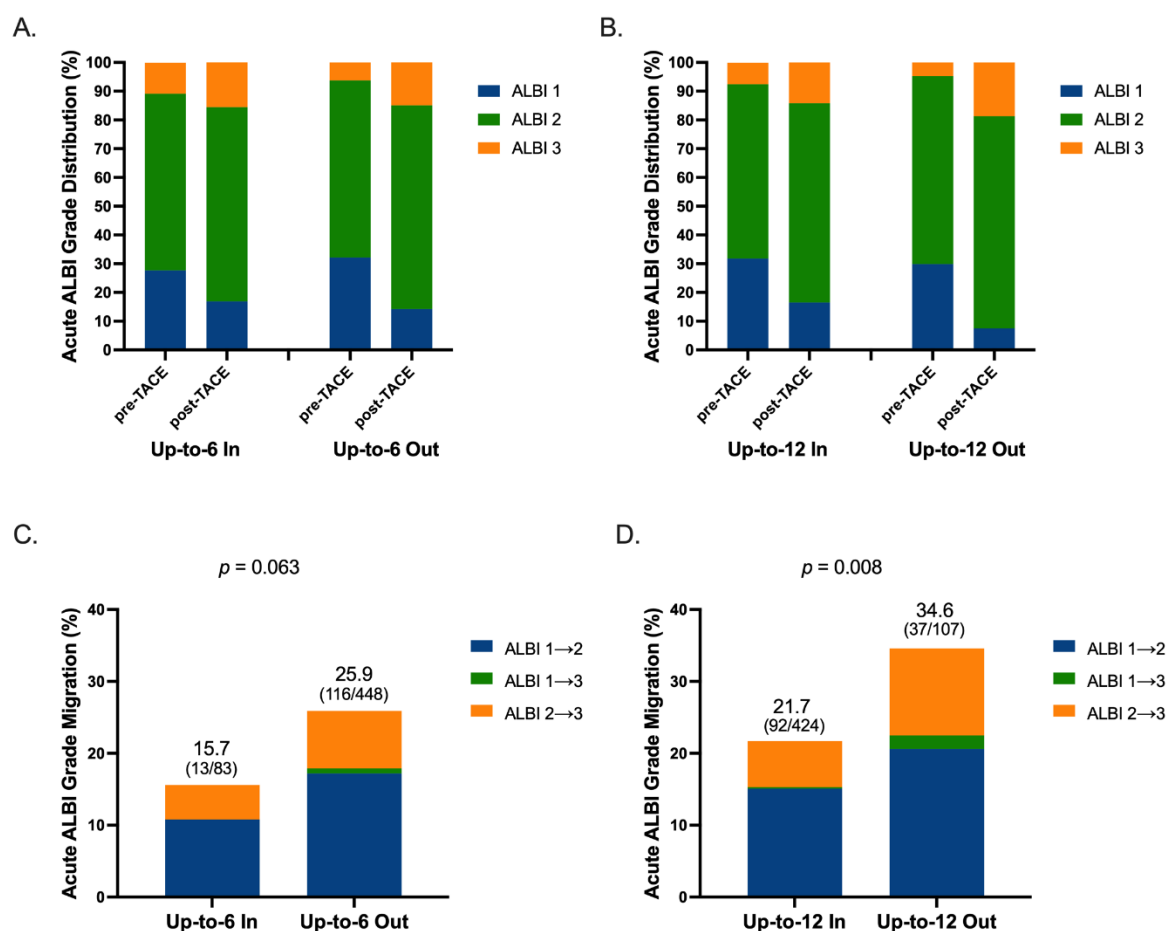


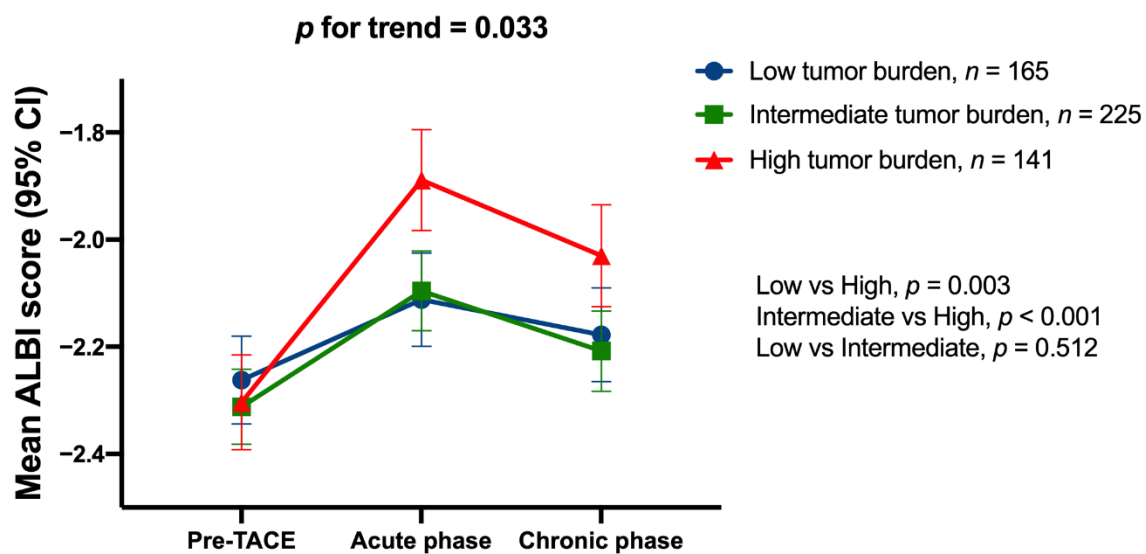
## Supplementary Materials

# Effect of Transarterial Chemoembolization on ALBI Grade in Intermediate-Stage Hepatocellular Carcinoma: Criteria for Unsuitable Cases Selection

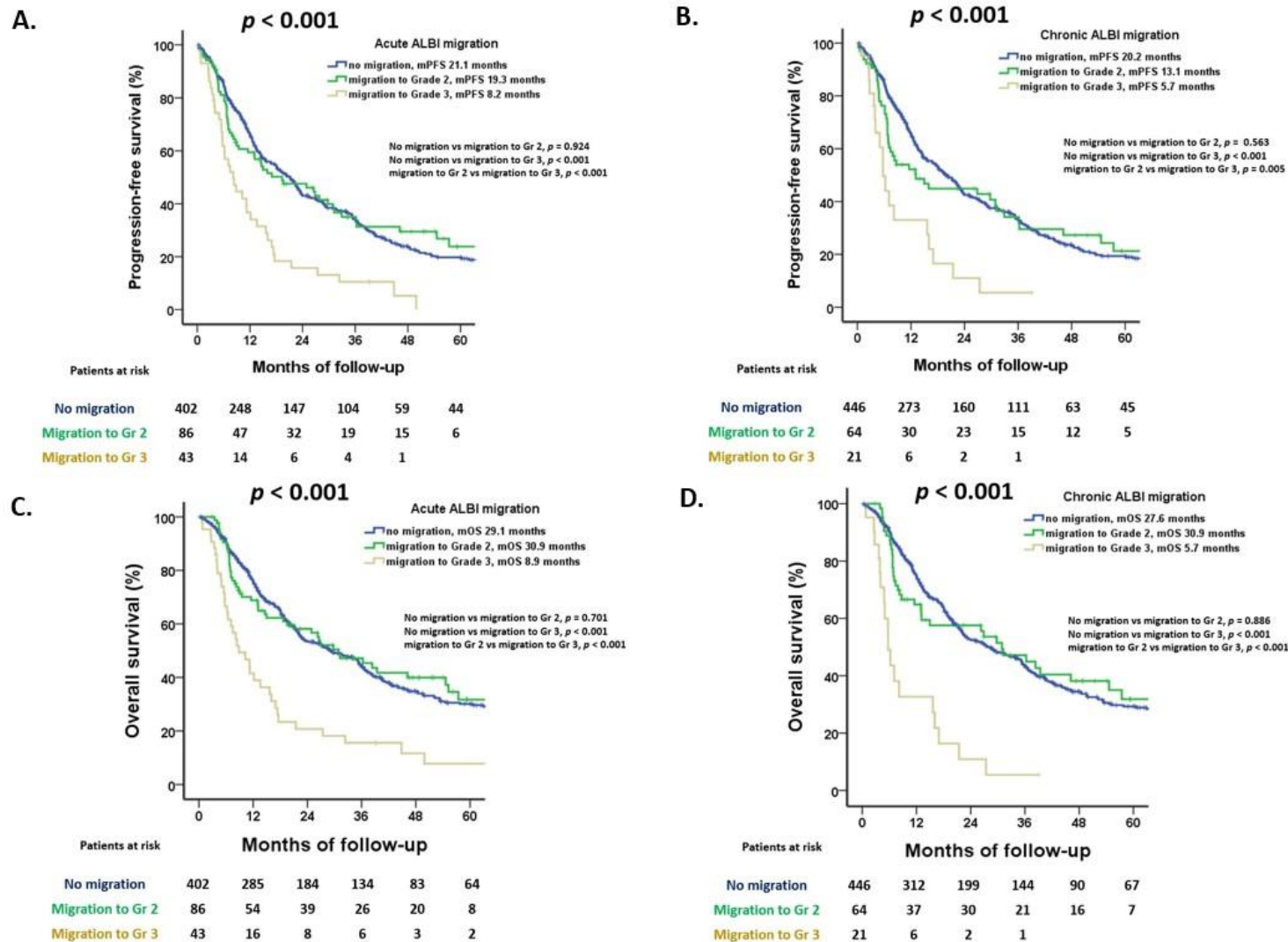
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**Figure S1.** Distribution of ALBI grade and rates of acute ALBI migration. Distribution of ALBI grade stratified by (A) up-to-6 and (B) up-to-12, and acute ALBI grade migration rate stratified by (C) up-to-6 and (D) up-to-12. Abbreviations: ALBI, Albumin-Bilirubin; TACE, transarterial chemoembolization.



