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REVIEW

# Living-donor *vs* deceased-donor liver transplantation for patients with hepatocellular carcinoma

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## Abstract

With the increasing prevalence of living-donor liver transplantation (LDLT) for patients with hepatocellular carcinoma (HCC), some authors have reported a potential increase in the HCC recurrence rates among LDLT recipients compared to deceased-donor liver transplantation (DDLT) recipients. The aim of this review is to encompass current opinions and clinical reports regarding differences in the outcome, especially the recurrence of HCC, between LDLT and DDLT. While some studies report impaired recurrence - free survival and increased recurrence rates among LDLT recipients, others, including large database studies, report comparable recurrence - free survival and recurrence rates between LDLT and DDLT. Studies supporting the increased recurrence in LDLT have linked graft regeneration to tumor progression, but we found no association between graft regeneration/initial graft volume and tumor recurrence among our 125 consecutive LDLTs for HCC cases. In the absence of a prospective study regarding the use of LDLT *vs* DDLT for HCC patients, there is no evidence to support the higher HCC recurrence after LDLT than DDLT, and LDLT remains a reasonable treatment option for HCC patients with cirrhosis.



**Key words:** Deceased donor liver transplantation; Hepatocellular carcinoma; Living donors; Living-donor liver transplantation; Recurrence

**Core tip:** The current opinions and clinical reports regarding differences in the recurrence of hepatocellular carcinoma (HCC) between living donor liver transplantation (LDLT) and deceased donor liver transplantation (DDLT) were reviewed. In the absence of a prospective study regarding the use of LDLT *vs* DDLT for HCC patients, only with some retrospective studies with conflicting results, there is no evidence to support the higher HCC recurrence after LDLT than DDLT, and LDLT remains a reasonable treatment option for HCC patients with cirrhosis.

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## INTRODUCTION

Hepatocellular carcinoma (HCC) is the 7th most common cancer overall and the 3rd most common cause of cancer-related death worldwide[1,2]. Since the landmark report of the Milan criteria by Mazzaferro *et al*[3], which demonstrated comparable outcomes of patients with HCC having a single tumor smaller than 5 cm in diameter or up to 3 tumors smaller than 3 cm in diameter with no vascular invasion or extra-hepatic disease determined by preoperative imaging studies, deceased - donor liver transplantation (DDLT) has become an established treatment for cirrhotic patients with HCC[4,5]. Similarly, in Asian countries where living-donor liver transplantation (LDLT) comprises the majority of liver transplantation procedures, LDLT has become an established treatment

**Table 1 Studies comparing living - donor liver transplantation and deceased - donor liver transplantation for hepatocellular carcinoma**

