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ORIGINAL RESEARCH

Nutritional–Inflammatory Recovery After Metal versus Plastic Biliary Stenting in Elderly Cholangiocarcinoma: A Prospective Observational Cohort Study

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Background: Malignant biliary obstruction (MBO) in elderly cholangiocarcinoma is frequently accompanied by systemic inflammation and impaired immune–nutritional reserve. We compared stent durability and early nutrition-inflammation recovery after self-expandable metal stents (SEMS) versus plastic stents.

Methods: We conducted a single-center prospective observational cohort of consecutive patients aged ≥65 years undergoing first-time biliary stenting (2019–2024; N=188; SEMS n=109; plastic stent n=79). The primary endpoint was time to recurrent biliary obstruction (TRBO; TOKYO criteria), with death treated as a competing event. Confounding was addressed using propensity score overlap weighting. Competing-risk outcomes were analyzed with Fine–Gray regression overall survival (OS) with weighted Cox models, longitudinal GNRI, PNI, NLR, and log(SII) trajectories with mixed-effects models. Prognostic associations were evaluated using a prespecified 30-day landmark analysis.

Results: At 6 months, the overlap-weighted cumulative incidence of TRBO was 35.6% with SEMS versus 52.9% with plastic (sHR 0.64, 95% CI 0.44–0.93). SEMS was associated with fewer biliary reinterventions (any intervention 44.1% vs 68.2%; sHR 0.58, 95% CI 0.41–0.82). From baseline to day ~30, SEMS recipients had greater recovery in GNRI (mean difference +1.9; 95% CI 0.4–3.4) and PNI (+1.8; 95% CI 0.5–3.1) and a larger reduction in log(SII) (−0.10; 95% CI −0.19 to −0.01). In the landmark cohort (n=153), each 3-point increase in ΔPNI was associated with lower mortality (HR 0.86, 95% CI 0.78–0.95), while higher day-30 SII predicted higher mortality (per doubling HR 1.22, 95% CI 1.05–1.42). OS and 30-day adverse events did not differ significantly.

Conclusion: In elderly cholangiocarcinoma with MBO, SEMS was associated with lower TRBO and fewer reinterventions, and with more favorable early nutrition–inflammation recovery. Early PNI improvement and residual inflammatory burden at ~30 days provided prognostic information, supporting integrated post-drainage nutrition–inflammation monitoring.

Keywords: cholangiocarcinoma, malignant biliary obstruction, recurrent biliary obstruction, geriatric nutritional risk index, systemic immune-inflammation index

Introduction

Malignant biliary obstruction (MBO) in cholangiocarcinoma is common in older adults and is frequently accompanied by cholestasis, recurrent cholangitis, systemic inflammation, and catabolic stress. These pathophysiologic consequences contribute to rapid deterioration in immune–nutritional reserve and may worsen outcomes and procedural tolerance.[1] In parallel, inflammation-integrated nutritional indices have gained attention in cholangiocarcinoma. For example, composite immune–inflammation–nutrition scores incorporating albumin-based and leukocyte-based markers have shown prognostic value in intrahepatic cholangiocarcinoma (iCCA).[2] In older biliary tract cancer populations, adverse body composition and low prognostic nutritional index (PNI) have been associated with poorer survival, highlighting the importance of immune–nutritional reserve in geriatric oncology care.[3]

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Biliary drainage is central to palliation and supportive care in MBO, improving cholestasis-related symptoms and enabling subsequent treatment in selected patients. Both endoscopic and percutaneous approaches are used in routine practice.[4,5] However, recurrent biliary obstruction remains common and triggers repeat procedures, infections, and clinical deterioration. Metal stents generally provide larger luminal diameter and lower stent dysfunction and recurrent obstruction compared with plastic stents in malignant extrahepatic strictures.[6,7] A major challenge in interpreting observational evidence is outcome heterogeneity, because "reintervention" depends on local practice and may be confounded by elective exchange patterns for plastic stents. The TOKYO criteria standardized the concept of recurrent biliary obstruction (RBO), including occlusion and migration, enabling more comparable reporting through TRBO (time to RBO).[8,9]

Despite growing evidence that metal stents reduce obstruction-related events, less is known about whether stent strategy is associated with differential early recovery trajectories of nutrition–inflammation phenotypes in real-world elderly cholangiocarcinoma cohorts, and whether early post-drainage changes provide prognostic information beyond patency outcomes. Accordingly, we conducted a single-center cohort study in China among patients aged ≥65 years with cholangiocarcinoma undergoing first-time biliary stenting for MBO. Our primary aim was to compare TRBO between SEMS and plastic stents using a competing-risk framework with death as a competing event. Secondary aims were to compare 6-month reintervention outcomes and to evaluate early trajectories and recovery contrasts in immune–nutritional and inflammatory indices (GNRI, PNI, NLR, SII) at baseline, day 7–14, and approximately day 30 after drainage (We selected the 30-day window as a pragmatic early recovery interval because clinical and laboratory stabilization after drainage commonly occurs within the first month and this timing aligns with typical early follow-up assessment). Finally, we tested whether early recovery indices and residual inflammatory burden at ~30 days predicted subsequent survival using a prespecified 30-day landmark design. By linking stent durability with early nutrition–inflammation recovery in a real-world geriatric cohort, these findings inform pragmatic post-drainage monitoring and procedure-sparing stent selection.