**Figure S2.** Dynamics of ALBI score in pre-TACE phase, acute phase, and chronic phase, stratified by seven-eleven criteria. Abbreviations: ALBI, Albumin-Bilirubin; TACE, transarterial chemoembolization; CI, confidence interval.



**Figure S3.** Progression-free survival (PFS) stratified by different degree of ALBI-grade migration, (A) acute ALBI-grade migration, and (B) chronic ALBI-grade migration. Overall survival (OS) stratified by different degree of ALBI-grade migration, (C) acute ALBI-grade migration, and (D) chronic ALBI-grade migration. Abbreviations: ALBI, Albumin-Bilirubin; mPFS, median progression-free survival; mOS, median overall survival; Gr.2, grade 2; Gr.3, grade 3.

**Table S1.** The impact of NUCs on ALBI-grade migration in HBV-HCC patients undergoing TACE.

| Events                               | HBsAg Positive ( <i>n</i> = 244) |                                | <i>p</i> |
|--------------------------------------|----------------------------------|--------------------------------|----------|
|                                      | On NUCs ( <i>n</i> = 69)         | Without NUCs ( <i>n</i> = 175) |          |
| Acute ALBI migration, <i>n</i> (%)   | 22 (31.9)                        | 49 (28.0)                      | 0.536    |
| Chronic ALBI migration, <i>n</i> (%) | 15 (21.7)                        | 31 (17.7)                      | 0.472    |
| Without NUCs ( <i>n</i> = 175)       | Acute ALBI grade migration       |                                |          |
|                                      | Yes ( <i>n</i> = 49)             | No ( <i>n</i> = 126)           | <i>p</i> |
| HBV reactivation, <i>n</i> (%)       | 3 (6.1)                          | 5 (4.0)                        | 0.688    |

Abbreviations: ALBI, Albumin-Bilirubin; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization; NUCs, nucleos(t)ide analogs; HBV, hepatitis B virus; HBsAg, hepatitis B surface antigen.

