

Comparing the Lifetime Survival in Patients with Early-Stage Hepatocellular Carcinoma (HCC) Receiving Two Competitive Treatments: Liver Transplantation (LT) Versus Hepatic Resection (HR) – An Analysis of Nationwide 17-year Follow-up

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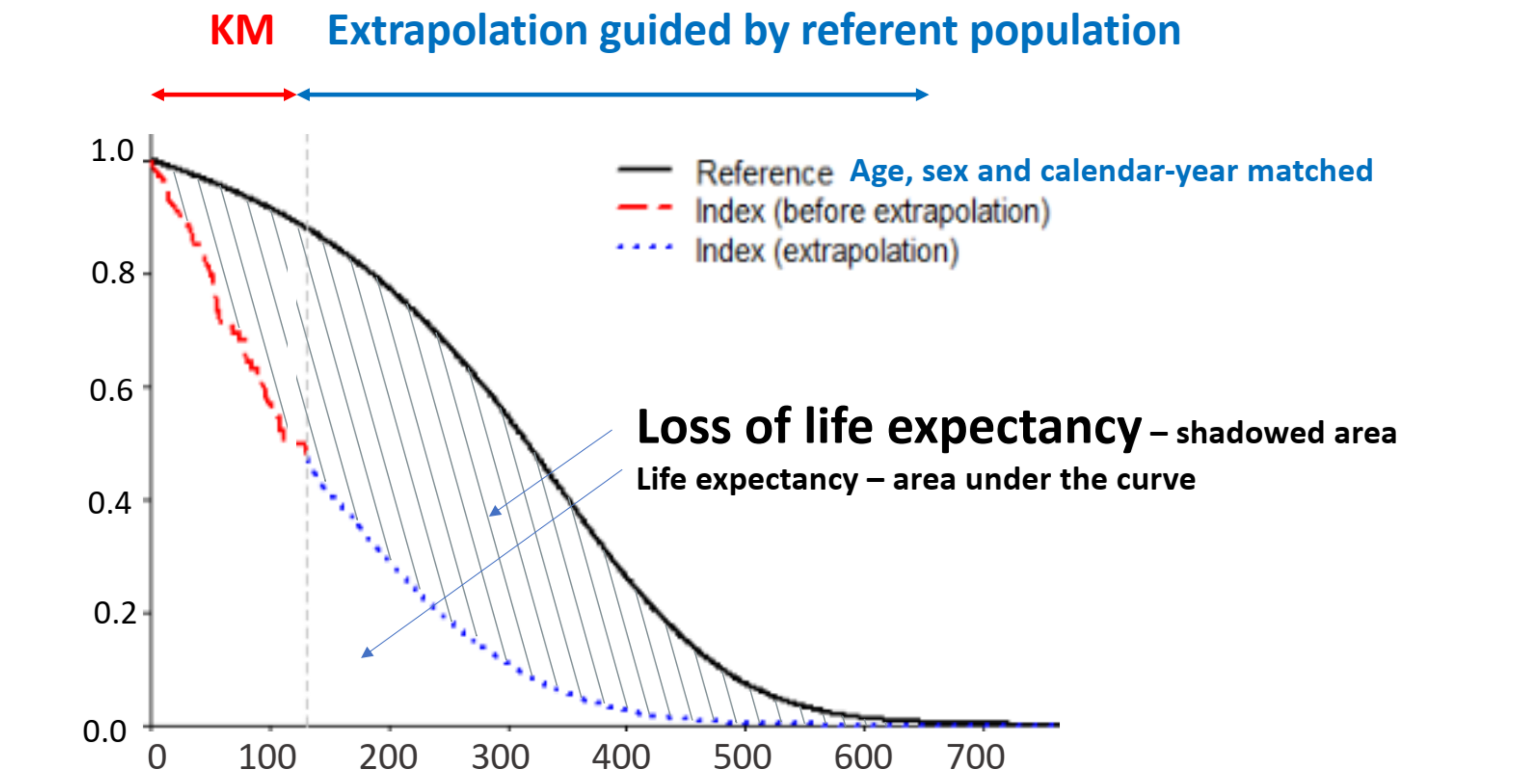
Introduction

Liver transplantation (LT) and hepatic resection (HR) represent two competitive treatments which provide with potential chance of cure for cirrhotic patients with early hepatocellular carcinoma (HCC). Many surgeons favor LT over HR because of the better 5 or 10-year survival rates reported in observational studies. Direct comparison of Kaplan-Meier(K-M) derived survival when analyzing the longitudinal data with extended period of time might be confounded by different distributions of age, sex, and calendar year of treatment. We hypothesized that lifetime estimates would be more unbiased indicator. Based on a nationwide 17-year follow-up data, we compared the lifetime survival of patients with early HCC who underwent LT versus HR.

