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## Optimal Timing Of Surgery After Neoadjuvant Treatment In Resected Borderline Resectable Pancreatic Cancer

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**Background** : Neoadjuvant treatment (NAT) in borderline resectable pancreatic cancer (BRPC) has become an accepted treatment in the last decade. However, there is no consensus regarding the optimal timing of surgery for patients with BRPC undergoing neoadjuvant treatment. This study is aimed to investigate prognostic factors for overall and recurrence-free survival and to suggest optimal resection timing during or after NAT in the patients with borderline resectable disease.

**Methods** : Between January 2007 and December 2019, prospectively collected data of 282 consecutive patients with BRPC who underwent upfront surgery (n=73) or NAT followed by resection (n=164) or not (n=45) were retrospectively analyzed. Among them, 146 patients who received R0 or R1 resection after NAT were included to identify prognostic parameters and survival outcomes.

**Results** : The mean age was 62.3 years and the ratio of male to female was 1.3:1 in the entire cohort. The median OS from the diagnosis was 20, 27.5, and 16 months for patients with upfront surgery, NAT followed by surgery, and NAT without surgery. When comparing NAC regimens, patients treated with FOLFIRINOX presented significantly improved resection rate (95.5% vs 83.0%,  $p = 0.003$ ) and R0 resection rate (82.9% vs 75.5%,  $P = 0.022$ ), lower LN ratio (0.15 vs 0.19,  $P = 0.029$ ) compared to those with gemcitabine-based regimen respectively. The number of NAC cycle ( $< 6$  vs  $\geq 6$ , HR 0.440), NAC regimen (Gemcitabine-based vs FOLFIRINOX, HR 0.461), delta log CA 19-9 ( $> -1.75$  vs  $\leq -1.75$ , HR 0.403), margin status (R1 vs R0 resection, HR 0.440), LN metastasis (Node-negative, HR 0.529) were associated with OS in the univariate analysis. NAC cycles  $\geq 6$  (HR:0.545, 95% CI: 0.330-0.900) and node-negativity (HR:0.566, 95% CI: 0.349-0.916) were independently associated with better OS. Patients with NAC cycles  $\geq 8$  were significantly better OS than those with 6 or 7 cycles (median OS, not-reached vs 35months,  $P = 0.025$ ). Regarding the recurrence, patients with NAT followed by surgery had a lower risk of recurrence compared to those who underwent upfront surgery (60.7% vs 75.0%,  $P = 0.044$ ). Neoadjuvant radiotherapy did not significantly reduce locoregional recurrence ( $P = 0.056$ ). Delta log CA 19-9  $\leq -1.75$  (HR:0.467, 95% CI: 0.233-0.939), R0 resection (HR:0.443, 95% CI: 0.246-0.798) and node-negativity (HR: 0.450, 95% CI: 0.292-0.695) were independently associated with better recurrent-free survival.

**Conclusions** : We suggest optimal timing of resection following NAT might be at the time serum CA 19-9 is nearly normalized after at least 6 cycles of chemotherapy.

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