

Table S1 Steyerberg checklist

Step	Specific issues	Model in our study
General considerations		
Research question	Aim: predictors/predictions?	Emphasis on prediction
Intended application	Clinical practice/research?	Clinical practice
Outcome	Clinically relevant?	Overall survival
Predictors	Reliable measurement? Comprehensiveness	Systematic review of literature
Study design	Retrospective/prospective?	Retrospective cohort
Statistical model	Appropriate for research question and type of outcome?	Cox regression
Sample size	Sufficient for aim?	174 patients, 111 events: Moderate
Seven modeling steps		
Data inspection	Distribution of data	Table 1
	Missing values	Single imputation
Coding of predictors	Continuous predictors	Truncation and spline transformations
	Combining categorical predictors	Cluster analysis
	Combining predictors with similar effects	Cluster analysis
Model specification	Appropriate selection of main effects?	Backward stepwise selection with high P-value and Lasso
	Assessment of assumptions (distributional, linearity, and additivity)?	Additivity checked with interaction terms Proportional hazards checked
Model estimation	Shrinkage included?	Penalized estimation with Lasso
	External information used?	No
Model performance	Appropriate measures used?	Discrimination: KM curves and c-index Calibration: calibration curves
Model validation	Internal validation, including model specification and estimation?	Bootstrap
	External validation?	Data from Chongming Branch Hospital, including 38 patients with 26 events
Model presentation	Format appropriate for audience	Nomogram
Validity		
Internal: overfitting	Sufficient attempts to limit and correct for overfitting?	Predictors from literature, Lasso for selection and shrinkage
External: generalizability	Predictions valid for plausibly related populations?	Routinely available predictors, representing important domains; external validated

Table S2 Cox regression coefficients in the full model

Predictor	P value	β coefficient
Sex		
Female		
Male	0.2618	-0.2799
Age	0.5165	-0.0133
Age**	0.4731	0.0173
Differentiation		
Well		
Moderate	0.6363	-0.1192
Poor	0.4787	-0.4042
T stage, AJCC 7th edn		
Tis		
T1	0.6809	-0.3351
T2	0.6081	0.3698
T3	0.3668	0.6510
T4	0.8274	0.1821
Lymph node		
Positive	<0.0001	1.4773
NA**		
Concomitant cholelithiasis	0.1911	-0.3084
TBIL	0.3838	0.0071
TBIL'	0.4592	-0.0637
CA199	0.0362	-0.0018
CA199'	0.0597	0.0306
CA125	0.3542	0.0052
CA125'	0.3060	-0.0299
CEA	0.0262	0.1466
CEA'	0.0297	-0.4085
Fibrinogen	0.4331	-0.1707
Fibrinogen'	0.0440	0.5384
INR	0.2602	-3.4033
INR'	0.3279	2.8306
Year of Surgery	0.5881	0.0318

*Continuous variables were fitted with restricted cubic spline functions, requiring 2 independent coefficients respectively, like: AGE, AGE'.

**As the "N negative and nodes examined ≥ 6 " group was too small to analyze, it was merged with the "N negative and nodes examined <6" group, and renamed "not available".

