

Adjuvant Chemotherapy After R0/N0 Biliary Tract Cancer Resection: Utilization and Survival by Subtype

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Introduction: The BILCAP trial informed adoption of adjuvant capecitabine as standard treatment for resected biliary tract cancer (BTC), but approximately 38% of participants had R1 margins and 47% had node-positive disease, leaving the benefit in lower-risk R0/N0 patients uncertain. We evaluated utilization and survival associations of adjuvant chemotherapy (AC) following R0/N0 resection and tested whether these associations differed among intrahepatic cholangiocarcinoma (iCCA), perihilar cholangiocarcinoma (pCCA), distal cholangiocarcinoma (dCCA), and gallbladder cancer (GBC).

Methods: Using the National Cancer Database from 2010 through 2022, we identified adults with R0/N0-resected BTC, at least three lymph nodes examined, and survival of at least 90 days after surgery. Subtypes were assigned using ICD-O-3 topography and histology codes, supplemented by site-specific AJCC staging schemas to distinguish pCCA from dCCA. The primary exposure was AC receipt within 90 days of surgery. Overall survival from a 90-day landmark was evaluated using multivariable and propensity score-based Cox models. A chemotherapy-by-subtype interaction was tested in pooled models. Temporal utilization trends were assessed within each subtype during the pre-BILCAP era, 2010–2016, and post-BILCAP era, 2018–2022, with 2017 excluded as a transition year.

Results: Among 3,008 patients with R0/N0-resected BTC, 756 had iCCA, 281 pCCA, 1,132 dCCA, and 839 GBC. AC utilization increased from 47.1% to 68.8% (P for trend <0.0001). Utilization was stable before BILCAP (P=0.88) and increased by 2.4 percentage points annually post-BILCAP (P=0.0024), without significant variation by subtype (interaction P=0.44). Single-agent chemotherapy utilization differed by subtype over time (interaction P=0.03), with post-BILCAP increases in GBC, iCCA, and dCCA and no significant increase in pCCA. AC receipt was associated with improved overall survival in covariate-adjusted (HR, 0.66; 95% CI, 0.53–0.82; P=0.0002) and propensity-score-matched models (HR, 0.70; 95% CI, 0.54–0.90; P=0.0054). Similar associations were observed for single-agent (HR, 0.67) and multi-agent chemotherapy (HR, 0.61), each compared with no AC. Chemotherapy-by-subtype interactions were nonsignificant across models (interaction P=0.55–0.95), providing no evidence that the association between AC and survival differed by subtype.

Conclusion: Among 90-day survivors following R0/N0 resection of BTC, AC utilization increased post-BILCAP. AC receipt was associated with improved overall survival, and this association did not significantly differ among iCCA, pCCA, dCCA, and GBC. Although overall AC utilization increased similarly across subtypes, adoption of single-agent chemotherapy varied, with no significant post-BILCAP increase in pCCA. These findings suggest that the survival association of AC was not confined to a particular anatomic subtype.