A novel scoring system predicts adjuvant chemolipiodolization benefit for hepatocellular carcinoma patients after hepatectomy

Supplementary Materials

Supplementary Table S1: Univariable analysis of tumor recurrence and OS in the primary cohort

| | T | umor recurrence | | OS | | |
|--------------------------|----------------|------------------|---------|------------------|--|--|
| Variable | P HR (95.0%CI) | | P | HR (95.0% CI) | | |
| Age, years | | | | | | |
| > 50 vs. ≤ 50 | 0.50 | 0.95 (0.81–1.11) | 0.09 | 0.84 (0.69–1.03) | | |
| Gender | | | | | | |
| Male vs. Female | 0.13 | 1.21 (0.95–1.55) | 0.40 | 1.14 (0.84–1.57) | | |
| HBsAg, | | | | | | |
| Positive vs. Negative | 0.02 | 1.31 (1.04–1.64) | 0.04 | 1.36 (1.02–1.82) | | |
| HBeAg | | | | | | |
| Positive vs. Negative | 0.02 | 1.23 (1.04–1.45) | 0.07 | 1.22 (0.98–1.51) | | |
| HBcAb | | | | | | |
| Positive vs. Negative | 0.10 | 1.29 (0.95–1.76) | 0.23 | 1.26 (0.86–1.86) | | |
| HCVAb | | | | | | |
| Positive vs. Negative | 0.46 | 0.83 (0.51–1.37) | 0.10 | 0.51 (0.23–1.13) | | |
| Cirrhosis | | | | | | |
| Positive vs. Negative | 0.78 | 1.02 (0.87–1.20) | 0.93 | 1.01 (0.82–1.24) | | |
| AFP, ng/mL | | | | | | |
| > 400 vs. ≤ 400 | < 0.001 | 1.39 (1.18–1.64) | 0.02 | 1.30 (1.05–1.60) | | |
| PT, second | | | 1 | Ì | | |
| > 12 vs. ≤ 12 | 0.11 | 1.14 (0.97–1.34) | 0.91 | 1.01 (0.83–1.24) | | |
| PLT, ×10 ⁹ /L | | | 1 | | | |
| >100 vs. ≤ 100 | 0.46 | 1.08 (0.89–1.30) | 0.12 | 1.22 (0.95–1.56) | | |
| ALB, g/L | | | | | | |
| > 40 vs. ≤ 40 | 0.27 | 0.91 (0.77-1.07) | 0.70 | 1.04 (0.84–1.30) | | |
| ALT, U/L | | | | | | |
| >40 vs. ≤40 | 0.004 | 1.26 (1.08–1.48) | 0.32 | 1.11 (0.91–1.36) | | |
| TBIL, μmol/L | | | | | | |
| ≤ 34 vs. > 34 | 0.70 | 1.15 (0.57–2.30) | 0.70 | 0.83 (0.31–2.21) | | |
| WBC, ×10°/L | | | | | | |
| > 4 vs. ≤ 4 | 0.26 | 1.12(0.92–1.38) | 0.10 | 1.25(0.96–1.63) | | |
| Tumor number | | | | | | |
| Multiple vs. Single | < 0.001 | 1.94(1.60-2.35) | < 0.001 | 2.06 (1.63–2.60) | | |
| Tumor diameter, cm | | | | | | |
| 3–5 vs. ≤ 3 | < 0.001 | 1.60 (1.24–2.06) | < 0.001 | 1.96 (1.35–2.85) | | |
| > 5 vs. 3–5 | < 0.001 | 2.86 (2.28–3.57) | < 0.001 | 4.50 (3.23–6.26) | | |
| MVI | | | | | | |
| Presence vs. Absence | < 0.001 | 3.12 (2.66–3.66) | < 0.001 | 3.10 (2.53–3.80) | | |

