**SUPPLEMENTARY FILE**

**Supplementary Table 1. Multivariable Cox regression analyses of various normal bilirubin thresholds at 1 year for the prediction of liver transplantation and death**

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| **Bilirubin at 1 year (n=2382)** |
| **Threshold (×ULN)** | **C-statistic (95%CI)** | **HR (95% CI)** | ***P* value** | **No. of patients ≤/> threshold** |
| 0.30 | 0.7223 (0.6930-0.7515) | 1.63 (1.04-2.58) | 0.04 | 302/2080 |
| 0.40 | 0.7240 (0.6948-0.7531) | 1.51 (1.12-2.06) | 0.008 | 712/1670 |
| 0.50 | 0.7366 (0.7081-0.7651) | 1.85 (1.46-2.36) | <0.001 | 1243/1139 |
| 0.55 | 0.7357 (0.7073-0.7642) | 1.90 (1.51-2.40) | <0.001 | 1416/966 |
| 0.59 | 0.7400 (0.7114-0.7686) | 2.02 (1.61-2.54) | <0.001 | 1573/809 |
| 0.60 | 0.7429 (0.7144-0.7713) | 2.12 (1.69-2.66) | <0.001 | 1619/763 |
| 0.61 | 0.7423 (0.7137-0.7710) | 2.09 (1.67-2.62) | <0.001 | 1630/752 |
| 0.62 | 0.7385 (0.7095-0.7676) | 2.00 (1.60-2.50) | <0.001 | 1676/706 |
| 0.63 | 0.7385 (0.7095-0.7675) | 2.02 (1.61-2.52) | <0.001 | 1687/695 |
| 0.65 | 0.7351 (0.7061-0.7642) | 1.89 (1.51-2.37) | <0.001 | 1751/631 |
| 0.66 | 0.7354 (0.7063-0.7645) | 1.90 (1.52-2.38) | <0.001 | 1755/627 |
| 0.67 | 0.7361 (0.7070-0.7652) | 1.92 (1.53-2.40) | <0.001 | 1821/561 |
| 0.68 | 0.7354 (0.7064-0.7644) | 1.89 (1.51-2.37) | <0.001 | 1824/558 |
| 0.69 | 0.7341 (0.7051-0.7631) | 1.88 (1.50-2.36) | <0.001 | 1854/528 |
| 0.70 | 0.7344 (0.7055-0.7633) | 1.91 (1.52-2.40) | <0.001 | 1889/493 |
| 0.75 | 0.7346 (0.7052-0.7640) | 1.96 (1.54-2.49) | <0.001 | 1999/383 |
| 0.80 | 0.7336 (0.7045-0.7626) | 2.14 (1.67-2.75) | <0.001 | 2085/297 |
| 0.85 | 0.7291 (0.6997-0.7584) | 1.89 (1.41-2.52) | <0.001 | 2175/207 |
| 0.90 | 0.7253 (0.6959-0.7546) | 1.86 (1.34-2.59) | <0.001 | 2242/140 |

ULN, upper limit of normal; HR, hazard ratio; CI, confidence interval.

**Supplementary Table 2. Survival estimates at 15 years according to bilirubin quartiles and bilirubin threshold of 0**.**6×ULN**

|  |  |
| --- | --- |
|  | **15-year survival rates (%)** |
| **Bilirubin quartiles**  | **Time zero cohort** | **1-year cohort**  |
| Q1 | 83.4  | 82.3  |
| Q2 | 82.6 | 85.4  |
| Q3 | 77.6 | 74.6  |
| Q4 | 71.3 | 64.6  |
| **Bilirubin threshold** | **Time zero cohort** | **1-year cohort**  |
| <0.6×ULN | 82.0 | 82.9 |
| 0.6-1.0×ULN | 73.0 | 65.1  |
| >1×ULN | 33.4  | 30.0 |

ULN, upper limit of normal.

