Prognosis of liver transplantation and hepatectomy in patients with hepatocellular carcinoma meeting the Milan criteria: A systematic review and meta-analysis

JILING WANG[1,2], ZHENG PAN[1], YONGZHENG WANG[1], YANSHUO YE[1] and WEI LI[1]

[1]Department of Hepatobiliary-Pancreatic Surgery, China-Japan Union Hospital of Jilin University, Changchun, Jilin 130033, P.R. China; [2]Department of Hepatobiliary Surgery, Tengzhou Central People's Hospital, Zaozhuang, Shandong 277500, P.R. China

Received February 14, 2025; Accepted September 18, 2025

DOI: 10.3892/ol.2026.15447

Abstract. Liver transplantation (LT) and liver resection (LR) are two curative treatment options for patients with hepatocellular carcinoma (HCC) meeting the Milan criteria. However, the optimal choice between LT and LR remains contentious. The present meta-analysis aimed to provide additional evidence to optimize treatment decisions for patients with HCC. A comprehensive literature search was conducted across multiple databases, including PubMed, Embase, Cochrane, Web of Science (Medline), OVID, Scopus, China National Knowledge Infrastructure, Value-Added Information Provider, Wanfang and China Biology Medicine, focusing on studies reporting on the prognosis of LR and LT in patients with HCC. The data were analyzed using Review Manager 5.4 software. Random-effects models were employed to compare the 1-, 3-, 5- and 10-year overall survival (OS) rates, disease-free survival (DFS) rates and recurrence rate (RR) between patients who underwent LT and those who underwent LR. In total, 36 studies encompassing 6,839 patients (3,894 in the LR group and 2,945 in the LT group) were included. The analysis revealed no significant difference in 1-year OS rate between the two groups. However, the LT group demonstrated significantly improved OS rates at 3, 5 and 10 years. Additionally, the LT group indicated significantly improved DFS rates at all time points (1, 3, 5 and 10 years) compared with the LR group. Postoperative RR was significantly lower in the LT group compared with that in the LR group. In conclusion, in patients with HCC meeting the Milan criteria, LT provides improvements in OS and DFS rates, and results in a lower RR compared with LR. Therefore, LT should be considered the preferred treatment option for these patients within the Milan criteria if donor organs are available.

Correspondence to: Dr Wei Li, Department of Hepatobiliary-Pancreatic Surgery, China-Japan Union Hospital of Jilin University, 126 Xiantai Street, Changchun, Jilin 130033, P.R. China
E-mail: weili888@jlu.edu.cn

Abbreviations: DFS, disease-free survival; HCC, hepatocellular carcinoma; LR, liver resection; LT, liver transplantation; MVI, microvascular invasion; OS, overall survival; RR, recurrence rate

Key words: liver transplantation, liver resection, hepatocellular carcinoma, Milan criteria, meta-analysis

Introduction

Hepatocellular carcinoma (HCC) ranks as the sixth most prevalent cancer globally and the fourth leading cause of cancer-related mortality. There were an estimated 905,000 new cases and 830,000 associated deaths worldwide in 2020 (1). The primary curative treatment options for HCC include liver transplantation (LT) and liver resection (LR). Currently, LR is the most commonly employed treatment, aimed at tumor eradication and extending overall survival (OS) time in patients with compensated liver function (2). However, HCC resectability is contingent on several factors, including liver function, cirrhosis status with portal hypertension, tumor size and number, tumor location, clinical staging and the overall health of the patient. LR is generally more effective in patients with HCC who have Child-Pugh A liver function, with or without cirrhosis and portal hypertension (3). However, the recurrence rate (RR) of HCC after LR can approach 50% within the first few years, likely due to the presence of occult HCC foci in the residual liver, circulating cancer cells returning to the liver to form novel tumors or *de novo* HCC development due to the underlying liver disease in the remnant liver (4).

By contrast, the HCC RR following LT has been recorded as ~17% (range, 15-19%) (5), with a >30% reduction in absolute RR post-LT compared with that observed in LR (4). LT not only removes the tumor but also addresses the underlying chronic liver disease and associated complications, such as portal hypertension (6). However, LT has its limitations, including organ donor shortages, extended waiting times, the need for lifelong immunosuppressive therapy and the associated risk of infections. Therefore, the debate continues regarding which treatment, LR or LT, should be the preferred initial option for HCC.

The core requirements of Milan criteria are as follows: A single tumor with a diameter ≤5 cm, or up to 3 tumors each ≤3 cm in diameter, with no vascular invasion or extrahepatic metastasis, represent the first internationally recognized

guidelines for LT in liver cancer (7). Patients with HCC meeting these criteria who undergo LT achieve a 4-year OS rate of up to 85% and a disease-free survival (DFS) rate of 92%. The efficacy of LT within the Milan criteria has been validated by multiple transplant centers globally. Previous studies have indicated that 20-25% of patients with liver cancer are eligible for both LT and LR, making the decision for first-line treatment more complex (8-11). Due to the numerous factors that complicate direct comparisons between these two surgical approaches, their respective advantages and prognostic differences remain contentious. Therefore, the present study utilized a meta-analysis to compare the prognosis of patients with HCC undergoing LT and LR within the Milan criteria, specifically focusing on differences in OS and DFS rates, to provide additional evidence-based guidance for clinical decision-making in the future.

Materials and methods

Search strategy. A systematic search was conducted across multiple databases, including PubMed (https://pubmed.ncbi.nlm.nih.gov/), Embase (http://www.embase.com/), Cochrane (http://www.cochranelibrary.com/), Web of Science (Medline) (https://www.webofscience.com/), OVID (https://www.ovid.com/), Scopus (https://www.scopus.com/), China National Knowledge Infrastructure (http://www.cnki.net/), Value-Added Information Provider (https://qikan.cqvip.com/), Wanfang (https://www.wanfangdata.com.cn/index.html) and China Biology Medicine (http://www.sinomed.ac.cn/zh/), to identify studies evaluating the prognosis of LT and LR in patients with HCC meeting the Milan criteria. The search, which spanned from the inception of each database to June 2024, utilized a combination of index terms and text words. Key search terms included 'liver cancer', 'hepatocellular carcinoma', 'HCC', 'liver transplantation', 'LT', 'liver resection' and 'LR' (the terms HCC, LT and LR were also searched for separately as the abbreviations), among others (Data S1). Furthermore, references cited in relevant studies were also reviewed to ensure comprehensive retrieval.

Inclusion and exclusion criteria. The inclusion criteria were as follows: i) Studies comparing the efficacy and prognosis of LT and LR for HCC; ii) patients with HCC meeting the Milan criteria, with pathological confirmation; iii) interventions involving LR or LT; iv) studies providing relevant outcome data, including 1-, 3-, 5- and 10-year OS, DFS and RR; and v) full-text articles available in either Chinese or English. The exclusion criteria were as follows: i) Animal studies; ii) meta-analyses, systematic reviews, reviews, case reports, degree thesis, editorials and conference abstracts; iii) studies lacking primary research indicators or duplicated from Surveillance, Epidemiology and End Results Program database data (https://seer.cancer.gov/); iv) studies with <10 cases in either the LT or LR groups; and v) studies where full text could not be accessed.

Data extraction and quality assessment. Data extraction was performed independently by two reviewers using a standardized table, with discrepancies resolved by a third reviewer. Extracted data included: i) Study details [author, publication date, country, sample size for LT and LR groups, transplant center name, treatment intent, sex, liver function classification (12), vascular invasion and follow-up period]; and ii) outcome measures (OS and DFS rates, and RR, at 1-, 3-, 5- and 10-years post-treatment). The quality of retrospective cohort studies was assessed using the Newcastle-Ottawa Scale (NOS) (13), evaluating study subject selection, group comparability and outcome measurement. The total score of the scale was 9 points, with a score of ≥7 points indicating high-quality studies.

Statistical analysis. Statistical analysis was performed using Review Manager software (version 5.4; The Cochrane Collaboration). Odds ratios (OR) were calculated for binary variables, with 95% confidence interval (CI) provided for each estimate. Heterogeneity among studies was assessed using the χ^2 test, with I^2 quantifying the degree of heterogeneity. High heterogeneity was defined by $P<0.05$ and $I^2>50\%$, while low heterogeneity was indicated by $P\geq0.05$ and $I^2\leq50\%$. A random effects model was used for all comparisons, in line with previous evidence suggesting its greater reliability compared with the fixed effects model (14). Sensitivity analysis was conducted to explore sources of heterogeneity and publication bias was evaluated using a funnel plot. The χ^2 test was also used to analyze differences in cirrhosis severity, sex and microvascular invasion (MVI), with $P<0.05$ considered to indicate a statistically significant difference.

Results

Characteristics of the included studies and quality assessment. As illustrated in Fig. 1, a total of 25,712 articles were retrieved. After applying the inclusion and exclusion criteria, 36 articles were selected, comprising 30 English-language studies (15-43) and 6 Chinese-language studies (44-49), all of which were retrospective cohort studies. The included studies involved a total of 6,839 patients, with 3,894 in the LR group and 2,945 in the LT group. The basic characteristics of these studies are summarized in Tables I and II, while the quality assessment results are presented in Table III. All studies were of high quality, scoring ≥7 according to the NOS. Table IV provides a detailed description of the basic characteristics of the patients with HCC. For patients with liver cancer undergoing LR or LT, sex, liver function and tumor vascular invasion status are closely related to the prognosis. As the hormone levels influence tumor progression, and microvascular invasion reflects the tumor's aggressiveness and is directly linked to the risk of recurrence, liver function reserve determines treatment tolerance and recovery capacity. There were no statistically significant differences between the LR and LT groups in terms of sex distribution ($P=0.697$). However, a significant difference was observed in the severity of cirrhosis and MVI distribution between the two groups, ($P<0.001$ and $P=0.006$, respectively) (Table V). In addition, among the 36 included articles, 5 did not provide a detailed description of the dropout rate (18,25,32,36,49), 4 had dropout rates (15,16,33,44) and the remaining 27 did not have dropout rates.

