraindication for donation. To determine whether this is justified, a systematic review and meta-analysis were carried out to compare perioperative outcome of live donor nephrectomy between donors with high and low BMI. A comprehensive literature search was performed in MEDLINE, Embase, and CENTRAL (the Cochrane Library). All aspects of the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement were followed. Of 14 studies reviewed, eight perioperative donor outcome measures were meta-analyzed, and, of these, five were not different between BMI categories. Three found significant differences in favor of low BMI (29.9 and less) donors with significant mean differences in operation duration (16.9 min (confidence interval (CI) 9.1–24.8)), mean difference in rise in serum creatinine (0.05 mg/dl (CI 0.01–0.09)), and risk ratio for conversion (1.69 (CI 1.12–2.56)). Thus, a high body mass index (BMI) alone is no contraindication for live kidney donation regarding short-term outcome.

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Kidney transplantation is the treatment of choice for end-stage renal disease.[1] In the United States, more than 88,000 people are currently on the waiting list for a kidney transplant. However, in 2010, only 16,898 patients received a donor kidney, of which 37% were from a live donor. However, end-stage renal disease patients are dependent on hemodialysis or peritoneal dialysis, which in itself has a high morbidity and mortality rate.[2–5] After kidney transplant, life expectancy and the quality of life improve markedly.[6] As the deceased donor pool remains more or less stable, and the donor shortage increases, it is important to assess whether the live kidney donor pool can be expanded. Careful decisions with respect to including and excluding criteria for possible live donors are warranted.

In the Erasmus MC, Rotterdam, The Netherlands, in 2010 135 kidney transplantations were performed with kidneys from a live donor (75% of the total). Especially in a program of this magnitude, the need for careful donor selection is of critical importance. One of the parameters used for donor selection is the BMI. In most transplant centers, a BMI higher than 35 is considered a relative contraindication for donation,[7,8] which is in accordance with the guidelines formulated during the Amsterdam Forum in 2005[9] and other international guidelines.[10–12] This is because donors with a higher BMI are said to be more prone to complications.[13,14] Furthermore, obesity is correlated with chronic kidney disease[15,16] and with several risk factors for kidney disease, such as diabetes, cardiovascular diseases, and hypertension. In addition, a BMI higher than 30 may predispose for more postoperative pain.[17,18] However, the level of evidence of published studies may not be sufficient to answer the question whether a high BMI leads to more complications of live donor nephrectomy (LDN). The incidence of obesity is increasing in the general population, and thus in possible live kidney donors. Lumsdaine *et al.*[19] carried out a survey in the United Kingdom and demonstrated that only one center accepted donors with a BMI greater than 30 in 1999. Six years later, a US survey reported that in 10 years the acceptance of a donor with a BMI higher than 30 had increased from 86 to

90%.[20] On the basis of these numbers, we conclude that in most centers obesity is no longer considered a contraindication. The question is whether or not BMI is a reliable parameter for the selection of live kidney donors. The aim of this review is to evaluate the literature systematically to examine the relation between BMI and outcome of LDN. We aimed to specifically investigate perioperative outcome measures and did not focus on long-term outcome as there is little literature available.

RESULTS

Study selection

Publications were selected for review if they investigated two or more groups of donors divided into BMI categories. Of the 529 publications found after the initial search, 102 publications were screened according to abstract or full text. After screening, 14 publications fell in the scope of our study. One article was excluded because of missing s.d. values.[21] Fourteen studies were included for review and meta-analysis. Three additional articles were found by scrutinizing the reference lists.[22–24] These three articles were not identified in the original search, because these were conference abstracts or were not indexed. A flow diagram is presented in Figure 1. The characteristics of included studies are presented in Table 1. A detailed morbidity report of all included studies is available in Supplementary Data online. Not all studies used the same cutoff value for BMI according to standards set by the World Health Organization.[25] After careful consideration, consensus was reached to compare all studies based on 'high BMI' versus 'low BMI'. For the pooled cohorts, a BMI of 29.9 was used as the cutoff value, according to the World Health Organization definitions. Furthermore, we chose this value because the prevalence of overweight is relatively high in developed countries. To adequately differentiate between donor BMI groups, we classified a BMI >30 as 'high BMI'.

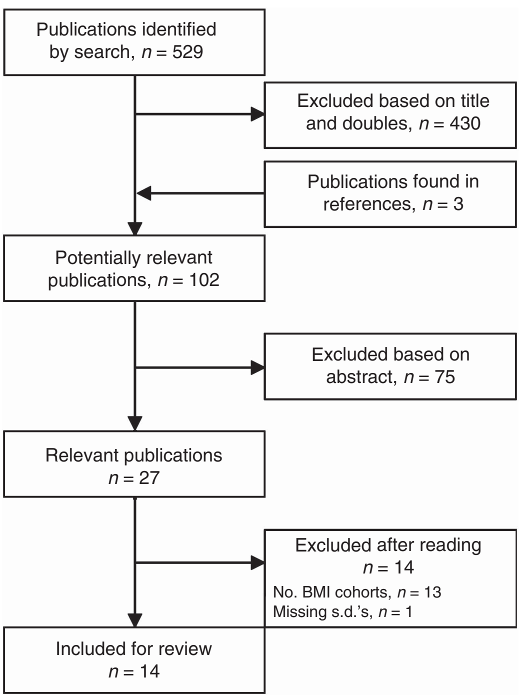

Figure 1 | Flow diagram outlining selection of studies.