| Ref. | Country | Year | Study period | Type of LT | Case number | Recurrence - free survival | | | *P* | % Recurrence rate | *P* | Criteria used | % Outside Milan | Difference in tumor characteristics | Median follow-up period (mo) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 1-yr | 3-yr | 5-yr | | | | | | | |
| Impaired results in LDLT | | | | | | | | | | | | | | | |
| Park *et al*[10] | South Korea | 2014 | 1999-2010 | LDLT | 166 | 89 | | 81 | 0.045 | 19 | 0.045 | UCSF | NA | none | 35 |
| | | | | DDLT | 50 | 96 | | 94 | | 6 | | | | | |
| Vakili *et al*[13] | United States | 2009 | 1999-2007 | LDLT | 28 | | | | | 29 | < 0.05 | UNOS | 25 | none | 41 |
| | | | | DDLT | 65 | | | | | 12 | | | | | |
| Kulik *et al*[12] | United States | 2012 | 1998-2010 | LDLT | 100 | 80 | 66 | 56 | 0.05 | 38 | 0.0004 | UNOS | 59 | More aggressive | 60 |
| | Multi-center | | | DDLT | 97 | 90 | 81 | 73 | | 11 | | | 30 | in LDLT | |
| Lo *et al*[14] | Hong Kong | 2007 | 1995-2004 | LDLT | 43 | 93 | 71 | 71 | 0.029 | 29 | 0.029 | UCSF | 26 | More aggressive | 33 |
| | | | | DDLT | 17 | 100 | 100 | 100 | | 0 | | | 29 | in LDLT | |
| Comparable results | | | | | | | | | | | | | | | |
| Sandhu *et al*[15] | Canada | 2013 | 1996-2009 | LDLT | 58 | 88 | 75 | 70 | NS | 17 | NS | Toronto | 28 | none | 38 |
| | | | | DDLT | 287 | 86 | 75 | 70 | | 15 | | criteria | 32 | | 31 |
| Bhangui *et al*[16] | France | 2011 | 2000-2009 | LDLT | 36 | 100 | 89 | 88 | NS | 13 | NS | UCSF | 27 | none | 58 |
| | | | | DDLT | 120 | 93 | 89 | 86 | | 13 | | | 21 | | 50 |
| Li *et al*[36] | China | 2010 | 2005-2009 | LDLT | 38 | 71 | 42 | | NS | 50 | NS | UCSF | 79 | none | 25 |
| | | | | DDLT | 101 | 76 | 41 | | | 55 | | | 68 | | |
| Di Sandro *et al*[35] | Italy | 2009 | 2000-2007 | LDLT | 25 | | 96 | 96 | NS | 4 | NS | Milan | 20 | none | NA |
| | | | | DDLT | 154 | | 91 | 89 | | 11 | | | 31 | | |
| Sotiropoulos *et al*[20] | Germany | 2007 | 1998-2006 | LDLT | 45 | 88 | 75 | | NS | 12 | NS | UCSF | 44 | none | NA |
| | | | | DDLT | 55 | | 81 | | | 14 | | | | | |
| Hwang *et al*[8] | South Korea | 2005 | 1992-2002 | LDLT | 237 | 83 | 80 | | NS | 18 | NS | | 27 | none | 26 |
| | Multi-center | | | DDLT | 75 | 88 | 82 | | | 16 | | | 29 | | 45 |
| Gondolesi *et al*[17] | United States | 2004 | 1988-2002 | LDLT | 36 | 82 | 74 | | NS | 19 | NS | UNOS | 53 | none | 15 |
| | | | | DDLT | 165 | 90 | 83 | | | 19 | | | | | |

DDLT: Deceased - donor liver transplantation; HCC: Hepatocellular carcinoma; LDLT: Living - donor liver transplantation; LT: Liver transplantation; UCSF: University of California, San Francisco; UNOS: United Network for Organ Sharing; NA: Not applicable; NS: Not significant.

for HCC patients with end-stage liver disease[6,7]. LDLT is now considered a promising treatment for HCC patients in Western countries, not only to compensate for the shortage of donor organs but also to reduce the dropout rate on the waiting list[8].

With the accumulation of LDLTs for HCC patients, the impact of LDLT on recipient outcome compared with DDLT, especially the recurrence of HCC after liver transplantation, has become an important topic of debate[9]. The aim of this review was to encompass the current opinions and clinical reports regarding the differences in outcome, especially the recurrence of HCC, between LDLT and whole liver DDLT.

## STUDIES COMPARING LDLT AND DDLT FOR HCC PATIENTS

Studies comparing LDLT and DDLT for HCC patients are summarized in Table 1. All DDLTs reviewed here were done with the whole liver graft.

### *Studies reporting a poorer outcome in the LDLT setting*

Park *et al*[10] recently reported poorer recurrence-free survival among 166 LDLT recipients (81% at 5 years) compared to 50 DDLT recipients (94% at 5 years; $P = 0.045$). The noteworthy finding of this study was that the smaller the LDLT graft, the poorer the recurrence - free survival. Based on this finding, Park *et al*[10] suggested that the physiology of the small graft may stimulate tumor recurrence.

The results of the A2ALL cohort in United States also demonstrated an impaired outcome in LDLT recipients. In their initial report[11], they found a higher rate of recurrence within 3 years in LDLT than in DDLT (29% *vs* 0%, $P = 0.002$), but there was a clear tendency toward more aggressive tumor characteristics in the LDLT group. The same group recently published an updated report[12], in which HCC recurrence remained significantly different between LDLT and DDLT after adjustment for tumor characteristics. They concluded that the higher recurrence observed after LDLT was likely due to differences in the tumor characteristics, pretransplant HCC management, and waiting time.