Methods

Study Design, Setting, and Data Sources

This single-center, non-interventional prospective cohort study was conducted at Xi'an Honghui Hospital using collected data from the electronic medical record, endoscopy/interventional radiology procedure reports, the laboratory information system, and imaging reports. Consecutive patients evaluated for malignant biliary obstruction requiring biliary drainage between January 2019 and December 2024 were screened. The index date was defined as the date of initial biliary stent placement. Follow-up continued until the first occurrence of the relevant endpoint, last documented clinical contact, or administrative censoring in June 2025. The protocol conformed to the Declaration of Helsinki and was approved by the ethics committee of Xi'an Honghui Hospital (KYY-022). All participants provided written informed consent.

Participants and Eligibility Criteria

Patients were included if they were aged ≥65 years at index stenting, had cholangiocarcinoma with malignant biliary obstruction requiring drainage based on imaging and cholangiography/procedural documentation, underwent first-time biliary stenting during the study window, and had baseline laboratory data available within 0–7 days prior to the index procedure. Patients were excluded if they were younger than 65 years, had malignant biliary obstruction due to a non-cholangiocarcinoma primary malignancy, or had prior biliary stenting before the index procedure. Because this was an observational study with a fixed cohort size, all eligible consecutive patients were included and no formal a priori sample size calculation was performed.

Disease Definition, Diagnostic Confirmation, and Baseline Clinical Assessment

Cholangiocarcinoma was classified anatomically as intrahepatic (iCCA), perihilar (pCCA), or distal (dCCA) based on cross-sectional imaging reports (contrast-enhanced CT and/or MRI/MRCP when available) and cholangiography/procedural descriptions. For drainage-focused analyses, the level of obstruction was operationalized as distal versus perihilar based on procedural and imaging descriptions of the dominant stricture location.

Diagnostic confirmation was established by histopathology or cytology when available from clinically obtained specimens. When tissue confirmation was not feasible, patients were included if a multidisciplinary clinical–radiologic diagnosis was documented and the clinical course was consistent with cholangiocarcinoma. Serum tumor markers were treated as supportive information and were not used alone to establish malignancy.

Baseline assessment included demographics, performance status when documented (ECOG), obstruction level (distal vs perihilar), metastatic/unresectable status based on imaging and oncology evaluation, drainage route (ERCP vs PTBD), baseline liver biochemistry including total bilirubin, baseline nutritional/inflammatory laboratory measures, and the presence of acute cholangitis at presentation using Tokyo Guidelines 2018 (TG18) diagnostic criteria when sufficient documentation was available.

Frailty and comorbidity burden, which are common in older oncology populations and may influence recovery and tolerance,[10] however, formal frailty instruments and patient-reported mental/psychological or quality-of-life measures were not routinely collected. ECOG performance status, when documented, served as the available functional status indicator.

Exposure Definition and Procedural Characteristics

The exposure of interest was the initial stent type placed at the index procedure, categorized as SEMS or plastic stent, reflecting routine clinician choice without protocolized assignment. Procedural descriptors abstracted from reports included drainage route (ERCP vs PTBD), obstruction level (distal vs perihilar), number of stents placed, and stent specifications recorded in the procedure note when available. Peri-procedural antibiotics, supportive care, and subsequent oncologic treatments were delivered per standard practice and were not influenced by the study.

Outcomes and Endpoint Adjudication

The prespecified primary endpoint was time to recurrent biliary obstruction (TRBO), defined using the TOKYO criteria concept of recurrent biliary obstruction (RBO) as the first occurrence of stent occlusion or stent migration after index stenting, with event timing assigned as the earliest date on which clinical documentation and objective evidence supported RBO. Stent occlusion was identified by recurrence of cholestasis symptoms and/or cholangitis with corroborating laboratory or imaging findings leading to stent-directed management, and migration was identified by endoscopic, radiologic, or procedural documentation of displacement. Death before TRBO was treated as a competing event.

Elective/planned stent exchange does not meet RBO criteria. In the primary TRBO analysis, elective exchange did not terminate follow-up for TRBO. A prespecified sensitivity analysis censored follow-up at elective exchange to approximate index-stent patency.

Key secondary endpoints included time to unplanned biliary reintervention (RBO-driven or complication-driven), time to any biliary reintervention (including elective exchanges), time to elective/planned stent exchange, total post-index biliary procedures within 6 months (excluding the index procedure) as a measure of procedure burden, functional success within 14 days defined as a $\geq$50% reduction or normalization of total bilirubin without additional biliary drainage (with absence of a qualifying bilirubin assessment within the window treated conservatively as not meeting functional success), 30-day adverse events captured from clinical documentation using standard post-ERCP/PTBD adverse event definitions, and overall survival defined as time from index stenting to death from any cause with censoring at last known follow-up.

Laboratory Measurements and Nutrition–Inflammation Indices

Routine laboratory data were obtained from the central hospital laboratory and included serum albumin and total bilirubin from clinical chemistry assays and complete blood counts with differential including absolute neutrophil and lymphocyte counts and platelet counts.

Laboratory timepoints were defined as baseline (closest measurement within 0–7 days prior to index stenting), early follow-up (closest measurement within 7–14 days after stenting), and approximately 30-day follow-up (closest measurement to day 30 within ±10 days).

Immune–nutritional status was assessed using GNRI and PNI and systemic inflammation using NLR and SII. GNRI was calculated as 1.489×albumin (g/L) + 41.7×(weight/ideal body weight), where ideal body weight was

estimated using the BMI-22 method ($22\times\text{height}^2$). PNI was calculated as albumin (g/L) + 5×lymphocyte count (10^9/L). NLR was calculated as absolute neutrophils divided by absolute lymphocytes, and SII as platelets×neutrophils/lymphocytes using absolute counts from the same blood draw. Because SII was right-skewed, longitudinal models used the natural logarithm transformation log(SII). For recovery analyses, baseline-to-day-~30 changes were computed as $\Delta\text{index} = \text{index}_{\text{day30}} - \text{index}_{\text{baseline}}$.

