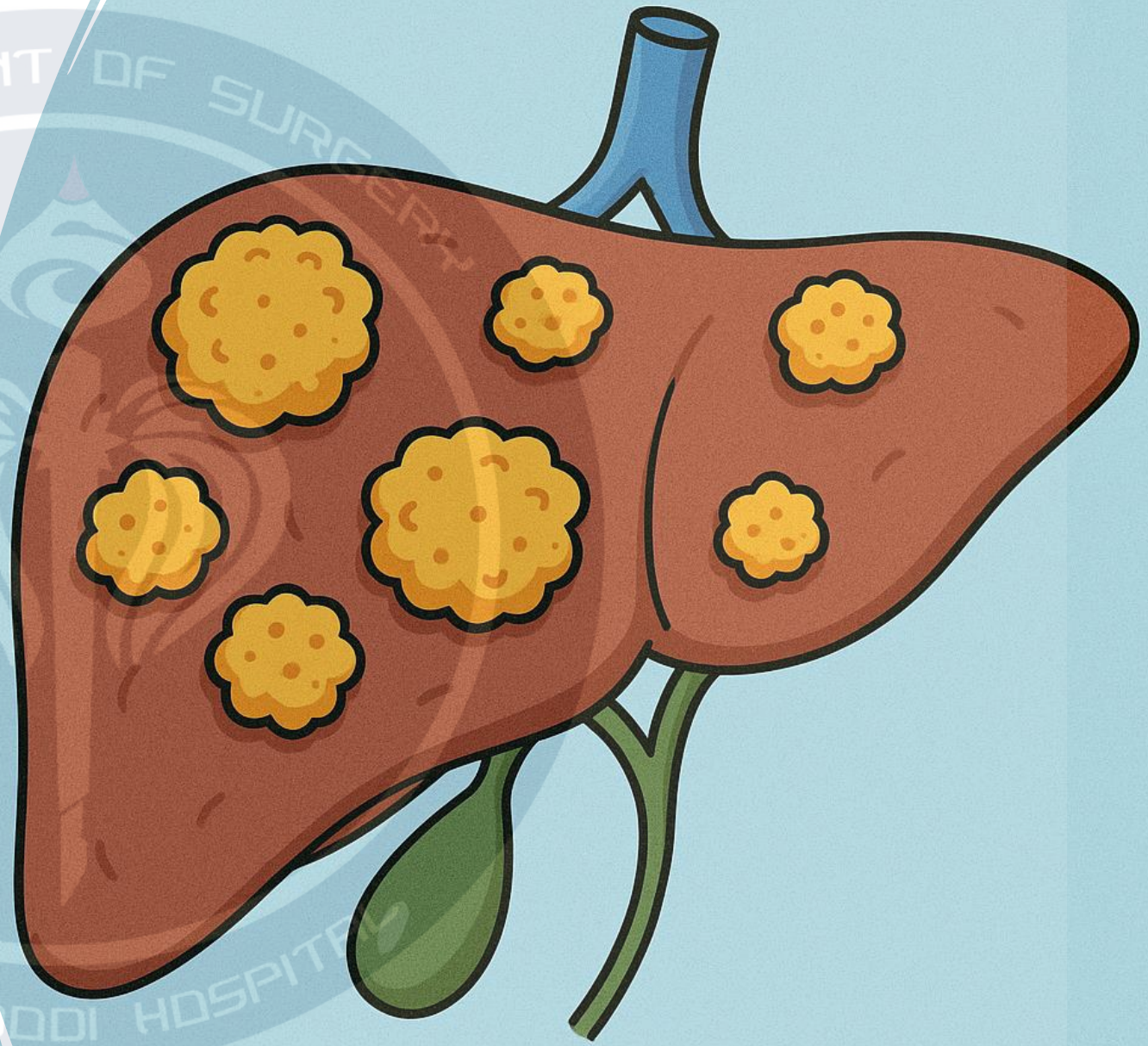
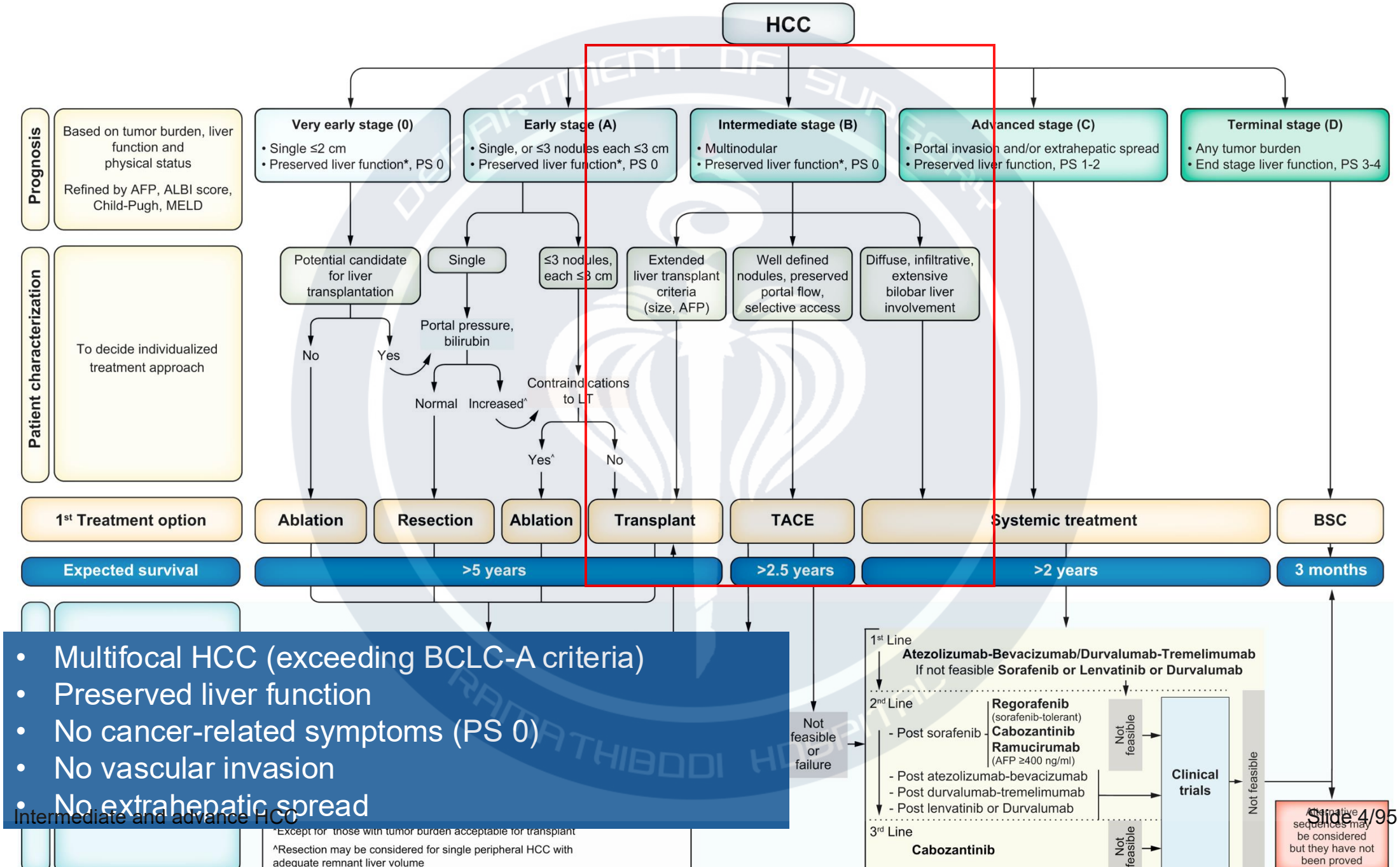
Surgical management in intermediate and advance HCC

Outline

- Intermediate stage HCC
- Advance satge HCC
  - PVTT,HVTT
  - BDTT
- Rupture HCC

Intermediate stage HCC





- Multifocal HCC (exceeding BCLC-A criteria)
- Preserved liver function
- No cancer-related symptoms (PS 0)
- No vascular invasion
- No extrahepatic spread

Biondi's Subclassification

BCLC Sub-Stage	B1	B2	B3	B4
CPT score	5-6-7	5-6	7	8-9*
Beyond Milan and within Ut-7	IN	OUT	OUT	ANY
ECOG (Tumor Related) PS	0	0	0	0-1
PVT	NO	NO	NO	NO
1st option	**TACE**	TACE or TARE		**BSC**
Alternative	LT TACE + ablation	SOR	Research trials TACE SOR	LT**

Fig. 3 Substaging and treatment indications for patients at first observation with intermediate hepatocellular carcinoma. Bold letters mean stronger scientific evidence. *, with severe/refractory ascites and/or jaundice; ** only if Up-to-7 IN and PS0; BSC, best supportive care; LT, liver transplantation; SOR, sorafenib; TARE, transarterial radioembolization.

Bolondi L, Burroughs A, Dufour JF, Galle PR, Mazzaferro V, Piscaglia F, Raoul JL, Sangro B. **Heterogeneity of Patients with Intermediate (BCLC B) Hepatocellular Carcinoma: Proposal for a Subclassification to Facilitate Treatment Decisions.** *Semin Liver Dis*. 2012;32(4):348–359.

Modified Biondi's Subclassification(Kinki)

Table 3. Subclassification and treatment strategy of intermediate-stage HCC (modified Bolondi)

BCLC substage	B1	B2	B3	
Child-Pugh score	5–7	5–7	8, 9	
Beyond Milan and within up-to-7	IN	OUT	ANY	
			IN	OUT
Sub-substage			B3-a	B3-b
Concept of treatment strategy	Curative intent	Non-curative, palliative	Curative intent if within up-to-7	Palliative, no treatment
Treatment option	Resection Ablation Superselective c-TACE	DEB-TACE[1] HAIC[2] Sorafenib[3]	Transplantation Ablation Superselective cTACE	HAIC Selective DEB-TACE
Alternative	DEB-TACE (large, C-P 7) B-TACE[4]	cTACE	DEB-TACE B-TACE, HAIC	BSC

[1] DEB-TACE is recommended for huge tumors that are >6 cm. [2] HAIC is recommended for multiple tumors >6. [3] Sorafenib is recommended for patients with liver function of Child-Pugh score 5 and 6. [4] B-TACE is recommended for fewer tumors.

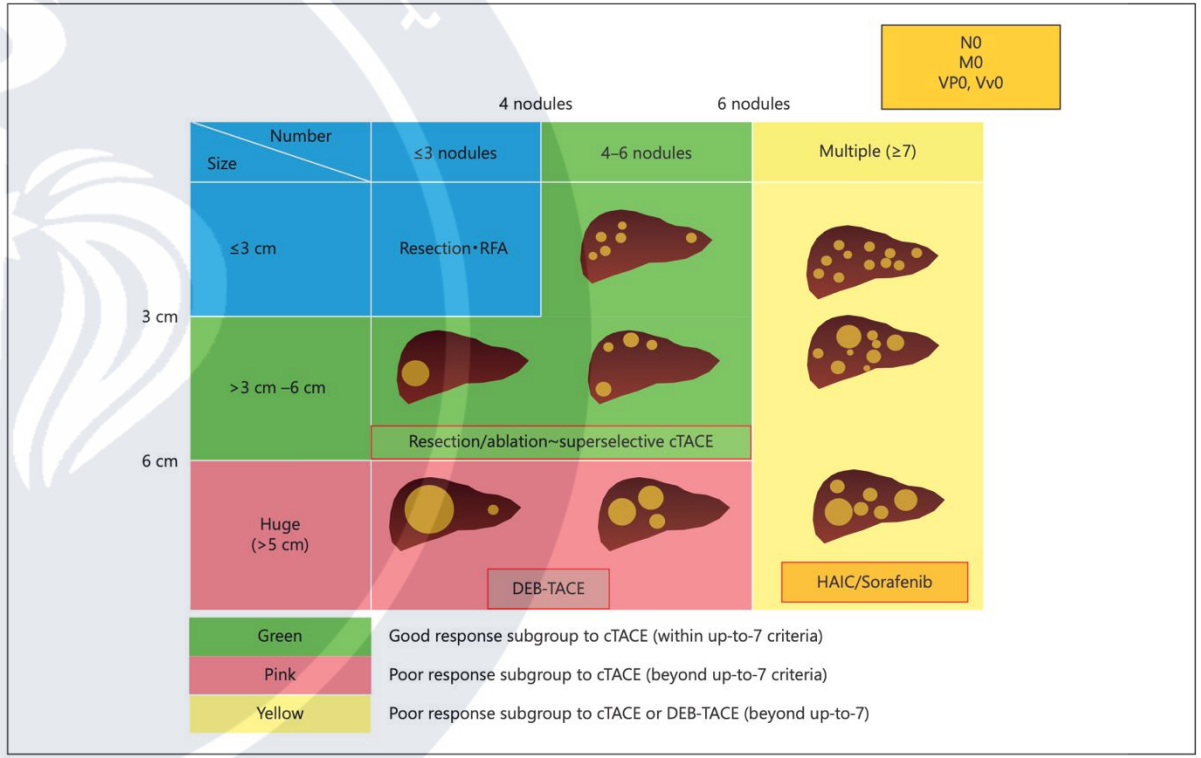


Fig. 6. Heterogeneity and treatment strategy of intermediate stage HCC (sub-stage B1, B2).

Kudo M, Arizumi T, Ueshima K, Sakurai T, Kitano M, Nishida N. Subclassification of BCLC B stage hepatocellular carcinoma and treatment strategies: Proposal of modified Bolondi's subclassification (Kinki criteria). *Dig Dis*. 2015;33(6):751-8.

RESEARCH Open Access

Significance of liver resection for intermediate stage hepatocellular carcinoma according to subclassification

Masateru Yamamoto[1,2], Tsuyoshi Kobayashi[1,2*], Masakazu Hashimoto[1,2], Shintaro Kuroda[1,2], Tomokazu Kawaoka[2,3], Hiroshi Aikata[2,3], Kazuaki Chayama[2,3] and Hideki Ohdan[1,2]

Abstract

Background: Patients diagnosed with Barcelona Clinic Liver Cancer (BCLC) intermediate stage hepatocellular carcinoma (HCC) encompass a broad clinical population. Kinki criteria subclassifications have been proposed to better predict prognoses and determine appropriate treatment strategies for these patients. This study validated the prognostic significance within the Kinki criteria substages and analyzed the role of liver resection in patients with intermediate stage HCC.

Methods: Patients with intermediate stage HCC ($n = 378$) were retrospectively subclassified according to the Kinki criteria (B1, $n = 123$; B2, $n = 225$; and B3, $n = 30$). We analyzed the overall survival (OS) and treatment methods.

Results: The OS was significantly different between adjacent substages. Patients in substage B1 who underwent liver resection had a significantly better prognosis than those who did not, even after propensity score matching (PSM). Patients in substage B2 who underwent liver resection had a significantly better prognosis than those who did not; however, there was no difference after PSM. There was no difference in prognosis based on treatments among patients in substage B3.

Conclusions: The Kinki criteria clearly stratify patients with intermediate stage HCC by prognosis. For substage B1 HCC patients, liver resection provides a better prognosis than other treatment modalities. In patients with substage B2 and B3, an alternative approach is required.

Keywords: BCLC staging system, Hepatocellular carcinoma, Intermediate stage, Kinki criteria, Liver resection

Intermediate and advance HCC

Yamamoto M, Kobayashi T, Hashimoto M, Kuroda S, Kawaoka T, Aikata H, et al. Significance of liver resection for intermediate stage hepatocellular carcinoma according to subclassification. *BMC Cancer*. 2021;21:668.

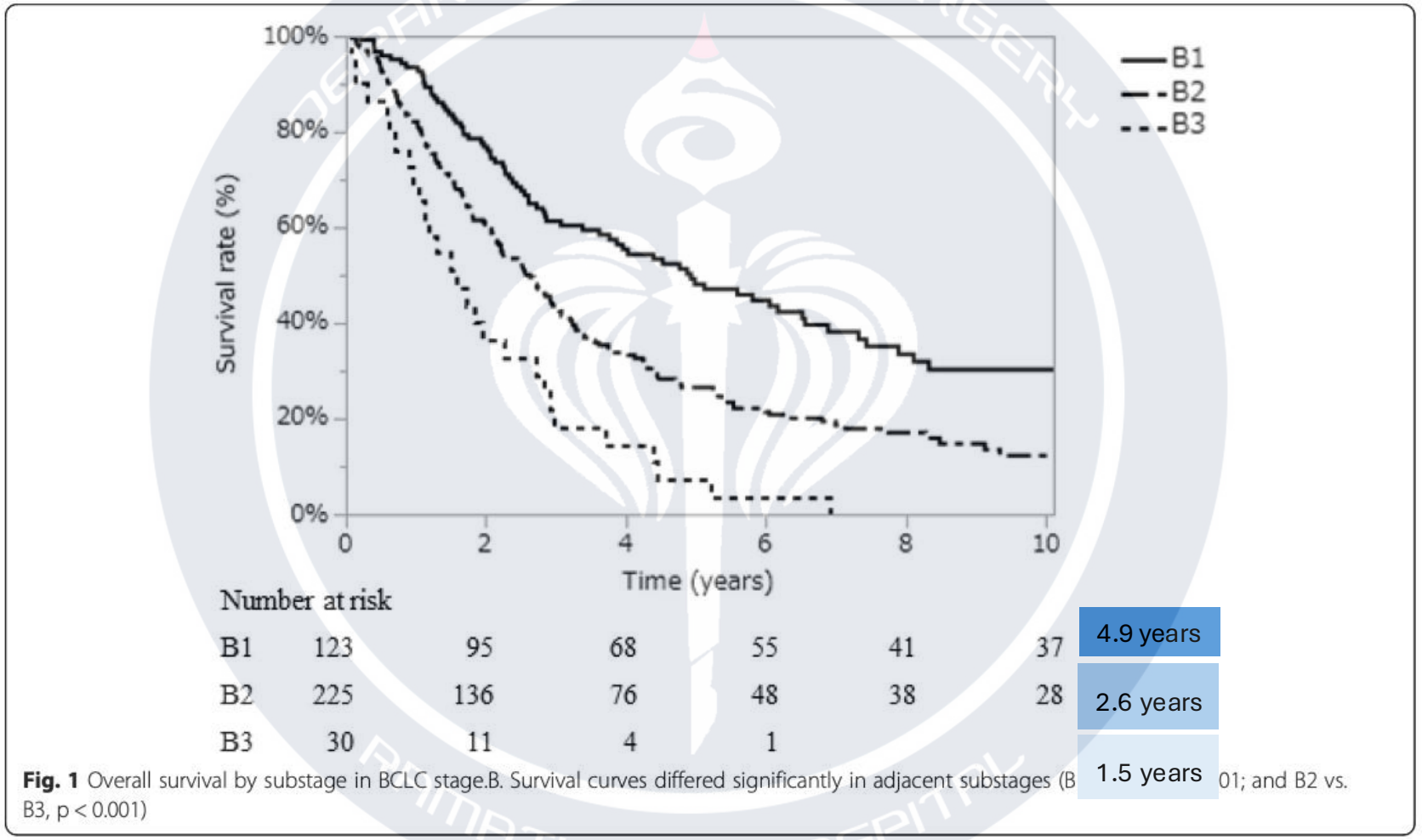


Fig. 1 Overall survival by substage in BCLC stage.B. Survival curves differed significantly in adjacent substages (B 01; and B2 vs. B3, $p < 0.001$)

Intermediate and advance HCC

Yamamoto M, Kobayashi T, Hashimoto M, Kuroda S, Kawaoka T, Aikata H, et al. Significance of liver resection for intermediate stage hepatocellular carcinoma according to subclassification. *BMC Cancer*. 2021;21:668

Subgroup B1

7.9 years (range 0.5–16.3)

2.4 years (range, 0.2–10.0)

2.0 years (range, 0.4–10.8)

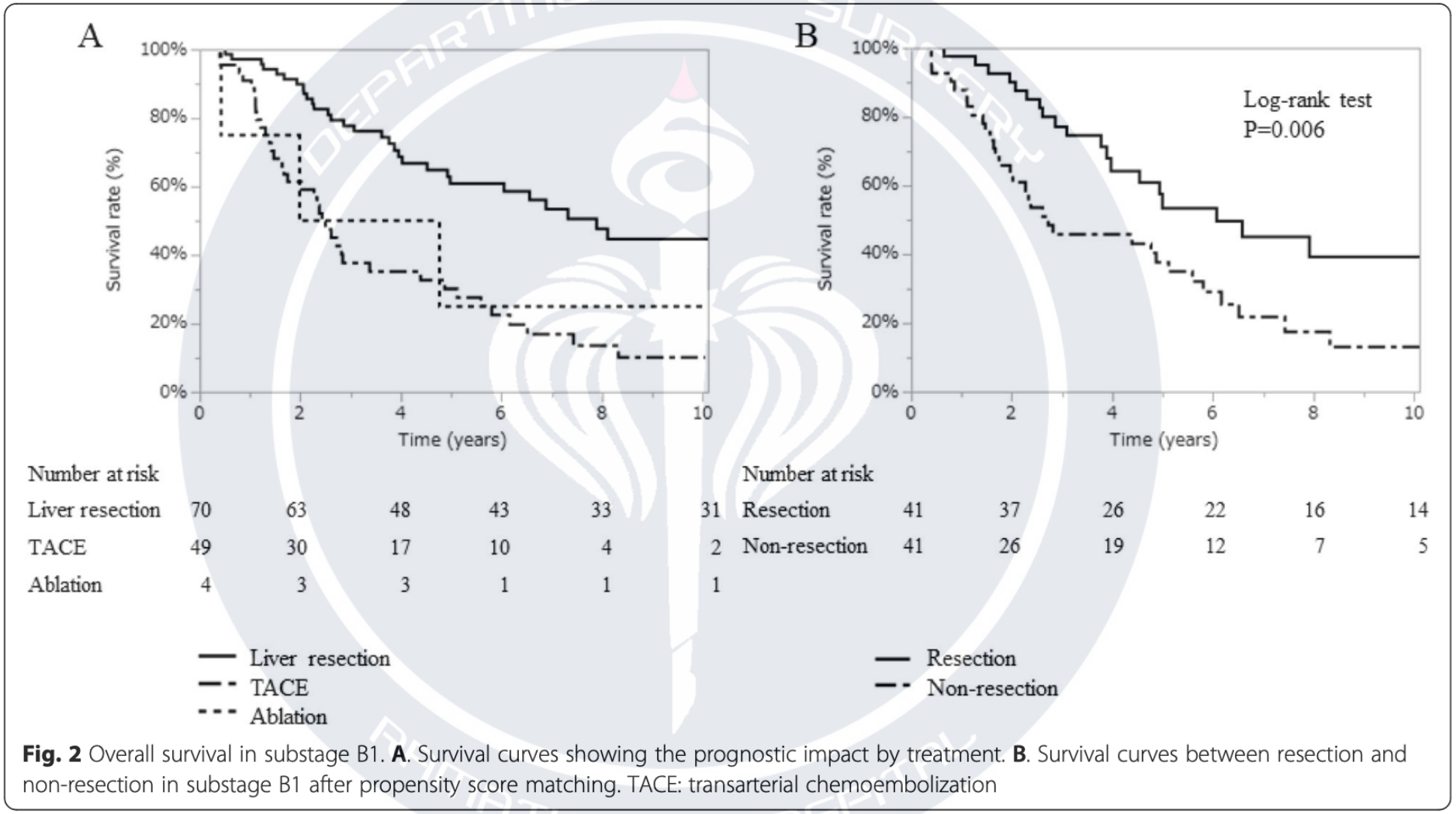


Fig. 2 Overall survival in substage B1. **A**. Survival curves showing the prognostic impact by treatment. **B**. Survival curves between resection and non-resection in substage B1 after propensity score matching. TACE: transarterial chemoembolization

Intermediate and advance HCC

Yamamoto M, Kobayashi T, Hashimoto M, Kuroda S, Kawaoka T, Aikata H, et al. Significance of liver resection for intermediate stage hepatocellular carcinoma according to subclassification. *BMC Cancer*. 2021;21:668

Subgroup B2

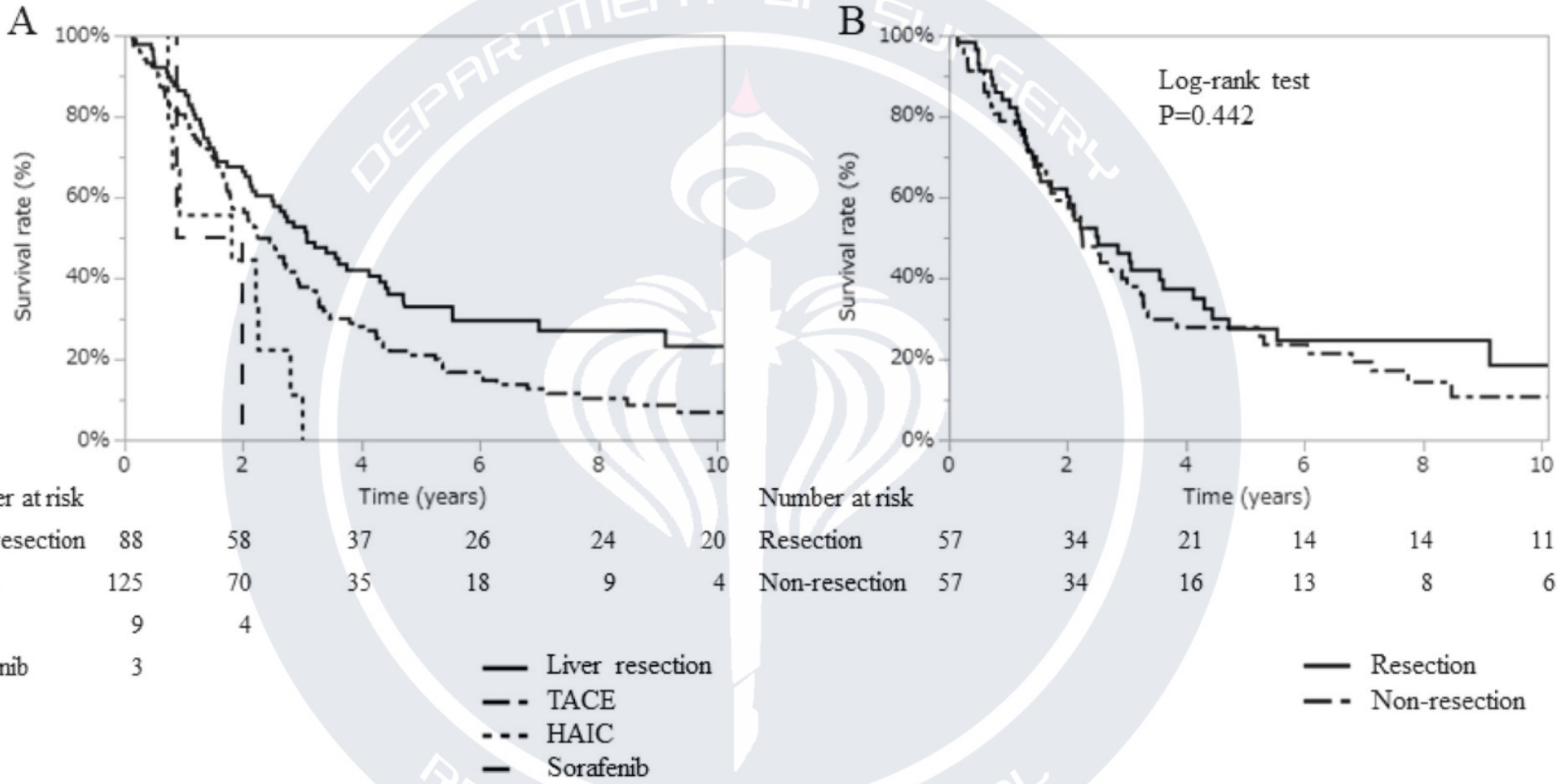


Fig. 3 Overall survival in substage B2. **A**. Survival curves showing the prognostic impact by treatment. **B**. Survival curves between resection and non-resection in substage B2 after propensity score matching. HAIC: hepatic arterial infusion chemotherapy, TACE: transarterial chemoembolization

Yamamoto M, Kobayashi T, Hashimoto M, Kuroda S, Kawaoka T, Aikata H, et al. Significance of liver resection for intermediate stage hepatocellular carcinoma according to subclassification. *BMC Cancer*. 2021;21:668

Subgroup B3

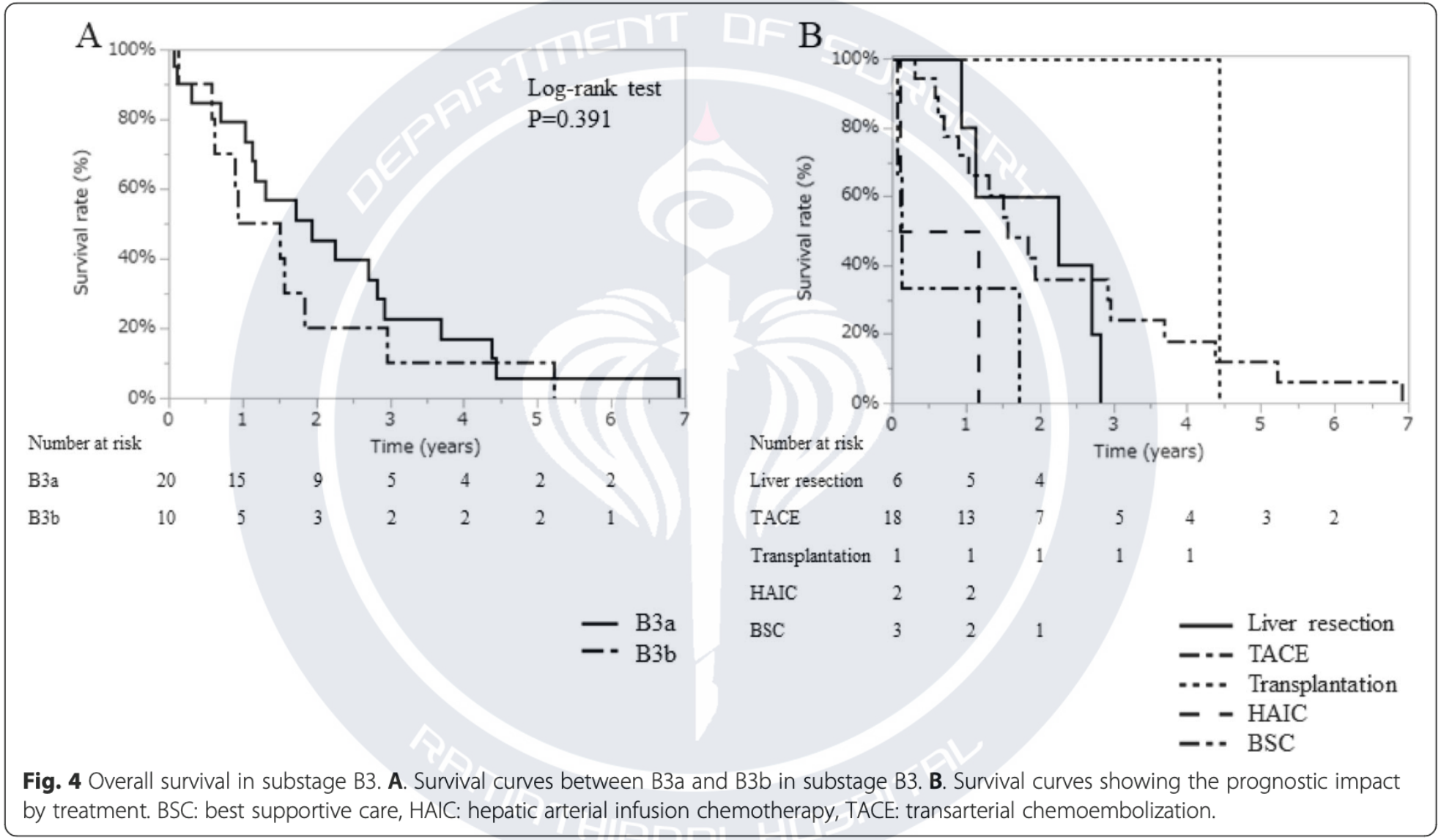


Fig. 4 Overall survival in substage B3. **A**. Survival curves between B3a and B3b in substage B3. **B**. Survival curves showing the prognostic impact by treatment. BSC: best supportive care, HAIC: hepatic arterial infusion chemotherapy, TACE: transarterial chemoembolization.

Yamamoto M, Kobayashi T, Hashimoto M, Kuroda S, Kawaoka T, Aikata H, et al. Significance of liver resection for intermediate stage hepatocellular carcinoma according to subclassification. *BMC Cancer*. 2021;21:668

Partial hepatectomy *vs.* transcatheter arterial chemoembolization for resectable multiple hepatocellular carcinoma beyond Milan criteria: A RCT

Lei Yin[1], Hui Li[2,†], Ai-Jun Li[1,†], Wan Yee Lau[1,3], Ze-ya Pan[1], Eric C.H. Lai[1,3], Meng-chao Wu[1], Wei-Ping Zhou[1,*]

[1]*The Third Depart ment of Hepatic Surgery, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai 200438, China;* [2]*The Department of Dermatology, Changhai Hospital, Second Military Medical University, Shanghai 200438, China;* [3]*Faculty of Medicine, The Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, Hong Kong Special Administrative Region*

See Editorial, pages 3–4

Background & Aims: The aim of this randomized comparative trial (RCT) is to compare partial hepatectomy (PH) with transcatheter arterial chemoembolization (TACE) to treat patients with resectable multiple hepatocellular carcinoma (RMHCC) outside of Milan Criteria.

Methods: This RCT was conducted on 173 patients with RMHCC outside of Milan Criteria (a solitary tumor up to 5 cm or multiple tumors up to 3 in number and up to 3 cm for each tumor) who were treated in our centre from November 2008 to September 2010. The patients were randomly assigned to the PH group or the TACE group. The primary outcome measure was overall survival (OS) from the date of treatment. A multivariate Cox proportional hazards regression analysis was performed to assess the prognostic risk factors associated with OS.

Results: The 1-, 2-, and 3-year OS rates were 76.1%, 63.5%, and 51.5%, respectively, for the PH group compared with 51.8%, 34.8%, and 18.1%, respectively, for the TACE group (Log-rank test, $\chi^2 = 24.246$, $p < 0.001$). Multivariate Cox proportional hazards regression analysis revealed the type of treatment (hazard ratio, 0.434; 95% CI, 0.293 to 0.644, $p < 0.001$), number of tumor (hazard ratio, 1.758; 95% CI, 1.213 to 2.548, $p = 0.003$) and gender (hazard ratio, 0.451; 95% CI, 0.236 to 0.862, $p = 0.016$) were significant independent risk factors associated with OS.

Conclusions: PH provided better OS for patients with RMHCC outside of Milan Criteria than conventional TACE. The number of tumor and gender were also independent risk factors associated with OS for RMHCC.

Keywords: Multiple hepatocellular carcinoma; Partial hepatectomy; Transcatheter arterial chemoembolization; Overall survival; RCT.

Received 4 August 2013; received in revised form 10 February 2014; accepted 10 March 2014; available online 17 March 2014

☆ DOI of original article: http://dx.doi.org/10.1016/j.jhep.2014.04.005.

* Corresponding author. Tel.: +86 21 81875521/65341828; fax: +86 21 81875529.

E-mail address: EHPHWP@126.com (W.-P. Zhou).

† These authors contributed equally to this work.

Introduction

Hepatocellular carcinoma (HCC) is a common malignancy especially in East-Asian countries [1]. Partial hepatectomy (PH) is the most commonly used curative therapy for HCC [2]. The results of PH for small HCC are good [3]. However, its role for multiple HCC is less well-defined. Multiple HCC have been shown to have a poor impact on survival after PH [4]. The use of Milan Criteria to select patients for liver transplantation (LT) produces good results for a solitary HCC up to 5 cm or for multiple HCC up to 3 in number and up to 3 cm for each tumor [5]. In most centers, LT is not recommended for HCC beyond Milan Criteria [6,7].

In non-randomized studies, PH has the potential to improve

Intermediate and advance HCC

Yin, L., Li, H., Li, A. J., Lau, W. Y., Pan, Z. Y., Lai, E. C., ... & [et al.] (2014). Partial hepatectomy vs. transcatheter arterial chemoembolization for resectable multiple hepatocellular carcinoma beyond Milan Criteria: a randomized controlled trial. *Journal of Hepatology, 61*(1), 82–88.

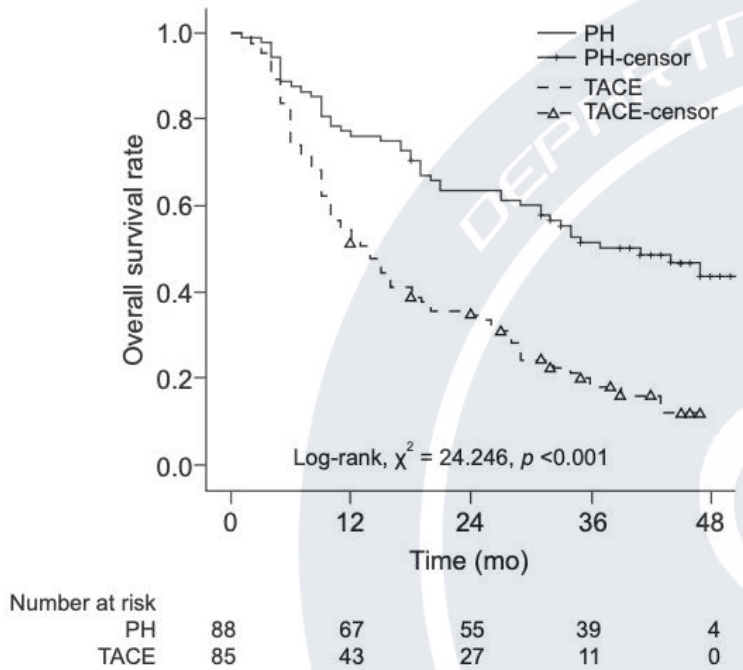


Fig. 2. Overall survival curves for PH and TACE.

OS	1-year	2-year	3-year
Resection (41month)	76.1	63.5	51.1
TACE(14month)	51.8	34.8	18.1

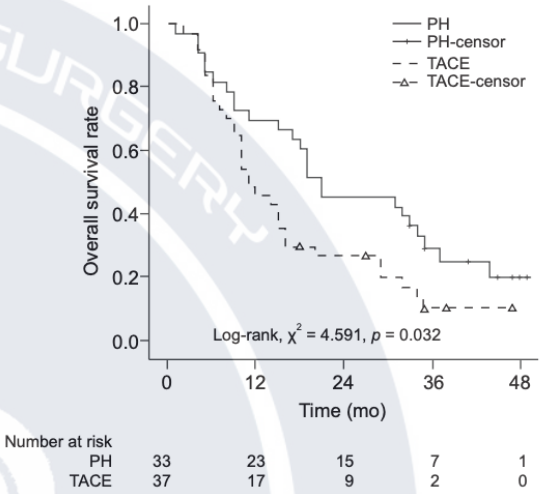


Fig. 4. Overall survival curves for patients with >2 tumors after PH or TACE.

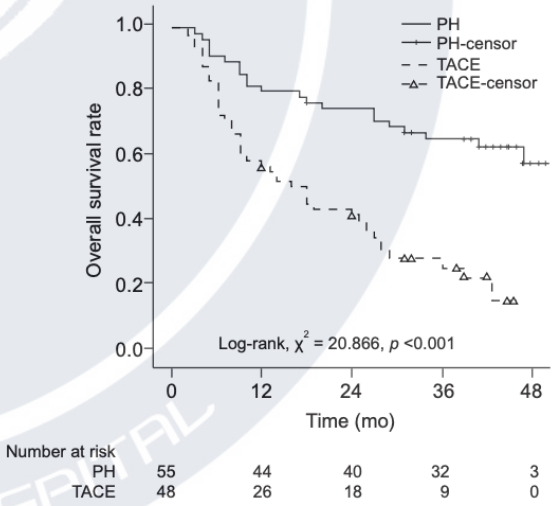


Fig. 3. Overall survival curves for patients with 2 tumors after PH or TACE.

Intermediate and advance HCC

Yin, L., Li, H., Li, A. J., Lau, W. Y., Pan, Z. Y., Lai, E. C., ... & [et al.] (2014). Partial hepatectomy vs. transcatheter arterial chemoembolization for resectable multiple hepatocellular carcinoma beyond Milan Criteria: a randomized controlled trial. *Journal of Hepatology, 61*(1), 82–88.

Table 4. Univariate and multivariate analysis of prognostic factors of OS.

Variable	Univariate		Multivariate	
	χ^2 value (Log-rank)	*p* value	HR (95% CI)	*p* value
Treatment (PH *vs.* TACE)	24.246	<0.001	0.434 (0.293, 0.644)	<0.001
Number of tumor (>2 *vs.* 2)	12.800	<0.001	1.758 (1.213, 2.548)	0.003
Sex (female *vs.* male)	11.282	0.001	0.451 (0.236, 0.862)	0.016
Serum AFP* (ng/ml) (>400 *vs.* ≤400)	6.204	0.013	1.362 (0.920, 2.016)	0.122
Total tumor size (cm) (>10 *vs.* ≤10)	5.235	0.022	1.142 (0.776, 1.681)	0.501
Child-Pugh classification (B *vs.* A)	0.001	0.973	1.204 (0.434, 3.344)	0.722
Age (yr) (>50 *vs.* ≤50)	1.478	0.224	-	n.a.
HBsAg (positive *vs.* negative)	0.273	0.601	-	n.a.
HBeAg (positive *vs.* negative)	0.981	0.322	-	n.a.
HBV-DNA (IU/ml) (>1000 *vs.* ≤1000)	0.233	0.630	-	n.a.
HCV (positive *vs.* negative)	0.038	0.845	-	n.a.
Cirrhosis (normal *vs.* cirrhosis)	0.010	0.919	-	n.a.
Tumor location (same hepatic segment *vs.* different hepatic segment)	0.001	0.976	-	n.a.