Vakili *et al*[13] reporting the Lahey Clinic experience, demonstrated that the HCC recurrence rate of LDLT (29%) was significantly higher than that of DDLT (12%) ($P < 0.05$), but survival after LDLT was significantly better than that following DDLT for HCC during the same

period ($P = 0.02$).

Lo *et al*[14] from Hong Kong also reported a significantly higher incidence of HCC recurrence, 29% in LDLT and 0% in DDLT ($P = 0.029$). While the tumor characteristics were comparable between groups, the authors speculated that LDLT as a salvage transplantation, microscopic vascular invasion, and liver regeneration led to the difference in the recurrence rate.

### *Studies reporting a comparable outcome*

Sandhu and colleagues of the Toronto group[15] reported that LDLT and DDLT both provide similarly low recurrence rates and high survival rates. They compared the results of 58 LDLT cases with those of 287 DDLT cases having comparable tumor characteristics, in which the 1-, 3-, and 5-year recurrence-free survival rates were 88%, 75%, and 70%, and 86%, 75%, and 70%, respectively.

In a well-designed study by Bhangui *et al*[16], an intention-to-treat analysis was conducted with recurrence rate representing the primary endpoint, comparing 36 LDLT cases and 147 DDLT cases. The authors demonstrated that both LDLT and DDLT provided similar recurrence - free survival rates (88% *vs* 86% at 5 years) for patients with HCC. The dropout rate and waiting time were significantly lower in the LDLT group than in the DDLT group, and there was also a trend toward a longer time to recurrence in the LDLT group, which may guarantee additional advantages with LDLT.

The Mount Sinai group[17,18] reported comparable recurrence - free survival between LDLT ($n = 36$) and DDLT ($n = 165$; 74% *vs* 83% at 2 years, $P = 0.3$). When stratified by tumor size (5 cm diameter) and the existence of microvascular invasion, there was still no difference between groups.

Sotiropoulos and colleagues of Essen, Germany[19,20], also supported the comparable recurrence - free survival rates between LDLT and DDLT for HCC (75% *vs* 81% at 3 years).

Hwang *et al*[21] of South Korea performed a nationwide survey regarding this issue. Among 237 LDLTs and 75 DDLTs for HCC, the 1 - and 3 - year recurrence - free survival rates were 83% and 80%, and 88% and 82%, respectively, with no significant difference between them.

A comparison of outcomes after liver transplantation obtained from database studies revealed comparable patient survival rates between LDLT and DDLT. According to a report from the Japanese Liver Transplantation Society Registry[22], a total of 6097 LDLTs were performed in Japan by the end of 2010, and 1225 (32%) were indicated for HCC, which was the most common indication in adult patients. The 1-, 3-, 5-, and 10-year cumulative survival rates of LDLT for HCC were 85%, 74%, 69%, and 60%, respectively. Todo and colleagues[23] performed a detailed survey using the same database (up to the end of 2005), comprising 653 patients who had undergone LDLT for HCC in Japan. At 1, 3, and 5 years, overall patient survival was 83%, 73%, and 69%, and disease-free survival was 77%, 65%, and 61%, respectively. Based on preoperative imaging studies, 62% were within the Milan criteria and 38% were beyond the Milan criteria, with 5-year recurrence-free survival rates of 90% and 61%, respectively ($P < 0.001$). These findings do not differ much from those obtained in the DDLT database of the United States and Europe[24-27], and may validate the use of LDLT for HCC patients.

## CURRENT OPINIONS REGARDING THE DIFFERENCE BETWEEN LDLT AND DDLT

A randomized clinical study would be best to settle the controversy regarding the use of LDLT *vs* DDLT for HCC patients, but this is indeed difficult, if not impossible, to realize given the complicated decision-making process involved in LDLT. No prospective study has been conducted to date.

