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Original Article

Repeat liver resection versus salvage liver transplant for recurrent hepatocellular carcinoma: A propensity score-adjusted and -matched comparison analysis

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Backgrounds/Aims: Repeat liver resection (RLR) and salvage liver transplantation (SLT) are viable treatment options for recurrent hepatocellular carcinoma (HCC). With possibly superior survival outcomes than RLR, SLT is however, limited by liver graft availability and poses increased perioperative morbidity. In this study, we seek to compare the outcomes of RLR and SLT for patients with recurrent HCC. **Methods:** Between 1999 and 2018, 94 and 16 consecutive patients who underwent RLR and SLT respectively were identified. Further retrospective subgroup analysis was conducted, comparing 16 RLR with 16 SLT patients via propensity-score matching. **Results:** After propensity-score adjusted analyses, SLT demonstrated inferior short-term perioperative outcomes than RLR, with increased major morbidity (57.8% vs 5.4 %, p=0.0001), reoperations (39.1% vs 0, $p<0.0001$), renal insufficiency (30.1% vs 3%, p=0.0071), bleeding (19.8% vs 2.2%, p=0.0289), prolonged intensive care unit stay (median=4 vs 0 days, $p<0.0001$) and hospital stay (median= 19.8 vs 7.1days, $p<0.001$). However, SLT showed significantly lower recurrence rate (15.4% versus 70.3%, p=0.0005) and 5-year cumulative incidence of recurrences (19.4% versus 68.4%, p=0.005). Propensity-matched subgroup analysis showed concordant findings. **Conclusions:** While SLT offers potentially reduced risks of recurrence and trended towards improved long-term survival outcomes relative to RLR, it has poorer short-term perioperative outcomes. Patient selection is prudent amidst organ shortages to maximise allocated resources and optimise patient outcomes. **(Ann Hepatobiliary Pancreat Surg 2019;23:305-312)**

Key Words: Hepatocellular carcinoma; Salvage liver transplantation; Repeat liver resection; Tumour recurrence; Survival analysis; Propensity score

INTRODUCTION

Tumour recurrence remains a pertinent issue in the management of hepatocellular carcinoma (HCC), with recurrence rates of up to 76%.[1-3] As HCC recurrences compromise patient survival outcomes, it is imperative that these patients receive prompt treatment. Curative surgical options for HCC include liver resection and liver transplantation. In the case of recurrent tumours, repeat liver resection (RLR) and salvage liver transplantation (SLT) are viable therapeutic options.

Often perceived as the less complicated procedure without limitations imposed by the availability of liver grafts, RLR has been widely adopted in the treatment of HCC recurrence. However, its successes are often limited by inadequate future liver remnant and exceedingly high postoperative cancer recurrences.[3-7] On the other hand, SLT is performed infrequently due to limited liver grafts with strict criteria imposed for transplantation. Several studies have also reported greater perioperative morbidity and mortality associated with the procedure.[8-10] Furthermore, patients awaiting SLT are at risk of disease progression while waiting for an available organ, denying patients of curative options.[2,11,12] In view of these contentious issues

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surrounding the management of recurrent HCC, we reviewed and compared our institution's experience with SLT and RLR.

MATERIALS AND METHODS

Between 1999 and 2018, 94 consecutive RLR cases in 84 patients and 16 consecutive SLT were performed at the Singapore General Hospital. Patient details were reviewed from a prospectively maintained database for individuals with HCC. Institutional review board approval was obtained beforehand. Some of these patients have been included in our previous studies.[13,14]

Patient clinicopathological factors and perioperative survival outcomes were reviewed retrospectively from the computerised clinical and operative databases (Sunrise Clinical Manager version 5.8, Eclipsys Corporation, Atlanta, Georgia, USA and OTM 10, IBM, Armonk, New York, USA), as well as patient charts where necessary. Preoperative details were assessed at the point of listing for liver transplant or collected closest to the date of re-resection. Haematological and biochemical data (complete blood count, renal and liver function tests, coagulation profile and serum alpha-fetoprotein (AFP)) and imaging in the form of computed tomography (CT) and/or magnetic resonance imaging (MRI) were retrieved and assessed.

HCC and its recurrences are diagnosed via a combination of imaging, presence of risk factors and/or serum AFP. Certain patients slated for transplant but exceeded the Milan criteria, underwent biopsies to rule out those with poorly differentiated tumours. Postoperative monitoring was conducted via regular clinical reviews with liver function tests, serum AFP and surveillance imaging.

