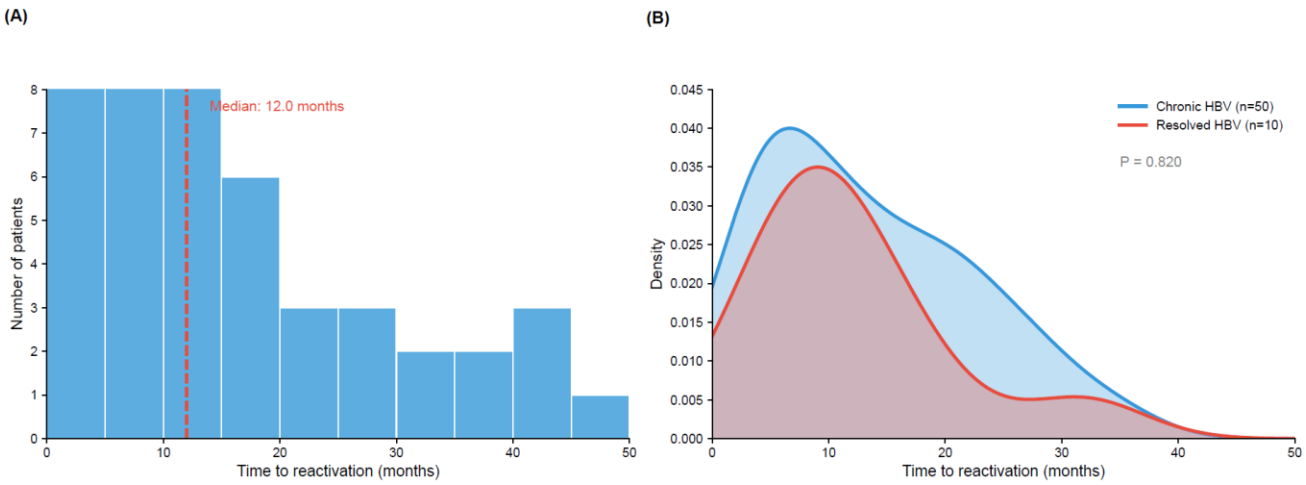
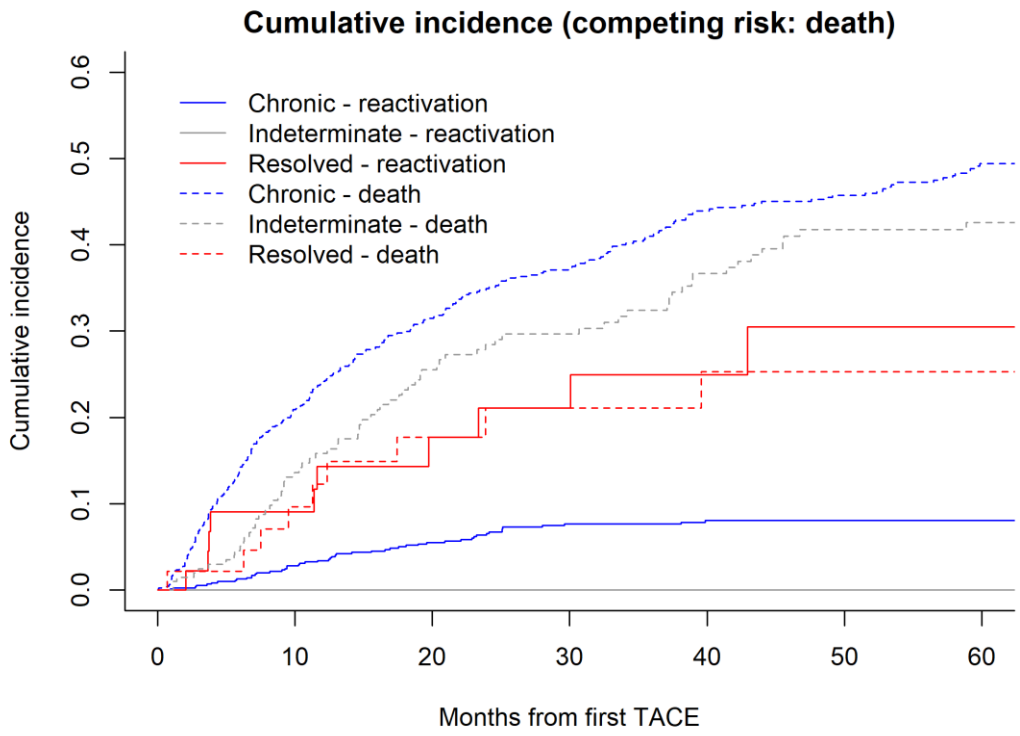