The Toronto group[28] recently performed a meta-analysis on 12 retrospective studies comparing the recurrence rates and recurrence - free survival between LDLT and DDLT recipients. A total of 633 LDLTs and 1232 DDLTs were enrolled, and the study provided evidence of lower disease - free survival after LDLT compared with DDLT for HCC (HR = 1.59, 95%CI: 1.02-2.49; $P = 0.041$). In contrast, there was no difference in overall survival between LDLT and DDLT (HR = 0.97, 95%CI: 0.73-1.27; $P = 0.808$). As mentioned by the authors of the paper, however, all involved studies were retrospective, had a low data quality score with poor reporting of baseline patient characteristics and an inadequate statistical approach, and were heterogeneous in critical aspects such as indication criteria and basal tumor characteristics, which warrant further well-designed studies to determine whether differences in HCC recurrence are due to study biases or biologic differences.

A recent review article by experts[29] concluded as follows: Although there is no strong evidence to support the higher HCC recurrence rates in LDLT than DDLT, the higher recurrence rates in LDLT recipients reported by several authors cannot be ignored. Actually, there are critical differences among societies such as: (1) differences in the allocation system for DDLT and LDLT; (2) differences in the availability of deceased donors; (3) differences in the potential waiting time; and (4) the differences in regional and national organ transplant law. In addition to taking into account these differences, liver transplant candidates with HCC and their potential live donors should be informed following risks and benefits; the waiting time for DDLT may lead to the dropout due to HCC progression which could be avoided by the prompt LDLT, however, the prompt LDLT may mask the aggressive tumor characteristics which may lead to a higher HCC recurrence rates. Although the currently available literatures can provide a low evidence for the difference of HCC recurrence between DDLT and LDLT, the tumor characteristics and biology seem to significantly influence on the recurrence, while the graft type and waiting time are less likely important as a possible risk factor.

**Table 2 Graft characteristics and hepatocellular carcinoma recurrence**

| | Patients with recurrence ($n$ = 11) | Patients without recurrence ($n$ = 114) | $P$ |
|---|---|---|---|
| Regeneration rate at 3 mo (%) | 90 ± 24 | 93 ± 34 | 0.732 |
| Graft type: right/left | 4/7 | 36/78 | 0.702 |
| Initial graft volume ratio to standard liver volume (%) | 46 ± 9 | 47 ± 9 | 0.842 |

## POSTULATED THEORIES FOR DIFFERENCES BETWEEN LDLT AND DDLT

LDLT provides several advantages compared with DDLT, such as a shorter waiting time, good quality graft with normal liver function and shorter ischemic time, and pretransplant treatment optimization, which might contribute to improved survival in LDLT recipients. Some of these characteristics, on the other hand, may lead to a favorable milieu for tumor progression[9].

There are several hypotheses other than tumor characteristics to explain the inferior outcome of LDLT. One explanation for the higher recurrence rates in LDLT is fast-tracking patients into liver transplantation, the so - called fast-track effect[11,30]. Some patients with more biologically aggressive HCC might drop off the waiting list due to tumor progression beyond the criteria during the wait-time in the DDLT setting. In contrast, due to the shortened wait time for LDLT candidates, progression of HCC with an aggressive tumor biology might not be recognized during such a short wait-time. This scenario might account for the higher HCC recurrence in the LDLT setting.

Another hypothesized mechanism for the higher recurrence rates in LDLT is that growth factors and cytokines released during rapid regeneration of the partial grafts from living donors might contribute to tumor progression and recurrence[31-34]. A rapidly regenerating liver parenchyma and ischemic-reperfusion injury facilitated by a small-for-size graft in LDLT setting might be a more favorable environment for tumor progression and HCC recurrence.

Additionally, some authors[11,35,36] insist that the technique of LDLT per se foregoes the principles of oncologic surgery. During LDLT, the meticulous dissection and mobilization of the liver might increase the possibility of tumor capsule violation or tumor embolization through the hepatic veins, thus promoting tumor dissemination. Preserving the native vena cava and the bile duct/hepatic artery/portal vein in the hepatic hilum might increase the risk of leaving the residual tumors.