Definitions

RLR refers to the surgical removal of the hepatic segment affected by recurrent HCC while SLT involves transplantation of a liver graft following HCC recurrence after previous resection or deterioration in liver function.[1,11] Transplantation for tumour recurrences after other treatment modalities such as ablation or transarterial chemoembolization were not considered SLT. Major liver resection referred to the resection of three or more liver segments.[15] Wait time entails the duration between date of documented recurrence to operation date. Any complication or death within 30 days of surgery or within the same hospitalisation contributed to postoperative morbidity and mortality. The Clavien-Dindo classification was used to classify complications into major (grade $\geq$ 3) and minor (grade $\leq$ 2) grades.[16]

Survival analysis

Overall survival (OS) was defined as the time of surgery until death. Recurrence-free survival (RFS) was defined as the time from surgery until radiologically and clinically-documented recurrence, or death. Time-to-recurrence (TTR) was calculated as the time from surgery to the first documented recurrence, with death regarded as a competing risk since it precludes the observation of cancer recurrence. Patients without these events were censored at their last follow-up visit. Accordingly, OS and RFS were analysed using standard Cox regression models, while TTR was analysed using Fine & Gray's competing risk regression model. Median follow-up for overall survival was calculated using the reverse Kaplan Meier method.[17]

Propensity score model and analyses

Propensity score (PS) analyses were undertaken to reduce treatment selection bias and confounding by accounting for clinical and surgical characteristics which are regarded to influence a patient's likelihood of undergoing SLT or RLR. Multiple alternative PS models were developed using semi-automated algorithms and manual selection of covariates (Supplementary Table S1). The final PS model was selected on the basis of the Bayesian information criterion (BIC) and adequacy of covariate balancing within the PS-matched patient subset after greedy matching, and took into account the following covariates: age at surgery, prior re-resection, presence of cirrhosis, and whether patients were within Milan criteria (Supplementary Table S2). Goodness-of-fit, calibration and discrimination were assessed using the methods of Lemeshow and Hosmer and receiver operating curves. The PS model exhibited good calibration (Supplementary Fig. S1) and discrimination (area under the receiver operating curve=0.7953, bias-corrected bootstrapped 95% CI: 0.6496-0.8987) (Supplementary Fig. S2).

We undertook three PS methodologies for comparing outcomes of patients who underwent SLT versus RLR: (1)

covariate adjustment using the linear predictor (log odds) of the PS was used as the primary analysis, and (2) PS-matching and (3) inverse probability of treatment-weighting (IPTW) were conducted as additional sensitivity analyses.[18]

For the primary analysis, baseline characteristics shown in Table 1 were analysed using tests for independent samples. Accordingly, the Mann-Whitney U test and χ^2 tests were utilised to compare distributions and proportions respectively. The number of previous resections was modelled as a count data, and was therefore analysed using a Poisson model with a time-exposure offset. Differences in peri-operative and oncologic outcomes between the SLT and RLR groups in Table 2 were adjusted using the linear predictor of the propensity scores in multivariable regression models (quantile, logistic, and Cox models for conditional medians, proportions, and time-to-event outcomes respectively). Model-adjusted medians, proportions, and rates were obtained using post-hoc estimation commands immediately after fitting regression models.

Next, sensitivity analyses by way of PS matching were conducted to verify the robustness of conclusions from PS

Table 1. Patient characteristics at time of recurrence before salvage transplant or repeat liver resection for recurrent HCC

