

# Do extensive pancreatic resections improve survival?

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## INTRODUCTION

Despite the progress in diagnostics, surgical techniques, neoadjuvant and adjuvant therapy there is a lack of improvement in outcomes of the patients with pancreatic cancer. Surgical resection is the only potential curative treatment, however only 15 to 20% of patients are candidates for surgery at the time of the diagnosis. Even after a curative resection, the prognosis is relatively poor, with a median survival of 15–23 months and a 5-year survival of 30% for node negative and 10% for node positive disease (1). The prognosis of a patients undergoing surgical resection is highly dependent on margin status. Resections with histologically negative margins provide the best outcome while resections with positive histological margins have reduced survival rate and resections with residual tumor have a prognosis similar to patients treated with non-operative therapies (1). Only patients with high probability of R0 resection are good candidates for upfront surgery (2).

In pancreatic cancer patients with involvement of the adjacent vascular structures, lymph node involvement beyond the field of resection and distant metastasis are deemed unresectable. Resectability of a pancreatic tumor is determined by preoperative imaging evaluation. Thin-cut pancreatic protocol computed tomography (CT) scan is the method of choice for pancreatic cancer diagnostics. Positive predictive value of a CT scan for unresectability (89–100%) is high, however the positive predictive value of CT scan for predicting resectability is low (45–79%) (3). Magnetic reso-

nance imaging (MRI) can be useful in detection of hepatic lesions that cannot be characterized by a CT (2). The sensitivity and specificity of a CT scan for lymph nodes are low, especially after a patient has undergone neoadjuvant treatment. In such cases exploration might be the only method to assess true resectability. The value of diagnostic laparoscopy is not universally accepted and should be limited to patients with the highest likelihood of occult metastatic disease.

Preoperative histological verification in patients with a typical clinical presentation and resectable malignant disease on imaging is not necessary. It is reasonable to proceed to surgery, due to high negative predictive value of a biopsies.

## RESULTS

According to the guidelines from the National Comprehensive Cancer Network (NCCN) all patients with distant metastases and metastases to the lymph nodes beyond resection are deemed unresectable. Patients are considered unresectable also when tumor surrounds  $> 180^\circ$  of SMA or celiac axis or is in contact with the first jejunal SMA branch, and if SMV or portal vein due to tumor involvement or occlusion can't be reconstructed. While unresectable disease definitions are widely accepted there is less consensus on the definition of the "borderline" resectable disease (1). European Society for Medical Oncology (ESMO) recommends chemotherapy for patients with locally advanced disease and recognizes a minor role in of the addition of chemoradiation. If sufficient downsta-

ging response is achieved, subsequent surgical exploration can be considered. Oncological treatment is adjusted based on the patient's performance status.

The NCCN considers patients as borderline resectable when tumor is in contact with the IVC or surrounds SMV or portal vein in more than  $> 180^\circ$  and in presence of vein thrombosis when resection and reconstruction is possible. Tumors in contact with common hepatic artery without involvement of celiac axis or hepatic artery bifurcation and SMA  $\leq 180^\circ$  allowing resection and reconstruction are also considered resectable. Tumors of body and tail are considered as borderline resectable when tumor is in contact less  $\leq 180^\circ$  with the celiac axis or more but without involvement of the aorta and with an intact and uninvolved gastroduodenal artery.

Due to high probability of an incomplete resection of borderline resectable tumors, strategies to "downstage" the tumour prior to the resection, using chemotherapy with or without radiotherapy, developed. ESMO and NCCN all favor initial period of chemotherapy followed by a reassessment of resectability (4). However, there is no consensus for the best approach to those patients and it is unclear whether neoadjuvant therapy provides benefit compared to modern adjuvant therapy. Most institutions and guidelines encourage enrolment of such patients in trials.

Portal vein (PV) or superior mesenteric vein (SMV) resection is supported when a R0 or R1 resection can be accomplished and if good inflow and outflow veins are present. It is suggested that in high-volume centers patients undergoing venous reconstructions have similar morbidity and perioperative mortality and it is recommended for selected groups of patients where R0/R1 resection can be accomplished (5).

While venous resection is supported, arterial resection is generally not recommended by guidelines such as ESMOs (6). However, with the advancements in operative techniques current evidence suggests that it might be appropriate for selected group of patients.

In high volume centers this is a viable option and may provide survival benefit (6).

Lymph node status is one of the most important prognostic factors after pancreatectomy and at least 15 lymph nodes should be sampled. Early recurrence and poor survival is inevitable when paraaortic nodes are infiltrated. Extended lymphadenectomy does not improve long term survival or lower recurrence rate in pancreatic cancer surgery and is not recommended (7).

Prognosis of patients with liver metastasis from pancreatic cancer is very poor and hepatic resection is generally not recommended. However, some authors have shown survival benefit in patients with synchronous solitary metastasis (8). A multicentric, prospective, randomized phase III control trial (CSPAC-1) is currently in progress to evaluate the benefits of synchronous resection of pancreatic cancer and liver metastases (9).

Sometimes resection of nearby organs is necessary to achieve radical resection. There is limited data on such resections and their oncological benefit remains controversial.

A systematic review of pancreaticoduodenectomy with colon resections showed that they are associated with increased morbidity and mortality compared to a standard resection, however survival was comparable (10).

## CONCLUSIONS

Although surgical resection is the only potentially curative treatment of pancreatic cancer for now, due to poor results, it is obviously not the best or the last answer.

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