As opposed with the above-mentioned anecdotal explanations, the advanced tumor characteristics of LDLT recipients can reasonably explain the higher recurrence rate in the LDLT setting. Grafts from living donors are not limited by restrictions imposed by the organ allocation system, meaning that the relation of the graft and recipient is usually one-on-one. Consequently, selection criteria based on the tumor burden, such as the tumor size and number, can be considered relative on a case-by-case basis, taking into account the presence of risk factors for recurrence and the chance of survival, as well as the wishes of the donor[37]. Consequently, the majority of Asian transplant centers have adopted extended criteria beyond those of Milan or the University of California, San Francisco (UCSF)[38]. Based on some studies, differences in patient tumor characteristics between LDLT and DDLT remain a main reason for the higher recurrence rate in LDLT. Additionally, in the majority of the aforementioned studies comparing LDLT and DDLT for HCC patients, tumor burdens such as the size, number, vascular invasion, and poor differentiation have proved to be independent risk factors for HCC recurrence after liver transplantation, all of which may lead to a rational explanation for the impaired recurrence - free survival of LDLT compared to DDLT.

## OUR EXPERIENCE

At our institution, the University of Tokyo Hospital, a total of 423 adult recipients underwent LDLT by the end of 2012. Among them, 125 (30%) patients had HCC. The principle criterion for LDLT for HCC at our center is "up to 5 nodules with a maximum tumor diameter within 5 cm", which we call the "5-5 rule"[39]. Of the 125 patients, 118 (94%) were within the 5-5 rule criteria and 109 (87%) were within the Milan criteria. Overall survival of the 125 recipients at 1, 3, and 5 years was 88%, 82%, and 76%, respectively, with a median follow-up period of 8 years. A total of 11 (9%) patients developed HCC recurrence with a cumulative recurrence rate at 1, 3, and 5 years of 6%, 9%, and 11%, respectively.

We compared the graft regeneration rate between patients with HCC recurrence ($n$ = 11) and those without recurrence ($n$ = 114) to confirm the association of liver regeneration with HCC recurrence. The regeneration rate was calculated as follows: (graft volume at 3 mo after LDLT- initial graft volume)/initial graft volume × 100 (%). As shown in Table 2, there was no difference in the regeneration rate between those with HCC recurrence and those without recurrence. At the same time, the graft type (right *vs* left) and the initial graft volume ratio to the recipient's standard liver volume were also compared between groups, revealing no difference. A similar result was reported by the Asan group of South Korea[40], in which the graft-recipient weight ratio had no impact on HCC recurrence after LDLT among 181 LDLT recipients with HCC. Our result as well as the report of the Asan group clearly demonstrated that graft regeneration of the partial liver graft has no impact on HCC recurrence, at least in a clinical setting. The independent predictors for HCC recurrence in our series were tumors not within the 5-5 rule (Tokyo criteria), AFP level over 400 ng/mL, and des-

gamma-carboxy prothrombin levels over 200 mAU/mL.

## CONCLUSION

In conclusion, there is no strong evidence to support higher HCC recurrence after LDLT than DDLT, and it may be reasonable to use different indication criteria for LDLT and DDLT, while there could be a potential bias in choosing the articles in the present study. LDLT should always be considered as a treatment option for HCC patients with advanced cirrhosis in areas where deceased donors are scarce or for patients whose tumor status interrupts access to DDLT.

## REFERENCES


1 **Ferlay J**, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer* 2010; **127**: 2893-2917 [PMID: 21351269 DOI: 10.1002/ijc.25516]

2 **Forner A**, Llovet JM, Bruix J. Hepatocellular carcinoma. *Lancet* 2012; **379**: 1245-1255 [PMID: 22353262 DOI: 10.1016/S0140-6736(11)61347-0]

3 **Mazzaferro V**, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, Montalto F, Ammatuna M, Morabito A, Gennari L. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. *N Engl J Med* 1996; **334**: 693-699 [PMID: 8594428 DOI: 10.1056/NEJM199603143341104]

4 **Bruix J**, Gores GJ, Mazzaferro V. Hepatocellular carcinoma: clinical frontiers and perspectives. *Gut* 2014; **63**: 844-855 [PMID: 24531850]