Statistical Analysis

Continuous variables were summarized as mean ± standard deviation (SD) or median (interquartile range (IQR)) and categorical variables as counts with percentages. Unweighted group comparisons used Student's *t*-test or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher's exact tests for categorical variables.

To address confounding by indication, propensity scores (PS) for receiving SEMS versus plastic were estimated using logistic regression with prespecified baseline covariates reflecting demographics, disease severity/anatomy, infection status, and procedure characteristics, including age, sex, BMI, obstruction level (distal vs perihilar), baseline acute cholangitis, metastatic/unresectable status, ECOG performance status category (≥2 vs <2/unknown), drainage route (ERCP vs PTBD), baseline total bilirubin, baseline albumin, baseline SII, and calendar year. Overlap weights were defined as 1−PS for SEMS recipients and PS for plastic recipients. Covariate balance was assessed using standardized mean differences (SMDs), with SMD <0.10 indicating acceptable balance.

The primary endpoint TRBO was analyzed using overlap-weighted cumulative incidence functions (CIFs) with death as a competing event and overlap-weighted Fine–Gray subdistribution hazard models with robust (sandwich) standard errors to estimate subdistribution hazard ratios (sHRs) and 95% confidence intervals (CIs), with 6-month CIF as the prespecified primary summary timepoint. Secondary competing-risk endpoints (unplanned reintervention, any reintervention, elective exchange) were analyzed similarly. Overall survival was analyzed using overlap-weighted Cox proportional hazards regression with robust standard errors. Median overall survival was summarized descriptively using Kaplan–Meier estimates by group. Binary outcomes (functional success and 30-day adverse events) were analyzed using overlap-weighted logistic regression. Procedure burden (number of post-index biliary procedures within 6 months) was analyzed using overlap-weighted negative binomial regression with an offset for log(time at risk) truncated at 6 months to account for shortened observation time due to early death.

Longitudinal trajectories of GNRI, PNI, NLR, and log(SII) across baseline, day 7–14, and day ~30 were evaluated using linear mixed-effects models with time treated as a categorical fixed effect and patient-specific random intercepts. Overlap weights were applied as case weights. Adjusted mean profiles with standard errors, and adjusted baseline-to--day-~30 contrasts.

Prognostic associations of recovery indices were evaluated using a prespecified 30-day landmark design restricted to patients alive and under observation at day 30 and with an available day-~30 laboratory assessment within the ±10-day window, with follow-up time re-indexed at the landmark. Multivariable Cox models estimated hazard ratios for scaled predictors including ΔPNI per 3-point increase, day-30 SII per doubling (modeled as $\log_2[\text{SII}]$), ΔGNRI per 3-point increase, and day-30 total bilirubin per 50 μmol/L alongside prespecified clinical covariates.

Multiplicity was controlled using the Benjamini–Hochberg false discovery rate (FDR) procedure applied separately to the clinical endpoint family and the nutrition–inflammation recovery endpoint family and to the biomarker hypotheses, with both nominal P values and FDR-adjusted q values reported. Robustness of the primary endpoint was assessed via prespecified sensitivity analyses including cause-specific hazards modeling, a doubly robust weighted specification, alternative handling of elective exchange, and subgroup restrictions. All tests were two-sided with $\alpha=0.05$, and analyses were conducted using R (version 4.4). A technical roadmap summarizing the prespecified analytic workflow is provided in Figure 1.

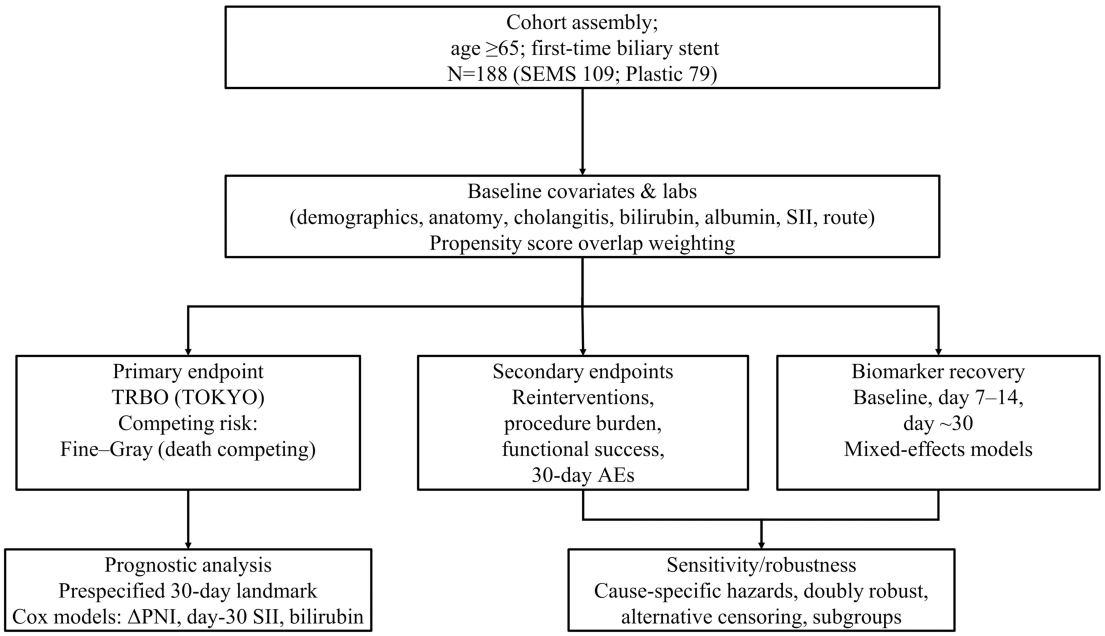

Figure 1 Study technical roadmap and analytic workflow. Flow diagram summarizing cohort assembly, propensity score overlap weighting, and the prespecified analytic context of primary and secondary endpoints, longitudinal recovery models, 30-day landmark prognostic analysis, and sensitivity analyses.