	All patients			Propensity-score matched subset		
	SLT (n=16)	RLR (n=94)	*p*-value	SLT (n=16)	RLR (n=16)	*p*-value
Median age at surgery, years (range)	58.5 (26-72)	63.5 (34-83)	0.0579	58.5 (26-72)	59.5 (39-69)	0.3011
Male gender (%)	15/16 (93.8)	83/94 (88.3)	0.5178	15/16 (93.8)	14/16 (87.5)	1.0000
Hepatitis B (%)	12/16 (75.0)	70/94 (74.5)	0.9640	12/16 (75.0)	11/16 (68.8)	0.7389
Hepatitis C (%)	1/16 (6.3)	7/94 (7.5)	0.8647	1/16 (6.3)	2/16 (12.5)	0.5637
Non-B/C (%)	3/16 (18.8)	15/94 (16.0)	0.7802	3/16 (18.8)	3/16 (18.8)	1.0000
Major liver resection (%)	3/16 (18.8)	10/94 (10.6)	0.3528	3/16 (18.8)	2/16 (12.5)	0.6547
Median no. of previous liver resections (range)	1 (1-2)	1 (1-3)	0.2513	1 (1-2)	1 (1-2)	0.3524
No. of patients with ≥1 previous liver re-resection	4/16 (25.0)	11/94 (11.7)	0.1519	4/16 (25.0)	4/16 (25.0)	1.0000
Child-Pugh status (%)			<0.0001			0.0703
A	9/16 (56.3)	89/91 (97.8)		9/16 (56.3)	15/16 (93.8)	
B	6/16 (37.5)	2/91 (2.2)		6/16 (37.5)	1/16 (6.3)	
C	1/16 (6.3)	0/91 (0)		1/16 (6.3)	0/16 (0)	
Within Milan criteria (%)	12/16 (75.0)	81/91 (89.0)	0.1254	12/16 (75.0)	14/16	0.5000
Median tumour size (scan), cm (range)	2.8 (1.0-4.6)	2.2 (0.6-10.5)	0.5329	2.8 (1.0-4.6)	1.95 (0.90-5.0)	0.8360
AFP, ng/ml (IQR)	14.3 (8.4-68.8)	5.6 (2.9-28.1)	0.0531	14.3 (8.4-68.8)	14.5 (4.6-39.1)	0.2775
Pre-operative locoregional treatment (%)						
RFA	11/16 (68.8)	36/94 (38.3)	0.0228	11/16 (68.8)	7/16 (43.8)	0.1025
TACE	7/16 (43.8)	32/94 (34.0)	0.4530	7/16 (43.8)	6/16 (37.5)	0.4142
Y-90	3/16 (18.8)	4/94 (4.3)	0.0281	3/16 (18.8)	0/16 (0)	0.2500
Pathological characteristic						
Liver cirrhosis (%)	15/16 (93.8)	59/91 (64.8)	0.0209	15/16	15/16	1.0000
Median tumour size (pathology), cm (range)	2.7 (0.6-5.0)	2.5 (0.6-10.0)	0.7343	2.7 (0.6-5.0)	2.0 (1.2-6.8)	0.5694
Median number of nodules (range)	1.5 (1-7)	1 (1-3)	<0.0001	1.5 (1-7)	1 (1-3)	0.1094
Tumour differentiation (%)			0.0699			0.6061
1	2/16 (12.5)	7/93 (7.4)		2/16 (12.5)	0/16 (0)	
2	5/16 (31.3)	44/93 (47.3)		5/16 (31.3)	10/16 (62.5)	
3	7/16 (43.8)	30/93 (32.3)		7/16 (43.8)	4/16 (25.0)	
4	2/16 (12.5)	13/93 (14.0)		2/16 (12.5)	2/16 (12.5)	
Vascular invasion (%)	4/16 (25.0)	18/94 (19.2)	0.5886	4/16 (25.0)	4/16 (25.0)	1.0000
Satellite nodules (%)	8/16 (50.0)	7/94 (8.5)	<0.0001	8/16 (50.0)	1/16 (6.3)	0.0156
Median wait time* (IQR)	15.7 (10.7-21.0)	1.2 (0.7-2.2)	<0.0001	15.7 (10.7-21.0)	0.7 (0.4-1.3)	0.0004

AFP, alpha-fetoprotein; RFA, radiofrequency ablation; TACE, transarterial chemoembolization; Y-90, Yttrium-90 microspheres radioembolization

*Wait time, time from date of recurrence to date of operation

Table 2. Post-operative outcomes of patients with recurrent HCC after salvage liver transplant and repeat liver resection

