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META-ANALYSIS

Different techniques for harvesting grafts for living donor liver transplantation: A systematic review and meta-analysis

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Abstract

AIM

To perform a systematic review and meta-analysis on minimally *vs* conventional invasive techniques for harvesting grafts for living donor liver transplantation.

METHODS

PubMed, Web of Science, EMBASE, and the Cochrane Library were searched comprehensively for studies comparing MILDH with conventional living donor hepatectomy (CLDH). Intraoperative and postoperative outcomes (operative time, estimated blood loss, postoperative liver function, length of hospital stay, analgesia use, complications, and survival rate) were analyzed in donors and recipients. Articles were included if they: (1) compared the outcomes of MILDH and CLDH; and (2) reported at least some of the above outcomes.

RESULTS

Of 937 articles identified, 13, containing 1592 patients, met our inclusion criteria and were included in the meta-analysis. For donors, operative time [weighted mean difference (WMD) = 20.68, 95%CI: -6.25-47.60, P = 0.13] and blood loss (WMD = -32.61, 95%CI: -80.44-5.21, P = 0.18) were comparable in the two groups. In contrast, analgesia use (WMD = -7.79, 95%CI: -14.06-1.87, P = 0.01), postoperative complications [odds ratio (OR) = 0.62, 95%CI: 0.44-0.89, P = 0.009], and length of hospital stay (WMD): -1.25, 95%CI: -2.35-0.14, P = 0.03) significantly favored MILDH. No differences were observed in recipient outcomes, including postoperative complications (OR = 0.93, 95%CI: 0.66-1.31, P = 0.68) and survival rate (HR = 0.96, 95%CI: 0.27-3.47, P = 0.95). Funnel plot and statistical methods showed a low probability of publication bias.

CONCLUSION

MILDH is safe, effective, and feasible for living donor liver resection with fewer donor postoperative complications, reduced length of hospital stay and analgesia requirement than CLDH.

Key words: Living donor hepatectomy; Graft harvesting; Minimally invasive techniques; Conventional invasive approaches; Meta-analysis

Core tip: Minimally invasive procedures have been increasingly used in liver resection, as they are considered safe and effective. Concerns have been raised, however, about the feasibility and donor safety of minimally invasive living donor hepatectomy. We analyzed 13 articles, containing 1592 patients, to compare two techniques for harvesting grafts for living donor liver transplantation. Finally, we concluded that minimally invasive procedures are safe, effective, and feasible for living donor liver resection, with fewer donor postoperative complications and reduced length of hospital stay and analgesia requirement than conventional approaches.

Li H, Zhang JB, Chen XL, Fan L, Wang L, Li SH, Zheng QL, Wang XM, Yang Y, Chen GH, Wang GS. Different techniques for harvesting grafts for living donor liver transplantation: A systematic review and meta-analysis. *World J Gastroenterol* 2017; 23(20): 3730-3743 Available from: URL: http://www.wjgnet.com/1007-9327/full/v23/i20/3730.htm DOI: http://dx.doi.org/10.3748/wjg.v23.i20.3730

INTRODUCTION

Since the first reported successful human liver transplantation in 1967[1], this technique has gained worldwide acceptance, becoming the best and most common treatment for patients with end-stage liver disease. Because of the shortage of deceased donor organs, especially in East Asian countries, living donor liver transplantation (LDLT) has become an established treatment modality for patients with end-stage liver disease[2]. In 1990, the first successful pediatric LDLT, using a left lateral section graft from a mother to her son, was reported in Australia[3]. Since then, the feasibility and safety of pediatric LDLT have been well documented[4]. Donor safety is considered paramount, as donor hepatectomy is a major surgery for healthy individuals[5]. However, the large permanent abdominal incision scar resulting from conventional open surgery may cause mental and physical stress among some putative living donors, especially young unmarried women, resulting in hesitation or unwillingness to donate liver tissue[4,6].

Although conventional living donor hepatectomy (CLDH) is safe, approximately 40% of donors have experienced postoperative complications[7-9]. Minimally invasive liver surgery has been widely used to treat patients with various liver diseases. Although laparoscopic liver surgery has resulted in lower rates of surgical morbidity and reduced postoperative pain and recovery time when compared with standard liver surgery[10,11], minimally invasive approaches to living donor hepatectomy are not generally performed. Minimally invasive living donor hepatectomy (MILDH), involving either a laparoscopic approach or a hybrid technique, has been compared with CLDH in several centers.

Although studies have compared outcomes following MILDH and CLDH, most of these studies were small series with unclear results[12-15]. Thus, their relative benefits for donors have not been investigated. This systematic review and meta-analysis analyzed studies comparing MILDH with CLDH to evaluate the safety, efficacy, and potential advantages of MILDH.

MATERIALS AND METHODS

Objective and groups

This meta-analysis was performed to compare the feasibility and donor safety of MILDH with CLDH, including evaluations of recipient survival rates. Outcomes compared included perioperative complications, estimated blood loss (EBL), requirement for analgesics, overall survival, operative time, postoperative liver function and hospital costs. MILDH in this study included fully laparoscopic and laparoscopy-assisted approaches, upper midline incision with or without laparoscopic assistance, and a hybrid approach

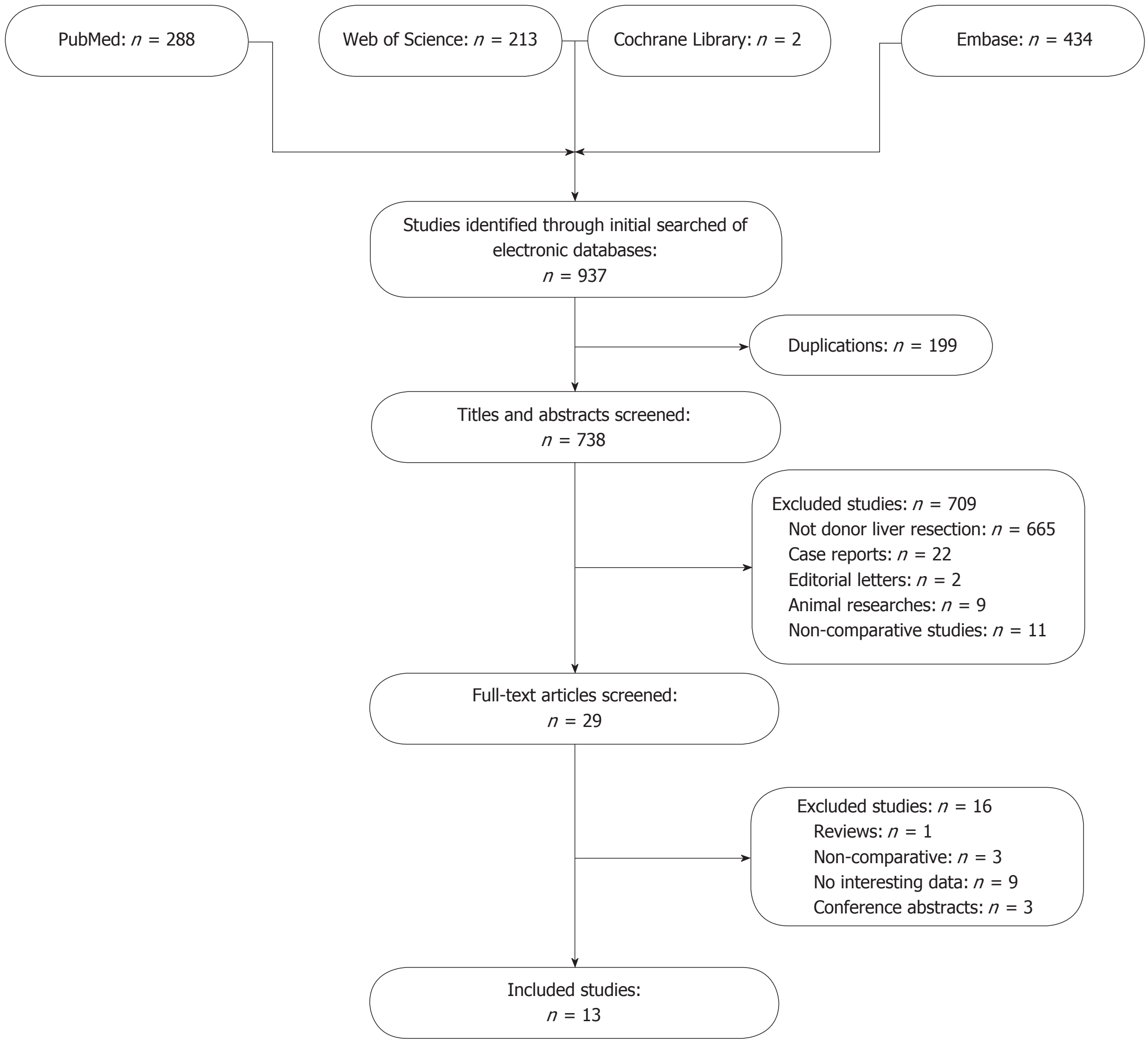


Figure 1 Flow diagram of study identification, inclusion and exclusion.

with incision length ≤ 15 cm. CLDH included standard open donation with a large subcostal incision, Mercedes incision, L-shaped incision, and a large J-shaped or midline skin incision.