*AFP, alpha-fetoprotein.
n.a., not applicable.

Intermediate and advance HCC

Yin, L., Li, H., Li, A. J., Lau, W. Y., Pan, Z. Y., Lai, E. C., ... & [et al.] (2014). Partial hepatectomy vs. transcatheter arterial chemoembolization for resectable multiple hepatocellular carcinoma beyond Milan Criteria: a randomized controlled trial. *Journal of Hepatology, 61*(1), 82–88.

Article

Surgical Resection Is Superior to TACE in the Treatment of HCC in a Well Selected Cohort of BCLC-B Elderly Patients—A Retrospective Observational Study

Stefania Brozzetti [1], Chiara D'Alterio [1,*], Simone Bini [2], Jessica Antimi [1], Bianca Rocco [3], Alessia Fassari [1], Pierleone Lucatelli [3], Piergiorgio Nardis [3], Michele Di Martino [3], Giuseppe Maria De Sanctis [4], Mario Corona [3], Oreste Bagni [5], Enrico Cortesi [3], Mario Bezzi [3] and Carlo Catalano [3]

[1] Department of Surgery "Pietro Valdoni", Policlinico Umberto I., University of Rome-Sapienza, 00161 Rome, Italy
[2] Department of Translational and Precision Medicine, Policlinico Umberto I., University of Rome-Sapienza, 00161 Rome, Italy
[3] Department of Radiological, Oncological and Pathological Sciences, University-Sapienza, 00161 Rome, Italy
[4] Department of Tropical and Infectious Diseases, Policlinico Umberto I., University of Rome-Sapienza, 00161 Rome, Italy
[5] Dipartimento di Medicina Nucleare, Ospedale Santa Maria Goretti, 04100 Latina, Italy
* Correspondence: chiara.dalterio@uniroma1.it

Simple Summary: Hepatocellular carcinoma (HCC) is the most common primary liver malignancy. Liver transplantation (LT) and surgical resection (SR) are currently the primary treatments with curative intent. Nevertheless, more than two-thirds of patients are elderly and, therefore, excluded from LT; while, according to the Barcelona Clinic Liver Cancer (BCLC) system, SR should only be offered to a small group of patients with early stage HCC. The identification in stage B of an intermediate subgroup of patients that fulfill the criteria for surgery may play an important role in the implementation of potentially curative treatments.

Abstract: Hepatocellular carcinoma (HCC) usually develops in cirrhotic liver, with high recurrence rates. However, considering its increasing detection in non-cirrhotic liver, the choice of treatment assumes particular relevance. This study aimed to investigate outcomes of patients among BCLC stages and enrolled for surgical resection (SR) according to a more complex evaluation, to establish its safety and efficacy. A total of 186 selected HCC patients (median age 73.2 yrs) submitted to SR between January 2005 and January 2021, were retrospectively analyzed. Of which, 166 were staged 0, A, B according to the BCLC system, while 20 with a single large tumor (>5 cm) were classified as stage AB. No perioperative mortality was recorded; complications occurred in 48 (25.80%) patients, and all but two were Clavien–Dindo grade I–II. Median follow-up was 9.2 years. Subsequently, 162 recurrent patients (87,1%) were selected for new treatments. Comparable overall survival rates (OS) were observed at 1, 3, 5, and 10 years in 0, A, B and AB stages ($p = 0.2$). Eventually, the BCLC-B group was matched to 40 BCLC-B patients treated (2015-2021) with TACE. Significant differences in baseline characteristics ($p < 0.0001$) and in OS were observed at 1 and 3 years ($p < 0.0001$); a significant difference was also observed in oncological outcomes, in terms of the absence, residual, or relapse of disease ($p < 0.05$). Surgery might be a valid treatment in HCC for patients affected by chronic liver disease in a condition of compensation, up to BCLC-B stage. Surgical indication for liver resection in case of HCC should be extensively revised.

check for updates

Citation: Brozzetti, S.; D'Alterio, C.; Bini, S.; Antimi, J.; Rocco, B.; Fassari, A.; Lucatelli, P.; Nardis, P.; Di Martino, M.; De Sanctis, G.M.; et al. Surgical Resection Is Superior to TACE in the Treatment of HCC in a Well Selected Cohort of BCLC-B Elderly Patients—A Retrospective Observational Study. *Cancers* **2022**, *14*, 4422. https://doi.org/10.3390/cancers14184422

Academic Editor: Dimitrios Moris

Received: 29 August 2022
Accepted: 8 September 2022
Published: 12 September 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Intermediate and advance HCC

Brozzetti S, D'Alterio C, Bini S, Antimi J, Rocco B, Fassari A, Lucatelli P, Nardis P, Di Martino M, De Sanctis GM, Corona M, Bagni O, Cortesi E, Bezzi M, Catalano C. Surgical resection is superior to TACE in the treatment of HCC in a well selected cohort of BCLC-B elderly patients—A retrospective observational study. *Cancers*. 2022;14(18):4422.

Table 2. Tumor features and treatments. Perioperative outcomes. Recurrence treatments.

	Stage 0 (n = 9)	Stage A (n = 99)	Stage AB (n = 20)	Stage B (n = 58)	*p* Value
Nodules resected/ablated, n (%)					
1	9 (100)	60 (60.6)	20 (100)	0	
2	0 (0)	30 (30.3)/ 10 * (10.1)	0 (0)	40 (51.3)/ 10 * (12.82)	
3	0 (0)	9 (9.1)/ 5 * (5.05)	0 (0)	18 (23)/ 13 * (16.7)	
HCC size (cm), median, (Range)	1.7 (1.3–2)	3.2 (0.8–4.5)	7.5 (5–11)	2.6 (0.8-4.5)	
Type of resection, n (%)					*0.00008*
Extended Right Hepatectomy	0 (0)	0 (0)	1 (5)	0 (0)	
Right Hepatectomy	0 (0)	1 (1)	0 (0)	9 (15.51)	
Left hepatectomy	0 (0)	0 (0)	1 (5)	2 (3.45)	
Bi-Segmentectomy	0 (0)	52 (52.5)	17 (85)	26 (44.83)	
Segmentectomy	9 (100)	45 (45.4)	1 (5)	20 (34.48)	
Wedge	0 (0)	2 (2%)	0 (0)	4 (6.9)	
Morbidity n, (%)					*0.54*
I-II (Clavien-Dindo)	1 (11.1)	22 (22.2)	3 (15)	17 (29.31)	
III (Clavien-Dindo)	0 (0)	1 (1.01)	0 (0)	1 (1.72)	
Length of hospital stay, mean (range)	6 (5–8)	7 (6–15)	7 (6–10)	8 (6–15)	
ICU length of stay, mean (range)	0.5 (0–1)	1.2 (0–3)	1 (0–1)	1.3 (0–3)	
90-days mortality	0 (0)	0 (0)	0 (0)	(0)	
I recurrence treatment, n (%)	6 (66.66)	86 (86.87)	12 (60)	58 (100)	
Curative Treatments	6 (100)	47 (54.65)	11 (91.67)	23 (39.66)	*0.003*
Palliative Treatments	0	39 (45.35)	1 (8.33)	35 (60.34)	
II recurrence treatments, n (%)	3 (33.33)	38 (38.4)	6 (30)	24 (41.38)	
Curative	3 (100)	9 (23.7)	4 (66.67)	5 (20.83)	*0.013*
Palliative	0 (0)	29 (76.3)	2 (33.33)	19 (79.17)	
III recurrence treatments, n (%)	1 (11.11)	19 (19.2)	0 (0)	9 (15.5)	
Curative	1 (100)	6 (31.6)	0 (0)	2 (22.22)	0.6
Palliative	0 (0)	13(68.4)	0 (0)	7 (77.78)	

* Patients who received RFA combined with surgery.

Table 3. Overall survival.

	Stage 0	Stage A	Stage AB	Stage B	*p* Value
1-yr OS, survival % (IC 95%)	100% [IC: 1–1]	100% [IC:1–1]	100% [IC: 1–1]	100% [IC: 1–1]	*0.2*
3-yrs OS, survival % (IC 95%)	100% [IC: 1–1]	96.03% [IC: 0.917–0.999]	95.21% [IC: 0.813–0.946]	97.43% [IC: 0.891–0.992]	*0.2*
5-yrs OS, survival % (IC 95%)	88.9% [IC: 0.706–1]	80.8% [IC: 0.589–0.779]	78.7% [IC: 0.532–0.755]	67.2% [IC: 0.507–0.718]	*0.2*
10.yrs OS, survival % (IC 95%)	66.66% [IC: 0.507–0.718]	62.2% [IC: 0.542–0.753]	58.3% [IC: 0.492–0.723]	50.3% [IC: 0.464–0.690]	*0.2*
Death, n (%)	3 (33.33)	37 (37.4)	7 (35)	28 (48.28)	*0.015*
HCC	0(0)	6 (16.2%)	2 (28.57)	15 (53.571)	
Liver disease/Cirrhosis	0 (0)	21 (56.8)	3 (42.86)	10 (35.71)	
Other causes	3 (100)	10 (27)	2 (28.57)	3 (10.71)	

Intermediate and advance HCC

Brozzetti S, D'Alterio C, Bini S, Antimi J, Rocco B, Fassari A, Lucatelli P, Nardis P, Di Martino M, De Sanctis GM, Corona M, Bagni O, Cortesi E, Bezzi M, Catalano C. Surgical resection is superior to TACE in the treatment of HCC in a well selected cohort of BCLC-B elderly patients—A retrospective observational study. *Cancers*. 2022;14(18):4422.

	SR/RF 58 pts, n 134 HCC (%)	TACE 40 pts, n 69 HCC (%)	*p* Value
Number of nodules n, (%)	134 target HCC 108/26 *	69 target HCC	*<0.00001*
2	40/10 * (68.97)	11 (27.5)	
3	18/13 * (31.03)	9 (22.5)	
>3	0	20 (50)	
HCC site			*<0.00001*
Unilobar	55 (94.83)	18 (45)	
Bilobar	3 (5.17)	22 (55)	
HCC nodules/pts, n (range)	2 (2–3)	4 (2–9)	
HCC, Median size (cm), (Range)	2.6 (0.8–4.5)	2.4 (0.7–12)	

Figure 2. Follow-up in patients submitted to TACE.

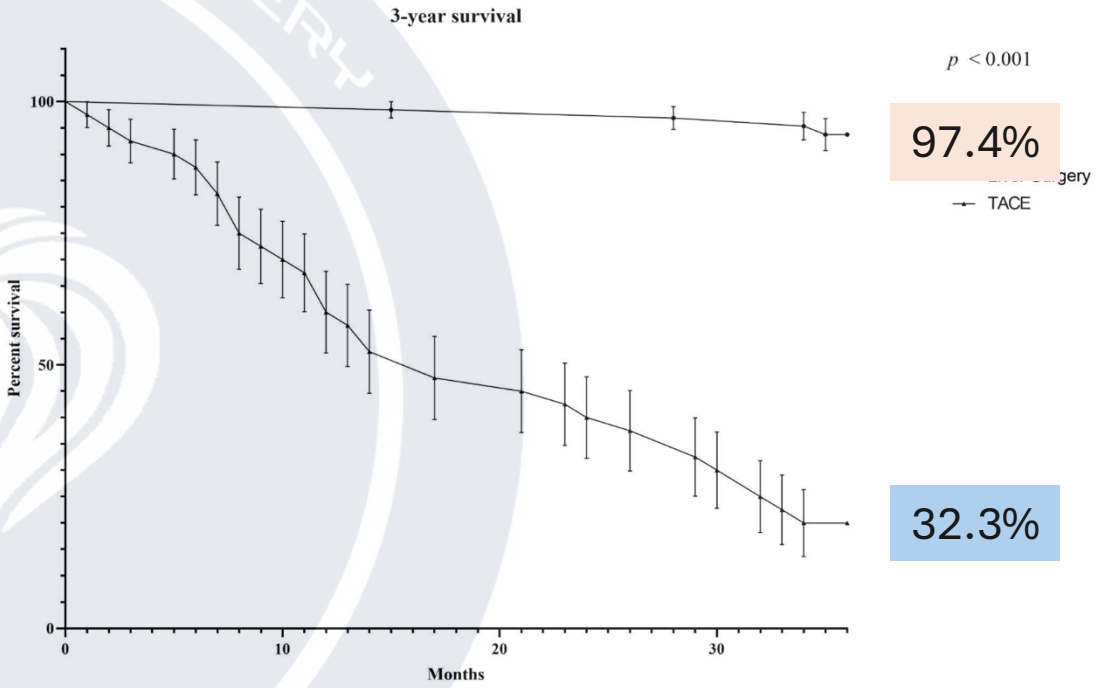


Figure 3. Comparison of OS between the surgical group and the TACE group.

Intermediate and advance HCC

Brozzetti S, D'Alterio C, Bini S, Antimi J, Rocco B, Fassari A, Lucatelli P, Nardis P, Di Martino M, De Sanctis GM, Corona M, Bagni O, Cortesi E, Bezzi M, Catalano C. Surgical resection is superior to TACE in the treatment of HCC in a well selected cohort of BCLC-B elderly patients—A retrospective observational study. *Cancers*. 2022;14(18):4422.

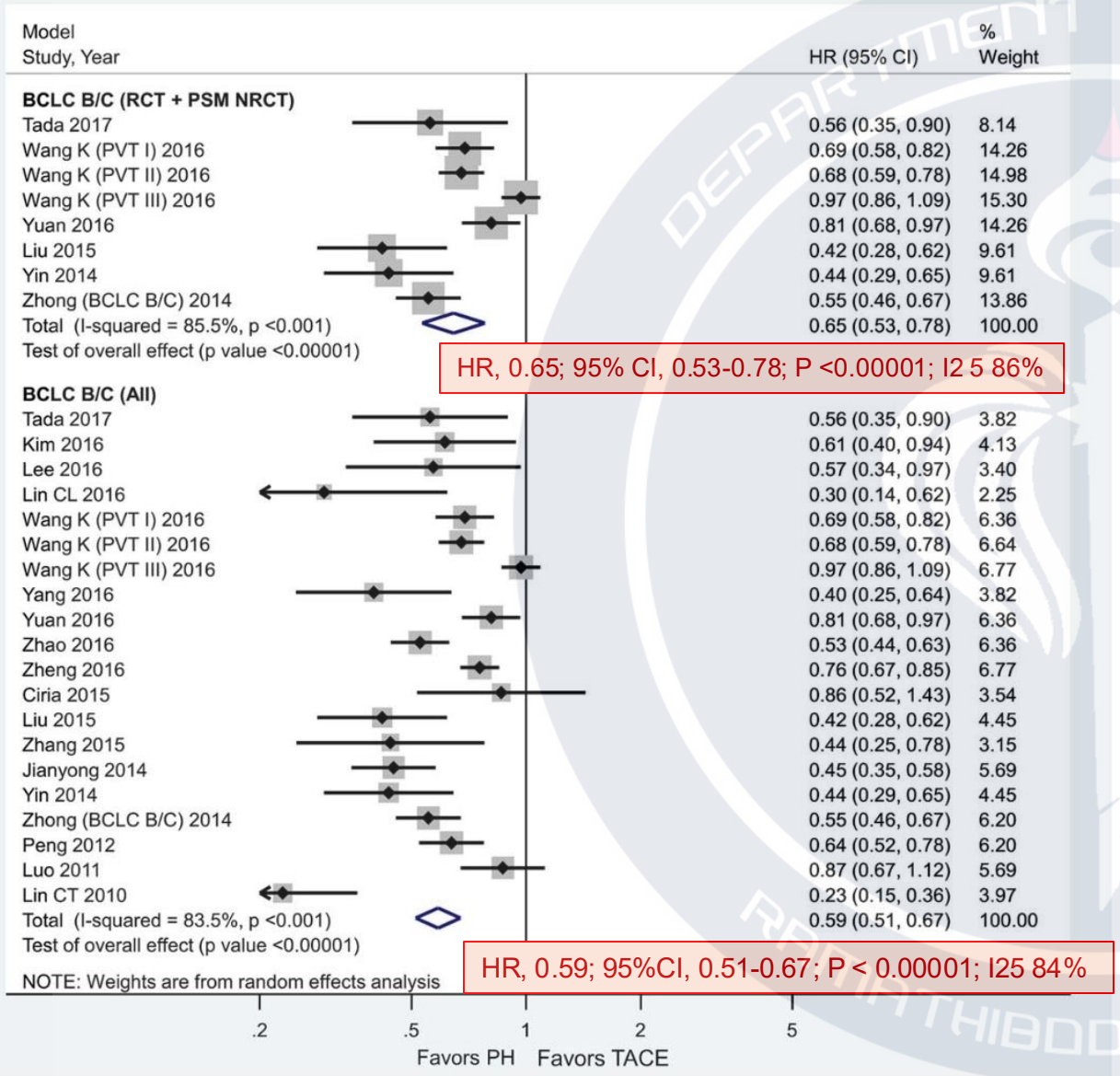
Hepatic Resection Compared to Chemoembolization in Intermediate- to Advanced-Stage Hepatocellular Carcinoma: A Meta-Analysis of High-Quality Studies

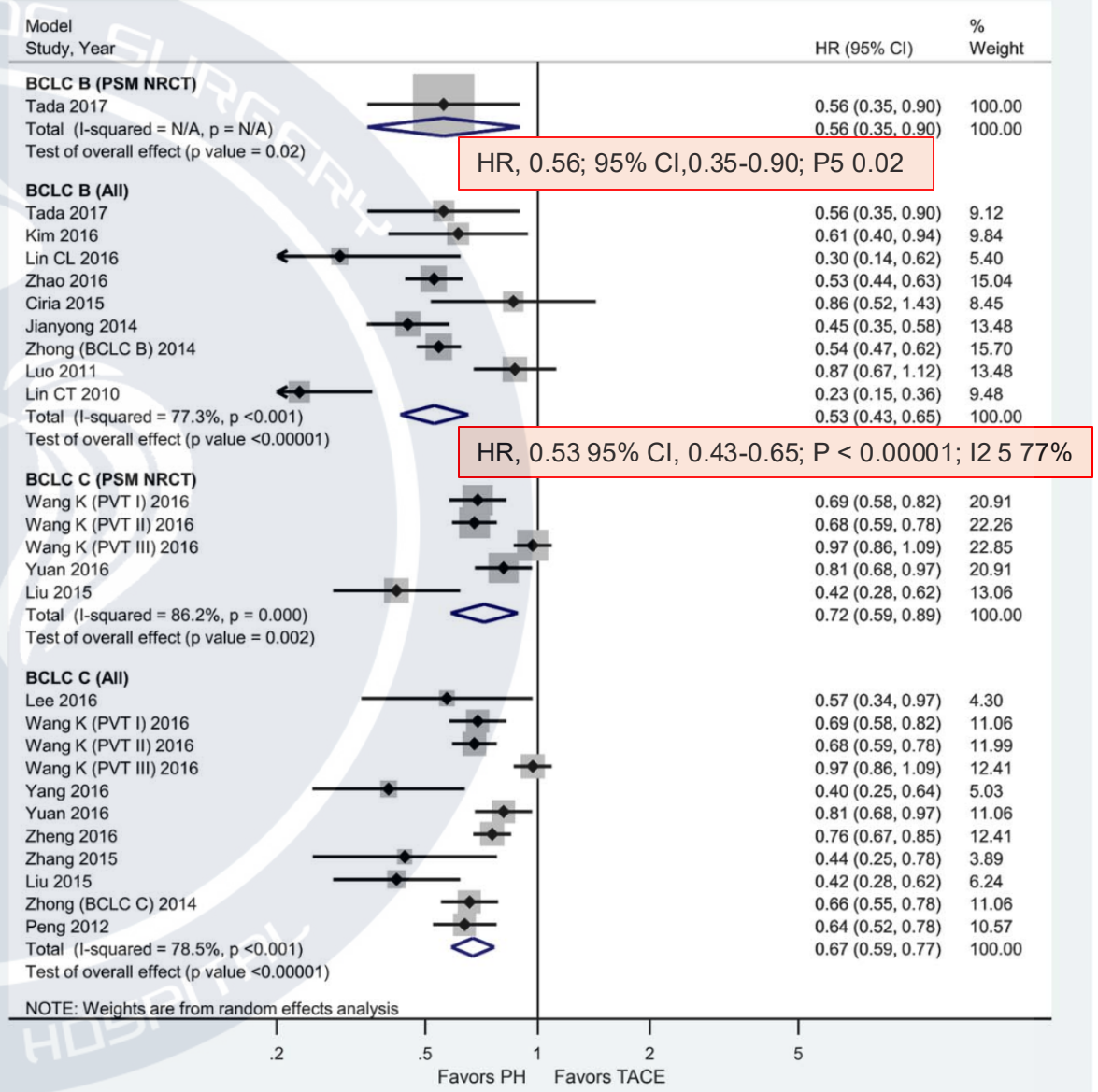
Myung Han Hyun [1*] Young-Sun Lee [2*] Ji Hoon Kim,[2] Chan Uk Lee,[2] Young Kul Jung,[2] Yeon Seok Seo,[2] Hyung Joon Yim,[2] Jong Eun Yeon,[2] and Kwan Soo Byun[2]

According to the American Association for the Study of Liver Diseases (AASLD) treatment guidelines for hepatocellular carcinoma (HCC), the role of surgery has been expanded beyond the Barcelona Clinic Liver Cancer (BCLC) algorithm. We compared primary hepatectomy (PH) with transarterial chemoembolization (TACE) in patients with intermediate- to advanced-stage (BCLC stage B/C) HCC to determine the current evidence. Through a database search, we included 18 high-quality studies (one randomized controlled trial [RCT], five propensity-score matching nonrandomized comparative trials [NRCTs], and 12 NRCTs) that compared survival outcomes of 5,986 patients after PH and TACE. We found significant survival benefits for PH over TACE in BCLC stage B/C patients (hazard ratio [HR], 0.59; 95% confidence interval [CI], 0.51-0.67; $P < 0.00001$; $I^2 = 84\%$). According to the BCLC, both stage B and stage C patients showed significantly better overall survival (OS) for PH compared to TACE (HR, 0.53; 95% CI, 0.43-0.65; $P < 0.00001$; $I^2 = 77\%$; HR, 0.67; 95% CI, 0.59-0.77; $P < 0.00001$; $I^2 = 79\%$, respectively). Five-year survival rates for PH were significantly higher than those for TACE in BCLC stage B/C, stage B, and BCLC stage C patients (odds ratio [OR], 2.71, 2.77, and 3.03, respectively; all $P < 0.00001$). Survival benefits persisted across subgroup, sensitivity, and metaregression analyses; interstudy heterogeneity remained constant. *Conclusion:* This meta-analysis suggests that surgical resection provides survival benefits in patients with intermediate- to advanced-stage HCC. The evidence found herein may assist in the choice of treatment modality based on diverse definitions of operability. (HEPATOLOGY 2018; 68:977-993).

Intermediate and advance HCC

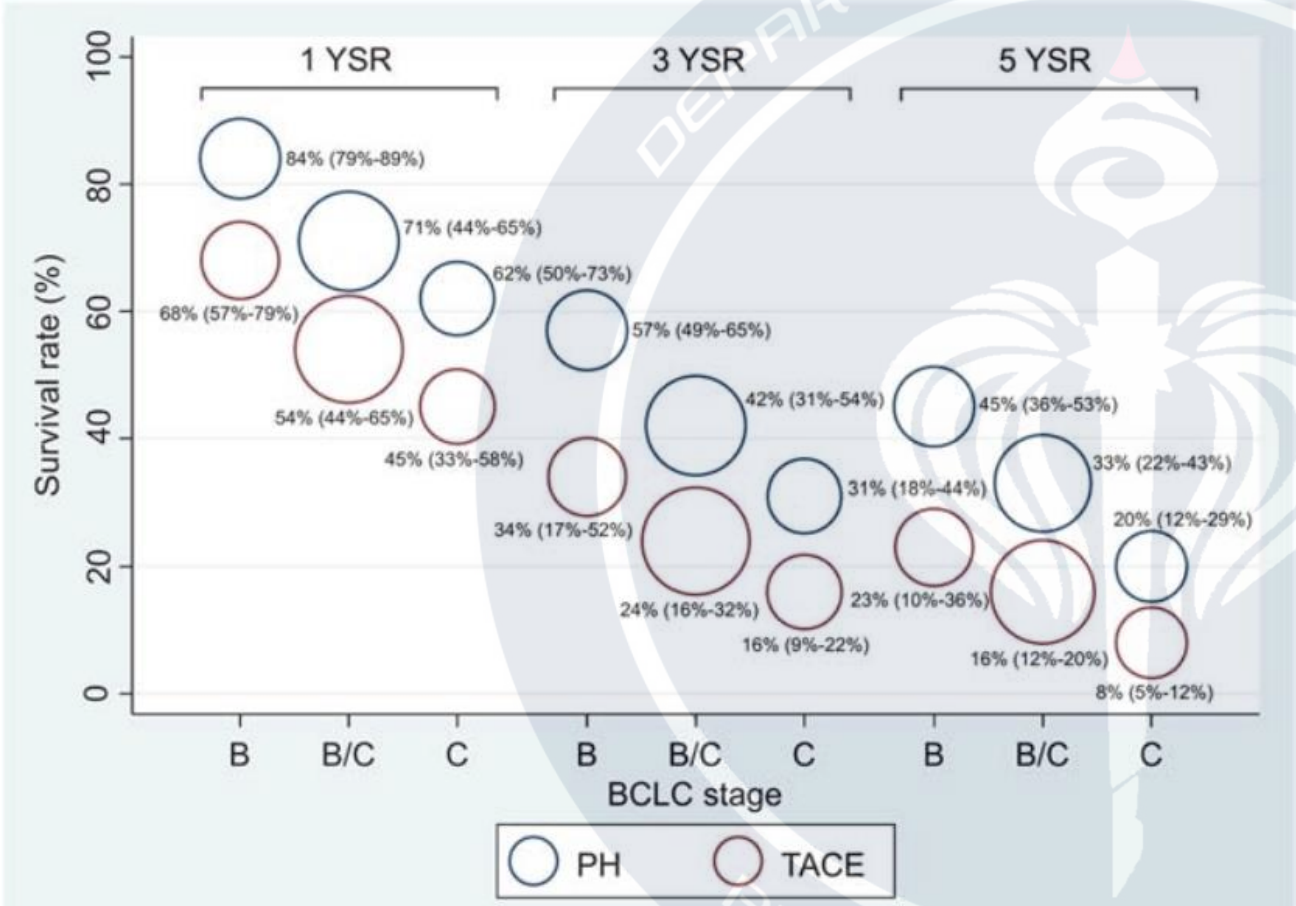
Hyun, M. H., Lee, Y.-S., Kim, J. H., Lee, C. U., Jung, Y. K., Seo, Y. S., Yim, H. J., Yeon, J. E., & Byun, K. S. (2018). Hepatic resection compared to chemoembolization in intermediate- to advanced-stage hepatocellular carcinoma: A meta-analysis of high-quality studies. *Hepatology, 68*(3), 977–99





Intermediate and advance HCC

Hyun, M. H., Lee, Y.-S., Kim, J. H., Lee, C. U., Jung, Y. K., Seo, Y. S., Yim, H. J., Yeom, J. E., & Byun, K. S. (2018). Hepatic resection compared to chemoembolization in intermediate- to advanced-stage hepatocellular carcinoma: A meta-analysis of high-quality studies. *Hepatology, 68*(3), 977–99



B/C Procedure-related mortality was not statistically different between the two treatment modalities in BCLC stage B plus stage C patients (OR, 1.27; 95% CI,0.70-2.30)

Intermediate and advance HCC

Hyun, M. H., Lee, Y.-S., Kim, J. H., Lee, C. U., Jung, Y. K., Seo, Y. S., Yim, H. J., Yeon, J. E., & Byun, K. S. (2018). Hepatic resection compared to chemoembolization in intermediate- to advanced-stage hepatocellular carcinoma: A meta-analysis of high-quality studies. *Hepatology, 68*(3), 977–99

Liver resection versus transarterial chemoembolisation for the treatment of intermediate hepatocellular carcinoma: a systematic review and meta-analysis

Aleksandar Bogdanovic, PhD[a,c,*], Jelena Djokic Kovac, PhD[b,c], Predrag Zdujic, MD[a], Uros Djindjic, MD[a], Vladimir Dugalic, PhD[a,c]

Background: Transarterial chemoembolisation (TACE) is the primary treatment for intermediate-stage hepatocellular carcinoma (HCC), according to the updated Barcelona Clinic Liver Cancer (BCLC) staging system. Although growing evidence favours liver resection (LR) over TACE for intermediate-stage HCC, the best treatment option remains controversial. This meta-analysis aimed to compare the overall survival (OS) after LR versus TACE for intermediate-stage HCC.

Methods: A comprehensive literature review of PubMed, Embase, Cochrane Library, and Web of Science was performed. Studies that compared the efficacy of LR and TACE in patients with intermediate (BCLC stage B) HCC were selected. According to the recent updated BCLC classification, intermediate stage of HCC was defined as follows: (a) four or more HCC nodules of any size, or (b) two or three nodules, but if at least one tumour is larger than 3 cm. The main outcome was OS, expressed as the hazard ratio.

Results: Nine eligible studies of 3355 patients were included in the review. The OS of patients who underwent LR was significantly longer than that of patients who underwent TACE (hazard ratio = 0.52; 95% CI: 0.39–0.69; $I^2 = 79\%$). Prolonged survival following LR was confirmed after sensitivity analysis of five studies using propensity score matching (HR = 0.45; 95% CI: 0.34–0.59; $I^2 = 55\%$).

Conclusion: Patients with intermediate-stage HCC who underwent LR had a longer OS that those who underwent TACE. The role of LR in patients with BCLC stage B should be clarified in future randomised controlled trials.

Keywords: Barcelona Clinic Liver Cancer staging, hepatocellular carcinoma, intermediate-stage B, liver resection, transarterial chemoembolization

Bogdanovic A, Djokic Kovac J, Zdujic P, Djindjic U, Dugalic V. Liver resection versus transarterial chemoembolisation for the treatment of intermediate hepatocellular carcinoma: a systematic review and meta-analysis. *Int J Surg*. 2023;109:1439–1446.

Table 3

Survival outcome.

First Author	Median follow-up (months)			1-year survival (%)		3-year survival (%)		5-year survival (%)		
	Overall	LR	TACE	LR	TACE	LR	TACE	LR	TACE	*P*
Ruben Ciria[12]	28.2	nr	nr	83.3	68.2	52.8	47.7	44.4	38.6	0.229
Jun Young Kim[13]	30.0	nr	nr	92.3	78.2	65	39.2	51.8	27.9	0.002
Linbin Lu[21]	nr	67.4	18.5	85.8	76.9	68.6	52.7	63.3	46.7	< 0.0001
Jun Luo[22]	nr	nr	nr	70.6	67.2	35.3	26	23.9	18.9	0.26
Yufu Peng[23]	13	nr	nr	nr	nr	nr	nr	nr	nr	nr
Toshifumi Tada[24]	26	nr	nr	nr	nr	nr	nr	nr	nr	nr
Chih-Wen Lin[25]	nr	39.0	22	89.2	69.5	69.4	37.0	61.2	15.2	< 0.0001
Wei Xu[26]	37.6	nr	nr	86.5	73.9	53.8	45.7	33.8	28.9	0.03
Lei Yin[27]	nr	33.3	13.5	76.1	51.8	63.5	34.8	51.5	18.1	< 0.001

LR, liver resection; nr, not reported; TACE, transarterial chemoembolisation.

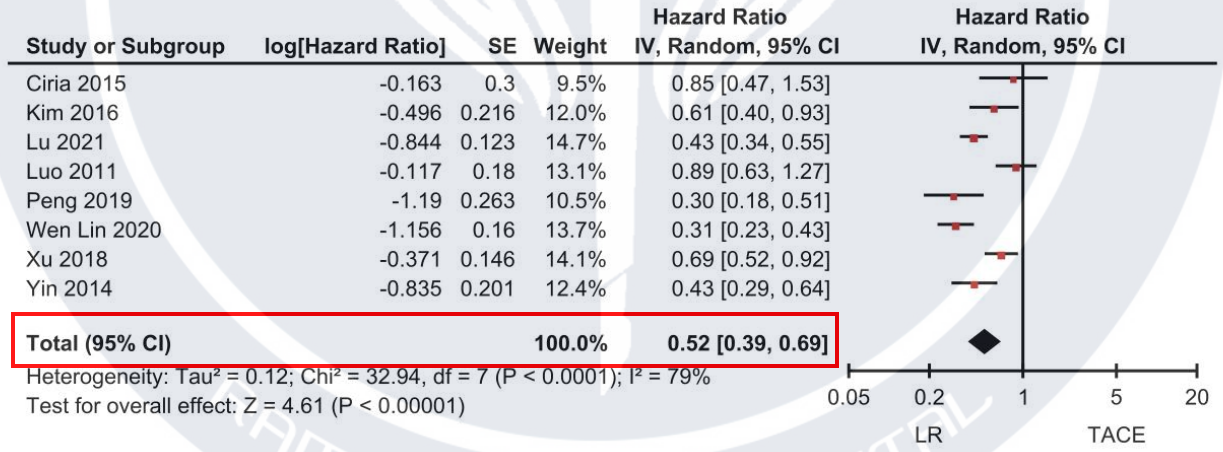


Figure 2. Overall survival according to therapeutic intervention (LR versus TACE) in patients with intermediate-stage hepatocellular carcinoma. LR, liver resection; TACE, transarterial chemoembolization.

Intermediate and advance HCC

Bogdanovic A, Djokic Kovac J, Zdujic P, Djindjic U, Dugalic V. Liver resection versus transarterial chemoembolisation for the treatment of intermediate hepatocellular carcinoma: a systematic review and meta-analysis. *Int J Surg*. 2023;109:1439–1446.

Retrospective Cohort Study

INTERNATIONAL JOURNAL OF SURGERY

OPEN

Identification of patients with favorable prognosis after resection in intermediate-stage-hepatocellular carcinoma

Han Ah Lee, MD, PhD[a,b,c], Minjong Lee, MD, PhD[a,b,c,*], Jeong-Ju Yoo, MD, PhD[g], Ho Soo Chun, MD, PhD[a,b], Yewan Park, MD[e], Hwi Young Kim, MD, PhD[a,b], Tae Hun Kim, MD, PhD[a,b], Yeon Seok Seo, MD, PhD[f], Dong Hyun Sinn, MD, PhD[d,*]

Backgrounds: It is unclear which patients benefit from resection in intermediate-stage-hepatocellular carcinoma (HCC). The authors aimed to identify high-risk patients for early recurrence among patients with resectable intermediate-stage HCC.

Methods: This multicenter retrospective study included patients who underwent resection or trans-arterial chemoembolization (TACE) for intermediate-stage HCC (2008–2019). Multivariable Cox proportional analysis was performed to identify high-risk patients when treated with resection. A prediction score for 2-year recurrence-free survival (RFS) was developed using the training cohort and validated. The 2-year RFS in each risk group was compared with that in TACE group, after propensity score matching (PSM).

Results: A total of 1686 patients were included (480 and 1206 patients in the resection and TACE groups). During a median follow-up of 31.4 months, the 2-year RFS was significantly higher in the resection (47.7%) than in the TACE group (19.8%) [adjusted hazard ratio (aHR) = 1.471, 95% CI: 1.199–1.803, $P < 0.001$). On multivariate analysis, alpha-fetoprotein ≥ 5.0 ng/ml (aHR = 0.202), ALBI grade ≥ 2 (aHR = 0.709), tumor number ≥ 3 (aHR = 0.404), and maximal tumor size ≥ 5 cm (aHR = 0.323) were significantly associated with the lower risk of 2-year RFS in the resection group. The newly developed Surgery Risk score in BCLC-B (SR-B score) with four significant risk factors showed an area under the curve of 0.801 for the 2-year RFS and was validated. Based on the SR-B score, low-risk patients had a significantly higher 2-year RFS (training: aHR = 5.834; validation: aHR = 5.675) than high-risk patients (all $P < 0.001$) did. In a PSM cohort, a low-risk resection group had a significantly higher (aHR = 3.891); a high-risk resection group had a comparable 2-year RFS to those treated with TACE (aHR = 0.816).

Conclusions: Resection may be beneficial for resectable intermediate-stage HCC based on the SR-B score.

Keywords: hepatocellular carcinoma, intermediate-stage, resection, trans-arterial chemoembolization

Intermediate and advance HCC

Lee HA, Lee M, Yoo JJ, Chun HS, Park Y, Kim HY, Kim TH, Seo YS, Sinn DH. *Identification of patients with favorable prognosis after resection in intermediate-stage hepatocellular carcinoma*. **Int J Surg.** 2024;110:1008–1018.

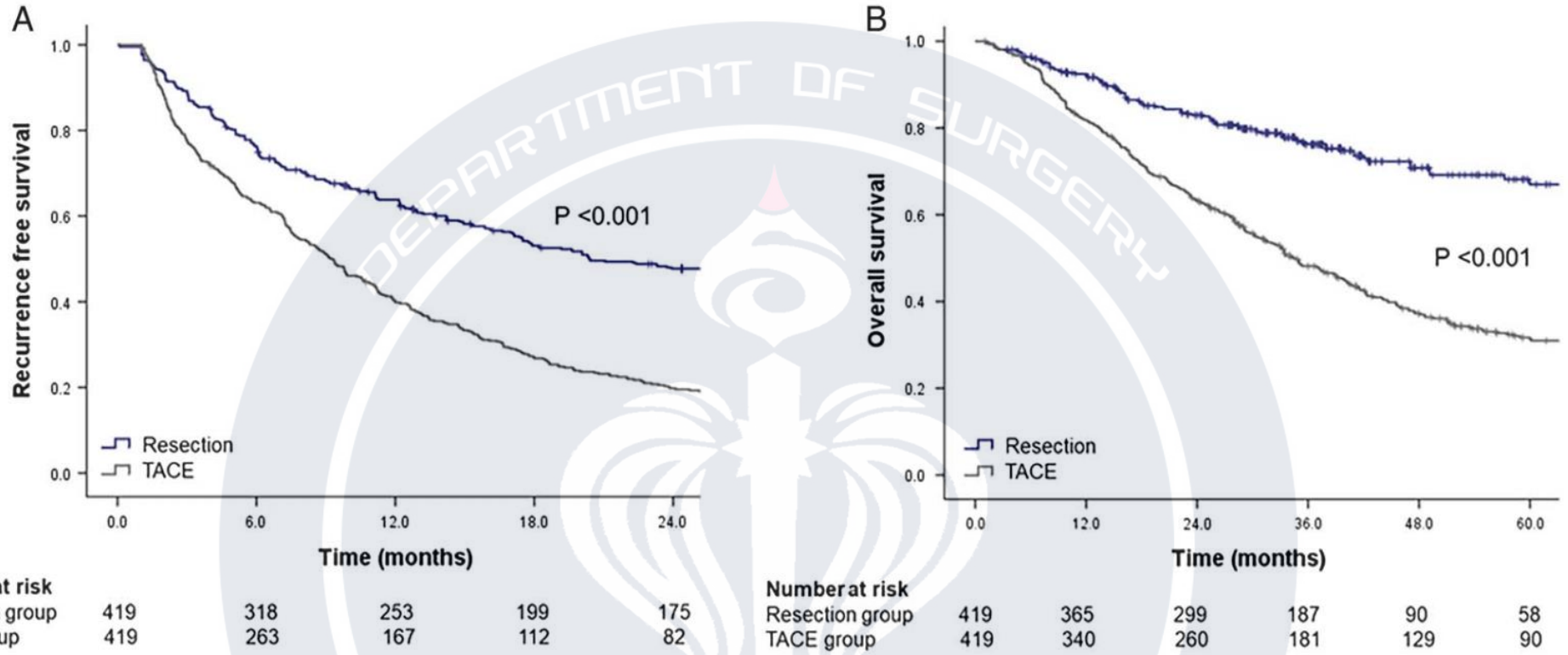


Figure 1. The survival outcomes of resection and TACE groups.The 2-year recurrence-free survival was significantly higher in the resection group than in the TACE group (A), and The 5-year overall survival was significantly higher in the resection group than in the TACE group in propensity score-matched cohorts (B). TACE, trans-arterial chemoembolization.

DFS	1-year	2-year	5-year
Resection (20.4month)	63.8	47.7	20.1
TACE (9.2month)	40.3	19.8	6.4

OS	1-year	2-year	5-year
Resection	92.5	83.0	67.0
TACE	81.8	63.2	31.7

Intermediate and advanced HCC

Lee HA, Lee M, Yoo JJ, Chun HS, Park Y, Kim HY, Kim TH, Seo YS, Sinn DH. *Identification of patients with favorable prognosis after resection in intermediate-stage hepatocellular carcinoma*. **Int J Surg.** 2024;110:1008–1018.

Table 3

Predictors for 2-year recurrence-free survival in the training cohort of the resection group.