5 **Bruix J**, Sherman M. Management of hepatocellular carcinoma: an update. *Hepatology* 2011; **53**: 1020-1022 [PMID: 21374666 DOI: 10.1002/hep.24199]

6 **de Villa V**, Lo CM. Liver transplantation for hepatocellular carcinoma in Asia. *Oncologist* 2007; **12**: 1321-1331 [PMID: 18055852 DOI: 10.1634/theoncologist.12-11-1321]

7 **Lee Cheah Y**, K H Chow P. Liver transplantation for hepatocellular carcinoma: an appraisal of current controversies. *Liver Cancer* 2012; **1**: 183-189 [PMID: 24159583 DOI: 10.1159/000343832]

8 **Hwang S**, Lee SG, Belghiti J. Liver transplantation for HCC: its role: Eastern and Western perspectives. *J Hepatobiliary Pancreat Sci* 2010; **17**: 443-448 [PMID: 19885638 DOI: 10.1007/s00534-009-0241-0]

9 **Quintini C**, Hashimoto K, Uso TD, Miller C. Is there an advantage of living over deceased donation in liver transplantation? *Transpl Int* 2013; **26**: 11-19 [PMID: 22937787]

10 **Park MS**, Lee KW, Suh SW, You T, Choi Y, Kim H, Hong G, Yi NJ, Kwon CH, Joh JW, Lee SK, Suh KS. Living-donor liver transplantation associated with higher incidence of hepatocellular carcinoma recurrence than deceased-donor liver transplantation. *Transplantation* 2014; **97**: 71-77 [PMID: 24056623 DOI: 10.1097/TP.0b013e3182a68953]

11 **Fisher RA**, Kulik LM, Freise CE, Lok AS, Shearon TH, Brown RS, Ghobrial RM, Fair JH, Olthoff KM, Kam I, Berg CL. Hepatocellular carcinoma recurrence and death following living and deceased donor liver transplantation. *Am J Transplant* 2007; **7**: 1601-1608 [PMID: 17511683 DOI: 10.1111/j.1600-6143.2007.01802.x]

12 **Kulik LM**, Fisher RA, Rodrigo DR, Brown RS, Freise CE, Shaked A, Everhart JE, Everson GT, Hong JC, Hayashi PH, Berg CL, Lok AS. Outcomes of living and deceased donor liver transplant recipients with hepatocellular carcinoma: results of the A2ALL cohort. *Am J Transplant* 2012; **12**: 2997-3007 [PMID: 22994906 DOI: 10.1111/j.1600-6143.2012.04272.x]

13 **Vakili K**, Pomposelli JJ, Cheah YL, Akoad M, Lewis WD, Khettry U, Gordon F, Khwaja K, Jenkins R, Pomfret EA. Living donor liver transplantation for hepatocellular carcinoma: Increased recurrence but improved survival. *Liver Transpl* 2009; **15**: 1861-1866 [PMID: 19938113 DOI: 10.1002/lt.21940]

14 **Lo CM**, Fan ST, Liu CL, Chan SC, Ng IO, Wong J. Living donor versus deceased donor liver transplantation for early irresectable hepatocellular carcinoma. *Br J Surg* 2007; **94**: 78-86 [PMID: 17016793 DOI: 10.1002/bjs.5528]

15 **Sandhu L**, Sandroussi C, Guba M, Selzner M, Ghanekar A, Cattral MS, McGilvray ID, Levy G, Greig PD, Renner EL, Grant DR. Living donor liver transplantation versus deceased donor liver transplantation for hepatocellular carcinoma: comparable survival and recurrence. *Liver Transpl* 2012; **18**: 315-322 [PMID: 22140013 DOI: 10.1002/lt.22477]

16 **Bhangui P**, Vibert E, Majno P, Salloum C, Andreani P, Zocrato J, Ichai P, Saliba F, Adam R, Castaing D, Azoulay D. Intention-to-treat analysis of liver transplantation for hepatocellular carcinoma: living versus deceased donor transplantation. *Hepatology* 2011; **53**: 1570-1579 [PMID: 21520172 DOI: 10.1002/hep.24231]