Search strategy and criteria

PubMed, EMBASE, the Web of Science, and Cochrane Library were searched for studies comparing MILDH with CLDH published through December 2015. There were no restrictions on publication date, type or language. Search terms included "donor hepatectomy" OR "liver transplantation" OR "donor liver resection" OR "donor sectionectomy" AND "open surgery" OR "right subcostal incision" OR "regular surgery" OR "conventional surgery" AND "laparoendoscopic" OR "laparoscopic". The reference lists of all selected articles were manually searched to determine if they should be included.

The literature search identified 937 articles, of which 288 from PubMed, 434 from EMBASE, 213 from Web of Science, and two from the Cochrane Library (Figure 1). Two reviewers browsed the titles and abstracts independently. Articles were included if they: (1) compared the outcomes of MILDH and CLDH; and (2) reported at least some of the above outcomes. Articles were excluded if were submitted by the same authors or the same institutions to avoid duplication of patient populations.

Of the 937 identified articles, 199 were duplications; 665 did not focus on donor liver resection; nine were in animals; 11 did not compare MILDH with CLDH; two were editorials; and 22 were case reports. The full texts of the remaining 29 articles were carefully reviewed. Of these, three did not compare MILDH with CLDH; nine did not include outcomes of interest; one was a review article; and three were conference abstracts. Finally, 13 articles[12-24] were included in this meta-analysis.

Data management

Data were analyzed by three authors (Li H, Zhang JB and Chen XL) independently. These reviewers were

Table 1 Quality of cohort studies evaluated with modified Newcastle-Ottawa scale

Ref.	Case definition	Selection		Definition of controls	Comparability		Outcomes		Quality score
		Representativeness	Selection of controls		Comparable for 1, 2, 3	Comparable for 4, 5	Assessment of outcomes	Integrity of follow-up	
Choi *et al*[16], 2012	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Choi *et al*[17], 2014	Yes	No	Yes	Yes	No	No	Yes	Yes	5
Makk *et al*[19], 2014	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	8
Marubashi *et al*[20], 2013	Yes	No	Yes	Yes	2, 3	4	Yes	Yes	7
Nagai *et al*[21], 2012	Yes	No	Yes	Yes	1, 3	4	Yes	Yes	7
Samstein *et al*[22], 2015	Yes	No	Yes	Yes	Yes	No	Yes	Yes	7
Soubrane *et al*[12], 2006	Yes	No	Yes	Yes	1,3	4	Yes	Yes	7
Suh *et al*[23], 2015	Yes	No	Yes	Yes	No	No	Yes	Yes	5

1 = gender; 2 = body max index; 3 = graft generation; 4 = age; 5 = haemoglobin.

Table 2 Quality of case-controlled studies evaluated with modified Newcastle-Ottawa scale

Ref.	Case definition	Selection		Definition of controls	Comparability		Outcomes		Quality score
		Representativeness	Selection of controls		Comparable for 1, 2, 3	Comparable for 4, 5	Ascertainment of exposure	Non-response	
Baker *et al*[13], 2009	Yes	No	Yes	Yes	Yes	4	Yes	Yes	7
Kim *et al*[14], 2009	Yes	No	Yes	Yes	Yes	4	Yes	Yes	7
Kim *et al*[18], 2011	Yes	No	Yes	Yes	1, 3	Yes	Yes	Yes	6
Thenappan *et al*[15], 2011	Yes	No	Yes	Yes	No	No	Yes	Yes	7
Zhang *et al*[24], 2014	Yes	No	Yes	Yes	Yes	4	Yes	Yes	7

1 = gender; 2 = body max index; 3 = graft generation; 4 = age; 5 = haemoglobin.

blinded to the authors, institutions, and journals of publication of all selected articles. Any disagreements between the reviewers were settled by the senior author (Wang GS).

Donor outcomes of interest included operative time, EBL, hospital costs, length of hospital stay, postoperative complications, analgesic use, graft weight, and postoperative liver function. Liver function was evaluated based on peak serum levels of aspartate transaminase (AST), alanine aminotransferase (ALT), and total bilirubin (TB). Recipient outcomes of interest included postoperative complications, postoperative liver function, and survival rate. If survival rate did not appear directly in an article, it was determined using Engauge software.

Quality assessment

The methodological quality of retrospective studies was assessed using the modified Newcastle-Ottawa scale, which consists of three factors: patient selection, comparability of the study groups, and assessment of outcome[25,26]. As the maximum total score on this scale is 9, studies with scores $\geqslant$ 7 were defined as high-quality studies (Tables 1 and 2).

Data were pooled with the Cochrane Collaboration's Review Manager 5.3 (Cochrane Collaboration, Oxford, United Kingdom). Mean differences and 95%CIs were calculated to pool functional outcomes. Statistical heterogeneity among studies was assessed using the χ^2 test with significance set at P < 0.1, and heterogeneity was quantified using the I^2 statistic. A random-effects model was used if there was heterogeneity among studies; otherwise, a fixed-effects model was used[27].

Subgroups and publication bias

Grafts harvested from the left and right sides of the liver differ in weight, vascularity, and bile duct distribution, affecting outcomes in both donors and recipients. Therefore, subgroup analyses were performed on donors who underwent left hepatectomy (LH) and right hepatectomy (RH). Operative time, postoperative complications, and EBL were analyzed in these subgroups.

The publication bias of selected articles was analyzed by funnel plots, which were produced by Review Manager 5.3. If outcomes were associated with significant heterogeneity among studies, a random-effects model was used to minimize bias resulting from this heterogeneity.

Table 3 Characteristics of included studies

Ref.	Level of evidence	Patient no.		Left/right	Recipients	TMI	TCI	Matching	Quality score
		MILDH	CLDH						
Baker *et al*[13], 2009	3b	33	33	Right	W	LA	Midline epigastric	1, 2, 3, 4	7
Choi *et al*[16], 2012	2b	60	90	Right	W/O	LA	Right subcostal	1, 2, 3, 4, 5	8
Choi *et al*[17], 2014	4	25	484	Right	W/O	HAL or LA	Mercedes-Benz or L-shaped	NA	5
Kim *et al*[14], 2009	3b	23	23	Right	W	Upper midline	J-shaped	1, 2, 3, 4	7
Kim *et al*[18], 2011	3b	11	11	Left	W	L	J-shaped or midline	1, 3, 4, 5	7
Makk *et al*[19], 2014	2b	26	24	Right	W	LA	Right subcostal with midline extension	1, 2, 3, 4, 5	8
Marubashi *et al*[20], 2013	2b	31	79	Left	W	LA	Mercedes	2, 3, 4	7
Nagai *et al*[21], 2012	2b	28	30	Right	W	Hal or upper midline	Mercedes	1, 3, 4	7
Samstein *et al*[22], 2015	2b	22	20	Left	W	L	Midline	1, 2, 3	7
Soubrane *et al*[12], 2006	2b	16	14	Left	W	L	Subcostal	1, 3, 4	7
Suh *et al*[23], 2015	4	161	268	Un	W	LA or Upper midline	L-shaped	NA	5
Thenappan *et al*[15], 2011	3b	15	15	Un	W	LA or Minimally-access	Midline epigastric with subcostal	NA	6
Zhang *et al*[24], 2014	3b	25	25	Right	W	LA	Right subcostal	1, 2, 3, 4	7

MILDH: Minimally invasive living donor hepatectomy; CLDH: Conventional living donor hepatectomy; Left/right: Graft from left or right liver lobe of donors; Recipients: With or without analyzing recipients; TMI: Type of minimally incisions; TCI: Type of conventional incisions; W: With; W/O: Without; Un: Unclear or not only one kind; L: Laparoscopic approach; LA: Laparoscopy-assisted; HAL: Hand-assisted laparoscopic; Matching: 1 = gender; 2 = body max index; 3 = graft generation; 4 = age; 5 = haemoglobin; NA: No data available.