Results

Study Cohort and Data Availability

Among 205 screened patients, 17 were excluded due to age <65 years (n=8), non-cholangiocarcinoma malignancy (n=5), or prior biliary stenting before the index procedure (n=4), leaving 188 eligible patients included in the analytic cohort, of whom 109 received SEMS and 79 received plastic stents (Figure 2). Baseline laboratory data within 0–7 days pre-stent were available in all patients (188/188, 100.0%), early follow-up laboratories at day 7–14 were available in 172/188 (91.5%), and day-~30 laboratories (±10 days) were available in 160/188 (85.1%). The prespecified 30-day landmark cohort comprised 153/188 (81.4%) patients who were alive and under observation at day 30 and had an eligible day-~30 laboratory assessment (Figure 2).

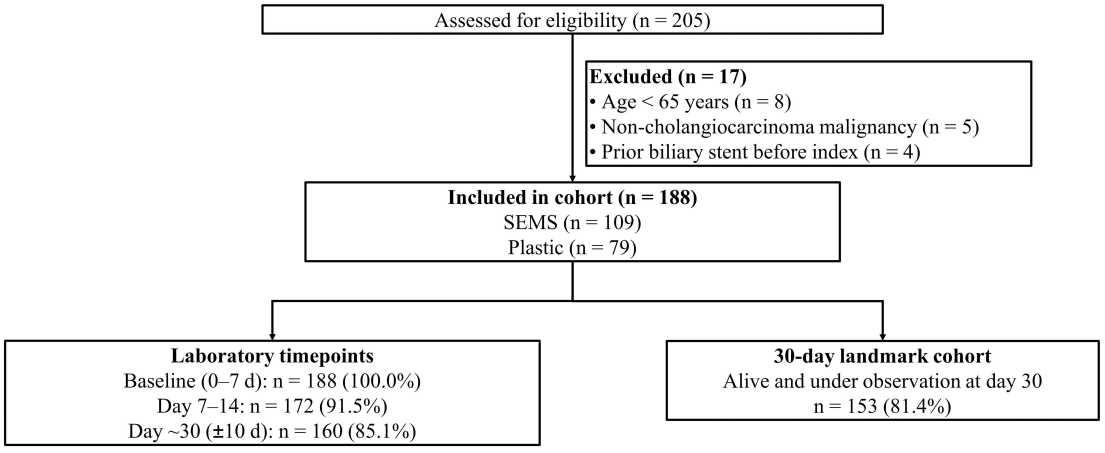

Figure 2 Study flow and data availability. Flow diagram of cohort assembly and laboratory timepoint availability in a single-center elderly cholangiocarcinoma cohort undergoing first-time biliary stenting. Baseline labs were defined as within 0–7 days pre-stent, and follow-up windows were day 7–14 and day ~30 (±10 days).

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Baseline Characteristics and Covariate Balance

In unweighted comparisons, SEMS recipients were more likely to have distal obstruction than plastic recipients (62.4% vs 48.1%, p=0.049), had higher baseline albumin (32.5±4.0 vs 31.1±4.3 g/L, p=0.030), and had lower baseline SII (median 1060.0 [IQR 760.0–1520.0] vs 1220.0 [860.0–1760.0], p=0.040), whereas age, sex, BMI, metastatic/unresectable disease, baseline cholangitis prevalence, and drainage route were otherwise broadly comparable between groups (Table 1). After overlap weighting, covariate balance improved substantially, with all displayed SMDs reduced to <0.10, supporting adequate overlap and reduced measured confounding for the weighted outcome analyses (Table 1).

Primary Endpoint: Time to Recurrent Biliary Obstruction

The overlap-weighted cumulative incidence of TRBO at 6 months was lower in the SEMS group than in the plastic group (35.6% vs 52.9%), with divergence of the cumulative incidence curves over time (Figure 3). In overlap-weighted Fine–Gray competing-risk regression treating death as a competing event, SEMS was associated with a significantly lower subdistribution hazard of TRBO compared with plastic (sHR 0.64, 95% CI 0.44–0.93; P=0.021), and this finding remained statistically significant after FDR correction within the clinical endpoint family (q=0.034) (Table 2).

Table 1 Baseline Characteristics (Unweighted) and Covariate Balance After Overlap Weighting