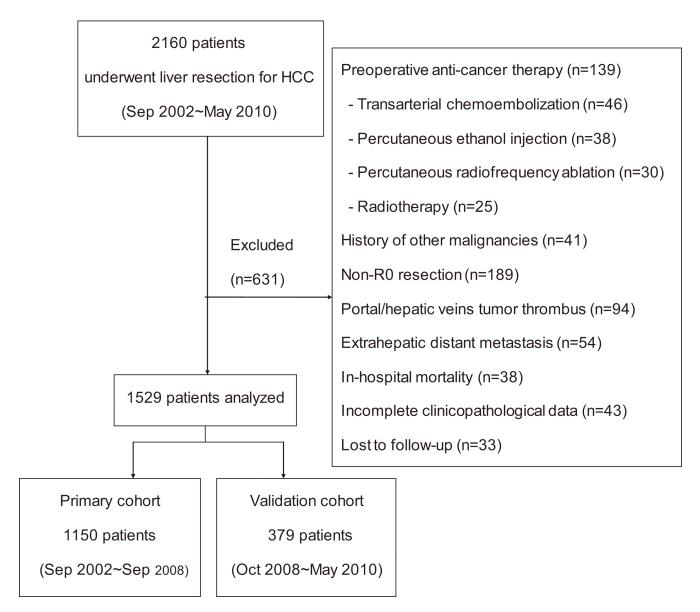
| 37 - 11 | Tu | mor recurrence | OS | | |
|-------------------------------|---------|------------------|---------|------------------|--|
| Variable | P | HR (95.0%CI) | P | HR (95.0% CI) | |
| Tumor capsule | | | | | |
| Incomplete vs. Complete | < 0.001 | 1.48 (1.26–1.74) | < 0.001 | 2.16 (1.76–2.65) | |
| Edmondson-Steiner | | | | | |
| III/IV vs. I/II | < 0.001 | 1.43 (1.19–1.72) | < 0.001 | 1.59 (1.25–2.03) | |
| Blood transfusion | | | | | |
| Yes vs. No | 0.01 | 1.34 (1.06–1.69) | 0.22 | 1.21 (0.89–1.64) | |
| Surgical margin, cm | | | | | |
| ≤ 1 vs. >1 | 0.003 | 1.29 (1.09–1.52) | 0.001 | 1.46 (1.17–1.81) | |
| Hepatectomy | | | | | |
| Anatomical vs. Non-anatomical | 0.98 | 1.00 (0.85–1.18) | 0.65 | 1.05 (0.85–1.29) | |
| ACL | | | 1 | | |
| ACL vs. non–ACL | 0.52 | 0.95 (0.80–1.12) | 0.76 | 0.97 (0.78-1.20) | |

Supplementary Table S2: Clinicopathologic characteristics of patients treated with or without ACL with a score of ≥ 10