**Supplementary Figure 1 Distribution of time to HBV reactivation after TACE.** A: Histogram showing the distribution of time from first TACE to HBV reactivation in 60 patients who developed reactivation. The dashed line indicates the median time to reactivation (12.0 months). B: Kernel density plots comparing time to reactivation between patients with chronic HBV (n = 50) and those who previously had HBV (n = 10). The *P* value was calculated using the Mann–Whitney U test. HBV, hepatitis B virus; TACE, transarterial chemoembolization.




**Supplementary Figure 2 Cumulative incidence of hepatitis B virus reactivation by serological group.** Cumulative incidence functions for HBV reactivation (solid lines) and the competing event of death without HBV reactivation (dashed lines) are shown, stratified by baseline HBV serological group: chronic HBV infection (blue), indeterminate serostatus (gray), and resolved HBV infection (red). The Fine–Gray model was used, with death without HBV reactivation specified as the competing event. The cumulative incidence of HBV reactivation differed significantly between the chronic and resolved HBV groups (Gray's test, $P < 0.001$). Abbreviations: HBV, hepatitis B virus.

**Supplementary Table 1 HBV DNA measurement profile**

| Variable | Value |
|---|---|
| Number of HBV DNA measurements per patient | 5 [3–10] |
| Distribution of DNA follow-up duration (months) | 16.7 [2.1–51.3] |
| Number of patients with at least three HBV DNA measurements | 752 (77.0) |
| Maximum number of serial DNA tests | 10 |
| | |
| **Distribution of DNA measurement counts** | |
| 2 measurements | 224 (23.0) |
| 3 measurements | 139 (14.2) |
| 4 measurements | 91 (9.3) |
| 5 measurements | 75 (7.7) |
| 6 measurements | 53 (5.4) |
| 7 measurements | 53 (5.4) |
| 8 measurements | 49 (5.0) |
| 9 measurements | 42 (4.3) |
| 10 measurements | 250 (25.6) |

Data are presented as the median [quartiles 1–3] or n (%). DNA follow-up duration was calculated as the interval between the first and last HBV DNA measurements for each patient.

Abbreviations: HBV, hepatitis B virus.

**Supplementary Table 2 Hepatitis B virus DNA monitoring intensity according to baseline serological status**

| HBV Serological Status | Total Patients (n) | Number of DNA Measurements | Monitoring Interval (months) | Follow-up Duration (months) |
|---|---|---|---|---|
| Chronic HBV | 727 | 5 [3–10] | 4 [3–7] | 21 [7–52] |
| Resolved HBV | 47 | 3 [2–6] | 9 [4–17] | 17 [7–40] |
| Indeterminate | 202 | 6 [3–10] | 5 [3–9] | 33 [12–79] |
| P value* | — | <0.001 | <0.001 | 0.245 |

Data are presented as the median [quartiles 1–3]. *P values were calculated using the Mann–Whitney U test comparing the chronic HBV and resolved HBV groups only; the indeterminate group is shown for reference. Abbreviations: HBV, hepatitis B virus.

**Supplementary Table 3 Comparison of viral dynamics during HBV reactivation**

| Variable | Chronic HBV n=50 | Resolved HBV n=10 | *P* value |
|---|---|---|---|
| Baseline HBV DNA ($log_{10}$ IU/mL) | | | |
| Median [Q1–3] | 1.74 [1.00–3.45] | Undetectable | — |
| Peak HBV DNA ($log_{10}$ IU/mL) | | | |
| Median [Q1–3] | 5.33 [3.92–6.81] | 1.49 [1.09–1.56] | <0.001 |
| Magnitude of viral surge ($\Delta log_{10}$) | | | |
| Median [Q1–3] | 3.24 [2.39–4.00] | 1.00 [0.88–1.43] | <0.001 |
| Mean ± SD | 3.32 ± 1.41 | 1.08 ± 0.41 | |
| Viral surge magnitude, n (%) | | | |
| ≥1 $log_{10}$ increase | 47 (94.0) | 7 (70.0) | 0.052 |

This table includes only the 60 patients who developed HBV reactivation. *P* values were calculated using the Mann–Whitney U test for continuous variables and Fisher's exact test for categorical variables.