	Propensity-score adjusted comparison†				Propensity-score matched comparison			
	SLT† (n=16)	RLR† (n=94)	Effect size (95% CI)	*p*-value	SLT (n=16)	RLR (n=16)	Effect size (95% CI)	*p*-value
Post-operative morbidity, %								
Minor morbidity (grade≤2)	14.8% (4.3-40.4%)	25.8% (17.7-35.9%)	OR:0.50 (0.12-2.13)	0.3484	3/16 (18.8%)	4/16 (25.0%)	OR: 0.67 (0.06-5.82)	0.6547
Major morbidity (grade≥3)	57.8% (29.8-81.6%)	5.4% (2.2-12.5%)	23.90 (5.08-112.54)	0.0001	9/16 (56.3%)	2/16 (12.5%)	NE	0.0082
Reoperation	39.1% (13.8-72.2%)	0%	NE	<0.0001*	6/16 (37.5%)	0/16 (0%)	NE	0.0143
Renal insufficiency	30.1% (10.4-61.5%)	3.0% (0.9-9.5%)	OR:13.84 (2.04-93.73)	0.0071	4/16 (25.0%)	0/16 (0%)	NE	0.0455
Sepsis	14.0% (2.9-47.3%)	2.1% (0.5-8.4%)	OR:7.53 (0.72-78.78))	0.0919	2/16 (12.5%)	0/16 (0%)	NE	0.1573
Bleeding	19.8% (5.2-52.7%)	2.2% (0.5-8.4%)	OR:11.1 (1.28-96.41)	0.0289	3/16 (18.8%)	1/16 (6.3%)	OR: 3.00 (0.31-28.84)	0.3173
Median ICU stay, days	4 (range: 1-10)	0 (range: 0-35)	MD:4.0 (3.7-4.4)	<0.0001	4 (range: 1-10)	0 (range: 0-2)	MD: 4.0 (1.9-6.1)	0.0002
Median LOS, days	19.8 (IQR: 19.3-19.9)	7.1 (IQR: 6.9-7.4)	MD:13.0 (8.1-17.9)	<0.0001	19.5 (IQR: 14-44.5)	6.5 (IQR: 6-9.5)	MD: 13.0 (6.7-19.3)	0.0001
Recurrence, %	15.4% (4.5-40.9%)	70.3% (59.9-78.9%)	OR:0.08 (0.02-0.33)	0.0005	3/16 (18.8%)	66/94 (70.2%)	OR: 0.20 (0.04-0.91)	0.0209
Median time-to-recurrence, months	NR (IQR: NR-NR)	16.8 (IQR: 8.0-61.8)	SHR:0.18 (0.05-0.59)	0.0050	NR (IQR: NR-NR)	16.0 (IQR: 6.4-119.8)	SHR: 0.19 (0.05-0.70)	0.0066
1-year CIF rate, %	12.5% (2.1-32.8%)	34.9% (25.3-44.6%)			12.5% (2.1-32.8%)	33.5% (12.2-56.6%)		
2-year CIF rate, %	19.4% (4.7-41.4%)	53.4% (42.5-63.1%)			19.4% (4.7-41.4%)	53.6% (26.5-74.6%)		
5-year CIF rate, %	19.4% (4.7-41.4%)	68.4% (56.7-77.5%)			19.4% (4.7-41.4%)	67.0% (37.9-84.7%)		
Median RFS, months	NR (4.7-NR)	16.8 (8.0-61.8)	HR: 0.46 (0.20-1.07)	0.0707	NR (4.7-NR)	16.0 (6.4-119.8)	HR: 0.63 (0.24-1.63)	0.3427
1-year RFS rate, %	84.2%	61.0%			68.8% (40.5-85.6%)	64.3% (34.3-83.3%)		
2-year RFS rate, %	75.1%	40.9%			55.0% (27.9-75.6%)	42.9% (17.7-66.0%)		
5-year RFS rate, %	75.1%	24.9%			55.0% (27.9-75.6%)	35.7% (13.0-59.4%)		
Median OS, months	NR (12.3-NR)	102.0 (34-NR)	HR: 0.88 (0.35-2.23)	0.7882	NR (12.3-NR)	71.4 (19.6-NR)	HR: 0.80 (0.21-2.98)+	0.7394
1-year OS rate, %	92.6%	88.4%			81.3% (52.5-93.5%)	87.1% (57.3-96.6%)		
2-year OS rate, %	81.2%	81.2%			60.9% (32.7-80.3%)	73.1% (43.0-89.0%)		
5-year OS rate, %	81.2%	63.3%			60.9% (32.7-80.3%)	58.4% (29.6-78.9%)		

ICU, intensive care unit; LOS, length of stay; RFS, recurrence-free survival; OS, overall survival; IQR, interquartile range; NR, not reached; NE, not estimable; OR, odds ratio; MD, difference in medians; HR, hazard ratio; SHR, subhazard ratio; CIF, cumulative incidence function

†Model-predicted proportions, medians, and rates were obtained using post-estimation commands immediately after adjusting for the linear predictor of propensity scores. All values given in brackets represent 95% confidence intervals unless specified otherwise