Variable	SEMS (n=109)	Plastic (n=79)	*p*	SMD (Unweighted)	SMD (After Overlap Weighting)
Age (years)	73.4 ± 5.8	72.9 ± 6.1	0.550	0.08	0.03
Male	69 (63.3%)	47 (59.5%)	0.610	0.08	0.02
BMI (kg/m^2)	22.1 ± 3.2	21.7 ± 3.4	0.410	0.12	0.04
Distal obstruction (vs perihilar/hilar)	68 (62.4%)	38 (48.1%)	0.049	0.30	0.06
Baseline acute cholangitis (TG18)	37 (33.9%)	36 (45.6%)	0.100	0.24	0.07
Metastatic/unresectable disease	49 (45.0%)	31 (39.2%)	0.440	0.12	0.05
ECOG performance status ≥2	43 (39.4%)	37 (46.8%)	0.310	0.15	0.04
Drainage route: ERCP (vs PTBD)	85 (78.0%)	55 (69.6%)	0.190	0.19	0.05
Baseline total bilirubin, μmol/L	228.0 (156.0–320.0)	260.0 (180.0–350.0)	0.120	0.22	0.06
Baseline albumin (g/L)	32.5 ± 4.0	31.1 ± 4.3	0.030	0.33	0.08
Baseline WBC (×10^9/L)	8.2 (6.4–10.6)	8.7 (6.8–11.8)	0.210	0.18	0.06
Baseline lymphocytes (×10^9/L)	1.1 (0.9–1.5)	1.1 (0.8–1.4)	0.160	0.20	0.05
Baseline platelets (×10^9/L)	225.0 (175.0–290.0)	235.0 (180.0–310.0)	0.380	0.10	0.03
Baseline GNRI (score)	92.1 ± 6.0	90.8 ± 6.4	0.160	0.21	0.05
Baseline PNI (score)	38.0 ± 4.3	37.2 ± 4.6	0.240	0.18	0.04
Baseline SII	1060.0 (760.0–1520.0)	1220.0 (860.0–1760.0)	0.040	0.29	0.09
Baseline NLR	5.0 (3.4–7.2)	5.4 (3.8–7.8)	0.150	0.20	0.07

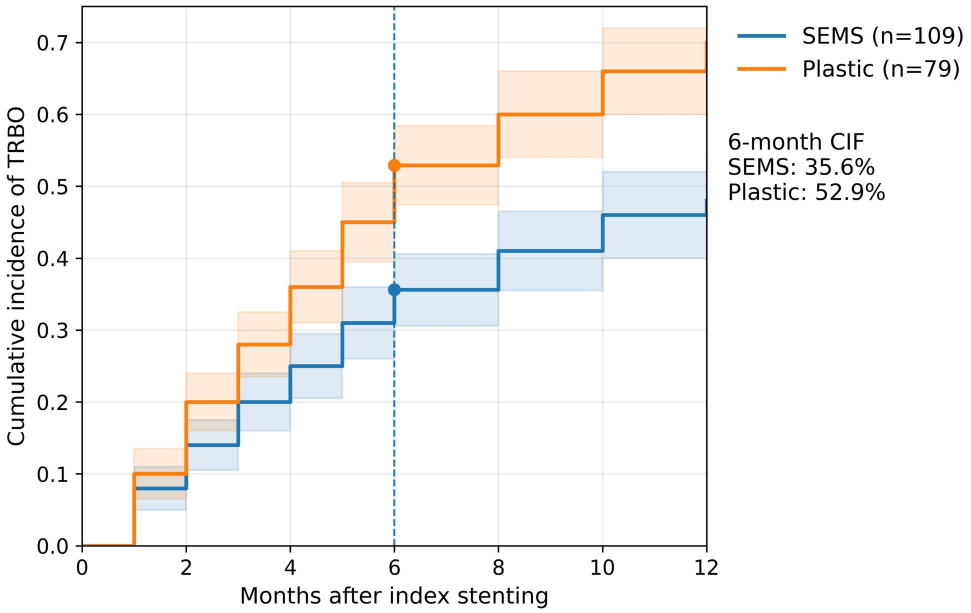

Figure 3 Cumulative incidence of TRBO by initial stent type. Cumulative incidence functions (CIF) for time to recurrent biliary obstruction (TRBO) comparing SEMS vs plastic stents, with death treated as a competing event. Shaded bands indicate illustrative 95% confidence intervals.

Secondary Clinical Endpoints

Across secondary endpoints analyzed under the overlap-weighted framework, SEMS was associated with a lower 6-month cumulative incidence of unplanned biliary reintervention compared with plastic (38.0% vs 55.0%; sHR 0.63, 95% CI 0.43–0.91; p=0.014; q=0.028) and a lower cumulative incidence of any biliary reintervention when elective

Table 2 Clinical Outcomes and Nutrition–Inflammation Recovery

Endpoint	SEMS (n=109)	Plastic (n=79)	Effect Estimate	95% CI	*p*	FDR q value
Clinical endpoints						
TRBO at 6 months (primary), CIF	35.6%	52.9%	sHR 0.64	0.44–0.93	0.021	0.034
Unplanned biliary reintervention at 6 months, CIF	38.0%	55.0%	sHR 0.63	0.43–0.91	0.014	0.028
Any biliary reintervention at 6 months (incl. elective), CIF	44.1%	68.2%	sHR 0.58	0.41–0.82	0.002	0.012
Elective/planned stent exchange at 6 months, CIF	8.5%	20.0%	sHR 0.40	0.20–0.78	0.006	0.016
Total post-index biliary procedures within 6 months, mean±SD	1.4 ± 0.9	2.0 ± 1.1	RR 0.71	0.58–0.87	0.003	0.012
Functional success within 14 days, n (%)	89 (81.7%)	61 (77.2%)	OR 1.30	0.65–2.60	0.460	0.460
30-day adverse events, n (%)	20 (18.3%)	19 (24.1%)	OR 0.70	0.35–1.42	0.330	0.440
Overall survival, median OS (months)	9.6	8.8	HR 0.88	0.66–1.18	0.390	0.446
Nutrition–inflammation recovery (baseline to day ~30)						
ΔGNRI (adjusted mean change)	+3.8	+1.9	Mean diff +1.9	0.4–3.4	0.018	0.036
ΔPNI (adjusted mean change)	+3.4	+1.6	Mean diff +1.8	0.5–3.1	0.012	0.036
Δlog(SII) (adjusted mean change)	−0.32	−0.22	Mean diff −0.10	−0.19 to −0.01	0.031	0.041
ΔNLR (adjusted mean change)	−1.2	−1.0	Mean diff −0.2	−0.5 to 0.0	0.072	0.072

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exchanges were included (44.1% vs 68.2%; sHR 0.58, 95% CI 0.41–0.82; p=0.002; q=0.012) (Table 2). Elective/planned exchange was less frequent after SEMS (6-month cumulative incidence 8.5% vs 20.0%; sHR 0.40, 95% CI 0.20–0.78; p=0.006; q=0.016) (Table 2). The mean number of post-index biliary procedures within 6 months (excluding the index procedure) was 1.4±0.9 in the SEMS group and 2.0±1.1 in the plastic group. In overlap-weighted negative binomial regression accounting for time at risk, SEMS was associated with a lower procedure rate (RR 0.71, 95% CI 0.58–0.87; p=0.003; q=0.012) (Table 2).