Operative outcome measures

The operation duration of laparoscopic LDN was investigated in eight studies.[23,26–32] All studies showed a longer operation time in the high BMI group, except for one. The overall mean difference, based on a total of 1105 observations, was 16.9 min (CI 9.06–24.76; $P<0.0001$) in favor of donors with a low BMI (Figure 2). The incidence of conversion from laparoscopic LDN to an open procedure was assessed in seven studies, which included a total of 5869 patients.[22,27–29,31–33] All studies found a risk ratio higher than 1 for donors with a high BMI. Overall, there is a risk ratio of 1.69 (CI 1.12–2.56; $P=0.01$) (Figure 3). The duration of the warm ischemia in seconds was assessed in three studies.[28,30,32] All studies except for one reported a longer warm ischemia time for donors with a high BMI. Overall, the meta-analysis shows no significant difference between groups (mean difference: -0.21 s CI -28.89 to 28.47; $P=0.99$) based on 284 observations (Figure 4). Seven studies investigated the estimated blood loss in milliliters during LDN, in a total of 939 donors.[22,23,26–28,30,32] Five studies reported more blood loss in the high BMI group. However, in two studies, less blood loss was observed in the group with high BMI donors. Overall, the meta-analysis shows no significant difference between groups (mean difference = 34.46 ml; CI -6.73 to 75.66; $P=0.10$) (Figure 5).

Perioperative outcome measures

The length of hospital stay after LDN was investigated in 10 studies in a total of 6019 patients.[22,23,26–33] Eight studies showed a longer length of stay in the high BMI group. Two studies found a shorter length of stay for the group with high BMI, and one reported no difference. Overall, there is no significant difference between groups (mean difference = 0.18 days; CI -0.02 to 0.39; $P=0.08$). (Figure 6) The amount of perioperative complications, such as bleeding, wound complications, urinary tract infections, readmission, and reoperation, was assessed in eight studies in a total of 5869 patients.[22,27–29,31–33] Three studies reported a higher risk of complications for donors with a high BMI. Overall, the meta-analysis shows no significant difference between groups (risk ratio = 1.01; CI 0.75–1.36; $P=0.94$) (Figure 7).

Kidney function outcome measures

The difference in preoperative and postoperative serum creatinine in mg/dl was analyzed in eight studies in a total of 3511 patients.[24,27,30,31,33–36] Although not all studies reported the exact time points of serum measurements postoperatively, best matches were acquired for optimal comparison. Five studies reported a higher increase in serum creatinine in the group with high BMI donors. Two studies showed no mean difference, and one study reported a lower increase in the group with high BMI donors. Overall, the

Table 1 | Characteristics of studies comparing outcome of LDN between BMI groups

Reference	Study type	Groups (BMI)	*N*	NOS	Outcome measures	Follow-up
Hakaim *et al.*[26]	Retrospective cohort	IBW FAIBW MAIBW	6 5 5	6	OD, EBL, CI, UP, FD, SCr	2 Months
Jacobs *et al.*[28]	Retrospective cohort	<30 >35	41 41	7	OD, C, DR, LP	1 Week
Kuo *et al.*[27]	Retrospective cohort	⩽31 >31	28 12	8	OD, EBL, LoS, SC	4.2 ± 0.4 Months
Chavin[23]	Retro/ prospective cohort	17–25 25–27 27–30 30–35 35–40	28 17 19 16 7	7	LoS, OD, EBL, ME	Not reported
Chow *et al.*[29]	Prospective cohort	<30 ⩾30	75 34	6	OD, C, SC, LoS	Not reported
Mateo *et al.*[30]	Prospective cohort	<30 ⩾30	35 12	8	WIT, OD, EBL, UP, LoS, SCr	
Leventhal *et al.*[22]	Retrospective cohort	⩽30 >30	390 110	7	EBL, LoS, SC, C	Not reported
Heimbach *et al.*[31]	Retrospective cohort	<25 25⩽BMI<30 30⩽BMI<35 ⩾35	170 211 114 58	8	C, OD, LoS, SC, SCr, BP	11 ± 0.34 Months
Espinoza *et al.*[24]	Prospective cohort	20⩽BMI⩽25 >30	37 37	6	SCr, GFR, SC, M	50.8 ± 28.5 Months
Rea *et al.*[34]	Retrospective cohort	<30 ⩾30	41 49	8	SCr, BP	Median 340 (21–963) days
Kok *et al.*[32]	Prospective cohort	<25 >27	91 76	8	C, WIT, OD, EBL, SC, LoS, PC	1 Year
Rook *et al.*[35]	Retrospective cohort	<25 25–29.9 ⩾30	87 70 21	7	GFR, SCr	2 Months
Tavakol *et al.*[36]	Retrospective cohort	<30 ⩾30	82 16	8	GFR, 24-h ur. prot., SCr, HT, Chol, BP	11 ± 7 Years
Reese *et al.*[33]	Retrospective cohort	<25 25⩽BMI<30 30⩽BMI<35 ⩾35	2002 2108 944 250	6	LoS, SCr, C, SC, GFR, HT	1 Year