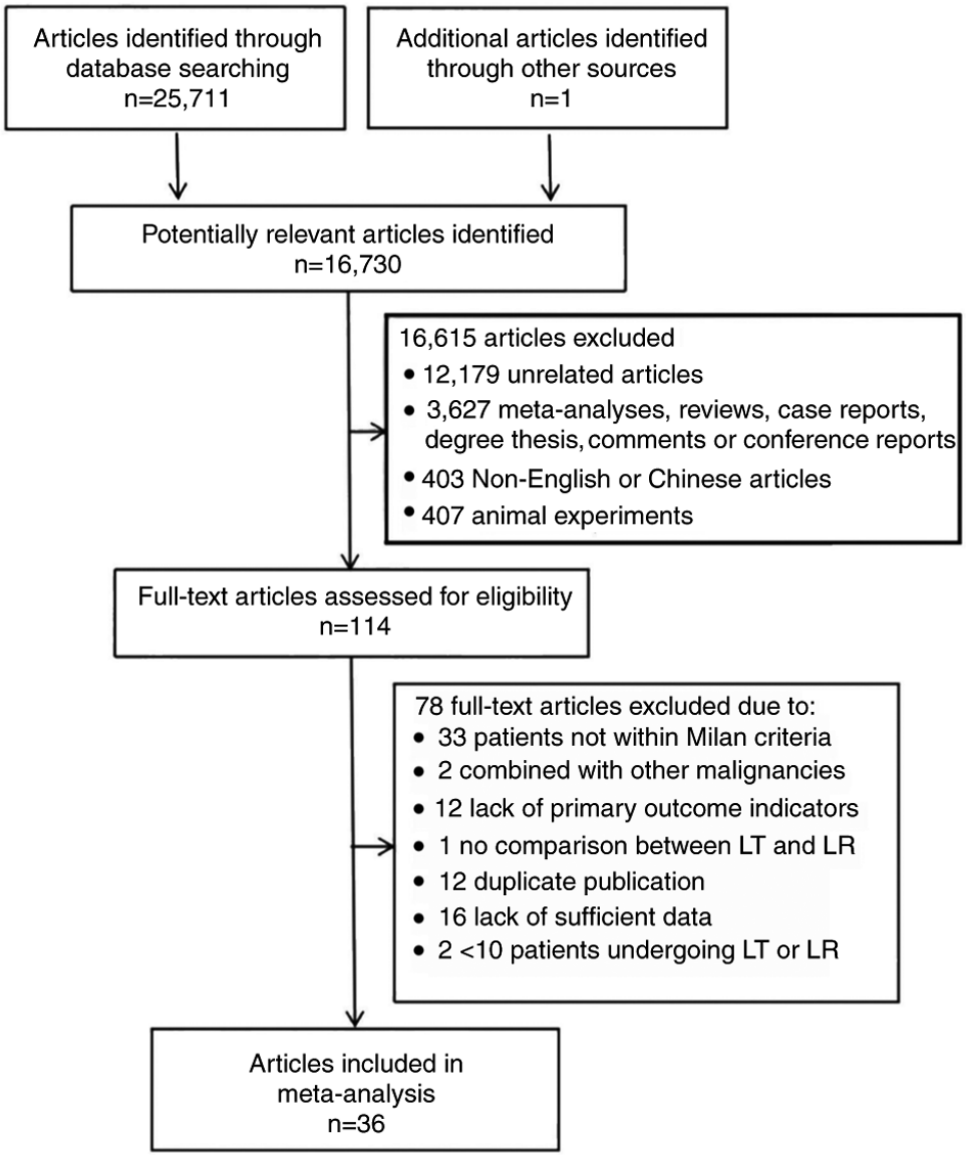

Figure 1. Flow diagram for included articles. LT, liver transplantation; LR, liver resection; HCC, hepatocellular carcinoma.

Results of meta-analysis

OS rate analysis. i) 1-year OS rate. In total, 23 studies assessed the 1-year OS rate, comprising 3,860 patients with HCC (2,437 in the LR group and 1,423 in the LT group). The meta-analysis revealed no significant difference in the 1-year OS rates between the LR and LT groups, which were 92.2 and 89.9%, respectively (OR, 1.03; 95% CI, 0.79-1.34; P=0.85). No heterogeneity was observed among the studies (P=0.75; I^2=0%) (Fig. 2A).

ii) 3-year OS rate. In total, 23 studies evaluated the 3-year OS rate, involving 3,635 patients with HCC (2,439 in the LR group and 1,196 in the LT group). The meta-analysis demonstrated a statistically significant difference in the 3-year OS rates between the LR and LT groups, with patients with LT demonstrating a slightly higher 3-year OS rate (77.4 vs. 76.8%) (OR, 0.70; 95% CI, 0.53-0.93; P=0.01). There was moderate heterogeneity among the studies (P=0.002; I^2=52%) (Fig. 2B).

iii) 5-year OS rate. In total, 32 studies assessed the 5-year OS rate, involving 5,870 patients with HCC (3,277 in the LR group and 2,593 in the LT group). The meta-analysis revealed a significant difference in the 5-year OS rate between the two groups, with the LT group having a higher 5-year OS rate (70.3 vs. 61.6%) (OR, 0.52; 95% CI, 0.43-0.63; P<0.00001). There was moderate heterogeneity among the studies (P=0.0009; I^2=50%) (Fig. 2C).

iv) 10-year OS rate. In total, 5 studies evaluated the 10-year OS rate, involving 1,532 patients with HCC (754 in the LR group and 778 in the LT group). The meta-analysis indicated a significantly higher 10-year OS rate for the LT group compared with that in the LR group (57.8 vs. 40.6%) (OR, 0.39; 95% CI, 0.25-0.61; P<0.0001). There was significant heterogeneity among the studies (P=0.02; I^2=67%) (Fig. 2D).

DFS rate analysis. i) 1-year DFS rate. In total, 19 studies evaluated the 1-year DFS rate, including 3,510 patients with HCC (2,302 in the LR group and 1,208 in the LT group). The meta-analysis revealed that the 1-year DFS rate was significantly higher in the LT group compared with the LR group (89.7 vs. 78.8%) for patients with HCC meeting the Milan

Table I. Characteristics of the included studies.

First author, year	LR, n	LT, n	OS (LR/LT), %				DFS (LR/LT), %				Number of recurrences		(Refs.)
			1-year	3-year	5-year	10-year	1-year	3-year	5-year	10-year	LR	LT	
Margarit *et al*, 2005	37	36	92.0/78.0	NA	70.0/65.0	50.0/60.0	84.0/77.0	NA	39.0/64.0	18.0/56.0	22	4	(19)
Jiang *et al*, 2014	33	34	84.8/94.1	64.0/91.2	51.2/76.5	NA	NA	35.6/72.0	19.8/41.0	NA	22	6	(15)
Foltys *et al*, 2014	30	31	NA	NA	57.9/42.0	NA	NA	NA	NA	NA	NA	NA	(20)
Bigourdan *et al*, 2003	20	17	NA	67.0/87.0	36.0/71.0	NA	NA	52.0/87.0	40.0/80.0	NA	NA	NA	(21)
Sogawa *et al*, 2013	56	52	85.1/75.0	65.4/59.4	51.6/51.3	NA	NA	NA	NA	NA	34	12	(22)
Moon *et al*, 2007	100	17	92.9/94.1	79.0/94.1	66.5/94.1	NA	78.1/100	65.4/75.0	54.5/75.0	NA	36	1	(23)
Bellavance *et al*, 2008	245	134	93.0/91.0	71.0/79.0	46.0/66.0	NA	88.0/96.0	62.0/89.0	40.0/82.0	NA	122	19	(24)
Squires *et al*, 2014	45	131	NA	NA	43.8/65.7	NA	NA	NA	22.7/85.3	NA	NA	NA	(25)
Michelakos *et al*, 2019	95	89	NA	76.0/82.0	62.0/77.0	41.0/53.0	NA	48.0/96.0	44.0/94.0	31.0/94.0	NA	NA	(18)
Meyerovich *et al*, 2019	30	54	92.1/81.2	78.1/56.4	55.2/47.0	NA	73.4/89.4	53.6/62.4	27.8/56.2	NA	4	15	(26)
Krenzien *et al*, 2018[a]	30	123	NA	NA	36.0/77.0	NA	NA	NA	29.0/76.0	NA	NA	NA	(27)
Krenzien *et al*, 2018[b]	29	91	NA	NA	61.0/73.0	NA	NA	NA	40.0/70.0	NA	NA	NA	(27)
Park *et al*, 2017	199	137	NA	NA	NA	NA	73.9/92	54.6/87.1	NA	NA	79	19	(14)
Li *et al*, 2017	61	31	93.4/100	63.1/91.1	51.2/85.4	NA	68.9/100	48.4/87.4	38.6/80.1	NA	NA	NA	(16)
Huang *et al*, 2016	254	49	NA	NA	NA	NA	82.0/86.0	61.0/80.0	45.0/80.0	31.0/68.0	140	8	(28)
Li *et al*, 2014	243	39	96.3/100	83.9/85.2	76.2/81.0	NA	79.8/89.7	59.7/83.5	50.9/79.3	NA	NA	NA	(29)
Dai *et al*, 2014	25	13	100/100	93.3/91.7	93.3/91.7	NA	92.0/92.3	71.7/92.3	64.5/92.3	NA	NA	NA	(30)
Poon *et al*, 2007	204	43	NA	NA	68.0/81.0	NA	NA	NA	44.0/84.0	NA	NA	NA	(31)
Baccarani *et al*, 2008	38	48	82.0/85.0	61.0/79.0	26.0/74.0	NA	79.0/82.0	41.0/74.0	11.0/74.0	NA	13	1	(32)
Sung *et al*, 2017	89	67	NA	NA	63.0/78.0	43.0/75.0	NA	NA	57.0/88.0	37.0/86.0	50	8	(33)
Hsueh *et al*, 2016	184	65	94.9/96.9	82.2/86.7	71.4/76.4	NA	81.2/92.2	58.4/80.9	46.6/70.5	NA	NA	NA	(17)
Lee *et al*, 2010	82	48	87.7/85.1	74.9/78.1	58.4/78.1	NA	74.3/91.5	59.3/89.1	57.4/89.1	NA	NA	NA	(34)
Shabahang *et al*, 2002	44	65	NA	57.0/66.0	NA	NA	NA	36.0/66.0	NA	NA	NA	NA	(35)
Chapman *et al*, 2015	248	496	NA	NA	52.8/74.3	21.7/53.7	NA	NA	30.1/71.8	11.7/53.4	NA	NA	(36)
Koniaris *et al*, 2011	33	205	94.0/87.0	NA	59.0/63.0	NA	94.0/84.0	NA	NA	NA	NA	NA	(37)
Sotiropoulos *et al*, 2009	26	26	NA	NA	26.0/56.0	NA	NA	NA	NA	NA	NA	NA	(38)
Shah *et al*, 2007	121	140	89.0/90.0	70.0/75.0	56.0/64.0	NA	NA	NA	NA	NA	53	17	(39)
Fan *et al*, 2011	287	50	93.4/92.0	82.1/86.0	72.8/81.0	NA	77.4/92.0	59.5/83.0	54.7/83.0	NA	135	5	(40)
Del Gaudio *et al*, 2008	80	147	90.0/90.0	NA	66.0/73.0	NA	72.0/85.0	NA	41.0/71.0	NA	7	1	(41)
Adam *et al*, 2012	97	101	NA	67.0/79.0	52.0/75.0	36.0/65.0	NA	33.0/76.0	20.0/72.0	12.0/64.0	60	10	(42)

Table I. Continued.

