

Association of Diagnosis-to-Surgery Interval With Survival Across Cholangiocarcinoma Subtypes

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Introduction: Cholangiocarcinoma (CCA) is an aggressive biliary tract malignancy for which resection offers the principal potentially curative treatment. The association between time from diagnosis to surgery and postoperative outcomes remains uncertain, and prior studies have been limited to institutional cohorts or selected CCA subtypes. We evaluated the non-linear association between diagnosis-to-surgery interval (DSI) and postoperative all-cause survival and whether this relationship differs among intrahepatic (iCCA), perihilar (pCCA), and distal (dCCA) CCA.

Methods: Adults with nonmetastatic iCCA, pCCA, or dCCA who underwent definitive-intent resection were identified using the National Cancer Database from 2010 through 2022. Subtypes were classified using ICD-O-3 topography and histologic codes, and staging was handled within AJCC 7th- and AJCC 8th-Edition eras. The primary exposure was DSI and the primary outcome was overall survival measured from surgery. Multivariable Cox proportional hazards regression modeled as a restricted cubic spline, a spline-by-subtype interaction, and baseline hazards stratified by staging era. Multivariable regression models evaluated 30- and 90-day mortality, 30-day readmission, margin positivity, and pathologic nodal positivity among node evaluated patients.

Results: The cohort included 7466 patients: 3240 with iCCA, 944 with pCCA, 3282 with dCCA. Median DSI was 30 days and varied by subtype: 39 days for iCCA, 26 days for pCCA, and 24 days for dCCA ($p < 0.001$). The association between DSI and postoperative all-cause survival differed by CCA subtype ($p = 0.0275$). Relative to an interval of 30 days, adjusted postoperative mortality ratio remained [HR 1.00 (95% CI: (0.93-1.15); CI: (0.87-1.18)] for iCCA and pCCA, respectively, whereas for dCCA DSI of 60-120 days had increased postoperative mortality compared to those with DSI of 30 days or less [HR (95% CI: 1.23 (1.06-1.43)]. DSI was not associated with 30-day mortality, 90-day mortality, readmission, and margin positivity. However, the relationship between DSI and pathologic nodal positivity varied significantly by subtype ($p < 0.001$). Predicted nodal positivity peaked when day of surgery coincided with day of diagnosis for iCCA, 30 days after for pCCA, and approximately 45 days after for dCCA.

Conclusion: Among patients who ultimately underwent resection, the association between DSI and postoperative all-cause survival differed by CCA subtype. Adjusted survival was largely stable over the interval containing most patients, although dCCA demonstrated a possible increase in postoperative mortality hazard beyond approximately 60 days. These findings support further evaluation of subtype-specific measures of surgical timeliness but do not establish a safe delay threshold or support a universal quality benchmark.