Methods

Taiwan’s nationwide data on HCC primarily treated with LT and HR were collected from 2002 to 2017 and followed until 2018. There were 14,004 AJCC stage I and 9,301 stage II patients. After excluding severe cirrhosis, we applied a rolling-over algorithm to extrapolate the survival function to lifetime and estimated life expectancy (LE) and loss-of-LE. The results were corroborated with 1:1 matching of age, sex, calendar year of treatment and major comorbidities.

Figure 1. Rolling-over algorithm to extrapolate the survival function to lifetime and estimated life expectancy (LE) and loss-of-LE by iSQoL2 package.



Results

The 5 and 10-year survival rate of LT patients appeared better than HR patients for early-stage HCC, but the average age of LT patients was five years younger.

Figure 2. Kaplan-Meier analysis revealed the cross-over of survival curves of stage I HCC patients with tumor size ≤ 2 cm receiving LT versus HR.

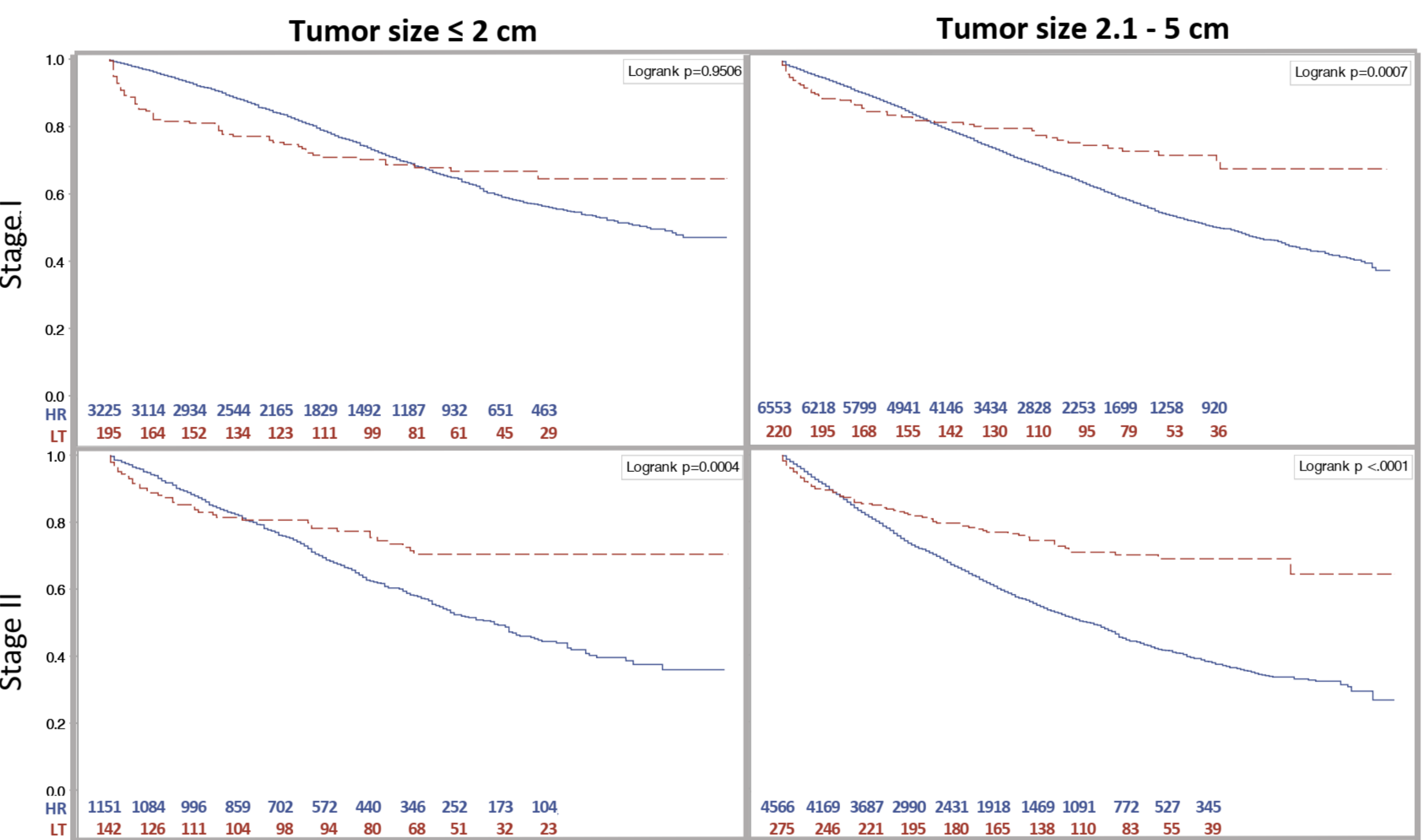


Figure 3. Comparison of LE and loss-of-LE estimation of the whole cohort without severe liver cirrhosis and with direct 1:1 matching for age, sex, and calendar year of operation. Loss-of-LE is less confounded by these factors.