First author, year	LR, n	LT, n	OS (LR/LT), %				DFS (LR/LT), %				Number of recurrences		(Refs.)
			1-year	3-year	5-year	10-year	1-year	3-year	5-year	10-year	LR	LT	
Llovet *et al*, 1999	77	87	NA	85.0/82.0	62.0/69.0	51.0/69.0	NA	NA	NA	NA	NA	NA	(43)
Xia *et al*, 2021	285	90	96.3/95.4	87.1/79.4	76.9/77.4	54.7/71.7	NA	NA	NA	NA	136	13	(44)
Yu *et al*, 2014	227	36	96.9/100	83.8/87.5	76.1/83.1	NA	80.6/91.7	59.8/85.3	50.8/81.0	NA	100	6	(45)
Huang *et al*, 2014	55	33	87.3/90.9	69.3/87.7	57.3/70.1	NA	71.0/96.7	52.6/85.3	40.6/64.6	NA	29	6	(46)
Xu *et al*, 2013	31	22	87.0/86.0	71.0/68.0	NA	NA	84.0/77.0	74.0/59.0	NA	NA	7	5	(47)
Xia *et al*, 2012	89	32	86.0/87.0	63.0/70.0	44.0/62.0	NA	68.0/80.0	44.0/65.0	26.0/52.0	NA	NA	NA	(48)
Zhu *et al*, 2011	65	66	92.3/93.9	67.7/87.9	NA	NA	NA	NA	NA	NA	15	4	(49)

[a]Patients who received treatment between 1989 and 2004; [b]patients who received treatment between 2005 and 2011. LR, liver resection; LT, liver transplantation; OS, overall survival; DFS, disease-free survival; NA, not available.

criteria (OR, 0.38; 95% CI, 0.27-0.55; P<0.00001). Statistical heterogeneity was present among the studies (P=0.03; I^2=41%) (Fig. 3A).

ii) 3-year DFS rate. In total, 21 studies assessed the 3-year DFS rate, involving 3,664 patients with HCC (2,485 in the LR group and 1,179 in the LT group). The meta-analysis indicated a statistically significant difference in the 3-year DFS rates between the LR and LT groups (OR, 0.24; 95% CI, 0.18-0.31; P<0.00001), with the LT group exhibiting a significantly higher 3-year DFS rate (82.2 vs. 56.3%). Statistical heterogeneity was present (P=0.02; I^2=44%) (Fig. 3B).

iii) 5-year DFS rate. In total, 28 studies assessed the 5-year DFS rate, comprising 5,343 patients with HCC (3,027 in the LR group and 2,316 in the LT group). The meta-analysis indicated a significant difference in the 5-year DFS rates between the LR and LT groups (OR, 0.20; 95% CI, 0.16-0.26; P<0.00001), with the LT group demonstrating a considerably higher 5-year DFS rate (74.0 vs. 43.1%). There was statistical heterogeneity among the studies (P=0.0002; I^2=56%) (Fig. 3C).

iv) 10-year DFS rate. In total, 5 studies evaluated the 10-year DFS rate, including 1,460 patients with HCC (723 in the LR group and 737 in the LT group). The meta-analysis demonstrated that the 10-year DFS rate was significantly higher in the LT group compared with that in the LR group (59.7 vs. 22.5%) (OR, 0.12; 95% CI, 0.07-0.23; P<0.00001). There was high heterogeneity among the studies (P=0.005; I^2=73%) (Fig. 3D).

RR analysis. A total of 19 studies with 3,453 patients with HCC (2,274 in the LR group and 1,179 in the LT group) assessed RR. The meta-analysis revealed that the RR after LT was significantly lower compared with that after LR (12.6 vs. 47.3%), with a statistically significant difference (OR, 6.21; 95% CI, 4.92-7.85; P<0.00001). No heterogeneity was observed among the studies (P=0.21; I^2=20%) (Fig. 4).

Sensitivity analysis and publication bias. A sensitivity analysis was conducted by sequentially excluding each study with high heterogeneity for outcome indicators. The results revealed that the combined effect of the outcome indicators did not change notably compared with the previous analysis. Publication bias was assessed using funnel plots and all plots displayed varying degrees of asymmetry, indicating potential publication bias (Figs. 5 and 6). These results reflected the limitation of the present analysis due to the lack of published RCT studies.

Discussion

The present meta-analysis compared the prognosis of patients with HCC within the Milan criteria who received either LT or LR. The results demonstrated no significant difference in the 1-year OS rate between the LR and LT groups. However, the LT group demonstrated significantly higher 3-, 5- and 10-year OS rates compared with the LR group. Similarly, the DFS rates were consistently higher in the LT group at 1-, 3-, 5- and 10-year intervals. The present study updates the literature on the prognosis of patients with HCC within the Milan criteria undergoing LT and LR, offering more precise information and clinical outcomes for patients with early-stage HCC.

Varying degrees of heterogeneity were observed among the studies included in the present meta-analysis. The studies by

Table II. Characteristics of the included studies.

First author, year	Region	Transplant centers	ITT	(Refs.)
Margarit *et al*, 2005	Spain	Single	No	(19)
Jiang *et al*, 2014	China	Single	No	(15)
Foltys *et al*, 2014	USA	Single	Yes	(20)
Bigourdan *et al*, 2003	France	Single	No	(21)
Sogawa *et al*, 2013	USA	Single	Yes	(22)
Moon *et al*, 2007	Korea	Single	No	(23)
Bellavance *et al*, 2008	USA	Multiple	Yes	(24)
Squires *et al*, 2014	USA	Single	No	(25)
Michelakos *et al*, 2019	USA	Single	Yes	(18)
Meyerovich *et al*, 2019	Israel	Single	Yes	(26)
Krenzien *et al*, 2018[a]	Germany	Single	No	(27)
Krenzien *et al*, 2018[b]	Germany	Single	No	(27)
Park *et al*, 2017	Korea	Single	No	(14)
Li *et al*, 2017	China	Single	No	(16)
Huang *et al*, 2016	China	Multiple	No	(28)
Li *et al*, 2014	China	Single	No	(29)
Dai *et al*, 2014	China	Single	No	(30)
Poon *et al*, 2007	China	Single	No	(31)
Baccarani *et al*, 2008	Italy	Single	Yes	(32)
Sung *et al*, 2017	Korea	Single	No	(33)
Hsueh *et al*, 2016	China	Multiple	No	(17)
Lee *et al*, 2010	Korea	Single	No	(34)
Shabahang *et al*, 2002	USA	Single	No	(35)
Chapman *et al*, 2015	USA	Multiple	No	(36)
Koniaris *et al*, 2011	USA	Multiple	Yes	(37)
Sotiropoulos *et al*, 2009	Germany	Single	No	(38)
Shah *et al*, 2007	Canada	Single	Yes	(39)
Fan *et al*, 2011	China	Single	No	(40)
Del Gaudio *et al*, 2008	Italy	Single	Yes	(41)
Adam *et al*, 2012	France	Single	Yes	(42)
Llovet *et al*, 1999	Spain	Single	Yes	(43)
Xia *et al*, 2021	China	Single	No	(44)
Yu *et al*, 2014	China	Single	No	(45)
Huang *et al*, 2014	China	Single	No	(46)
Xu *et al*, 2013	China	Single	No	(47)
Xia *et al*, 2012	China	Single	No	(48)
Zhu *et al*, 2011	China	Multiple	No	(49)

[a]Patients who received treatment between 1989 and 2004; [b]patients who received treatment between 2005 and 2011. ITT, intention-to-treat.

Meyerovich *et al* (26) and Xia *et al* (44) were notable contributors to the high heterogeneity observed in the 3- and 5-year OS rates. A previous study by Meyerovich *et al* (26), conducted in Israel, reported a median waiting time of 304 days for LT, with a 24% dropout rate, which suggested that LR provided a higher 5-year OS rate compared with LT. This result contrasts with the present study findings, possibly due to the lower organ donation rates in Israel, which result in longer waiting times for LT. Shorter waiting times might reduce dropout rates and improve post-transplant survival. Similarly, Xia *et al* (44)

Table III. Quality assessment results (Newcastle-Ottawa Scale).

	Selection				Comparability		Outcome				
First author, year	Representation of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Study controls to select the most key factor	Study controls for any additional factor	Assessment of outcome	Whether follow-up was long enough for outcomes to occur	Integrity of follow-up	Score	(Refs.)
Margarit *et al*, 2005	*	*	*	*	*	*	*	*	/	8	(19)
Jiang *et al*, 2014	*	*	*	*	*	*	*	*	*	9	(15)
Foltys *et al*, 2014	*	*	*	*	*	/	*	*	*	8	(20)
Bigourdan *et al*, 2003	*	*	*	*	*	/	*	*	*	8	(21)
Sogawa *et al*, 2013	*	*	*	*	/	/	*	*	*	7	(22)
Moon *et al*, 2007	*	*	*	*	*	*	*	*	*	9	(23)
Bellavance *et al*, 2008	*	*	*	*	*	/	*	*	/	7	(24)
Squires *et al*, 2014	*	*	*	*	/	*	*	*	/	7	(25)
Michelakos *et al*, 2019	*	*	*	*	*	/	*	*	/	7	(18)
Meyerovich *et al*, 2019	*	*	*	*	*	/	*	*	/	7	(26)
Krenzien *et al*, 2018	*	*	*	*	*	/	*	*	*	8	(27)
Park *et al*, 2017	*	*	*	*	*	/	*	/	*	7	(14)
Li *et al*, 2017	*	*	*	*	/	*	*	*	*	8	(16)
Baccarani *et al*, 2008	*	*	*	*	*	/	*	*	/	7	(32)
Huang *et al*, 2016	*	*	*	*	/	*	*	*	*	8	(28)
Li *et al*, 2014	*	*	*	*	*	/	*	*	*	8	(29)
Dai *et al*, 2014	*	*	*	*	*	*	*	*	*	9	(30)
Poon *et al*, 2007	*	*	*	*	/	/	*	*	*	7	(31)
Sung *et al*, 2017	*	*	*	*	*	/	*	*	*	8	(33)
Hsueh *et al*, 2016	*	*	*	*	/	*	*	*	/	7	(17)
Lee *et al*, 2010	*	*	*	*	*	*	*	*	/	8	(34)
Shabahang *et al*, 2002	*	*	*	*	*	/	*	/	*	7	(35)
Chapman *et al*, 2015	*	*	*	*	*	/	*	*	/	7	(36)
Koniaris *et al*, 2011	*	*	*	*	*	*	*	*	/	8	(37)
Sotiropoulos *et al*, 2009	*	*	*	*	/	/	*	*	*	7	(38)
Shah *et al*, 2007	*	*	*	*	/	*	*	*	/	7	(39)

Table III. Continued.