Functional success within 14 days occurred in 81.7% of SEMS and 77.2% of plastic recipients (OR 1.30, 95% CI 0.65–2.60; p=0.460), and 30-day adverse events occurred in 18.3% and 24.1%, respectively (OR 0.70, 95% CI 0.35–1.42; p=0.330), with neither comparison statistically significant after correction (Table 2). Overall survival was similar between groups, with median OS of 9.6 months in SEMS recipients and 8.8 months in plastic recipients and no evidence of a survival difference in the overlap-weighted Cox model (HR 0.88, 95% CI 0.66–1.18; p=0.390) (Table 2).

Nutrition–Inflammation Recovery After Biliary Drainage

In longitudinal analyses, both groups demonstrated improvement in immune–nutritional indices and reduction in inflammation indices from baseline through day 7–14 and day ~30 (Figure 4). Model-based baseline-to-day-~30 recovery contrasts favored SEMS, including larger increases in GNRI (ΔGNRI +3.8 vs +1.9; mean difference +1.9, 95% CI 0.4–3.4; p=0.018; q=0.036) and PNI (ΔPNI +3.4 vs +1.6; mean difference +1.8, 95% CI 0.5–3.1; p=0.012; q=0.036) and a greater reduction in log(SII) (Δlog[SII] −0.32 vs −0.22; mean difference −0.10, 95% CI −0.19 to −0.01; p=0.031; q=0.041), whereas the between-group difference in ΔNLR was not statistically significant (mean difference −0.2, 95% CI −0.5 to 0.0; p=0.072; q=0.072) (Table 2).

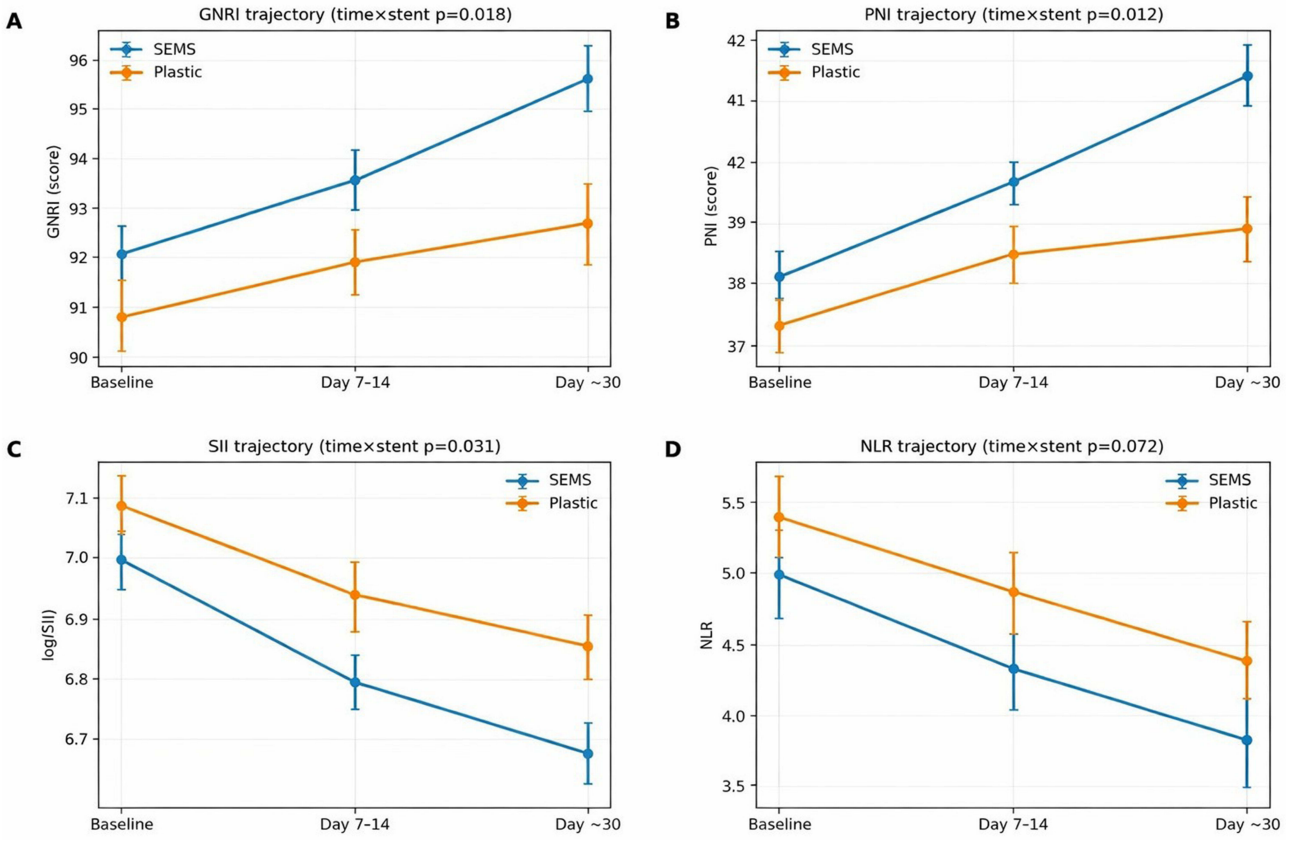

Figure 4 Adjusted nutrition–inflammation trajectories after biliary drainage. Adjusted mean trajectories (±SE) for immune–nutritional and inflammation indices at baseline, day 7–14, and day ~30: (**A**) GNRI, (**B**) PNI, (**C**) log(SII), and (**D**) NLR.

