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Surgical strategy for borderline resectable pancreatic cancer

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The survival of the patients with pancreatic cancer has been still dismal despite of the development of surgical techniques. To improve the survival after pancreatic surgery, postoperative adjuvant therapy is reported to be an independent prognostic factor and surgery without morbidity is strongly required.

The definition of borderline resectable (BR) cancer has been proposed by NCCN-guideline, and briefly it should be the cancer with difficulty of R0 with pancreatic surgery. R0 surgery is an essential requirement for long survival in patients with pancreatic cancer, however, pancreatic cancer should be considered as a systemic disease in the view point of its tumor biology. Therefore, one should consider that R0 surgery is an only issue for the impact of survival in patients with advanced pancreatic cancer (*Hirono,*

Yamaue, et al. pancreas 2016).

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 (*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.

The indications for distal pancreatectomy with en-bloc celiac axis resection (DP-CAR) were extended recently to increase the R0 rate for advanced pancreatic body/tail carcinoma. Moreover, it is well recognized that neoadjuvant chemotherapy (NAC) or chemoradiotherapy (NACRT) is essential for obtaining R0 resection in patients with borderline resectable pancreatic cancer. We have conducted the clinical trial for NAC using gemcitabine and alternative day administration of S-1, and the incidence of R0 reached 81% by NAC in borderline resectable patients, whereas it was only 35% without NAC treatment (*Okada, Yamaue, et al. Surgery 2013*).

Another problem of DP-CAR is a delayed gastric emptying (DGE) due to

the ischemic gastropathy after resection of left gastric artery (LGA). We have attempted preservation of LGA (modified DP-CAR) if the patients have a tumor situated more than 10mm away from the antecedent branching LGA. The ISGPS grades of DGE were: grade A = 26%, B = 13% and C = 17% in the conventional DP-CAR group, and grade A = 7%, grade B/C = 0% in the modified DP-CAR group. Thus, we conclude that Modified DP-CAR significantly reduced the incidence of DGE in comparison to conventional DP-CAR (*Okada, Yamaue et al. World J Surg 2014*).

Third problem that one should address is how to decrease the incidence of pancreatic fistula (PF) after DP and DP-CAR. We have examined whether anastomosis of pancreatic remnant and jejunum (PJ) by duct-to-mucosa fashion will have a less incidence of PF comparing to conventional stapler closure method by multicenter randomized controlled trial, and anastomosis of PJ has some clinical benefit in patients with thicker pancreas more than 12mm at the cut surface of the pancreas (*Kawai, Yamaue et al. Ann Surg 2016*).

According to the results of RCTs, the surgical technique should be improved to get zero morbidity and mortality, and allow the patients to be given a suitable postoperative adjuvant therapy. The treatment strategy for patients with borderline resectable pancreatic cancer has been still controversial, and further studies and discussion will be needed to confirm the appropriate treatment.