Peak HBV DNA represents the maximum HBV DNA level observed during follow-up. The magnitude of viral surge was calculated as the difference between peak and baseline HBV DNA levels ($\Delta log_{10}$ IU/mL).

Resolved HBV: HBsAg negative, anti-HBc positive.

Abbreviations: HBV, hepatitis B virus; Q, quartile; SD, standard deviation; HBsAg, hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core antigen.

**Supplementary Table 4 Clinical and biochemical outcomes by hepatitis B virus reactivation status and baseline serological status**

| | Full Cohort (N = 976) | | | Within Reactivators (n = 60) | | |
|---|---|---|---|---|---|---|
| **Outcome** | **No Reactivation (n = 916)** | **Reactivation (n = 60)** | **P value** | **Chronic (n = 50)** | **Resolved (n = 10)** | **P value** |
| ALT >2x ULN | 155/916 (16.9%) | 17/60 (28.3%) | 0.038 | 16/50 (32.0%) | 1/10 (10.0%) | 0.255 |
| ALT flare >3x ULN | 108/916 (11.8%) | 16/60 (26.7%) | 0.002 | 15/50 (30.0%) | 1/10 (10.0%) | 0.263 |
| Severe ALT flare >5x ULN | 58/916 (6.3%) | 10/60 (16.7%) | 0.005 | 9/50 (18.0%) | 1/10 (10.0%) | >0.99 9 |
| Total bilirubin >2 mg/dL | 345/916 (37.7%) | 28/60 (46.7%) | 0.210 | 25/50 (50.0%) | 3/10 (30.0%) | 0.312 |
| INR >1.5 | 204/916 (22.3%) | 19/60 (31.7%) | 0.128 | 17/50 (34.0%) | 2/10 (20.0%) | 0.480 |
| Albumin <2.8 g/dL | 267/916 (29.1%) | 22/60 (36.7%) | 0.276 | 19/50 (38.0%) | 3/10 (30.0%) | 0.732 |
| Any decompensation indicator | 427/916 (46.6%) | 34/60 (56.7%) | 0.168 | 30/50 (60.0%) | 4/10 (40.0%) | 0.305 |
| All-cause mortality | 416/916 (45.4%) | 34/60 (56.7%) | 0.119 | 29/50 (58.0%) | 5/10 (50.0%) | 0.733 |

Values represent the proportion of patients meeting each criterion at the last available laboratory assessment during follow-up. This time point was not standardized between groups: for reactivators, it typically coincides with or

follows the reactivation event, whereas for non-reactivators it reflects the end of routine surveillance. The left panel compares all patients by reactivation status (full cohort, N = 976); the right panel compares reactivators by baseline HBV serological group (n = 60). P values were calculated using the chi-square or Fisher's exact test. The upper limit of normal (ULN) for ALT was defined as 40 IU/L for men and 33 IU/L for women. Abbreviations: ALT, alanine aminotransferase; ULN, upper limit of normal; INR, international normalized ratio; HBV, hepatitis B virus.

**Supplementary Table 5 Sensitivity/Subgroup analyses for the effect of a resolved HBV status**

| Subgroup | HR (95% CI) | *P* value |
|---|---|---|
| Overall | 4.02 (2.04–7.93) | <0.001 |
| Baseline DNA detectable | — | — |
| Baseline DNA undetectable | 4.59 (2.15–9.82) | <0.001 |
| TACE, at least three sessions | 4.43 (1.65–11.88) | 0.003 |
| TACE fewer than three sessions | 3.86 (1.50–9.95) | 0.005 |
| Liver cirrhosis | 3.63 (1.78–7.42) | <0.001 |
| No liver cirrhosis | 12.82 (1.42–115.82) | 0.023 |

Cox proportional-hazards regression was performed within each subgroup to assess the effect of a resolved HBV status (vs. a chronic HBV status) on the HBV reactivation risk.

Resolved HBV: HBsAg negative, anti-HBc positive.

Abbreviations: HR, hazard ratio; CI, confidence interval; HBV, hepatitis B virus; TACE, transarterial chemoembolization; HBsAg, hepatitis B surface antigen; anti-HBc, antibody to hepatitis B core antigen.

