

Pancreatic Head Mass: How Can We Treat It ? Tumor: Surgical Treatment

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Summary

Pancreatic carcinoma is a devastating disease. Untreated 5-year survival is 0%. The only possibility of being cured is given by surgical removal of the tumor. Pancreatoduodenectomy previously involved high morbidity and mortality rates until it was postulated that palliation gave better results. Today, morbidity and mortality rates have been decreased to an acceptable level, mortality rates in specialized centers being under 5%. Prognostic factors determining survival were found to be the size of the tumor, grade, lymph node involvement and stage. In order to be able to compare results of the different centers, standardization of the surgical technique is mandatory. It is unanimously accepted that in order to improve survival in pancreatic carcinoma, the radicality of the surgical procedure should be increased to include lymphadenectomy. Postoperative adjuvant therapy could also be a determinant factor. Prospective randomized clinical trials will give an answer to these still unanswered questions.

Introduction

The incidence of pancreatic cancer has increased in the last decades and reached an incidence of 8-12/100,000 inhabitants in Europe and the United States. In recent years, the frequency of new occurrences has not changed. In Hungary, 1500 new cases can be expected yearly from 10 million inhabitants. It is the fourth leading cause of death in gastrointestinal malignancies. Therefore, it is considered a frequently occurring disease. Untreated one-year survival is less than 20 %

while 5-year survival is 0%. Even today pancreatic cancer should be considered as incurable, since even after radical surgery, the majority of patients die from the consequences of the disease. Pancreatoduodenectomy has been advocated as the method of surgical treatment since 1935, when Whipple published the initial results of his method [1]. In spite of several modifications in the technique, the so-called Kausch-Whipple pancreatoduodenectomy was the method of choice for several decades. Because of high morbidity and mortality rates reaching 50% and 20% respectively, it was postulated by Crile in the 1970s, that palliation of pancreatic cancer provides better survival than radical surgery, and many have rejected resection as the method of treatment [2-4]. Experience gained as a result of the surgical technique, achievements of intensive postoperative care have considerably improved the results of resection treatment. During the last decades morbidity and mortality rates have decreased to an acceptable level in specialized centers and are below the 5% limit [5-7]. However, long-term survival, as reported in the literature, is a disappointingly low 0-24% [8-10].

Historical Background

Early reports of surgery for pancreatic carcinoma go back to the end of the 19th century, when Trendelenbourg resected the left side of the pancreas in 1882 [11]. Halsted resected the ampulla of Vater for malignant tumors in 1989 [12]. In 1898, Codivilla performed the first pancreatic head resection followed by Kausch in 1912 and Whipple, who did it in two stages, in 1935 [1,

13, 14]. These operations were performed for periampullary tumors. Brunschwig was the first to perform pancreatoduodenectomy for pancreatic cancer in 1937 [15]. The procedure was carried out in one stage from that time on and many modifications were introduced during the following decades. These included changing sequences of the anastomosis and the different techniques of gastrointestinal reconstruction. In spite of the technical modifications mortality and morbidity rates were disappointingly high. Therefore, in the early 70s Crile postulated that palliation provides better and longer survival than radical surgery in pancreatic cancer [3].

The introduction of pylorus preservation technique by Traverso and Longmire made a great impact on pancreatic surgery [16]. The safety of pancreatic anastomosis was enhanced by the use of pancreatogastrostomy as advocated by Flautner and Tihanyi [17].

Resecability

After the nihilistic attitude of surgeons in the 1970s many specialized centers demonstrated that the mortality rate after radical surgery can be kept low, even nil in some series [6, 18]. In the meantime, after R0 resection, a 5 year survival rate of 28% was reported by Trede [19].

Resectability of pancreatic cancer is very low. In 1987 Gudjonsson reviewing the results of 50 years of literature demonstrated that of 37,000 patients studied the resectability rate was 11% with a five year survival of only 0.4% [20]. Many factors may effect the resectability rates reported: the attitude of the surgeon toward radical surgery, the selection of the patients, and the institutional case load to mention a few. Resectability rates between 2.6–99% were reported in a collected series [21, 22]. These studies should be evaluated carefully, as the 99% figure was reported in a Japanese study performed in selected centers and for small tumors less than 2 cm in size while the 2.6% was observed in the West Midland region of England and included all patients having pancreatic cancer.

Resectability can be improved upon careful preoperative assessment. Besides the recent development of basic imaging techniques such as computed tomography and ultrafast magnetic resonance imaging, endoscopic and laparoscopic ultrasonography are the new diagnostic modalities of preoperative staging [23-25]. Thirty to forty percent of patients with potentially resectable cancer evaluated were found to have liver metastases and peritoneal spread unseen by conventional computed tomography or ultrasonography. Thus an unnecessary laparotomy can be spared in these patients. If needed, less invasive palliative procedures can be applied with decreased morbidity.