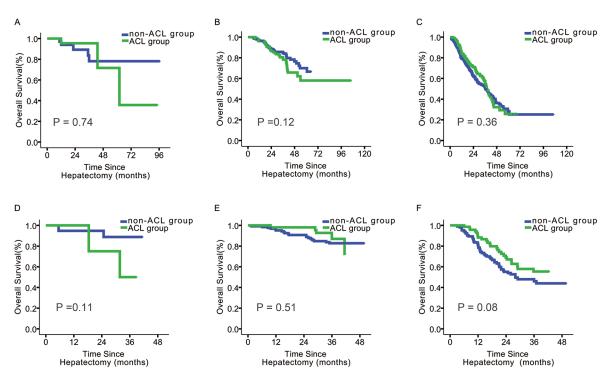
| | Primary cohort | | ' | Validation cohort | | |
|------------|----------------|------------|---------|-------------------|-------------|---------|
| Variable | Non-ACL | ACL | P value | Non-ACL | ACL | P value |
| | (n=71) | (n = 36) | | (n = 24) | (n = 17) | |
| Age, years | | | | | | |
| ≤ 50 | 32 (45.1%) | 26 (72.2%) | 0.008** | 15 (62.5%) | 8 (47.1%) | 0.33 |
| > 50 | 39 (54.9%) | 10 (27.8%) | | 9 (37.5%) | 9 (52.9%) | |
| Gender | | | | | | |
| Male | 64 (90.1%) | 31 (86.1%) | 0.53 | 19 (79.2%) | 14 (82.4%) | 0.99* |
| Female | 7 (9.9%) | 5 (13.9%) | | 5 (20.8%) | 3 (17.6%) | |
| HBsAg | | | | | | |
| Positive | 62 (87.3%) | 30 (83.3%) | 0.57 | 20 (83.3%) | 12 (70.6%) | 0.56* |
| Negative | 9 (12.7%) | 6 (16.7%) | | 4 (16.7%) | 5 (29.4%) | |
| HBeAg | | | | | | |
| Positive | 20 (28.2%) | 10 (27.8%) | 0.97 | 6 (25.0%) | 2 (11.8%) | 0.51* |
| Negative | 51 (71.8%) | 26 (72.2%) | | 18 (75.0%) | 15 (88.2%) | |
| HBcAb | | | | | | |
| Positive | 66 (93.0%) | 34 (94.4%) | 0.99* | 24 (100.0%) | 17 (100.0%) | 0.99* |
| Negative | 5 (7.0%) | 2 (5.6%) | | 0 (0.0%) | 0 (0.0%) | |
| HCVAb | | | | | | |
| Positive | 0 (0%) | 1 (2.8%) | 0.73* | 1 (4.2%) | 1 (5.9%) | 0.99* |
| Negative | 71 (100.0%) | 35 (97.2%) | | 23 (95.8%) | 16 (94.1%) | |
| Cirrhosis | | | | | | |
| Yes | 40 (56.3%) | 16 (44.4%) | 0.24 | 11 (45.8%) | 8 (47.1%) | 0.94 |
| No | 31 (43.7%) | 20 (55.6%) | | 13 (54.2%) | 9 (52.9%) | |
| AFP, ng/mL | | | | | | |
| ≤ 400 | 30 (42.3%) | 19 (52.8%) | 0.30 | 10 (41.7%) | 11 (64.7%) | 0.15 |
| > 400 | 41 (57.7%) | 17 (47.2%) | | 14 (58.3%) | 6 (35.3%) | |
| PT, second | | | | | | |
| ≤ 12 | 34 (47.9%) | 19 (52.8%) | 0.63 | 11 (45.8%) | 7 (41.2%) | 0.77 |
| > 12 | 37 (52.1%) | 17 (47.2%) | | 13 (54.2%) | 10 (58.8%) | |

