One of the debate sessions during the recent IHPBA World Congress in Tokyo was dedicated to the extent of resection for pancreatic cancer. Under the title ‘Extended resection for pancreatic adenocarcinoma: Yes or no?’, the current status of extended radical resection for pancreatic adenocarcinoma was put into perspective. The framework of the debate was provided by the panellists and basically covered the views held at the Academic Medical Center in Amsterdam and at the University Hospital in Nagoya. One might say in the end that the whole issue of extended radical resection comes down to a discussion between Japanese pancreatic surgeons and their Western colleagues.

Reports in the late 1980s on the outcome of management of pancreatic cancer were not very encouraging. Subsequently experience has increased with Kausch-Whipple pancreatoduodenectomy (according to the Italians, Codivilla is entitled to this eponym too), and the mortality rate of surgical treatment has dropped to less than 2% in high-volume centres. When considering survival after resection, however, we are looking at five-year survival rates of 5–20 per cent at best and, as sometimes pointed out by our non-surgical colleagues, we can ask ourselves if we are really doing a good job. Clearly, this dismal outcome is caused, apart from liver metastasis, by the high rate of local recurrence encountered after resection of these tumours. Lymphatic spread, neural invasion, soft tissue infiltration and involvement of adjacent structures are crucial factors underlying recurrence, and obviously expectations were high that by extending surgical resection, next to development of effective (neo)adjuvant treatment protocols, survival could be improved. This notion triggered a modification of the technique of pancreatoduodenectomy, aiming at extending the limits of the standard resection initially set out by the Kausch-Whipple operation.

The concept of wide lymphatic clearance in the surgical treatment of pancreatic cancer was pioneered by Dr JG Fortner in the early seventies. He introduced radical excision encompassing wide dissection of lymph nodes, extended resection of soft tissue as well as nerve plexus and vascular removal and reconstruction. One third of patients in his series had lymph node metastases that would have not been included with the standard resection, proving his point of extending lymphadenectomy with resection. However, the toll of this extensive surgical procedure was an increased morbidity and mortality rate, and for this reason the technique of wide excision at that time was not taken up by many surgeons. Fortner called the technique of wide excision for pancreatic cancer ‘regional resection’, a term that may now raise confusion in light of later nomenclature in which regional lymphadenectomy refers to a limited lymph node dissection as opposed to radical lymphadenectomy.

In the late 1980s, the technique of extended lymphadenectomy was picked up again by Japanese surgeons. The rationale for extended radical resection was based on the high incidence of intra- and extrapancreatic neural invasion (65%) in pancreatic cancer as well as the high incidence of lymph node metastases (50–75%) found in various (mainly Japanese) studies. Several reports showed improved survival times (three-year survival rate 38% and five-year survival rate 33.4%), but these were all non-controlled studies. Interestingly, one report demonstrated improved survival with extended radical resection in lymph node-negative patients.

What is the available evidence to justify adoption of extended radical lymphadenectomy? To begin with, there is no level I evidence that extended radical lymphadenectomy results in improved survival. There are two randomised clinical trials (RCTs) addressing this question, but one may argue whether these studies meet the criteria to qualify as level II evidence. The first RCT has been undertaken by the Baltimore group as a prospective, single-institution study. According to an interim analysis, 114 patients with periamullary cancer were included in this study of which only 34, however, had pancreatic ductal carcinoma. No significant differences were found in survival of patients after standard resection or radical resection. Apart from the fact that this study is underpowered with respect to the number of patients with pancreatic cancer.
ductal carcinoma, the resection carried out in this study is less extensive than understood with the extended radical type of resection: Only the lymph nodes on the right lateral aspect of the superior mesenteric artery (not all station #14 nodes) are removed, while the lymph nodes of the coeliac axis (station #9) are not always removed nor yet the para-aortic lymph nodes (station #16).