Abbreviations: BP, blood pressure; C, conversion; Chol, cholesterol; CI, crystalloid infusion; DR, donor recovery; EBL, estimated blood loss; FD, furosemide dose; F/MAIBW, female/male above ideal body weight; GFR, glomerular filtration rate; HT, hypertension; IBW, ideal body weight; M, mortality; ME, morphine equivalents; LoS, length of stay; LP, laparoscopic ports; Nos, Newcastle–Ottawa Scale, SCr, serum creatinine; OD, operation duration; PC, postoperative complications; SC, surgical complications; UP, urine production; WIT, warm ischemia time.

Follow-up is in years ± s.d. unless otherwise reported.

Study or subgroup	High BMI Mean	High BMI s.d.	High BMI Total	Low BMI Mean	Low BMI s.d.	Low BMI Total	Weight	Mean difference IV, random, 95% CI	Year
Hakaim	213.5	28	10	205	19	10	10.8%	8.50 (−12.47, 29.47)	1997
Kuo	182	31	12	165	22	28	12.1%	17.00 (−2.34, 36.34)	2000
Jacobs	236.5	60.1	41	194.7	54.8	41	8.2%	41.80 (16.90, 66.70)	2000
Chow	216.6	44.9	34	191.6	44.8	75	13.3%	25.00 (6.82, 43.18)	2002
Chavin	299.2	60.9	23	282.98	73.3	64	5.7%	16.22 (−14.47, 46.91)	2002
Mateo	307	75	12	291	67	35	2.5%	16.00 (−31.89, 63.89)	2003
Heimbach	149.3	43.7	172	130.8	34.1	381	32.8%	18.50 (11.13, 25.87)	2005
Kok	296.9	51.4	76	298.4	61	91	14.5%	−1.50 (−18.55, 15.55)	2007
Total (95% CI)			380			725	100.0%	16.91 (9.06, 24.76)	

Heterogeneity: $\tau^2 = 34.70$; $\chi^2 = 9.87$, df = 7 ($P = 0.20$); $I^2 = 29\%$
Test for overall effect: $Z = 4.22$ ($P < 0.0001$)

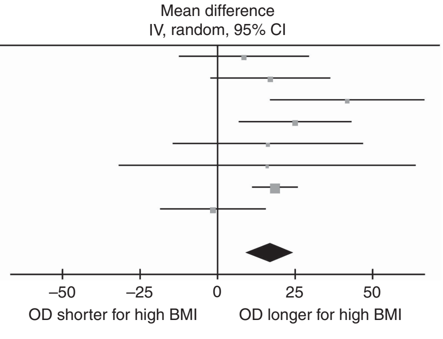

Figure 2 | Forest plot of comparison: high versus low BMI donors; outcome: operation duration (OD) in minutes. BMI, body mass index; CI, confidence interval.

meta-analysis shows a mean difference of 0.05 mg/dl (0.01–0.09; $P = 0.02$) in favor of low BMI donors (Figure 8). Four studies assessed the change in glomerular filtration rate after LDN at different time points after donor nephrectomy. All except one reported a greater decrease in glomerular filtration rate (GFR) in the group with high BMI

Study or subgroup	High BMI Events	High BMI Total	Low BMI Events	Low BMI Total	Weight	Risk ratio M–H, random, 95% CI	Year
Kuo	1	12	1	28	2.4%	2.33 (0.16, 34.31)	2000
Jacobs	3	41	0	41	2.0%	7.00 (0.37, 131.38)	2000
Chow	2	34	1	75	3.1%	4.41 (0.41, 47.01)	2002
Leventhal	4	110	5	390	10.2%	2.84 (0.77, 10.38)	2004
Heimbach	2	172	3	381	5.4%	1.48 (0.25, 8.76)	2005
Kok	7	76	4	91	12.1%	2.10 (0.64, 6.89)	2007
Reese	20	997	50	3421	64.9%	1.37 (0.82, 2.29)	2009
Total (95% CI)		1442		4427	100.0%	1.69 (1.12, 2.56)	
Total events	39		64				