Characteristics of selected articles

The meta-analysis included 13 articles[12-24] involving 1592 patients; the characteristics of the selected articles are shown in Table 3. Primary outcomes of interest included donor safety, as determined by perioperative complications and EBL; donor requirement for analgesics after hepatectomy; and recipient survival rate. Secondary outcomes included postoperative liver function, length of hospital stay, and total hospital cost. The level of evidence of these articles was estimated using the United Kingdom Cochrane Centre of Evidence (2001)[28]. Six articles described cohort studies comparing contemporary series of patients (level of evidence: 2b)[12,16,19-22]; five articles were retrospective case-control studies (level of evidence: 3b)[13-15,18,24], and two articles were retrospective studies using historical series as controls (level of evidence: 4)[17,23].

RESULTS

Donor outcomes

Of the 1592 donors included in the 13 articles, 476 underwent MILDH and 1116 underwent CLDH (Table 4)[12-24]. Operative times were similar in the two groups [weighted mean difference (WMD) = 20.68, 95%CI: -6.25-47.60, P = 0.13] (Figure 2). Twelve studies[12-18,20-24] analyzed EBL among 1542 donors, finding no significant difference between those who underwent MILDH and CLDH (WMD = -32.61, 95%CI: -80.44-5.21, P = 0.18). Hospital costs were reported by only two articles[18,24], finding no significant difference between the two donor groups (WMD = 0.56, 95%CI: -0.62-0.74, P = 0.35). Ten studies[12,14-16,18,20-24], including 967 patients, evaluated the length of hospital stay, finding that donors who underwent MILDH group had a significantly shorter hospital stay than those who underwent CLDH (WMD: -1.25, 95%CI: -2.35-0.14, P = 0.03). Twelve articles[12-16,18-24] analyzed postoperative complications, finding that the rate of postoperative complications was significantly lower in the MILDH than in the CLDH group (OR = 0.62, 95%CI: 0.44-0.89, P = 0.009). Ten articles[12-16,18-24] compared postoperative complications of donors between the two groups, finding no statistical difference (WMD = 0.56, 95%CI: 0.27-1.18, P = 0.13) (Figure 3). Five articles[12,14-16,24] reported analgesic use, finding that the total analgesic use among donors was significantly lower in the MILDH than in the CLDH group (WMD = -7.79, 95%CI: -14.06-1.87, P = 0.01) (Figure 4). Five studies[12-14,19,24] reported graft weight, finding no significant difference between the two groups (WMD = -3.32, 95%CI: -22.25-15.61, P = 0.73). Seven articles[14,16,18,19,21,23,24] compared postoperative liver function, finding no significant difference between the two groups in peak AST (WMD = 6.41, 95%CI: -3.79-16.60, P = 0.50), ALT (WMD = 11.86, 95%CI: -10.84-34.56, P = 0.031), and TB (WMD = -0.10, 95%CI: -0.26-0.06, P = 0.21) concentrations (Figure 5).

Recipient outcomes

Six studies[12,13,18,19,23,24] compared postoperative complications in recipients, finding no significant difference in postoperative complication rates between the two groups (OR = 0.93, 95%CI: 0.66-1.31, P = 0.68).

Table 4 Results of meta-analysis comparison of minimally invasive living donor hepatectomy and conventional living donor hepatectomy

Outcome of interest	Study (*n*)	MILDH (*n*)	CLDH (*n*)	WMD/OR (95%CI)	*P* value	Study heterogeneity			*P* value
						I^2	df	I^2, %	
Graft weight (g)	5	123	119	-3.32 (-22.25,15.61)	0.73	6.56	4	39	0.16
Donor outcomes									
Operative time (min)	13	476	1116	20.68 (-6.25,47.60)	0.13	147.62	12	92	< 0.01
Estimated blood loss (mL)	12	450	1092	-32.61 (-80.44,15.21)	0.18	61.26	11	82	< 0.01
Hospital cost (dollar)	2	36	36	0.56 (-0.62,1.74)	0.35	4.24	1	76	0.04
Length of hospital stay (d)	10	392	575	-1.25 (-2.35,-0.14)	0.03	99.31	9	91	< 0.01
Post complications	12	451	632	0.62 (0.44,0.89)	0.009	4.40	11	0	0.96
Analgesic use (h)	5	139	167	-7.97 (-14.06,-1.87)	0.01	7.50	4	47	0.11
Liver function									
Post AST peak (IU/L)	7	334	471	6.41 (-3.79.16.60)	0.22	13.60	6	56	0.03
Post ALT peak (IU/L)	8	350	485	11.86 (-10.84,34.57)	0.31	15.39	7	55	0.03
Post TB peak (mg/dL)	7	324	461	-0.10 (-0.26,0.06)	0.21	2.10	6	0	0.91
Recipient outcomes									
Liver function									
Post AST peak (IU/L)	3	59	59	-28.73 (-86.76,29.31)	0.33	0.90	2	0	0.64
Post ALT peak (IU/L)	3	59	59	-29.98 (-87.65,27.7)	0.31	0.31	2	0	0.86
Post TB peak (mg/dL)	3	59	59	-0.96 (-2.57,0.65)	0.24	1.26	2	0	0.53
Surviving	3			0.96 (0.27,3.47)	0.95	0.11	2	0	0.95
Post complications	6	272	375	0.93 (0.66,1.31)	0.68	3.28	5	0	0.66

MILDH: Minimally invasive living donor hepatectomy; CLDH: Conventional living donor hepatectomy; WMD/OR: Weight mean difference/odds ratio; df: Degree of freedom; Post: Postoperative.

Seven studies[12,13,18,19,23,24] analyzed postoperative biliary complications for recipients, showing no significant difference between the two groups (WMD = 1.10, 95%CI: 0.73-1.66, *P* = 0.65) (Figure 6). Three studies[14,18,24] compared postoperative liver function in recipients, finding no significant differences between the two groups in peak AST (WMD = -28.73, 95%CI: -86.76-29.31, *P* = 0.33), ALT (WMD = -29.98, 95%CI: -87.65-27.7, *P* = 0.31), and TB (WMD = -0.96, 95%CI: -2.57-0.65, *P* = 0.24) concentrations. Three articles[13,20,22] compared overall recipient survival, finding no significant difference between the two groups in recipient survival rate (HR = 0.96, 95%CI: 0.27-3.47, *P* = 0.95) (Figure 7).

Subgroup analysis

Postoperative complications, operative time, and EBL were analyzed in donors who underwent RH and LH. In assessing postoperative complications, three studies[15,17,23] were excluded, as data were unmatched. Pooled data of six studies[13,14,16,19,21,24] showed no significant difference in postoperative complication rates in donors who underwent RH by MILDH and CLDH, but did favor MILDH (OR = 0.73, 95%CI: 0.45-1.19, *P* = 0.21). In contrast, pooled data of four studies[12,18,20,22] that evaluated donors who underwent LH showed that the postoperative complication rate was significantly lower in patients who underwent MILDH (OR = 0.37, 95%CI: 0.16-0.87, *P* = 0.02) (Figure 8).

Seven studies[13,14,16,17,19,21,24] compared operative time for RH, finding no significant difference between MILDH and CLDH (WMD = 14.99, 95%CI: -22.52-52.50, *P* = 0.43). In contrast, four studies[12,18,20,22] that compared operative time for LH found that this time was significantly shorter for CLDH (WMD = 62.04, 95%CI: 37.04-87.03, *P* < 0.0001). The remaining two studies[15,23] were excluded (Figure 9).

Six studies[13,14,16,17,21,24] reported EBL in donors who underwent RH, finding no significant difference between the MILDH and CLDH groups (WMD = -1.67, 95%CI: -66.05-62.72, *P* = 0.96). Similarly, four studies[12,18,20,22] compared EBL in donors who underwent LH, finding no significant difference between the two groups (WMD = -93.04, 95%CI: -215.56-29.48, *P* = 0.14) (Figure 10).

Publication bias

The funnel plot of postoperative complications showed that all articles included in this meta-analysis were symmetrically distributed around the center line, indicating a lack of obvious publication bias (Figure 11).

