Supplementary material

Supplementary Table 1 Baseline characteristics of patients with and without complete three-time-point measurements

Variable	Complete 3-time-point data	Incomplete 3-time-point data	P value
n	836	60	
Age, years	58.00 [48.00, 69.00]	61.00 [51.75, 69.25]	0.400
Common bile duct diameter, mm	10.00 [6.00, 15.00]	10.00 [6.00, 15.00]	0.952
Baseline Tbil	49.55 [15.65, 128.82]	41.10 [19.50, 98.40]	0.583
Baseline Dbil	37.55 [7.80, 105.17]	28.55 [8.57, 78.67]	0.432
Baseline TBA	129.25 [23.67, 329.25]	57.40 [12.85, 142.00]	0.011
Baseline ALP	186.50 [109.25, 299.75]	168.00 [111.00, 240.00]	0.363
Baseline GGT	281.00 [107.50, 546.50]	330.00 [136.50, 570.25]	0.438
Baseline WBC	7.29 [5.51, 9.87]	7.65 [5.96, 10.54]	0.380
Baseline albumin	37.50 [33.40, 41.10]	37.70 [32.08, 42.42]	0.899
Baseline creatinine	77.00 [64.00, 92.00]	73.00 [58.50, 87.50]	0.146
Male sex, n (%)	551 (65.9)	38 (63.3)	0.685
Initial ERCP, n (%)	630 (75.4)	50 (83.3)	0.163
Complete stone clearance, n (%)	582 (90.5)	53 (100.0)	0.010
Early biochemical drainage response, n (%)	250 (29.9)	28 (46.7)	0.007
Main diagnosis, n (%)			0.134
Benign stricture	88 (10.5)	4 (6.7)	
Biliary dilation of unknown cause	3 (0.4)	0 (0.0)	
Other biliary disease	6 (0.7)	0 (0.0)	
Clonorchiasis	6 (0.7)	3 (5.0)	

Malignant stricture	117 (14.0)	8 (13.3)	
Stone disease	616 (73.7)	45 (75.0)	
Drainage strategy, n (%)			0.013
ENBD only	502 (60.0)	48 (80.0)	
ENBD + stent	110 (13.2)	3 (5.0)	
Stent only	212 (25.4)	8 (13.3)	
No continuous drainage device	12 (1.4)	1 (1.7)	

Note: Continuous variables are presented as median [interquartile range], and categorical variables as n (%). P values were calculated using the Mann-Whitney U test, χ^2 test, or Fisher exact test, as appropriate. TBA: Total bile acid; Dbil: Direct bilirubin; Tbil: Total bilirubin; ALP: Alkaline phosphatase; GGT: Gamma-glutamyl transferase; WBC: White blood cell count; ERCP: Endoscopic retrograde cholangiopancreatography.

Supplementary Table 2 Cross-marker comparison of 24-h relative decline in patients with available baseline and 24-h measurements

Section	Marker	N	Median [IQR]
Part A. Descriptive 24-h relative declines	TBA	873	80.20 [44.64, 95.58]
Part A. Descriptive 24-h relative declines	Dbil	893	6.63 [-31.58, 36.16]
Part A. Descriptive 24-h relative declines	Tbil	895	4.63 [-36.17, 33.56]

Section	Comparison	N	Median decline of TBA (%)	Median decline of comparator	P value	Adjusted P value

					(%)		
Part B. Paired within-patient comparisons	TBA vs Dbil	870	80.39	6.19	<0.001	<0.001	
Part B. Paired within-patient comparisons	TBA vs Tbil	872	80.17	4.42	<0.001	<0.001	

Note: Relative decline was calculated as (baseline value - 24-h postoperative value)/baseline value × 100%. This analysis required baseline and 24-h data only and did not require complete 5-d measurements. P values were calculated using paired Wilcoxon signed-rank tests. Adjusted P values were corrected using the Holm method. ERCP: Endoscopic retrograde cholangiopancreatography; TBA: Total bile acid; Dbil: Direct bilirubin; Tbil: Total bilirubin.