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 2.99$, df = 6 ($P = 0.81$); $I^2 = 0\%$
Test for overall effect: $Z = 2.49$ ($P = 0.001$)

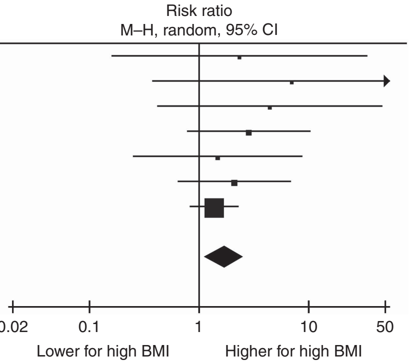

Figure 3 | Forest plot of comparison: high versus low BMI donors; outcome: conversion (risk ratio). BMI, body mass index; CI, confidence interval.

Study or subgroup	High BMI Mean	High BMI s.d.	High BMI Total	Low BMI Mean	Low BMI s.d.	Low BMI Total	Weight	Mean difference IV, random, 95% CI	Year
Jacobs	156.4	46.3	41	167.2	111.5	41	60.2%	−10.80 (−47.76, 26.16)	2000
Mateo	227	101	7	208	89	28	12.3%	19.00 (−62.76, 100.76)	2003
Kok	418.8	177.2	76	404.4	182.5	91	27.5%	14.40 (−40.31, 69.11)	2007
Total (95% CI)			124			160	100.0%	−0.21 (−28.89, 28.47)	

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 0.80$, df = 2 ($P = 0.67$); $I^2 = 0\%$
Test for overall effect: $Z = 0.01$ ($P = 0.99$)

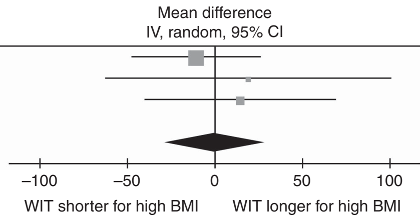

Figure 4 | Forest plot of comparison: high versus low BMI donors; outcome: warm ischemia time (WIT) in seconds. BMI, body mass index; CI, confidence interval.

Study or subgroup	High BMI Mean	High BMI s.d.	High BMI Total	Low BMI Mean	Low BMI s.d.	Low BMI Total	Weight	Mean difference IV, random, 95% CI	Year
Hakaim	303	148.96	10	258	55	6	11.8%	45.00 (−57.28, 147.28)	1997
Kuo	310	302	12	278	325	28	3.6%	32.00 (−177.02, 241.02)	2000
Jacobs	170.1	201.6	41	112.9	162.4	41	16.7%	57.20 (−22.04, 136.44)	2000
Chavin	193.26	171	23	268.53	241.32	64	13.9%	−75.27 (−166.81, 16.27)	2002
Mateo	296	232	12	170	139	35	7.3%	126.00 (−13.11, 265.11)	2003
Leventhal	181	145	110	125	126	390	35.7%	56.00 (26.16, 85.84)	2004
Kok	272.7	287.1	76	275.8	418.6	91	11.0%	−3.10 (−110.63, 104.4.43)	2007
Total (95% CI)			284			655	100.0%	34.46 (−6.73, 75.66)	

Heterogeneity: $\tau^2 = 1005.79$; $\chi^2 = 9.33$, df = 6 ($P = 0.16$); $I^2 = 36\%$
Total for overall effect: $Z = 1.64$ ($P = 0.10$)

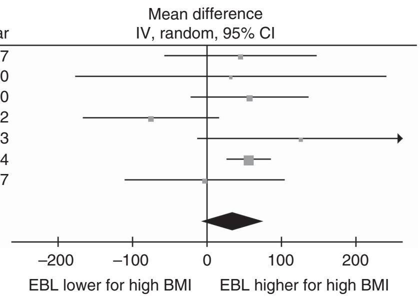

Figure 5 | Forest plot of comparison: high versus low BMI donors; outcome: estimated blood loss (EBL) in milliliters. BMI, body mass index; CI, confidence interval.

Study or subgroup	High BMI Mean	High BMI s.d.	High BMI Total	Low BMI Mean	Low BMI s.d.	Low BMI Total	Weight	Mean difference IV, random, 95% CI	Year
Hakaim	7.4	1.01	10	5.8	0.3	6	6.1%	1.60 (0.93, 2.27)	1997
Kuo	2.1	0.9	12	1.6	0.5	28	7.8%	0.50 (−0.04, 1.04)	2000
Jacobs	2.72	0.87	41	2.74	0.88	41	10.8%	−0.02 (−0.40, 0.36)	2000
Chow	2.4	0.9	34	2.1	0.8	75	11.4%	0.30 (−0.05, 0.65)	2002
Chavin	2.43	0.95	23	2.35	0.84	64	9.6%	0.08 (−0.36, 0.52)	2002
Mateo	4.17	1.42	12	4	1.38	35	3.9%	0.17 (−0.75, 1.09)	2003
Leventhal	1.7	0.7	110	1.7	0.7	390	15.6%	0.00 (−0.15, 0.15)	2004
Heimbach	2.27	1.01	172	2.24	1.41	381	14.5%	0.03 (−0.18, 0.24)	2005
Kok	3.33	1.4	76	3.65	1.4	91	9.9%	−0.32 (−0.75, 0.11)	2007
Reese	3.32	5.87	997	3.05	4.53	3421	10.5%	0.27 (−0.12, 0.66)	2009
Total (95% CI)			1487			4532	100.0%	0.18 (−0.02, 0.39)	