DISCUSSION

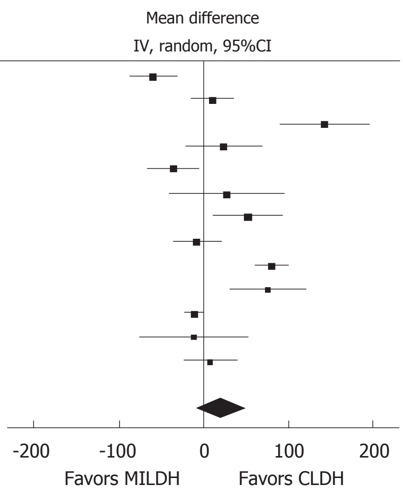
Primary laparoscopic living donor hepatectomy was introduced in 2002 to reduce the impact of open hepatectomy on donors[29]. Since then, minimally invasive approaches have been considered safe and effective, reducing postoperative pain and surgical morbidity and providing a faster recovery time[9,11,30,31]. Despite these findings, minimally invasive approaches to living donor hepatectomy have not been accepted by consensus guidelines. A hybrid technique for donor hepatectomy was introduced in 2006[32], and subsequent studies have compared minimally invasive and conventional donor liver resection[33]. To date, however, these two methods have not been

Operative time

Study or subgroup	MILDH Mean (min)	MILDH SD (min)	MILDH Total	CLDH Mean (min)	CLDH SD (min)	CLDH Total	Weight	Mean difference IV, random, 95%CI
Baker 2009	256	48	33	316	61	33	8.3%	-60.00 (-86.48, -33.52)
Choi H 2012	313.52	80.66	60	303.22	61.49	90	8.5%	10.30 (-13.74, 34.34)
Choi Y 2014	415.4	131.89	25	272.4	49.7	484	6.8%	143.00 (91.11, 194.89)
Kim 2011	330	68	11	306	29	11	7.3%	24.00 (-19.69, 67.69)
Kim S 2009	232.3	29.2	23	268.8	67.1	23	8.2%	-36.50 (-66.41, -6.59)
Makk 2014	702.5	124.11	26	675.21	117.54	24	5.8%	27.29 (-39.70, 94.28)
Marubashi 2013	435	103	31	383	73	79	7.6%	52.00 (12.33, 91.67)
Nagai 2012	363	53	28	371	52	30	8.3%	-8.00 (-35.05, 19.05)
Samstein 2015	478	8	22	398	42	20	8.7%	80.00 (61.29, 98.71)
Soubrane 2006	320	67	16	244	55	14	7.3%	76.00 (32.32, 119.68)
Suh 2015	265	52.09	161	275.9	45.7	268	9.0%	-10.90 (-20.63, -1.17)
Thenappan 2011	312	67.8	15	324	105.6	15	6.0%	-12.00 (-75.51, 51.51)
Zhang 2013	385.9	47.7	25	378.1	59	25	8.2%	7.80 (-21.87, 37.47)
Total (95%CI)			476			1116	100.0%	20.68 (-6.25, 47.60)

Heterogeneity: $Tau^2 = 2078.56$; $\chi^2 = 147.62$, df = 12 ($P < 0.00001$); $I^2 = 92\%$

Test for overall effect: $Z = 1.51$ ($P = 0.13$)



Estimated blood loss

Study or subgroup	MILDH Mean (min)	MILDH SD (min)	MILDH Total	CLDH Mean (min)	CLDH SD (min)	CLDH Total	Weight	Mean difference IV, random, 95%CI
Baker 2009	417	217	33	550	305	33	6.5%	-133.00 (-260.71, -5.29)
Choi H 2012	590	616.98	60	531.7	322.59	90	4.8%	58.30 (-111.45, 228.05)
Choi Y 2014	339.7	240.6	25	310.5	206.2	484	8.2%	29.20 (-66.89, 125.29)
Kim 2011	396	72	11	464	78	11	10.1%	-68.00 (-130.73, -5.27)
Kim S 2009	185.6	59.2	23	218.8	67.1	23	11.4%	-33.20 (-69.77, 3.37)
Marubashi 2013	435	103	31	383	73	79	11.2%	52.00 (12.33, 91.67)
Nagai 2012	316	121	28	212	114	30	10.2%	104.00 (43.40, 164.60)
Samstein 2015	177.3	100.6	22	375.3	190.9	20	8.3%	-198.00 (-291.63, -104.37)
Soubrane 2006	18.7	44.2	16	199.2	185.4	14	8.0%	-180.50 (-280.00, -81.00)
Suh 2015	318	194.5	161	333	215.2	268	11.2%	-15.00 (-54.58, 24.58)
Thenappan 2011	1033	1096	15	733	457	15	0.6%	300.00 (-300.93, 900.93)
Zhang 2013	378.4	112.5	25	422.6	139.3	25	9.6%	-44.20 (-114.39, 25.99)
Total (95%CI)			450			1092	100.0%	-32.61 (-80.44, 15.21)

Heterogeneity: $Tau^2 = 4896.48$; $\chi^2 = 61.26$, df = 11 ($P < 0.00001$); $I^2 = 82\%$

Test for overall effect: $Z = 1.34$ ($P = 0.18$)

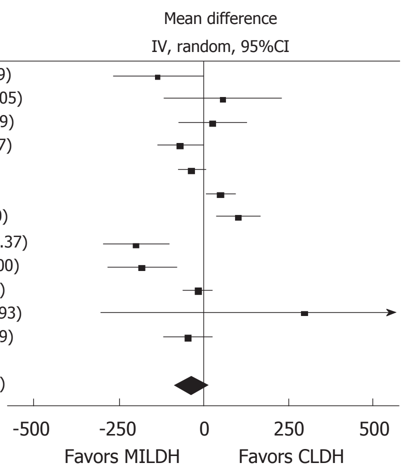


Figure 2 Forest plots and meta-analysis of intraoperative outcomes of donors.

Study or subgroup	MILDH Events	MILDH Total	CLDH Events	CLDH Total	Weight	Odds ratio M-H, fixed, 95%CI
Baker 2009	1	35	1	35	4.8%	1.00 (0.06, 16.65)
Choi H 2012	3	60	8	90	30.0%	0.54 (0.14, 2.12)
Choi Y 2014	1	25	28	484	13.0%	0.68 (0.09, 5.20)
Kim S 2009	0	23	1	23	7.3%	0.32 (0.01, 8.25)
Nagai 2012	1	28	2	30	9.2%	0.52 (0.04, 6.06)
Samstein 2015	1	22	2	20	9.9%	0.43 (0.04, 5.13)
Soubrane 2006	1	14	0	16	2.1%	3.67 (0.14, 97.49)
Suh 2015	0	161	2	268	9.3%	0.33 (0.02, 6.92)
Thenappan 2011	0	15	1	15	7.2%	0.31 (0.01, 8.28)
Zhang 2013	0	25	1	25	7.3%	0.32 (0.01, 8.25)
Total (95%CI)		408		1006	100.0%	0.56 (0.27, 1.18)
Total events	8		46			

Heterogeneity: $\chi^2 = 1.98$, df = 9 ($P = 0.99$); $I^2 = 0\%$

Test for overall effect: $Z = 1.51$ ($P = 0.13$)

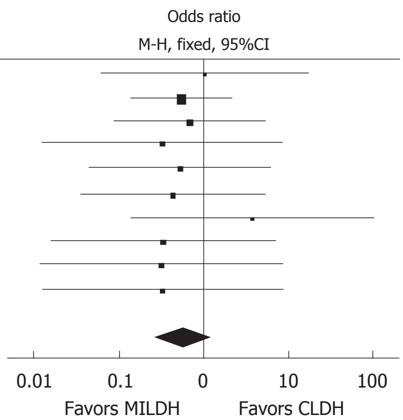


Figure 3 Forest plot and meta-analysis of postoperative biliary complications for donors.

systematically analyzed in large donor populations.

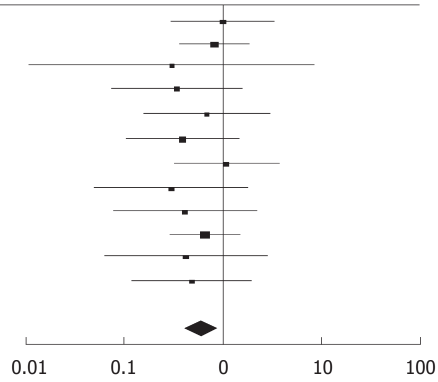
This systematic review and meta-analysis of 13 studies, involving 1592 patients, compared minimally invasive with conventional methods for living donor hepatectomy, finding that MILDH was not less safe than CLDH. MILDH was associated with a significantly lower postoperative complication rate, a significantly lower analgesic requirement, and a significantly shorter hospital stay for donors than CLDH. However, operative time, EBL, graft weight, hospital costs, and postoperative liver function for donors were similar in the two groups. Moreover, comparisons of