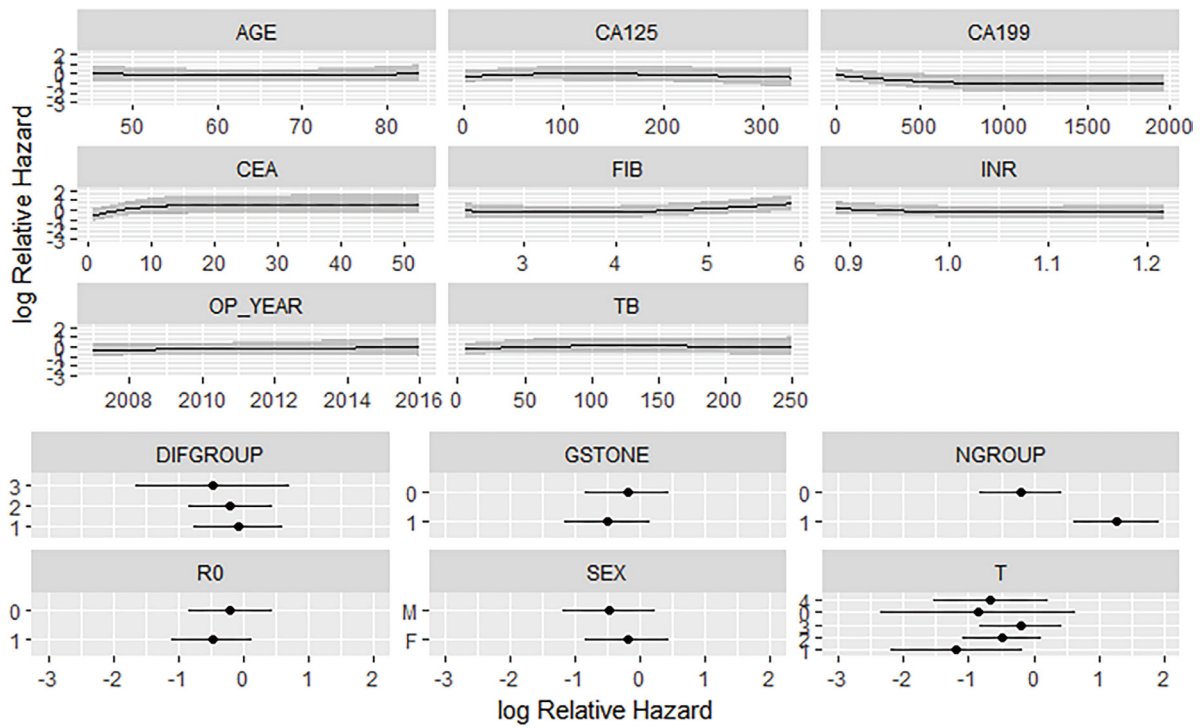


Figure S1 Trend of predictors on log hazard of death in the full model. DIFGROUP: level of differentiation, 1-well, 2-moderate, 3-poor. GSTONE: concomitant cholestasis, 1-positive, 0-negative. NGROUP: lymph node involved, 1-positive, 0-not available. R0: 1-margin negative, 0-margin positive. SEX: M-male, F-female.

Table S3 Cox regression coefficients in the simplified full model, then the stepwise selection and Lasso results

Predictor	Simplified full model		Stepwise (AIC)		Lasso
	P value	β coefficient	P value	β coefficient	β coefficient
Sex			Not selected		Not selected
Female					
Male	0.7136	-0.0789			
Age	0.7869	-0.0026	Not selected		Not selected
Differentiation			Not selected		Not selected
Well					
Moderate/poor	0.6472	-0.1968			
T stage, AJCC 7th edn					
Tis/T1					
T2–T4	0.0652	0.7564	0.012	0.9280	0.465
Lymph node					
Positive	<0.0001	1.4155	<0.001	1.3839	1.10
NA*					
Concomitant cholelithiasis	0.3015	-0.2250	Not selected		Not selected
TBIL	0.2346	0.0018	Not selected		Not selected
CA199	0.0941	0.0002	Not selected		Not selected
CA125	0.2610	0.0014	Not selected		0.0006
CEA	0.7561	0.0008	Not selected		Not selected
Fibrinogen	0.0408	0.2310	0.2826	0.004	0.120
R0	0.1521	-0.3063	Not selected		Not selected
INR	0.8813	-0.1546	Not selected		Not selected
Year of Surgery	0.6438	0.0246	Not selected		Not selected

*As the “N negative and nodes examined ≥ 6 ” group was too small to analyze, it was merged with the “N negative and nodes examined < 6 ” group, and renamed “not available”.