Heterogeneity: $\tau^2 = 0.07$; $\chi^2 = 29.47$, df = 9 ($P = 0.0005$); $I^2 = 69\%$
Total for overall effect: $Z = 1.74$ ($P = 0.08$)

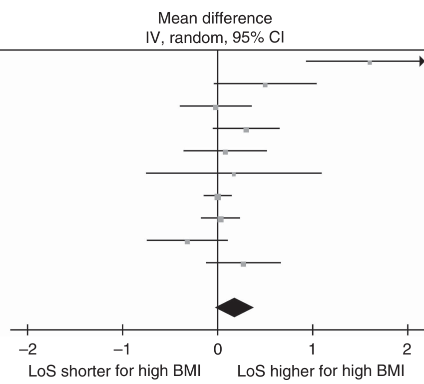

Figure 6 | Forest plot of comparison: high versus low BMI donors; outcome: length of stay (LoS) in days. BMI, body mass index; CI, confidence interval.

donors. Overall, the meta-analysis shows a mean difference of 1.78 ml/min (−1.62 to 5.18; $P = 0.31$) (Figure 9).

An additional subgroup analysis was performed to gain better insight into differences within the high BMI group. Three studies of our original analysis could be used,[23,31,33] as they described multiple cohorts. Kidney donors with a BMI of 30–34.9 were compared with those with a BMI of 35 and higher. For none of the outcome measures were significant differences found

Study or subgroup	High BMI Events	High BMI Total	Low BMI Events	Low BMI Total	Weight	Risk ratio M–H, random, 95% CI	Year
Kuo	0	12	1	28	0.9%	0.74 (0.03, 17.06)	2000
Jacobs	9	41	10	41	11.2%	0.90 (0.41, 1.98)	2000
Chow	8	34	13	75	11.4%	1.36 (0.62, 2.97)	2002
Leventhal	4	110	17	390	6.8%	0.83 (0.29, 2.43)	2004
Heimbach	21	172	28	381	19.6%	1.66 (0.97, 2.84)	2005
Kok	12	76	27	91	16.6%	0.53 (0.29, 0.98)	2007
Reese	48	997	161	3421	33.5%	1.02 (0.75, 1.40)	2009
Total (95% CI)		1442		4427	100.0%	1.01 (0.75, 1.36)	
Total events	102		257				

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 8.36$, df = 6 ($P = 0.21$); $I^2 = 28\%$
Test for overall effect: $Z = 0.07$ ($P = 0.94$)

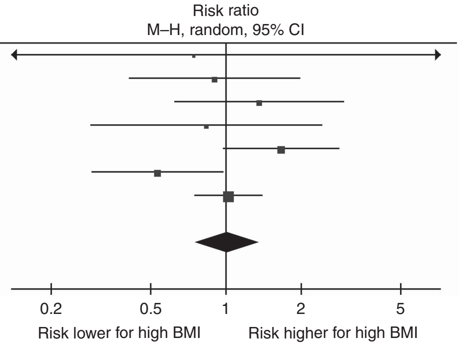

Figure 7 | Forest plot of comparison: high versus low BMI donors; outcome: perioperative complications (risk ratio). BMI, body mass index; CI, confidence interval.

Study or subgroup	High BMI Mean	High BMI s.d.	High BMI Total	Low BMI Mean	Low BMI s.d.	Low BMI Total	Weight	Mean difference IV, random, 95% CI	Year
Kuo	0.4	0.2	12	0.4	0.17	28	6.8%	0.00 (–0.13, 0.13)	2000
Mateo	0.29	0.27	12	0.3	0.23	35	4.4%	–0.01 (–0.18, 0.16)	2003
Heimbach	0.35	0.21	104	0.31	0.19	221	19.4%	0.04 (–0.01, 0.09)	2005
Rea	0.3	0.17	49	0.2	0.2	41	13.1%	0.10 (0.02, 0.18)	2006
Espinoza	0.5	0.26	37	0.3	0.17	37	9.7%	0.20 (0.10, 0.30)	2006
Rook	0.4	0.17	21	0.4	0.17	157	13.1%	0.00 (–0.08, 0.08)	2008
Tavakol	0.27	0.2	16	0.24	0.21	82	8.8%	0.03 (–0.08, 0.14)	2009
Reese	0.39	0.24	600	0.37	0.35	2059	24.6%	0.02 (–0.00, 0.04)	2009
Total (95% CI)			851			2660	100.0%	0.05 (0.01, 0.09)	