Postoperative complications

Study or subgroup	MILDH Events	MILDH Total	CLDH Events	CLDH Total	Weight	Odds ratio M-H, fixed, 95%CI
Baker 2009	7	33	7	33	7.0%	1.00 (0.31, 3.26)
Choi H 2012	12	60	21	90	17.1%	0.82 (0.37, 1.83)
Kim 2011	0	11	1	11	1.8%	0.30 (0.01, 8.32)
Kim S 2009	3	23	7	23	7.7%	0.34 (0.08, 1.54)
Makk 2014	4	26	5	24	5.6%	0.69 (0.16, 2.95)
Marubashi 2013	3	31	17	79	11.0%	0.39 (0.11, 1.44)
Nagai 2012	7	28	7	30	6.4%	1.10 (0.33, 3.65)
Samstein 2015	2	22	5	20	6.1%	0.30 (0.05, 1.76)
Soubrane 2006	3	16	5	14	5.5%	0.42 (0.08, 2.19)
Suh 2015	9	161	22	268	19.8%	0.66 (0.30, 1.48)
Thenappan 2011	2	15	4	15	4.4%	0.42 (0.06, 2.77)
Zhang 2013	4	25	7	25	7.5%	0.49 (0.12, 1.95)
Total (95%CI)		451		632	100.0%	0.62 (0.44, 0.89)
Total events	56		108			

Heterogeneity: χ^2 = 4.40, df = 11 (P = 0.96); I^2 = 0%

Test for overall effect: Z = 2.60 (P = 0.009)

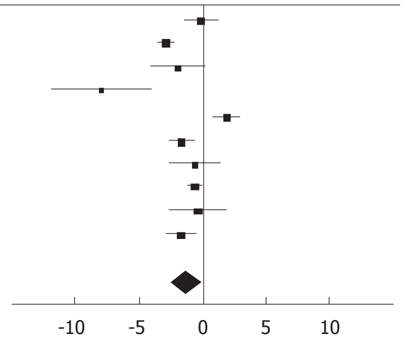


Length of hospital stay

Study or subgroup	MILDH Mean (d)	MILDH SD (d)	MILDH Total	CLDH Mean (d)	CLDH SD (d)	CLDH Total	Weight	Mean difference IV, random, 95%CI (d)
Choi H 2012	11.9	3.96	60	12	3.61	90	10.7%	-0.10 (-1.35, 1.15)
Kim 2011	6.9	0.3	11	9.8	0.9	11	12.0%	-2.90 (-3.46, -2.34)
Kim S 2009	10	2.9	23	11.9	4.1	23	8.7%	-1.90 (-3.95, 0.15)
Marubashi 2013	10.33	3.3	31	18.3	16.7	79	4.9%	-7.97 (-11.83, -4.11)
Nagai 2012	7.8	2.3	28	5.9	1.2	30	11.4%	1.90 (0.95, 2.85)
Samstein 2015	4.27	1.5	22	5.95	1.5	20	11.5%	-1.68 (-2.59, -0.77)
Soubrane 2006	7.5	2.3	16	8.1	3	14	9.0%	-0.60 (-2.53, 1.33)
Suh 2015	8.6	2.04	161	9.2	3.3	268	12.1%	-0.60 (-1.11, -0.09)
Thenappan 2011	6	2	15	6.4	3.68	15	8.5%	-0.40 (-2.52, 1.72)
Zhang 2013	7	1.4	25	8.7	2.4	25	11.1%	-1.70 (-2.79, -0.61)
Total (95%CI)			392			575	100.0%	-1.25 (-2.35, -0.14)

Heterogeneity: Tau^2 = 2.56; χ^2 = 99.31, df = 9 (P < 0.00001); I^2 = 91%

Test for overall effect: Z = 2.21 (P = 0.03)



Analgesics use

Study or subgroup	MILDH Mean (h)	MILDH SD (h)	MILDH Total	CLDH Mean (h)	CLDH SD (h)	CLDH Total	Weight	Mean difference IV, fixed, 95%CI (h)
Choi H 2012	58.4	24.6	60	61.2	26.4	90	54.3%	-2.80 (-11.08, 5.48)
Kim S 2009	91.2	57.6	23	134.4	76.8	23	2.4%	-43.20 (-82.43, -3.97)
Soubrane 2006	48	21.6	16	52.8	21.6	14	15.5%	-4.80 (-20.29, 10.69)
Thenappan 2011	47.6	23.2	15	56.8	40.2	15	6.7%	-9.20 (-32.69, 14.29)
Zhang 2013	57.6	24	25	76.8	24	25	21.0%	-19.20 (-32.50, -5.90)
Total (95%CI)			139			167	100.0%	-7.97 (-14.06, -1.87)

Heterogeneity: χ^2 = 7.50, df = 4 (P = 0.11); I^2 = 47%

Test for overall effect: Z = 2.56 (P = 0.01)

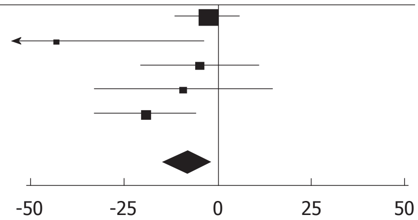


Figure 4 Forest plots and meta-analysis of postoperative outcomes of donors.

postoperative recipient liver function, complication rate, and survival rate showed no differences between these two groups.

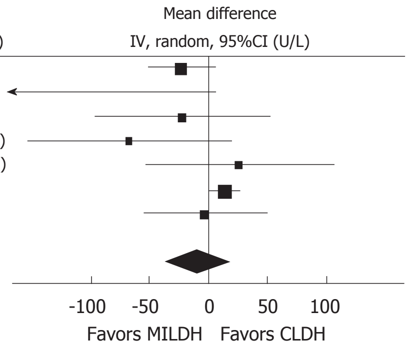
Donor safety is of paramount importance during LDLT, regardless of the technique used. Our pooled data on perioperative outcomes indicated that MILDH was as safe and effective for LDLT as CLDH.

Our finding that operative times were comparable in the two groups is inconsistent with several studies suggesting that MILDH was associated with a shorter average operative time[13,14]. This may have been owing to the dissimilarity of operative procedures in different institutions. Nevertheless, the operative time for making an upper midline incision was generally shorter in the MILDH group, as the incision was shorter. Although the small incision reduced the time spent in opening and closing the abdomen, it was apparently balanced by the additional time required to mobilize grafts laparoscopically, as this approach required frequent installation and removal of laparoscopic devices, application of the hanging maneuver, and dissection of the deep parenchyma.

EBL did not differ significantly between the MILDH and CLDH groups, although it was lower in the MILDH group. Laparoscopic parenchymal dissection and the high intra-abdominal pressure attained by pneumoperitoneum use apparently resulted in lower blood loss in the MILDH group[34]. Furthermore, Peak AST

Study or subgroup	MILDH Mean (U/L)	MILDH SD (U/L)	MILDH Total	CLDH Mean (U/L)	CLDH SD (U/L)	CLDH Total	Weight	Mean difference IV, random, 95%CI (U/L)
Choi H 2012	169.2	78.4	60	191.8	93.2	90	25.4%	-22.60 (-50.25, 5.05)
Kim 2011	191	124.2	11	459.4	444.9	11	0.9%	-268.40 (-541.37, 4.57)
Kim S 2009	166.6	117.3	23	189.1	137.8	23	9.6%	-22.50 (-96.46, 51.46)
Makk 2014	261.96	114.11	26	329.04	182.81	24	7.7%	-67.08 (-152.36, 18.20)
Nagai 2012	345	173	28	319	131	30	8.6%	26.00 (-53.39, 105.39)
Suh 2015	159.99	56.4	161	145.9	63.8	268	32.6%	14.09 (2.50, 25.68)
Zhang 2013	185.8	96.7	25	188.3	89.9	25	15.2%	-2.50 (-54.26, 49.26)
Total (95%CI)			334			471	100.0%	-9.14 (-36.00, 17.72)

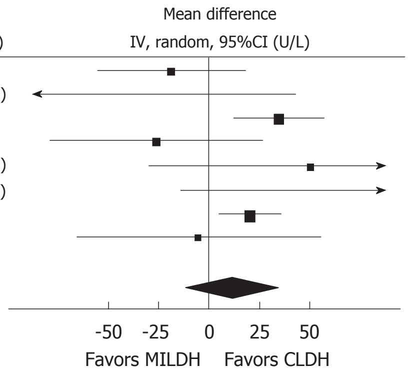
Heterogeneity: Tau^2 = 540.95; χ^2 = 13.60, df = 6 (P = 0.03); I^2 = 56%
Test for overall effect: Z = 0.67 (P = 0.50)