First author, year	Selection				Comparability		Outcome			Score	(Refs.)
	Representation of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Study controls to select the most key factor	Study controls for any additional factor	Assessment of outcome	Whether follow-up was long enough for outcomes to occur	Integrity of follow-up		
Fan *et al*, 2011	*	*	*	*	*	*	*	/	*	8	(40)
Adam *et al*, 2012	*	*	*	*	/	*	*	*	*	8	(42)
Del Gaudio *et al*, 2008	*	*	*	*	*	/	*	*	/	7	(41)
Llovet *et al*, 1999	*	*	*	*	/	*	*	*	*	8	(43)
Xia *et al*, 2021	*	*	*	*	/	*	*	*	*	8	(44)
Yu *et al*, 2014	*	*	*	*	*	/	*	*	*	8	(45)
Huang *et al*, 2014	*	*	*	*	/	*	*	*	/	7	(46)
Xu *et al*, 2013	*	*	*	*	*	*	*	/	*	8	(47)
Xia *et al*, 2012	*	*	*	*	*	*	*	*	*	9	(48)
Zhu *et al*, 2011	*	*	*	*	*	*	*	/	/	7	(49)

*, score; /, no score.

Table IV. Basic characteristics of patients with hepatocellular carcinoma.

	Sex				Child-Pugh score										
	LR		LT		LR			LT			MVI		Follow-up, months[a]		
First author, year	Male	Female	Male	Female	A	B	C	A	B	C	LR	LT	LR	LT	(Refs.)
Adam *et al*, 2012	84	13	85	16	80	10	1	19	45	37	NA	NA	36	83	(42)
Baccarani *et al*, 2008	28	10	42	6	28	10	0	19	20	8	29	8	36±25	28±26	(32)
Bellavance *et al*, 2008	203	42	110	24	233	12	0	75	59	0	60	11	27.60	39.60	(24)
Bigourdan *et al*, 2003	NA	NA	NA	NA	20	0	0	17	0	0	3	0	55	55	(21)
Chapman *et al*, 2015	170	78	372	124	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(36)
Dai *et al*, 2014	22	3	12	1	25	0	0	13	0	0	3	4	NA	NA	(30)
Del Gaudio *et al*, 2008	63	17	126	21	66	14	0	66	53	88	NA	NA	NA	NA	(41)
Fan *et al*, 2011	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(40)
Foltys *et al*, 2014	NA	NA	NA	NA	30	0	0	31	0	0	NA	NA	22.30	47.50	(20)
Hsueh *et al*, 2016	139	45	49	16	179	5	0	20	24	21	45	13	NA	NA	(17)
Huang *et al*, 2016	227	29	43	8	241	15	0	23	15	13	NA	NA	62.40	30	(28)
Jiang *et al*, 2014	28	5	29	5	33	0	0	34	0	0	13	10	31.40±15.50	43.50±22.10	(15)
Koniaris *et al*, 2011	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(37)
Krenzien *et al*, 2018[b]	18	12	101	22	NA	NA	NA	NA	NA	NA	20	89	NA	NA	(27)
Krenzien *et al*, 2018[c]	21	8	72	19	NA	NA	NA	NA	NA	NA	7	11	NA	NA	(27)
Lee *et al*, 2010	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	66.50	49.10	(34)
Li *et al*, 2017	NA	NA	NA	NA	61	31	0	NA	NA	NA	NA	NA	NA	NA	(16)
Li *et al*, 2014	211	32	35	4	243	0	0	39	0	0	44	12	40.26±19.72	40.26±19.72	(29)
Llovet *et al*, 1999	48	29	65	22	74	3	0	37	38	12	11	22	32	26	(43)
Margarit *et al*, 2005	29	8	22	14	37	0	0	36	0	0	6	2	50	44	(19)
Meyerovich *et al*, 2019	21	9	37	17	NA	NA	NA	NA	NA	NA	15	4	27.70	23.30	(26)
Michelakos *et al*, 2019	74	21	76	13	95	0	0	89	0	0	NA	NA	NA	NA	(18)
Moon *et al*, 2007	78	22	16	1	100	0	0	17	0	0	9	0	22	77	(23)
Park *et al*, 2017	150	49	107	30	194	5	0	32	60	45	47	21	28.70	37.80	(14)
Poon *et al*, 2007	165	39	35	8	195	4	0	8	15	20	61	6	49	53	(31)
Shabahang *et al*, 2002	26	18	45	20	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(35)
Shah *et al*, 2007	56	65	76	64	NA	NA	NA	NA	NA	NA	25	22	NA	35	(39)
Sogawa *et al*, 2013	41	15	60	15	55	1	0	28	47	0	34	22	58.30	74.30	(22)

Table IV. Continued.

	Sex				Child-Pugh score										
	LR		LT		LR			LT			MVI		Follow-up, months[a]		
First author, year	Male	Female	Male	Female	A	B	C	A	B	C	LR	LT	LR	LT	(Refs.)
Sotiropoulos *et al*, 2009	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(38)
Squires *et al*, 2014	NA	NA	NA	NA	39	6	0	37	75	19	14	33	45	40.20	(25)
Sung *et al*, 2017	71	18	54	13	87	2	0	18	35	14	9	12	NA	NA	(33)
Huang *et al*, 2014	51	4	28	5	49	6	0	15	10	8	10	7	NA	NA	(46)
Xia *et al*, 2021	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(44)
Xia *et al*, 2012	80	9	26	6	89	0	0	32	0	0	25	8	37	37	(48)
Xu *et al*, 2013	22	9	19	3	27	4	0	11	11	0	NA	NA	35	35	(47)
Yu *et al*, 2014	197	30	32	4	227	0	0	36	0	0	41	11	41.84±19.37	41.84±19.37	(45)
Zhu *et al*, 2011	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	(49)

[a]Data are presented as the median or mean. [b]Patients who received treatment between 1989 and 2004; [c]patients who received treatment between 2005 and 2011. MVI, microvascular invasion; LR, liver resection; LT, liver transplantation; NA, not available.

Table V. Comparisons of sex and Child-Pugh scores calculated using the χ^2 test.

Characteristics	LR, n	LT, n	P-value
Sex (male/female)	2,323/639	1,774/501	0.697
MVI (yes/no)	531/1,378	328/1,063	0.006
Child-Pugh score			
A	2,507	752	<0.001
B	128	507	
C	1	285	

LR, liver resection; LT, liver transplantation; MVI, microvascular invasion.

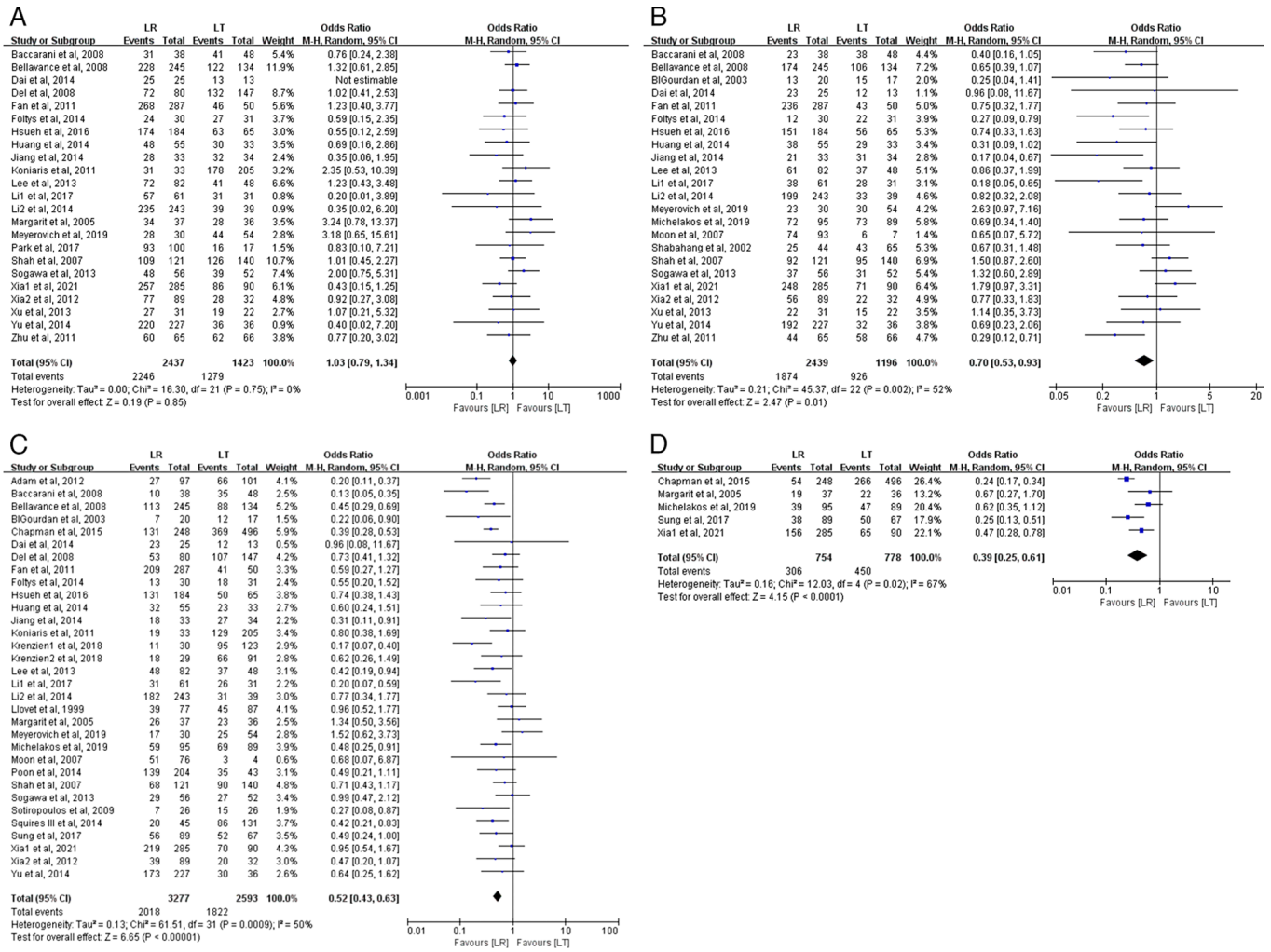

Figure 2. Forest plot of overall survival in patients meeting the Milan criteria at the (A) 1-year, (B) 3-year, (C) 5-year and (D) 10-year follow-ups. All comparisons were based on random-effects meta-analysis. Boxes represent the odds ratio of each study, with box sizes proportional to the study weight in the analysis. Segments represent the 95% CI of each study. Diamonds represent the overall effect size and diamond widths represent the overall 95% CI. CI, confidence interval; M-H, Mantel-Haenszel test; random, random effect; LT, liver transplantation; LR, liver resection.