Heterogeneity: $\tau^2 = 0.00$; $\chi^2 = 15.93$, df = 7 ($P = 0.03$); $I^2 = 56\%$
Test for overall effect: $Z = 2.39$ ($P = 0.02$)

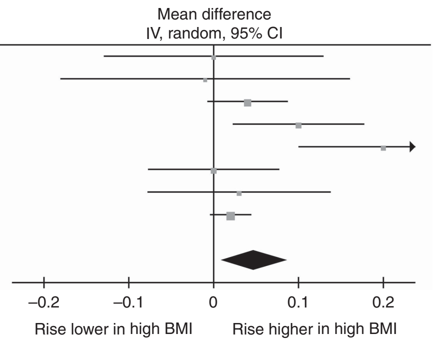

Figure 8 | Forest plot of comparison: high versus low BMI donors; outcome: difference in serum creatinine in mg/dl. BMI, body mass index; CI, confidence interval.

Study or subgroup	High BMI Mean	High BMI s.d.	High BMI Total	Low BMI Mean	Low BMI s.d.	Low BMI Total	Weight	Mean difference IV, random, 95% CI	Year
Espinoza	46.3	12.2	37	38.4	15.9	37	19.2%	7.90 (1.44, 14.36)	2006
Rook	45	20.8	21	44.7	19.8	157	10.8%	0.30 (–9.12, 9.72)	2008
Tavakol	23	13.5	16	24	16.8	82	15.3%	–1.00 (–8.55, 6.55)	2009
Reese	30.9	17.1	600	30.2	17.7	2059	54.8%	0.70 (–0.87, 2.27)	2009
Total (95% CI)			674			2335	100.0%	1.78 (–1.62, 5.18)	

Heterogeneity: $\tau^2 = 4.86$; $\chi^2 = 4.82$, df = 3 ($P = 0.19$); $I^2 = 38\%$
Test for overall effect: $Z = 1.02$ ($P < 0.31$)

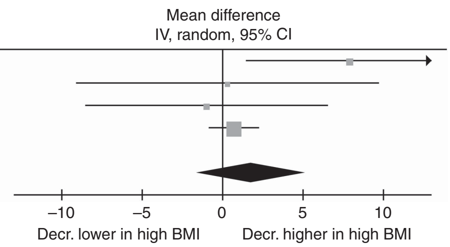

Figure 9 | Forest plot of comparison: high versus low BMI donors; outcome: decrease in glomerular filtration rate in ml/min. BMI, body mass index; CI, confidence interval; Decr., decrease.

between these BMI groups based on a meta-analysis (data not shown). A total of 1192 donors were analyzed in this respect.

DISCUSSION

In the literature, there seems to be a slowly increasing trend of accepting overweight people as live kidney donors.[20,22,31,37,38] By conducting this review and meta-analysis, we aimed to obtain a better insight into the relationship that exists between BMI and short-term outcome after LDN. To compare all groups described in the studies, we justified pooling the cohorts for mathematical reasons, being aware of the possible implications and limitations such as statistical bias and heterogeneity. Of the studies included, 14 examined obese living donors based on their BMI class. Five studies used a cutoff value of 29.9 kg/m^2 for high versus low BMI,[22,29,30,34,36] according to the World Health Organization classification. In four studies, more than two cohorts of BMI categories were defined, but from these we were able to pool the cohorts into two cohorts with a cutoff value of 29.9 kg/m^2.[23,31,33,35] The other five studies used a different cutoff point (summarized in Table 1). To include as many studies as is statistically valid, a consensus was reached to pool these data with the two BMI groups. Nine studies were retrospective cohort studies, one collected retrospective and prospective data[23,] and four studies were prospective cohort studies.

Several authors have already indicated the advantages of laparoscopic LDN over the open approach.[39–44] The BMI was taken into account in some of these studies; however, no hard statements were made regarding the relation between BMI and outcome of LDN. We aimed to include only those studies that assessed laparoscopic LDN to enable the most sound comparison; however, in some publications, we were unable to identify whether a laparoscopic or an open LDN had been performed.[24,26,35,36] As significance did not change whether we included or excluded these studies, we decided to include them in the analysis. A meta-analysis by Young *et al.*[45] performed in 2008 also partially investigated the influence of BMI on outcome after LDN. Only a limited number of outcome measures, i.e., operative time, blood loss, and length of hospital stay, were meta-analyzed. Differences in serum creatinine and GFR were summarized, but not meta-analyzed. The authors concluded that more research should be conducted to investigate whether high-risk donors can be safely accepted for live kidney donation.