Peak ALT

Study or subgroup	MILDH Mean (U/L)	MILDH SD (U/L)	MILDH Total	CLDH Mean (U/L)	CLDH SD (U/L)	CLDH Total	Weight	Mean difference IV, random, 95%CI (U/L)
Choi H 2012	205.7	98.6	60	224.6	128.6	90	17.2%	-18.90 (-55.35, 17.55)
Kim 2011	269.6	256.7	11	492	367.2	11	0.7%	-222.40 (-487.16, 42.36)
Kim S 2009	188.4	47.1	23	153.9	26.5	23	24.0%	34.50 (12.41, 56.59)
Makk 2014	194	87.88	26	220.29	100.3	24	11.7%	-26.29 (-78.74, 26.16)
Nagai 2012	361	159	28	311	150	30	6.4%	50.00 (-29.68, 129.68)
Soubrane 2006	349.7	223.5	16	239.6	110.3	14	3.0%	110.10 (-13.72, 233.92)
Suh 2015	162.8	74.1	161	142.6	83.6	268	27.2%	20.20 (5.00, 35.40)
Zhang 2013	253	115.8	25	258.4	100.7	25	9.8%	-5.40 (-65.56, 54.76)
Total (95%CI)			350			485	100.0%	11.86 (-10.84, 34.57)

Heterogeneity: Tau^2 = 433.35; χ^2 = 15.39, df = 7 (P = 0.03); I^2 = 55%
Test for overall effect: Z = 1.02 (P = 0.31)



Peak TB

Study or subgroup	MILDH Mean (mg/dL)	MILDH SD (mg/dL)	MILDH Total	CLDH Mean (mg/dL)	CLDH SD (mg/dL)	CLDH Total	Weight	Mean difference IV, fixed, 95%CI (mg/dL)
Choi H 2012	2.05	0.78	60	2.28	0.87	90	34.2%	-0.23 (-0.50, 0.04)
Kim 2011	1.59	0.7	11	1.5	0.5	11	9.4%	0.09 (-0.42, 0.60)
Kim S 2009	2.9	1.5	23	3.2	1.2	23	4.0%	-0.30 (-1.09, 0.49)
Nagai 2012	2.8	1.9	28	2.8	1.3	30	3.4%	0.00 (-0.84, 0.84)
Soubrane 2006	1.08	0.32	16	1.11	0.33	14	44.8%	-0.03 (-0.26, 0.20)
Suh 2015	3.01	186	161	3.1	1.8	268	0.0%	-0.09 (-28.82, 28.64)
Zhang 2013	3.06	1.26	25	3.15	1.5	25	4.1%	-0.09 (-0.86, 0.68)
Total (95%CI)			324			461	100.0%	-0.10 (-0.26, 0.06)

Heterogeneity: χ^2 = 2.10, df = 6 (P = 0.91); I^2 = 0%
Test for overall effect: Z = 1.25 (P = 0.21)

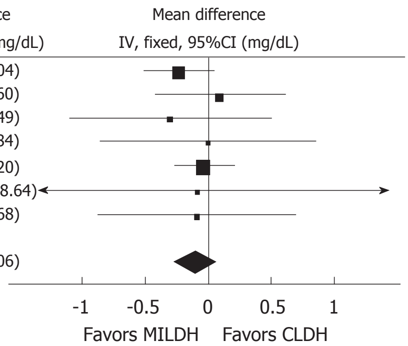


Figure 5 Forest plots and meta-analysis of postoperative liver function of donors.

Study or subgroup	MILDH Events	MILDH Total	CLDH Events	CLDH Total	Weight	Odds ratio M-H, fixed, 95%CI
Baker 2009	14	33	15	33	19.8%	0.88 (0.33, 2.34)
Kim 2011	1	11	0	11	1.0%	3.29 (0.12, 89.81)
Makk 2014	2	26	2	24	4.4%	0.92 (0.12, 7.07)
Soubrane 2006	3	16	4	14	8.0%	0.58 (0.10, 3.19)
Suh 2015	31	161	45	268	62.6%	1.18 (0.71, 1.96)
Thenappan 2011	2	15	1	15	2.0%	2.15 (0.17, 26.67)
Zhang 2013	1	25	1	25	2.2%	1.00 (0.06, 16.93)
Total (95%CI)		287		390	100.0%	1.10 (0.73, 1.66)
Total events	54		68			

Heterogeneity: χ^2 = 1.55, df = 6 (P = 0.96); I^2 = 0%
Test for overall effect: Z = 0.45 (P = 0.65)

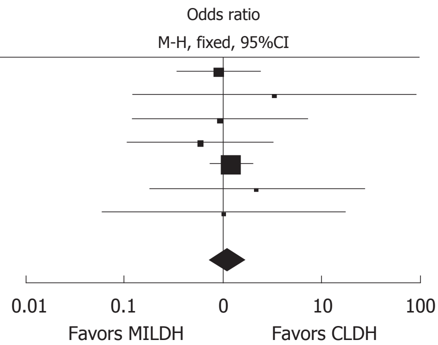


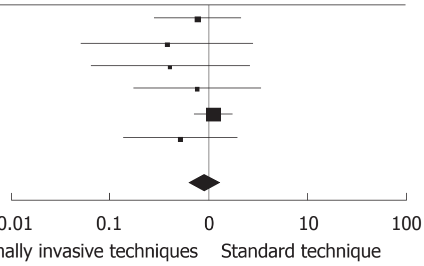
Figure 6 Forest plot and meta-analysis of postoperative biliary complications for recipients.

Postoperative complications

Study or subgroup	Minimally invasive techniques Events	Total	Standard technique Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
Baker 2009	17	33	19	33	13.6%	0.78 (0.30, 2.07)
Kim 2011	2	11	4	11	4.8%	0.39 (0.05, 2.77)
Makk 2014	2	26	4	24	5.7%	0.42 (0.07, 2.52)
Soubrane 2006	7	16	7	14	6.2%	0.78 (0.18, 3.28)
Suh 2015	53	161	81	268	60.2%	1.13 (0.74, 1.72)
Zhang 2013	5	25	8	25	9.5%	0.53 (0.15, 1.93)
Total (95%CI)		272		375	100.0%	0.93 (0.66, 1.31)
Total events	86		123			

Heterogeneity: χ^2 = 3.28, df = 5 (P = 0.66); I^2 = 0%

Test for overall effect: Z = 0.42 (P = 0.68)



Surviving

Study or subgroup	Log (Hazard ratio)	SE	Weight	Hazard ratio IV, fixed, 95%CI
Baker 2009	0.21	1.42	21.3%	1.23 (0.08, 19.95)
Marubashi 2013	-0.03	0.8	67.2%	0.97 (0.20, 4.66)
Samstein 2015	-0.57	1.94	11.4%	0.57 (0.01, 25.34)
Total (95%CI)			100.0%	0.96 (0.27, 3.47)

Heterogeneity: χ^2 = 0.11, df = 2 (P = 0.95); I^2 = 0%

Test for overall effect: Z = 0.06 (P = 0.95)

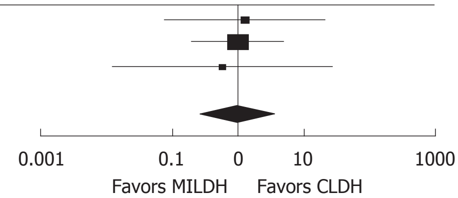


Figure 7 Forest plots and meta-analysis of postoperative outcomes of recipients.

Study or subgroup	MILDH Events	Total	CLDH Events	Total	Weight	Odds ratio M-H, fixed, 95%CI
3.1.1 Right hepatectomy						
Baker 2009	7	33	7	33	9.5%	1.00 (0.31, 3.26)
Choi H 2012	12	40	21	60	20.3%	0.80 (0.34, 1.88)
Kim S 2009	3	23	7	23	10.5%	0.34 (0.08, 1.54)
Makk 2014	4	26	5	24	7.6%	0.69 (0.16, 2.95)
Nagai 2012	7	28	7	30	8.8%	1.10 (0.33, 3.65)
Zhang 2013	4	25	7	25	10.2%	0.49 (0.12, 1.95)
				195	66.9%	0.73 (0.45, 1.19)
Subtotal (95%CI)		175				
Total events	37		54			
Heterogeneity: χ^2 = 2.04, df = 5 (P = 0.84); I^2 = 0%						
Test for overall effect: Z = 1.25 (P = 0.21)						
3.1.2 Left hepatectomy						
Kim 2011	0	11	1	11	2.5%	0.30 (0.01, 8.32)
Marubashi 2013	3	31	17	79	14.9%	0.39 (0.11, 1.44)
Samstein 2015	2	22	5	20	8.2%	0.30 (0.05, 1.76)
Soubrane 2006	3	16	5	14	7.5%	0.42 (0.08, 2.19)
				124	33.1%	0.37 (0.16, 0.87)
Subtotal (95%CI)		80				
Total events	8		28			
Heterogeneity: χ^2 = 0.09, df = 3 (P = 0.99); I^2 = 0%						
Test for overall effect: Z = 2.28 (P = 0.22)						
Total (95%CI)		255		319	100.0%	0.61 (0.40, 0.93)
Total events	45		82			

