

intrapapillary mucinous tumors (IPMN) or mucinous cystic tumors (MCN) and other rare tumors are increasing. However, in almost 40% of the patients with potentially resectable pancreatic cancer surgery is not offered, although 5-year survival rates are up to 40% or even higher in selected patients depending on tumor stage and histology [1]. Therefore surgical skills and techniques and the perioperative management have to be improved to obtain curative resection and increase survival. Further factors influencing the outcome are the hospital volume and surgical experience [2]. Standard procedures for tumors in the head of the pancreas are the Kausch–Whipple- or pylorus-preserving Whipple procedure including local lymphadenectomy. For tumors left to the portal vein the procedure of choice is the left lateral pancreas resection, generally including lymphadenectomy and splenectomy. Whereas pancreatic fistulas after a Whipple procedure is as low as 2% in experienced hands [3], the fistula rate after left resection increases up to 40% depending on the technique used. Indications for extended pancreatic surgery are increasing including venous and arterial infiltration, involvement of surrounding organs indicating multivisceral resections and surgery for metastatic disease or palliative pancreas resection. Nowadays, portal vein resection for local infiltration with or without replacement by a graft is established without change of morbidity or mortality or an increased rate for R1 resection. Although arterial resection is in many cases technically feasible its oncologic impact remains questionable and is reserved to rare indications. Although the value of extended lymphadenectomy is frequently debated, recent studies show no advantage (evidence level I) [4]. Multivisceral resections, i.e. in tumors of the tail of the pancreas invading the colon or stomach or other surrounding tissues are associated with an increased and a longer stay in the hospital. But they show comparable mortality- and survival rates to those without infiltration and therefore should be performed if technically feasible [5]. Data of surgical treatment in patients with metastatic pancreatic disease do not show any advantage to palliative treatment but can be an option in selective patients with easily removable metastasis. Although some data indicate an increased 2-year survival for patients with palliative resection (R2) due to those only with palliative surgery (bypass surgery) it does not justify its increased morbidity and mortality and especially loss of quality of life [6]. Cystic tumors of the pancreas are increasing, probably due to earlier detection by high resolution imaging. Serous cystic tumors rarely become malignant and therefore do not need surgery except they become symptomatic. Due to its high malignant potential mucinous cystic tumors (MCN) should generally be operated such as main-duct IPMN's. Branch-duct IPMN have to be operated when they are larger than three centimeters or when they show nodal involvement or signs of malignancy. Parenchyma sparing procedures such as enucleation are reserved for benign diseases i.e. cystic tumors (branch-type IPMN). In conclusion pancreatic surgery beyond the traditional limits is established in tumors infiltration the venous system and may be an approach in patients with locally infiltrating pancreatic cancer or metastasis but is not an option for palliative surgery.

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SPEAKER ABSTRACT

Adjuvant therapy in resected pancreatic cancer

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Resection rates of above 15% can be achieved in specialised centres with 5y survival rates of 10% and can be improved to 25–30% with adjuvant systemic chemotherapy. GITSG randomised 43 patients between chemoradiation (40 Gy with weekly 5-Fluorouracil (5FU) for two years) vs. surgery alone [1]. Median survival was increased in the treated group (20m vs. 11m, $p=0.035$). The ESPAC1 trial was the first adequately powered, randomised study in resected pancreatic cancer [2]. Initial analysis of all 541 patients indicated no survival benefit for adjuvant chemoradiotherapy but the results for chemotherapy were inconclusive with only ten months' median follow-up. The final results of this trial in the 289 patients restricted to the original 2×2 factorial design definitively demonstrated a survival benefit for chemotherapy, but not for chemoradiotherapy [3]. The 5y survival for chemoradiation was 10.0% and 19.6% without ($p=0.05$) and 21.1% for chemotherapy and 8.4% without ($p=0.009$). Quality of life improved after adjuvant therapy irrespective of the modality or combination of modalities [4]. A survival advantage was also demonstrated for adjuvant combination chemotherapy using 5FU, doxorubicin and mitomycin C in another randomised controlled trial [5]. A metaanalysis using individual patient data showed that the survival benefit of adjuvant chemotherapy extended to patients with R1 resection margins although the treatment effect was much less [6]. The EORTC randomised 218 patients