In 2010, Friedman *et al.*[46] reported that obesity is associated with a higher complication rate. However, as commented in the article, complications are not segregated by severity and thus can consist of a large number of minor complications. Segev *et al.*[47] demonstrated in 2010 that no statistically significant difference in surgical mortality was observed by BMI. Overall, various outcomes have been reported in literature and this emphasizes the need for a systematic review.

According to this systematic review and meta-analysis, only in three out of eight short-term outcome measures were significant differences seen between low and high BMI donors. With regard to the operative outcome measures, only operation duration and conversion rate were significantly lower in favor of low BMI donors. Importantly, no higher complication rates were found in the high BMI group. The fact that operation duration is longer for high BMI donors is plausible, as in this group the operation is technically more challenging because of more (perirenal) fat and more difficulties in identifying the vessels in the hilum.[48,49] The overall difference in operation duration found in our meta-analysis is only 17 min, which is not necessarily of great clinical relevance. Furthermore, there is no evidence in the literature that such a small increase in general anesthesia time has disadvantages for a patient. Low BMI donors were found to have a significantly lower conversion rate compared with the high BMI group. Nowadays, the overall conversion rate from laparoscopic LDN to the open approach is very low. Large case series nowadays report a conversion rate of 0.6–0.7%.[50,51] In the studies we included, conversion rates for high BMI donors range from 1.2 to 9.2%. In our opinion, a conversion rate of 9.2% is very high; however, we should take into account that experience and laparoscopic skills have increased over the years. However, although conversion rates are higher for the high BMI donors, it does not seem to affect complication rates and length of hospital stay. The difference found in warm ischemia time is not significant between donor groups. In 2006, Simforoosh *et al.*[52] showed in a prospective study that prolonged warm ischemia time up to 17 min does not lead to impaired graft function, which was confirmed in another retrospective study.[53] However, these studies did not include donors with a BMI >30.

Of the two perioperative outcome measures, none was significantly different between BMI groups. In 2005, Bachmann *et al.* described that obese donors have significantly higher visual analog scale scores compared with donors with a normal weight.[17] Visual analog scale scores were not reported in included studies and therefore not a part of our meta-analysis. However, it appears that the higher conversion rate in high BMI donors does not lead to more postoperative pain necessitating longer hospital stay.

Authors describing their early LDN experience report higher complication rates in donors with BMI >30.[54,55] More recent publications show that overall complication rates of LDN range from 4 to 30%,[44,56] which is in line with the complication rates we found. One could argue that the included studies in our analysis are hard to compare because not all of them assessed the same type of complications. Therefore, we decided to pool complication data into one group, i.e., perioperative complications, and found no difference between BMI cohorts.

Five of the included studies in the review reported zero donor deaths, and the other nine did not report on mortality.

A statistically significant difference in increase in postoperative serum creatinine was found, but no difference was found in GFR between the two BMI groups. A study conducted by Rizvi *et al.*[57] also shows that obese donors have no greater decline in GFR compared with nonobese donors.

Tavakol *et al.*[36] and Reese *et al.*[33] assessed kidney function using the estimated GFR calculated with the modification of diet in renal diseases equation.[58] As this is an estimation of the GFR, reported values may differ from the actual GFR.

We should acknowledge the fact that not all of the included studies used the same postoperative schedule of follow-up visits for the donors.

Limitations

A concern that could not be entirely analyzed is the long-term effect of LDN on overweight or obese live kidney donors. Even though this was not the primary aim of our meta-analysis, we felt the need to address this matter. The main reason why clinicians are reluctant to include high BMI donors is because of the increased risk for the metabolic syndrome. Hsu *et al.*[59] showed in 2006 that, with increasing BMI, the relative risk of developing end-stage renal disease is also increasing. Persons with a BMI between 30 and 34.9 already have an adjusted risk ratio of 3.57. However, we should note that the subjects described were people with a high BMI and not a highly selected group of live kidney donors with a high BMI (and thus otherwise healthy). Interestingly, Ibrahim *et al.*[60] demonstrated in 2009 that, overall, kidney donors have a better long-term outcome in terms of developing end-stage renal disease than do nondonors and that no major elevations in serum creatinine occur even 30 years after donation. Hypertension and estimated GFR <60 were associated with BMI, however with relatively low odds ratios (both 1.12). Recent data by Tent *et al.*[61] demonstrate that, in 100 donors (5-year follow-up), only the filtration fraction is significantly higher compared with that before donation. However, the filtration fraction is equal to that of the lean donors and is therefore not determined by BMI. Wu *et al.*[62] reported no significant difference in the 3-year follow-up of serum creatinine and blood pressure between low and high BMI donors. Amin *et al.*[63] stated that obese kidney donors are not at higher risk for renal dysfunction but do have an increased incidence of several cardiovascular disease risk factors. However, the number of analyzed donors is small. Aggarwal *et al.*[64] showed that, at 1 year post donation, there is no increased incidence of hypertension, proteinuria, or renal dysfunction in obese kidney donors compared with nonobese donors.