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Prognostic Associations in the 30-Day Landmark Cohort

Among 153 patients in the 30-day landmark cohort, nutrition–inflammation recovery and residual inflammatory burden were associated with subsequent survival in multivariable Cox models (Table 3). Each 3-point increase in PNI from baseline to day ~30 was associated with lower post-landmark mortality (HR 0.86, 95% CI 0.78–0.95; p=0.003; q=0.012), whereas higher day-30 SII remained associated with increased mortality risk (per doubling HR 1.22, 95% CI 1.05–1.42; p=0.009; q=0.018). Higher day-30 total bilirubin was also associated with worse survival (per 50 μmol/L HR 1.10, 95% CI 1.02–1.19; p=0.014; q=0.019) (Table 3). ΔGNRI showed a directionally protective association that did not reach statistical significance (per 3 points HR 0.92, 95% CI 0.84–1.02; p=0.108). Stent type was not independently associated with post-day-30 mortality in the landmark model (SEMS vs plastic HR 0.94, 95% CI 0.70–1.26; p=0.680), while metastatic/unresectable disease remained strongly associated with worse survival (HR 1.61, 95% CI 1.17–2.22; p=0.004) (Table 3).

Sensitivity Analyses for the Primary Endpoint

Prespecified sensitivity analyses supported the robustness of the association between SEMS and lower TRBO risk (Table 4). Findings were consistent in an overlap-weighted cause-specific hazards model (HR 0.67, 95% CI 0.47–0.96; p=0.029) and in a doubly robust Fine–Gray specification adding covariate adjustment to overlap weighting (sHR 0.62, 95% CI 0.42–0.92; p=0.018). The association remained statistically significant when censoring at elective exchange (sHR 0.66, 95% CI 0.45–0.98; p=0.038) (Table 4). In exploratory subgroup analyses, the association appeared similar or stronger in distal obstruction (sHR 0.60, 95% CI 0.38–0.95; p=0.031), while estimates in perihilar obstruction were directionally consistent but imprecise (sHR 0.70, 95% CI 0.41–1.19; p=0.186). Exclusion of baseline acute cholangitis did not materially change the effect estimate (sHR 0.63, 95% CI 0.41–0.98; p=0.041) (Table 4).

Table 3 30-Day Landmark Analysis for Post-Day-30 Overall Survival

Predictor (30-Day Landmark Cohort, n=153)	Adjusted HR	95% CI	*p*	FDR q Value
ΔPNI (per +3 points)	0.86	0.78–0.95	0.003	0.012
Day-30 SII (per doubling)	1.22	1.05–1.42	0.009	0.018
ΔGNRI (per +3 points)	0.92	0.84–1.02	0.108	0.108
Day-30 total bilirubin (per 50 μmol/L)	1.10	1.02–1.19	0.014	0.019
Stent type (SEMS vs plastic)	0.94	0.70–1.26	0.680	—
Metastatic/unresectable disease	1.61	1.17–2.22	0.004	—
Age (per +5 years)	1.07	0.96–1.19	0.210	—

Table 4 Sensitivity Analyses for Primary Endpoint (TRBO)

Sensitivity Analysis for TRBO (Primary Endpoint)	Effect Estimate	95% CI	*p*
Primary: overlap-weighted Fine–Gray (death competing)	sHR 0.64	0.44–0.93	0.021
Cause-specific Cox (overlap-weighted)	HR 0.67	0.47–0.96	0.029
Doubly robust: overlap weighting + covariate adjustment	sHR 0.62	0.42–0.92	0.018
Censor at elective exchange (sensitivity)	sHR 0.66	0.45–0.98	0.038
Restricted to distal obstruction (n=106)	sHR 0.60	0.38–0.95	0.031
Restricted to perihilar/hilar obstruction (n=82)	sHR 0.70	0.41–1.19	0.186
Exclude baseline acute cholangitis (n=115)	sHR 0.63	0.41–0.98	0.041

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Discussion

In this single-center cohort of elderly patients with cholangiocarcinoma and malignant biliary obstruction undergoing first-time biliary stenting, initial SEMS placement was associated with a lower 6-month competing-risk–adjusted incidence of recurrent biliary obstruction than plastic stenting. Consistent with this patency advantage, SEMS recipients also had lower 6-month incidences of unplanned reintervention and any reintervention including elective exchange, and experienced a lower post-index procedure burden within 6 months. In contrast, functional success, 30-day adverse events, and overall survival were broadly similar between groups.