17 **Gondolesi GE**, Roayaie S, Muñoz L, Kim-Schluger L, Schiano T, Fishbein TM, Emre S, Miller CM, Schwartz ME. Adult living donor liver transplantation for patients with hepatocellular carcinoma: extending UNOS priority criteria. *Ann Surg* 2004; **239**: 142-149 [PMID: 14745320 DOI: 10.1097/01.sla.0000109022.32391.eb]

18 **Roayaie S**, Schwartz JD, Sung MW, Emre SH, Miller CM, Gondolesi GE, Krieger NR, Schwartz ME. Recurrence of hepatocellular carcinoma after liver transplant: patterns and prognosis. *Liver Transpl* 2004; **10**: 534-540 [PMID: 15048797 DOI: 10.1002/lt.20128]

19 **Malagó M**, Sotiropoulos GC, Nadalin S, Valentin-Gamazo C, Paul A, Lang H, Radtke A, Saner F, Molmenti E, Beckebaum S, Gerken G, Frilling A, Broelsch CE. Living donor liver transplantation for hepatocellular carcinoma: a single-center preliminary report. *Liver Transpl* 2006; **12**: 934-940 [PMID: 16528715 DOI: 10.1002/lt.20677]

20 **Sotiropoulos GC**, Lang H, Nadalin S, Neuhäuser M, Molmenti EP, Baba HA, Paul A, Saner FH, Weber F, Hilgard P, Frilling A, Broelsch CE, Malagó M. Liver transplantation for hepatocellular carcinoma: University Hospital Essen experience and meta-analysis of prognostic factors. *J Am Coll Surg* 2007; **205**: 661-675 [PMID: 17964442 DOI: 10.1016/j.jamcollsurg.2007.05.023]

21 **Hwang S**, Lee SG, Joh JW, Suh KS, Kim DG. Liver transplantation for adult patients with hepatocellular carcinoma in Korea: comparison between cadaveric donor and living donor liver transplantations. *Liver Transpl* 2005; **11**: 1265-1272 [PMID: 16184545 DOI: 10.1002/lt.20549]

22 Liver transplantation in Japan- registry by the Japnese Liver Transplantation Society. *Ishoku* 2012; **46**: 524-536

23 **Todo S**, Furukawa H, Tada M. Extending indication: role of living donor liver transplantation for hepatocellular carcinoma. *Liver Transpl* 2007; **13**: S48-S54 [PMID: 17969069]

24 **Mazzaferro V**, Bhoori S, Sposito C, Bongini M, Langer M, Miceli R, Mariani L. Milan criteria in liver transplantation for hepatocellular carcinoma: an evidence-based analysis of 15 years of experience. *Liver Transpl* 2011; **17** Suppl 2: S44-S57 [PMID: 21695773]

25 **Adam R**, Karam V, Delvart V, O'Grady J, Mirza D, Klempnauer J, Castaing D, Neuhaus P, Jamieson N, Salizzoni M, Pollard S, Lerut J, Paul A, Garcia-Valdecasas JC, Rodríguez FS, Burroughs A. Evolution of indications and results of liver transplantation in Europe. A report from the European Liver Transplant Registry (ELTR). *J Hepatol* 2012; **57**: 675-688 [PMID: 22609307 DOI: 10.1016/j.jhep.2012.04.015]

26 **Singal AK**, Guturu P, Hmoud B, Kuo YF, Salameh H, Wiesner RH. Evolving frequency and outcomes of liver transplantation based on etiology of liver disease. *Trans-*