Surgical Procedures

The original Kausch-Whipple pancreatoduodenectomy is still considered as the “gold standard” for pancreatic carcinoma. Two-thirds of the surgeons in the USA prefer this technique [26]. Clinical trials comparing the classical Whipple with pylorus preserving pancreatoduodenectomy have proven the superiority of the latter with respect to metabolic function, hormonal regulation and the gastrointestinal quality of life [27-30]. In spite of some concern [31, 32], the fact that the pylorus preserving procedure neither compromises oncological radicality nor survival in comparison to the traditional Whipple resection has been well-demonstrated [33-36]. Both procedures can be performed with equally low operative mortality. Among the post operative morbidity, delayed gastric emptying is said to be the most frequent complication following the pylorus-preserving procedures. Braasch [37] observed delayed recovery of normal gastric function in as much as 50% of his 87 patients. Many factors were proposed for the mechanism of delayed gastric emptying: the decreased circulating level of motilin, gastric dysrhythmia caused by intra-abdominal complications, decreased blood supply to the antropyloric region and gastric atony due to disruption of gastroduodenal neural connections. In the John Hopkins Hospital

experience the administration of Erythromycin, a motilin agonist significantly decreased the incidence of gastric motility disturbances [38].

Management of the Pancreatic Remnant

Whipple originally ligated the pancreatic duct oversewing the stump. Later on pancreaticojejunostomy was introduced. Most of the post operative complications were related to leakage of the pancreatic anastomosis. The friable pancreas encountered in cases of carcinoma of the head is rather difficult to manage. Among the different options for the management of the pancreatic remnant, closure of the duct by ligation or duct occlusion have been suggested with limited success. Pancreatogastrostomy has gained the widest acceptance worldwide. Although in comparative studies the superiority of pancreatogastrostomy over pancreaticojejunostomy could not be proven, pancreatogastrostomy is thought to be at least as feasible as its counterpart [39, 40].

Extent of Radicality

In spite of improvement in the surgical techniques and perioperative care, the long term survival was still disappointing. In 1973 Fortner introduced his technique of extended regional resection with regional lymphadenectomy and portal vein and/or mesenteric artery resection [41]. High morbidity and mortality rates associated with this procedure prevented it from being widely applied. Survival data were not improved either. Cubilla demonstrated that 1/3 of the patients undergoing extended resection had lymph node metastases, which are not removed by a standard pancreatoduodenectomy [42]. Following this observation, there was a renewed interest in the role of lymphadenectomy in prolonging survival. Ishikawa in 1988 showed an apparent improvement of the 5 year survival rate following extended lymphadenectomy

[43]. Many retrospective studies coming from Japan reported similar promising results [44-46]. Only few prospective randomized trials have been conducted in recent years. Pedrazzoli *et al.* [47] could not demonstrate differences in survival between traditional and extended radical lymphadenectomy. The difficulties in comparing the results of the various centers and, in particular, the very different results of the Japanese and Western countries, made it evident that a standardization of the procedures used in the surgical treatment of pancreatic cancer should be put into force.

Standardisation of the Surgical Technique

To achieve these goals the most important event in recent years occurred in Castelfranco Veneto, Italy in 1998, where an international meeting of the European experts of pancreatology took place. A consensus was reached to classify the surgical procedures according to the extent of pancreatic resection and lymph node dissection [48]. According to this new classification three types of resection for pancreatic head cancer have been formulated: "standard", "radical" and "extended radical". Common to all three is the fact that the gall bladder is removed. Either a pylorus preserving pancreatoduodenectomy or the classical Kausch-Whipple procedure can be performed with any technique of reconstruction, the exception being tumors extending to the duodenum and pyloric region. Resection of adjacent organs, Gerota's fascia and/or the mesenterico-portal vein is accepted in order to reach clear tumor-free margins. Resection of the lymph node groups differs in the three procedures, as well as the transection line of the pancreas; the latter is in the mid part of the mesenterico-portal vein in the standard resection and to the left side of the vein in the radical and extended radical resections. Lymph node groups were defined according to the rules of the Japanese Pancreas Society in order to be able to define the precise extent of lymphatic dissection.

It is clear, that any further clinical study should be based on this classification in order to obtain comparable results.

Conclusions

The standard treatment of pancreatic head cancer is pancreaticoduodenal resection. It has been shown by means of clinical studies, that the pylorus preserving technique has many advantages with respect to the lower morbidity and the better quality of life without compromising oncological principals. In the reconstruction of pancreatico-enteral continuity, pancreatogastric anastomosis proved to be at least equally effective if not superior to pancreatojejunostomy. Lymphadenectomy should be included in the procedure to achieve R0 resection, although the advantages of the extended lymphadenectomy and/or mesenterico-portal vein resection are still not demonstrated by randomized clinical trials. Therefore further prospective trials are necessary to demonstrate any beneficial effect of the extended surgical radicality in improving long-term survival. It is also evident from the literature, that surgery alone has its limitations in treating pancreatic cancer. Therefore the inclusion of different adjuvant and/or neoadjuvant treatment modalities should be considered in the complex therapy of patients with pancreatic cancer.

Key words Digestive System Surgical Procedures; Lymph Node Excision; Neoplasm Staging; Pancreatectomy; Pancreatic Neoplasms; Pancreaticoduodenectomy; Pancreaticojejunostomy; Prognosis; Survival

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