| Variable | Primary cohort | | | Validation cohort | | P value |
|--------------------------|----------------|---------------------------------------|----------|-------------------|-------------|---------|
| | Non-ACL ACL | | P value | Non-ACL ACL | | |
| | (n = 71) | (n = 36) | - | (n = 24) | (n = 17) | |
| PLT, ×10 ⁹ /L | | | | | | |
| ≤ 100 | 11 (15.5%) | 4 (11.1%) | 0.54 | 1 (4.2%) | 4 (23.5%) | 0.17* |
| > 100 | 60 (84.5%) | 32 (88.9%) | | 23 (95.8%) | 13 (76.5%) | |
| ALB, g/L | | | | | | |
| ≤ 40 | 33 (46.5%) | 10 (27.8%) | 0.06 | 7 (29.2%) | 7 (41.2%) | 0.42 |
| > 40 | 38 (53.5%) | 26 (72.2%) | | 17 (70.8%) | 10 (58.8%) | |
| ALT, U/L | | | | | | |
| ≤ 40 | 36 (50.7%) | 11 (30.6%) | 0.05 | 14 (58.3%) | 6 (35.3%) | 0.15 |
| > 40 | 35 (49.3%) | 25 (69.4%) | | 10 (41.7%) | 11 (64.7%) | |
| TBIL, μmol/L | | | | | | |
| ≤ 34 | 2 (2.8%) | 0 (0.0%) | 0.79* | 0 (0.0%) | 0 (0.0%) | 0.99* |
| > 34 | 69 (97.2%) | 36 (100.0%) | | 24 (100%) | 17 (100%) | |
| WBC, ×10 ⁹ /L | ì | | | | | |
| ≤ 4 | 10 (14.1%) | 3 (8.3%) | 0.58* | 4 (16.7%) | 5 (29.4%) | 0.56* |
| > 4 | 61 (85.9%) | 33 (91.7%) | | 20 (83.3%) | 12 (70.6%) | |
| Tumor number | ì | | | , , , | | |
| Single | 30 (42.3%) | 22 (61.1%) | 0.07 | 15 (62.5%) | 15 (88.2%) | 0.14* |
| Multiple | 41 (57.7%) | 14 (38.9%) | | 9 (37.5%) | 2 (11.8%) | |
| Tumor diameter, cm | <u> </u> | | | | , , , | |
| ≤3 | 0 (0.0%) | 0 (0.0%) | 0.99* | 0 (0.0%) | 0 (0.0%) | 0.99* |
| 3–5 | 0 (0.0%) | 0 (0.0%) | | 0 (0.0%) | 0 (0.0%) | |
| > 5 | 71 (100.0%) | 36 (100.0%) | | 24 (100.0%) | 17 (100.0%) | |
| MVI | , , | | | | | |
| Presence | 71 (100.0%) | 36 (100.0%) | 0.99* | 24 (100.0%) | 17 (100.0%) | 0.99* |
| Absence | 0 (0.0%) | 0 (0.0%) | | 0 (0.0%) | 0 (0.0%) | |
| Tumor capsule | | | | , , , | | |
| Complete | 0 (0.0%) | 0 (0.0%) | 0.99* | 0 (0.0%) | 0 (0.0%) | 0.99* |
| Incomplete | 71 (100.0%) | 36 (100.0%) | | 24 (100.0%) | 17 (100.0%) | |
| Edmondson-Steiner | | | | | | |
| I/II | 8 (11.3%) | 3 (8.3%) | 0.89* | 4 (16.7%) | 1 (5.9%) | 0.58* |
| III/IV | 63 (88.7%) | 33 (91.7%) | | 20 (83.3%) | 16 (94.1%) | |
| Blood transfusion | | | | | | |
| Yes | 18 (25.4%) | 7 (19.4%) | 0.50 | 3 (12.5%) | 6 (35.3%) | 0.18* |
| No | 53 (74.6%) | 29 (80.6%) | | 21 (87.5%) | 11 (64.7%) | |
| Surgical margin, cm | (| \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ | 1 | | | 1 |
| ≤1 | 70 (98.6%) | 32 (88.9%) | 0.08* | 22 (91.8%) | 17 (100.0%) | 0.63* |
| >1 | 1 (1.4%) | 4 (11.1%) | 1 | 2 (8.3%) | 0 (0.0%) | |
| Hepatectomy | (, 5) | | <u> </u> | () | . (, | |
| Anatomical | 48 (67.6%) | 19 (52.8%) | 0.13 | 17 (70.8%) | 12 (70.6%) | 0.99* |
| Non-anatomical | 23 (32.4%) | 17 (47.2%) | 1 | 7 (29.2%) | 5 (29.4%) | 10.27 |