Supplementary Table 3 Exploratory ROC analysis for 24-h relative decline in total bile acid

Predictor	Outcome	N	AUC	95%CI lower	95%CI upper	Youden cutoff (%)	Sensitivity	Specificity	PPV	NPV
24-h relative decline in TBA	Bilirubin-defined early biochemical drainage response	873	0.675	0.638	0.713	75.1	0.73	0.526	0.405	0.816

Note: The outcome was bilirubin-defined early biochemical drainage response, defined as a ≥30% decline in total bilirubin or direct bilirubin within 24 h after ERCP. The cutoff was derived using the Youden index and should be regarded as exploratory. ROC: Receiver operating characteristic; AUC: Area under the curve; CI: Confidence interval; TBA: Total bile acid; PPV: Positive predictive value; NPV: Negative predictive value.

Supplementary Table 4 Sensitivity analyses using alternative bilirubin-based response thresholds

Bilirubin-	N	Responders	Non-	AUC	95%CI	95%CI	Youden cutoff	Sensitivity	Specificity

response threshold			responders		lower	upper	for TBA decline (%)		
20%	873	352	521	0.674	0.638	0.709	72.85	0.727	0.536
30%	873	267	606	0.675	0.638	0.713	75.1	0.73	0.526
50%	873	142	731	0.696	0.65	0.742	80.01	0.739	0.543

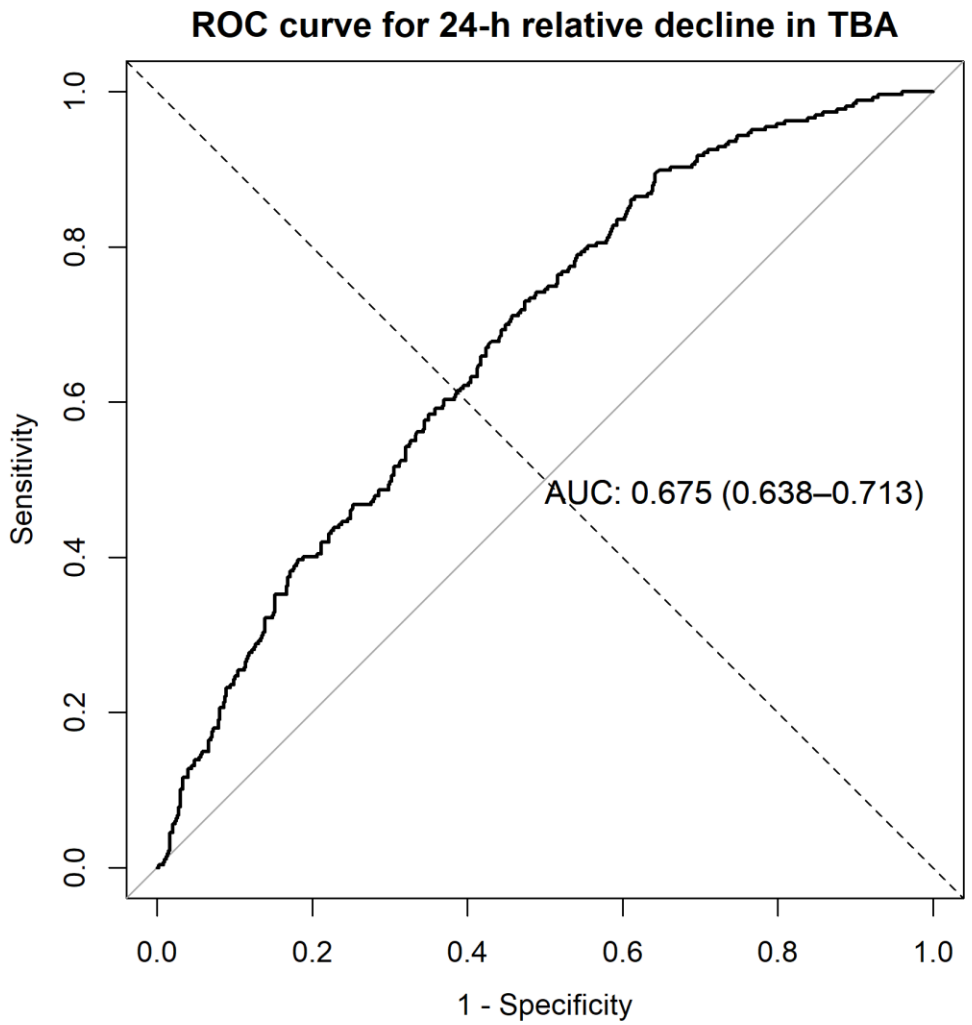
Note: The predictor was 24-h relative decline in total bile acid. Alternative outcomes were defined as ≥20%, ≥30%, or ≥50% decline in total bilirubin or direct bilirubin within 24 h after ERCP. The cutoff was derived using the Youden index and should be regarded as exploratory. TBA: Total bile acid; AUC: Area under the receiver operating characteristic curve; CI: Confidence interval.