**Table S2.** Factors associated with progression-free survival of the 531 BCLC-B HCC patients undergoing TACE.

| Factors                          | No.     | Univariate          |          | Multivariate        |          |                     |          |
|----------------------------------|---------|---------------------|----------|---------------------|----------|---------------------|----------|
|                                  |         |                     |          | Model 1             |          | Model 2             |          |
|                                  |         | HR (95% CI)         | <i>p</i> | HR (95% CI)         | <i>p</i> | HR (95% CI)         | <i>p</i> |
| Age (years), >70/≤70             | 265/266 | 1.063 (0.872–1.296) | 0.546    |                     | -        |                     |          |
| Gender, Male/Female              | 412/119 | 1.046 (0.820–1.332) | 0.719    |                     | -        |                     |          |
| HBV vs HCV †                     | 220/156 | 1.163 (0.919–1.471) | 0.209    |                     | -        |                     |          |
| Alcoholic, Yes/No                | 66/465  | 1.057 (0.789–1.416) | 0.709    |                     | -        |                     |          |
| Cirrhosis, Yes/No                | 379/152 | 1.021 (0.820–1.270) | 0.855    |                     | -        |                     |          |
| PLT ≤120 K/>120 K                | 196/335 | 0.868 (0.707–1.066) | 0.178    |                     | -        |                     |          |
| ALT (IU/L), >40/≤40              | 306/225 | 0.928 (0.759–1.134) | 0.465    |                     | -        |                     |          |
| AST (IU/L) ‡, >45/≤45            | 325/205 | 1.183 (0.964–1.451) | 0.109    |                     | -        |                     |          |
| INR, >1.0/≤1.0                   | 427/104 | 1.100 (0.860–1.405) | 0.449    |                     | -        |                     |          |
| Tumor location, Bilobar/Unilobar | 258/273 | 1.033 (0.848–1.260) | 0.746    |                     | -        |                     |          |
| Tumor size, per cm               | 531     | 1.081 (1.056–1.107) | <0.001   | 1.071 (1.044–1.098) | <0.001   | 1.072 (1.045–1.099) | <0.001   |
| Tumor number, ≥3/<3              | 269/262 | 1.078 (0.884–1.314) | 0.461    | -                   | -        | -                   | -        |
| AFP (ng/ml), >400/≤ 400          | 149/382 | 1.943 (1.566–2.410) | <0.001   | 1.753 (1.408–2.182) | <0.001   | 1.763 (1.418–2.193) | <0.001   |
| Acute ALBI grade migration       |         |                     |          |                     |          |                     |          |
| No                               | 402     | 1                   | Ref      | 1                   | Ref      | -                   | -        |
| Migration to Grade 2             | 86      | 0.985 (0.743–1.305) | 0.916    | 0.865 (0.650–1.150) | 0.318    | -                   | -        |
| Migration to Grade 3             | 43      | 2.272 (1.616–3.196) | < 0.001  | 1.637 (1.150–2.329) | 0.006    | -                   | -        |
| Chronic ALBI grade migration     |         |                     |          |                     |          |                     |          |
| No                               | 446     | 1                   | Ref      | -                   | -        | 1                   | Ref      |
| Migration to Grade 2             | 64      | 1.094 (0.803–1.490) | 0.569    | -                   | -        | 0.948 (0.692–1.300) | 0.742    |
| Migration to Grade 3             | 21      | 2.733 (1.694–4.410) | < 0.001  | -                   | -        | 2.029 (1.247–3.302) | 0.004    |

† exclude 24 co-infection patients; ‡ 1 missing data; Abbreviations: ALBI, Albumin-Bilirubin; BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization; HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; PLT, platelet count; K, kilo; ALT, alanine transaminase; AST, aspartate aminotransferase; IU, international unit; INR, international normalized ratio; AFP, alpha-fetoprotein

