

BP SY 1-3

Treatment Options For Stable Locally Advanced Pancreatic Cancer After Chemotherapy

Hiroki YAMAUE

Second Department Of Surgery, Wakayama Medical University, JAPAN

Lecture : Background and Purpose: To improve the survival of patients with pancreatic cancer, preoperative neoadjuvant therapy has been reported to be an independent prognostic factor especially in borderline resectable cancer, and conversion surgery should be considered after intensive chemotherapy even in locally advanced pancreatic cancer. The clinical question is arising who can receive the conversion surgery if the pancreatic cancer is still stable disease (SD) and when the conversion surgery is performed in patients with stable disease. Moreover, in conversion surgery, aggressive surgical techniques including arterial resection should be required to obtain R0 status without increasing incidence of the postoperative complications. Surgical procedures of arterial resection during pancreatoduodenectomy: The overall survival (OS) of BR-artery (A) patients was significantly shorter than that of the patients with borderline resectable pancreatic cancer with portal vein/ superior mesenteric vein (PV/SMV) involvement (n=76) and resectable pancreatic cancer (n=105) who underwent surgical resection (median OS: 13.6 vs. 20.6 months, $P<0.001$). The OS of BR-A patient with neoadjuvant therapy followed by surgical resection was significantly longer than those with upfront surgery (median OS: 20.2 vs. 12.9 months, $P=0.047$). Therefore, some additional strategy is strongly needed, especially recently developed chemotherapeutic regimen including FOLFIRINOX and Gemcitabine plus nab-paclitaxel (Okada, Yamaue et al. Cancer Chemother Pharmacol 2016, Okada, Yamaue et al. Anticancer Res 2017). First, neoadjuvant chemotherapy (NAC) and chemoradiotherapy (NACRT) will be discussed in this lecture, using new regimen (Okada, Yamaue et al. Oncology 2017). PancreatoDuodenectomy with Common Hepatic Artery Resection; PD-CHAR Next, advanced surgery is combined arterial resection during pancreatoduodenectomy, and common hepatic artery (CHA) is resected and reconstructed by splenic artery. The borderline resectable or locally advanced pancreatic cancer located in pancreatic neck or dorsal pancreas tends to invade CHA, and also bifurcation of CHA and gastroduodenal artery. In these cases, CHA has to resect to obtain R0 status and reconstructed by other arteries including jejunal artery, middle colic artery, and splenic artery. Splenic artery has been preferably used in our institution and the patients had a good response regarding short- and long- term outcomes (Okada, Yamaue et al. Anticancer Res 2022). However, it has remains unclear and debatable whether arterial resection really bring a good outcome. Molecular analysis using liquid biopsy to determine the feasibility and timing of conversion surgery: In terms of feasibility and timing of conversion surgery, liquid biopsy has been performing in WMUH to determine the cell free tumor DNA (ctDNA) in the peripheral blood between March 2017 and April 2020. The study enrolled 55 patients with locally advanced PC, and each patient consented to inclusion in the study. The study investigated the relationship between KRAS status in ctDNA and clinicopathologic features, analyzing ctDNA at three time points: pretreatment, post-NAC, and post-operation. The patients with positive pretreatment and post-NAC ctDNA status had no significant decrease in median relapse-free survival (RFS) or overall survival (OS). However, the patients with positive postoperation ctDNA status had a significantly shorter median OS (723 days) than the patients with negative ctDNA results (not reached; $P = 0.0148$). A combined analysis of postoperative ctDNA and



CA19-9 values showed the cumulative effect on both RFS ($P = 0.0066$) and OS ($P = 0.0046$). The adjusted hazard ratio for risk of survival computed for the patients carrying risk factors (either detectable ctDNA or CA19-9[37 U/ml]) increased from 4.13-fold to 17.71-fold (both $P = 0.0055$) compared with the patients who had no risk factors. Conclusion: The treatment strategy for patients with borderline resectable and locally advanced pancreatic cancer has been still controversial, and further studies and discussion will be needed to confirm the appropriate treatment. Especially, according to the results of RCTs, the surgical technique should be improved to get R0 surgical margin in borderline resectable pancreatic cancer, and allow the patients to be given a suitable preoperative and postoperative adjuvant therapy. Moreover, Positive ctDNA predicts poor survival for patients with BR-PC who undergo NAC followed by pancreatectomy. Keywords: pancreatic cancer, conversion surgery, neoadjuvant chemotherapy, liquid biopsy, gene mutation