**p*-value from likelihood ratio test for the *difference* between independent proportions, since the P value corresponding to the odds ratio from logistic regression cannot be estimated

+Estimated hazard ratio may not be valid due to significant deviation from proportional hazards requirement

adjustment analyses. The SLT and RLR patients were paired 1:1 using a greedy algorithm without replacement, and adequacy of matching was assessed using kernel density and histogram plots (Supplementary Figs. S3, S4). In the PS-matched subset of patients, the Wilcoxon signed-rank test and McNemar's test (or the Cochran Q test when there are more than two levels) were respectively utilized to compare continuous and binary variables shown in Table 1. Mixed-effects quantile regression, McNemar's test, and stratified Cox regressions taking into account the matched pairs were used to estimate effect sizes and p values for continuous, binary, and time-to-event outcomes in Table 2.

A final sensitivity analysis was undertaken by conducting weighted survival analyses using the inverse probability of treatment-weighting (IPTW) methodology. Statistical analyses were performed in STATA version 13.0 (StataCorp) and $p < 0.05$ were regarded to indicate nominal statistical significance.

RESULTS

Comparison of clinicopathologic features between RLR and SLT (Table 1)

The PS model created 2 patient cohorts for comparison with a PS-adjusted group comparing 16 SLT to 94 RLR cases and a PS-matched cohort comparing 16 SLT to 16 RLR cases. Comparisons between all operative cases of RLR and SLT revealed statistically significant differences in Child-Pugh status, preoperative locoregional treatment for radiofrequency ablation (RFA) and Yttrium-90 therapy, liver cirrhosis, median number of tumour nodules as well as satellite nodules. Following propensity-score matching, our 2 patient groups are comparable with the exception of the SLT cohort having a significantly higher occurrence of satellite nodules (50% vs 6.3%, p=0.0156, Table 1). Other patient characteristics including age, gender, underlying aetiology, major hepatic resections and frequency of previous liver resections were similar between the 2 groups. No significant difference was demonstrated for tumour characteristics including tumours within the Milan criteria, median tumour size, AFP, preoperative transarterial chemoembolization (TACE), tumour differentiation and vascular invasion. Not unexpectedly, both PS-adjusted and PS-matched SLT groups had significantly longer median wait times at 15.7 months.

Comparison of post-operative outcomes between RLR and SLT (Table 2)

The SLT group consistently demonstrated higher postoperative major morbidity (Clavien-Dindo grade $\geq$ 3), reoperation rate and renal insufficiency for both PS-adjusted and PS-matched comparisons. Significantly more SLT patients had longer median intensive care unit (ICU) stay (PS-matched 4 vs 0 days, p=0.0002) and median length of stay (LOS) (PS-matched 19.5 vs 6.5 days, p=0.0001).

In spite of greater perioperative morbidity, there was no statistical difference for postoperative 30-day mortality (SLT=1/16=6.3% vs RLR=3/94=3.2%, p=0.472). One SLT patient died due to hepatic artery thrombosis causing massive liver infarct and consequent failure. Two cases of postoperative liver decompensation with liver failure and one case of acute myocardial infarction contributed to the demise of 3 RLR patients.

Total recurrence was significantly higher in the RLR group (PS-adjusted RLR=70.3% versus SLT=15.4%, p=0.0005 and PS-matched RLR=70.2% versus SLT=18.8%, p=0.0209), as were the recurrence cumulative incidence rate (CIF) (PS-adjusted RLR 5-year CIF=68.4% versus SLT=19.4%, p=0.005 and PS-matched RLR 5-year CIF=67% versus SLT=19.4%, p=0.0066). However, 5-year RFS and OS were not shown to be significantly different between RLR and SLT for both PS-adjusted and PS-matched analyses.

The median duration of follow-up from point of initial liver resection to RLR and SLT were 74.3 months (interquartile range: 44-133.3) and 94.8 months (interquartile range: 61.1-94.8) respectively.

DISCUSSION

As the second most common cause of cancer-related deaths worldwide,[19] there is a need to devise novel methods and/or revise existing treatment strategies to improve survival outcomes for patients with HCCs. A multitude of factors including chronic hepatitis infection, liver cirrhosis, presence of other liver diseases contribute to the prevalence of disseminated or *de novo* HCC recurrences.[20-23] As such, curative options involve the direct removal of tumour via hepatic resection or elimination of the under-

lying aetiology in the form of a liver transplant. Repeat liver resections are, however, limited by functionality of the liver remnant and high cancer recurrences while transplantation depends on liver graft availability and transplant expertise. While RLR has become commonplace in the treatment of recurrent HCCS, SLT has gained traction in recent years to maximise the use of scarce liver grafts where appropriate. This study serves to evaluate perioperative outcomes of those undergoing RLR and SLT, and improve on treatment strategies for recurrent HCCS.