		Univariate analysis			Multivariable analysis		
Variables	**Rating**	**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Age	years	1.006	0.992–1.022	0.398			
Sex	0 = women; 1 = men	0.981	0.647–1.489	0.929			
Diabetes	0 = no; 1 = yes	0.892	0.608–1.307	0.557			
Viral etiology	0 = other; 1 = viral	0.710	0.471–1.069	0.101			
Alanine aminotransferase	IU/l	1.001	0.999–1.004	0.283			
Platelet count	$\times 10^9$/l	1.000	0.997–1.003	0.989			
Alpha-fetoprotein	≥5.0 ng/ml	0.240	0.145–0.398	<0.001	0.202	0.121–0.336	<0.001
ALBI grade	≥2	1.488	1.053–2.101	0.024	0.709	0.511–0.983	0.039
Tumor number	≥3	0.512	0.366–0.716	<0.001	0.404	0.287–0.568	<0.001
Maximal tumor size	≥5 cm	0.372	0.270–0.512	<0.001	0.323	0.233–0.448	<0.001

ALBI, albumin-bilirubin; HR, hazard ratio; MELD, model for end-stage liver disease; TACE, trans-arterial chemoembolization.

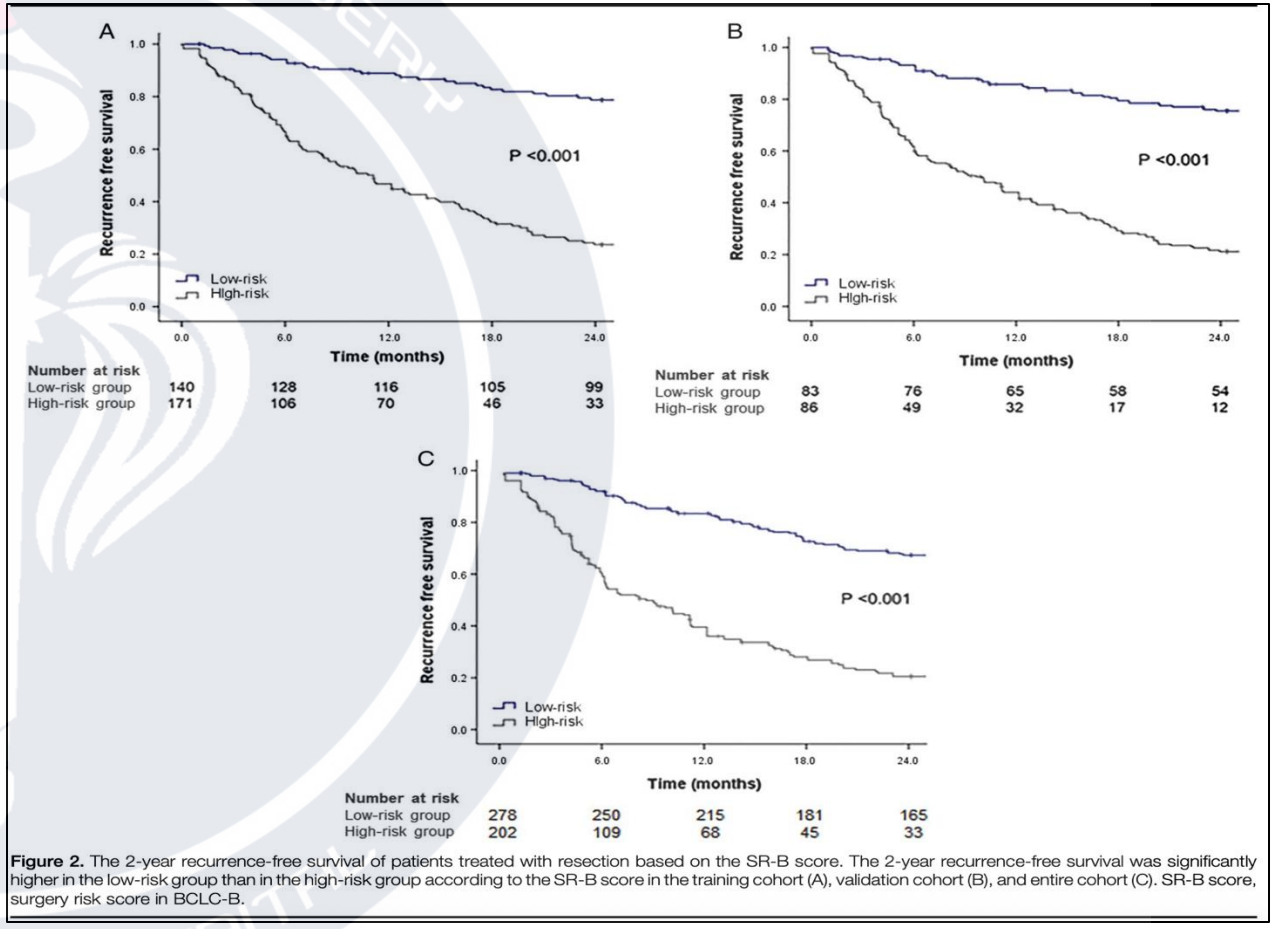


Figure 2. The 2-year recurrence-free survival of patients treated with resection based on the SR-B score. The 2-year recurrence-free survival was significantly higher in the low-risk group than in the high-risk group according to the SR-B score in the training cohort (A), validation cohort (B), and entire cohort (C). SR-B score, surgery risk score in BCLC-B.

BCLC-B (SR-Bscore) using the following formula:

- The SR-B score= 2.361 × AFP(0: <5.0 ng/ml; 1: ≥ 5.0 ng/ml)
- + 0.581 × ALBI grade (0: Grade1; 1: Grade 2 or 3)
- + 1.460 × tumor number (0: two; 1: three or more)
- + 1.624 × maximal tumor size (0: <5 cm; 1: ≥ 5 cm)
- + 1.154.

The AUC of the SR-B score for predicting 2-year RFS after resection was 0.801 (95% CI: 0.753–0.849)
Cut point >> 4.24

Intermediate and advance HCC

Lee HA, Lee M, Yoo JJ, Chun HS, Park Y, Kim HY, Kim TH, Seo YS, Sinn DH. *Identification of patients with favorable prognosis after resection in intermediate-stage hepatocellular carcinoma*. **Int J Surg.** 2024;110:1008–1018.

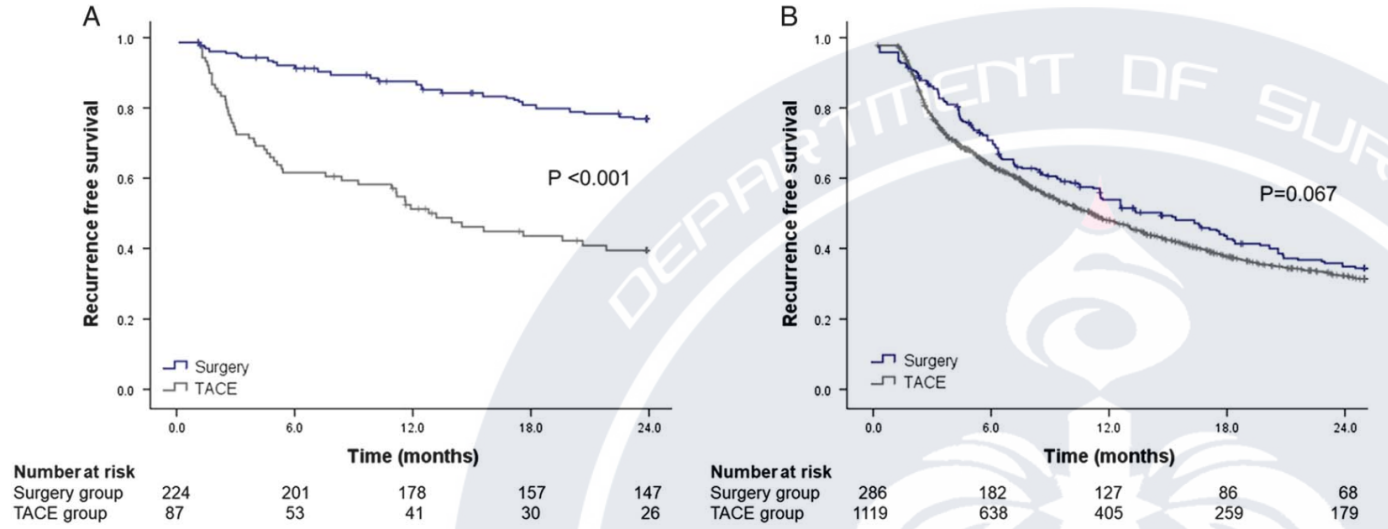


Figure 3. The 2-year recurrence-free survival of resection and TACE groups according to the risk groups classified with the SR-B score. In the low-risk group, the 2-year recurrence-free survival was significantly higher in the resection group than in the TACE group (A). In the high-risk group, the 2-year recurrence-free survival was comparable between the resection and TACE groups (B). SR-B score, surgery risk score in BCLC-B; PS, propensity score; TACE, trans-arterial chemoembolization.

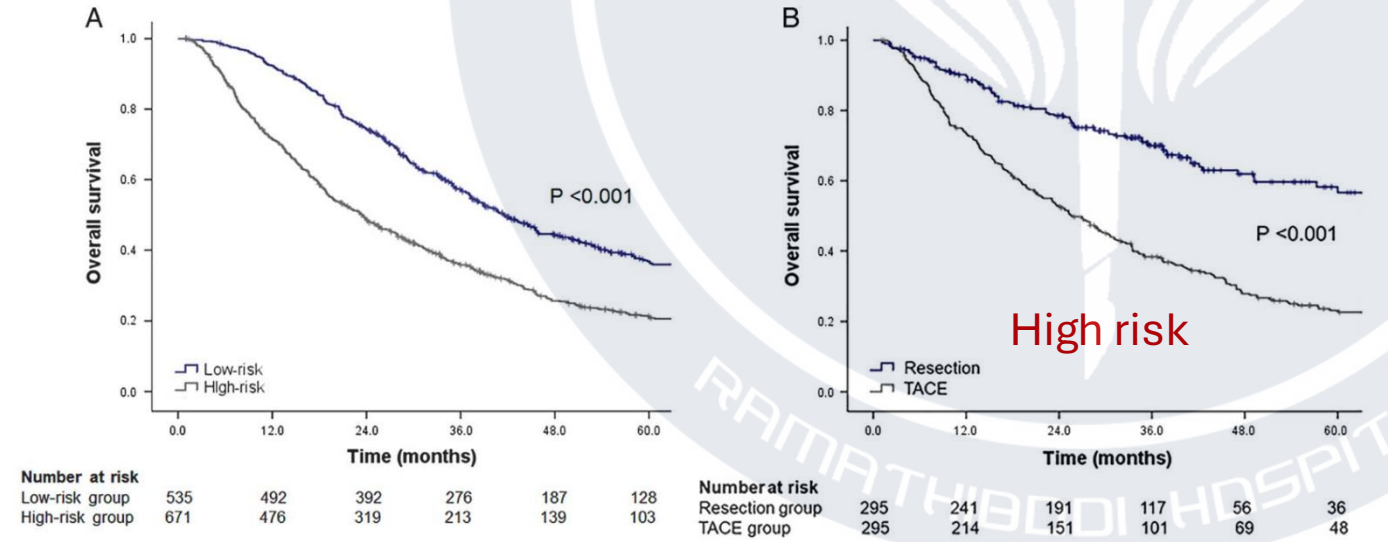


Figure 4. The 5-year overall survival of risk groups based on the HAP score. In the TACE group, the 5-year overall survival was significantly higher in the low-risk group than in the high-risk group according to the HAP score (A). The 5-year overall survival was significantly higher in the PS-matched resection group than in the high-risk TACE group according to the HAP score (B). PS, propensity score; TACE, trans-arterial chemoembolization; HAP, hepatoma arterial embolization prognostic score.

Conclusion

Resection may be beneficial for resectable intermediate-stage HCC based on the SR-B score.

(AFP ≥ 5.0 ng/ml, ALBI grade ≥ 2, Tumor number ≥ 3, Maximal tumor size ≥ 5 cm)

Lee HA, Lee M, Yoo JJ, Chun HS, Park Y, Kim HY, Kim TH, Seo YS, Sinn DH. *Identification of patients with favorable prognosis among Barcelona Clinic Liver Cancer intermediate-stage hepatocellular carcinoma.* **Int J Surg.** 2024;110:1008–1018.

Article

Surgical Resection plus Intraoperative Radiofrequency Ablation versus Chemoembolization for the Treatment of Intermediate-Stage (BCLC B) Hepatocellular Carcinoma with Preserved Liver Function: A Propensity Score-Matched Analysis

Gun Ha Kim [1], Jin Hyoung Kim [1,*], Heung Kyu Ko [1,*], Hee Ho Chu [1], Seong Ho Kim [1], Ji Hoon Shin [1], Dong Il Gwon [1], Gi-Young Ko [1], Hyun-Ki Yoon [1], Ki-Hun Kim [2], Ju Hyun Shim [3] and Nayoung Kim [4]

[1] Department of Radiology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea; kimgh.rad@amc.seoul.kr (G.H.K.); angiochu@amc.seoul.kr (H.H.C.); evazzang23@amc.seoul.kr (S.H.K.); jhshin@amc.seoul.kr (J.H.S.); radgwon@amc.seoul.kr (D.I.G.); kogy@amc.seoul.kr (G.-Y.K.); hkyoon@amc.seoul.kr (H.-K.Y.)
[2] Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea; khkim620@amc.seoul.kr
[3] Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea; s5854@amc.seoul.kr
[4] Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea; nyny0803@amc.seoul.kr
* Correspondence: jhkimrad@amc.seoul.kr (J.H.K.); hk.ko@amc.seoul.kr (H.K.K.); Tel.: +82-2-3010-4384 (J.H.K.); +82-2-3010-3974 (H.K.K.); Fax: +82-2-476-0090 (J.H.K.); +82-2-3010-6645 (H.K.K.)

check for updates

Citation: Kim, G.H.; Kim, J.H.; Ko, H.K.; Chu, H.H.; Kim, S.H.; Shin, J.H.; Gwon, D.I.; Ko, G.-Y.; Yoon, H.-K.; Kim, K.-H.; et al. Surgical Resection plus Intraoperative Radiofrequency Ablation versus Chemoembolization for the Treatment of Intermediate-Stage (BCLC B) Hepatocellular Carcinoma with Preserved Liver Function: A Propensity Score-Matched Analysis. *Cancers* **2022**, *14*, 2440. https://doi.org/10.3390/cancers14102440

Academic Editor: Dimitrios Moris

Received: 28 April 2022
Accepted: 13 May 2022
Published: 15 May 2022

Simple Summary: Surgical resection plus intraoperative radiofrequency ablation showed better survival outcomes than transarterial chemoembolization in selected patients with intermediate-stage hepatocellular carcinoma and Child–Pugh class A liver function. These findings suggest that surgical resection plus intraoperative radiofrequency ablation may provide an opportunity for curative treatment to selected patients deemed eligible only for palliative treatment.

Abstract: The purpose of this study was to compare the efficacy and safety of surgical resection (SR) plus intraoperative radiofrequency ablation (IORFA) with transarterial chemoembolization (TACE) in patients with intermediate-stage HCC and Child–Pugh class A liver function. Treatment-naïve patients who received SR plus IORFA (n = 104) or TACE (n = 513) were retrospectively evaluated. Patients were subjected to a maximum 1:3 propensity score matching (PSM), yielding 95 patients who underwent SR plus IORFA and 252 who underwent TACE. Evaluation of the entire study population showed that progression-free survival (PFS) and overall survival (OS) were significantly better in the SR plus IORFA than in the TACE group. After PSM, the median PFS (18.4 vs. 15.3 months) and OS (88.6 vs. 56.2 months) were significantly longer, and OS rate significantly higher (HR: 0.65, p = 0.026), in the SR plus IORFA group than in the TACE group. Stratified Cox regression analysis and doubly robust estimation revealed that treatment type was significantly associated with both OS and PFS. Rates of major complications were similar in the SR plus IORFA and TACE groups. In conclusion, SR plus IORFA showed better survival outcomes than TACE. SR plus IORFA may provide curative treatment to patients with intermediate-stage HCC with ≤4 tumors and Child–Pugh class A.

Intermediate and advance HCC

Kim GH, Kim JH, Ko HK, Chu HH, Kim SH, Shin JH, Gwon DI, Ko GY, Yoon HK, Kim KH, Shim JH, Kim N. Surgical resection plus intraoperative radiofrequency ablation versus chemoembolization for the treatment of intermediate-stage (BCLC B) hepatocellular carcinoma with preserved liver function: a propensity score-matched analysis. *Cancers (Basel)*. 2022 May 15;14(10):2440.

SR plus IORFA in patients with BCLC B HCC and preserved liver function include

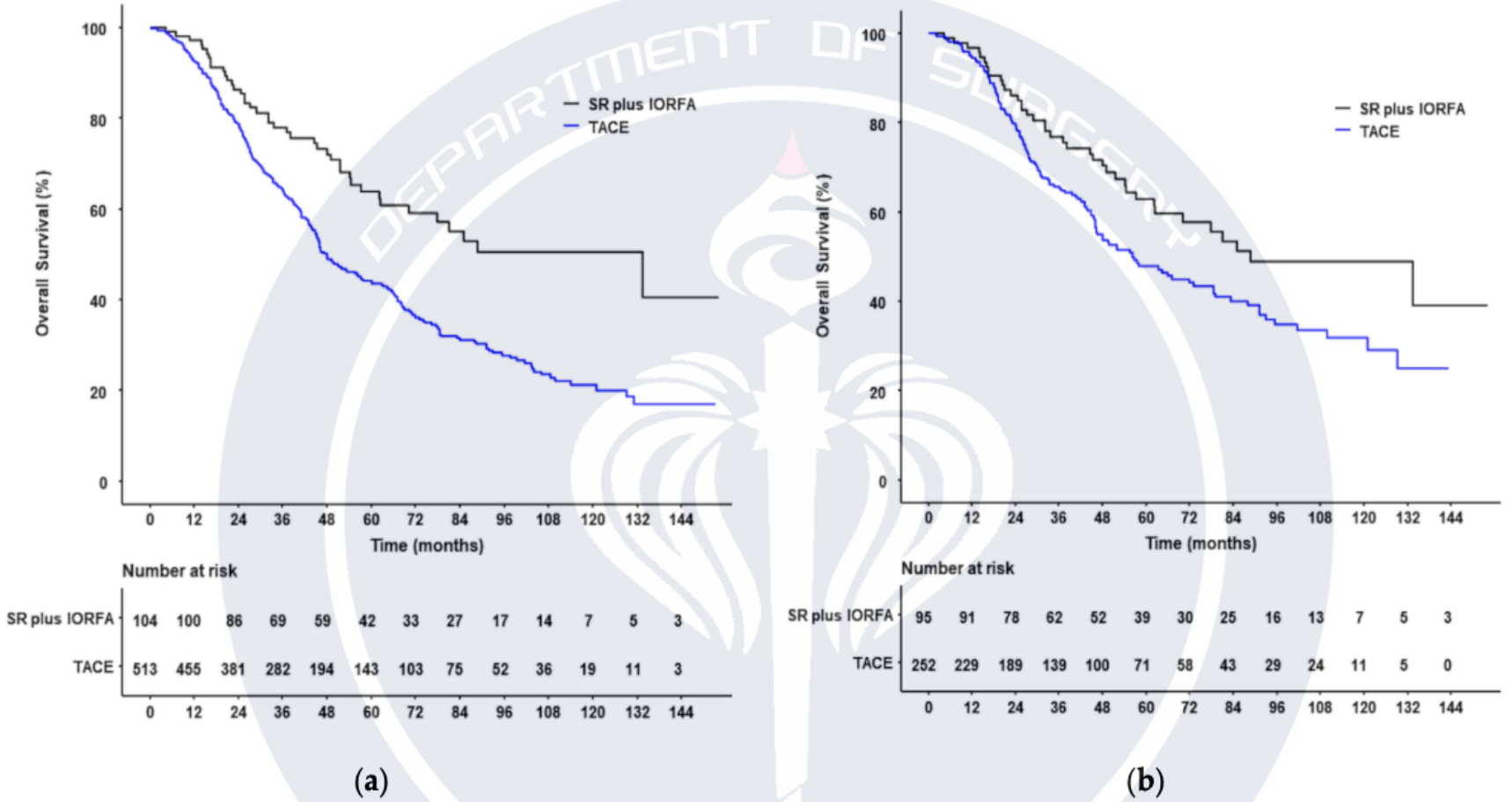
- A completely resectable main HCC
- ≤3 remnant HCC nodules, each ≤3 cm in maximum diameter
- If SR alone had a high risk of insufficient FLR or was impossible due to unfavorable tumor locations

Both group HCC ≤ 4 nodule

Table 1. Demographic and clinical characteristics of patients before and after propensity score matching.

Variables	Before PSM			After PSM		
	SR plus IORFA	TACE	SMD	SR plus IORFA	TACE	SMD
No. of patients	104	513		95	252	
Age > 60 years, *n* (%)	43 (41.3%)	265 (51.7%)	0.208	40 (42.1%)	112 (44.4%)	0.047
Male sex, *n* (%)	90 (86.5%)	443 (86.4%)	0.005	81 (85.3%)	226 (89.7%)	0.134
Etiology			0.143			0.067
HBV	74 (71.2%)	373 (72.7%)		70 (73.7%)	191 (75.8%)	
HCV	8 (7.7%)	61 (11.9%)		8 (8.4%)	21 (8.3%)	
Alcohol	8 (7.7%)	46 (9.0%)		8 (8.4%)	17 (6.7%)	
Others	14 (13.5%)	33 (6.4%)		9 (9.5%)	23 (9.1%)	
Maximal tumor size > 5 cm, *n* (%)	44 (42.3%)	183 (35.7%)	0.136	38 (40.0%)	98 (38.9%)	0.023
Tumor number > 2, *n* (%)	35 (33.7%)	238 (46.4%)	0.262	33 (34.7%)	101 (40.1%)	0.111
Bilobar tumor extent, *n* (%)	65 (62.5%)	210 (40.9%)	0.442	56 (58.9%)	133 (52.8%)	0.124
Bilirubin > 0.9 mg/dL, *n* (%)	25 (24.0%)	154 (30.0%)	0.135	25 (26.3%)	66 (26.2%)	0.003
Albumin ≤ 3.5 mg/dL, *n* (%)	19 (18.3%)	170 (33.1%)	0.345	19 (20.0%)	55 (21.8%)	0.045
Portal hypertension, *n* (%)	9 (8.7%)	104 (20.3%)	0.335	9 (9.5%)	32 (12.7%)	0.103
AFP ≥ 200 ng/mL, *n* (%)	25 (24.0%)	155 (30.2%)	0.139	25 (26.3%)	54 (21.4%)	0.115

Kim GH, Kim JH, Ko HK, Chu HH, Kim SH, Shin JH, Gwon DI, Ko GY, Yoon HK, Kim KH, Shim JH, Kim N. Surgical resection plus intraoperative radiofrequency ablation versus chemoembolization for the treatment of intermediate-stage (BCLC B) hepatocellular carcinoma with preserved liver function: a propensity score-matched analysis. *Cancers (Basel)*. 2022 May 15;14(10):2440.



OS	1-year	3-year	5-year	10-year
Resection+ IORFA	97.1	77.9	63.8	50.6
TACE	92.4	64.1	21.3	21.3

Intermediate and advance HCC

Figure 2. Kaplan–Meier analyses of overall survival (OS) in patients who underwent SR plus IORFA or TACE before (**a**) and after (**b**) PSM. (**a**,**b**) OS rates were significantly higher in patients who underwent SR plus IORFA than in those who underwent TACE both (**a**) before PSM (HR: 0.52 (95% CI, 0.37–0.71), $p < 0.001$) and (**b**) after PSM (HR: 0.65 (95% CI, 0.44–0.95), $p = 0.026$).

Kim GH, Kim JH, Ko HK, Chu HH, Kim SH, Shin JH, Gwon DI, Ko GY, Yoon HK, Kim KH, Shim JH, Kim N. Surgical resection plus intraoperative radiofrequency ablation versus chemoembolization for the treatment of intermediate-stage (BCLC B) hepatocellular carcinoma with preserved liver function: a propensity score-matched analysis. *Cancers (Basel)*. 2022 May 15;14(10):2440.

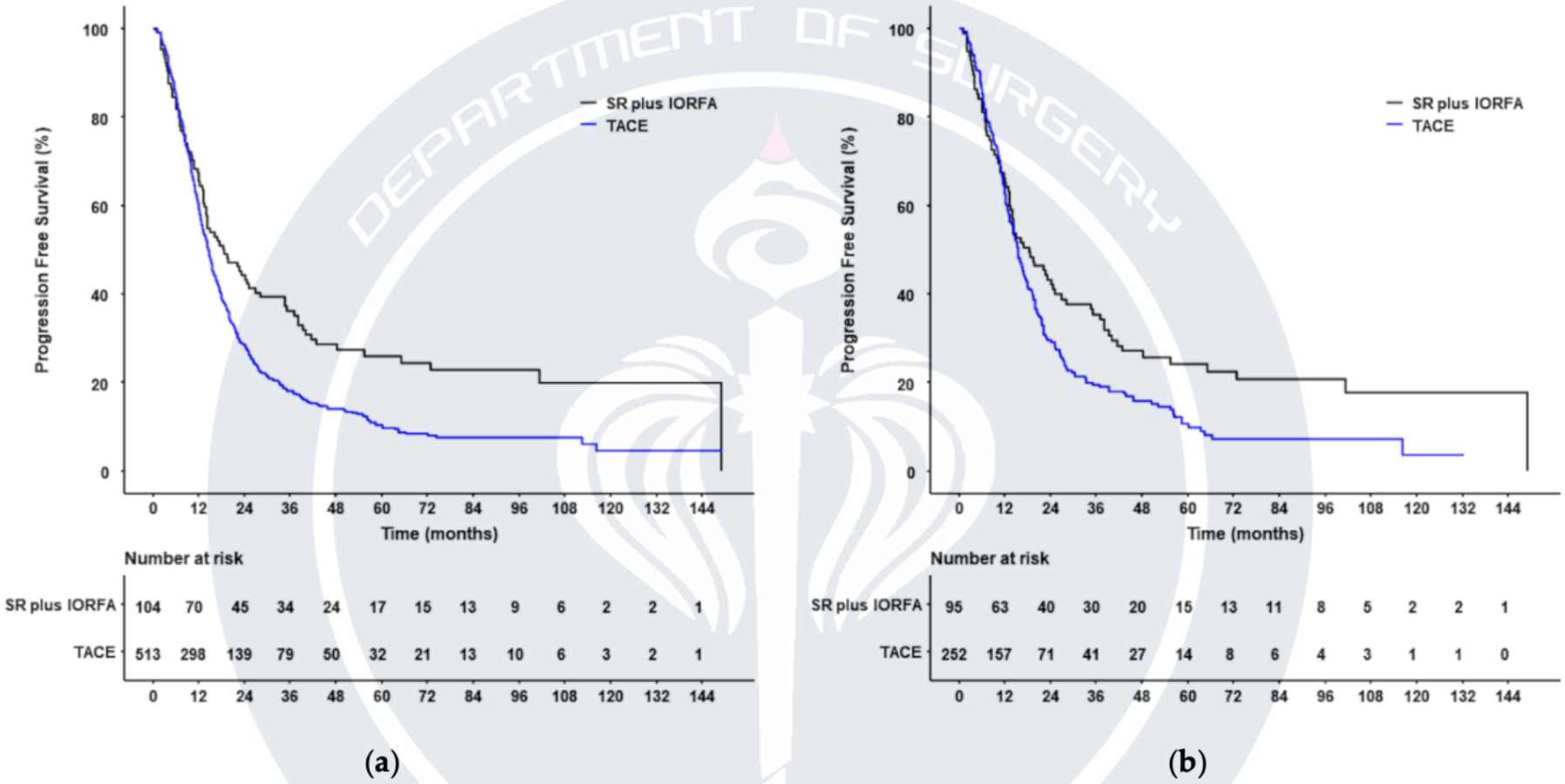


Figure 4. Kaplan–Meier analyses of progression-free survival (PFS) in patients who underwent SR plus IORFA or TACE before (**a**) and after (**b**) PSM. (**a**,**b**) PFS rates were significantly higher in patients who underwent SR plus IORFA group than in those who underwent TACE both (**a**) before PSM (HR: 0.67 (95% CI, 0.52–0.85), $p < 0.001$) and (**b**) after PSM (HR: 0.72 (95% CI, 0.54–0.96), $p = 0.023$).

PFS	1-year	3-year	5-year	10-year
Resection+ IORFA	65.4	36.1	25.9	19.1
TACE	59.1	18.1	9.8	4.6

Intermediate and advance HCC

Kim GH, Kim JH, Ko HK, Chu HH, Kim SH, Shin JH, Gwon DI, Ko GY, Yoon HK, Kim KH, Shim JH, Kim N. Surgical resection plus intraoperative radiofrequency ablation versus chemoembolization for the treatment of intermediate-stage (BCLC B) hepatocellular carcinoma with preserved liver function: a propensity score-matched analysis. *Cancers (Basel)*. 2022 May 15;14(10):2440.

Long-term outcomes and salvageability in patients undergoing liver resection for intermediate- and advanced-stage hepatocellular carcinoma

Tomoaki Yoh, MD, PhD*, Takamichi Ishii, MD, PhD, Satoshi Ogiso, MD, PhD, Hiroto Nishino, MD, PhD, Takahiro Nishio, MD, PhD, Yukinori Koyama, MD, PhD, Yoichiro Uchida, MD, PhD, Takashi Ito, MD, PhD, Etsuro Hatano, MD, PhD

Department of Surgery, Graduate School of Medicine, Kyoto University, Japan

ARTICLE INFO

Article history:
Accepted 18 June 2023
Available online 24 July 2023

ABSTRACT

Backgrounds: The prognosis of intermediate- and advanced-stage hepatocellular carcinoma after liver resection should be comprehensively analyzed due to the high incidence of tumor recurrence and the availability of salvage therapy. This study evaluated the long-term outcome and salvageability in these patients after liver resection.

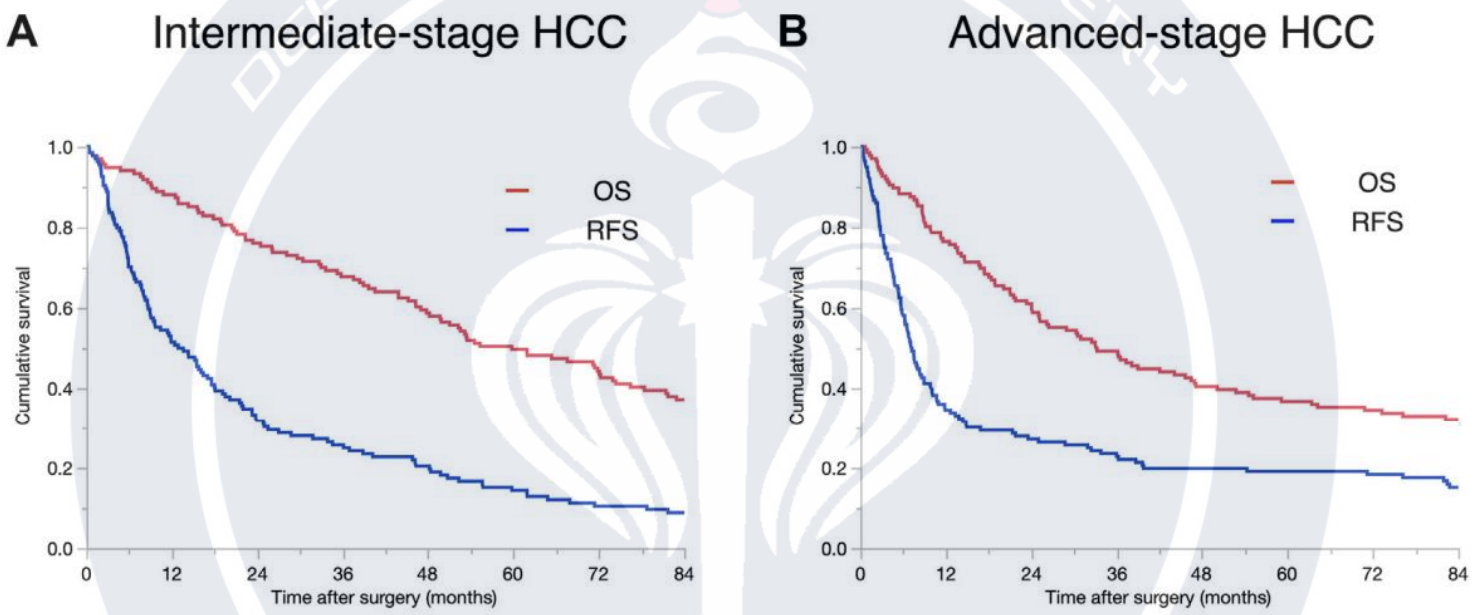
Methods: Data from consecutive patients with intermediate- and advanced-stage hepatocellular carcinoma who underwent initial liver resection from 2000 to 2016 were retrospectively reviewed. Analyses were performed in the setting of the initial liver resection and the recurrence(s). Active salvage therapy for recurrence was defined as the implementation of each therapy with curative intent—repeat surgery, ablative therapy, and liver transplantation.

Results: Among the 1,013 liver resections for hepatocellular carcinoma, a total of 270 patients were eligible for this study (intermediate hepatocellular carcinoma, $n = 134$; advanced hepatocellular carcinoma, $n = 136$). The 5-year overall survival rates for intermediate and advanced-stage hepatocellular carcinoma were 49.7% and 36.8%, respectively; meanwhile, the actual recurrence rates excluding patients who died without recurrence were 94.7% and 90.7%, respectively. Active salvage therapy was performed in 43 (39.8%) patients with intermediate-stage hepatocellular carcinoma and 25 (23.4%) patients with advanced-stage hepatocellular carcinoma. Overall survival after initial liver resection, first active salvage therapy, and second/more active salvage therapy were comparable in both stages.

Conclusions: This study suggests that although liver resection alone may not yield remission in most patients with intermediate and advanced-stage hepatocellular carcinoma, active salvage therapy can potentially prolong survival. Further study to identify approaches to decrease recurrence rates and increase salvageability for these patients would be warranted.

Intermediate and advance HCC

Yoh T, Ishii T, Ogiso S, Nishino H, Nishio T, Koyama Y, Uchida Y, Ito T, Hatano E. Long-term outcomes and salvageability in patients undergoing liver resection for intermediate- and advanced-stage hepatocellular carcinoma. **Surgery.** 2023;174(4):858–864.



No at risk	N	1 year	3 years	5 years
OS	136	104	67	50
RFS	136	47	31	26

No at risk	N	1 year	3 years	5 years
OS	134	118	90	65
RFS	134	69	34	19

Figure 1. Overall survival, and recurrence-free survival, in (A) intermediate- and (B) advanced-stage hepatocellular carcinoma. *HCC*, hepatocellular carcinoma; *OS*, overall survival; *RFS*, recurrence-free survival.

Intermediate and advance HCC

Yoh T, Ishii T, Ogiso S, Nishino H, Nishio T, Koyama Y, Uchida Y, Ito T, Hatano E. Long-term outcomes and salvageability in patients undergoing liver resection for intermediate- and advanced-stage hepatocellular carcinoma. **Surgery.** 2023;174(4):858–864.

Conclusion

- **Patient selection:**
  - Good performance status
  - Preserved liver function
- **Treatment outcomes:**
  - **Liver resection (LR)** → superior to **TACE**
  - Better **overall survival (OS)** and **disease-free survival (DFS)**
- **Careful selection needed**
- High-risk features:
  - Elevated **AFP**
  - **ALBI grade ≥2**
  - **≥3 tumors**
  - **Tumor size >5 cm**

Japan Society of hepatology(2021)

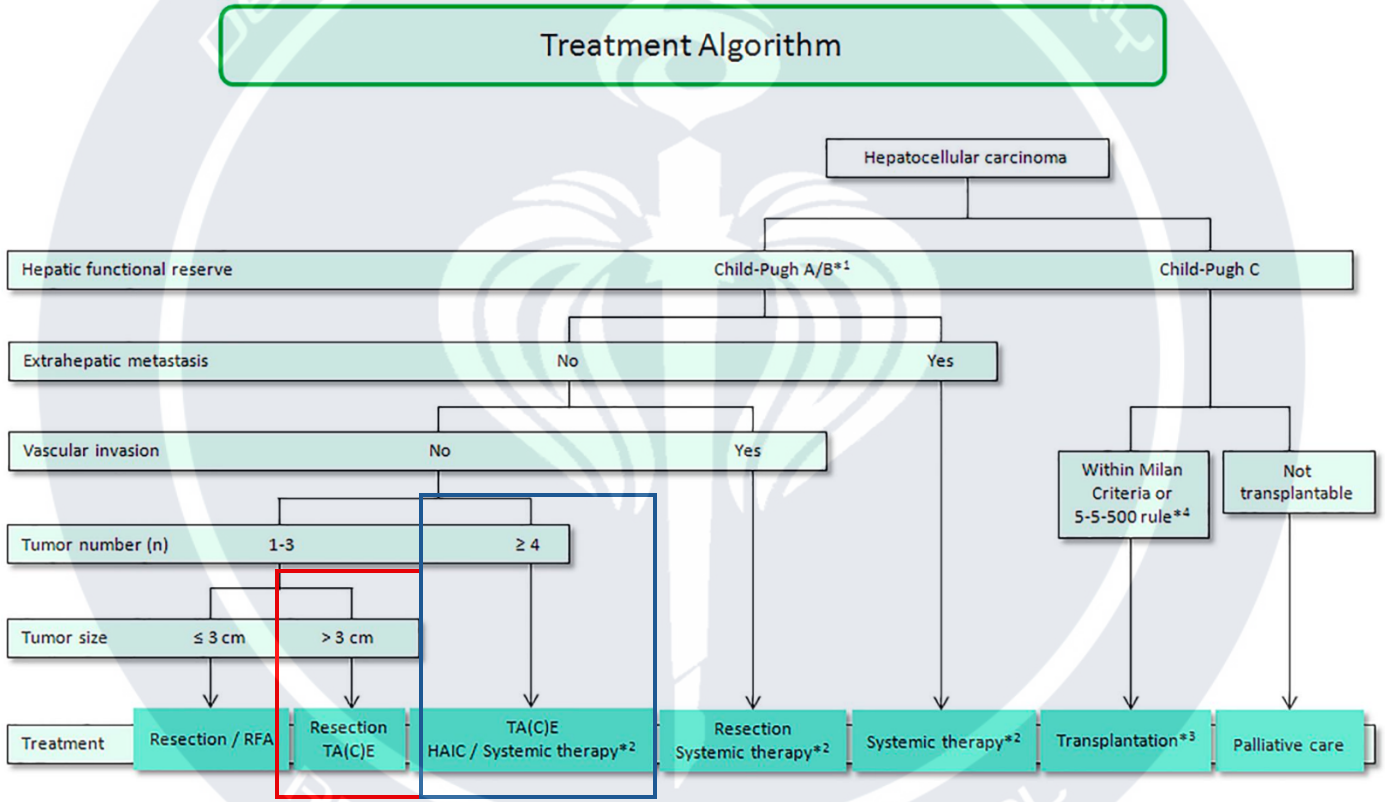


FIGURE 3 Algorithm for treatment. For the treatment modalities of the upper and lower layers, the upper layer should be prioritized. Treatment modalities separated by slashes are equally recommended. *[1]Assessment based on liver damage is recommended in the case of hepatectomy. *[2]Patients with Child–Pugh A only. *[3]Patients age ≤65 years. *[4]Tumor diameter ≤5 cm, ≤5 tumors and alpha-fetoprotein ≤500 ng/mL, with no distant metastasis or vascular invasion. HAIC, hepatic arterial infusion chemotherapy; RFA, radiofrequency ablation; TA (C)E, transcatheter arterial (chemo)embolization.

Hasegawa K, Takemura N, Yamashita T, Watadani T, Kaibori M, Kubo S, et al. Clinical practice guidelines for hepatocellular carcinoma: The Japan Society of Hepatology 2021 version (5th JSH-HCC guidelines). *Hepatol Res*. 2023;53(5):383-390.