reported that the 3-year OS rate in the LT group was lower compared with that in the LR group, although the difference was not statistically significant. The heterogeneity in the 10-year OS rate was primarily influenced by the study by Chapman *et al* (36), which identified the type of surgery as an independent risk factor for prognosis in multivariate analysis. The present study, which retrospectively analyzed data from five transplant centers, noted marked variation in surgical approaches and its large sample size further contributed to the observed heterogeneity in the 10-year OS rate.

The present analysis indicated that the 1-, 3-, 5- and 10-year DFS rates were all significantly higher in the LT group compared

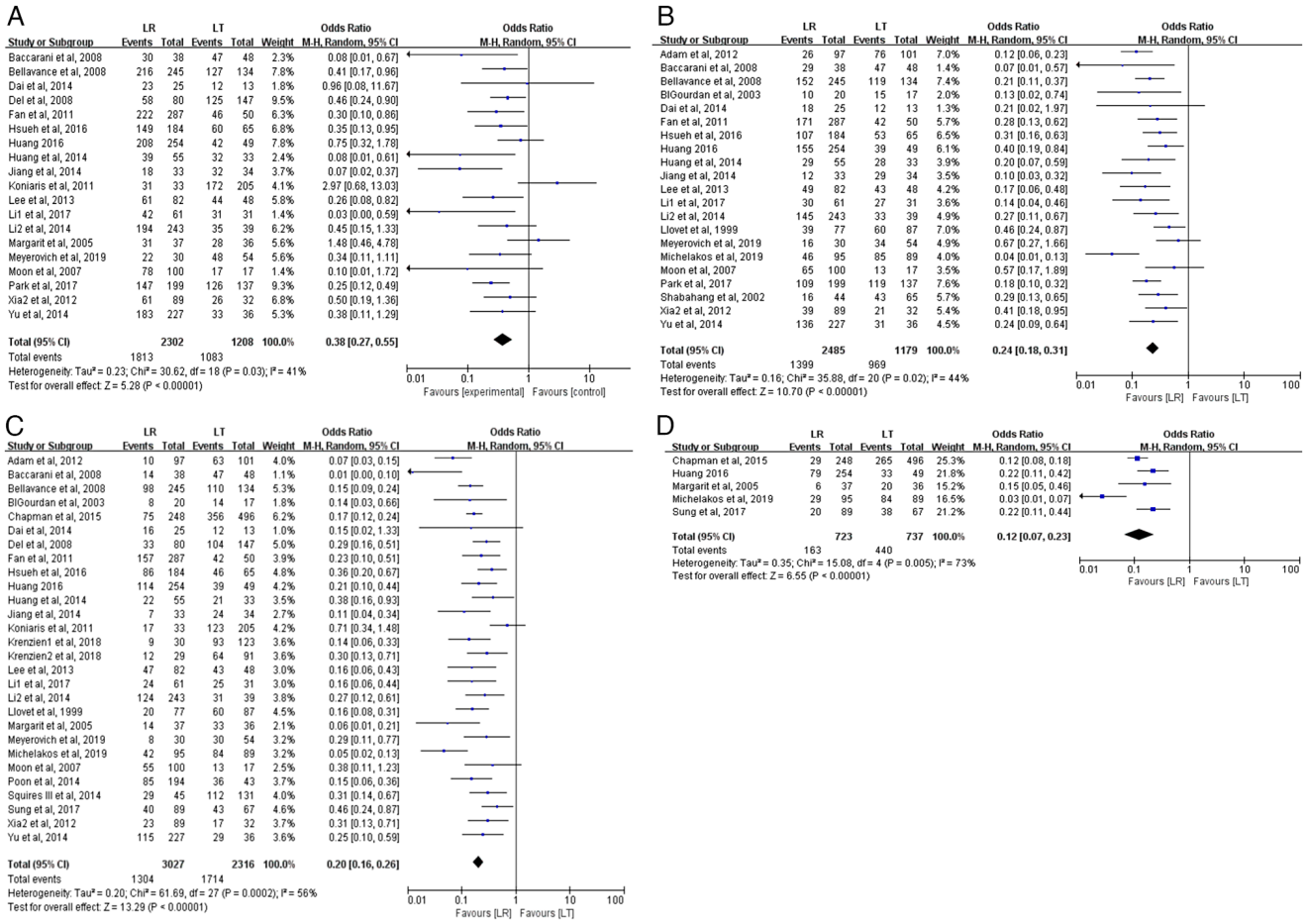

Figure 3. Forest plot of disease-free survival in patients meeting the Milan criteria at the (A) 1-year, (B) 3-year, (C) 5-year and (D) 10-year follow-ups. All comparisons were based on random-effects meta-analysis. Boxes represent the odds ratio of each study, with box sizes proportional to the study weight in the analysis. Segments represent the 95% CI of each study. Diamonds represent the overall effect size and diamond widths represent the overall 95% CI. CI, confidence interval; M-H, Mantel-Haenszel test; random, random effect; LT, liver transplantation; LR, liver resection.

with those in the LR group for patients with HCC meeting the Milan criteria. This finding is consistent with the report by Michelakos *et al* (18), which indicated that patients with LT had smaller maximum tumor diameters and included more patients with T0 stage. By contrast, Koniaris *et al* (37) reported a higher 1-year DFS rate in the LR group compared with that in the LT group, although the difference was not statistically significant. This discrepancy may be attributed to the technical challenges and complications arising from immunosuppressive therapy in transplantation surgery. The recurrence of HCC within the first year after LT may be influenced by several factors. First, despite meeting the Milan criteria, certain tumors may exhibit high invasiveness or micrometastasis that current diagnostic methods (such as computed tomography and magnetic resonance imaging) cannot detect prior to surgery (50). Second, the use of immunosuppressants in LT recipients may impair the immune system, creating an environment conducive to tumor recurrence and growth. Furthermore, delayed postoperative follow-up or failure to detect and treat recurrent tumors early could increase the RR. A recently proposed deep learning model has exhibited notable accuracy in the prediction of postoperative recurrence compared with the Milan criteria and could potentially identify high-risk subgroups, thereby improving recurrence management after LT (51).

The present study included patients with HCC with Child-Pugh B/C liver cirrhosis, revealing significant differences in cirrhosis severity between the two groups. Most patients in the LR group had Child-Pugh A liver function, whereas the LT group predominantly consisted of patients with Child-Pugh B/C liver function, a factor that may have contributed to the observed heterogeneity. Cirrhosis severity serves a key role in the prognosis of patients with HCC. For those with mild or non-cirrhotic liver disease (Child-Pugh A), both LR and LT yield favorable therapeutic outcomes. However, LT is typically recommended for patients with moderate to severe cirrhosis.

The present study findings indicated that LT resulted in significantly higher 1-, 3-, 5- and 10-year DFS rates compared with LR for patients with HCC meeting the Milan criteria. This may be attributed to the fact that LT addresses both the tumor and the underlying liver disease (52). By contrast, residual liver tissue following LR may harbor micrometastases, increasing the risk of tumor recurrence or liver decompensation. While no significant difference was found in the 1-year OS rate between LR and LT for patients within the Milan criteria in the present study, LT demonstrated improved 3-, 5- and 10-year OS outcomes. The minimal difference in 1-year OS rate could be attributed to complications such as acute graft rejection (53),