Beyond procedural outcomes, we observed a more favorable early shift in the nutrition–inflammation phenotype among SEMS recipients. By approximately 30 days, adjusted improvements in GNRI and PNI were larger and the reduction in inflammatory burden was greater, while the between-group difference in NLR change was not statistically significant. These patterns are biologically plausible: more durable drainage may reduce recurrent cholestasis and infection risk, thereby enabling earlier stabilization and recovery. TG18 emphasizes the central role of biliary obstruction in the pathogenesis of acute cholangitis and the need for drainage as source control.[11] In addition, relief of obstructive jaundice can improve appetite and functional recovery, and restoring bile flow can plausibly improve fat and fat-soluble vitamin absorption.[1] Importantly, GNRI and PNI incorporate serum albumin, which is inflammation-sensitive and reflects inflammatory burden and disease severity in addition to dietary intake. Thus, GNRI/PNI should be interpreted as immune–nutritional/inflammatory reserve rather than "pure nutrition".[12]

In our elderly cholangiocarcinoma cohort, the main clinical value of SEMS appears to be procedure sparing rather than survival prolongation. Despite similar median OS, SEMS was associated with lower 6-month TRBO and fewer downstream interventions, translating into a lower 6-month post-index procedure burden. This patient-centered benefit is consistent with the ASGE guideline framework for malignant hilar obstruction.[13] Randomized evidence in unresectable complex hilar cholangiocarcinoma further supports a durability/adequacy-of-drainage advantage for SEMS over plastic stents, reinforcing the plausibility of our lower RBO and reintervention rates.[14] Beyond procedural endpoints, we observed larger early gains in GNRI and PNI and a greater reduction in inflammatory burden among SEMS recipients, aligning with the intended use of GNRI for nutrition-related risk stratification in older adults and with evidence that both PNI and SII carry prognostic information.[15–18] Taken together with our landmark findings, these data support incorporating a pragmatic 30-day reassessment of nutrition–inflammation indices to triage intensified nutrition and inflammation/infection management after biliary drainage.

Our TRBO findings align with the broader SEMS-versus-plastic evidence base in malignant biliary obstruction, where metal stents generally demonstrate lower dysfunction/occlusion and fewer reinterventions than plastic stents in meta-analyses and guideline syntheses.[7,19] Location-specific evidence suggests benefits may be particularly pronounced in distal malignant strictures.[20] Even in the preoperative drainage setting for resectable perihilar cholangiocarcinoma, contemporary expert-center data suggest lower stent failure with SEMS than plastic, consistent with a durable patency signal across clinical contexts.[21] Recent multicenter propensity score-matched data in inoperable perihilar cholangiocarcinoma similarly showed fewer reinterventions with metal stents among longer-term survivors.[22]

From a geriatric supportive-care perspective, these findings support an implementable workflow based on routine lab tests. Assessment of baseline immune–nutritional reserve and inflammation burden around the time of drainage, and reassess at ~30 days when early stabilization has occurred. Poor ΔPNI recovery or persistently elevated SII at ~30 days may serve as pragmatic triggers for early dietitian referral and escalation of nutrition support. This approach is consistent with oncology nutrition guidance advocating systematic screening and timely intervention.[23] GLIM criteria also emphasize the etiologic role of disease burden/inflammation in malnutrition, which is particularly relevant in cholangiocarcinoma patients experiencing cholestasis and cholangitis.[24] Although stent selection is not a nutrition intervention and causality cannot be inferred from this observational design, minimizing recurrent obstruction and procedure burden may indirectly facilitate nutritional intake and rehabilitation in frail elderly patients. In other malignant biliary obstruction cohorts undergoing PTBD, PNI thresholds in the mid-30s have been used to stratify short-term outcomes, providing context that the magnitude of ΔPNI observed here could be clinically meaningful.[25] Recent metastatic biliary tract cancer cohorts likewise support PNI as a prognostic marker during systemic therapy.[26]

Important limitations should be acknowledged. First, as a single-center study, external validity may be limited and residual confounding remains possible even after overlap weighting, particularly from unmeasured factors such as frailty, tumor burden details, stent design features, and subsequent oncologic therapy. Second, outcome ascertainment was based on the institutional medical record. Obstruction or reinterventions managed outside the institution may have been missed if not documented, and differential capture by stent group could bias event estimates. Third, missing laboratory measurements and potential informative dropout among the sickest patients could bias trajectory estimates. Fourth, GNRI depends on body weight and may be affected by fluid shifts in patients with cholestasis and advanced malignancy. Therefore, GNRI changes should be interpreted cautiously and ideally complemented by direct nutritional phenotyping in future studies. Finally, the sample size limited precision for subgroup analyses, particularly for perihilar obstruction. In addition, formal frailty/comorbidity assessments and patient-reported psychological, functional, or quality-of-life outcomes were not available, which limits interpretation of patient-centered recovery.

Conclusion

In conclusion, in elderly cholangiocarcinoma with malignant biliary obstruction, initial SEMS placement was associated with a lower incidence of recurrent biliary obstruction and fewer downstream biliary procedures compared with plastic stents, alongside more favorable early recovery in immune–nutritional reserve and inflammatory burden over the first month after drainage. Early post-stent PNI change and residual day-30 SII provided prognostic signals for subsequent mortality, supporting integrated nutrition–inflammation monitoring after biliary drainage. A 3-point increase in PNI corresponds approximately to a 3 g/L increase in albumin or a 0.6×10^9/L increase in lymphocyte count (or a combination), providing a clinically tangible scale for the observed recovery effects. These conclusions pertain primarily to short- to mid-term outcomes in this geriatric cohort.

Data Sharing Statement

Deidentified individual participant data (where permitted by ethics) and the statistical code used for the analyses are available from the corresponding author on reasonable request, subject to institutional approval and a data use agreement.

Ethics Approval and Consent to Participate

The protocol conformed to the Declaration of Helsinki and was approved by the ethics committee of Xi'an Honghui Hospital (KYY-022). All participants provided written informed consent prior to any study procedures.

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Disclosure

The authors have no conflicts of interest to declare for this work.

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