Intermediate and advance HCC

HongKong Liver Cancer Stanging System

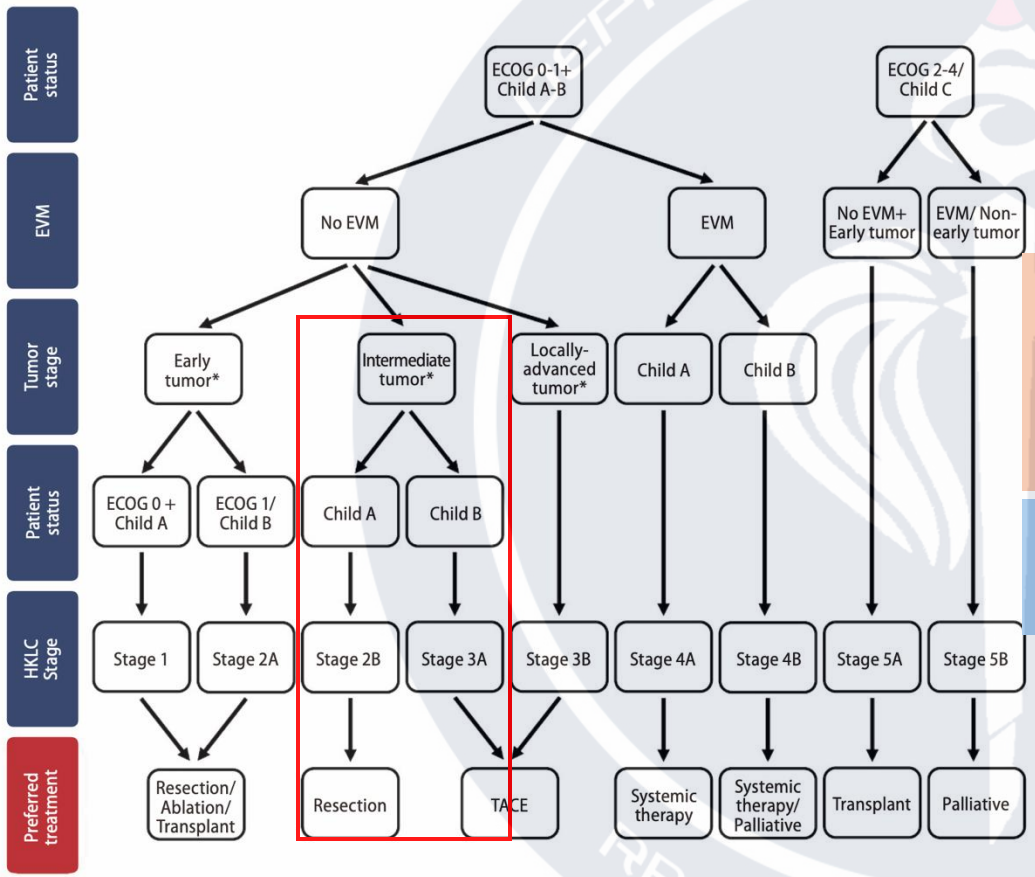


Figure 2. Staging and preferred treatment in the Hong Kong Liver Cancer Staging System. ECOG, Eastern Cooperative Oncology Group; EVM, extrahepatic vascular invasion or metastasis; TACE, transarterial chemoembolization; HKLC, Hong Kong Liver Cancer. *Early tumor: ≤5 cm+≤3 tumor nodules+No intrahepatic venous invasion; Intermediate tumor: ≤5 cm+>3 tumor nodules/Intrahepatic venous invasion OR >5 cm+≤3 tumor nodules+No intrahepatic venous invasion; Locally-advanced tumor: ≤5 cm+>3 tumor nodules+intrahepatic venous invasion OR >5 cm+>3 tumor nodules+intrahepatic venous invasion OR diffuse tumor.

Hong Kong Consensus recommends liver resection as the first-line treatment for HCC with solitary lesion or with several lesions limited to segment(s) with resectable potential, given satisfactory liver function reserve.

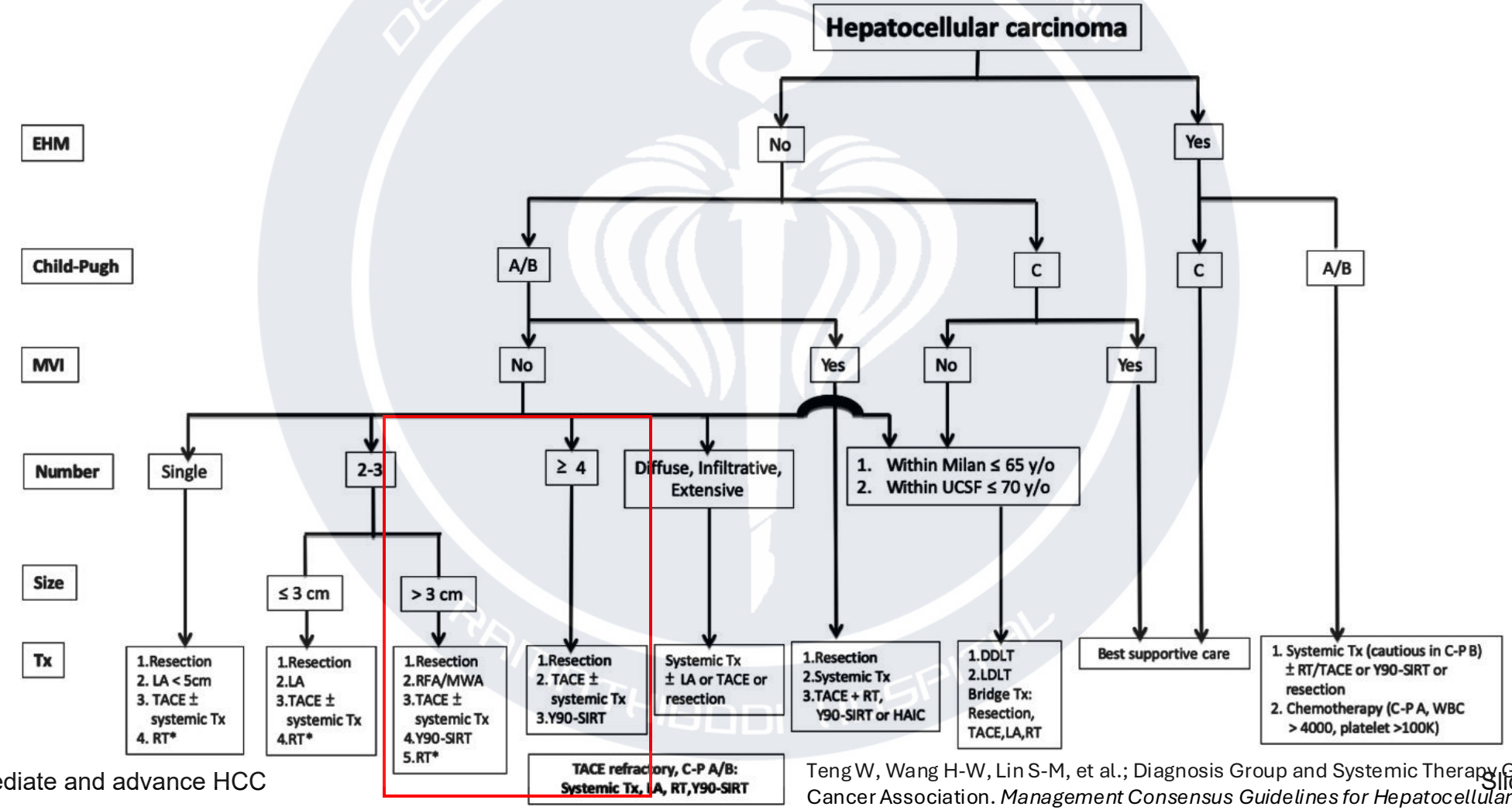
Inadequate future liver remnant

- PVE or ALPPS

Intermediate and advance HCC

Hui RWH, Mak LY, Cheung TT, Lee VHF, Seto WK, Yuen MF. Clinical practice guidelines and real-life practice in hepatocellular carcinoma: A Hong Kong perspective. *Clin Mol Hepatol.* 2023;29(2):217-229

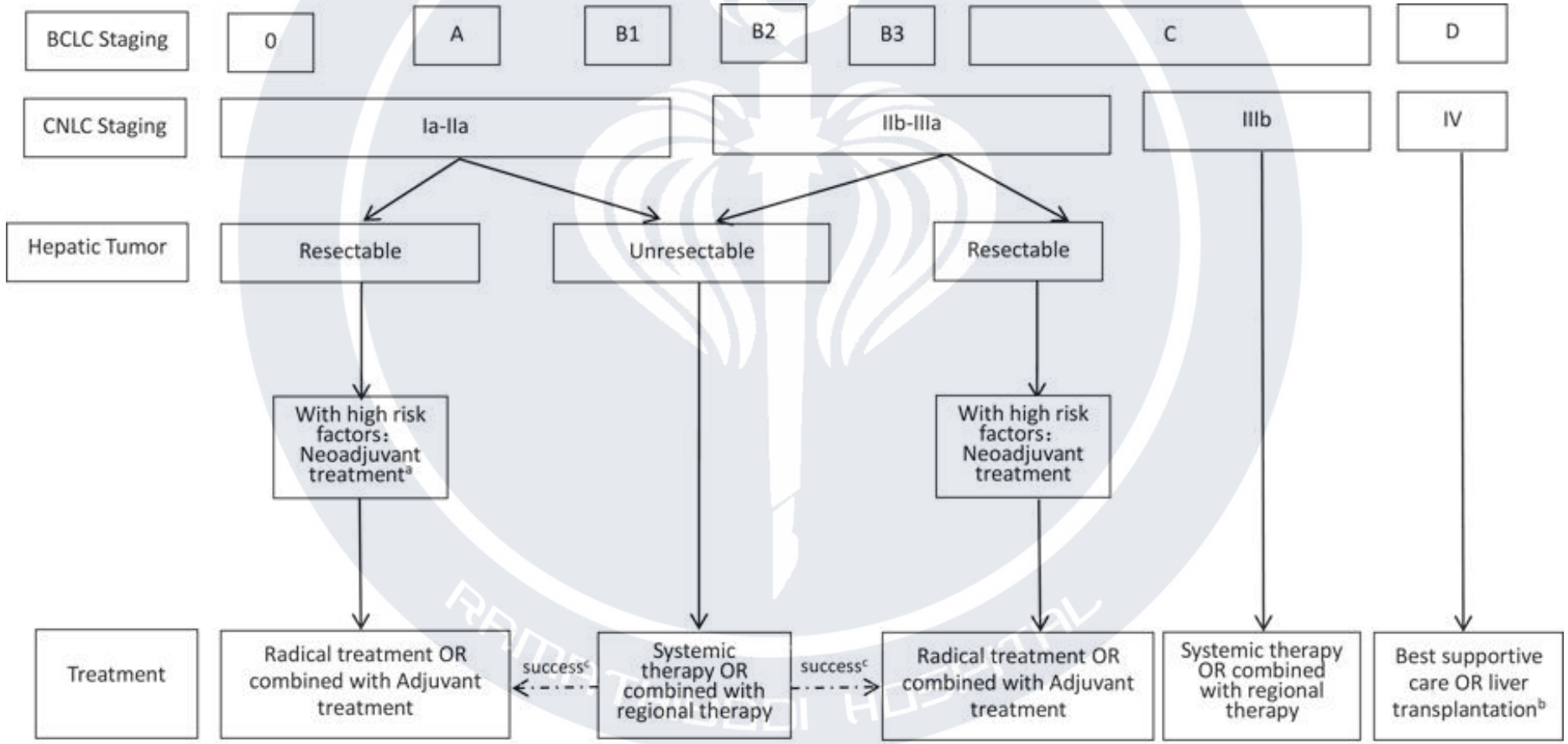
Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan(2016)



Intermediate and advance HCC

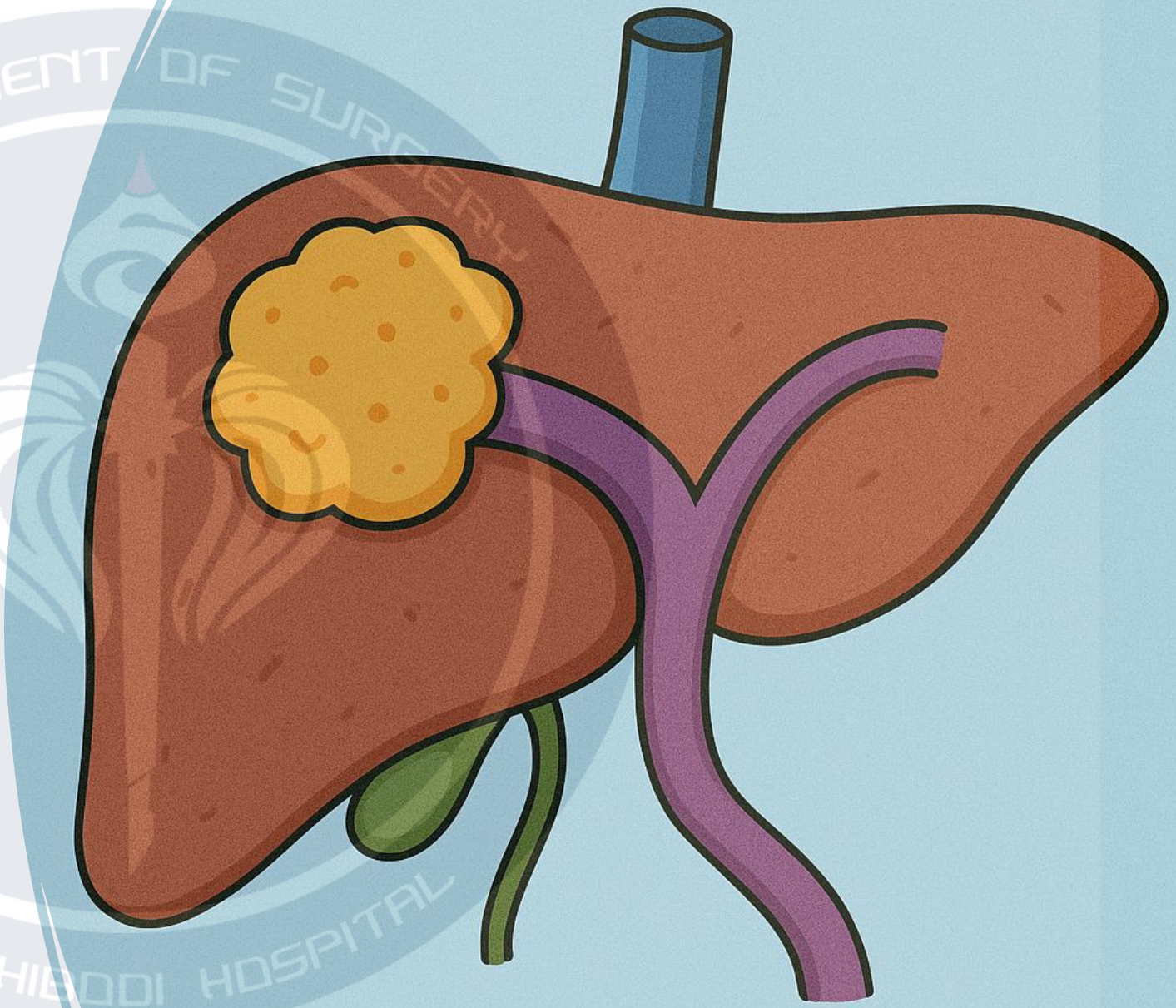
Teng W, Wang H-W, Lin S-M, et al.; Diagnosis Group and Systemic Therapy Group of the Taiwan Liver Cancer Association. *Management Consensus Guidelines for Hepatocellular Carcinoma: 2023 Update on Surveillance, Diagnosis, Systemic Treatment, and Posttreatment Monitoring*. Liver Cancer. 2024

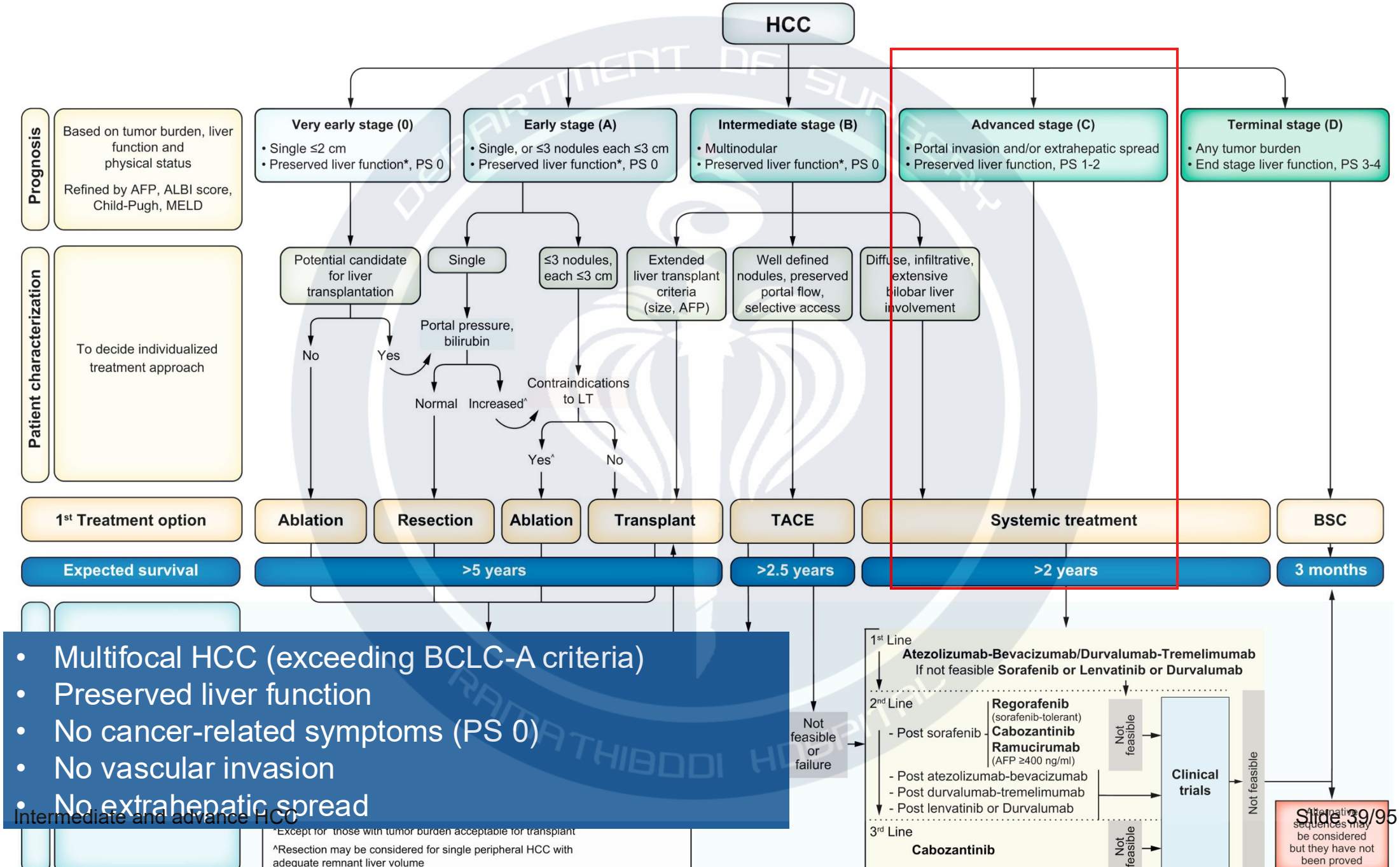
Chinese Expert Consensus on the Whole-Course Management of Hepatocellular Carcinoma (2023 Edition)



[a]Still being studied; [b]Patients who meet the criteria for liver transplantation: Milan standard /UCSF standard/Other standard; [c]Successful conversion

Advance stage HCC





- Multifocal HCC (exceeding BCLC-A criteria)
- Preserved liver function
- No cancer-related symptoms (PS 0)
- No vascular invasion
- No extrahepatic spread

PVTT Classification

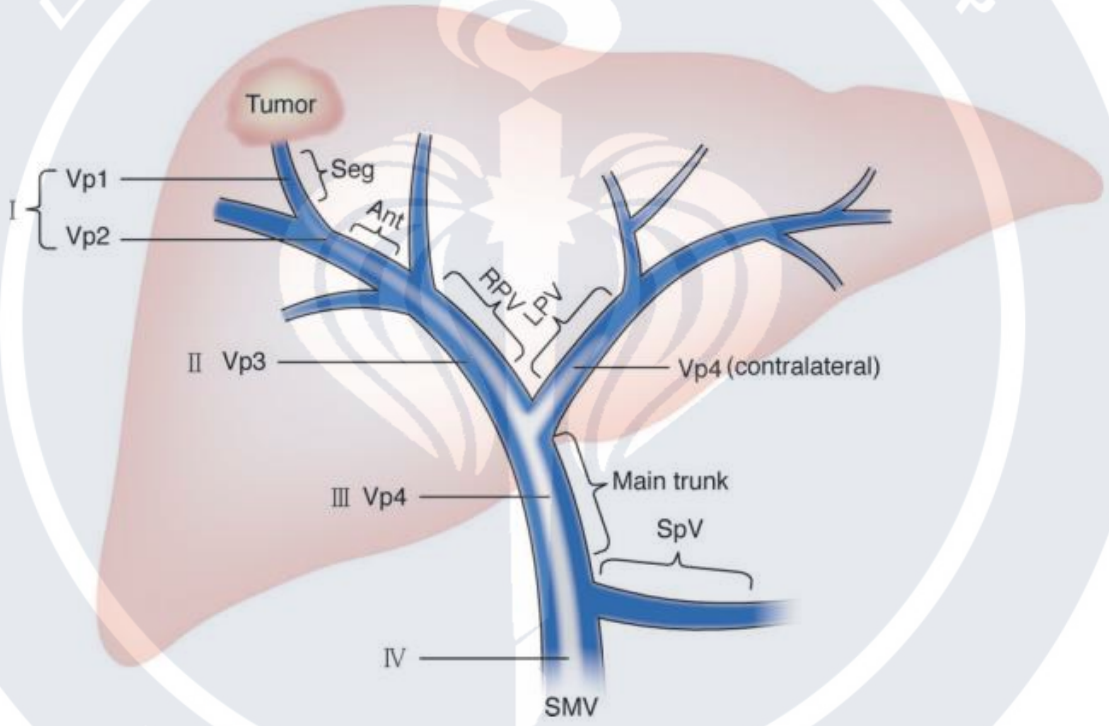


Fig. 1. Classification of hepatocellular carcinoma with portal vein tumor thrombus. Vp and Roman numerals express Japan's VP classification and Cheng's classification, respectively. Vp4, Vp3, Vp2 and Vp1 are categorized as an extension to the main trunk/contralateral branch, first-order branch, second-order branch, and third-order branch, respectively. Abbreviations: Ant, anterior branch; LHV, left portal vein; RPV, right portal vein; Seg, segmental branch; SMV, superior mesenteric vein; SpV, splenic vein.

Survival benefit of liver resection for hepatocellular carcinoma associated with portal vein invasion

Takashi Kokudo[1,2], Kiyoshi Hasegawa[1], Yutaka Matsuyama[3], Tadatoshi Takayama[4], Namiki Izumi[5], Masumi Kadoya[6], Masatoshi Kudo[7], Yonson Ku[8], Michiie Sakamoto[9], Osamu Nakashima[10], Shuichi Kaneko[11], Norihiro Kokudo[1,*], for the Liver Cancer Study Group of Japan

[1]*Hepato-Biliary-Pancreatic Surgery Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, Japan;* [2]*Division of Gastroenterological Surgery, Saitama Cancer Center, Japan;* [3]*Department of Biostatistics, School of Public Health, The University of Tokyo, Japan;* [4]*Department of Digestive Surgery, Nihon University School of Medicine, Japan;* [5]*Department of Gastroenterology, Musashino Red Cross Hospital, Japan;* [6]*Department of Radiology, Shinshu University School of Medicine, Japan;* [7]*Department of Gastroenterology and Hepatology, Kinki University School of Medicine, Japan;* [8]*Division of Hepato-Biliary-Pancreatic Surgery, Department of Surgery, Kobe University Graduate School of Medicine, Japan;* [9]*Department of Pathology, Keio University School of Medicine, Japan;* [10]*Department of Clinical Laboratory Medicine, Kurume University Hospital, Japan;* [11]*Department of Gastroenterology, Kanazawa University Hospital, Japan*

Background & Aims: The presence of portal vein tumor thrombosis (PVTT) in patients with hepatocellular carcinoma (HCC) is regarded as indicating an advanced stage, and liver resection (LR) is not recommended. The aim of this study was to evaluate the survival benefit of LR for HCC patients with PVTT through the analysis of the data from a Japanese nationwide survey.

Methods: We analyzed data for 6474 HCC patients with PVTT registered between 2000 and 2007. Of these patients, 2093 patients who underwent LR and 4381 patients who received other treatments were compared. The propensity scores were calculated and we successfully matched 1058 patients (66.1% of the LR group).

Results: In the Child-Pugh A patients, the median survival time (MST) in the LR group was 1.77 years longer than that in the non-LR group (2.87 years *vs.* 1.10 years; p <0.001) and 0.88 years longer than that in the non-LR group (2.45 years *vs.* 1.57 years; p <0.001) in a propensity score-matched cohort. A subgroup analysis revealed that LR provides a survival benefit regardless of age, etiology of HCC, tumor marker elevation, and tumor number. The survival benefit was not statistically significant only in patients with PVTT invading the main trunk or contralateral branch. In the LR group, the postoperative 90-day mortality rate was 3.7% (68 patients).

Conclusions: As long as the PVTT is limited to the first-order branch, LR is associated with a longer survival outcome than non-surgical treatment.

Lay summary: The presence of portal vein tumor thrombosis in patients with hepatocellular carcinoma is regarded as indicating an advanced stage, and liver resection is not recommended. We performed a multicenter, nationwide study to assess the survival benefit of liver resection in hepatocellular carcinoma patients with portal vein tumor thrombosis using propensity score-based matching. As long as the portal vein tumor thrombosis is limited to the first-order branch, liver resection is associated with a longer survival outcome than non-surgical treatment.

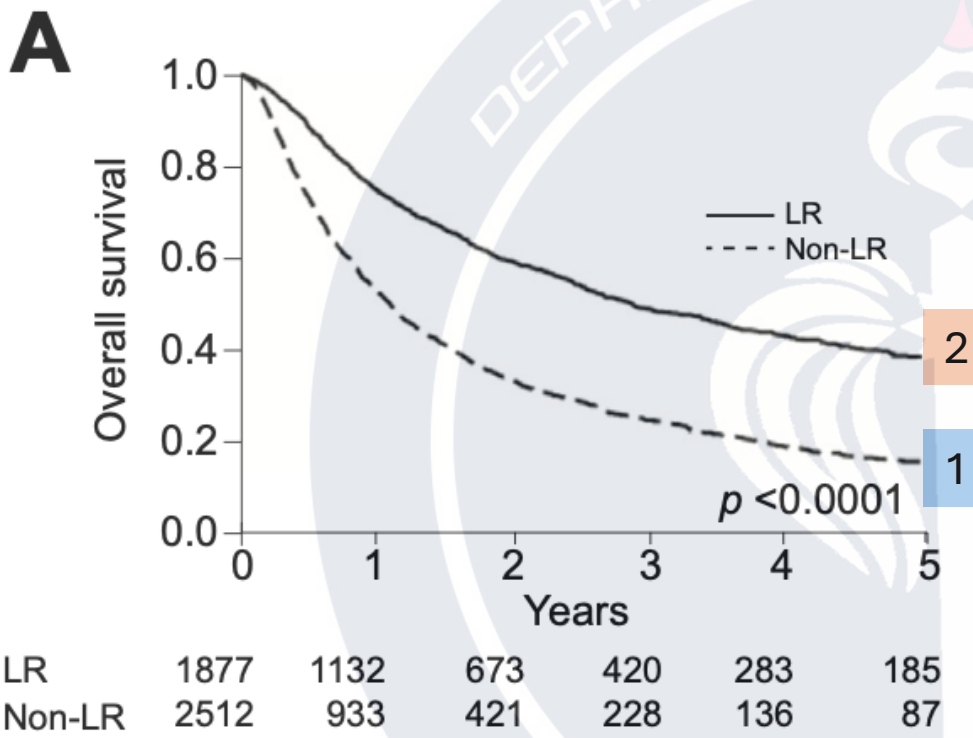
- Retrospective 2000-2007
- 2093 LR VS 4381 Non-LR

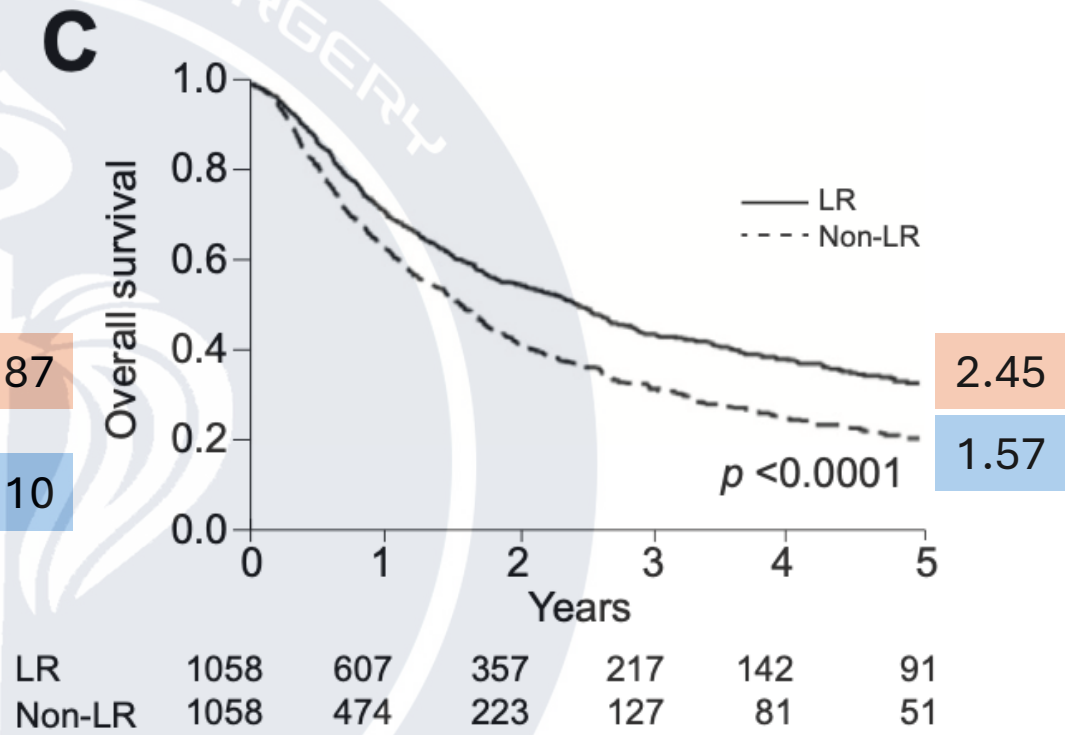
Introduction

Patients with advanced hepatocellular carcinoma (HCC) showing macroscopic vascular invasion have been reported to have an extremely poor prognosis [1]. According to the American Association for the Study of the Liver Disease/Barcelona Clinic for Liver Cancer (AASLD/BCLC) Staging System and treatment guidelines, portal vein invasion, or portal vein tumor thrombosis (PVTT), is regarded as an advanced stage of the disease with almost zero hope for a cure [2]. The only proposed treatment option for this group of patients is sorafenib chemotherapy, and the reported median survival time (MST) of patients with advanced HCC treated with sorafenib is as short as 10.7 months [3]. Therefore, surgical intervention may play some role in the treatment of

Non LR

- TACE
- CHEMOTHERAPY
- HAIC
- PALLATIVE

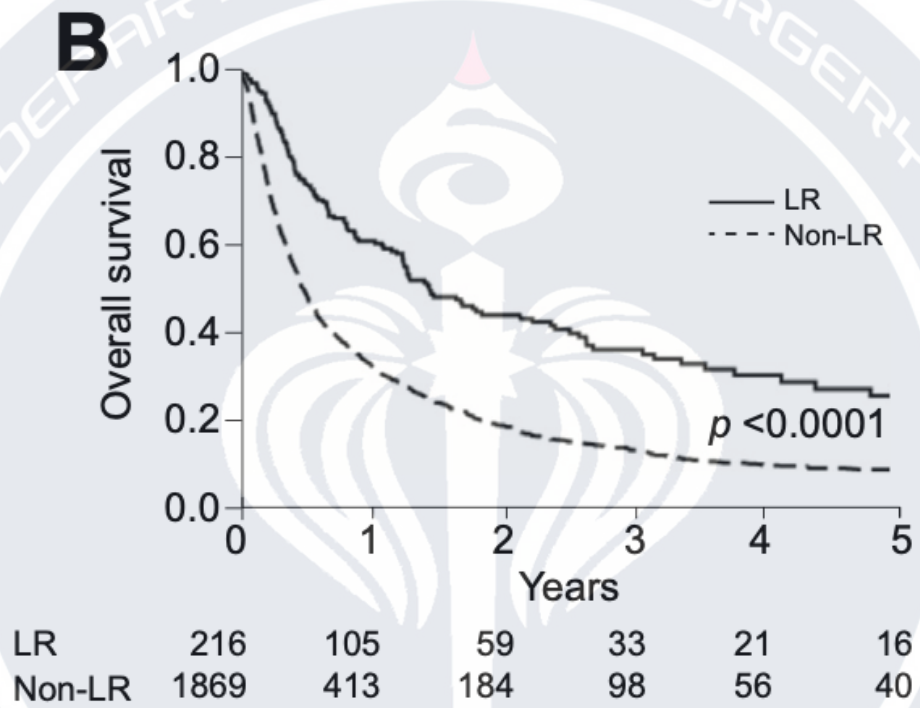




OS	1-year	3-year	5-year
Resection	74.9	49.1	39.1
Non-LR	53.1	25.3	16.0

After PPS

OS	1-year	3-year	5-year
Resection	70.9	43.5	32.9
Non-LR	62.9	31.6	20.1



1.44

0.48

OS	1-year	3-year	5-year
Resection	61.3	35.2	25.6
Non-LR	32.2	13.0	7.9

Intermediate and Advance HCC

Child-Pugh B

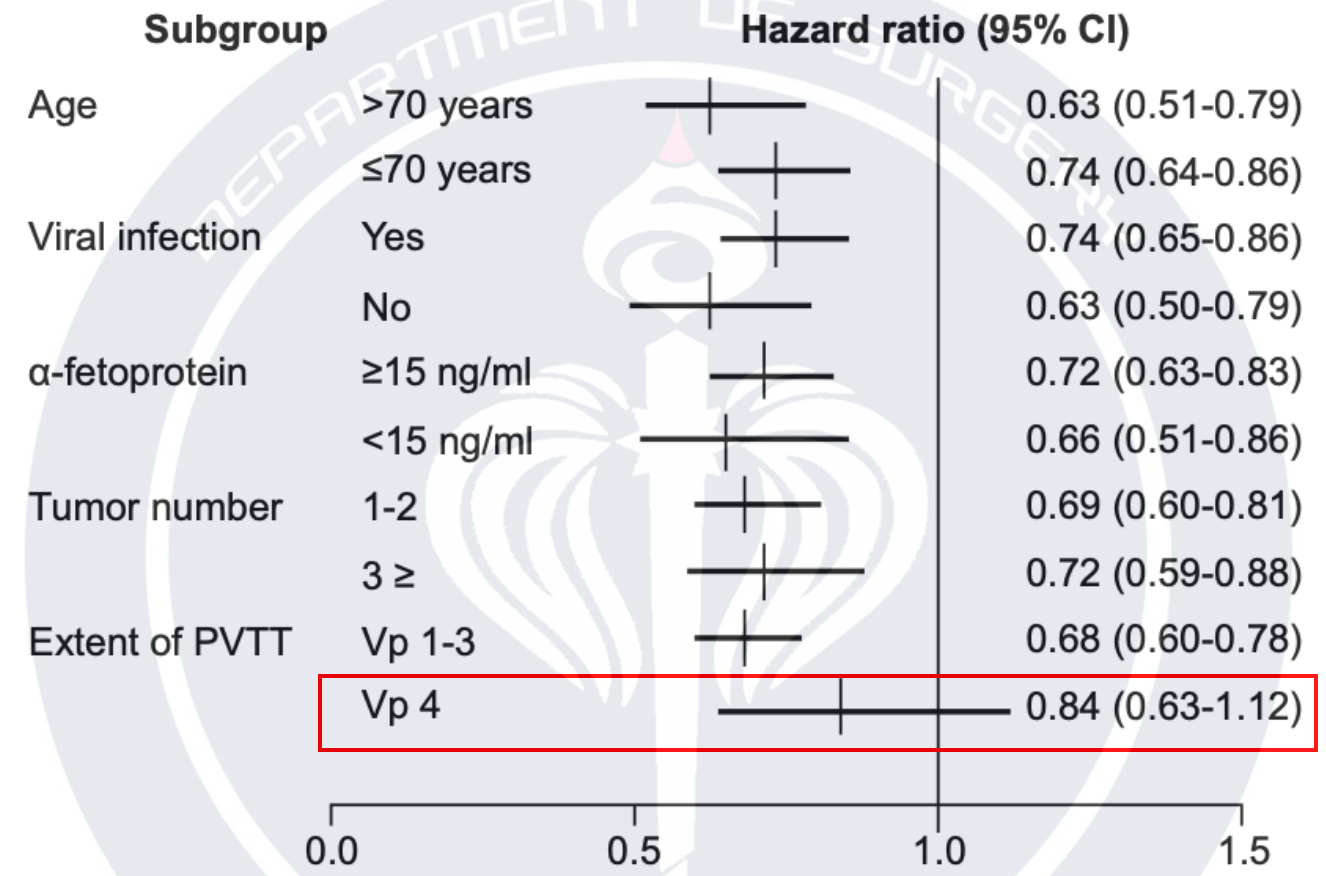


Fig. 2. Hazard ratios for death associated with liver resection in the subgroups of patients matched by propensity score. PVTT, portal vein tumor thrombosis; CI, confidence interval.

Table 3. Operative procedures and outcomes.

	Vp1 (n = 819)*	Vp2 (n = 475)*	Vp3 (n = 404)*	Vp4 (n = 179)*
Major hepatectomy§	379 (49.0)	310 (68.4)	338 (87.1)	158 (90.8)
Extent of resection				
R1	333 (61.1)	215 (65.4)	134 (45.0)	51 (38.1)
R2	64 (11.7)	73 (22.2)	139 (46.6)	81 (60.5)
Median survival time (yr)	4.13 (95% CI 3.40-5.81)	2.49 (95% CI 1.92-3.08)	1.58 (95% CI 1.22-2.17)	0.91 (95% CI 0.75-1.23)
Recurrence-free survival (yr)	1.23 (95% CI 1.04-1.73)	0.82 (95% CI 0.65-1.05)	0.56 (95% CI 0.46-0.69)	0.38 (95% CI 0.29-0.45)
Site of the first recurrence				
Intrahepatic	263 (36.2)	168 (39.3)	149 (41.3)	88 (56.4)
Distant metastasis	71 (9.8)	35 (8.2)	34 (9.4)	17 (10.9)
Both	35 (4.8)	47 (11.0)	47 (13.0)	16 (10.3)
90-day mortality	19 (2.4)	14 (3.0)	21 (5.3)	14 (8.2)

Data are the mean (standard deviation) or number (%) unless otherwise indicated.
*Missing data were not imputed for baseline characteristics.
§More than three Couinaud's segments.
CI, confidence interval.

Table 4. Multivariate analysis to identify prognostic factors associated with survival after liver resection.

Risk factors	*p* value	Hazard ratio (95% CI)
Liver cirrhosis	0.011	1.25 (1.05-1.48)
Tumor size (cm)	<0.001	1.02 (1.01-1.04)
Number of tumors ≥3	0.016	1.27 (1.05-1.53)
Serum alpha-fetoprotein ≥15 ng/ml	<0.001	1.53 (1.25-1.87)
Vp4	<0.001	1.63 (1.27-2.06)
R2 resection	<0.001	1.59 (1.32-1.91)

- LR significantly improves survival in HCC patients with PVTT limited to **first-order or more peripheral branches (Vp1–Vp3)** and preserved liver function.
- Benefit not proven in **Vp4 (main trunk/contralateral invasion)** due to high R2 resection rate and poor outcomes.

HVTT classification

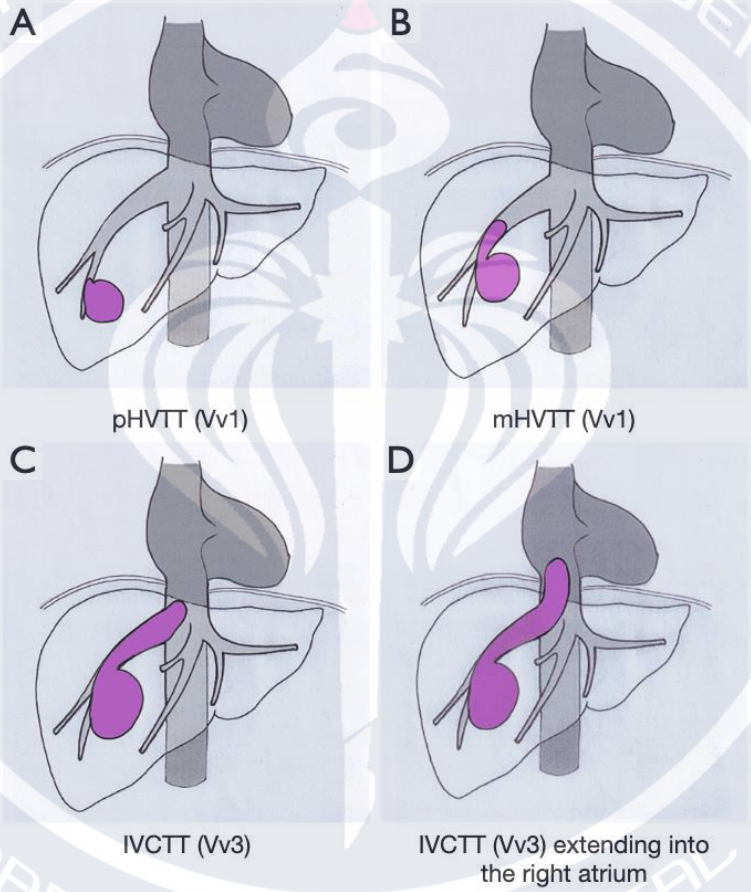


Figure 1 Diagram of the Japanese classification of HVTT/IVCTT (6). (A) tumor thrombus (TT) in a peripheral hepatic vein (pHVTT, Vv1), (B) TT in a major hepatic vein (mHVTT, Vv2), (C) TT in the inferior vena cava (IVCTT, Vv3), (D) IVCTT extending into the right atrium.