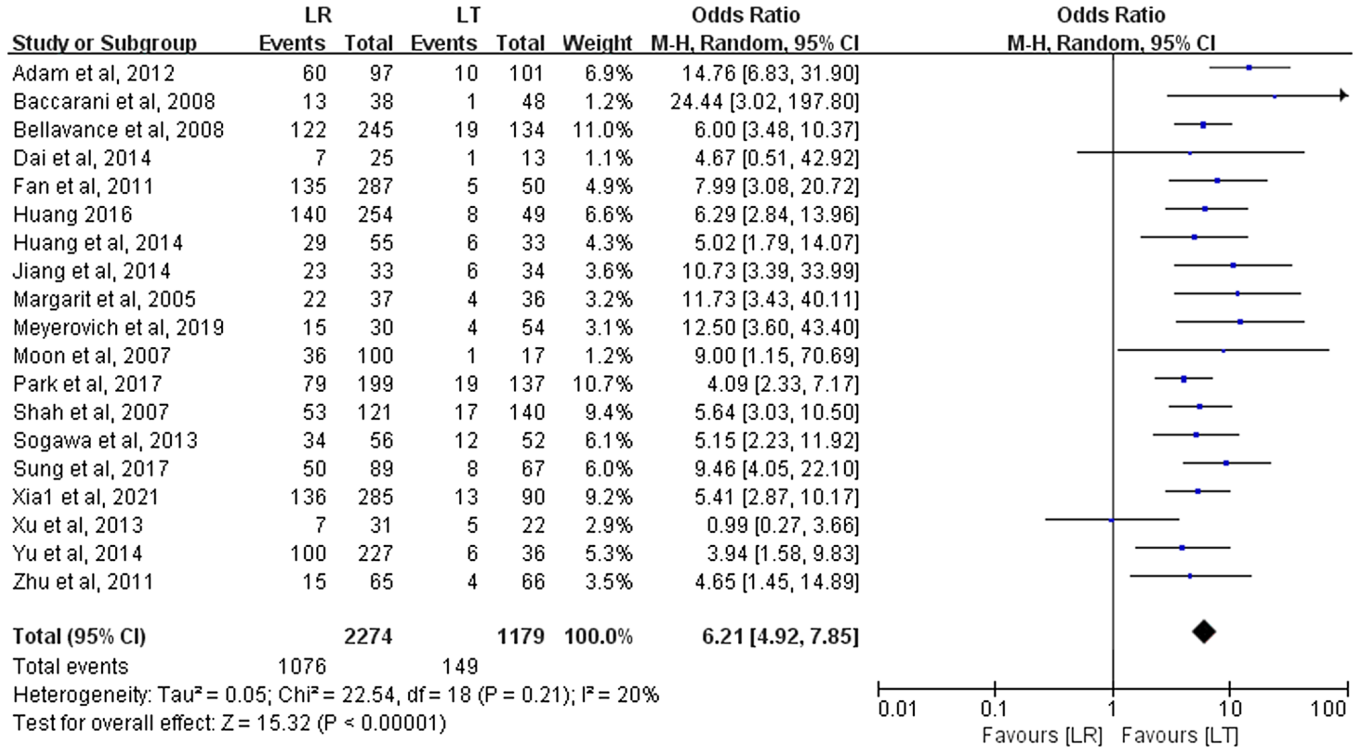

Figure 4. Forest plot of recurrence rate in patients meeting the Milan criteria. All comparisons were based on random-effects meta-analysis. Boxes represent the odds ratio of each study, with box sizes proportional to the study weight in the analysis. Segments represent the 95% CI of each study. Diamonds represent the overall effect size and diamond widths represent the overall 95% CI. CI, confidence interval; M-H, Mantel-Haenszel test; random, random effect; LT, liver transplantation; LR, liver resection.

infections due to immunosuppressants and renal failure (54), rather than the cancer itself. Long-term survival outcomes (3-, 5- and 10-year) were predominantly influenced by tumor recurrence. The present analysis demonstrated that LT reduced RR by 29.2% compared with LR, further supporting its long-term survival benefits. The risk of death within 5 years post-LT in elderly patients was not higher compared with that in younger patients and the OS rate in elderly patients with LT was higher compared with those who underwent LR. Thus, while elderly patients >70 may experience decline in organ function, poor surgical tolerance, slower recovery and coexisting chronic conditions, age alone should not exclude patients from liver transplant consideration (55-57).

Due to factors such as organ shortage, liver donor waiting times, hospitalization durations and associated costs, certain studies have recommended LR as the initial treatment for patients with HCC eligible for either LR or LT, with LT being considered as a salvage method for tumor recurrence (58,59). Several studies reported that the median hospitalization time for patients with HCC undergoing LT was 9-14 days longer compared with that for those patients who underwent LR (28,31). Michelakos *et al* (18) highlighted that the average cost of LT was markedly higher compared with that of LR, considering the expenses associated with preoperative bridging therapy and postoperative recurrence management (18). Shah *et al* (39) suggested that LT offers improved survival outcomes compared with LR only if the waiting time for a liver transplant is <4 months, as patients with HCC may lose the opportunity for transplantation due to tumor progression during the waiting period. However, certain studies have noted that the prognosis of salvage LT after recurrence post-resection is worse compared with that of primary LT, and the risks associated with sequential LT following resection should be carefully considered (60,61).

The present meta-analysis provided a comprehensive evaluation of the prognostic outcomes of LT and LR for patients with HCC within the Milan criteria, offering the latest reliable data and insights key for guiding the selection of LT candidates in liver cancer treatment. Nonetheless, several limitations should be acknowledged. First, due to ethical considerations, all included studies were retrospective, with no randomized controlled trials available, preventing assessment of blinding and potentially introducing selection bias. Second, most studies did not adequately report loss-to-follow-up rates, limiting the ability to evaluate attrition bias. Third, funnel plots indicated the presence of publication bias, as studies with statistically significant positive results were more likely to be published, which may have influenced the present study findings. Lastly, relatively few studies that had smaller sample sizes compared the 10-year OS and DFS rates. These limitations present opportunities for future research. To address these issues, strategies such as mandatory clinical trial registration on public platforms before study initiation, ensuring transparency, establishing cross-regional or cross-institutional research networks to increase sample size and improve generalizability, and utilizing propensity score matching to correct for confounding factors could enhance the robustness and applicability of future studies.

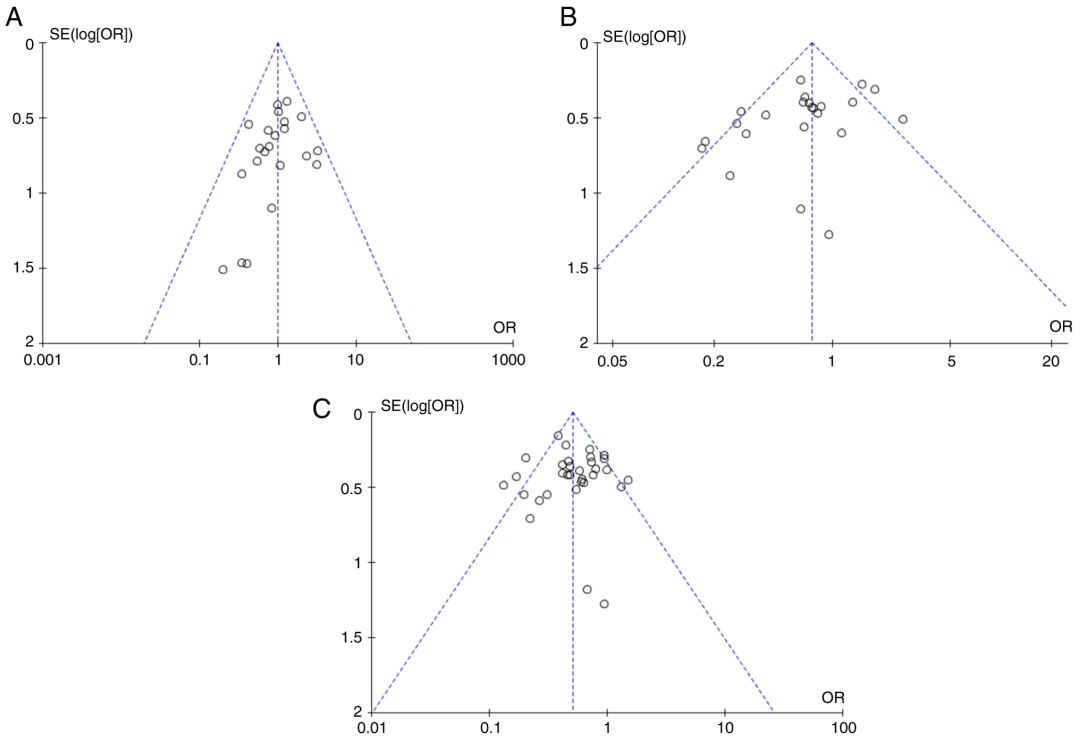

Figure 5. Funnel plots evaluating publication bias, including all studies assessing (A) 1-year, (B) 3-year and (C) 5-year OS rates. OS, overall survival; OR, odds ratio.

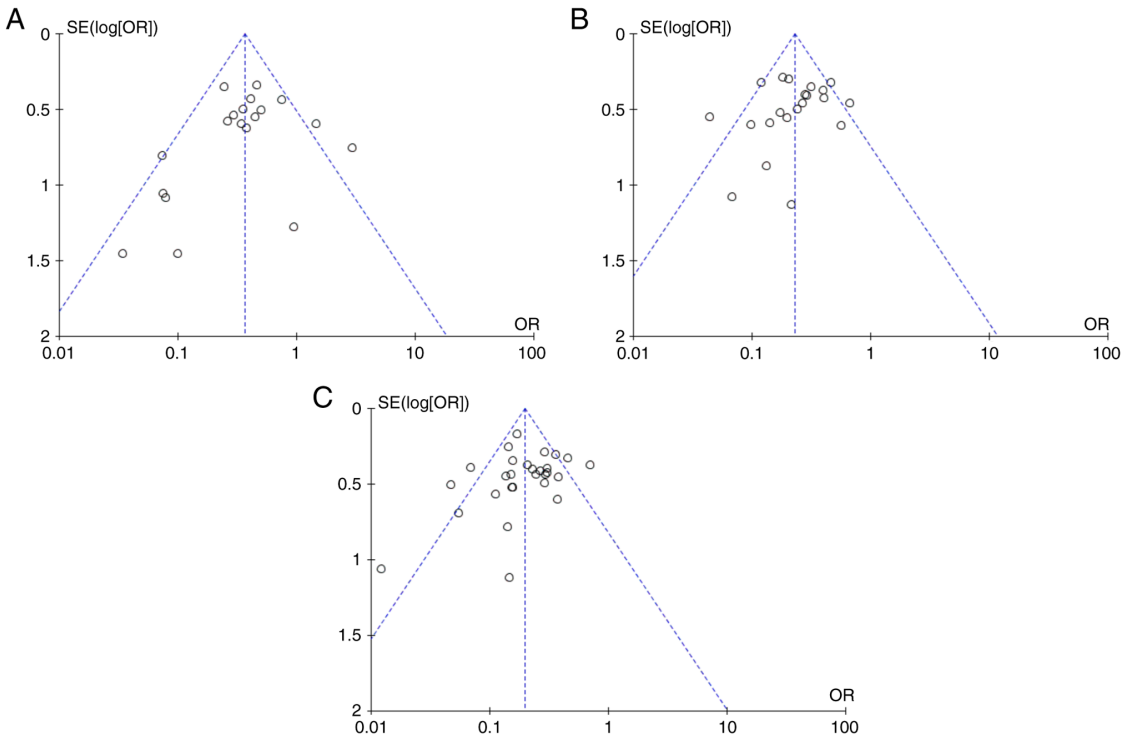

Figure 6. Funnel plots evaluating publication bias, including all studies assessing (A) 1-year, (B) 3-year and (C) 5-year DFS rates. DFS, disease-free survival; OR, odds ratio.