**Supplementary Table 6 Baseline characteristics of the analytic cohort and patients excluded due to indeterminate serostatus**

| Variable | Analytic cohort (n = 774) | Indeterminate cohort (n = 202) | P value |
|---|---|---|---|
| Age, years | 60.5 [53.3–68.0] | 59.8 [53.3–66.1] | 0.273 |
| Male, n (%) | 619 (80.0%) | 169 (83.7%) | 0.278 |
| Hypertension, n (%) | 194 (25.1%) | 51 (25.2%) | >0.999 |
| Diabetes mellitus, n (%) | 154 (19.9%) | 38 (18.8%) | 0.806 |
| Dyslipidemia, n (%) | 91 (11.8%) | 25 (12.4%) | 0.904 |
| Cirrhosis, n (%) | 679 (87.7%) | 165 (81.7%) | 0.034 |
| Child-Pugh B/C, n (%) | 77 (9.9%) | 8 (4.0%) | 0.011 |
| Albumin, g/dL | 4.0 [3.5–4.3] | 4.0 [3.7–4.3] | 0.249 |
| Total bilirubin, mg/dL | 0.7 [0.5–1.0] | 0.6 [0.5–0.9] | 0.030 |
| INR | 1.0 [1.0–1.1] | 1.0 [1.0–1.1] | 0.624 |
| Platelets, $\times 10^9$/L | 129.5 [89.0–169.0] | 134.0 [96.2–177.5] | 0.416 |
| AST, U/L | 33.0 [25.0–47.0] | 31.0 [25.0–41.0] | 0.127 |
| ALT, U/L | 26.0 [18.0–38.0] | 27.0 [21.0–36.0] | 0.253 |
| HBV DNA, $\log_{10}$ IU/mL | 1.6 [0.0–3.8] | 1.7 [0.0–3.7] | 0.826 |
| HBV DNA detectable, n (%) | 424 (54.8%) | 117 (57.9%) | 0.471 |
| Maximal tumor size, cm | 2.4 [1.6–4.0] | 2.2 [1.6–3.6] | 0.136 |

| | | | |
|---|---|---|---|
| AFP, ng/mL | 16.5 [4.7–168.3] | 14.2 [4.9–163.2] | 0.647 |
| PIVKA-II, mAU/mL | 44.0 [24.0–206.0] | 38.0 [22.0–163.0] | 0.193 |
| Tumor number | 1.0 [1.0–2.0] | 1.0 [1.0–2.0] | 0.615 |
| TACE sessions | 2.0 [1.0–3.0] | 2.0 [1.0–3.0] | 0.256 |
| HBV reactivation, n (%) | 60 (7.8%) | 0 (0.0%) | <0.001 |

Data are presented as the median [quartiles 1–3] or n (%). P values were calculated using the Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables. Abbreviations: HBV, hepatitis B virus; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; AFP, alpha-fetoprotein; PIVKA-II, protein induced by vitamin K absence or antagonist-II; TACE, transarterial chemoembolization.

**Supplementary Table 7 Multiple imputation sensitivity analysis for hepatitis B virus reactivation incorporating 202 patients with indeterminate serostatus**

| Variable | HR (95% CI) | P value |
|---|---|---|
| Resolved HBV infection | 2.97 (1.43–6.16) | 0.004 |
| AFP ($\log_{10}$ ng/mL) | 1.26 (0.98–1.62) | 0.072 |
| Tumor size (cm) | 1.09 (0.99–1.20) | 0.090 |

Multiple imputation by chained equations (MICE) was performed with m = 20 imputed datasets. The missing serostatus of 202 indeterminate patients was imputed using logistic regression, incorporating clinical, virological, and tumor-related covariates together with survival information (Nelson–Aalen cumulative hazard estimator and event indicator). Results were pooled using Rubin's rules. Main Table 3 reports the corresponding complete-case multivariable model in the analytic cohort (n = 774). Abbreviations: HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; MICE, multiple imputation by chained equations.

