**Table S1.** Univariate and multivariate Cox regression to identify factors associated with tumor-free survival in patients with a “low” Ki67 index (<30%) (n=253)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Factor** | **Univariate analysis** | |  | **Multivariate analysis** | |
| **HR** | **P-value** |  | **HR** | **P-value** |
| **Sex** |  |  |  |  |  |
| Male | 1.00 (reference) |  |  |  |  |
| Female | 0.971 (0.644-1.465) | 0.890 |  |  |  |
| **Age (years)** |  |  |  |  |  |
| <45 | 1.00 (reference) |  |  |  |  |
| ≥45 | 0.776 (0.583-1.034) | 0.083 |  | 0.794 (0.672-0.938) | 0.007\* |
| **HBsAg** |  |  |  |  |  |
| Negative | 1.00 (reference) |  |  |  |  |
| Positive | 1.498 (0.987-2.273) | 0.058 |  |  |  |
| **HBV-DNA (copies/ml)** |  |  |  |  |  |
| <500 | 1.00 (reference) |  |  |  |  |
| ≥500 | 1.297 (0.967-1.741) | 0.083 |  |  |  |
| **AFP level (ng/ml)** |  |  |  |  |  |
| <400 | 1.00 (reference) |  |  |  |  |
| ≥400 | 1.090 (0.832-1.427) | 0.533 |  |  |  |
| **Tumor capsuleb** |  |  |  |  |  |
| Complete | 1.00 (reference) |  |  |  |  |
| Incomplete | 2.001 (1.422-2.816) | <0.001\* |  | 1.827 (1.224-2.726) | 0.003\* |
| **Resection margin (cm)** |  |  |  |  |  |
| <1 | 1.00 (reference) |  |  |  |  |
| ≥1 | 1.071 (0.797-1.439) | 0.650 |  |  |  |
| **Tumor sizeb (cm)** |  |  |  |  |  |
| d<5 | 1.00 (reference) |  |  |  |  |
| d≥5 | 1.263 (0.876-1.822) | 0.211 |  |  |  |
| **Edmondson gradeb** |  |  |  |  |  |
| Poorly differentiated |  |  |  |  |  |
| Moderately and well differentiated | 0.688 (0.514-0.920) | 0.012\* |  | 0.821 (0.605-1.115) | 0.207 |
| (Continued to the next page) |  |  |  |  |  |
|  |  |  |  |  |  |
| **Table S1.** Continued |  |  |  |  |  |
| **Node number** |  |  |  |  |  |
| 1 | 1.00 (reference) |  |  |  |  |
| ≥2 | 1.684 (1.282-2.213) | <0.001\* |  | 2.190 (1.260-3.809) | 0.005\* |
| **CNLC stage** |  | <0.001\* |  |  | 0.060 |
| IA~IB | 1.00 (reference) |  |  |  |  |
| II | 1.540 (1.143-2.075) | 0.004\* |  | 0.860 (0.471-1.573) | 0.625 |
| IIA | 2.600 (1.716-3.939) | <0.001\* |  | 1.769 (0.515-6.078) | 0.365 |
| **MVI** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.574 (1.201-2.063) | 0.001\* |  | 1.700 (1.264-2.285) | <0.001\* |
| **PVTT** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 2.192 (1.440-3.339) | <0.001\* |  | 0.697 (0.196-2.475) | 0.577 |
| **Liver cirrhosis** |  |  |  |  |  |
| Without/Mild | 1.00 (reference) |  |  |  |  |
| Moderate-severe | 1.053 (0.787-1.410) | 0.728 |  |  |  |
| **Postoperative complications** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.668 (1.051-2.648) | 0.030\* |  | 2.083 (1.287-3.369) | 0.003\* |
| **PA-TACE** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 0.741 (0.556-0.970) | 0.029\* |  | 0.674 (0.507-0.894) | 0.006\* |

The HR was evaluated by Cox regression.

b In cases involving multiple nodes, only the largest was indicated.

\*p < 0.05 was considered as a significant difference between HR and HR+PA-TACE groups.