LT is the preferred treatment option for patients with HCC within the Milan criteria. However, in clinical practice, it faces multiple challenges across various dimensions. Technically, the LT procedure is complex and demanding, which requires a highly skilled and experienced surgical team to ensure optimal patient outcomes. Economically, LT is associated with notable costs, including high surgical expenses and the long-term financial burden of immunosuppressive therapy. The severe shortage of donor organs is a major limiting factor for the widespread adoption of LT, and the lack of

a global, comprehensive and equitable organ allocation system further complicates the process of securing suitable donors for patients. For example, in Singapore, patients with liver cancer have to meet the University of California San Francisco criteria (includes i) a single tumor ≤6.5 cm; ii) ≤3 lesions and maximum lesion diameter ≤4.5 cm, cumulative diameter ≤8 cm; and iii) no intrahepatic vascular infiltration or extrahepatic metastasis) to be eligible for the deceased donor liver transplant waiting list, which makes donor acquisition even more challenging (57). As a result, living donor LT has emerged as a key strategy to address the shortage of deceased donor organs (62).

Despite the benefits of LT, the 1-year OS rates post-transplant are typically ~90%, with ~10% mortality rates following both LT and LR. The high 1-year mortality rate after LR can be predicted preoperatively by factors such as multinodularity, Child-Pugh class and MVI (63). Therefore, a comprehensive and accurate preoperative assessment of patients with HCC is essential to guide the selection of the most appropriate treatment. In certain cases, LT or LR may not be the only viable options for treatment. Alternative approaches, such as transarterial chemoembolization (TACE) combined with radiofrequency ablation (RFA), may also offer curative outcomes. While the 3-year and 5-year DFS rates are higher in the LR group compared with those in the TACE + RFA group, no significant differences in the 1-, 3- and 5-year OS rates have been observed (64). Therefore, TACE + RFA is also considered a safe and effective treatment for early-stage HCC.

In conclusion, the present study demonstrated that LT provides significantly improved long-term OS and DFS rates, as well as a lower RR, compared with LR for patients with HCC meeting the Milan criteria. Therefore, LT is recommended as the preferred initial treatment for these patients, provided that a suitable liver donor is available. However, each case should be evaluated through multidisciplinary consultations to optimize patient outcomes while ensuring efficient use of limited donor resources. Although this conclusion is based on a comprehensive analysis of existing studies, clinical decisions must also consider specific patient circumstances. A notable limitation of the Milan criteria is its focus solely on tumor size and number, without incorporating liver function and cirrhosis in a more holistic evaluation. In cases of organ shortage, the degree of liver cirrhosis and liver reserve function should guide the decision between LT and LR. This approach would prioritize LR for patients with HCC with preserved liver function. The development of a more refined, comprehensive evaluation criteria for LT remains an area for future research. Furthermore, with the rapid advancements in cancer-targeted immunotherapy, the outcomes of LT and LR should be reassessed. It remains to be determined whether the combination of surgical resection and targeted immunotherapy can provide notably improved or similar results to LT, how immunotherapy should be managed post-LT and how HCC recurrence can be addressed after LT under immunosuppressive therapy, all of which warrant further investigation.

Acknowledgements

Not applicable.

Funding

The present study was supported in part by the International Cooperation Fund of the Science and Technology Bureau of Jilin Province (grant no. 20220402075GH), the Jilin Province Health Research Talent Project (grant no. 2022SCZ06) and the NSFC Regional Innovation and Development Fund (grant no. U20A20360).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

JW and YW conducted database searching and data analysis. JW wrote the manuscript. ZP conducted data analysis and revised the manuscript. YY conducted database searching, and data identification and analysis. WL participated in research design and wrote the manuscript. JW and YW confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A and Bray F: Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 71: 209-249, 2021.
2. Taefi A, Abrishami A, Nasseri-Moghaddam S, Eghtesad B and Sherman M: Surgical resection versus liver transplant for patients with hepatocellular carcinoma. Cochrane Database Syst Rev 6: CD006935, 2013.
3. Vibert E, Schwartz M and Olthoff KM: Advances in resection and transplantation for hepatocellular carcinoma. J Hepatol 72: 262-276, 2020.
4. Aufhauser DD Jr, Sadot E, Murken DR, Eddinger K, Hoteit M, Abt PL, Goldberg DS, DeMatteo RP and Levine MH: Incidence of occult intrahepatic metastasis in hepatocellular carcinoma treated with transplantation corresponds to early recurrence rates after partial hepatectomy. Ann Surg 267: 922-928, 2018.
5. Bzeizi KI, Abdullah M, Vidyasagar K, Alqahthani SA and Broering D: Hepatocellular carcinoma recurrence and mortality rate post liver transplantation: Meta-analysis and systematic review of real-world evidence. Cancers (Basel) 14: 5114, 2022.
6. Klupp J, Kohler S, Pascher A and Neuhaus P: Liver transplantation as ultimate tool to treat portal hypertension. Dig Dis 23: 65-71, 2005.
7. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, Montalto F, Ammatuna M, Morabito A and Gennari L: Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. N Engl J Med 334: 693-699, 1996.

8. Bhoori S, Schiavo M, Russo A and Mazzaferro V: First-line treatment for hepatocellular carcinoma: Resection or transplantation? Transplant Proc 39: 2271-2273, 2007.
9. European Association for the Study of the Liver: EASL clinical practice guidelines: Management of hepatocellular carcinoma. J Hepatol 69: 182-236, 2018.
10. Sala M, Fuster J, Llovet JM, Navasa M, Solé M, Varela M, Pons F, Rimola A, García-Valdecasas JC, Brú C, *et al*: High pathological risk of recurrence after surgical resection for hepatocellular carcinoma: An indication for salvage liver transplantation. Liver Transpl 10: 1294-1300, 2004.
11. Cherqui D, Laurent A, Mocellin N, Tayar C, Luciani A, Van Nhieu JT, Decaens T, Hurtova M, Memeo R, Mallat A and Duvoux C: Liver resection for transplantable hepatocellular carcinoma: Long-term survival and role of secondary liver transplantation. Ann Surg 250: 738-746, 2009.
12. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC and Williams R: Transection of the oesophagus for bleeding oesophageal varices. Br J Surg 60: 646-649, 1973.
13. Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, Petticrew M and Altman DG; International Stroke Trial Collaborative Group; European Carotid Surgery Trial Collaborative Group: Evaluating non-randomised intervention studies. Health Technol Assess 7: 3-10, 1-173, 2003.
14. Park MS, Lee KW, Kim H, Choi YR, Hong G, Yi NJ and Suh KS: Primary living-donor liver transplantation is not the optimal treatment choice in patients with early hepatocellular carcinoma with poor tumor biology. Transplant Proc 49: 1103-1108, 2017.
15. Jiang L, Liao A, Wen T, Yan L, Li B and Yang J: Living donor liver transplantation or resection for Child-Pugh A hepatocellular carcinoma patients with multiple nodules meeting the Milan criteria. Transpl Int 27: 562-569, 2014.
16. Li C, Liu JY, Peng W, Wen TF, Yan LN, Yang JY, Li B, Wang WT and Xu MQ: Liver resection versus transplantation for multiple hepatocellular carcinoma: A propensity score analysis. Oncotarget 8: 81492-81500, 2017.
17. Hsueh KC, Lee TY, Kor CT, Chen TM, Chang TM, Yang SF and Hsieh CB: The role of liver transplantation or resection for patients with early hepatocellular carcinoma. Tumour Biol 37: 4193-4201, 2016.
18. Michelakos T, Xourafas D, Qadan M, Pieretti-Vanmarcke R, Cai L, Patel MS, Adler JT, Fontan F, Basit U, Vagefi PA, *et al*: Hepatocellular carcinoma in transplantable Child-Pugh A cirrhotics: Should cost affect resection vs transplantation? J Gastrointest Surg 23: 1135-1142, 2019.
19. Margarit C, Escartín A, Castells L, Vargas V, Allende E and Bilbao I: Resection for hepatocellular carcinoma is a good option in Child-Turcotte-Pugh class A patients with cirrhosis who are eligible for liver transplantation. Liver Transpl 11: 1242-1251, 2005.
20. Foltys D, Zimmermann T, Kaths M, Strempel M, Heise M, Hoppe-Lotichius M, Weiler N, Scheuermann U, Ruckes C, Hansen T, *et al*: Hepatocellular carcinoma in Child's A cirrhosis: A retrospective analysis of matched pairs following liver transplantation vs liver resection according to the intention-to-treat principle. Clin Transplant 28: 37-46, 2014.
21. Bigourdan JM, Jaeck D, Meyer N, Meyer C, Oussoultzoglou E, Bachellier P, Weber JC, Audet M, Doffoël M and Wolf P: Small hepatocellular carcinoma in Child A cirrhotic patients: Hepatic resection versus transplantation. Liver Transpl 9: 513-520, 2003.
22. Sogawa H, Shrager B, Jibara G, Tabrizian P, Roayaie S and Schwartz M: Resection or transplant-listing for solitary hepatitis C-associated hepatocellular carcinoma: An intention-to-treat analysis. HPB (Oxford) 15: 134-141, 2013.
23. Moon DB, Lee SG and Hwang S: Liver transplantation for hepatocellular carcinoma: Single nodule with Child-Pugh class A sized less than 3 cm. Dig Dis 25: 320-328, 2007.
24. Bellavance EC, Lumpkins KM, Mentha G, Marques HP, Capussotti L, Pulitano C, Majno P, Mira P, Rubbia-Brandt L, Ferrero A, *et al*: Surgical management of early-stage hepatocellular carcinoma: Resection or transplantation? J Gastrointest Surg 12: 1699-1708, 2008.
25. Squires MH III, Hanish SI, Fisher SB, Garrett C, Kooby DA, Sarmiento JM, Cardona K, Adams AB, Russell MC, Magliocca JF, *et al*: Transplant versus resection for the management of hepatocellular carcinoma meeting Milan Criteria in the MELD exception era at a single institution in a UNOS region with short wait times. J Surg Oncol 109: 533-541, 2014.
26. Meyerovich G, Goykhman Y, Nakache R, Nachmany I, Lahat G, Shibolet O, Menachem Y, Katchman H, Wolf I, Geva R, *et al*: Resection vs transplant listing for hepatocellular carcinoma: An intention-to-treat analysis. Transplant Proc 51: 1867-1873, 2019.
27. Krenzien F, Schmelzle M, Struecker B, Raschzok N, Benzing C, Jara M, Bahra M, Öllinger R, Sauer IM, Pascher A, *et al*: Liver transplantation and liver resection for cirrhotic patients with hepatocellular carcinoma: Comparison of long-term survivals. J Gastrointest Surg 22: 840-848, 2018.
28. Huang ZY, Liang BY, Xiong M, Dong KS, Zhang ZY, Zhang EL, Li CH and Chen XP: Severity of cirrhosis should determine the operative modality for patients with early hepatocellular carcinoma and compensated liver function. Surgery 159: 621-631, 2016.
29. Li C, Zhu WJ, Wen TF, Dai Y, Yan LN, Li B, Yang JY, Wang WT and Xu MQ: Child-Pugh A hepatitis B-related cirrhotic patients with a single hepatocellular carcinoma up to 5 cm: Liver transplantation vs resection. J Gastrointest Surg 18: 1469-1476, 2014.
30. Dai Y, Li C, Wen TF and Yan LN: Comparison of liver resection and transplantation for Child-pugh A cirrhotic patient with very early hepatocellular carcinoma and portal hypertension. Pak J Med Sci 30: 996-1000, 2014.
31. Poon RTP, Fan ST, Lo CM, Liu CL and Wong J: Difference in tumor invasiveness in cirrhotic patients with hepatocellular carcinoma fulfilling the Milan criteria treated by resection and transplantation: Impact on long-term survival. Ann Surg 245: 51-58, 2007.
32. Baccarani U, Isola M, Adani GL, Benzoni E, Avellini C, Lorenzin D, Bresadola F, Uzzau A, Risaliti A, Beltrami AP, *et al*: Superiority of transplantation versus resection for the treatment of small hepatocellular carcinoma. Transpl Int 21: 247-254, 2008.
33. Sung PS, Yanf H, Na GH, Hwang S, Kang D, Jang JW, Bae SH, Choi JY, Kim DG, Yoon SK and You YK: Long-term outcome of liver resection versus transplantation for hepatocellular carcinoma in a region where living donation is a main source. Ann Transplant 22: 276-284, 2017.
34. Lee KK, Kim DG, Moon IS, Lee MD and Park JH: Liver transplantation versus liver resection for the treatment of hepatocellular carcinoma. J Surg Oncol 101: 47-53, 2010.
35. Shabahang M, Franceschi D, Yamashiki N, Reddy R, Pappas PA, Aviles K, Flores S, Chaparro A, Levi JU, Sleeman D, *et al*: Comparison of hepatic resection and hepatic transplantation in the treatment of hepatocellular carcinoma among cirrhotic patients. Ann Surg Oncol 9: 881-886, 2002.
36. Chapman WC, Klintmalm G, Hemming A, Vachharajani N, Majella Doyle MB, DeMatteo R, Zaydfudim V, Chung H, Cavaness K, Goldstein R, *et al*: Surgical treatment of hepatocellular carcinoma in North America: Can hepatic resection still be justified? J Am Coll Surg 220: 628-637, 2015.
37. Koniaris LG, Levi DM, Pedroso FE, Franceschi D, Tzakis AG, Santamaria-Barria JA, Tang J, Anderson M, Misra S, Solomon NL, *et al*: Is surgical resection superior to transplantation in the treatment of hepatocellular carcinoma? Ann Surg 254: 527-538, 2011.
38. Sotiropoulos GC, Drühe N, Sgourakis G, Molmenti EP, Beckebaum S, Baba HA, Antoch G, Hilgard P, Radtke A, Saner FH, *et al*: Liver transplantation, liver resection, and transarterial chemoembolization for hepatocellular carcinoma in cirrhosis: Which is the best oncological approach? Dig Dis Sci 54: 2264-2273, 2009.
39. Shah SA, Cleary SP, Tan JC, Wei AC, Gallinger S, Grant DR and Greig PD: An analysis of resection vs transplantation for early hepatocellular carcinoma: Defining the optimal therapy at a single institution. Ann Surg Oncol 14: 2608-2614, 2007.
40. Fan ST, Poon RT, Yeung C, Lam CM, Lo CM, Yuen WK, Ng KK, Liu CL and Chan SC: Outcome after partial hepatectomy for hepatocellular cancer within the Milan criteria. Br J Surg 98: 1292-1300, 2011.
41. Del Gaudio M, Ercolani G, Ravaioli M, Cescon M, Lauro A, Vivarelli M, Zanello M, Cucchetti A, Vetrone G, Tuci F, *et al*: Liver transplantation for recurrent hepatocellular carcinoma on cirrhosis after liver resection: University of Bologna experience. Am J Transplant 8: 1177-1185, 2008.
42. Adam R, Bhangui P, Vibert E, Azoulay D, Pelletier G, Duclos-Vallée JC, Samuel D, Guettier C and Castaing D: Resection or transplantation for early hepatocellular carcinoma in a cirrhotic liver: Does size define the best oncological strategy? Ann Surg 256: 883-891, 2012.