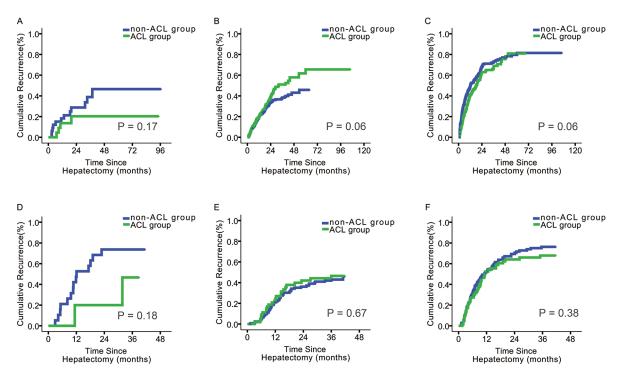
^{*}Continuity Correction test.
** The median ages of the non–ACL and ACL groups were 51.0 vs. 47.0 years (p=0.06).



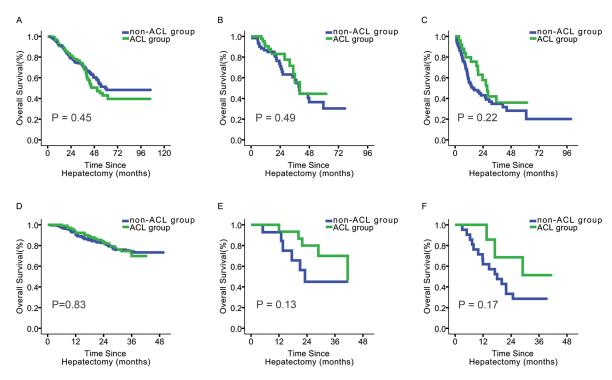
Supplementary Figure S1: Flow chart of the study.



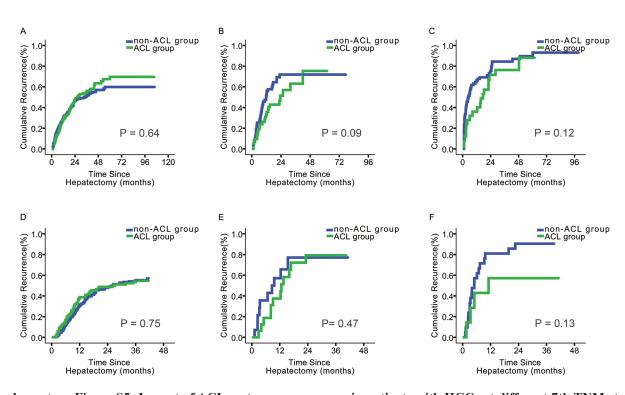
Supplementary Figure S2: Impact of ACL on OS in patients with HCCs at different BCLC stages. (A, B, C) OS of patients at stage 0, A and B in the primary cohort respectively; (p = 0.74, 0.12 and 0.36) (D, E, F) OS of patients at stage 0, A and B in the validation cohort respectively. (p = 0.11, 0.51 and 0.08).



Supplementary Figure S3: Impact of ACL on tumor recurrence in patients with HCCs at different BCLC stages. (A, B, C) Tumor recurrence of patients at stage 0, A and B in the primary cohort respectively; (p = 0.17, 0.06 and 0.06) (D, E, F) Tumor recurrence of patients at stage 0, A and B in the validation cohort respectively. (p = 0.18, 0.67 and 0.38).



Supplementary Figure S4: Impact of ACL on OS in patients with HCCs at different 7th TNM stages. (A, B, C) OS of patients at stage I, II and III in the primary cohort respectively; (p = 0.45, 0.49 and 0.22) (**D**, **E**, **F**) OS of patients at stage I, II and III in the validation cohort respectively. (p = 0.83, 0.13 and 0.17).



Supplementary Figure S5: Impact of ACL on tumor recurrence in patients with HCCs at different 7th TNM stages. (A, B, C) Tumor recurrence of patients at stage I, II and III in the primary cohort respectively; (p = 0.64, 0.09 and 0.12) (D, E, F) Tumor recurrence of patients at stage I, II and III in the validation cohort respectively. (p = 0.75, 0.47 and 0.13).