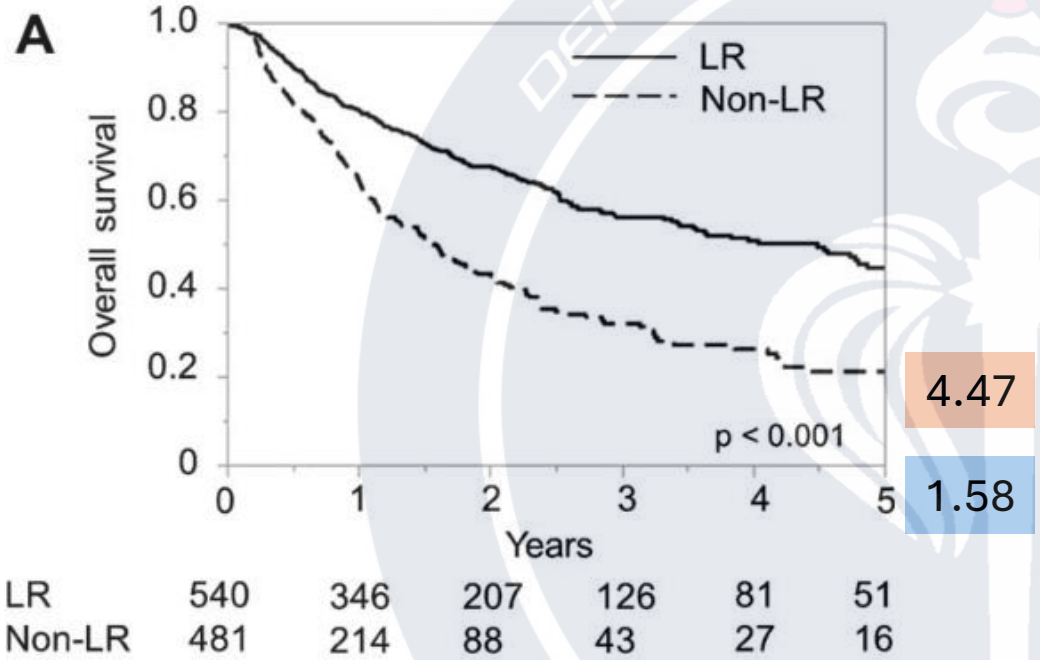
Liver Resection for Hepatocellular Carcinoma Associated With Hepatic Vein Invasion: A Japanese Nationwide Survey

Takashi Kokudo,[1,2] Kiyoshi Hasegawa,[1] Yutaka Matsuyama,[3] Tadatoshi Takayama,[4] Namiki Izumi,[5] Masumi Kadoya,[6] Masatoshi Kudo,[7] Shoji Kubo,[8] Michiie Sakamoto,[9] Osamu Nakashima,[10] Takashi Kumada,[11] and Norihiro Kokudo[1]; for the Liver Cancer Study Group of Japan

Because of the rarity of hepatic vein tumor thrombus (HVTT) compared with portal vein tumor thrombus (PVTT) in patients with hepatocellular carcinoma, little is known about this disease entity. The aim of this study was to evaluate the prognosis of each treatment modality for HVTT through an analysis of data collected in a Japanese nationwide survey. We analyzed data for 1,021 Child-Pugh A hepatocellular carcinoma patients with HVTT without inferior vena cava invasion registered between 2000 and 2007. Of these patients, 540 who underwent liver resection (LR) and 481 who received other treatments were compared. Propensity scores were calculated, and we successfully matched 223 patients (49.0% of the LR group). The median survival time in the LR group was 2.89 years longer than that in the non-LR group (4.47 versus 1.58 years, $P < 0.001$) and 1.61 years longer than that in the non-LR group (3.42 versus 1.81 years, $P = 0.023$) in a propensity score–matched cohort. After curative resection, median survival times were similar between patients with HVTT in the peripheral hepatic vein and those with HVTT in the major hepatic vein (4.85 versus 4.67 years, $P = 0.974$). In the LR group, the postoperative 90-day mortality rate was 3.4% (16 patients). In patients without PVTT, the median survival time was significantly better than that in patients with PVTT (5.67 versus 1.88 years, $P < 0.001$). *Conclusion:* LR is associated with a good prognosis in hepatocellular carcinoma patients with HVTT, especially in patients without PVTT. (HEPATOLOGY 2017;66:510-517).

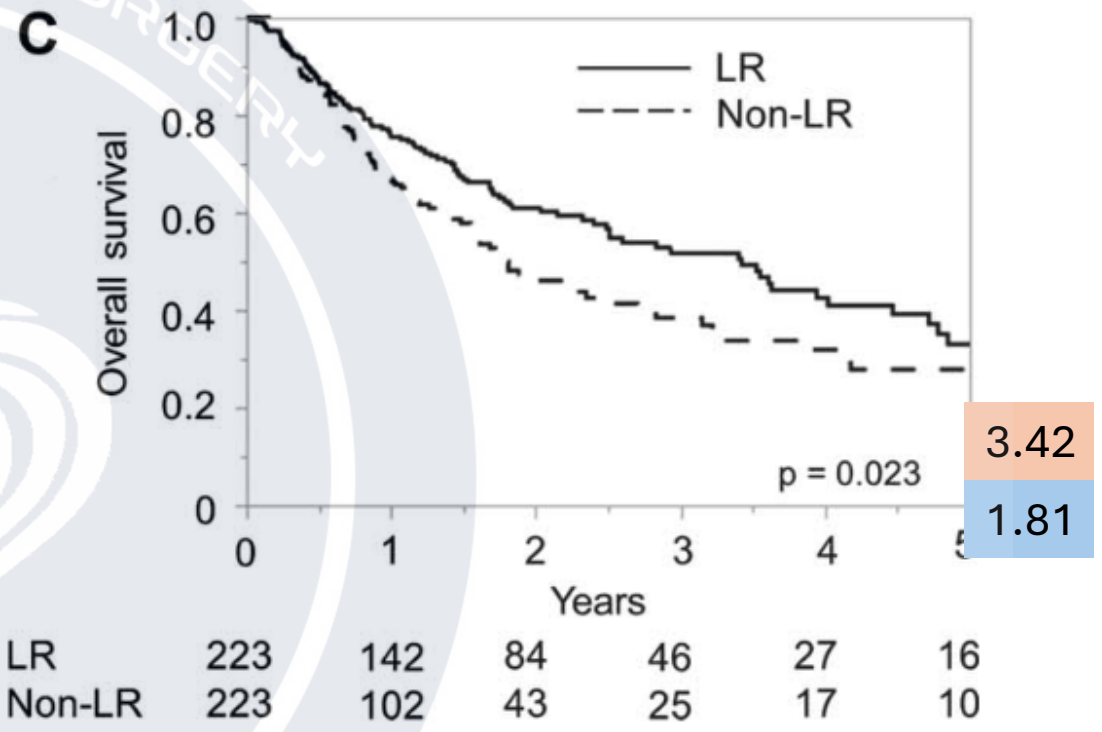
- Retrospective 2000-2007
- Child Pugh A
- 540 LR VS 481 Non-LR

Non LR
- TACE
- CHEMOTHERAPY
- HAIC
- PALLATIVE



4.47

1.58



3.42

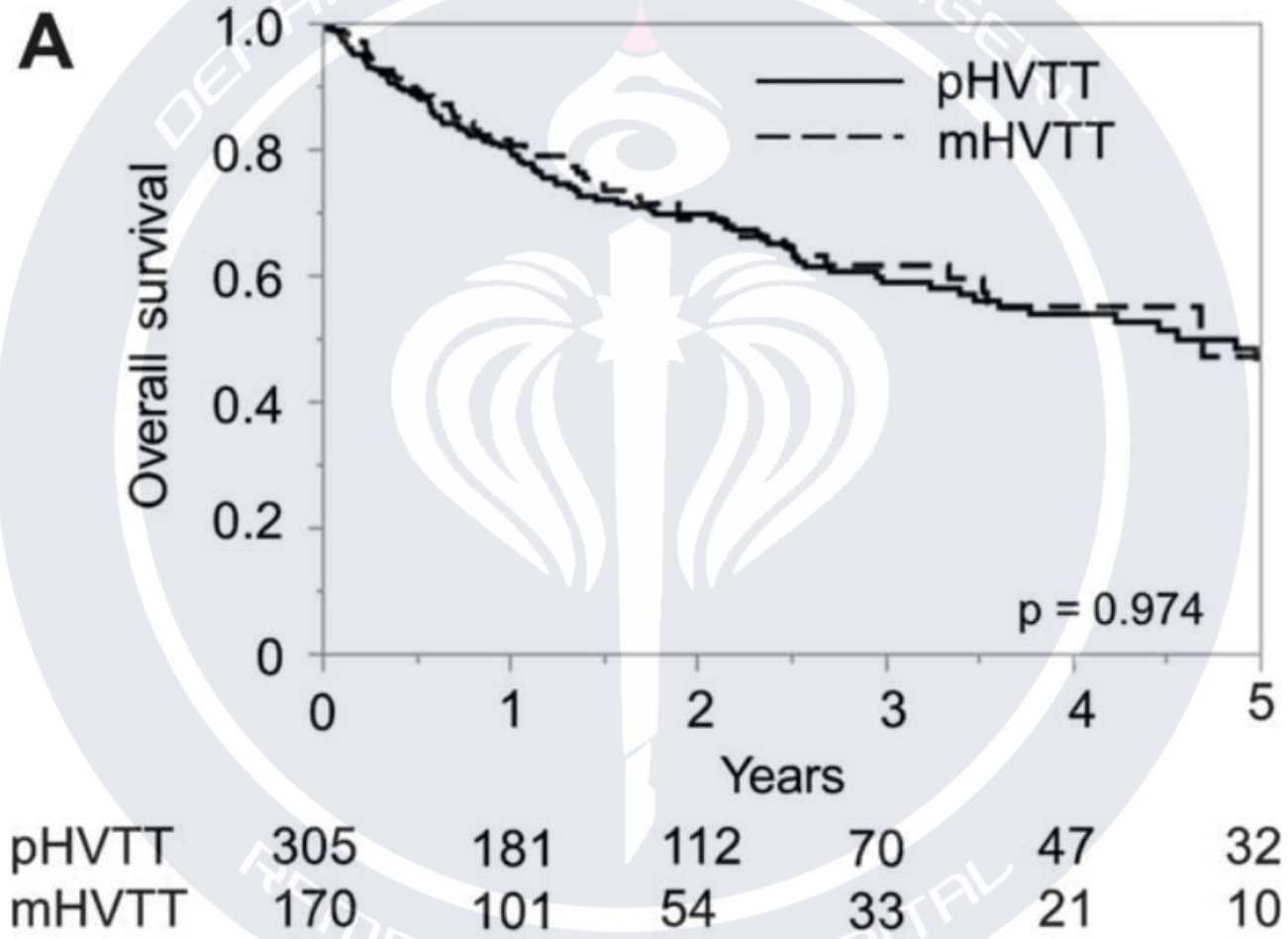
1.81

OS	1-year	3-year	5-year
Resection	80.0	56.6	44.2
Non-LR	63.7	32.6	20.3

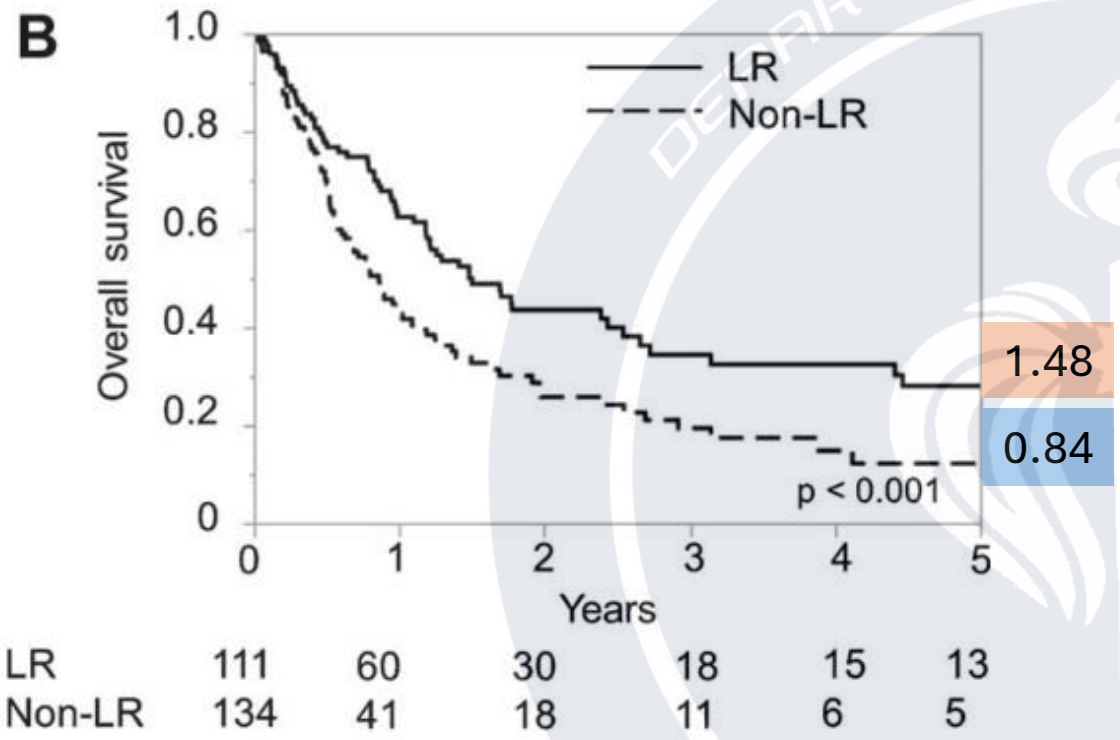
After PPS

OS	1-year	3-year	5-year
Resection	75.6	51.8	33.1
Non-LR	67.1	37.0	27.9

- Child Pugh A
- pHVTT/mHVTT

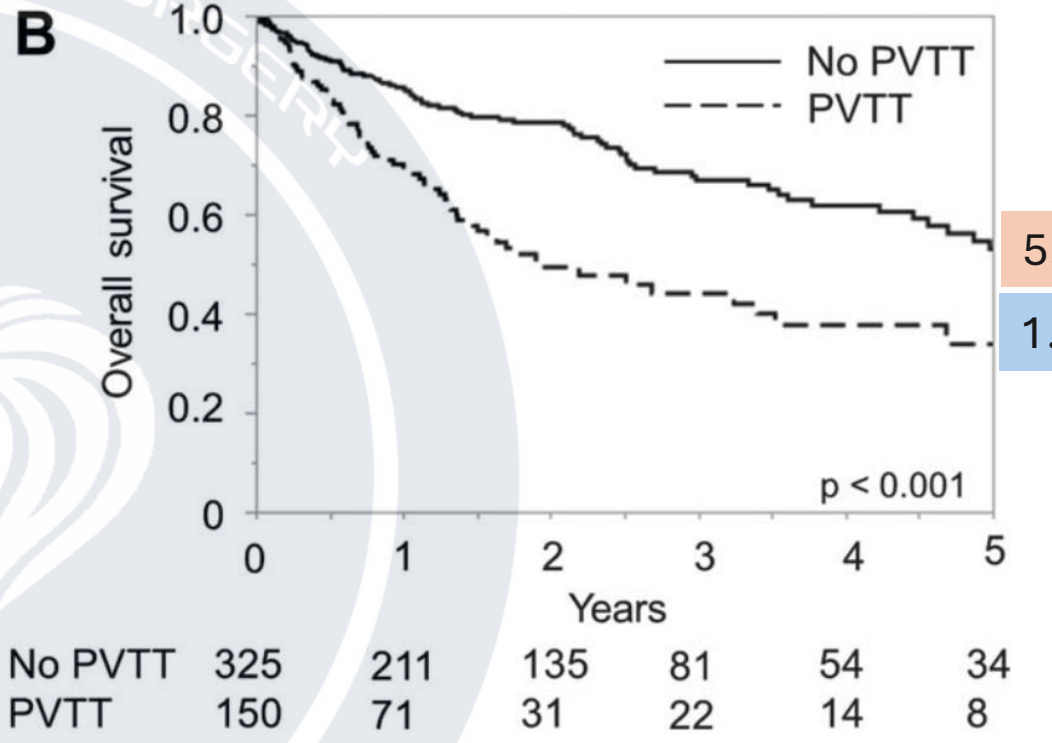


pHVTT Vs mHVTT



1.48

0.84



5.67

1.88

OS	1-year	3-year
Resection	63.2	33.1
Non-LR	42.3	20.1

PVTT >> vP2/vP3

- Child Pugh A
- IVCTT

TABLE 3. Operative Procedures and Outcomes for Patients Who Underwent Curative Resection

	pHVTT (n = 305)*	mHVTT (n = 170)*	IVCTT (n = 71)*
Major hepatectomy†	175 (59.9)	124 (76.5)	51 (75.0)
Median survival time (years)	4.85 (95% CI 3.38- n.a.)	4.67 (95% CI 3.32-5.88)	1.37 (95% CI 1.07-4.21)
Recurrence-free survival (years)	2.36 (95% CI 1.38-3.17)	0.88 (95% CI 0.75-1.32)	0.82 (95% CI 0.42-1.10)
Site of the first recurrence			
Intrahepatic	92 (32.7)	60 (38.0)	17 (23.9)
Distant metastasis	14 (5.0)	18 (11.4)	9 (12.7)
Both	17 (6.0)	16 (10.1)	15 (21.1)
Median hospital stay (days)	21 (IQR 15-36)	23 (IQR 16-46)	26 (IQR 18-55)
90-Day mortality	13 (4.3)	3 (1.8)	7 (9.9)

Data are the mean (standard deviation) or number (percentage) unless otherwise indicated.
*Missing data were not included for baseline characteristics.
†More than three Couinaud's segments.
Abbreviation: n.a., not available.

- Liver resection offers significant survival benefit with acceptable operative risk in HCC patients with HVTT, especially those without PVTT.

Liver resection is associated with good outcomes for hepatocellular carcinoma patients beyond the Barcelona Clinic Liver Cancer criteria: A multicenter study with the Hiroshima Surgical study group of Clinical Oncology

Masateru Yamamoto, MD[a], Tsuyoshi Kobayashi, MD, PhD[a,*], Naruhiko Honmyo, MD, PhD[a], Akihiko Oshita, MD, PhD[b], Tomoyuki Abe, MD, PhD[c], Toshihiko Kohashi, MD, PhD[d], Takashi Onoe, MD, PhD[e], Saburo Fukuda, MD, PhD[f], Ichiro Omori, MD, PhD[g], Yasuhiro Imaoka, MD, PhD[h], Hideki Ohdan, MD, PhD[a]

[a] *Department of Gastroenterological and Transplant Surgery, Graduate School of Biomedical and Health Science, Hiroshima University, Hiroshima, Japan*
[b] *Department of Gastroenterological Surgery, Hiroshima Prefectural Hospital, Hiroshima, Japan*
[c] *Department of Surgery, Onomichi General Hospital, Onomichi, Japan*
[d] *Department of Surgery, Hiroshima City Asa Citizens Hospital, Hiroshima, Japan*
[e] *National Hospital Organization, Kure Medical Center/Chugoku Cancer Center, Institute for Clinical Research, Hiroshima, Japan*
[f] *Department of Surgery, Chugoku Rosai Hospital, Kure, Japan*
[g] *Department of Surgery, National Hospital Organization Higashihiroshima Medical Center, Hiroshima, Japan*
[h] *Department of Surgery, National Hospital Organization Hiroshima-Nishi Medical Center, Hiroshima, Japan*

ARTICLE INFO

Article history:
Accepted 11 September 2021
Available online 30 October 2021

ABSTRACT

Background: Liver resection for hepatocellular carcinoma beyond the Barcelona Clinic Liver Cancer criteria remains controversial. Strict candidate selection is crucial to achieve optimal results in this population. This study explored postoperative outcomes and developed a preoperative predictive formula to identify patients most likely to benefit from liver resection.

Methods: In total, 382 patients who underwent liver resection for hepatocellular carcinoma beyond the Barcelona Clinic Liver Cancer resection criteria between 2000 and 2017 were identified from a multicenter database with the Hiroshima Surgical study group of Clinical Oncology. An overall survival prediction model was developed, and patients were classified by risk status.

Results: The 5-year overall survival after curative resection was 50.0%. Overall survival multivariate analysis identified that a high a-fetoprotein level, macrovascular invasion, and high total tumor burden were independent prognostic risk factors; these factors were used to formulate risk scores. Patients were divided into low-, moderate-, and high-risk groups; the 5-year overall survival was 65.7%, 49.5%, and 17.0% ($P < .001$), and the 5-year recurrence-free survival was 31.3%, 26.2%, and 0%, respectively ($P < .001$). The model performance was good (C-index, 0.76). Both the early and extrahepatic recurrence increased with higher risk score.

Conclusion: The prognosis of patients with hepatocellular carcinoma beyond the Barcelona Clinic Liver Cancer resection criteria depended on a high a-fetoprotein level, macrovascular invasion, and high total tumor burden, and risk scores based on these factors stratified the prognoses. Liver resection should be considered in patients with hepatocellular carcinoma beyond the Barcelona Clinic Liver Cancer criteria with a low or moderate-risk score.

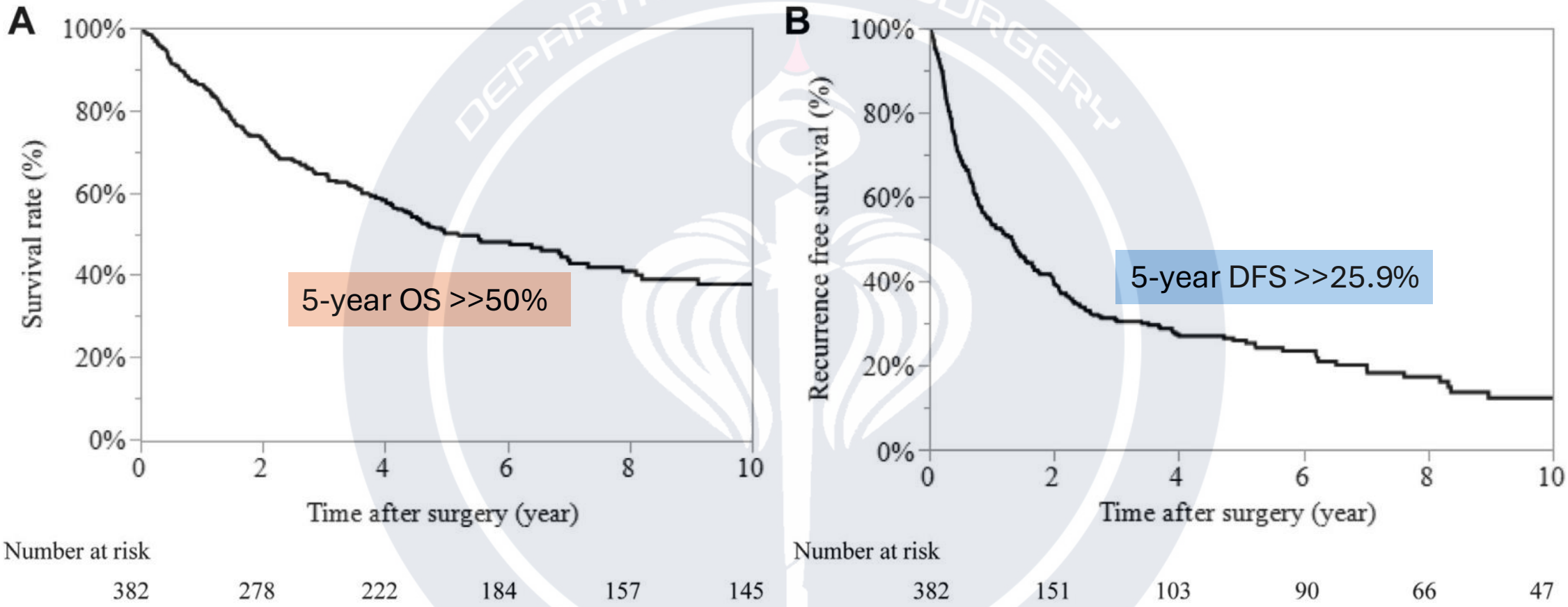


Fig 1. The overall survival (a) and recurrence-free survival (b) of 382 patients who underwent resection for HCC beyond the BCLC criteria.

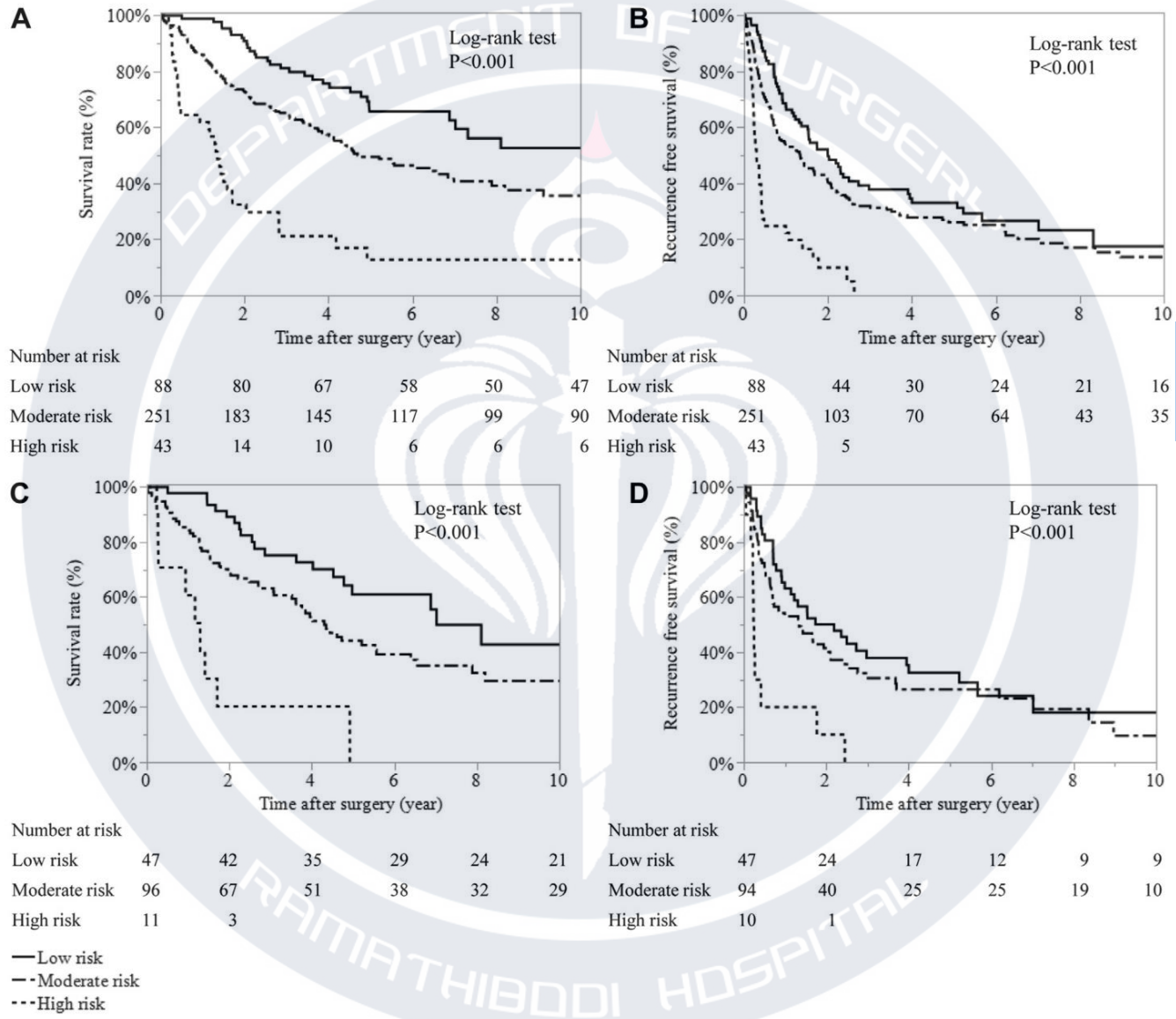
Table II
Univariate and multivariate analyses of prognostic factors for OS

Variable	N (%)	Univariate analysis			Multivariate analysis		
		P value	HR	95% CI	P value	HR	95% CI
Age >70 y	94 (24.6)	.633	1.086	.777-1.552			
Male	317 (83.0)	.799	1.049	.732-1.547			
HBV positive	59 (16.0)	.111	1.353	.931-1.919			
HCV positive	180 (48.8)	.941	1.011	.756-1.349			
Plt <14 ($\times 10^4$/mm^3)	164 (43.9)	.099	1.273	.955-1.697			
NLR >2.35	125 (32.7)	.595	1.085	.803-1.466			
Child-Pugh grade B	39 (10.2)	.014	1.746	1.128-2.593	0.054	1.548	0.912-2.366
AFP >50 (ng/mL)	173 (45.3)	<.001	1.989	1.496-2.653	0.001	1.629	1.206-2.199
DCP >1,000 (mAU/mL)	142 (37.2)	<.001	1.675	1.254-2.229	0.139	1.271	0.924-1.749
Macrovascular invasion	105 (27.5)	<.001	2.243	1.653-3.017	<0.001	1.984	1.441-2.732
High TTB	210 (55.0)	<.001	1.903	1.421-2.568	0.009	1.536	1.109-2.127
Major liver resection	141 (36.9)	.034	1.369	1.024-1.828	0.408	1.142	0.833-1.565
R1 margin	59 (15.4)	.005	1.671	1.165-2.392	0.206	1.229	0.892-1.692
poorly differentiated	99 (25.9)	.004	1.563	1.151-2.125			
LC	154 (40.3)	.419	1.125	.845-1.497			

AFP, alpha-fetoprotein levels; *DCP*, des-gamma-carboxyprothorombin; *HBV*, hepatitis B virus; *HCV*, hepatitis C virus; *LC*, liver cirrhosis; *NLR*, neutrophil-to-lymphocyte ratio; *TTB*, total tumor burden.
Data were presented as number and percentage for categorized variables.

$$\text{Linear predictor} = (0.56 \times \text{AFP}) + (0.74 \times \text{macrovascular invasion}) + (0.53 \times \text{TTB}).$$

< 0.53 = low risk,
0.53 -1.86 = intermediate
>1.86 = high risk



5-year OS 65.7%
5-year OS 49.5%
5-year OS 17.0%

5-year RFS 31.3%
5-year RFS 26.2%
5-year RFS 0%,

Cirrhosis
5-year OS 61%
5-year OS 41.6%
5-year OS 0%

Cirrhosis
5-year RFS 32.6%
5-year RFS 29.5%
5-year RFS 0%,

Liver resection should be considered in patients with HCC beyond the BCLC criteria with a low or moderate risk scores

Comparison of Surgical Resection and Systemic Treatment for Hepatocellular Carcinoma with Vascular Invasion: National Cancer Database Analysis

Rajalakshmi Govalan[a] Marie Lauzon[b, c] Michael Luu[b, c] Joseph C. Ahn[d] Kambiz Kosari[b, e, f] Tsuyoshi Todo[b, e, f] Irene K. Kim[e, f] Mazen Noureddin[a, e, g] Alexander Kuo[a, e, g] Ayoub S. Walid[a, e, g] Vinay Sundaram[a, e, g] Shelly C. Lu[a, b] Lewis R. Roberts[d] Amit G. Singal[h, i] Julie K. Heimbach[j, k] Vatche G. Agopian[l] Nicholas Nissen[b, e, f] Ju Dong Yang[a, b, e, g]

[a]Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [b]Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [c]Biostatistics and Bioinformatics Research Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [d]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, MN, USA; [e]Comprehensive Transplant Center, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [f]Department of Surgery, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [g]Karsh Division of Gastroenterology and Hepatology, Cedars-Sinai Medical Center, Los Angeles, CA, USA; [h]Harold C. Simmons Comprehensive Cancer Center, UT Southwestern Medical Center, Dallas, TX, USA; [i]Division of Digestive and Liver Diseases, UT Southwestern Medical Center, Dallas, TX, USA; [j]Department of Surgery, Mayo Clinic, Rochester, MN, USA; [k]Liver Transplant Program, Mayo Clinic, Rochester, MN, USA; [l]Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA

Retrospective in USA
- HCC with vascular invasion
- Resection VS systemic therapy

Keywords
Hepatocellular carcinoma · Vascular invasion · Surgical resection · Prognosis

Abstract
Introduction: Small studies from outside of the USA suggest excellent outcomes after surgical resection for hepatocellular carcinoma (HCC) with vascular invasion. The study aims to (1) compare overall survival after surgical resection and systemic therapy among patients with HCC and vascular invasion and (2) determine factors associated with receipt of surgical resection in a US population. ***Methods:*** HCC patients with AJCC clinical TNM stage 7th T3BN0M0 diagnosed between 2010 and 2017 from the National Cancer Database were analyzed. Cox and logistic regression analyses identified factors associated with overall survival and receipt of surgical resection. ***Results:*** Of 11,259 patients with T3BN0M0 HCC, 325 (2.9%) and 4,268 (37.9%) received surgical resection and systemic therapy, respectively. In multivariable analysis, surgical resection was associated with improved survival compared to systemic therapy (adjusted hazard ratio: 0.496, 95% confidence interval: 0.426–0.578) with a median survival of 21.4 and 8.1 months, respectively. Superiority of surgical resection was observed in noncirrhotic and cirrhotic subgroups and propensity score matching and inverse probability of treatment weighting adjusted analysis. Asians were more likely to receive surgical resection, whereas Charl-

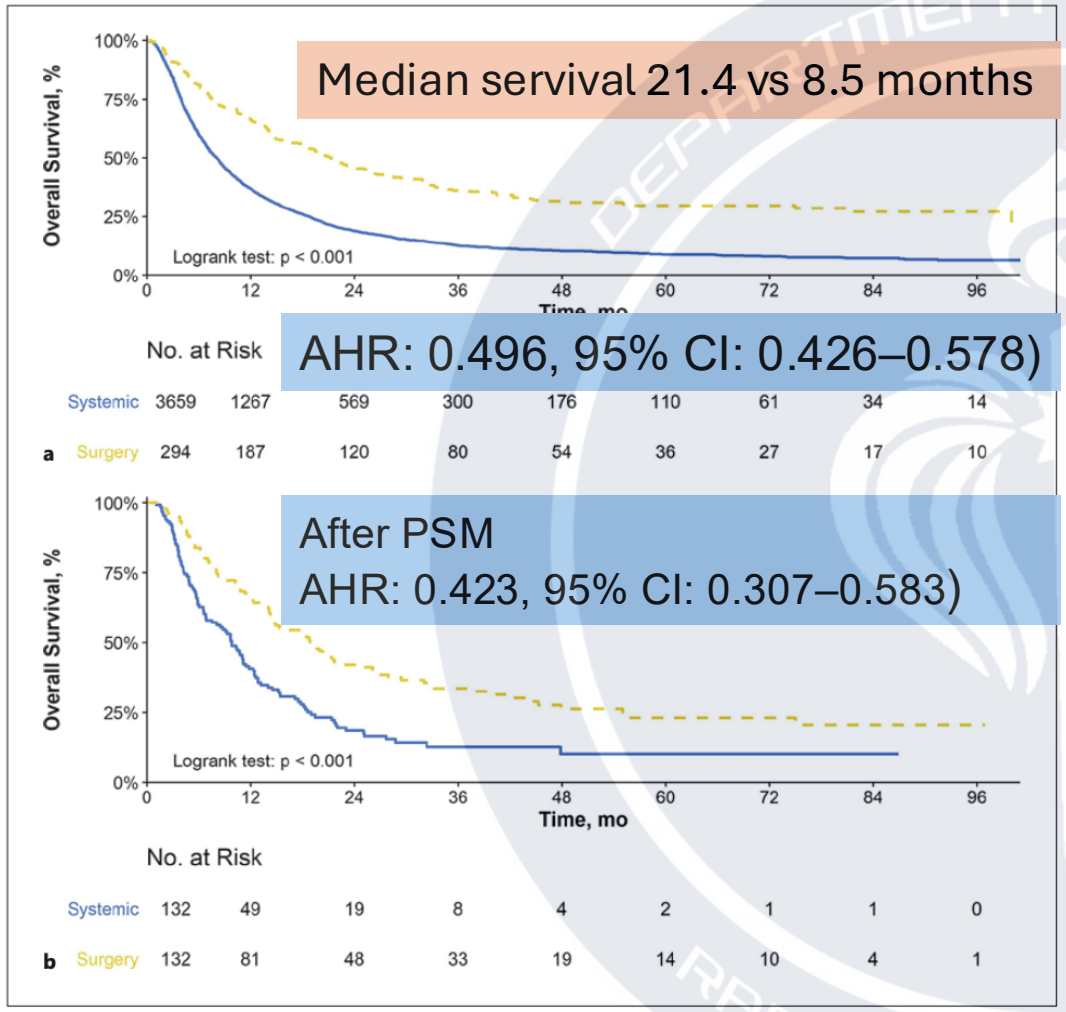


Fig. 1. Kaplan-Meier survival analysis of patients with surgical resection vs. systemic therapy for their HCC with vascular invasion. **a** Before propensity score matching. **b** After propensity score matching. HCC, hepatocellular carcinoma.

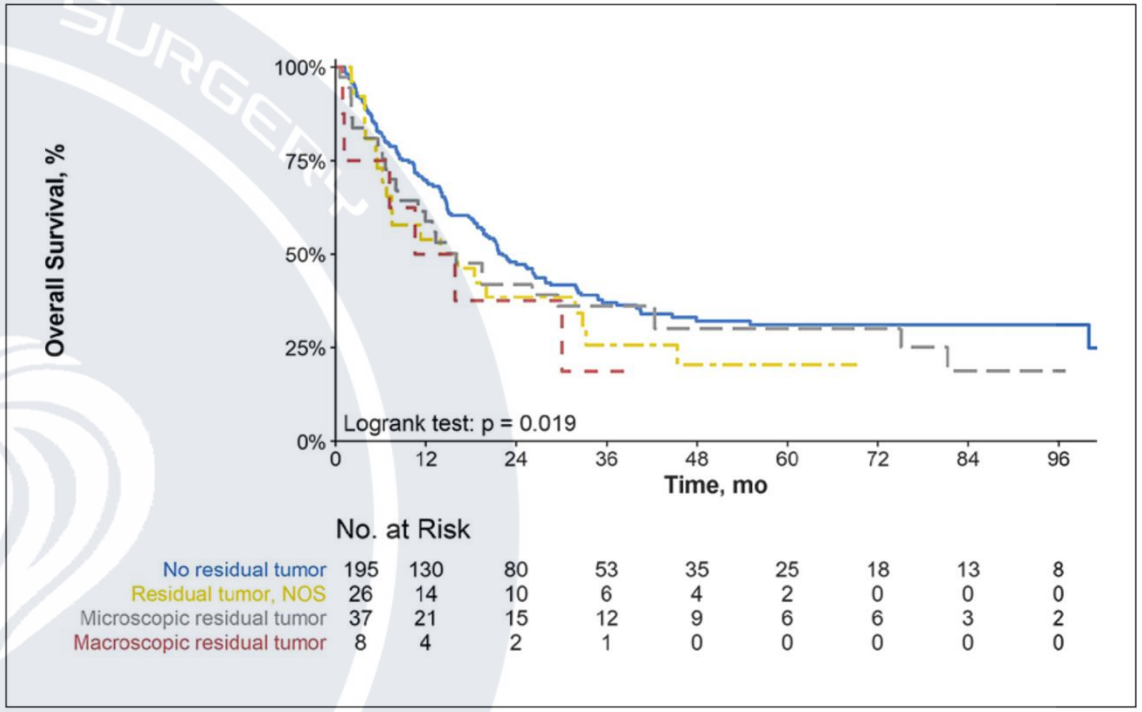


Fig. 2. Survival estimate for HCC patients with vascular invasion who underwent surgical resection by surgical margin status. HCC, hepatocellular carcinoma.

Median survival
- R0: 22.2 months
- R1: 16.0 months
- R2: 13.2 months

R1 vs Systemic :
AHR: 0.558, 95%CI 0.381–0.819)

Conclusion

- **PVTT**
  - **Vp1–3 PVTT**: LR provides survival benefit.
  - **Vp4 PVTT**: LR does **not** offer significant benefit.
  - **Independent risk factors for ineffective LR in PVTT**:
    - AFP levels >400 ng/mL
    - Tumor number >3
- HVTT
  - LR offers significant survival benefit with acceptable operative risk in patients with **hepatic vein tumor thrombus (HVTT)**, especially in the absence of PVTT.
  - Survival decreases in HVTT patients with **inferior vena cava (IVC) invasion**.