**Supplementary Table 8 Sensitivity analyses using alternative hepatitis B virus reactivation definitions: event counts and Cox regression hazard ratios**

| Definition | Total events | Chronic n (%) | Resolved n (%) | Univariable HR (95% CI) | P value | Multivariable Resolved HR (95% CI) | P value |
|---|---|---|---|---|---|---|---|
| Original (APASL/KASL, stratified) | 60 | 50 (6.9%) | 10 (21.3%) | 4.70 (2.38–9.29) | <0.001 | 4.86 (2.44–9.68) | <0.001 |
| Sensitivity A: AGA-based threshold | 47 | 47 (6.5%) | 0 (0.0%) | NE | — | NE | — |
| Sensitivity B: Uniform ≥2 $\log_{10}$ threshold | 61 | 61 (8.4%) | 0 (0.0%) | NE | — | NE | — |

Original = APASL/KASL guideline-concordant stratified definition (see Methods). Sensitivity A = AGA-based definition: ≥2 $\log_{10}$ increase if baseline HBV DNA detectable, or ≥1,000 IU/mL if baseline undetectable. Sensitivity B = uniform ≥2 $\log_{10}$ increase applied to both groups, with undetectable baseline set to a pseudo-baseline of 0.5 IU/mL. Event counts are restricted to the analytic cohort with confirmed serostatus (n = 774). Univariable and multivariable Cox regression models were fitted for each definition; the multivariable model was adjusted for AFP ($\log_{10}$ ng/mL). NE, not estimable. Abbreviations: HR, hazard ratio; CI, confidence interval; NE, not estimable; AFP, alpha-fetoprotein; APASL, Asian Pacific Association for the Study of the Liver; KASL, Korean Association for the Study of the Liver; AGA, American Gastroenterological Association.

**Supplementary Table 9 Fine–Gray subdistribution hazard regression for hepatitis B virus reactivation with death as a competing event**

| Variable | sHR (95% CI) | P value |
|---|---|---|
| **Univariable model** | | |
| Resolved HBV infection | 4.91 (2.50–9.64) | <0.001 |
| **Multivariable model adjusted for AFP** | | |
| Resolved HBV infection | 5.16 (2.62–10.15) | <0.001 |
| AFP ($log_{10}$ ng/mL) | 1.19 (0.96–1.48) | 0.110 |

The subdistribution hazard ratio (sHR) was estimated using the Fine–Gray model, with death without HBV reactivation specified as the competing event. The univariable model was fitted in the full cohort (N = 976); the multivariable model was adjusted for AFP ($log_{10}$ ng/mL) and excluded 66 patients with missing AFP data (n = 910). Abbreviations: sHR, subdistribution hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; HBV, hepatitis B virus.

**Supplementary Table 10 Sensitivity multivariable Cox regression for hepatitis B virus reactivation incorporating tumor number and multifocality**

| Variable | HR (95% CI) | P value |
|---|---|---|
| Model 1: Incorporating tumor number as a continuous variable | | |
| Resolved HBV infection | 4.56 (2.30–9.06) | <0.001 |
| AFP ($log_{10}$ ng/mL) | 1.36 (1.08–1.71) | 0.009 |
| Tumor number (continuous) | 1.05 (0.73–1.50) | 0.800 |
| Model 2: Incorporating multifocal HCC as a binary variable | | |
| Resolved HBV infection | 4.55 (2.29–9.03) | <0.001 |
| AFP ($log_{10}$ ng/mL) | 1.36 (1.08–1.71) | 0.009 |
| Multifocal HCC (≥2 nodules) | 1.17 (0.69–1.98) | 0.553 |

Each model extended the multivariable Cox model from Main Table 3 (resolved HBV, AFP, tumor size) by adding a tumor-burden variable. Model 1 added tumor number as a continuous variable; Model 2 added multifocal HCC (≥2 nodules vs. solitary) as a binary variable. Abbreviations: HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein; HCC, hepatocellular carcinoma; HBV, hepatitis B virus.

**Supplementary Table 11 Sensitivity Cox regression for hepatitis B virus reactivation restricted to antiviral-naive patients**

| Variable | HR (95% CI) | P value |
|---|---|---|
| Resolved HBV (univariable) | 3.06 (1.11–8.43) | 0.030 |
| Resolved HBV (multivariable, AFP-adjusted) | 3.69 (1.30–10.43) | 0.014 |
| AFP ($log_{10}$ ng/mL) | 1.32 (0.86–2.03) | 0.199 |

The analysis was restricted to patients who remained antiviral-naive throughout follow-up (n = 233: 160 chronic, 38 resolved, 35 indeterminate; 16 reactivation events: 10 chronic, 6 resolved). The multivariable model was adjusted for AFP ($log_{10}$ ng/mL). Abbreviations: HR, hazard ratio; CI, confidence interval; AFP, alpha-fetoprotein.