*plantation* 2013; **95**: 755-760 [PMID: 23370710 DOI: 10.1097/TP.0b013e31827afb3a]
27 **Taniguchi M**. Liver transplantation in the MELD era--analysis of the OPTN/UNOS registry. *Clin Transpl* 2012; **2012**: 41-65 [PMID: 23721009]
28 **Grant RC**, Sandhu L, Dixon PR, Greig PD, Grant DR, McGilvray ID. Living vs. deceased donor liver transplantation for hepatocellular carcinoma: a systematic review and meta-analysis. *Clin Transplant* 2013; **27**: 140-147 [PMID: 23157398 DOI: 10.1111/ctr.12031]
29 **Grant D**, Fisher RA, Abecassis M, McCaughan G, Wright L, Fan ST. Should the liver transplant criteria for hepatocellular carcinoma be different for deceased donation and living donation? *Liver Transpl* 2011; **17** Suppl 2: S133-S138 [PMID: 21634006]
30 **Kulik L**, Abecassis M. Living donor liver transplantation for hepatocellular carcinoma. *Gastroenterology* 2004; **127**: S277-S282 [PMID: 15508095]
31 **Man K**, Lo CM, Xiao JW, Ng KT, Sun BS, Ng IO, Cheng Q, Sun CK, Fan ST. The significance of acute phase small-for-size graft injury on tumor growth and invasiveness after liver transplantation. *Ann Surg* 2008; **247**: 1049-1057 [PMID: 18520234 DOI: 10.1097/SLA.0b013e31816ffab6XXX]
32 **Shi JH**, Huitfeldt HS, Suo ZH, Line PD. Growth of hepatocellular carcinoma in the regenerating liver. *Liver Transpl* 2011; **17**: 866-874 [PMID: 21542129 DOI: 10.1002/lt.22325]
33 **Efimova EA**, Glanemann M, Liu L, Schumacher G, Settmacher U, Jonas S, Langrehr JM, Neuhaus P, Nüssler AK. Effects of human hepatocyte growth factor on the proliferation of human hepatocytes and hepatocellular carcinoma cell lines. *Eur Surg Res* 2004; **36**: 300-307 [PMID: 15359093 DOI: 10.1159/000079915]
34 **Man K**, Fan ST, Lo CM, Liu CL, Fung PC, Liang TB, Lee TK, Tsui SH, Ng IO, Zhang ZW, Wong J. Graft injury in relation to graft size in right lobe live donor liver transplantation: a study of hepatic sinusoidal injury in correlation with portal hemodynamics and intragraft gene expression. *Ann Surg* 2003; **237**: 256-264 [PMID: 12560784 DOI: 10.1097/01.SLA.0000048976.11824.67]
35 **Di Sandro S**, Slim AO, Giacomoni A, Lauterio A, Mangoni I, Aseni P, Pirotta V, Aldumour A, Mihaylov P, De Carlis L. Living donor liver transplantation for hepatocellular carcinoma: long-term results compared with deceased donor liver transplantation. *Transplant Proc* 2009; **41**: 1283-1285 [PMID: 19460539 DOI: 10.1016/j.transproceed.2009.03.022]
36 **Li C**, Wen TF, Yan LN, Li B, Yang JY, Wang WT, Xu MQ, Wei YG. Outcome of hepatocellular carcinoma treated by liver transplantation: comparison of living donor and deceased donor transplantation. *Hepatobiliary Pancreat Dis Int* 2010; **9**: 366-369 [PMID: 20688599]
37 **Tamura S**, Sugawara Y, Kokudo N. Living donor liver transplantation for hepatocellular carcinoma: the Japanese experience. *Oncology* 2011; **81** Suppl 1: 111-115 [PMID: 22212944]
38 **Chan SC**. Liver transplantation for hepatocellular carcinoma. *Liver Cancer* 2013; **2**: 338-344 [PMID: 24400221 DOI: 10.1159/000343849]
39 **Sugawara Y**, Tamura S, Makuuchi M. Living donor liver transplantation for hepatocellular carcinoma: Tokyo University series. *Dig Dis* 2007; **25**: 310-312 [PMID: 17960065 DOI: 10.1159/000106910]
40 **Hwang S**, Lee SG, Ahn CS, Kim KH, Moon DB, Ha TY, Park KM, Song GW, Jung DH, Kim BS, Moon KM. Small-sized liver graft does not increase the risk of hepatocellular carcinoma recurrence after living donor liver transplantation. *Transplant Proc* 2007; **39**: 1526-1529 [PMID: 17580180 DOI: 10.1016/j.transproceed.2007.03.066]

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