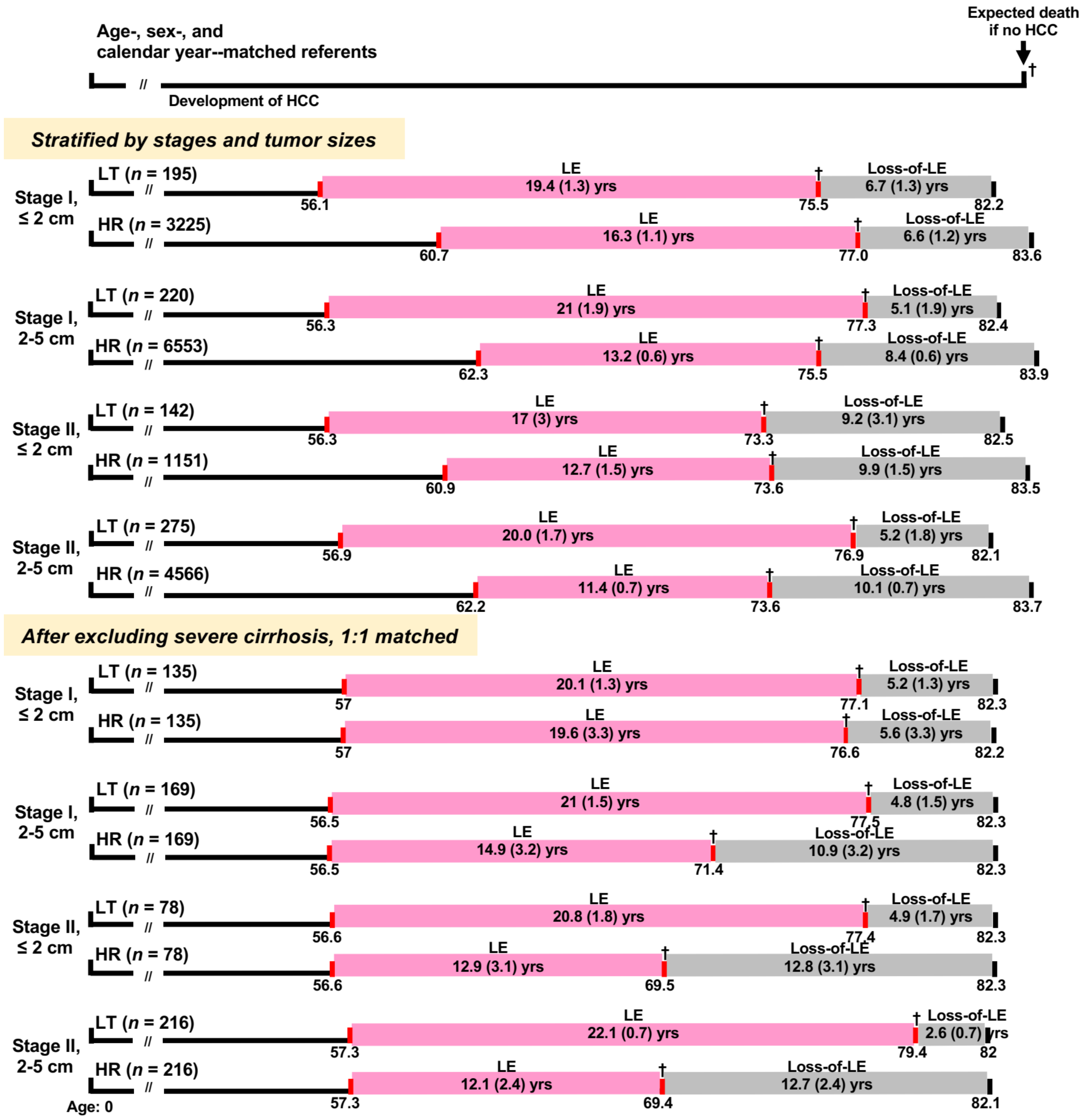


Table 1. Relative bias in lifetime estimations and the censored rate at the 14th year follow-up of patients with hepatocellular carcinoma receiving LT vs. HR. The relative bias represented the difference in the 14-year end survival between iSQoL2 R package-derived estimates and those from K-M method. Relative bias (%) = (extrapolated estimate by iSQoL2 – (K-M estimates))/(K-M estimate) × 100%

	LT				HR			
Subcohort/ stages/tumour size	Censored rate at 14 th year (%)	Extrapolated estimate† by iSQoL2†	K-M estimate‡	Relative bias* (%)	Censored rate at 14 th year (%)	Extrapolated estimate† by iSQoL2†	K-M estimate‡	Relative bias* (%)
AJCC, whole cohort	72.1	118.7 (2.7)	124.5 (2)	-4.6	58.0	99.1 (0.8)	103.2 (0.5)	-4
Stage I,	71.8	120.7 (3.5)	123.6 (2.9)	-2.4	61.9	106.4 (0.8)	110.7 (0.6)	-3.9
Stage II,	72.4	116.5 (4.4)	124.8 (2.8)	-6.6	52.0	86.6 (1)	90.8 (0.8)	-4.6
Stratified by AJCC staging and tumor sizes								
Stage I, ≤ 2 cm,	69.2	115.9 (5.6)	121 (5.3)	-4.3	68.4	110.9 (1.9)	119.3 (1.2)	-7
Stage I, 2.1-5 cm,	75.5	125.8 (6.7)	127.8 (4.6)	-1.6	62.5	106.2 (1.4)	109.7 (0.9)	-3.2