Table S4 Partial hazard test for the final model

Predictor	χ^2	P value
T stage (T0–1/T2–4)	0.8363	0.360
Positive lymph node	0.0092	0.924
Fibrinogen	0.0084	0.927
Global	0.879	0.831

Table S5 Redundancy analysis of final model

Predictor	R ²
T stage	0.158
Positive lymph node	0.144
Fibrinogen	0.071

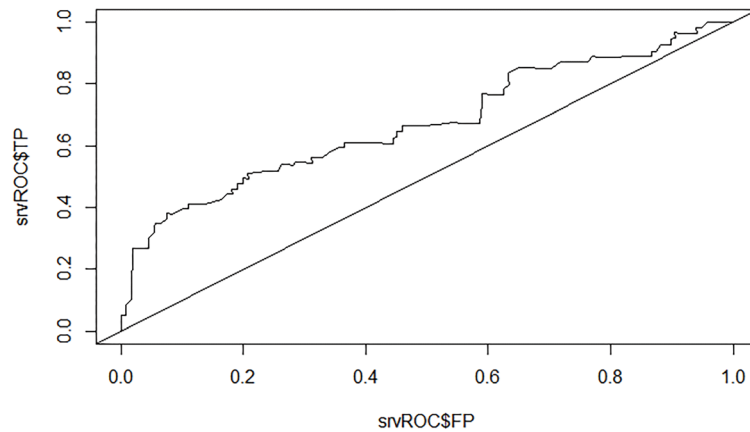


Figure S2 ROC of fibrinogen on predicting the prognosis (year =3).

Table S6 Demographic characteristics of GBC patients of validation cohort with and without hyperfibrinogenemia

Variable	Preoperative plasma fibrinogen		P-value*
	≤4.43g/L (N=27)	>4.43g/L (N=11)	
Female sex	20	9	0.93
Age	68.3±12.7	62.0±11.2	0.14
Moderate/Poor Differentiation	23	10	<0.01
T2–T4, 7 th edn	24	9	0.96
Positive lymph node	8	4	0.98
Concomitant cholelithiasis	21	7	0.62
TBIL, μmol/L (median, range)	14.0 (7–244)	12.0 (7–43)	0.50
CA199, U/mL (median, range)	31.0 (0.6–474)	37.6 (0.6–51.6)	0.69
CA125, U/mL (median, range)	15 (0.6–134)	20 (11.6–133.3)	0.03
CEA, ng/mL (median, range)	5.6 (1.9–18.0)	8.0 (3.0–14.9)	0.25
INR	0.97±0.15	0.97±0.12	0.94

* χ^2 test for discrete variables. T-test or Mann-Whitney U test for continuous variables.

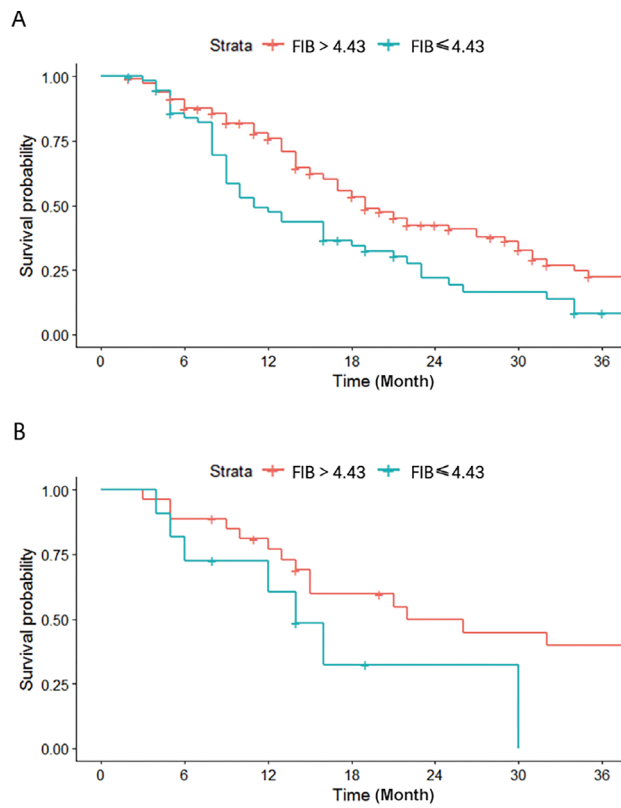


Figure S3 Survival analysis of the group dichotomized by preoperative serum fibrinogen level. (A) KM curve of the primary cohort. (B) KM curve of the validation cohort.