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Introduction: The management of locally advanced, non metastatic gall bladder cancers (GBC) is traditionally palliative chemotherapy. Down staging with neoadjuvant chemotherapy and attempting curative resection is an emerging option in this subset of tumors.

Methods: A prospectively maintained GBC database was screened for locally advanced disease, satisfying pre-defined criteria. Patients required histological proof of adenocarcinoma before entry into study. All patients with metastatic disease were excluded by performance of pre-treatment CT scans or PET-CT scans. Patients were treated with neoadjuvant chemotherapy (NACT) with Gemcitabine-Platinum doublet and assessed for response and potential resection after 3-4 cycles of chemotherapy. Prognostic factors for survival, response rates (RR), clinical benefit rate (CBR), resection rates, progression free survival (PFS) and overall survival (OS) were calculated.

Results: 160 patients were available for analysis in the time period between January 2010 and February 2016. Median age of the cohort was 52 years (range: 26-73), with a female predominance. 105 patients (65%) had node positive disease. Reasons for initial unresectability included pyloric infiltration in 10(6.3%), duodenal infiltration in 42 (26.3%), hepatic flexure in 25(15.6%), liver infiltration $>$ 2cm in 119 (75%), bile duct invasion in 31 (19.4%), vascular invasion in 8 (5%), nodal disease in 105 (65%) and doubtful margin status if resected in 26(16%), respectively. Median number of cycles administered as NACT was 4. RR and CBR after NACT was 52.5% and 70% respectively. 93 patients (58%) under surgical exploration after NACT, of which 48 patients underwent a radical cholecystectomy (30%), 18 underwent revision cholecystectomy (11%), while the remaining 27 patients were deemed unresectable intra-operatively (17%). Resection status was R0 in 63 patients (95%) and R+ in 3 patients (5%). Of the 67 patients who did not undergo surgical exploration, 10 were deemed unresectable on scans (6.3%), 43 had progressed on NACT (27%), while 14 patients (9%) defaulted/refused/progressed clinically prior to surgical assessment. 52 patients of those underwent resection (79%), received adjuvant therapy. With a median follow-up of 33 months, the median OS of the entire cohort was 13 months (95% CI: 8.7 to 17.2 months), with those having undergone curative surgery having a statistically superior OS as compared to those who did not (49 vs. 7 months; $p = 0.0001$). The median PFS of the entire cohort was 8 months (95% CI: 7 to 8.9 months). Patients having undergone curative surgery had a statistically superior PFS as compared to those who did not (25 months vs. 5 months; $p = 0.0001$). On multivariate analysis, pre-NACT higher T stage (T3,4$>$ T0,1,2) and CA 19-9 ($>$37 IU/ml) remained significant factors with poorer PFS and OS.

Conclusion: The strategy of neoadjuvant chemotherapy with potential down staging and attempted curative resection appears feasible in a selected group of 'locally advanced' GBC with improved survival outcomes as opposed to continuing palliative intent chemotherapy alone.

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