Stage II, ≤ 2 cm,	73.2	117.2 (8.2)	128.5 (5.7)	-8.8	58.8	97.8 (2.9)	102.6 (2.1)	-4.7
Stage II, 2.1-5 cm,	73.1	118.5 (5.2)	127.4 (4.4)	-7	52.6	88 (1.5)	92.5 (1.1)	-4.9
1:1 matched (AJCC)								
Stage I, ≤ 2 cm,	73.3	122.6 (6.7)	128 (6.1)	-4.3	75.6	127.2 (8.6)	128.9 (5.1)	-1.3
Stage I, 2.1-5 cm,	76.3	124.5 (6.7)	130.2 (5.1)	-4.3	74.6	127.2 (6.5)	126.1 (4.9)	0.8
Stage II, ≤ 2 cm,	74.4	121.2 (9.5)	127.2 (7.4)	-4.7	61.5	106.2 (8.9)	107.2 (6.7)	-0.9
Stage II, 2.1-5 cm,	75	121.4 (6.9)	129.6 (4.7)	-6.4	55.1	92.2 (6.4)	98 (4.8)	-6

Conclusion and Discussion

As more and more evidences are evolving from analyzing real world data, the quantification of the loss-of-LE proposed in this study provides a more valid estimation in the comparison of long-term outcome for different treatment modalities. Our analysis found that although LT would be suitable for stage II HCC, it did not show a survival advantage for stage I HCC with a tumor ≤ 2 cm and an equivocal advantage for those of 2.1–5 cm. Further studies with cost-effectiveness considerations are warranted for early-stage HCC.