**Table S3.** Factors associated with overall survival of the 531 BCLC-B HCC patients undergoing TACE.

| Factors                          | No.     | Univariate          |          | Multivariate        |          |                     |          |
|----------------------------------|---------|---------------------|----------|---------------------|----------|---------------------|----------|
|                                  |         |                     |          | Model 1             |          | Model 2             |          |
|                                  |         | HR (95% CI)         | <i>p</i> | HR (95% CI)         | <i>p</i> | HR (95% CI)         | <i>p</i> |
| Age (years), >70/≤70             | 265/266 | 1.230 (0.994–1.520) | 0.056    | 1.412 (1.134–1.757) | 0.002    | 1.445 (1.160–1.800) | 0.001    |
| Gender, Male/Female              | 412/119 | 1.114 (0.858–1.446) | 0.418    | -                   | -        | -                   | -        |
| HBV vs HCV <sup>†</sup>          | 220/156 | 1.032 (0.803–1.327) | 0.804    | -                   | -        | -                   | -        |
| Alcoholic, Yes/No                | 66/465  | 1.147 (0.846–1.557) | 0.377    | -                   | -        | -                   | -        |
| Cirrhosis, Yes/No                | 379/152 | 1.052 (0.834–1.328) | 0.667    | -                   | -        | -                   | -        |
| PLT, ≤120 K/>120 K               | 196/335 | 0.910 (0.731–1.132) | 0.398    | -                   | -        | -                   | -        |
| ALT (IU/L) >40/≤40               | 306/225 | 1.035 (0.834–1.283) | 0.757    | -                   | -        | -                   | -        |
| AST (IU/L) † >45/≤45             | 325/205 | 1.332 (1.067–1.662) | 0.011    | 1.256 (0.995–1.586) | 0.055    | 1.289 (1.025–1.622) | 0.030    |
| INR, >1.0/≤1.0                   | 427/104 | 1.102 (0.848–1.430) | 0.467    | -                   | -        | -                   | -        |
| Tumor location, Bilobar/Unilobar | 258/273 | 1.012 (0.819–1.250) | 0.913    | -                   | -        | -                   | -        |
| Tumor size, per cm               | 531     | 1.090 (1.063–1.118) | <0.001   | 1.083 (1.053–1.113) | <0.001   | 1.084 (1.055–1.114) | <0.001   |
| Tumor number, ≥3/<3              | 269/262 | 1.119 (0.905–1.383) | 0.298    | -                   | -        | -                   | -        |
| AFP (ng/ml) >400/≤ 400           | 149/382 | 1.985 (1.583–2.489) | <0.001   | 1.826 (1.448–2.303) | <0.001   | 1.825 (1.449–2.297) | <0.001   |
| Acute ALBI grade migration       |         |                     |          |                     |          |                     |          |
| No                               | 402     | 1                   | Ref      | 1                   | Ref      | -                   | -        |
| Migration to Grade 2             | 86      | 0.941 (0.693–1.277) | 0.697    | 0.784 (0.573–1.072) | 0.128    | -                   | -        |
| Migration to Grade 3             | 43      | 2.451 (1.726–3.481) | < 0.001  | 1.551 (1.070–2.251) | 0.021    | -                   | -        |
| Chronic ALBI grade migration     |         |                     |          |                     |          |                     |          |
| No                               | 446     | 1                   | Ref      | -                   | -        | 1                   | Ref      |
| Migration to Grade 2             | 64      | 0.970 (0.691–1.360) | 0.858    | -                   | -        | 0.791 (0.552–1.106) | 0.164    |
| Migration to Grade 3             | 21      | 3.899 (2.407–6.315) | < 0.001  | -                   | -        | 2.785 (1.697–4.570) | < 0.001  |

<sup>†</sup> exclude 24 co-infection patients; † 1 missing data; Abbreviations: ALBI, Albumin-Bilirubin; BCLC, Barcelona Clinic Liver Cancer; HCC, hepatocellular carcinoma; TACE, transarterial chemoembolization; HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; HCV, hepatitis C virus; PLT, platelet count; K, kilo; ALT, alanine transaminase; AST, aspartate aminotransferase; IU, international unit; INR, international normalized ratio; AFP, alpha-fetoprotein



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