**Supplementary Table 3.** **Multivariable Cox regression analyses of various normal bilirubin thresholds at time zero for the prediction of liver transplantation and death**

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| --- | --- | --- | --- | --- |
| **Threshold****(×ULN)** | **C-statistic (95% CI)** | **HR (95% CI)** | ***P* value** | **No. of patients ≤/> threshold** |
| 0.30 | 0.7335 (0.7021-0.7649) | 1.48 (0.90-2.43) | .13 | 228/1824 |
| 0.40 | 0.7363 (0.7053-0.7674) | 1.43 (1.00-2.05) | .05 | 522/1530 |
| 0.50 | 0.7404 (0.7098-0.7709) | 1.56 (1.19-2.05) | .001 | 979/1073 |
| 0.55 | 0.7380 (0.7069-0.7692) | 1.44 (1.11-1.86) | .006 | 1135/917 |
| 0.60 | 0.7403 (0.7093-0.7712) | 1.47 (1.15-1.89) | .002 | 1323/729 |
| 0.65 | 0.7467 (0.7162-0.7772) | 1.71 (1.33-2.19) | <.001 | 1435/617 |
| 0.66 | 0.7471 (0.7166-0.7776) | 1.70 (1.33-2.17) | <.001 | 1439/613 |
| 0.67 | 0.7452 (0.7146-0.7757) | 1.59 (1.24-2.03) | <.001 | 1492/560 |
| 0.68 | 0.7419 (0.7112-0.7726) | 1.52 (1.18-1.95) | .001 | 1503/549 |
| 0.69 | 0.7421 (0.7115-0.7728) | 1.52 (1.18-1.96) | .001 | 1527/525 |
| 0.70 | 0.7425 (0.7120-0.7730) | 1.54 (1.20-1.98) | .001 | 1551/501 |
| 0.75 | 0.7414 (0.7112-0.7717) | 1.60 (1.22-2.08) | .001 | 1681/371 |
| 0.80 | 0.7402 (0.7093-0.7711) | 1.57 (1.18-2.09) | .002 | 1769/283 |
| 0.85 | 0.7398 (0.7090-0.7706) | 1.66 (1.22-2.27) | .001 | 1860/192 |
| 0.90 | 0.7431 (0.7125-0.7737) | 2.17 (1.53-3.09) | <.001 | 1929/123 |

ULN, upper limit of normal; HR, hazard ratio; CI, confidence interval.



**Supplementary Figure 1. Distribution of clinical events from the 10-year survival rates associated with each bilirubin group.** Distribution of liver transplantation, liver-related death, and liver-unrelated death at (A) time zero and (B) 1 year. There was a significantly different distribution in the type of event according to bilirubin group at baseline and 1 year: *P* < .001 (Pearson Chi-square).



**Supplementary Figure 2. The association between bilirubin levels (****mg/dL) and risk for liver transplantation or death.** Hazard ratios and 95% CI were estimated by a restricted cubic spline function in (A) the time zero cohort and (B) the 1-year cohort. The bilirubin reference in each cohort is 0.65 mg/dL (11.1µmol/L).



**Supplementary Figure 3. The association between bilirubin level and risk for liver transplantation or death from 2-5 years.** Hazard ratios and 95% CI were estimated by a restricted cubic spline function at 2-5 years. The bilirubin reference in each cohort is 0.6×ULN.

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**Supplementary Figure 4. Mean bilirubin levels over 5 years in patients with normal bilirubin at study entry and stratified by outcome.** Trajectory of the mean bilirubin levels (×ULN) and 95% CI over the first 5 years depending on whether they experienced a late clinical event between 5 and 10 years (n=132) or no event within the first 10 years of follow-up (n=979). Clinical event is defined as liver transplantation or death. All patients without a clinical event had a follow-up of at least 10 years.



**Supplementary Figure 5. Survival estimates stratified by ALP levels in patients with normal bilirubin at 1 year.** Survival rates were significantly different between ALP≤1×ULN and 1.0-1.67×ULN (*P* = .001) and 1.67-3.0×ULN (*P* < .001), yet there was no significant difference between ALP 1.0-1.67 and ALP 1.67-3.0×ULN (*P* = .64). Survival was compared with the log-rank test.

 

**Supplementary Figure 6. Survival estimates according to the established thresholds for bilirubin and alkaline phosphatase.** Patients with normal bilirubin (≤1×ULN) and ALP≤1.67×ULN at 1 years were included.