

Prognostic Nodal Metrics in Resected Perihilar and Distal Cholangiocarcinoma

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Background: Perihilar cholangiocarcinoma (pCCA) and distal cholangiocarcinoma (dCCA) differ in surgical approach and the extent of lymph node evaluation. Although lymph node ratio (LNR) is an established prognostic marker, the relative prognostic value of lymph nodes examined (LNE) and LNR according to nodal status and anatomic subtype remains uncertain. We compared associations between nodal metrics and overall survival (OS) in resected pCCA and dCCA and explored subtype-specific prognostic cutpoints.

Methods: Adults with primary invasive, nonmetastatic pCCA or dCCA who underwent surgical resection were identified in the National Cancer Database from 2010 through 2022. Subtypes were assigned using ICD-O-3 topography, histology, and era-specific AJCC staging schemas. Patients with multiple primary malignancies or unknown LNE were excluded. LNR was defined as the number of positive lymph nodes divided by the number examined. OS was evaluated using multivariable Cox proportional hazards regression. LNE was modeled among patients with node-negative disease and LNR among those with node-positive disease using restricted cubic splines and subtype-by-metric interaction terms. Exploratory cutpoints were identified using maximally selected log-rank statistics.

Results: Among 4,284 patients, including 1,095 with pCCA and 3,189 with dCCA, 53.6% had node-positive disease. Nodal evaluation differed substantially by subtype, with a median of 6 nodes examined in pCCA and 16 in dCCA. Among patients with node-negative disease, greater LNE was associated with improved OS in both subtypes, without evidence that the association differed between pCCA and dCCA (interaction $p = 0.995$). Exploratory LNE cutpoints were 3 nodes for pCCA and 6 nodes for dCCA; LNE above the respective cutpoint was associated with lower mortality in pCCA (HR: 0.67; 95% CI: 0.53-0.85; $p = 0.001$) and dCCA (HR: 0.73; 95% CI: 0.63-0.86; $p = 0.0001$).

Among patients with node-positive disease, higher LNR was associated with worse OS in both subtypes, with no significant LNR-by-subtype interaction (interaction $p = 0.115$). Exploratory LNR cutpoints were 0.21 for pCCA and 0.12 for dCCA. LNR above the respective cutpoint was associated with higher adjusted mortality in pCCA (adjusted HR: 1.55; 95% CI: 1.19-2.01) and dCCA (adjusted HR: 1.73; 95% CI: 1.52-1.96).

Conclusions: Among patients with resected extrahepatic cholangiocarcinoma, the prognostic relevance of nodal metrics varied primarily by nodal status. LNE provided prognostic stratification among patients with node-negative disease, whereas LNR provided additional stratification among those with node-positive disease. Although exploratory cutpoints differed numerically between pCCA and dCCA, the nonsignificant interaction tests did not establish

distinct subtype-specific thresholds. These data-derived cutpoints should be considered prognostic stratification tools rather than minimum standards for adequate nodal evaluation.