Japan Society of hepatology(2021)

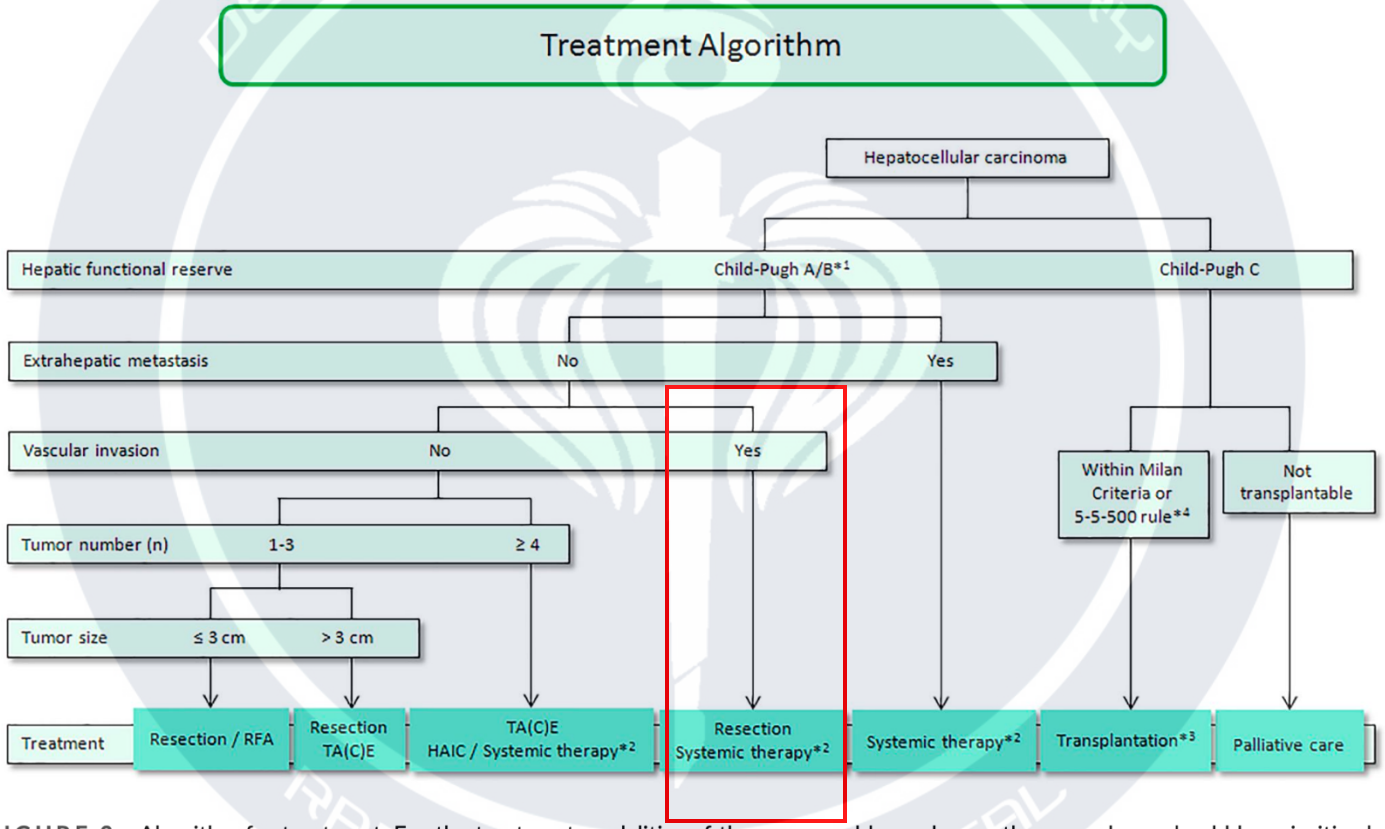
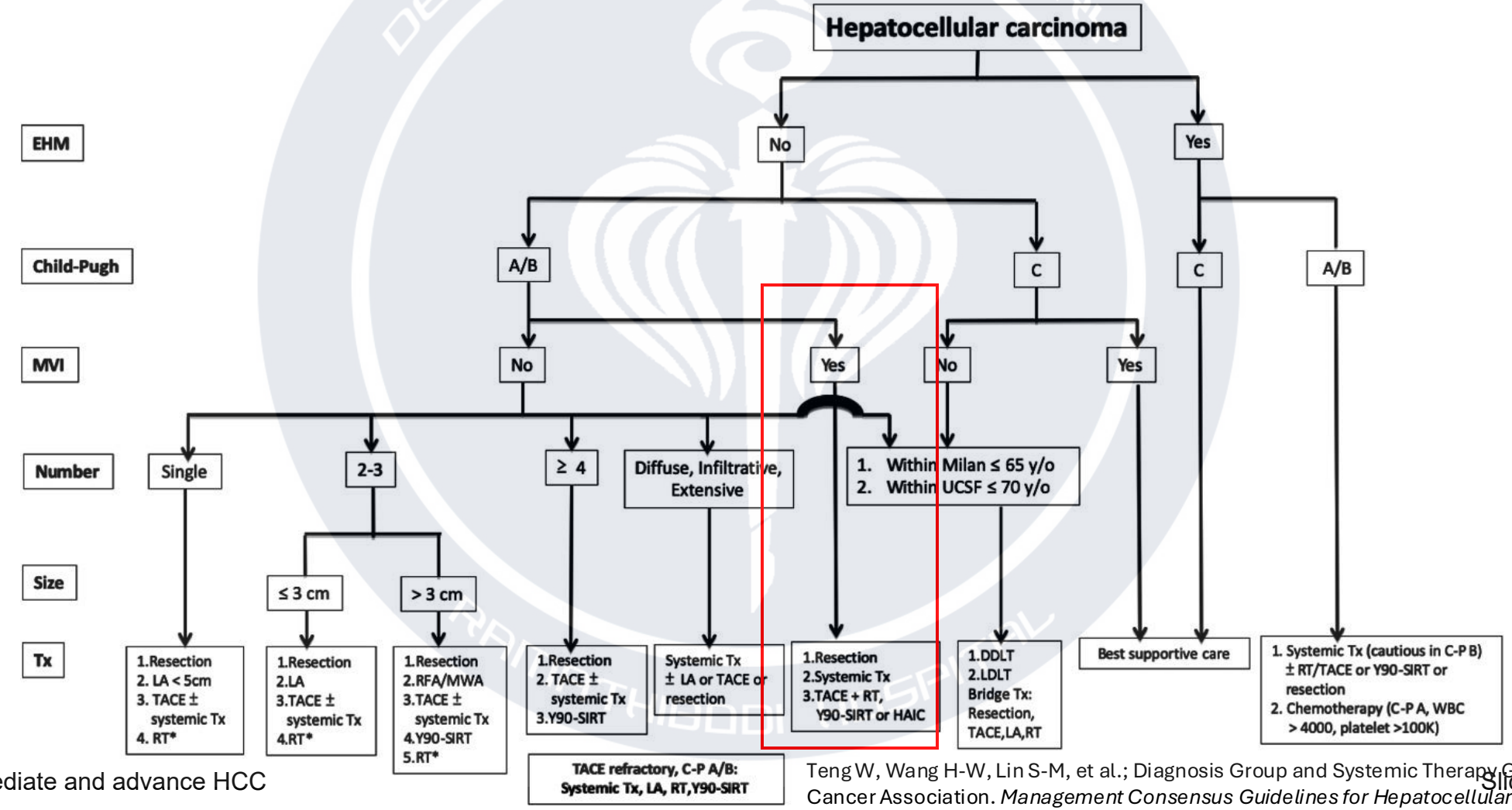


FIGURE 3 Algorithm for treatment. For the treatment modalities of the upper and lower layers, the upper layer should be prioritized. Treatment modalities separated by slashes are equally recommended. *[1]Assessment based on liver damage is recommended in the case of hepatectomy. *[2]Patients with Child–Pugh A only. *[3]Patients age ≤65 years. *[4]Tumor diameter ≤5 cm, ≤5 tumors and alpha-fetoprotein ≤500 ng/mL, with no distant metastasis or vascular invasion. HAIC, hepatic arterial infusion chemotherapy; RFA, radiofrequency ablation; TA (C)E, transcatheter arterial (chemo)embolization.

Hasegawa K, Takemura N, Yamashita T, Watadani T, Kaibori M, Kubo S, et al. Clinical practice guidelines for hepatocellular carcinoma: The Japan Society of Hepatology 2021 version (5th JSH-HCC guidelines). *Hepatol Res*. 2023;53(5):383-390.

Intermediate and advance HCC

Taiwan Liver Cancer Association and the Gastroenterological Society of Taiwan(2016)



Intermediate and advance HCC

Teng W, Wang H-W, Lin S-M, et al.; Diagnosis Group and Systemic Therapy Group of the Taiwan Liver Cancer Association. *Management Consensus Guidelines for Hepatocellular Carcinoma: 2023 Update on Surveillance, Diagnosis, Systemic Treatment, and Posttreatment Monitoring*. Liver Cancer. 2024

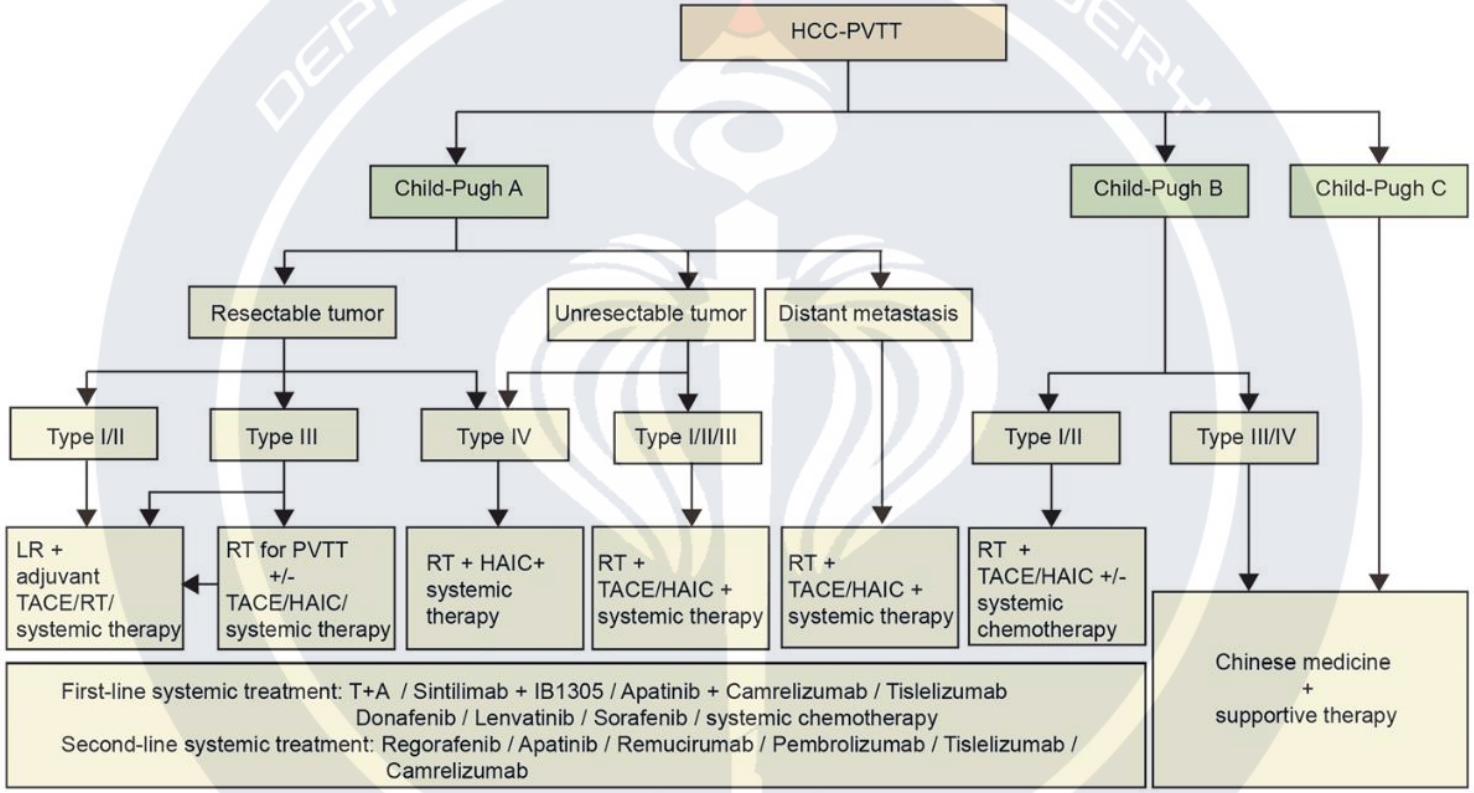
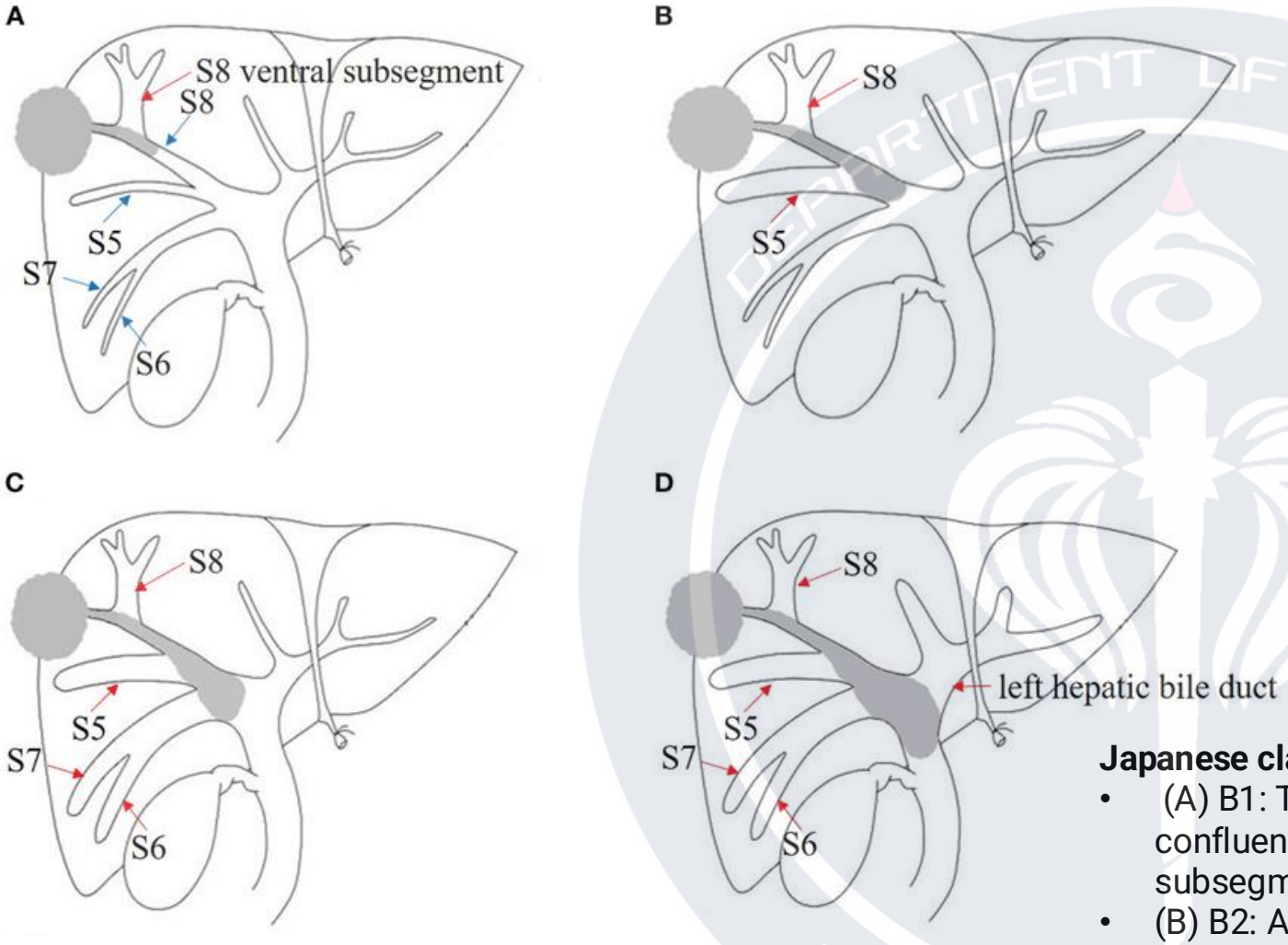


Figure 2. Treatment decision-making process for HCC-PVTT according to Cheng's classification [23]. HAIC, hepatic arterial infusion chemotherapy; HCC-PVTT, hepatocellular carcinoma with portal vein tumor thrombus; LR, liver resection; RT, radiotherapy; T + A, atezolizumab and bevacizumab; TACE, transcatheter arterial chemoembolization.

HCC with bile duct tumor thrombus (BDTT)

BDTT

- HCC with Bile duct tumor thrombus (BDTT) is a rare but recognized complication of hepatocellular carcinoma (HCC).
- Incidence 0.5–12.9%
- Standard practice guideline do not provide



Japanese classification of BDTT

- (A) B1: The tumor locates in S8 and the tumor thrombus invades the confluence of dorsal and ventral bile ducts; the bile duct dilation of ventral subsegment is observed.(>2 order)
- (B) B2: As the tumor thrombus further extends to the confluence of S5 and S8, bile duct dilation of S5 can be seen.(2nd order)
- (C) B3: The tumor thrombus extends to the right hepatic duct, and the bile duct dilation of the right posterior lobe can also be seen.(1st order)
- (D) B4: The tumor thrombus extends to the common bile duct, and the bile duct dilation of left hepatic lobe can be seen. (Main)

Usefulness of Resection for Hepatocellular Carcinoma with Macroscopic Bile Duct Tumor Thrombus

ATSUSHI OBA[1], SHINICHIRO TAKAHASHI[1], YUICHIRO KATO[1], NAOTO GOTOHDA[1], TAKAHIRO KINOSHITA[1], HIDEHITO SHIBASAKI[1], MASAFUMI IKEDA[2] and MASARU KONISHI[1]

Departments of [1]Digestive Surgical Oncology and [2]Hepatobiliary and Pancreatic Oncology, National Cancer Center Hospital East, Chiba, Japan

Abstract. *Background: The prognostic significance of bile duct tumor thrombus (BDTT) in hepatocellular carcinoma (HCC) is unclear and the usefulness of resection for HCC with BDTT is still controversial. The aim of the present study was to evaluate the impact of BDTT on prognosis in HCC and to determine whether resection of HCC with BDTT was useful. Patients and Methods: Out of 820 HCC patients who underwent hepatic resection from 1992 to 2012, 13 HCC patients (1.6%) had macroscopic BDTT. The results of resection for HCC patients with BDTT and the prognostic significance of BDTT were evaluated. Prognoses were also compared according to treatment in patients who had HCC with BDTT. Results: The overall 1-, 3- and 5-year survival rates after resection were 92%, 77% and 48%, respectively, for HCC patients with BDTT, and 88%, 67%, and 52%, respectively, for HCC patients without BDTT; there were no significant differences (p=0.833). In all HCC patients after resection, the unadjusted hazard ratio of the presence of BDTT was 1.08 (95%CI=0.49-2.05; p=0.835) and when adjusted for other significant prognostic factors, the hazard ratio of the presence of BDTT was 0.98 (95%CI=0.42-1.98; p=0.958). The overall 1-, 3- and 5-year survival rates were 14%, 5% and 0%, respectively, for 25 HCC patients with BDTT after other initial treatments. Conclusion: Bile duct tumor thrombus was not a prognostic factor in patients with resected HCC. In HCC with BDTT, surgical treatment is recommended whenever possible because only resected patients achieved long-term survival.*

Hepatocellular carcinoma (HCC) is responsible for approximately 600,000-700,000 deaths worldwide. It is highly prevalent in the Asia-Pacific region and Africa and is increasing in Western countries (1).

HCC usually spreads through the liver *via* the portal vein, and portal vein invasion is a well-documented prognostic marker (2-5). Meanwhile, bile duct tumor thrombus (BDTT) is relatively rare. The incidence of portal vein invasion is 26.1%, whereas the incidence of BDTT is 3.4%; the incidence of macroscopic BDTT is only 1.4% (6).

Several studies have reported that HCC patients with BDTT had poor survival because of obstructive jaundice, cholestasis, hepatic dysfunction and spread of tumors (7-13). On the other hand, good results of aggressive resection for HCC patients with BDTT have also been reported (14-16).

Survival of all HCC patients has improved due to advances in diagnostic and therapeutic modalities (6). However, the survival of HCC patients with BDTT is unclear.

In the present study, BDTT was assessed as a prognostic factor in patients with resectable HCC.

Patients and Methods

Patients. Between July 1992 and August 2012, 820 HCC patients underwent initial hepatic resection at the National Cancer Center Hospital East. A total of 13 HCC patients (1.6%) with macroscopic BDTT and 783 HCC patients (95.5%) without BDTT were retrospectively reviewed from our database.

Two pathologists evaluated the resected specimens macroscopically and microscopically according to the Japanese TNM Staging System by the Liver Cancer Study Group of Japan (17). Macroscopic BDTT was defined as b2-4 (tumor thrombus in

Retrospective
HCC with BDTT vs without BDTT

OS	1-year	3-year	5-year
BDTT (resection)	92%	77%	48%
Without BDTT	88%	67%	52%

No significant differences between the two groups (p=0.83)

OS	1-year	3-year	5-year
BDTT(13) (resection)	92%	77%	48%
BDTT(6) (no resection)	14%	5%	0%

Higher significant in resection group(p<0.001)

Surgical Outcomes of Hepatocellular Carcinoma With Bile Duct Tumor Thrombus

A Korea–Japan Multicenter Study

Dong-Sik Kim, MD, PhD, Bong-Wan Kim, MD, PhD,† Etsuro Hatano, MD, PhD,‡ Shin Hwang, MD, PhD,§ Kiyoshi Hasegawa, MD, PhD,¶ Atsushi Kudo, MD, PhD,|| Shunichi Ariizumi, MD, PhD,** Masaki Kaibori, MD, PhD,†† Takumi Fukumoto, MD, PhD,‡‡ Hideo Baba, MD, PhD,§§ Seong Hoon Kim, MD, PhD,¶¶ Shoji Kubo, MD, PhD,|||| Jong Man Kim, MD, PhD,*** Keun Soo Ahn, MD, PhD,††† Sae Byeol Choi, MD, PhD,* Chi-Young Jeong, MD, PhD,‡‡‡ Yasuo Shima, MD, PhD,§§§ Hiroaki Nagano, MD, PhD,¶¶¶ Osamu Yamasaki, MD, PhD,|||||| Hee Chul Yu, MD, PhD,**** Dai Hoon Han, MD,†††† Hyung-Il Seo, MD, PhD,‡‡‡‡ Il-Young Park, MD, PhD,§§§§ Kyung-Sook Yang, PhD,¶¶¶¶ Masakazu Yamamoto, MD, PhD,** and Hee-Jung Wang, MD, PhD†*

Objective: To identify optimal surgical methods and the risk factors for long-term survival in patients with hepatocellular carcinoma accompanied by macroscopic bile duct tumor thrombus (BDTT).

Summary Background Data: Prognoses of patients with hepatocellular carcinoma accompanied by BDTT have been known to be poor. There have been significant controversies regarding optimal surgical approaches and risk factors because of the low incidence and small number of cases in previous reports.

Methods: Records of 257 patients from 32 centers in Korea and Japan (1992-2014) were analyzed for overall survival and recurrence rate using the Cox proportional hazard model.

Results: Curative surgery was performed in 244 (94.9%) patients with an operative mortality of 5.1%. Overall survival and recurrence rate at 5 years was 43.6% and 74.2%, respectively. TNM Stage ($P < 0.001$) and the presence of fibrosis/cirrhosis ($P = 0.002$) were independent predictors of long-term survival in the Cox proportional hazards regression model. Both performing liver resection equal to or greater than hemihepatectomy and combined bile duct resection significantly increased overall survival [hazard ratio, HR = 0.61 (0.38-0.99); $P = 0.044$ and HR = 0.51 (0.31-0.84); $P = 0.008$, respectively] and decreased recurrence rate [HR = 0.59 (0.38-0.91); $P = 0.018$ and HR = 0.61 (0.42-0.89); $P = 0.009$, respectively].

Conclusions: Clinical outcomes were mostly influenced by tumor stage and underlying liver function, and the impact of BDTT to survival seemed less prominent than vascular invasion. Therefore, an aggressive surgical approach, including major liver resection combined with bile duct resection, to increase the chance of R0 resection is strongly recommended.

Keywords: bile duct resection, jaundice, liver resection, prognosis, survival, thrombectomy

(*Ann Surg* 2020;271:913–921)

Invasion of tumor cells into the bile duct and subsequent formation of bile duct tumor thrombus (BDTT) is an unusual but well-known presentation of hepatocellular carcinoma (HCC).[1-3] Although the incidence is low and the overall prognosis is poor, an adequate diagnosis followed by timely and aggressive management can provide long-term survival and a potential cure in selected cases.[4-7]

Often, patients with HCC and BDTT present with clinically evident obstructive jaundice, which is different in nature from

- Retrospective multicenter
- Surgical outcome in B3,B4
- N = 257

TABLE 2. Operative and Pathologic Data of Patients With Comparison Between B3 and B4 Groups

Parameters, n (%)	All (n = 257)	B3 (n = 151)	B4 (n = 106)	P
Surgery				0.321*
Right hemihepatectomy	121 (47.1)	64 (42.4)	57 (53.8)	
Right trisectionectomy	7 (2.7)	5 (3.3)	2 (1.9)	
Left hemihepatectomy	81 (31.5)	48 (31.8)	33 (31.1)	
Left trisectionectomy	2 (0.8)	1 (0.7)	1 (0.9)	
Posterior sectionectomy	5 (1.9)	3 (2.0)	2 (1.9)	
Anterior sectionectomy	12 (4.7)	9 (6.0)	3 (2.8)	
Left lateral sectionectomy	8 (3.1)	7 (4.6)	1 (0.9)	
Left medial sectionectomy	3 (1.2)	3 (2.0)	0 (0)	
Central bisectionectomy	6 (2.3)	4 (2.6)	2 (1.9)	
Nonsystematic resection	10 (3.9)	7 (4.6)	3 (2.8)	
Liver transplantation	2 (0.8)	0 (0)	2 (1.9)	
Liver resection ≥ hemihepatectomy	213 (82.9)	118 (78.1)	95 (89.6)	0.016
Resection of S1 included	69 (26.8)	33 (21.9)	36 (34.0)	0.031
BDR performed	68 (26.5)	19 (12.6)	49 (46.2)	<0.001
Postoperative complications	125 (48.6)	60 (39.7)	65 (61.3)	0.001
Grade in Clavien–Dindo classification†				0.017*
I	29 (11.3)	15 (9.9)	14 (13.2)	
II	27 (10.5)	11 (7.3)	16 (15.1)	
IIIa	52 (20.2)	27 (17.9)	25 (23.6)	
IIIb	3 (1.2)	1 (0.7)	2 (1.9)	
IV	1 (0.4)	0 (0)	1 (0.9)	
V	13 (5.1)	6 (4.0)	7 (6.6)	
Back ground liver status				0.456
Normal	21 (8.2)	13 (8.6)	8 (7.5)	
Chronic hepatitis	71 (27.6)	47 (31.1)	24 (22.6)	
Septal fibrosis	46 (17.9)	25 (16.6)	21 (19.8)	
Cirrhosis	119 (46.3)	66 (43.7)	53 (50.0)	
Multiple tumor	86 (33.5)	50 (33.1)	36 (34.0)	0.887
Tumor size ≥ 5 cm	125 (48.6)	74 (49.0)	51 (48.1)	0.888
Histologic differentiation				0.885
Well (G1)	10 (3.9)	7 (4.6)	3 (2.8)	
Moderate (G2)	136 (52.9)	80 (53.0)	56 (52.8)	
Poor (G3)	91 (35.4)	53 (35.1)	38 (35.8)	
Undifferentiated (G4)	20 (7.8)	11 (7.3)	9 (8.5)	
Microvascular invasion	176 (68.8)	104 (69.3)	72 (67.9)	0.872
Major vascular invasion	69 (26.8)	42 (27.8)	27 (25.5)	0.677
Combined HCC-CCC	12 (4.7)	9 (6.0)	3 (2.8)	0.369*
Microscopic resection margin involvement	58 (22.6)	33 (21.9)	25 (23.6)	0.744
AJCC Stage				0.052*
I	45 (17.5)	32 (21.2)	13 (12.3)	
II	107 (41.6)	52 (34.4)	55 (51.9)	
IIIA	24 (9.3)	15 (9.9)	9 (8.5)	
IIIB	60 (23.3)	39 (25.8)	21 (19.8)	
IIIC	8 (3.1)	4 (2.6)	4 (3.8)	
IVA	8 (3.1)	7 (4.6)	1 (0.9)	
IVB	5 (1.9)	2 (1.3)	3 (2.8)	

*Fisher exact test; others: chi-square test.
†In case a patient has more than 1 complication, the highest grade was counted.
CCC indicates cholangiocellular carcinoma.

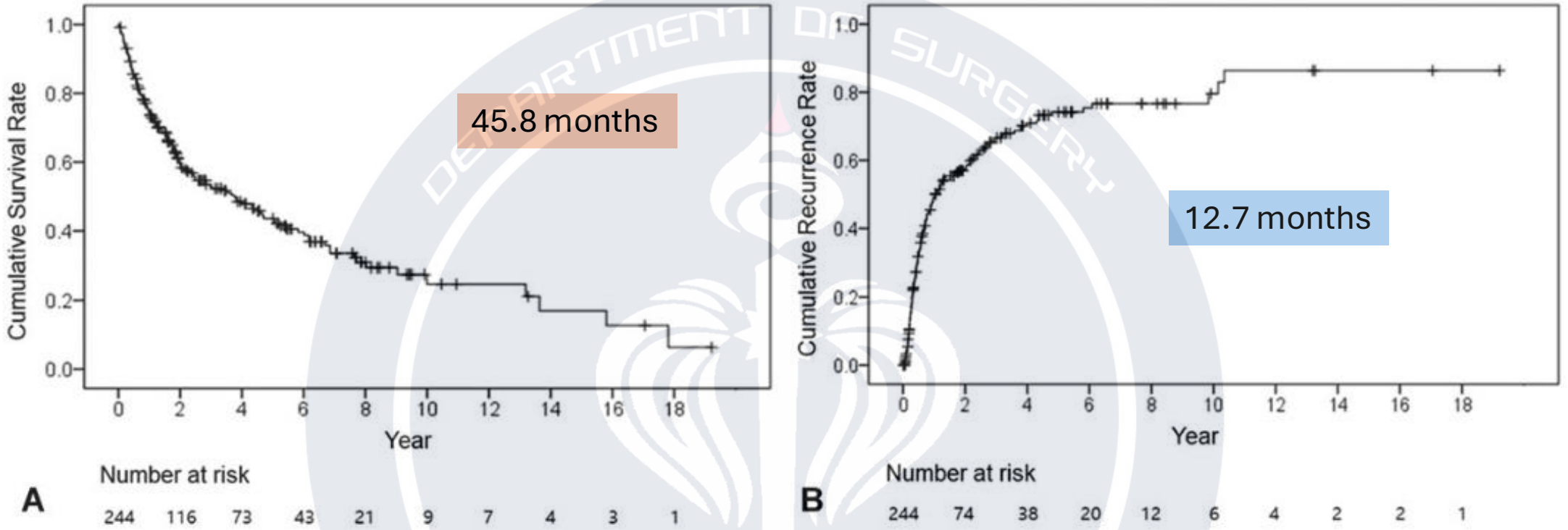
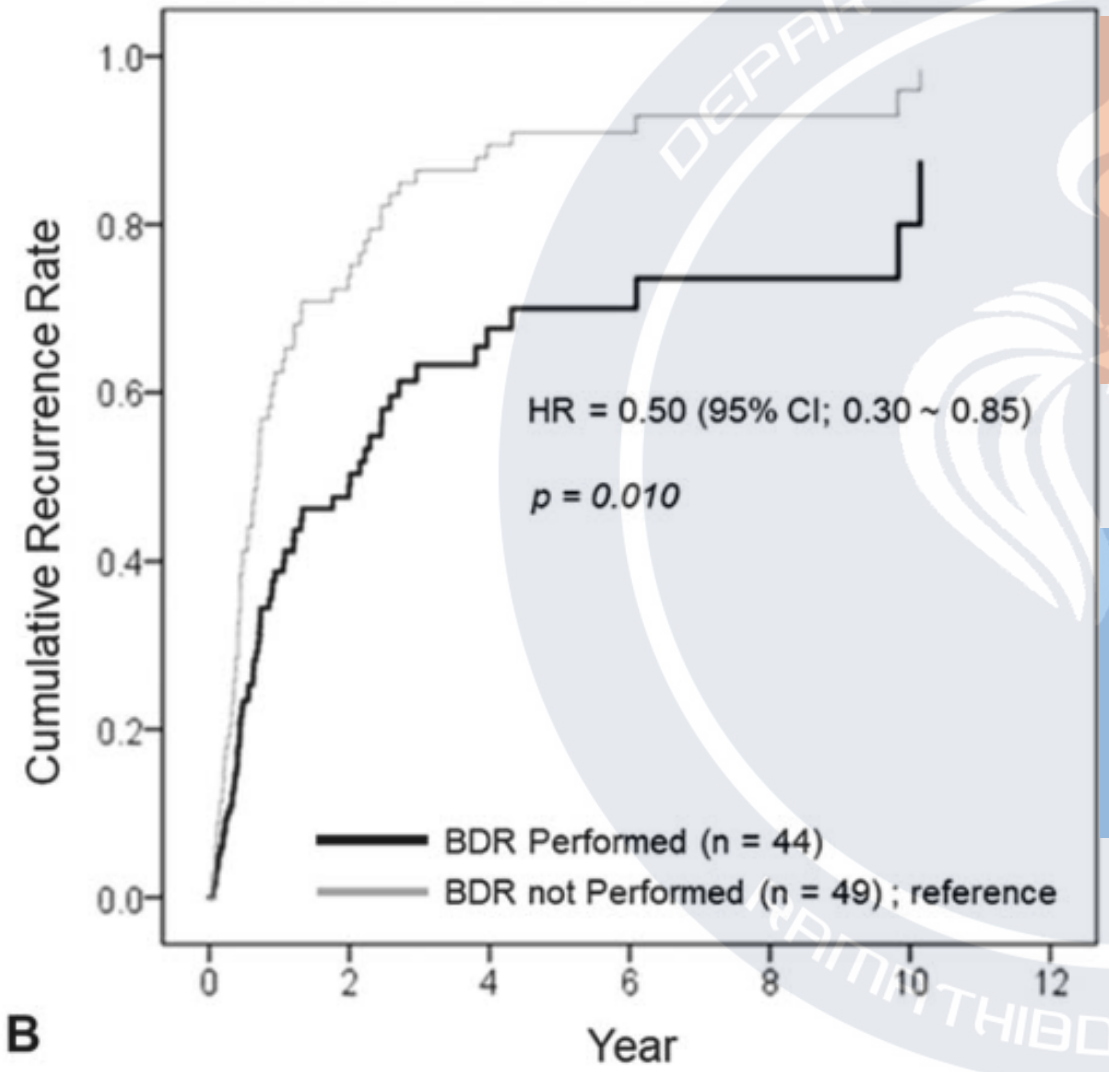


FIGURE 1. (A) Overall survival rate and (B) cumulative recurrence rate of 244 patients who underwent curative-intent surgery for HCC accompanied by macroscopic BDTT in Kaplan-Meier survival analysis.

OS	1-year	3-year	5-year	10-year
Resection	74.5	52.9	43.6	24.7

Cummerative recurrence rate	1-year	3-year	5-year	10-year
Resection	49.2	66.6	74.2	79.6

Overall survival rates and recurrnce rate not difference between at B3 and B4



Liver resection equal to or greater than hemi-hepatectomy + combined BDR

- Improved overall survival HR = 0.61 (0.38-0.99); p= 0.044 and HR= 0.51(0.31-0.84); P= 0.008, respectively
- Decreased recurrence HR = 0.59 (0.38-0.91); P= 0.018 and HR=0.61 (0.42-0.89);P= 0.009

B4 group, the influence of BDR was more significant for both overall survival and recurrence [HR = 0.40 (0.22-0.73); P= 0.003 and HR = 0.50 (0.30-0.85); P= 0.01, respectively

Prognostic Comparison Between Liver Resection and Transcatheter Arterial Chemoembolization for Hepatocellular Carcinoma Patients With Bile Duct Tumor Thrombus: A Propensity-Score Matching Analysis

Zong-Han Liu[1†], Ju-Xian Sun[1†], Jin-Kai Feng[1†], Shi-Ye Yang[1†], Zhen-Hua Chen[2], Chang Liu[1], Zong-Tao Chai[1], Fei-Fei Mao[3], Wei-Xing Guo[1], Jie Shi[1] and Shu-Qun Cheng[1]*

[1] Department of Hepatic Surgery VI, Eastern Hepatobiliary Surgery Hospital, Second Military Medical University, Shanghai, China, [2] Department of General Surgery, Zhejiang Provincial Armed Police Corps Hospital, Hangzhou, China, [3] Tongji University Cancer Center, Shanghai Tenth People's Hospital, Tongji University, Shanghai, China

Background: Hepatocellular carcinoma (HCC) with bile duct tumor thrombus (BDTT) is rare. The aim of this study is to evaluate the long-term prognosis of liver resection (LR) versus transcatheter arterial chemoembolization (TACE) in these patients.

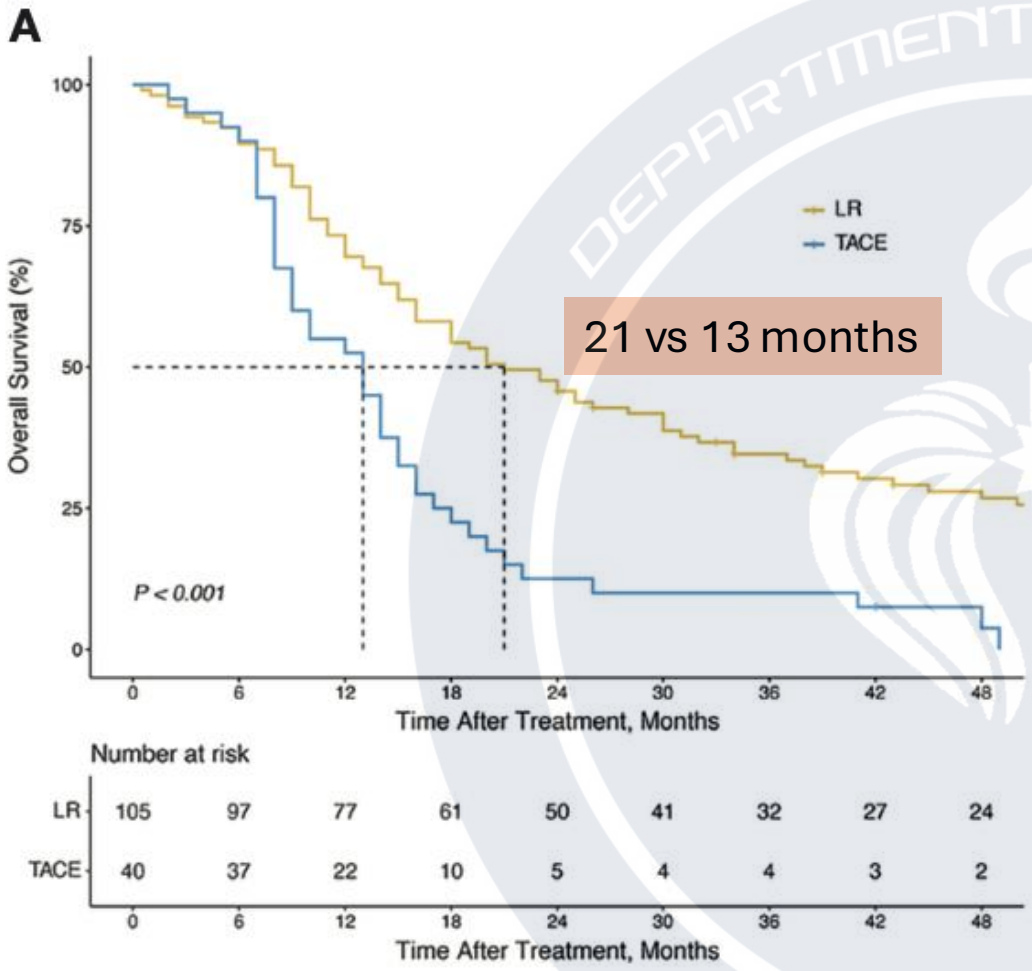
Methods: Data from HCC patients with BDTT who underwent liver resection and TACE were analyzed respectively. Propensity score matching (PSM) analysis was performed in these patients.

Results: A total of 145 HCC patients with BDTT were divided into two groups: the LR group (n = 105) and the TACE group (n = 40). The median OS in the LR group was 8.0 months longer than that in the TACE group before PSM (21.0 vs. 13.0 months, P <0.001) and 9.0 months longer after PSM (20.0 vs. 11.0 months, P <0.001). The median DFS in the LR group was 3.5 months longer than that in the TACE group before PSM (7.0 vs. 3.5 months, P = 0.007) and 5 months longer after PSM (7.0 vs. 2.0 months, P = 0.007).