Supplementary Table 5 Sensitivity analyses addressing potential hepatic and renal dysfunction

Analysis	Time point	N	TBA decline, median [IQR]	Dbil decline, median [IQR]	Tbil decline, median [IQR]	TBA vs Dbil P	TBA vs Dbil adjusted P	TBA vs Tbil P	TBA vs Tbil adjusted P
Primary complete-case analysis	24 h after ERCP	836	79.69 [42.81, 95.37]	5.70 [-31.98, 34.92]	3.98 [-35.82, 32.32]	<0.001	<0.001	<0.001	<0.001
Primary complete-case analysis	5 d after ERCP	836	92.00 [56.23, 98.52]	18.58 [-22.85, 52.99]	17.91 [-24.21, 52.57]	<0.001	<0.001	<0.001	<0.001
Excluding known albumin < 30 g/L	24 h after ERCP	757	80.00 [44.29, 95.58]	4.67 [-35.49, 36.32]	2.78 [-42.25, 33.56]	<0.001	<0.001	<0.001	<0.001
Excluding known	5 d after	757	92.86	18.76 [-	17.98 [-	<0.001	<0.001	<0.001	<0.001

albumin < 30 g/L	ERCP		[56.82, 98.70]	24.32, 54.52]	25.52, 53.59]				
Excluding known creatinine ≥ 177 μmol/L	24 h after ERCP	818	80.00 [43.69, 95.57]	5.70 [-32.11, 34.55]	3.98 [-36.21, 32.33]	<0.001	<0.001	<0.001	<0.001
Excluding known creatinine ≥ 177 μmol/L	5 d after ERCP	818	92.39 [56.98, 98.61]	18.53 [-22.86, 53.06]	17.91 [-24.75, 53.17]	<0.001	<0.001	<0.001	<0.001
Excluding known albumin < 30 g/L or creatinine ≥ 177 μmol/L	24 h after ERCP	741	80.03 [46.26, 95.72]	4.85 [-36.07, 36.32]	2.87 [-43.44, 33.88]	<0.001	<0.001	<0.001	<0.001
Excluding known albumin < 30 g/L or creatinine ≥ 177 μmol/L	5 d after ERCP	741	93.07 [58.02, 98.72]	18.76 [-24.59, 54.52]	18.25 [-25.82, 53.62]	<0.001	<0.001	<0.001	<0.001

Note: Albumin and serum creatinine were used as available proxy indicators of hepatic and renal dysfunction. PT/INR values were not systematically available in the analysis-ready database. Relative decline was calculated as (baseline value - postoperative value)/baseline value × 100%. P values were calculated using paired Wilcoxon signed-rank tests; adjusted P values were corrected using the Holm method. ERCP: Endoscopic retrograde cholangiopancreatography; TBA: Total bile acid; Dbil: Direct bilirubin; Tbil: Total bilirubin.



Supplementary Figure 1 Exploratory ROC curve for the 24-h relative decline in total bile acid to identify bilirubin-defined early biochemical drainage response. Note: The response outcome was defined as a ≥30% decline in total bilirubin or direct bilirubin within 24 h after ERCP. TBA: Total bile acid; ERCP: Endoscopic retrograde cholangiopancreatography; ROC: Receiver operating characteristic; AUC: Area under the curve.