**Table S2.** Univariate and multivariate Cox regression to identify factors associated with tumor-free survival in patients with a moderate Ki67 index (30-59%) (n=275)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Factor** | **Univariate analysis** | |  | **Multivariate analysis** | |
| **HR** | **P-value** |  | **HR** | **P-value** |
| **Sex** |  |  |  |  |  |
| Male | 1.00 (reference) |  |  |  |  |
| Female | 0.824 (0.564-1.203) | 0.315 |  |  |  |
| **Age (years)** |  |  |  |  |  |
| <45 | 1.00 (reference) |  |  |  |  |
| ≥45 | 0.718 (0.550-0.936) | 0.014\* |  | 0.750 (0.569-0.989) | 0.041\* |
| **HBsAg** |  |  |  |  |  |
| Negative | 1.00 (reference) |  |  |  |  |
| Positive | 1.052 (0.724-1.528) | 0.790 |  |  |  |
| **HBV-DNA (copies/ml)** |  |  |  |  |  |
| <500 | 1.00 (reference) |  |  |  |  |
| ≥500 | 1.080 (0.831-1.403) | 0.564 |  |  |  |
| **AFP level (ng/ml)** |  |  |  |  |  |
| <400 | 1.00 (reference) |  |  |  |  |
| ≥400 | 1.508 (1.167-1.948) | 0.002\* |  | 1.444 (1.114-1.872) | 0.006\* |
| **Tumor capsuleb** |  |  |  |  |  |
| Complete | 1.00 (reference) |  |  |  |  |
| Incomplete | 1.977 (1.502-2.604) | <0.001\* |  | 1.736 (1.283-2.350) | <0.001\* |
| **Resection margin (cm)** |  |  |  |  |  |
| <1 | 1.00 (reference) |  |  |  |  |
| ≥1 | 1.076 (0.805-1.439) | 0.621 |  |  |  |
| **Tumor sizeb (cm)** |  |  |  |  |  |
| d<5 | 1.00 (reference) |  |  |  |  |
| d≥5 | 1.324 (0.917-1.912) | 0.135 |  |  |  |
| **Edmondson gradeb** |  |  |  |  |  |
| Poorly differentiated | 1.00 (reference) |  |  |  |  |
| Moderately and well differentiated | 0.774 (0.599-0.999) | 0.049\* |  | 0.816 (0.628-1.061) | 0.130 |
| (Continued to the next page) |  |  |  |  |  |
| **Table S2.** Continued |  |  |  |  |  |
| **Node number** |  |  |  |  |  |
| 1 | 1.00 (reference) |  |  |  |  |
| ≥2 | 1.747 (1.343-2.274) | <0.001\* |  | 1.270 (0.819-1.969) | 0.285 |
| **CNLC stage** |  | <0.001\* |  |  | 0.060 |
| IA~IB | 1.00 (reference) |  |  |  |  |
| II | 1.771 (1.302-2.407) | <0.001\* |  | 1.521 (0.916-2.525) | 0.105 |
| IIIA | 2.365 (1.711-3.267) | <0.001\* |  | 3.466 (1.052-11.421) | 0.041 |
| **MVI** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.327 (0.973-1.809) | 0.074 |  |  |  |
| **PVTT** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.896 (1.398-2.571) | <0.001\* |  | 0.517 (0.158-1.690) | 0.275 |
| **Liver cirrhosis** |  |  |  |  |  |
| Without/Mild | 1.00 (reference) |  |  |  |  |
| Moderate-severe | 0.876 (0.654-1.173) | 0.373 |  |  |  |
| **Postoperative complications** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.619 (1.073-2.442) | 0.022\* |  | 1.473 (0.958-2.264) | 0.078 |
| **PA-TACE** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 0.753 (0.585-0.968) | 0.027\* |  | 0.670 (0.515-0.873) | 0.003\* |

The HR was evaluated by Cox regression.

b In cases involving multiple nodes, only the largest was indicated.

\*p < 0.05 was considered as a significant difference between HR and HR+PA-TACE groups.