Our meta-analysis combines data across studies to prove that at least the short-term outcome of high BMI kidney donors is acceptable. The main limitation of this meta-analysis, as with any overview, is that the outcome definitions (for serum creatinine, GFR, and complications) are not the same across studies. Sensitivity analyses were performed to check whether the results remained significant (or gained significance). Publication bias might account for some of the effects we observed. The comprehensive search in multiple databases and extensive scrutinizing of the reference lists minimized the presence of publication bias. On exploring heterogeneity using funnel plots and χ^2 and inconsistency (I^2) statistics, significant heterogeneity was found to be minimal.

Despite our conclusion that BMI only correlates with three outcome measures, we still advise that obese patients be encouraged to lose weight before kidney donation and be excluded if they have other associated comorbidities. Meticulous postoperative follow-up and prevention of weight gain of these donors would be very important. In line with this, according to several international guidelines, every person with a BMI above 40 or a BMI higher than 35 with comorbidities should be advised to undergo bariatric surgery.[65–67] Furthermore, as we do not know the exact number of donors with a BMI over 40 in our analysis, we should be careful in stating that a BMI higher than this value is no contraindication for LDN. Obese donors should be informed about possible risks, such as the general risk of complications during surgery. In addition to this, healthy lifestyle education should be available to all living donors.[9]

Overall, on the basis of the results of our systemic review and meta-analysis, we conclude, regarding short-term outcome, that a high BMI in itself is no contraindication for LDN. However, as long-term data are still scarce, careful selection of possible live kidney donors is of considerable importance.

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 (PRISMA) statement.[11]

Literature search strategy

A comprehensive database search was carried out. The following databases were searched from inception to January 2011: MEDLINE, Embase, and CENTRAL (the Cochrane Library 2011). Search terms were: (Living Donors [Mesh] AND "Body Weights and Measures"[Mesh]) OR (donor AND nephrectomy AND BMI) in PubMed. Other databases were searched with comparable terms, suitable for the specific database. We focused on the outcome of LDN and therefore excluded publications describing graft function or outcome in kidney transplant recipients. Additional articles or abstracts were retrieved by manually searching the reference lists of relevant publications. We excluded studies that assessed LDN using the open approach, as it is known that (post)operative outcome is significantly different than that of laparoscopic LDN.[40]

Literature screening

Studies were evaluated for inclusion by two independent reviewers for relevance to the subject. Study selection was accomplished through three levels of screening. At the first level, studies were excluded on the basis of title and if they were one of the following: review, case report, or comments. In addition, different studies describing the same population were excluded. At the second level, all abstracts were screened for relevance. If the abstract contained an indication that the article had several BMI cohorts, it was moved to the third level. For publications with no abstract, the full text was acquired. In level three, inclusion required that studies describe two or more groups of donors that were selected on the basis of their BMI or body weight and had relevant outcome measures in the donors.

Data extraction and critical appraisal

Data extraction was performed using electronic forms by two authors independently (JAL/SMH). All data regarding outcome in donors were extracted. Study authors were contacted to supply additional data or missing s.d.'s. In studies in which medians and ranges were given, raw data were requested to calculate means and s.d.'s. The quality of studies was assessed according to the Newcastle–Ottawa Scale for observational and cohort studies, which score selection, comparability, and outcome. Studies should have a Newcastle–Ottawa Scale-score equal to or greater than 6 in order to be included.[68]

Statistical analysis

A meta-analysis was performed using Review Manager version 5.1 (The Nordic Cochrane Center, Copenhagen, Denmark). Random-effects models were used.[69] Depending on the outcome, results were presented in forest plots with risk ratios or mean differences. Overall effects were determined using the *Z*-test. Ninety-five percent confidence intervals of these values were given and $P<0.05$ was considered statistically significant. Heterogeneity between studies was assessed by three methods. First, a Tau^2 test and a χ^2 test were conducted for statistical heterogeneity, with $P<0.05$ being considered statistically significant. In addition, I^2 statistics were used to assess clinical heterogeneity.[70] Some cohort studies could not be analyzed at first because of the fact that there were more than two cohorts.[23,26,31,33,35] To compare these studies, cohorts were pooled, and new means and s.d.'s were calculated.[18] Group means were weighted by the number of donors in each study group. Variance estimates for pre- to post-donation changes in outcomes were not reported in all studies; they were calculated as $\sigma^2_{\Delta}=\sigma^2_{pre}+\sigma^2_{post}—2\rho\sigma_{pre}\sigma_{post}$, where ρ represents the correlation between the pre- and post-donation values. A correlation of 0.5 was used to impute the missing change variance estimates.[71]

DISCLOSURE

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/ki

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