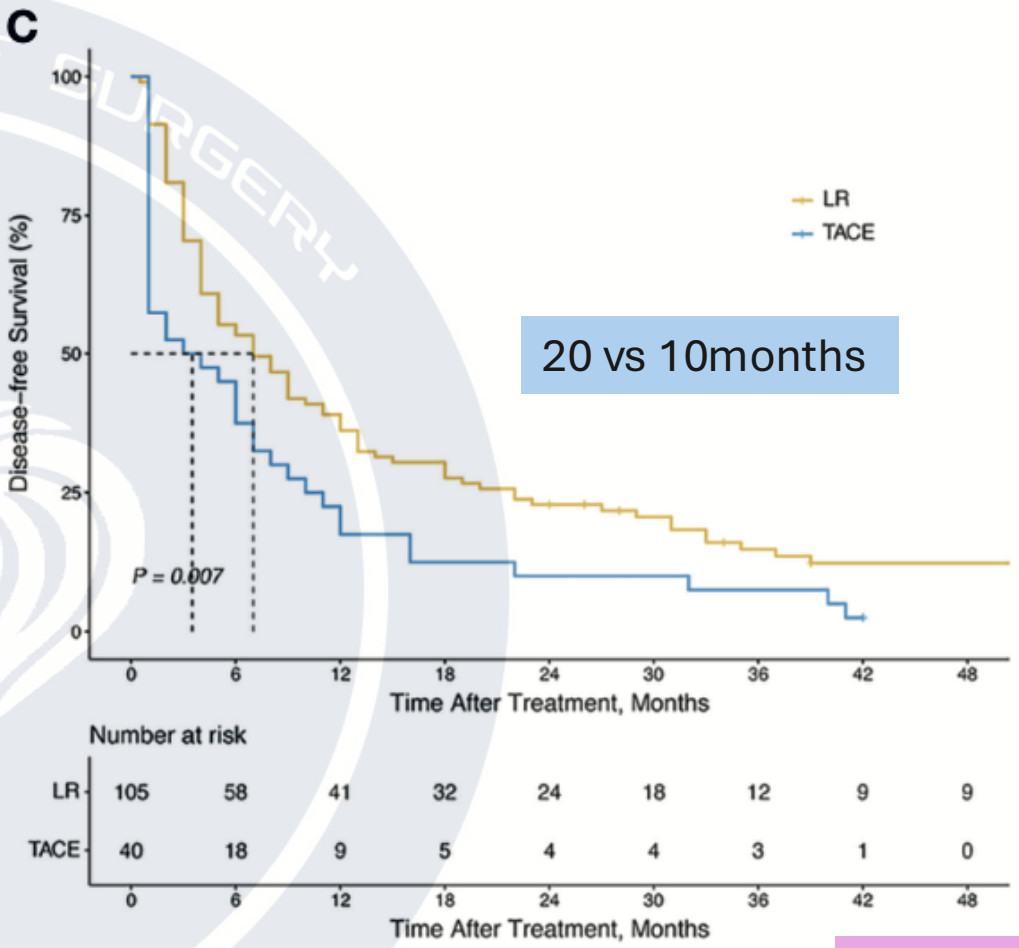
Conclusion: If surgery is technically feasible, liver resection provides better prognosis for HCC patients with BDTT compared with TACE.

Keywords: hepatocellular carcinoma (HCC), bile duct tumor thrombus (BDTT), liver resection, transcatheter arterial chemoembolization (TACE), prognosis

- Retrospective (PSM)
- LR vs TACE in HCC with BDTT
- M = 105 vs 40



21 vs 13 months

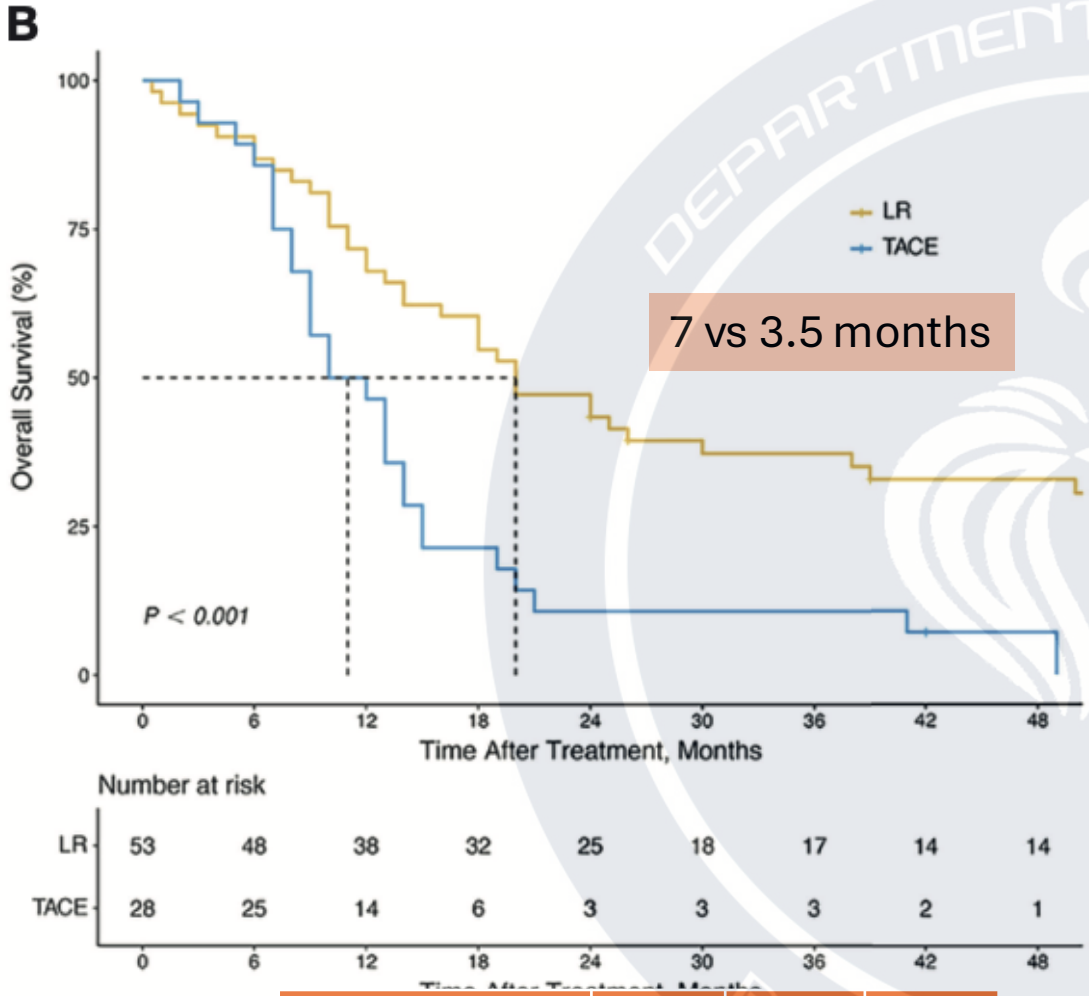


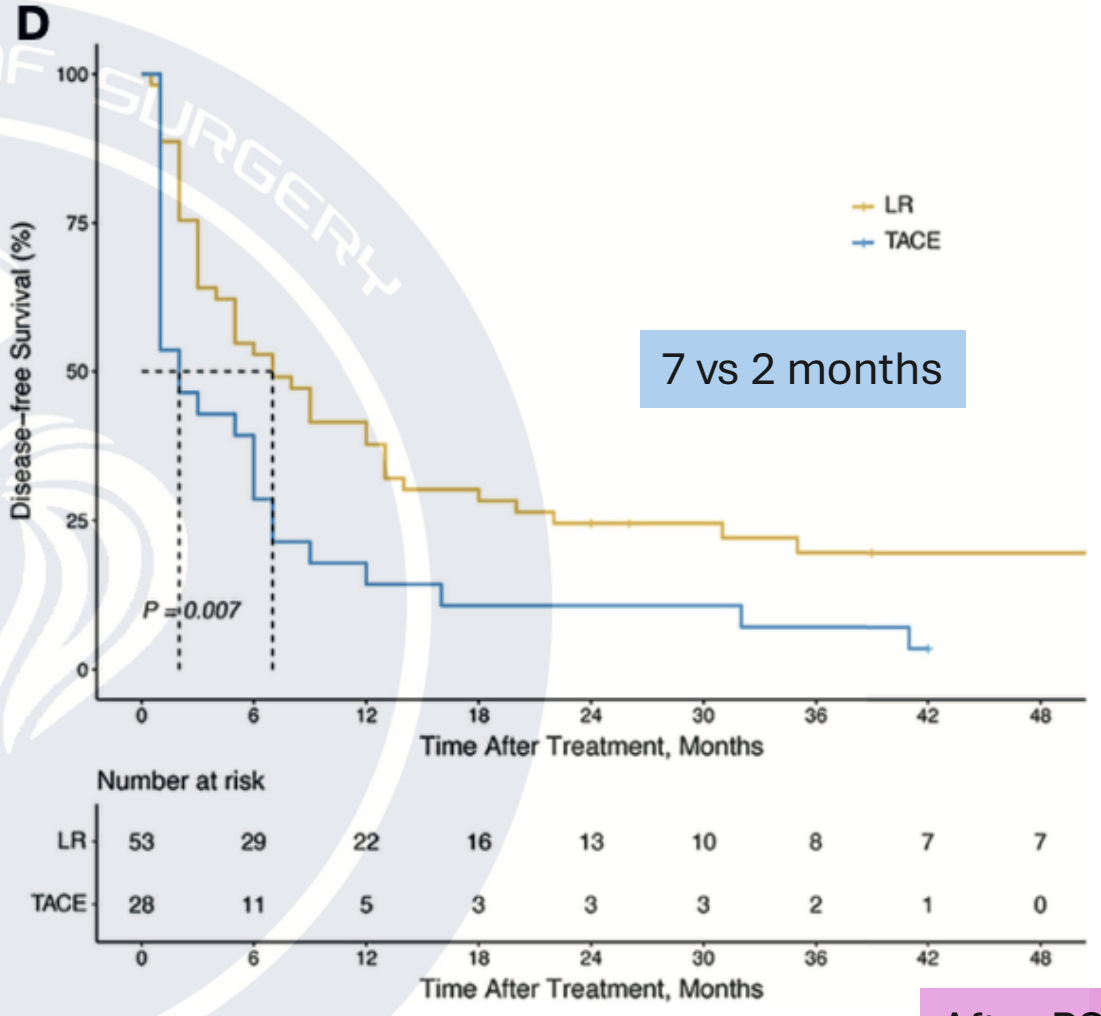
20 vs 10months

After PSM

OS	1-year	2-year	3-year
Resection	69.5	45.7	34.6
TACE	52.5	12.5	10.0

OS	1-year	2-year	3-year
Resection	67.9	43.4	37.7
TACE	46.6	14.3	10.7



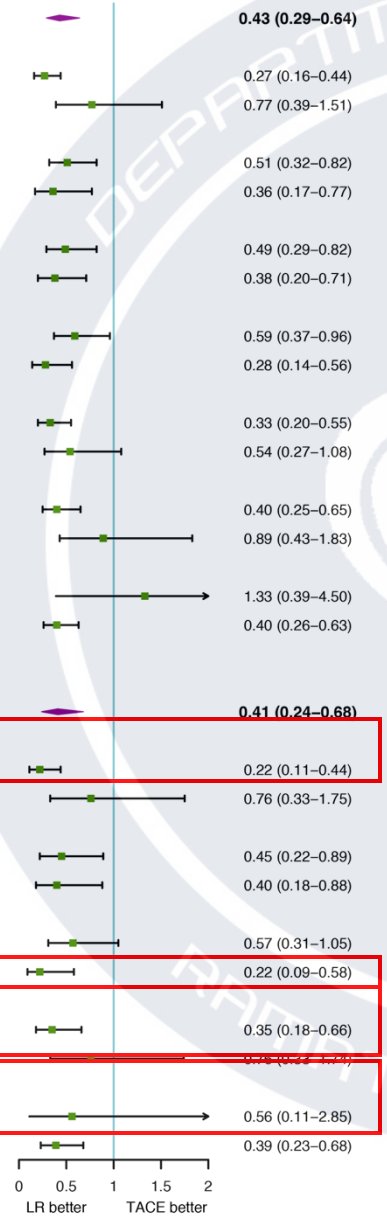


After PSM

DFS	1-year	2-year	3-year
Resection	69.5	45.7	34.6
TACE	52.5	12.5	10.0

DFS	1-year	2-year	3-year
Resection	38.5	25	20
TACE	14.3	14.3	7.1

Subgroup	No. of patients	LR group	TACE group	Hazard Ratio (95% CI)
		MOST (months)		
Before PSM				
All patients	**145**	**21**	**13**	**0.43 (0.29–0.64)**
Child–Pugh class				
A	91	30	13	0.27 (0.16–0.44)
B	54	12	9.5	0.77 (0.39–1.51)
HBsAg				
positive	94	18	12	0.51 (0.32–0.82)
negative	51	30	14	0.36 (0.17–0.77)
HGB				
≤ 30 g/L	81	20	11	0.49 (0.29–0.82)
> 130 g/L	64	30	15.5	0.38 (0.20–0.71)
ALB				
≤ 40 g/L	85	16	12.5	0.59 (0.37–0.96)
> 40 g/L	60	30	14	0.28 (0.14–0.56)
TBIL				
≤ 34 μmol/L	89	25	14	0.33 (0.20–0.55)
> 34 μmol/L	56	14.5	8	0.54 (0.27–1.08)
Tumor number				
solitary	112	25	13	0.40 (0.25–0.65)
multiple	33	11	11	0.89 (0.43–1.83)
Macrovascular invasion				
yes	14	12.5	16	1.33 (0.39–4.50)
no	131	23	12.5	0.40 (0.26–0.63)
After PSM				
All patients	**81**	**20**	**11**	**0.41 (0.24–0.68)**
Child–Pugh class				
A	48	30	13	0.22 (0.11–0.44)
B	33	11	9	0.76 (0.33–1.75)
HGB				
≤ 130 g/L	44	20	10	0.45 (0.22–0.89)
> 130 g/L	37	22.5	15	0.40 (0.18–0.88)
ALB				
≤ 40 g/L	52	17	12.5	0.57 (0.31–1.05)
> 40 g/L	29	39	9	0.22 (0.09–0.58)
Tumor number				
solitary	55	26	11	0.35 (0.18–0.66)
multiple	26	13.5	11	0.76 (0.33–1.72)
Macrovascular invasion				
yes	7	12.5	10	0.56 (0.11–2.85)
no	74	24	12	0.39 (0.23–0.68)



- When technically feasible, liver resection should be the preferred treatment for HCC with BDTT, offering superior OS and DFS compared with TACE.
- Best candidates: well-preserved liver function (Child–Pugh A),single tumor, and absence of major vascular invasion

Bile Duct Preserving Surgery for Hepatocellular Carcinoma With Bile Duct Tumor Thrombus

Peeling-off technique

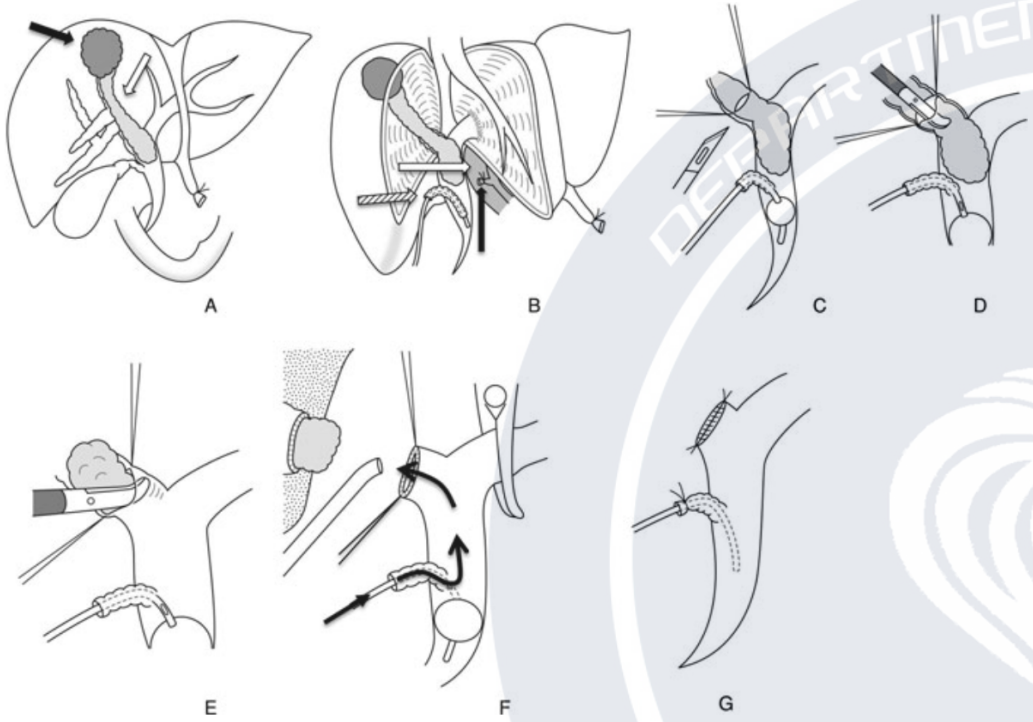


FIGURE 1. A typical case of bile duct preservation. (A) Closed arrow: main viable tumor located in Segment 8. Open arrow: bile duct tumor thrombus. The area from the anterior branch of bile duct to the common bile duct was filled by BDTT on IOUS. (B) Closed arrow: stump of right hepatic artery. The right hepatic artery was ligated and dissected. Open arrow: main portal trunk. Striped arrow: stump of the cystic duct, inserted 6-Fr IOC balloon catheter. Liver parenchymal transection was finished with Pringle maneuver. (C) After suturing 2 points of drawing string, anterior wall was transversely cut near the bifurcation with sharp-pointed scalpel. Before cutting the wall, IOC balloon was inflated. (D, E) BDTT was peeled off from the bile duct intimae using a pair of thin scissors. (F) After peeling off BDTT, right hepatic duct was completely divided. Normal saline was injected for flushing the bile duct with clamp of the left hepatic duct. Normal saline spilling from the stump of anterior branch was carefully sucked out. (G) The stump of the bile duct was closed by running suture and IOC balloon catheter was exchanged with 4- or 5-Fr feeding tube. IOUS indicates intraoperative ultrasonography.

	1-year	3-year	5-year
OS	82.5	38.8	32.5
RFS	35.1	21.9	14.6

Yamamoto S, Hasegawa K, Inoue Y, *et al*. Bile duct preserving surgery for HCC with bile duct tumor thrombus. *Ann Surg*. 2015;261(5):e123–e125.

Conclusion

- **BDTT is not an adverse prognostic factor** in resected HCC.
- When technically feasible, liver resection should be the preferred treatment for HCC with BDTT, offering superior OS and DFS compared with TACE.
- Best candidates: well-preserved liver function (Child–Pugh A), low tumor burden, and absence of major vascular invasion
- **Bile duct preserving surgery** using the peeling-off technique is feasible and safe for selected HCC with BDTT

Rupture HCC

Rupture HCC Management

- Transcatheter arterial embolization (TAE/TACE): effective for hemostasis
  - TACE alone or Bridge to surgery
- Surgery
  - emergency hepatectomy vs. staged hepatectomy
- Microwave coagulation, radiofrequency ablation (limited use)
  - Difficult technique in exophytic tumor or large tumor
- Perihepatic packing >> unstable patient with ineffective or contraindication for TAE
  - High rate of intraabdominal abscess
  - Poor survival
- Hepatic artery ligation >> unstable patient with ineffective or contraindication for TAE
  - High rate hemostasis but high in-hospital mortality
- Conservative: hemodynamic stable, limited role, poor prognosis
  - High rate rebleeding

Surgical Outcomes for the Ruptured Hepatocellular Carcinoma: Multicenter Analysis with a Case-Controlled Study

Shogo Tanaka[1] · Masaki Kaibori[2] · Masaki Ueno[3] · Hiroshi Wada[4] · Fumitoshi Hirokawa[5] · Takuya Nakai[6] · Hiroya Iida[2] · Hidetoshi Eguchi[4] · Michihiro Hayashi[5] · Shoji Kubo[1]

- Stage resection (TAE+conservative) >> 53
- Emergency resection >> 5
- Overall Perioperative mortality 12%
- 60%(3/5) in emergency resection group

Received: 20 July 2016 / Accepted: 13 September 2016 / Published online: 7 October 2016

Abstract

Background While spontaneously ruptured hepatocellular carcinoma (HCC) has a poor prognosis, the true impact of a rupture on survival after hepatic resection is unclear.

Methods Fifty-eight patients with ruptured HCC and 1922 with non-ruptured HCC underwent hepatic resection between 2000 and 2013. To correct the difference in the clinicopathological factors between the two groups, propensity score matching (PSM) was used at a 1:1 ratio, resulting in a comparison of 42 patients/group. We investigated outcomes in all patients with ruptured HCC and compared outcomes between the two matched groups.

Results Of the 58 patients with ruptured HCC, 7 patients (13 %) died postoperatively. Overall survival (OS) rate at 5 years after hepatic resection was 37 %. Emergency hepatic resection was an independent risk factor for in-hospital death and Child-Pugh class B for unfavorable OS in multivariate analysis. Clinicopathological variables were well-balanced between the two groups after PSM. No significant differences were noted in incidence of in-hospital death (ruptured HCC 12 % vs non-ruptured HCC 2 %, $p = 0.202$) or OS rate (5/10-year; 42 %/38 % vs 67 %/30 %, $p = 0.115$).

Conclusion Emergency hepatic resection should be avoided for ruptured HCC in Child-Pugh class B patients. Rupture itself was not a risk for unfavorable surgical outcomes.

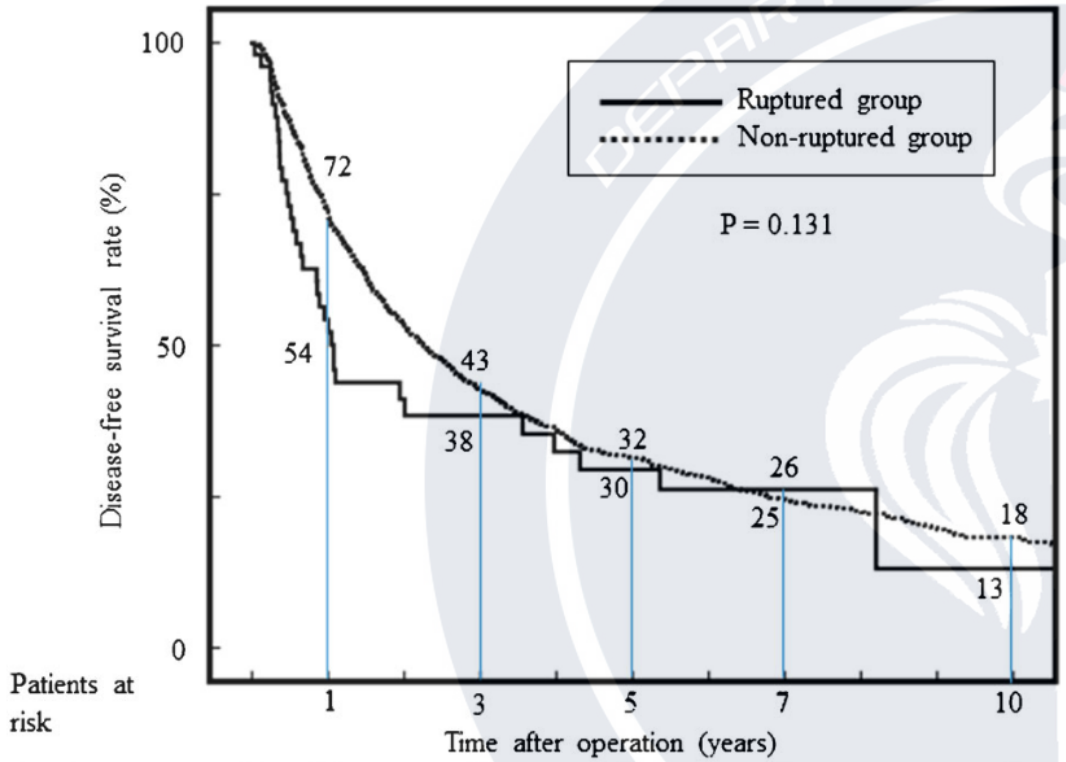


Fig. 1 The disease-free survival rate after hepatic resection for patients with a ruptured hepatocellular carcinoma (ruptured group) and those with a non-ruptured hepatocellular carcinoma (non-ruptured group) among all populations (before propensity score matching)

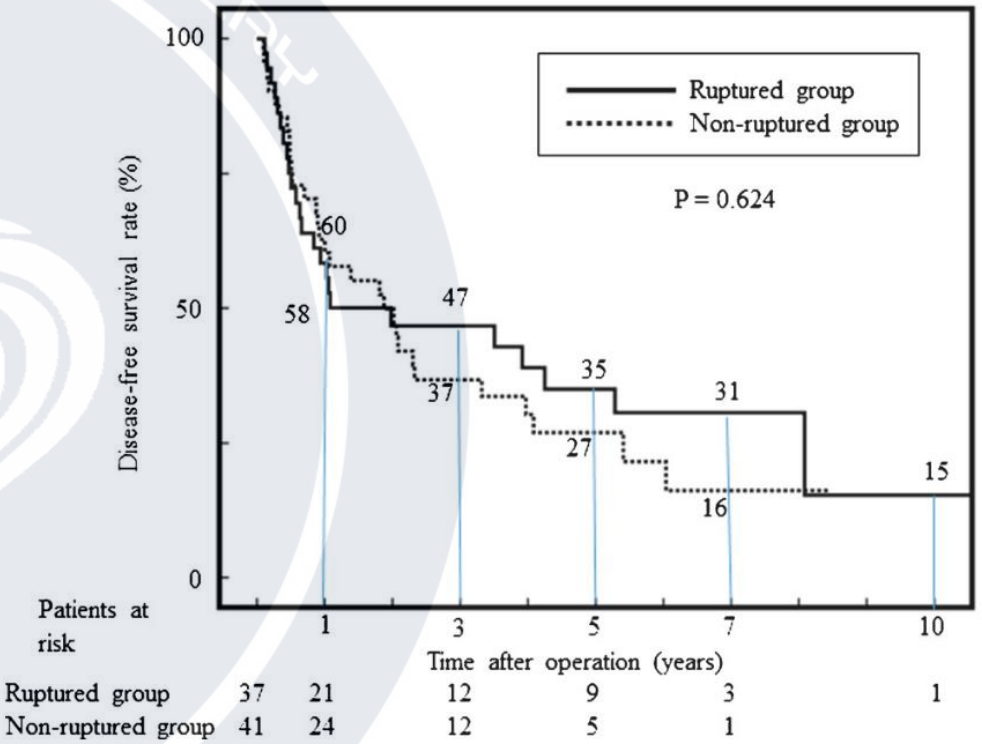


Fig. 3 The disease-free survival rate after hepatic resection for patients with a ruptured hepatocellular carcinoma (ruptured group) and those with a non-ruptured hepatocellular carcinoma (non-ruptured group) after propensity score matching

After PSM

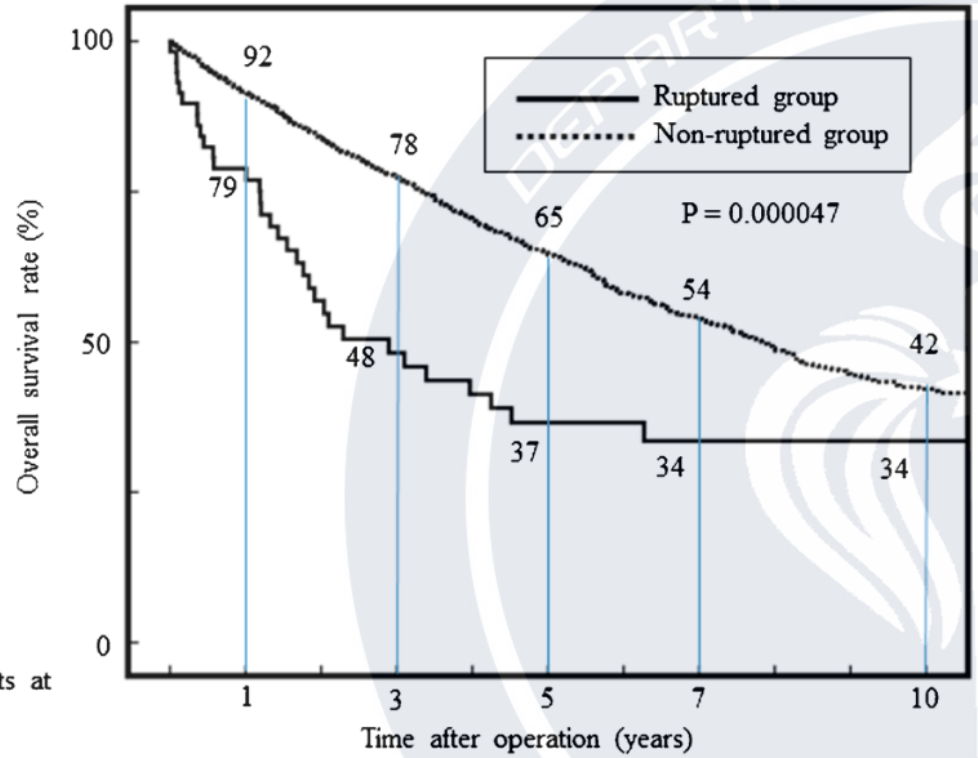


Fig. 2 The overall survival rate after hepatic resection for patients with a ruptured hepatocellular carcinoma (ruptured group) and those with a non-ruptured hepatocellular carcinoma (non-ruptured group) among all populations (before propensity score matching)

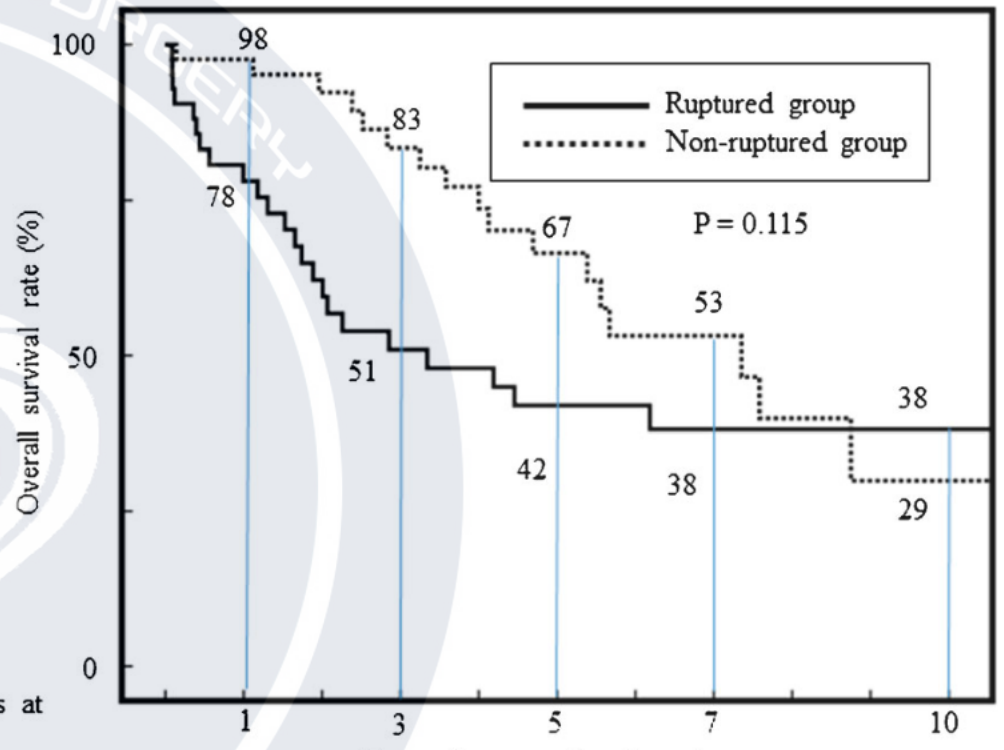


Fig. 4 The overall survival rate after hepatic resection for patients with a ruptured hepatocellular carcinoma (ruptured group) and those with a non-ruptured hepatocellular carcinoma (non-ruptured group) after propensity score matching

After PSM

Emergency transarterial embolization followed by staged hepatectomy versus emergency hepatectomy for ruptured hepatocellular carcinoma: a single-center, propensity score matched analysis

Chun Zhou[1] · Chu Zhang[1] · Qing-Quan Zu[1] · Bin Wang[1] · Chun-Gao Zhou[1] · Hai-Bin Shi[1] · Sheng Liu[1]

Received: 16 February 2020 / Accepted: 14 June 2020 / Published online: 20 June 2020

Retrospective
- Resectable rupture HCC
- Stage hepatectomy(after TAE) vs Emergency hepatectomy

Abstract

Purpose To compare the feasibility and efficacy of emergency transarterial embolization (TAE) follow tectomy (SH) with emergency hepatectomy (EH) for ruptured hepatocellular carcinoma (HCC).

Methods Between January 2012 and December 2017, 102 patients with HCC rupture received EH or emergency TAE followed by SH in our center. Patients were followed until April 2019. Propensity score matching (PSM) analysis was used at a 1:2 ratio, resulting in 20 patients in the SH group and 40 patients in the EH group. We retrospectively compared the operative variables, recurrence status, disease-free survival (DFS), and overall survival (OS) of patients between the two matched groups.

Results Compared with the matched EH group, the SH group showed significantly decreased perioperative blood loss or blood transfusion, shortened intraoperative duration of clamping and postoperative hospital stay ($P<0.05$), while achieving comparable long-term OS (SH group: 39.0 months vs. EH group: 38.1 months, $P=0.342$). There was no significant difference in the peritoneal metastasis rate (SH group: 20.0% vs. EH group: 25.6%, $P=0.874$), recurrence rate (SH group: 65.0% vs. EH group: 71.8%, $P=0.333$) or DFS (SH group: 9.4 months vs. EH group: 7.7 months, $P=0.602$) between the two matched groups.

Conclusion For resectable ruptured HCC, emergency TAE of rupture which followed by SH, could bring patients about intraoperative and postoperative benefits when compared to EH. Moreover, this combination treatment will not increase the rate of peritoneal metastasis or recurrence, and might achieve favorable survival benefits for patients.

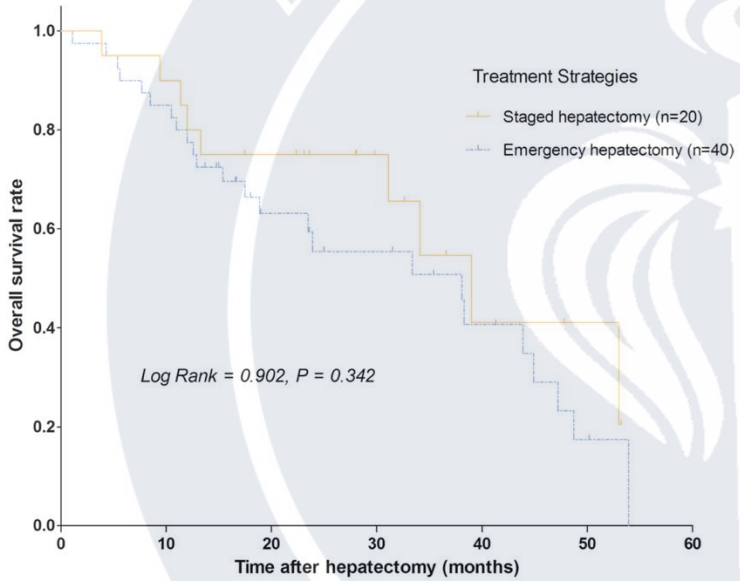
Keywords Hepatocellular carcinoma · Rupture · Emergency hepatectomy · Staged hepatectomy · Prognosis

Table 2 Participant operative variables of ruptured HCC patients treated with curative resection after PSM

Participant operative variables	SH group ($n=20$)	EH group ($n=40$)	χ^2/t	*P* value
Extent of hepatectomy			–	1.000
Minor, *n* (%)	17 (85.0)	35 (87.5)		
Major, *n* (%)	3 (15.0)	5 (12.5)		
Perioperative blood loss (mL)	588 ± 458	1855 ± 1292	5.546	< 0.001
RBC transfusion (mL)	420 ± 538	1223 ± 941	4.196	< 0.001
Operating time (min)	138 ± 31	153 ± 50	1.446	0.154
Duration of clamping (min)	16 ± 4	21 ± 9	2.778	0.007
Postoperative ICU admission, *n* (%)	1 (5.0)	8 (20.0)	1.324	0.250
Major complications, *n* (%)	2 (10.0)	9 (22.5)	0.682	0.409
Pneumonia	1	1		
Pleural effusion	1	2		
Perihepatic abscess	0	1		
Liver failure	0	4		
Heart failure	0	1		
Postoperative hospital stay (days)	11 ± 3	14 ± 6	2.120	0.038
In-hospital death, *n* (%)	0 (0.0)	1 (2.5)	–	1.000

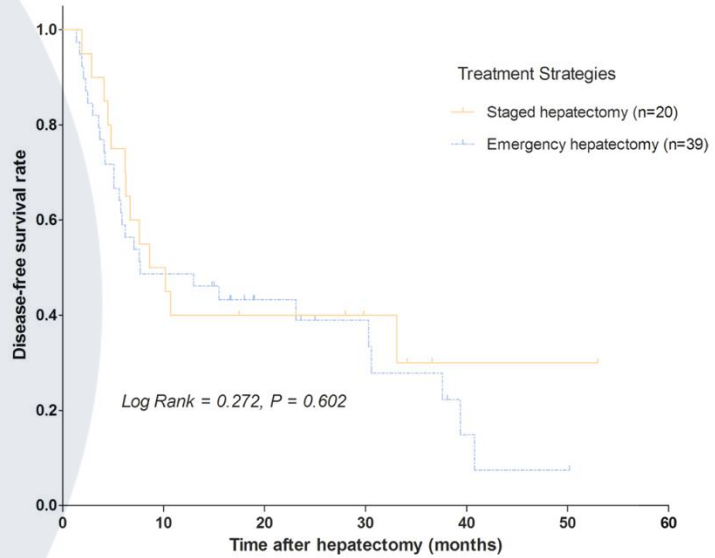
PSM propensity score matching, *SH* staged hepatectomy, *EH* emergency hepatectomy, *RBC* red blood cell

Fig. 2 Overall survival curves stratified according to different surgical methods (staged or emergency hepatectomy) after propensity score matching



No. at risk						
Staged hepatectomy	20	19	14	9	4	3
Emergency hepatectomy	40	34	18	13	8	2

Fig. 4 Disease-free survival curves stratified according to different surgical methods (staged or emergency hepatectomy) after propensity score matching



No. at risk						
Staged hepatectomy	20	10	8	5	2	1
Emergency hepatectomy	39	20	11	7	3	1

OS and DFS >> not significant

A Meta-analysis of TAE/TACE Versus Emergency Surgery in the Treatment of Ruptured HCC

Xinjian Xu[1,2] · Changsheng Chen[3] · Qiang Liu[1] · Xiangzhong Huang[2]

Received: 29 December 2019 / Accepted: 2 May 2020 / Published online: 21 May 2020

Abstract

Objectives To evaluate the efficacy and safety of TAE/TACE versus emergency surgery (ES) for spontaneous rupture of HCC (rHCC).

Methods Eight databases (Web of Science, Pubmed, Embase, Cochrane Library, ClinicalTrial.gov, Wanfang, CNKI and VIP) were searched to obtain all related literature from the inception dates to October 2019. Subgroup analyses based on the kind of study design and kind of embolization were conducted.

Results Twenty-one studies comparing TAE/TACE with ES were eligible. A total of 974 rHCC participants (485 participants treated with TACE/TAE and 489 participants treated with ES) were included in the present meta-analysis. TAE/TACE group was associated with lower risk of complications (OR = 0.36; 95% CI, 0.22–0.57; $P < 0.0001$) and in-hospital mortality (OR = 0.52; 95% CI, 0.29–0.94; $P = 0.03$) compared with ES group. In addition, no significant difference in successful hemostasis (OR = 1.67; 95% CI, 0.85–3.28; $P = 0.13$) and 1-year survival (OR = 1.08; 95% CI, 0.79–1.48; $P = 0.64$) between TAE/TACE and ES groups was demonstrated.

Conclusions TAE/TACE had comparable outcomes to ES in terms of successful hemostasis and 1-year survival. Meanwhile, TAE/TACE was significantly superior to ES in terms of complications and in-hospital mortality. Therefore, TAE/TACE may be recommended as a preferable treatment for rHCC.

Keywords Rupture · HCC · TAE · TACE · Emergency surgery

Xin Jian Xu and Changsheng Chen are contributed equally to this work and should be considered Co-first authors.

Xiang Zhong Huang and Qiang Liu are contributed equally to this work and should be considered Co-corresponding author.

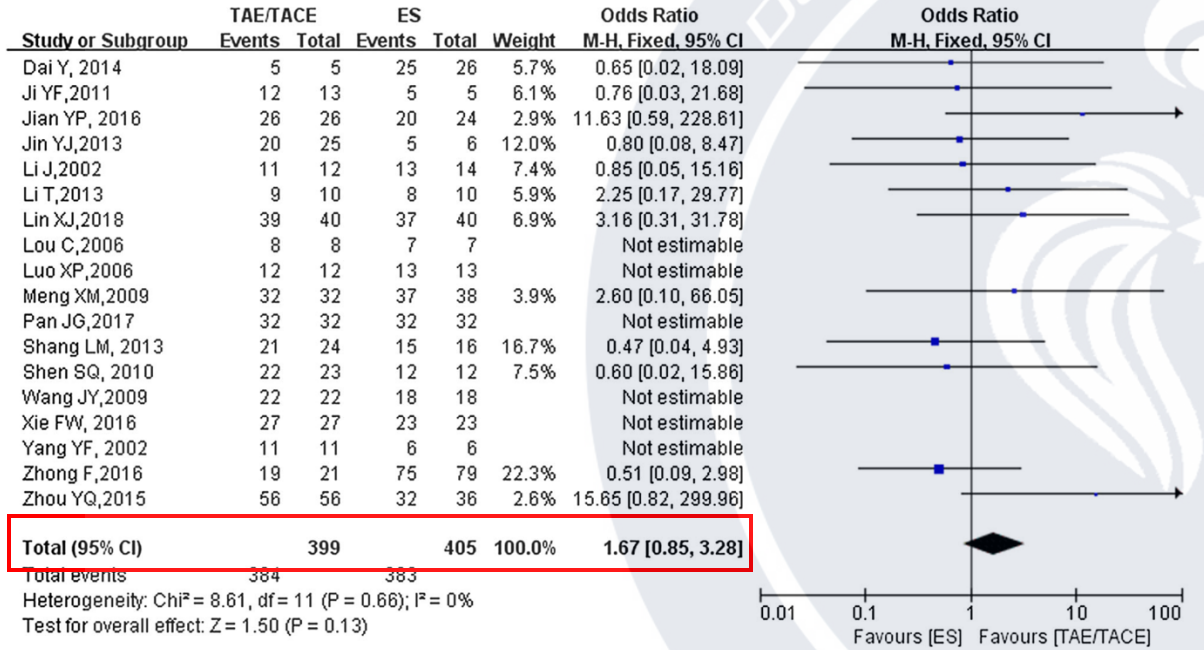
Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00270-020-02514-5) contains supplementary material, which is available to authorized users.