The second RCT is a prospective, multicentre trial coordinated by Pedrazzoli, including 81 patients with pancreatic head carcinoma [10]. Forty patients were randomised to resection with standard lymphadenectomy and 41 to resection with extended lymphadenectomy. The latter procedure comprised removal of lymph nodes along the aorta from the diaphragmatic hiatus to the origin of the inferior mesenteric artery (whereas the Japanese consider extended lymphadenectomy to include all the lymph nodes of station 16, onto the aorto-common iliac bifurcation). No difference in overall survival between the two groups was found. This study has been criticised for several reasons. Firstly, no power analysis underlies this study, potentially giving rise to a type 2 statistical error. Secondly, the number of extra lymph nodes retrieved with extended lymphadenectomy was considered modest (13.3 lymph nodes in the standard lymphadenectomy group versus 19.8 in the extended lymphadenectomy group). Together with an operation time that was not significantly different and a relatively low incidence of postoperative diarrhoea (25–20%) in the group with extended lymphadenectomy, there are concerns as to the completeness of the wider lymphadenectomy performed in this study. A trend towards longer survival (p = 0.05) in node-positive patients was found in a post hoc analysis of this study, but on methodological grounds should be rejected.

This leaves us with no solid evidence that extended radical lymphadenectomy leads to better survival after pancreatoduodenectomy for pancreatic head adenocarcinoma. Non-randomised studies have shown either prolonged survival or no advantage for extended lymphadenectomy [11, 12]. Resection of a segment of the portal vein or superior mesenteric vein is dictated by the location of the tumour vis-à-vis the portal venous system and is not necessarily part of extended radical resection. Clearly, the problem is that variation in patient selection, variation in surgical technique, variation in terminology and variation in adjuvant protocols will lead to variation in patient outcome. The single, most important point therefore, is standardisation before any attempt at a new RCT should be made.

Regarding standardisation of terminology, an important step forward has been made during an international consensus meeting on surgical procedures in pancreatic cancer, held in Italy in 1998 [13]. A group of 29 experts in the field of pancreatic cancer, both surgeons and pathologists, reached an agreement on the definitions of standard, radical and extended radical pancreatoduodenectomy in terms of the scope of lymphadenectomy. The standard resection comprises regional lymphadenectomy around the duodenum and pancreas including the lymph nodes on the right side of the hepatoduodenal ligament, the right side of the superior mesenteric artery, and the anterior and posterior pancreaticoduodenal nodes, in addition to the usual (pylorus-preserving) Kausch-Whipple resection. The radical resection includes regional lymphadenectomy plus skeletonization of hepatic arteries, superior mesenteric artery between aorta and inferior pancreaticoduodenal artery, dissection of the coeliac trunk and anterolateral Gerota’s fascia. The extended radical resection encompasses radical lymphadenectomy plus clearance of the lymph node groups of station #16, between the diaphragmatic hiatus (above the coeliac trunk) and the origin of the common iliac arteries. The ideal study would then be a multicentre RCT with sufficient power, standardised surgical and pathological methods and involving no form of adjuvant therapy, to compare standard pancreatoduodenectomy with extended radical pancreatoduodenectomy, in which a strong emphasis should be placed on the assessment of quality of life. It goes without saying that this type of study is extremely difficult to carry out, and that is why many a review will still end with the proverbial statement that properly conducted, randomised controlled studies are necessary before concluding on the issue of extended radical pancreatoduodenectomy.

Even if we should succeed in putting together the ideal multicentre RCT, we may still be confronted with a controversial outcome. Looking at the Dutch gastric cancer trial completed in 1998, in which 996 patients were randomised to undergo either a D1 or D2 gastric resection according to the Japanese guidelines, no difference in survival was found [14]. Despite the fact that all the D2 operations were performed by a small number of surgeons trained under Japanese supervision, critics have attributed the negative outcome of this trial to a difference in surgical technique. So one might conclude that there are some innate believers in extended lymph node excision out there, who will not easily concede to the results of even a properly, conducted multicentre, RCT.
Remarkably, the discussants from Japan showed some reservation concerning the removal of all station #16 lymph nodes with pancreatoduodenectomy, especially when lymph nodes of these groups are found to be tumour-positive during the operation. There is now a multicentre RCT underway in Japan, conducted by Dr Y Nimura of Nagoya University Hospital, in which patients with pancreatic adenocarcinoma who do not have any evidence of involved para-aortic lymph nodes on frozen section examinations during the operation are randomised to undergo either a radical or extended radical pancreatoduodenectomy. The first results of this trial are expected in two years from now.

In the meantime, it seems that we are dealing with a battle of two principles. On the one hand, we have our scientific conscience which relies solely on evidence-based surgery and on the other hand, we have our professional conscience which tells us ‘never to give up’. At this point, we wish to compliment those who are exploring the field of extended radical pancreatoduodenectomy for all their efforts to push forward the frontier in what remains a dismal disease.

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**References**