Heterogeneity: χ^2 = 4.07, df = 9 (P = 0.91); I^2 = 0%

Test for overall effect: Z = 2.30 (P = 0.02)

Test for subgroup differences: χ^2 = 1.89, df = 1 (P = 0.17); I^2 = 47.2%

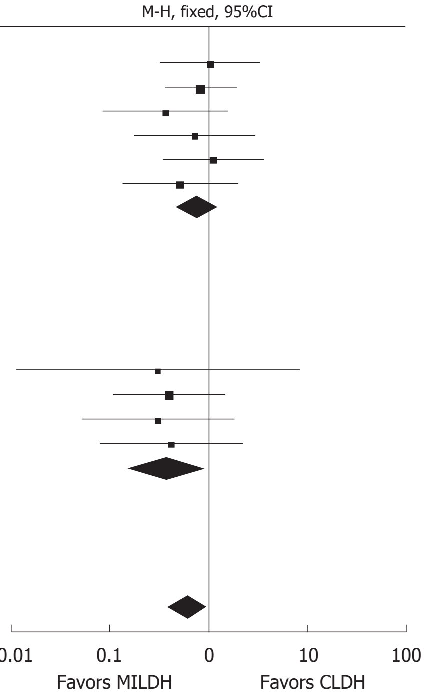


Figure 8 Forest plot and meta-analysis of postoperative complication rates for donors.

laparoscopy provided a magnified view of the liver, which was good for bleeding control.

Unlike intraoperative indices, postoperative outcomes favored MILDH. Our meta-analysis showed that postoperative complications (including wound-related, biliary, and vascular complications) occurred in 164 of 1093 patients in 12 studies, with a significantly lower postoperative donor complication rate in the MILDH group (12.4%) than in the CLDH group (17.1%). Few patients in either group experienced severe complications, including death or need for retransplantation. Our study also showed no statistical difference in the donor biliary complication rate between the MILDH group (1.96%) and CLDH group (4.57%), but favored the MILDH group. The incidence of postoperative biliary complications of donors was

Study or subgroup	MILDH Mean (min)	MILDH SD (min)	MILDH Total	CLDH Mean (min)	CLDH SD (min)	CLDH Total	Weight	Mean difference M-H, random, 95%CI
3.2.1 Right hepatectomy								
Baker 2009	265	48	33	316	61	33	9.7%	-51.00 (-77.48, -24.52)
Choi H 2012	313.52	80.66	60	303.22	61.49	90	9.8%	10.30 (-13.74, 34.34)
Choi Y 2014	415.4	131.89	25	272.4	49.7	484	8.2%	143.00 (91.11, 194.89)
Kim S 2009	232.3	29.2	23	268.8	67.1	23	9.5%	-36.50 (-66.41, -6.59)
Makk 2014	702.5	124.11	26	675.21	117.54	24	7.2%	27.29 (-39.70, 94.28)
Nagai 2012	389	69	28	359	54	30	9.4%	30.00 (-2.04, 62.04)
Zhang 2013	385.9	47.4	25	378.1	59	25	9.6%	7.80 (-21.87, 37.47)
Subtotal (95%CI)			220			709	63.5%	14.99 (-22.52, 52.50)
Heterogeneity: Tau^2 = 2185.47, χ^2 = 54.12, df = 6 (P < 0.00001); I^2 = 89%								
Test for overall effect: Z = 0.78 (P = 0.43)								
3.2.2 Left hepatectomy								
Kim 2011	330	68	11	306	29	11	8.7%	24.00 (-19.69, 67.69)
Marubashi 2013	435	103	31	383	73	79	9.0%	52.00 (12.33, 91.67)
Samstein 2015	478	8	22	398	42	20	10.0%	80.00 (61.29, 98.71)
Soubrane 2006	320	67	16	244	55	14	8.7%	76.00 (32.32, 119.68)
							36.5%	62.04 (37.04, 87.03)
Subtotal (95%CI)			80			124		
Heterogeneity: Tau^2 = 329.65, χ^2 = 6.21, df = 3 (P = 0.10); I^2 = 52%								
Test for overall effect: Z = 4.86 (P < 0.00001)								
Total (95%CI)			300			833	100.0%	31.29 (-1.08, 63.66)
Heterogeneity: Tau^2 = 2624.42, χ^2 = 110.54, df = 10 (P < 0.00001); I^2 = 91%								
Test for overall effect: Z = 1.89 (P = 0.06)								
Test for subgroup differences: χ^2 = 4.19, df = 1 (P = 0.04); I^2 = 76.1%								

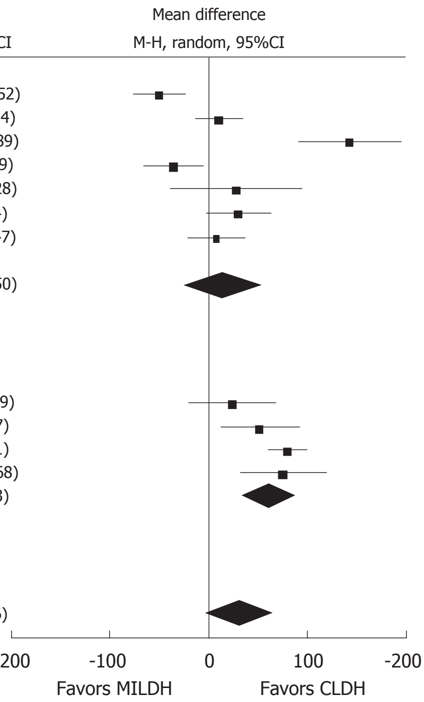


Figure 9 Forest plot and meta-analysis of operative time for donors.

Study or subgroup	MILDH Mean (min)	MILDH SD (min)	MILDH Total	CLDH Mean (min)	CLDH SD (min)	CLDH Total	Weight	Odds ratio M-H, fixed, 95%CI
3.3.1 Right hepatectomy								
Baker 2009	417	217	33	550	305	33	7.8%	-113.00 (-260.71, -5.29)
Choi H 2012	590	616.98	60	531.7	322.59	90	6.0%	58.30 (-111.45, 228.05)
Choi Y 2014	339.7	240.6	25	310.5	206.2	484	9.5%	29.20 (-66.89, 125.29)
Kim S 2009	185.6	59.2	23	218.8	67.1	23	12.3%	-33.20 (-69.77, 3.37)
Nagai 2012	316	121	28	212	114	30	11.3%	104.00 (43.40, 164.60)
Zhang 2013	378.4	112.5	25	422.6	139.3	25	10.8%	-44.20 (-114.39, 25.99)
						685		
Subtotal (95%CI)			194				57.7%	-1.67 (-66.05, 62.72)
Heterogeneity: Tau^2 = 4356.75, χ^2 = 20.78, df = 5 (P = 0.0009); I^2 = 76%								
Test for overall effect: Z = 0.05 (P = 0.96)								
3.3.2 Left hepatectomy								
Kim 2011	396	72	11	464	78	11	11.2%	-68.00 (-130.73, -5.27)
Marubashi 2013	435	103	31	383	73	79	12.2%	52.00 (12.33, 91.67)
Samstein 2015	177.3	100.8	22	375.3	190.9	20	9.6%	-198.00 (-291.63, -104.37)
Soubrane 2006	18.7	44.2	16	199.2	185.4	14	9.3%	-180.50 (-280.00, -81.00)
							42.3%	-93.04 (-215.56, 29.48)
Subtotal (95%CI)			80			124		
Heterogeneity: Tau^2 = 14109.01, χ^2 = 38.75, df = 3 (P < 0.00001); I^2 = 92%								
Test for overall effect: Z = 1.49 (P = 0.14)								
Total (95%CI)							100.0%	-38.27 (-95.00, 18.47)
Heterogeneity: Tau^2 = 6455.75, χ^2 = 60.21, df = 9 (P < 0.00001); I^2 = 85%								
Test for overall effect: Z = 1.32 (P = 0.19)								
Test for subgroup differences: χ^2 = 1.67, df = 1 (P = 0.20); I^2 = 40.3%								

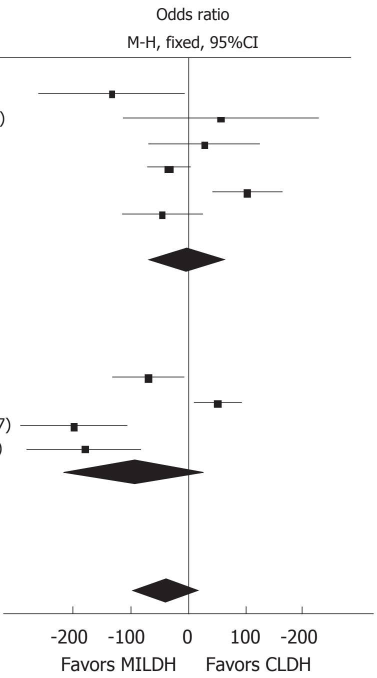


Figure 10 Forest plot and meta-analysis of estimated blood loss for donors.

closely related with the preoperative assessment of the biliary system and intraoperative anatomical techniques[35]. In laparoscopic liver resection, hepatic bile duct and artery could be identified more precisely with the amplification effect of laparoscopy, and the probability of bile duct injury would be reduced. We considered them as the main reasons for lower donor biliary complication rate in the MIDH group. In addition, preoperative magnetic resonance cholangiopancreatography (MRCP), intraoperative cholangiography and marking bile duct cut line would help to reduce postoperative biliary complications in donors[16].

