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Oncologic Benefits Of Neoadjuvant Treatment Versus Upfront Surgery In Borderline Resectable Pancreatic Cancer: A Systematic Review And Meta-analysis

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Background : Neoadjuvant treatment (NAT) followed by surgery is the primary treatment for borderline resectable pancreatic cancer (BRPC). However, there is limited high-level evidence supporting the efficacy of NAT for only BRPC patients.

Methods : A systematic literature search was performed in Medline (PubMed) to identify published articles reporting the oncological outcomes of BRPC patients treated with NAT or upfront surgery (UFS) up to February 11, 2022. Patient pool with “borderline resectable pancreatic ductal adenocarcinoma” was only included in this study. When the study included patients with not only BRPC but also other resectability types, only the BRPC patient pool was analyzed.

Results : A total of 1,204 publications were identified. Finally, 19 publications with 21 data sets were included in the analysis, with 2,906 patients (NAT, 1,516; UFS, 1,390). There were two RCTs, two prospective study designs, and fourteen retrospective analyses. Thirteen studies (15 data sets) performed ITT analysis, while six studies presented the data of resected patients. The NAT group had significantly better overall survival (OS) than the UFS group in the ITT analyses (HR: 0.63, 95% CI = 0.53–0.76, I2 = 58%) and in resected patients (HR: 0.68, 95% CI = 0.60-0.78, I2 =0%). Patients treated with both neoadjuvant gemcitabine or S-1-based chemotherapy and neoadjuvant FOLFIRINOX showed improved OS in the ITT analysis (gemcitabine, HR: 0.66, 95% CI = 0.56–0.78, I2 = 41%; FOLFIRINOX, HR: 0.56, 95% CI = 0.29–1.06, I2 = 82%) and in resected patients (gemcitabine, HR: 0.70, 95% CI = 0.60–0.80, I2 = 0%; FOLFIRINOX, HR: 0.54, 95% CI = 0.31–0.96, I2 = 65%). The resection rate (NAT, 67.9%; UFS, 81.4%), R0 rate (NAT, 81.7%; UFS, 58.7%), and lymph node (LN) positivity rate (NAT, 46.4%; UFS, 78.0%) were analyzed in ITT analysis and resected patients. The resection rate was higher in the UFS group in the ITT analysis (OR: 0.29, 95% CI = 0.23–0.36; I2 = 75%). The R0 resection rate among the resected patients in the NAT group was significantly improved (OR: 4.16, 95% CI = 3.35–5.17, I2 = 48%). The LN positivity rate among the resected patients in the NAT group was relatively lower (OR: 0.26, 95% CI = 0.21–0.32; I2 = 68%).

Conclusions : In conclusion, our meta-analysis, which only focused on BRPC patients, demonstrated that NAT provides survival benefits compared with UFS. Standardizing treatment regimens based on high-quality evidence is fundamental for developing an optimal protocol to improve the patient's survival.

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