43. Llovet JM, Fuster J and Bruix J: Intention-to-treat analysis of surgical treatment for early hepatocellular carcinoma: Resection versus transplantation. Hepatology 30: 1434-1440, 1999.
44. Xia YX, Zhang F, Li XC, Kong LB, Zhang H, Li DH, Cheng F, Pu LY, Zhang CY, Qian XF, *et al*: Surgical treatment of primary liver cancer: A report of 10 966 cases. Zhonghua Wai Ke Za Zhi 59: 6-17, 2021 (In Chinese).
45. Yu Y, Li C and Wen T: Child-Pugh A Class cirrhotic patients with a single hepatocellular carcinoma up to 5 cm in diameter: Liver transplantation versus resection. Chin J Bases Clin General Surg 21: 406-409, 2014 (In Chinese).
46. Huang JH and Zhou J: Factors for predicting outcomes of liver transplantation and liver resection for hepatocellular carcinoma meeting Milan criteria. J South Med Univ 34: 406-409, 2014.
47. Xu XS, Qu K, Zhou L, Song YZ, Zhang YL and Liu C: Selection of surgical procedure in the treatment of early hepatocellular carcinoma. Chin J Hepat Surg (Electronic Edition) 2: 80-85, 2013.
48. Xia Y, Jiang Y, Cai Q, Pan F, Zhang X and Lü L: Comparison of efficacies of hepatectomy and liver transplantion for patients with hepatocellular carcinoma fulfilling the Milan criteria. Chin J Dig Surg 11: 526-529, 2012 (In Chinese).
49. Zhu X, He X, Chen M, Yuan Y and Cui S: A multi-center comparative study of the effectiveness of three radical therapies on hepatocellular carcinoma. Chin J Hepatobiliary Surg 17: 372-375, 2011 (In Chinese).
50. Singal AG, Llovet JM, Yarchoan M, Mehta N, Heimbach JK, Dawson LA, Jou JH, Kulik LM, Agopian VG, Marrero JA, *et al*: AASLD practice guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma. Hepatology 78: 1922-1965, 2023.
51. Ko SH, Cao J, Yang YK, Xi ZF, Han HW, Sha M and Xia Q: Development of a deep learning model for predicting recurrence of hepatocellular carcinoma after liver transplantation. Front Med (Lausanne) 11: 1373005, 2024.
52. Clavien PA, Lesurtel M, Bossuyt PM, Gores GJ, Langer B and Perrier A; OLT for HCC Consensus Group: Recommendations for liver transplantation for hepatocellular carcinoma: An international consensus conference report. Lancet Oncol 13: e11-e22, 2012.
53. Matinlauri IH, Nurminen MM, HÖckerstedt KA and Isoniemi HM: Changes in liver graft rejections over time. Transplant Proc 38: 2663-2666, 2006.
54. Tinti F, Umbro I, Giannelli V, Merli M, Ginanni Corradini S, Rossi M, Nofroni I, Poli L, Berloco PB and Mitterhofer AP: Acute renal failure in liver transplant recipients: Role of pretransplantation renal function and 1-year follow-up. Transplant Proc 43: 1136-1138, 2011.
55. European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu. EASL clinical practice guidelines: Liver transplantation. J Hepatol 64: 433-485, 2016.
56. Mousa OY, Nguyen JH, Ma Y, Rawal B, Musto KR, Dougherty MK, Shalev JA and Harnois DM: Evolving role of liver transplantation in elderly recipients. Liver Transpl 25: 1363-1374, 2019.
57. Chow PKH, Choo SP, Ng DCE, Lo RH, Wang ML, Toh HC, Tai DW, Goh BK, Wong JS, Tay KH, *et al*: National cancer centre singapore consensus guidelines for hepatocellular carcinoma. Liver Cancer 5: 97-106, 2016.
58. Chan DL, Alzahrani NA, Morris DL and Chua TC: Systematic review of efficacy and outcomes of salvage liver transplantation after primary hepatic resection for hepatocellular carcinoma. J Gastroenterol Hepatol 29: 31-41, 2014.
59. De Carlis L, Di Sandro S, Giacomoni A, Mangoni I, Lauterio A, Mihaylov P, Cusumano C and Rampoldi A: Liver transplantation for hepatocellular carcinoma recurrence after liver resection: Why deny this chance of cure? J Clin Gastroenterol 47: 352-358, 2013.
60. Zheng Z, Liang W, Milgrom DP, Zheng Z, Schroder PM, Kong NS, Yang C, Guo Z and He X: Liver transplantation versus liver resection in the treatment of hepatocellular carcinoma: A meta-analysis of observational studies. Transplantation 97: 227-234, 2014.
61. Adam R, Azoulay D, Castaing D, Eshkenazy R, Pascal G, Hashizume K, Samuel D and Bismuth H: Liver resection as a bridge to transplantation for hepatocellular carcinoma on cirrhosis: A reasonable strategy? Ann Surg 238: 508-519, 2003.
62. Goldaracena N and Barbas AS: Living donor liver transplantation. Curr Opin Organ Transplant 24: 131-137, 2019.
63. Sheriff S, Madhavan S, Lei GY, Chan YH, Junnarkar SP, Huey CW, Low JK and Shelat VG: Predictors of mortality within the first year post-hepatectomy for hepatocellular carcinoma. J Egypt Natl Canc Inst 34: 14, 2022.
64. Gui CH, Baey S, D'cruz RT and Shelat VG: Trans-arterial chemoembolization + radiofrequency ablation versus surgical resection in hepatocellular carcinoma-A meta-analysis. Eur J Surg Oncol 46: 763-771, 2020.