

Neutrophil/lymphocyte ratio (NLR) as a prognostic factor in biliary tract cancer (BTC)

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Introduction BTCs include intrahepatic (IHC), hilar, distal bile duct (DBD), and gallbladder carcinoma (GBC). Risk factors include conditions associated with chronic inflammation. NLR, an inflammatory marker, is prognostic in several cancers but has not been reviewed in large BTC series, hilar or GBC.

Methods Baseline demographics and NLR at diagnosis were evaluated in 864 patients (pts) with BTC from 01/87 - 12/12 treated at Princess Margaret Cancer Center. Their prognostic significance for overall survival (OS) was determined using a Cox proportional hazards model.

Results High NLR ≥ 3.0 was associated with poor survival using univariable analysis as was stage/site of primary ($P < 0.05$), age > 65 yrs, lymphocytes ≤ 1.6 ($P < 0.01$), neutrophils ≥ 5.0 , platelets ≥ 280 , hemoglobin (Hb) < 110 g/L ($P < 0.001$). Median OS in pts with NLR < 3.0 was 21.6 mo, 12.0 mo with NLR ≥ 3.0 ($P < 0.001$). NLR retained its significance as a prognostic marker on multivariable analysis (Table), along with GBC ($P < 0.05$), age > 65 yrs, DBD primary ($P < 0.01$), stage and Hb < 110 g/L ($P < 0.001$). NLR was prognostic for OS on multivariable analysis for hilar: overall (Table) and advanced grp (n=102) (HR 1.68, 95%CI 1.07-2.64, $P < 0.05$) and in advanced DBD (n=102) (HR 1.63, 95%CI 1.03-2.57, $P < 0.05$). On subgrp analysis, NLR was prognostic for OS in advanced BTC (ABTC) (n=538) ($P < 0.01$) but not in surgical grp. NLR did not predict RECIST response to first line palliative chemotherapy in ABTC.

<i>Location</i>	<i>N</i>	<i>Variable</i>	<i>OS Univariable analysis HR (95% CI, P value)</i>	<i>OS Multivariable analysis HR (95% CI, P value)</i>
GBC	304	NLR ≥ 3.0	1.80 (1.39-2.34, < 0.001)	0.87 (0.58-1.30, 0.21)
DBD	220	NLR ≥ 3.0	1.21 (0.90-1.62, 0.21)	1.55 (1.12-2.13, 0.18)

Hilar	161	NLR \geq 3.0	1.53 (1.06-2.20, <0.05)	1.64 (1.12-2.41, <0.05)
IHC	179	NLR \geq 3.0	2.20 (1.49-3.26, <0.001)	1.38 (0.91-2.08, 0.13)
Overall	864	NLR \geq 3.0	1.60 (1.37-1.87, <0.001)	1.46 (1.25-1.72, <0.001)

Conclusion Baseline NLR is prognostic in BTC, specifically ABTC and hilar subgrp, suggesting the importance of systemic inflammation influencing outcome in pts with ABTC, thus providing a simple inexpensive prognostic biomarker while also possibly identifying pts that may benefit from antiinflammatory mediation. NLR was not predictive for response in BTC.