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**Prevalence and clinical significance of biliary intraepithelial neoplasia in
Cholangiocarcinoma**

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Purpose: Biliary intraepithelial neoplasia (BilIN) is often found synchronously adjacent to the tumor or at the surgical resection margin of resection CC. However, its prognostic significance on outcome after CC resection is unknown. The aim of this study was to elucidate the prevalence of BilIN in CC and to determine if the presence of BilIN has a prognostic or predictive effect on survival after resection for CC with curative intent.

Methods: We retrospectively analyzed the database of patients with CC who underwent curative surgery performed from 2010 to 2017. Patients whose resection margins were positive for invasive cancer were excluded. In addition, patients CC associated with IPNB were excluded from analysis.

Results: There were 142 patients who underwent curative surgery for CC. 104 and 38 patients had extrahepatic and intrahepatic CC respectively. BilIN was detected in 42 patients (29.5%) and showed a significantly higher prevalence in extrahepatic CC (90.5%) than in intrahepatic CC (9.5%; $p = 0.003$). Median follow up was 18 months. The median tumor size was 3.1cm. Of the patients with BilIN lesion, BilIN-3 was the most common type (64.2%). On univariate analysis, extrahepatic hepatic CC patients with BilIN lesions significantly showed better disease free survival ($p=0.05$). Also, although not statistically significant, extrahepatic CC patients with BilIN lesions revealed better overall survival ($p=0.09$). In addition, presence of any type of BilIN lesion at the surgical resection margin was not associated with disease free or overall survival. On multivariate analysis, presence of BilIN lesion, irrespective of location, was significantly associated with better disease free (HR=1.959, 95% CI 1.026-3.743, $p=0.042$) and overall survival (HR=2.140, 95% CI 1.006-4.552, $p=0.048$) in extrahepatic CC patients.

Conclusion: The presence of BilIN lesions was not uncommon in CC patients and was significantly associated with better disease free and overall survival in extrahepatic CC patients.