Liver transplantation is a complex procedure requiring a multidisciplinary team of skilled expertise for its success. Both primary and SLT are associated with increased mortality and major morbidity risks including bleeding, arterial thrombosis, sepsis and biliary complications.[24-28] In contrast, repeated hepatic resections demonstrated lower risks of mortality and morbidity.[29-32] Between SLT and RLR, liver transplantation is regarded as the more technically difficult procedure. The complexities of a liver transplant encompass precise dissection in liver mobilisation for total hepatectomy and various intricate anastomoses; the failure of which frequently results in disastrous complications. The hazards of surgery, in combination with patient factors, are likely to account for greater perioperative morbidity associated with SLT. Shown in Table 1, SLT patients were more likely to have poor baseline liver function with a greater proportion having a higher Child-Pugh score and liver cirrhosis. Remnant liver function has a direct implication on post-operative outcomes with cirrhosis, portal hypertension and coagulopathy heightening risks of bleeding, reoperation and renal insufficiency.[26,33,34]

While bleeding was not a significant complication in the PS-matched cohort, it was the predominant reason for reoperations with other contributions from intra-abdominal sepsis and arterial thrombosis. In the presence of portal hypertension and coagulopathy, the risk of intraoperative bleeding and reoperation increases with consequent compromise in patient outcomes.[26] Together with the high incidence of renal insufficiency as a result of nephrotoxic immunosuppressants, sepsis and pre-existing renal dysfunction,[35-38] one would expect greater perioperative morbidity associated with SLT with consequently longer ICU admissions and hospital LOS. Thereby, supporting our significant findings of increased major morbidity, reoperation rates and renal insufficiency for individuals undergoing SLT. These figures, along with the trend towards increased risks of sepsis and bleeding are congruent to those reported in the literature,[20,24,25,27,39] further establishing SLT as a more technically challenging operation with increased short-term morbidity compared to RLR.

Despite greater perioperative risks, SLT patients experienced similar survival outcomes with significantly lower tumour recurrences than those undergoing RLR (Table 2). The SLT cohort in our study also had a higher incidence of tumours with poorer prognostic factors including liver cirrhosis, higher median number of nodules and satellite nodules. While satellite nodules remained the only significant poor prognosticator after PS-matching, SLT still exhibited a trend towards higher 5-year RFS and OS than RLR. Although these figures are not statistically significant, they are, however, consistent with those reported in other studies; 5-year RFS=29-61% and 5-year OS=41-66%[10,24,25,39,40] for SLT as well as 5-year RFS=10-17%[29,41] and 5-year OS=40-69.3%[30,31,41-44] for RLR. These findings may therefore, suggest SLT's substantial role in providing long-term survival and RFS benefit for patients with recurrent HCCs.

Several limitations are acknowledged in this study. While our findings demonstrated results similar to those published in existing literature, it is nonetheless a retrospective study with small cohort sizes for analyses. Besides being inadequately powered, reducing effects of confounders via propensity score-matching does not eliminate confounding in its entirety compared to a completely randomized study. Of note, the significantly longer wait time depicted in our study for SLT patients may affect disease progression and alter survival outcomes. Moreover, the effects of variables including locoregional treatment (RFA, TACE, Yttrium-90) are not accounted for, all of which have proven survival benefit.[45-47]

SLT has been performed in a myriad of patients in a bid to maximise utility of scarce liver grafts. Its significant perioperative morbidity, however, requires further scrutiny before SLT is proposed as a safe alternative to RLR for recurrent HCCs. The advent of laparoscopic techniques may bolster the results of both SLT and RLR as fewer postoperative complications were depicted in several studies.[48-55] Careful patient selection based on survival prognosticators[56-63] will also play a greater role in a synergistic treatment framework offering patients the

best survival outcomes in the midst of inevitable tumour recurrences.

In conclusion, SLT may offer superior survival outcomes in view of its trend towards improved OS and RFS relative to RLR. However, its considerable perioperative risks of morbidity and mortality have to be weighed against its supposed benefits. Patient selection is therefore crucial to derive maximal benefit from the scarce resource of liver grafts.

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