**Table S3.** Univariate and multivariate Cox regression to identify factors associated with tumor-free survival in patients with a high Ki67 index (≥60%) (n=188)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Factor** | **Univariate analysis** | |  | **Multivariate analysis** | |
| **HR** | **P-value** |  | **HR** | **P-value** |
| **Sex** |  |  |  |  |  |
| Male | 1.00 (reference) |  |  |  |  |
| Female | 0.869 (0.576-1.309) | 0.500 |  |  |  |
| **Age (years)** |  |  |  |  |  |
| <45 | 1.00 (reference) |  |  |  |  |
| ≥45 | 0.684 (0.508-0.922) | 0.012\* |  | 0.794 (0.672-0.938) | 0.007\* |
| **HBsAg** |  |  |  |  |  |
| Negative | 1.00 (reference) |  |  |  |  |
| Positive | 1.054 (0.685-1.623) | 0.810 |  |  |  |
| **HBV-DNA (copies/ml)** |  |  |  |  |  |
| <500 | 1.00 (reference) |  |  |  |  |
| ≥500 | 1.096 (0.795-1.510) | 0.577 |  |  |  |
| **AFP level (ng/ml)** |  |  |  |  |  |
| <400 | 1.00 (reference) |  |  |  |  |
| ≥400 | 1.456 (1.071-1.978) | 0.016\* |  | 1.304 (0.944-1.802) | 0.108 |
| **Tumor capsuleb** |  |  |  |  |  |
| Complete | 1.00 (reference) |  |  |  |  |
| Incomplete | 1.936 (1.420-2.639) | <0.001\* |  | 1.668 (1.189-2.341) | 0.003\* |
| **Resection margin (cm)** |  |  |  |  |  |
| <1 | 1.00 (reference) |  |  |  |  |
| ≥1 | 1.067 (0.774-1.471) | 0.693 |  |  |  |
| **Tumor sizeb (cm)** |  |  |  |  |  |
| d<5 | 1.00 (reference) |  |  |  |  |
| d≥5 | 1.954 (1.055-3.618) | 0.033\* |  | 1.356 (0.712-2.583) | 0.354 |
| **Edmondson gradeb** |  |  |  |  |  |
| Poorly differentiated | 1.00 (reference) |  |  |  |  |
| Moderately and well differentiated | 0.892 (0.664-1.198) | 0.447 |  |  |  |
| (Continued to the next page) |  |  |  |  |  |
| **Table S3.** Continued |  |  |  |  |  |
| **Node number** |  |  |  |  |  |
| 1 | 1.00 (reference) |  |  |  |  |
| ≥2 | 1.311 (0.978-1.758) | 0.070 |  |  |  |
| **CNLC stage** |  | <0.001\* |  |  | 0.060 |
| IA~IB | 1.00 (reference) |  |  |  |  |
| II | 1.319 (0.908-1.917) | 0.146 |  | 1.390 (0.942-2.052) | 0.098 |
| IIIA | 1.901 (1.326-2.726) | <0.001\* |  | 2.660 (0.932-7.592) | 0.067 |
| **MVI** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 2.628 (1.467-4.710) | 0.001\* |  | 2.412 (1.305-4.457) | 0.005\* |
| **PVTT** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.585 (1.166-2.157) | 0.003\* |  | 0.522 (0.187-1.460) | 0.216 |
| **Liver cirrhosis** |  |  |  |  |  |
| Without/Mild | 1.00 (reference) |  |  |  |  |
| Moderate-severe | 0.805 (0.588-1.102) | 0.176 |  |  |  |
| **Postoperative complications** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 1.641 (1.113-2.419) | 0.012\* |  | 1.298 (0.870-1.935) | 0.201 |
| **PA-TACE** |  |  |  |  |  |
| No | 1.00 (reference) |  |  |  |  |
| Yes | 0.936 (0.691-1.269) | 0.671 |  |  |  |

The HR was evaluated by Cox regression.

b In cases involving multiple nodes, only the largest was indicated.

\*p < 0.05 was considered as a significant difference between HR and HR+PA-TACE groups.