Vascular complications (including postoperative bleeding and vascular embolization) of donors were related to the preoperative assessment of hepatic

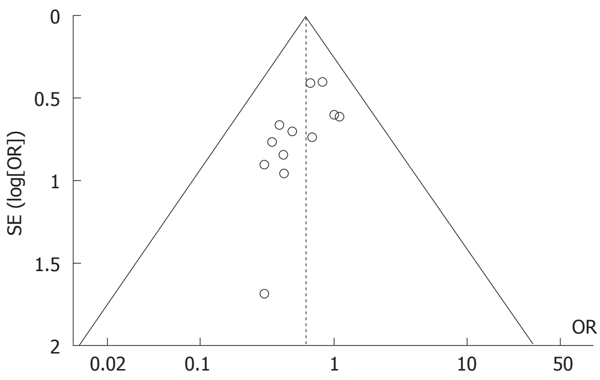


Figure 11 Funnel plot of postoperative complication rates.

vascular system and intraoperative anatomical techniques. Preoperative accurate assessment of hepatic vascular structures and careful intraoperative dissection techniques could reduce postoperative vascular complications effectively. Dissecting the liver precisely by minimally invasive approaches would also help to reduce donor vascular complications.

The rate of incision complications of the CLDH group was obviously higher than that of the MILDH group. The CLDH group adopted the "J" and "L" shape and "Mercedes" incision, which were larger compared to the other group. Large incision might cut off more abdominal nerves and was a high risk factor for incision complications. The smaller incision employed for MILDH, especially during laparoscopic surgery, could minimize surgical tissue trauma and abdominal nerve injury, thus reducing the rate of wound-related complications (infections, hematomas, and incisional hernias) and abdominal injuries. This finding is in good agreement with previous results[30]. Laparoscopic graft harvesting, in particular, could reduce incision hernia effectively. Smaller incision also contributes to reducing postoperative analgesia drug dose. Furthermore, minimally invasive approaches could result in earlier postoperative recovery of donors, thus minimizing other complications such as pleural effusion and intestinal obstruction.

Our study also found that the duration of continuous intravenous analgesic use was shorter in donors who underwent MILDH than in those who underwent CLDH. Minimally invasive approaches can reduce postoperative pain, as these approaches avoid cutting the subcostal muscle that is cut by conventional incisions, as well as minimizing surgical tissue trauma. Length of hospital stay was also significantly shorter for donors who underwent MILDH than in those who underwent CLDH, enabling the former to return to their normal lives earlier after surgery. A meta-analysis of 112 studies evaluating six laparoscopic surgical procedures showed a more rapid return to work after minimally invasive surgery[36]. Shorter hospital stay also contributed to lower hospital costs, increasing donor satisfaction with operative procedures. These outcomes were consistent with several studies of laparoscopic-assisted living donor hepatectomy, which found less pain, improved postoperative symptoms, and faster recovery compared with conventional open surgery[33,37].

Postoperative donor liver function was evaluated by measuring peak levels of serum AST, ALT, and TB. The pooled data showed no significant difference between the two groups. Reduced liver volume after donor liver resection may result in immediate, but transient, increases in peak AST, ALT, and TB. As the liver regenerates, all three indices would decline gradually. MILDH was a more difficult surgical procedure, but did not worsen liver function. Recovery time would be similar in donors who underwent MILDH and CLDH.

In subgroup analysis, we separately analyzed outcomes, including operative time, EBL, and postoperative complication rates, in patients who underwent LH or RH, to minimize any bias resulting from the side of liver resection. Donors who underwent minimally invasive LH had a lower rate of postoperative complications than those who underwent conventional LH; however, there was no between-group difference in donors who underwent RH. EBL and operative time were similar in donors who underwent minimally invasive and conventional LH and RH.

Evaluation of recipients showed no statistically significant differences in postoperative complication rate, postoperative liver function, or survival rate, although the complication rate was lower in the MILDH than in the CLDH group. There were also no significant differences in recipient postoperative liver function, as determined by peak serum AST, ALT, and TB levels. These findings indicate that the method of procuring liver grafts would have little effect on postoperative recipient liver function. Recovery times are similar in recipients who received grafts procured through MILDH and CLDH. The three studies[13,20,22] that evaluated recipient survival rate found no significant between-group difference. Other reports[38] evaluated several of the studies included in our meta-analysis, reporting survival rate but not postoperative liver function.

The biliary tree manipulation and identification have key impacts on the functions of graft. Our results showed no significant difference in the rate of recipient biliary complications between the MILDH group (18.8%) and CLDH group (17.4%). The recipient biliary complications include bile leakage and biliary stenosis and are closely related to the quality of liver graft[39]. Dissecting the liver precisely by minimally invasive approaches would help to harvest high-quality liver grafts and reduce the recipient biliary complications. In addition, comprehensive preoperative assessment of the biliary tract for donors (clear whether there are anomalies), familiarity with the hepatic biliary anatomy, cutting off donor bile duct precisely and feasible measures such as intraoperative cholangiography could minimize the risk of postoperative biliary complications[15].

This meta-analysis had several limitations, including the quality of the included studies. No randomized controlled trials were included, increasing the risk of bias owing to inadequate random sequence generation and blinding. In addition, all included articles were single-center studies, but differences in surgeons' experiences with the two techniques may have influenced patient outcomes. Moreover, within each study comparing MILDH with CLDH, not all operations were performed by a single surgeon, which may have introduced selection bias. Third, the follow-up period was generally short; therefore, long-term donor outcomes could not be evaluated. Finally, only three of the 13 included studies evaluated recipient survival rate. Because these recipients underwent LDLT with curative intent, their survival rate would be an important indicator of the safety and efficacy of these surgical procedures.

Nevertheless, the results of this meta-analysis are encouraging, as MILDH, which is more challenging to perform than CLDH, was always performed by experienced liver surgeons with a commitment to minimally invasive surgery[1]. Moreover, sufficient data on a large patient cohort that had undergone MILDH had accumulated, allowing evaluation by meta-analytical methods. Multiple strategies were used to identify applicable studies, with strict criteria used for study inclusion and evaluation. Subgroup analysis was performed to minimize heterogeneity. Future studies comparing MILDH and CLDH should include larger numbers of patients, with more data about recipients and a longer follow-up period.

In conclusion, the results of this meta-analysis comparing MILDH to CLDH show that MILDH could result in lower postoperative complication rate and analgesics requirement and shorter hospital stay with similar recipient outcomes. MILDH is safe, effective, and feasible for living donor liver resection. Nevertheless, MILDH, especially fully laparoscopic approach for the right lobe harvesting, is still an immature procedure with uncertain risk and effect, and should be performed cautiously.

COMMENTS

Background

Living donor liver transplantation has become an established treatment modality for patients with end-stage liver disease. With the wide use of minimally invasive techniques in hepatic surgery in recent years, more importance has been attached to minimally invasive living donor hepatectomy. Several centers considered minimally invasive approaches as safe and efficient techniques for graft harvested compared to conventional techniques. Despite this, no consensus is available in the literature about which of these two approaches is more beneficial to the patient.

Research frontiers

Nowadays living donor liver harvesting is performed with minimally invasive approaches in a growing number of centers. The worldwide research is directed towards a type of technique to guarantee the safety of donors.

Innovations and breakthroughs

In the present study, the authors investigated the outcomes of minimally invasive living donor liver resection and conventional approaches by pooling results from different centers. This is the first report of a meta-analysis comparing these two kinds of surgical approaches with concluding satisfactory results.

Applications

This report allows understanding the role of two surgical techniques for living donor hepatectomy.

Peer-review

This systematic review and meta-analysis of retrospective studies adds useful information for practice and research, and probably for policy.

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