(104 with ampullary tumours) to adjuvant chemoradiation (but with no follow-on chemotherapy) vs. surgery alone but survival was not improved [7,8]. The RTOG9704 trial randomised 538 patients to either pre- and post-chemoradiation gemcitabine or to pre- and post-chemoradiation 5FU [9]. The median survival in the 451 'eligible' patients was 16.7 mo and 18.8 mo respectively ($p=0.34$) and in the 388 patients with pancreas head cancer 20.5 mo vs. 16.9 mo ($p=0.09$). In the CONKO-001 trial DFS was 13.4 mo for gemcitabine and 6.9 mo for surgery alone ($p<0.001$); median overall survival was 22.1 mo and 20.5 mo respectively ($p<0.06$) [10]. A Japan trial which enrolled 119 patients showed longer DFS for gemcitabine than surgery-only (median 11.4 versus 5.0 mo; $p=0.01$) [11] but not overall survival (22.3 versus 18.4 mo; $p=0.19$). The ESPAC3 trial randomised 1088 patients to 5FU and folinic acid (FA) or to gemcitabine [12]. Median (95% CI) survival of patients treated with 5FU/FA was 23.0 mo (21.1, 25.0) and 23.6 mo (21.4, 26.4) for gemcitabine ($p=0.39$; 0.81, 1.08). There were no differences in either DFS or global quality of life scores. Thus, there were no significant differences between the two treatments although adjuvant gemcitabine had an improved safety profile. Using individual patient data from both ESPAC1 and ESPAC3 a composite data analysis confirmed that adjuvant 5FU/FA had a significant survival benefit compared to observation for patients with pancreatic cancer [13]. Two major Editorials have supported the conclusions of the ESPAC trials and raise very serious questions about the continued use of adjuvant chemoradiation [14,15]. ESPAC4 trial is comparing combination chemotherapy with gemcitabine plus capecitabine with gemcitabine alone [16]. There is already rapid recruitment with sites throughout the United Kingdom, Sweden, France and Germany.

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SPEAKER ABSTRACT

Radiochemotherapy of the pancreas: State of the art 2012

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Pancreatic ductal adenocarcinoma is the fourth leading cause of cancer-related mortality and is associated with an extremely poor prognosis, reflected by a median survival of 5–8 mo and a 5-y survival probability of less than 5% when all stages are combined. Currently, the only chance for cure and prolonged survival is surgical resection with macroscopic tumor clearance. However, only approximately 10%–20% of patients are candidates for curative resection. The majority of patients (50%–60%) present with metastatic disease, and thus palliative chemotherapy remains the only option for almost all of these patients [1]. Radiotherapy has a large role to play in the therapeutic management of this disease,

1. As a neoadjuvant approach for locally advanced resectable or borderline resectable tumors, most of the time in combination with chemotherapy. In a substantial number of patients (approximately 30%–40%) the disease is considered "locally advanced" at the time of diagnosis. This group of patients has been intensively discussed during the last years and neoadjuvant therapies have been proposed to achieve better local tumor control or tumor down-staging with a subsequent potentially resectable tumor [2]. Neoadjuvant therapy in this context is defined as any preoperative therapy aiming to convert unresectable to resectable tumors and/or to increase microscopic complete tumor resection rates [3, 4].
2. As an adjuvant approach, for R0 and/or R1 resected tumors, according with the literature.
3. For locally advanced unresectable tumors, in order to aim to cure the disease [5].
4. As a symptomatic treatment, either locally in case of local pain, or for a compressive effect relief, or for treating metastases.

In all these situations, radiotherapy benefits of the technical improvements like IGRT (Image Guided Radiation Therapy) which helps improving the tumor location immediately before and even during radiation delivery, for an optimal tumor targeting [6], like IMRT (Intensity Modulated Radiation Therapy) for