✉ Qiang Liu
liuqiangdoc@163.com

✉ Xiangzhong Huang
hxzdoc@163.com

Xinjian Xu
kg529452183@163.com

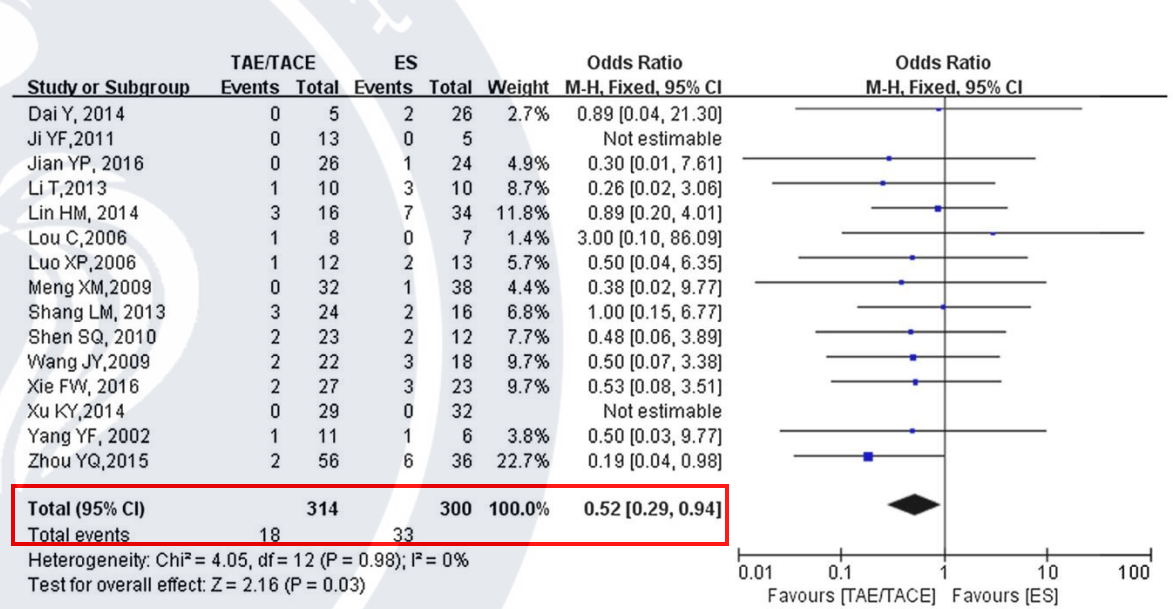
Changsheng Chen
ccsfsk@126.com



Study or Subgroup	TAE/TACE Events	TAE/TACE Total	ES Events	ES Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Dai Y, 2014	5	5	25	26	5.7%	0.65 [0.02, 18.09]
Ji YF,2011	12	13	5	5	6.1%	0.76 [0.03, 21.68]
Jian YP, 2016	26	26	20	24	2.9%	11.63 [0.59, 228.61]
Jin YJ,2013	20	25	5	6	12.0%	0.80 [0.08, 8.47]
Li J,2002	11	12	13	14	7.4%	0.85 [0.05, 15.16]
Li T,2013	9	10	8	10	5.9%	2.25 [0.17, 29.77]
Lin XJ,2018	39	40	37	40	6.9%	3.16 [0.31, 31.78]
Lou C,2006	8	8	7	7		Not estimable
Luo XP,2006	12	12	13	13		Not estimable
Meng XM,2009	32	32	37	38	3.9%	2.60 [0.10, 66.05]
Pan JG,2017	32	32	32	32		Not estimable
Shang LM, 2013	21	24	15	16	16.7%	0.47 [0.04, 4.93]
Shen SQ, 2010	22	23	12	12	7.5%	0.60 [0.02, 15.86]
Wang JY,2009	22	22	18	18		Not estimable
Xie FW, 2016	27	27	23	23		Not estimable
Yang YF, 2002	11	11	6	6		Not estimable
Zhong F,2016	19	21	75	79	22.3%	0.51 [0.09, 2.98]
Zhou YQ,2015	56	56	32	36	2.6%	15.65 [0.82, 299.96]
Total (95% CI)		**399**		**405**	**100.0%**	**1.67 [0.85, 3.28]**
Total events	384		383			

Heterogeneity: Chi² = 8.61, df = 11 (P = 0.66); I² = 0%
Test for overall effect: Z = 1.50 (P = 0.13)

Fig. 4 Forest plots for successful hemostasis between TAE/TACE and ES for rHCC



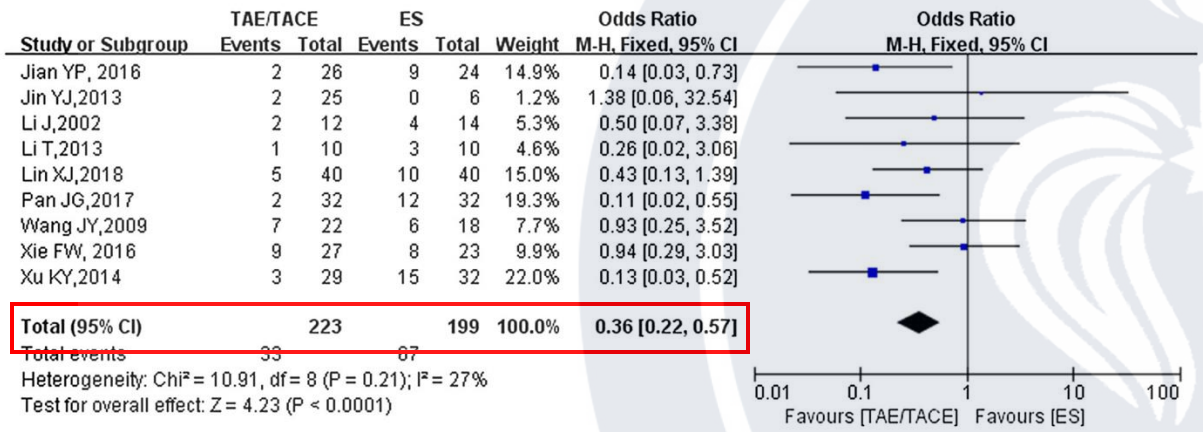
Study or Subgroup	TAE/TACE Events	TAE/TACE Total	ES Events	ES Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Dai Y, 2014	0	5	2	26	2.7%	0.89 [0.04, 21.30]
Ji YF,2011	0	13	0	5		Not estimable
Jian YP, 2016	0	26	1	24	4.9%	0.30 [0.01, 7.61]
Li T,2013	1	10	3	10	8.7%	0.26 [0.02, 3.06]
Lin HM, 2014	3	16	7	34	11.8%	0.89 [0.20, 4.01]
Lou C,2006	1	8	0	7	1.4%	3.00 [0.10, 86.09]
Luo XP,2006	1	12	2	13	5.7%	0.50 [0.04, 6.35]
Meng XM,2009	0	32	1	38	4.4%	0.38 [0.02, 9.77]
Shang LM, 2013	3	24	2	16	6.8%	1.00 [0.15, 6.77]
Shen SQ, 2010	2	23	2	12	7.7%	0.48 [0.06, 3.89]
Wang JY,2009	2	22	3	18	9.7%	0.50 [0.07, 3.38]
Xie FW, 2016	2	27	3	23	9.7%	0.53 [0.08, 3.51]
Xu KY,2014	0	29	0	32		Not estimable
Yang YF, 2002	1	11	1	6	3.8%	0.50 [0.03, 9.77]
Zhou YQ,2015	2	56	6	36	22.7%	0.19 [0.04, 0.98]
Total (95% CI)		**314**		**300**	**100.0%**	**0.52 [0.29, 0.94]**
Total events	18		33			

Heterogeneity: Chi² = 4.05, df = 12 (P = 0.98); I² = 0%
Test for overall effect: Z = 2.16 (P = 0.03)

Fig. 5 Forest plots for in-hospital mortality between TAE/TACE and ES for rHCC

Hemostasis >> not significant

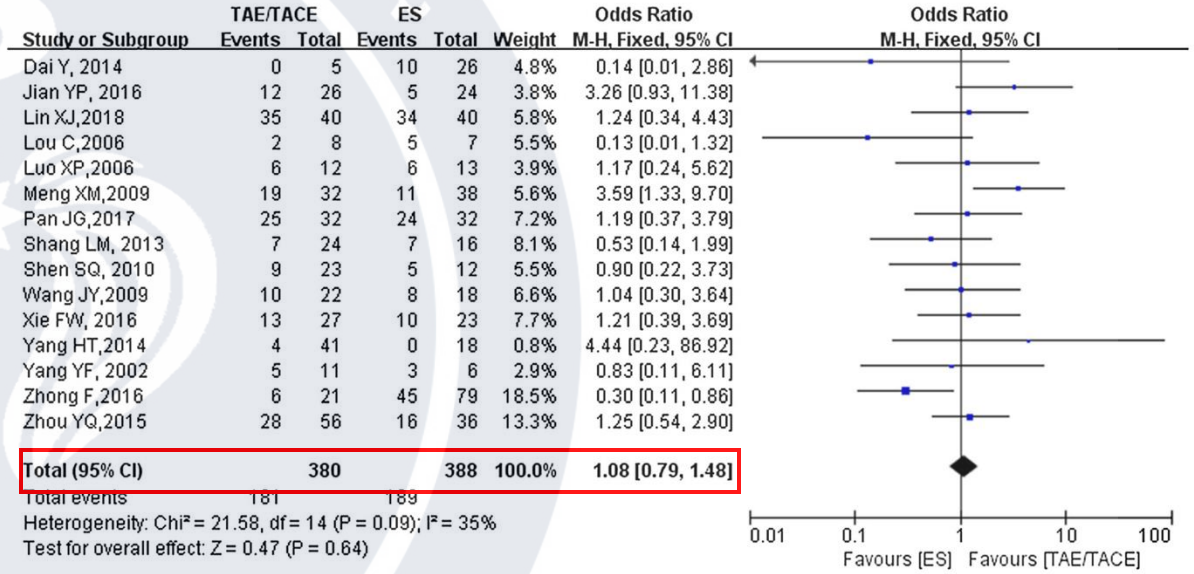
Mortality >> TAE group significant lower



Study or Subgroup	TAE/TACE Events	TAE/TACE Total	ES Events	ES Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Jian YP, 2016	2	26	9	24	14.9%	0.14 [0.03, 0.73]
Jin YJ,2013	2	25	0	6	1.2%	1.38 [0.06, 32.54]
Li J,2002	2	12	4	14	5.3%	0.50 [0.07, 3.38]
Li T,2013	1	10	3	10	4.6%	0.26 [0.02, 3.06]
Lin XJ,2018	5	40	10	40	15.0%	0.43 [0.13, 1.39]
Pan JG,2017	2	32	12	32	19.3%	0.11 [0.02, 0.55]
Wang JY,2009	7	22	6	18	7.7%	0.93 [0.25, 3.52]
Xie FW, 2016	9	27	8	23	9.9%	0.94 [0.29, 3.03]
Xu KY,2014	3	29	15	32	22.0%	0.13 [0.03, 0.52]
Total (95% CI)		**223**		**199**	**100.0%**	**0.36 [0.22, 0.57]**
Total events	33		67			

Heterogeneity: Chi² = 10.91, df = 8 (P = 0.21); I² = 27%
Test for overall effect: Z = 4.23 (P < 0.0001)

Fig. 6 Forest plots for complications between TAE/TACE and ES for rHCC



Study or Subgroup	TAE/TACE Events	TAE/TACE Total	ES Events	ES Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Dai Y, 2014	0	5	10	26	4.8%	0.14 [0.01, 2.86]
Jian YP, 2016	12	26	5	24	3.8%	3.26 [0.93, 11.38]
Lin XJ,2018	35	40	34	40	5.8%	1.24 [0.34, 4.43]
Lou C,2006	2	8	5	7	5.5%	0.13 [0.01, 1.32]
Luo XP,2006	6	12	6	13	3.9%	1.17 [0.24, 5.62]
Meng XM,2009	19	32	11	38	5.6%	3.59 [1.33, 9.70]
Pan JG,2017	25	32	24	32	7.2%	1.19 [0.37, 3.79]
Shang LM, 2013	7	24	7	16	8.1%	0.53 [0.14, 1.99]
Shen SQ, 2010	9	23	5	12	5.5%	0.90 [0.22, 3.73]
Wang JY,2009	10	22	8	18	6.6%	1.04 [0.30, 3.64]
Xie FW, 2016	13	27	10	23	7.7%	1.21 [0.39, 3.69]
Yang HT,2014	4	41	0	18	0.8%	4.44 [0.23, 86.92]
Yang YF, 2002	5	11	3	6	2.9%	0.83 [0.11, 6.11]
Zhong F,2016	6	21	45	79	18.5%	0.30 [0.11, 0.86]
Zhou YQ,2015	28	56	16	36	13.3%	1.25 [0.54, 2.90]
Total (95% CI)		**380**		**388**	**100.0%**	**1.08 [0.79, 1.48]**
Total events	181		189			

Heterogeneity: Chi² = 21.58, df = 14 (P = 0.09); I² = 35%
Test for overall effect: Z = 0.47 (P = 0.64)

Fig. 7 Forest plots for 1-year survival between TAE/TACE and ES for rHCC

Complication >> lower in TAE group

1-year survival >> not significant

Transarterial embolization followed by staged hepatectomy versus emergency hepatectomy for ruptured HCC: a meta-analysis

Tianfan Pan[1,2] · Feng Gao[1] · Xiangzhong Huang[1] · Xinjian Xu[1]

Received: 25 February 2023 / Accepted: 25 May 2023 / Published online: 16 June 2023

Abstract

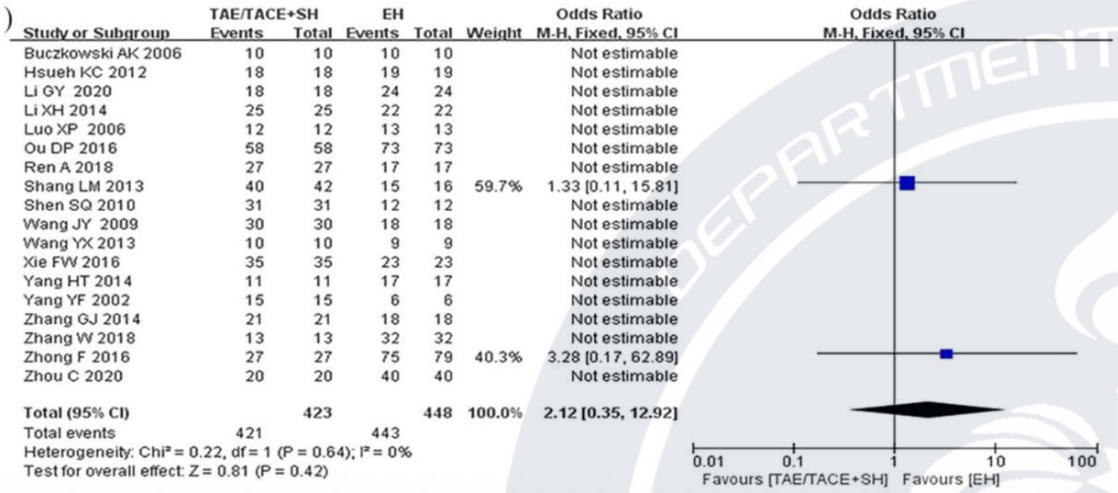
Background To compare the efficacy and safety between emergency hepatectomy (EH) and emergency transarterial embolization (TAE) followed by staged hepatectomy (SH) in the treatment of spontaneous ruptured hepatocellular carcinoma (rHCC).

Methods Databases (PubMed, EMBASE, Web of science, Cochrane Library, ClinicalTrial.gov, CNKI, Wanfang and VIP) were searched for all relevant comparative studies from January 2000 to October 2020. Odds ratio (*OR*) and mean difference (*MD*) with 95% confidence interval (*CI*) were pooled for dichotomous and continuous variables, respectively. Subgroup analyses based on the kind of embolization were conducted. RevMan 5.3 software was adopted for meta-analysis.

Results Eighteen studies with 871 patients were finally included in this meta-analysis, 448 in EH group and 423 in TAE + SH group. No significant difference was observed in successful hemostasis ($P = 0.42$), postoperative hospital stay ($P = 0.12$), complication rate ($P = 0.08$) between EH and TAE + SH group. However, TAE + SH group was associated with shorter operating time ($P < 0.00001$), fewer perioperative blood loss ($P = 0.007$), fewer blood transfusion ($P = 0.003$), lower in-hospital mortality ($P < 0.00001$) and higher 1-year survival as well as 3-year survival ($P < 0.0001$; $P = 0.003$) compared with EH group.

Conclusion Compared with EH, TAE + SH could reduce perioperative operating time, blood loss, blood transfusion, mortality rate and increase the long-term survival rate of the rHCC patients, which may be a better treatment for resectable rHCC.

(A)



Study or Subgroup	TAE/TACE+SH Events	Total	EH Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Buczkowski AK 2006	10	10	10	10		Not estimable
Hsueh KC 2012	18	18	19	19		Not estimable
Li GY 2020	18	18	24	24		Not estimable
Li XH 2014	25	25	22	22		Not estimable
Luo XP 2006	12	12	13	13		Not estimable
Ou DP 2016	58	58	73	73		Not estimable
Ren A 2018	27	27	17	17		Not estimable
Shang LM 2013	40	42	15	16	59.7%	1.33 [0.11, 15.81]
Shen SQ 2010	31	31	12	12		Not estimable
Wang JY 2009	30	30	18	18		Not estimable
Wang YX 2013	10	10	9	9		Not estimable
Xie FW 2016	35	35	23	23		Not estimable
Yang HT 2014	11	11	17	17		Not estimable
Yang YF 2002	15	15	6	6		Not estimable
Zhang GJ 2014	21	21	18	18		Not estimable
Zhang W 2018	13	13	32	32		Not estimable
Zhong F 2016	27	27	75	79	40.3%	3.28 [0.17, 62.89]
Zhou C 2020	20	20	40	40		Not estimable
Total (95% CI)		423		448	100.0%	2.12 [0.35, 12.92]
Total events	421		443			

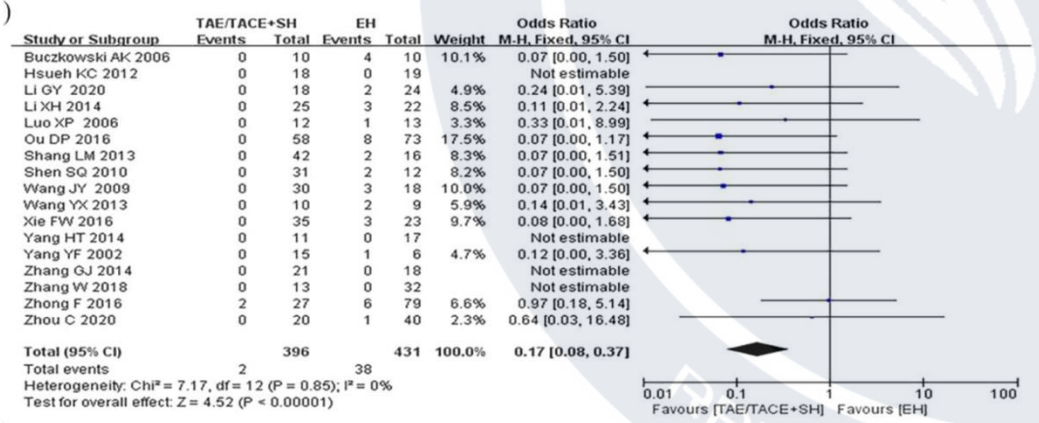
Heterogeneity: Chi² = 0.22, df = 1 (P = 0.64); I² = 0%
Test for overall effect: Z = 0.81 (P = 0.42)

Odds Ratio M-H, Fixed, 95% CI

0.01 0.1 1 10 100
Favours [TAE/TACE+SH] Favours [EH]

Successful hemostasis >> no significant

(B)

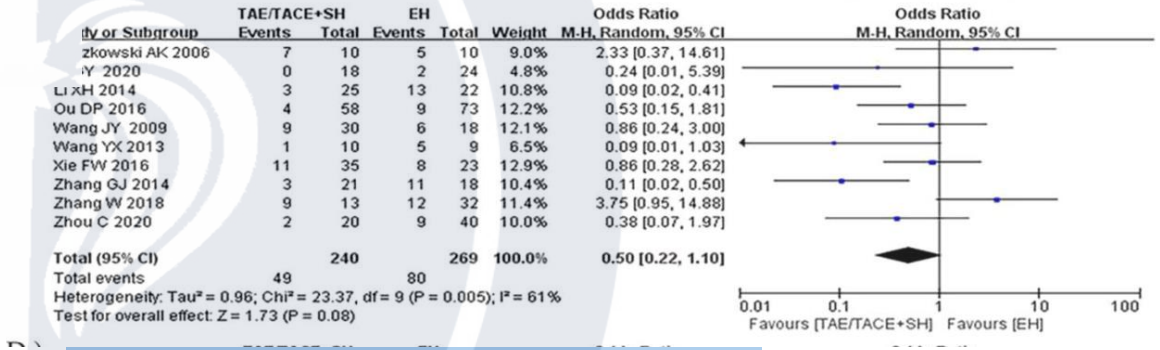


Study or Subgroup	TAE/TACE+SH Events	Total	EH Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Buczkowski AK 2006	0	10	4	10	10.1%	0.07 [0.00, 1.50]
Hsueh KC 2012	0	18	0	19		Not estimable
Li GY 2020	0	18	2	24	4.9%	0.24 [0.01, 5.39]
Li XH 2014	0	25	3	22	8.5%	0.11 [0.01, 2.24]
Luo XP 2006	0	12	1	13	3.3%	0.33 [0.01, 8.99]
Ou DP 2016	0	58	8	73	17.5%	0.07 [0.00, 1.17]
Shang LM 2013	0	42	2	16	8.3%	0.07 [0.00, 1.51]
Shen SQ 2010	0	31	2	12	8.2%	0.07 [0.00, 1.50]
Wang JY 2009	0	30	3	18	10.0%	0.07 [0.00, 1.50]
Wang YX 2013	0	10	2	9	5.9%	0.14 [0.01, 3.43]
Xie FW 2016	0	35	3	23	9.7%	0.08 [0.00, 1.68]
Yang HT 2014	0	11	0	17		Not estimable
Yang YF 2002	0	15	1	6	4.7%	0.12 [0.00, 3.36]
Zhang GJ 2014	0	21	0	18		Not estimable
Zhang W 2018	0	13	0	32		Not estimable
Zhong F 2016	2	27	6	79	6.6%	0.97 [0.18, 5.14]
Zhou C 2020	0	20	1	40	2.3%	0.64 [0.03, 16.48]
Total (95% CI)		396		431	100.0%	0.17 [0.08, 0.37]
Total events	2		38			

Heterogeneity: Chi² = 7.17, df = 12 (P = 0.85); I² = 0%
Test for overall effect: Z = 4.52 (P < 0.00001)

Odds Ratio M-H, Fixed, 95% CI

0.01 0.1 1 10 100
Favours [TAE/TACE+SH] Favours [EH]



Study or Subgroup	TAE/TACE+SH Events	Total	EH Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
zkowski AK 2006	7	10	5	10	9.0%	2.33 [0.37, 14.61]
Y 2020	0	18	2	24	4.8%	0.24 [0.01, 5.39]
Li XH 2014	3	25	13	22	10.8%	0.09 [0.02, 0.41]
Ou DP 2016	4	58	9	73	12.2%	0.53 [0.15, 1.81]
Wang JY 2009	9	30	6	18	12.1%	0.86 [0.24, 3.00]
Wang YX 2013	1	10	5	9	6.5%	0.09 [0.01, 1.03]
Xie FW 2016	11	35	8	23	12.9%	0.86 [0.28, 2.62]
Zhang GJ 2014	3	21	11	18	10.4%	0.11 [0.02, 0.50]
Zhang W 2018	9	13	12	32	11.4%	3.75 [0.95, 14.88]
Zhou C 2020	2	20	9	40	10.0%	0.38 [0.07, 1.97]
Total (95% CI)		240		269	100.0%	0.50 [0.22, 1.10]
Total events	49		80			

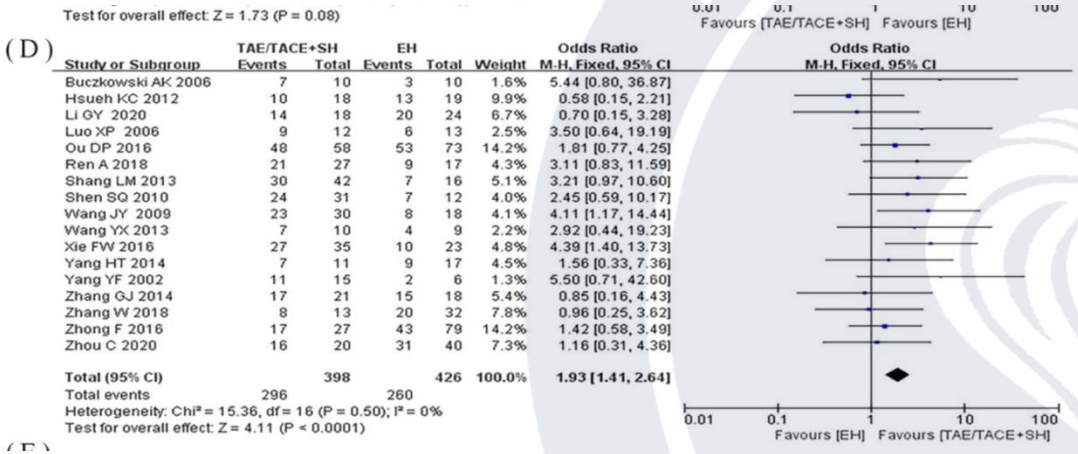
Heterogeneity: Tau² = 0.96; Chi² = 23.37, df = 9 (P = 0.005); I² = 61%
Test for overall effect: Z = 1.73 (P = 0.08)

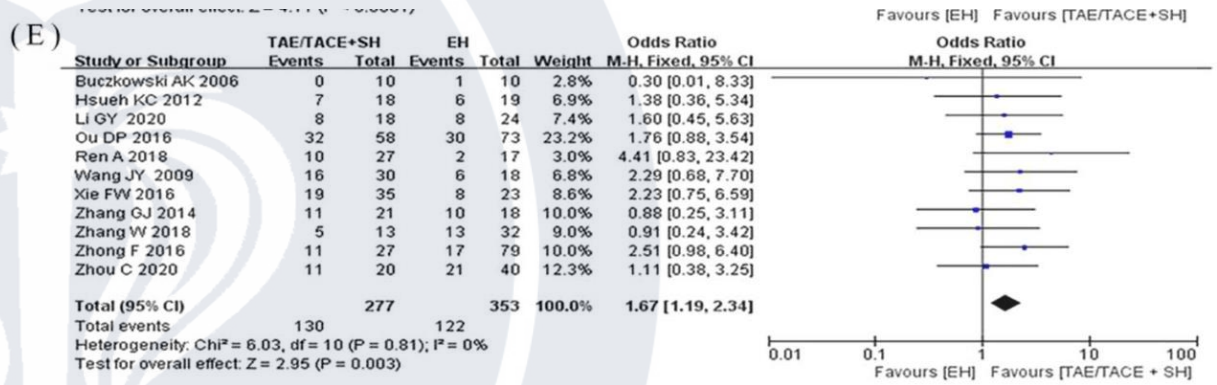
Odds Ratio M-H, Random, 95% CI

0.01 0.1 1 10 100
Favours [TAE/TACE+SH] Favours [EH]

Complication >> no significant

In-hospital mortality of rHCC patients in the TAE/TACE + SH group was lower than that of the EH group.





1-year survival of rHCC patients in the TAE/TACE + SH group was higher than that of the EH group.

3-year survival of rHCC patients in the TAE/TACE + SH group was higher than that of the EH group.

Staged partial hepatectomy versus transarterial chemoembolization for the treatment of spontaneous hepatocellular carcinoma rupture: a multicenter analysis in Korea

Hyung Soon Lee[1], Gi Hong Choi[2], Jin Sub Choi[2], Kwang-Hyub Han[3], Sang Hoon Ahn[3], Do Young Kim[3], Jun Yong Park[3], Seung Up Kim[3], Sung Hoon Kim[4], Dong Sup Yoon[5], Jae Keun Kim[5], Jong Won Choi[6], Soon Sun Kim[7], Hana Park[8]

[1]Department of Surgery, National Health Insurance Service Ilsan Hospital, Goyang, Korea
[2]Department of Surgery, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[3]Department of Internal Medicine, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[4]Department of Surgery, Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine, Wonju, Korea
[5]Department of Surgery, Gangnam Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[6]Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Goyang, Korea
[7]Department of Internal Medicine, Ajou University Medical Center, Ajou University School of Medicine, Suwon, Korea
[8]Department of Internal Medicine, CHA Bundang Medical Center, CHA University, Seongnam, Korea

Purpose: The aim of this study was to identify the prognostic factors and compare the long-term outcomes of staged hepatectomy and transarterial chemoembolization (TACE) for patients with spontaneous rupture of hepatocellular carcinoma (HCC).
Methods: This study is a multicenter, retrospective analysis of patients with newly diagnosed ruptured HCC. To compare overall survival between staged hepatectomy group and TACE alone group, we performed propensity score-matching to adjust for significant differences in patient characteristics. To identify prognostic factors, the clinical characteristics at the time of diagnosis of tumor rupture were investigated using Cox-regression analysis.
Results: From 2000 to 2014, 172 consecutive patients with newly diagnosed ruptured HCC were treated in 6 Korean centers. One hundred seventeen patients with Child-Pugh class A disease were identified; of which 112 were initially treated with transcatheter arterial embolization (TAE) for hemostasis and five underwent emergency surgery for bleeder ligation. Of the 112 patients treated with TAE, 44 underwent staged hepatectomy, 61 received TACE alone, and 7 received conservative treatment after TAE. Those that underwent staged hepatectomy had significantly higher overall survival than those that underwent TACE alone before matching ($P < 0.001$) and after propensity score-matching ($P = 0.006$). Multivariate analysis showed that type of treatment, presence of portal vein thrombosis, pretreatment transfusion >1,200 mL, and tumor size >5 cm were associated with poor overall survival.
Conclusion: Staged hepatectomy may offer better long-term survival than TACE alone for spontaneous rupture of HCC. Staged hepatectomy should be considered in spontaneous rupture of HCC with resectable tumor and preserved liver function.
[Ann Surg Treat Res 2019;96(6):275-282]

Key Words: Hepatocellular carcinoma, Spontaneous rupture, Hepatectomy, Therapeutic chemoembolization

After TAE
- Stage hepatectomy VS TACE alone

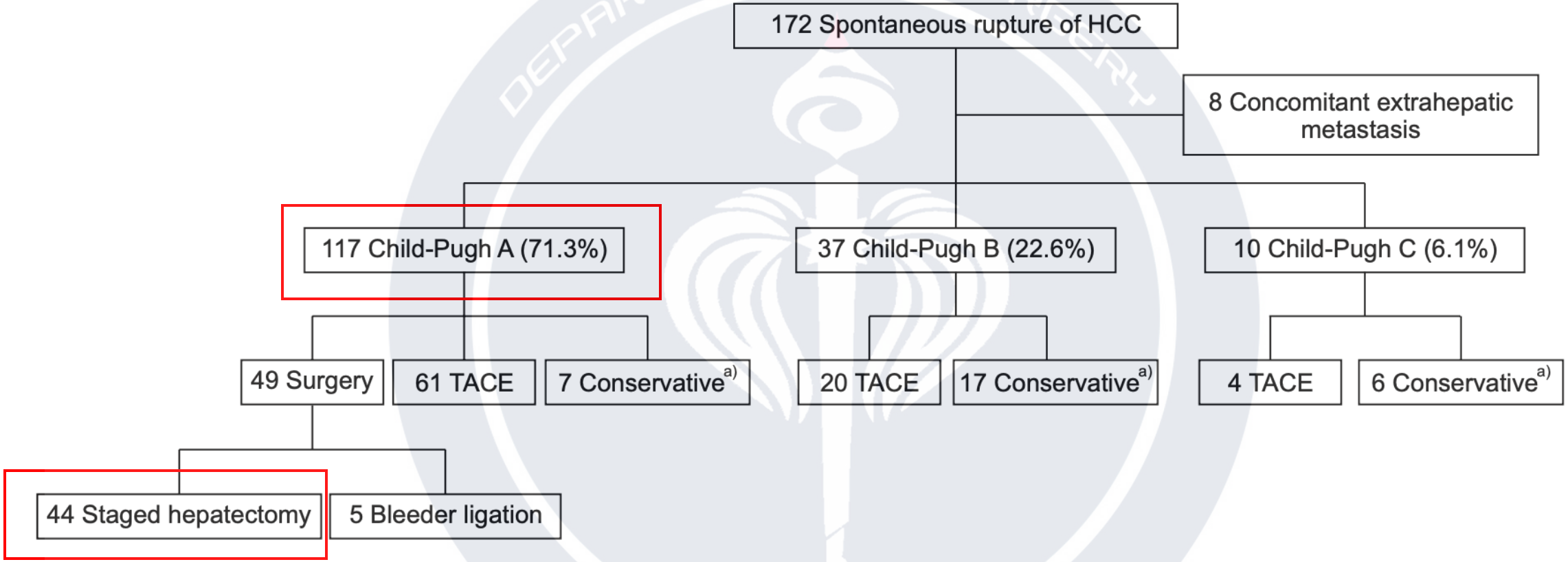


Fig. 1. Patient selection schematic. HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization. [a)]Supportive care, radiotherapy and chemotherapy.

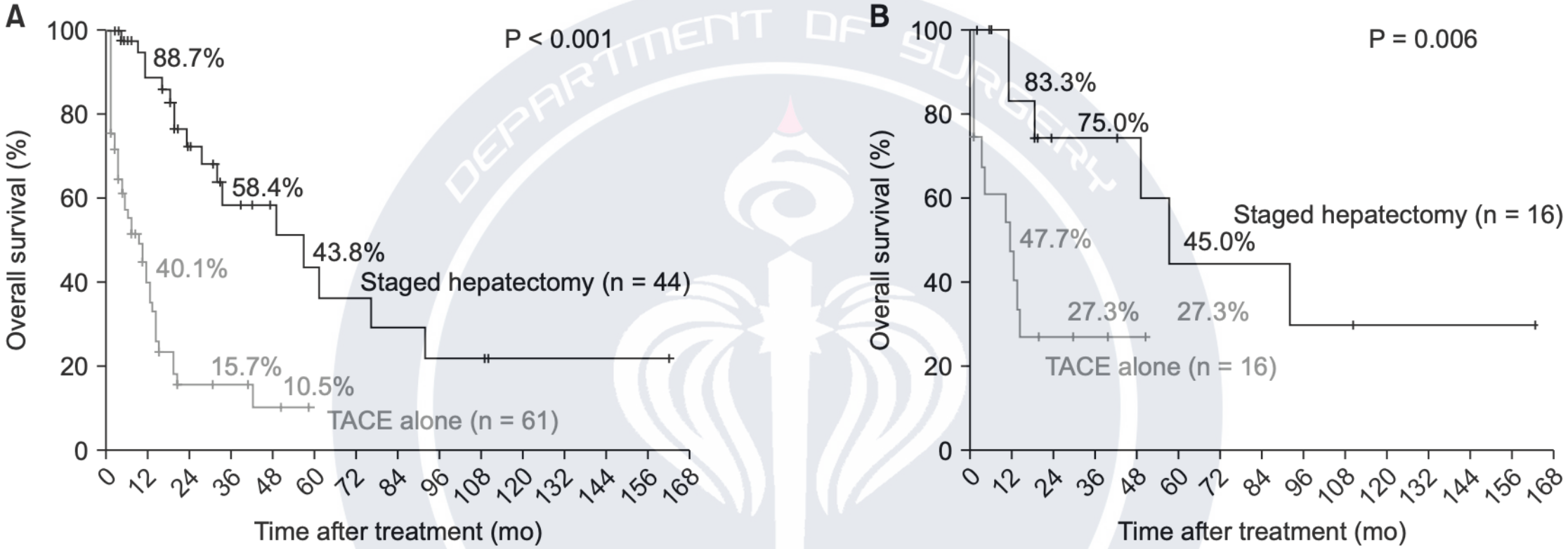


Fig. 2. Comparison of overall survival between staged hepatectomy and TACE alone before matching (A) and after propensity score-matching (B). TACE, transarterial chemoembolization.

OS	1-year	2-year	5-year
Resection	88.7	58.4	43.8
TACE	40.1	15.7	10.5

OS	1-year	2-year	5-year
Stage h	83.3	75	45
TACE	47.7	27.3	27.3

Conclusion

- Emergency hepatectomy is high mortality rate and complication
- Staged hepatectomy should be considered in cases of spontaneous HCC rupture with resectable tumor and preserved liver function.

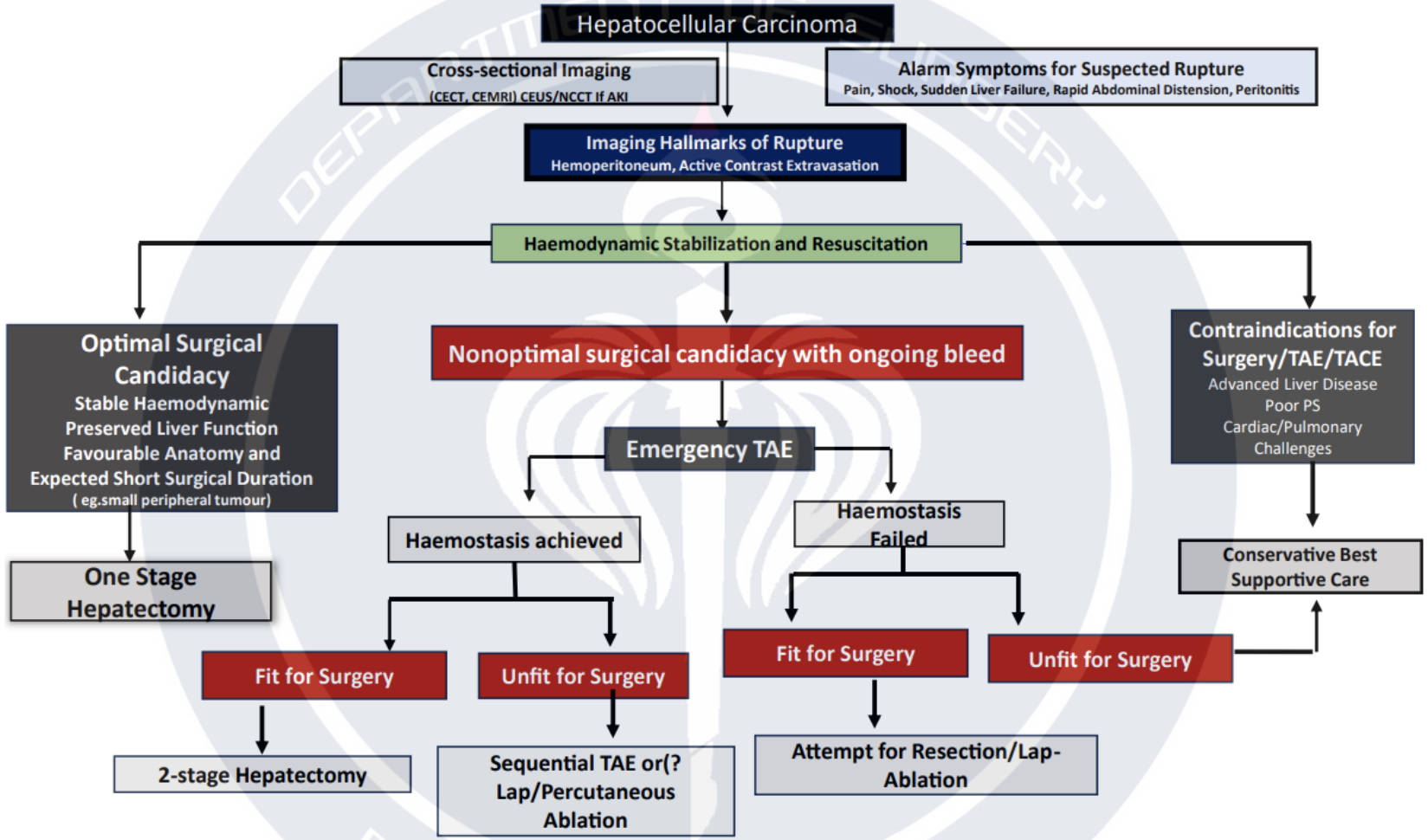


Figure 7 Algorithmic approach to ruptured HCC (AKI, acute kidney injury; CECT, contrast enhanced CT; CEMRI, contrast enhanced MRI; CEUS, contrast enhanced ultra sound; HCC, hepatocellular carcinoma; NCCT, non contrast CT; TACE, transarterial chemoembolisation; TAE, transarterial embolisation).