**Table S4****.** Chi-squared test to compare characteristics between patients who experienced early recurrence (<12 months) or delayed recurrence (≥12 months)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Characteristic** | **Delayed recurrence** | **Early recurrence** | **Chi-square value** | **P-value** |
| **Sex** |  |  | 0.515 | 0.473 |
| Male | 191 (85.7) | 376 (87.6) |
| Female | 32 (14.3) | 53 (12.4) |
| **Age (years)** |  |  |  |  |
| <45 | 58 (26.0) | 186 (43.4) |
| ≥45 | 165 (74.0) | 243 (56.6) | 18.856 | <0.001\* |
| **HBsAg** |  |  |  |  |
| Negative | 27 (12.1) | 54 (12.6) |
| Positive | 196 (87.9) | 375 (87.4) | 0.031 | 0.86 |
| **HBV-DNA (copies/ml)** |  |  |  |  |
| <500 | 70 (31.4) | 134 (32.1) |
| ≥500 | 153 (68.6) | 295 (68.8) | 0.002 | 0.968 |
| **AFP (ng/ml)** |  |  |  |  |
| <400 | 139 (62.3) | 157 (36.6) |
| ≥400 | 84 (37.7) | 272 (63.4) | 39.203 | <0.001\* |
| **Tumor sizeb (cm)** |  |  |  |  |
| d<5 | 41 (18.4) | 37 (8.6) |  |  |
| d≥5 | 182 (81.6) | 392 (91.4) | 13.274 | <0.001\* |
| **Edmondson gradeb** |  |  |  |  |
| Poorly differentiated | 70 (31.4) | 209 (48.7) |
| Moderately and well differentiated | 153 (68.6) | 220 (51.3) | 17.996 | <0.001\* |
| **Node number** |  |  |  |  |
| 1 | 155 (69.5) | 221 (51.5) |
| ≥2 | 68 (30.5) | 208 (48.5) | 19.456 | <0.001\* |
| **Tumor capsuleb** |  |  |  |  |
| Complete | 192 (86.1) | 236 (55.0) |
| Incomplete | 31 (13.9) | 193 (45.0) | 62.875 | <0.001\* |
| **Resection margin (cm)** |  |  |  |  |
| <1 | 153 (68.6) | 323 (75.3) |
| ≥1 | 70 (31.4) | 106 (24.7) | 3.324 | 0.068 |
| **Ki67 index** |  |  |  |  |
| <30% | 139 (62.3) | 83 (19.3) |  |  |
| 30-59% | 71 (31.8) | 177 (41.3) |  |  |
| ≥60 | 13 (5.8) | 169 (39.4) | 142.262 | <0.001\* |
| **MVI** |  |  |  |  |
| No | 100 (44.8) | 56 (13.1) |
| Yes | 123 (55.2) | 373 (86.9) | 81.465 | <0.001\* |
| (Continued to the next page) |  |  |  |  |
|  |  |  |  |  |
| **Table S4.** Continued |  |  |  |  |
| **PVTT** |  |  |  |  |
| No | 205 (91.9) | 298 (69.5) |
| Yes | 18 (8.1) | 131 (30.5) | 42.000 | <0.001\* |
| **Liver cirrhosis** |  |  |  |  |
| None/Mild | 151 (67.7) | 317 (73.9) |
| Moderate/Severe | 72 (32.3) | 112 (26.1) | 2.766 | 0.096 |
| **Postoperative complications** |  |  |  |  |
| No | 212 (95.1) | 361 (84.1) |
| Yes | 11 (4.9) | 68 (15.9) | 16.426 | <0.001\* |
| **CNLC stage** |  |  |  |  |
| IA~IB | 147 (65.9) | 156 (36.4) |
| II | 56 (25.1) | 134 (31.2) |
| IIIA | 20 (9.0) | 139 (32.4) | 62.505 | <0.001\* |
| **PA-TACE** |  |  |  |  |
| No | 114 (51.1) | 210 (49.0) |
| Yes | 109 (48.9) | 219 (51.0) | 0.276 | 0.599 |

Data were usedby Pearson Chi-square test or Fisher’s exact test if any cell number less than 5.

Abbreviations:

HBV: hepatitis B virus; AFP: alpha-fetoprotein; MVI: microvascular invasion; PVTT: portal vein tumor thrombus.

b In cases involving multiple nodes, the largest was indicated.

\*p < 0.05 was considered as a significant difference between HR and HR+PA-TACE groups.

**Table S5.** Binary logistic regression to identify factors associated with early recurrence (<12 months)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Factor** | **P-value** | **HR** | **95%CI** | |
| **Lower limit** | **Upper limit** |
| AFP | 0.001\* | 1.993 | 1.328 | 2.991 |
| Tumor sizeb | 0.029\* | 1.880 | 1.068 | 3.312 |
| Edmondson gradeb | 0.063 | 0.673 | 0.442 | 1.022 |
| Node number | 0.409 | 1.418 | 0.618 | 3.254 |
| Tumor capsuleb | 0.014\* | 1.935 | 1.142 | 3.280 |
| Ki67 index | <0.001\* | 79.869 | 25.464 | 250.520 |
| MVI | <0.001\* | 2.304 | 1.452 | 3.656 |
| PVTT | 0.819 | 1.261 | 0.173 | 9.216 |
| Postoperative complications | 0.005\* | 3.120 | 1.402 | 6.943 |
| CNLC stage | 0.592 |  |  |  |
| IA~IB |  |  |  |  |
| II | 0.323 | 1.584 | 0.636 | 3.945 |
| IIIA | 0.648 | 1.574 | 0.224 | 11.074 |
| Constant | 0.000 | 0.062 |  |  |

The OR was evaluated by Binary logistic regression.

Abbreviations:

HBV: hepatitis B virus; AFP: alpha-fetoprotein; MVI: microvascular invasion; PVTT: portal vein tumor thrombus.

b In cases involving multiple nodes, the largest was indicated.

\*p < 0.05 was considered was a significant difference between HR and HR+PA-TACE groups.