

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. Pancreato-duodenectomy 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. Pancreato-duodenectomy 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].

Extention 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, pancreaticogastric 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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References

1. Whipple AO, Parsons N, Mullins C. Treatment of carcinoma of the ampulla of Vater. *Ann Surg* 1935; 102:763-79.
2. Gilsdorf RB, Spanos P. Factors influencing morbidity and mortality in pancreatoduodenectomy. *Ann Surg* 1973; 177:332-7.
3. Crile G. The advantages of bypass operations over radical pancreatoduodenectomy in the treatment of pancreatic carcinoma. *Surg Gynecol Obstet* 1970; 130:1049-53.
4. Shapiro TM. Adenocarcinoma of the pancreas. A statistical analysis of biliary bypass vs. Whipple resection in good risk patients. *Ann Surg* 1975; 182:715-21.
5. Grace PA, Pitt HA, Tompkins RK, DenBesten L, Longmire WP Jr. Decreased morbidity and mortality after pancreatoduodenectomy. *Am J Surg* 1986; 151:141-9.
6. Trede M, Schwall G, Saeger HD. Survival after pancreatoduodenectomy. 118 consecutive resections without an operative mortality. *Ann Surg* 1990; 211:447-58. [90210738]
7. Neoptolemos JP, Russel RC, Bramhall S, Theis B. Low mortality following resection for pancreatic and periampullary tumours in 1026 patients. UK survey of specialist pancreatic units. UK Pancreatic Cancer Group. *Br J Surg* 1997; 84:1370-6. [98027662]
8. Yeo CJ, Cameron LJ, Lillemoe KD, Sitzmann JV, Hruban RH, Goodman SN, et al. Pancreatoduodenectomy for cancer of the

head of the pancreas in 201 patients. *Ann Surg* 1995; 221:721-31. [95314420]

9. Edge SB, Schmeig RE Jr, Rosenlof LK, Wilhelm LC. Pancreas cancer resection outcome in American university centres in 1989-1990. *Cancer* 1993; 71:3502-8.

10. Sperti C, Pasquali C, Piccoli A, Pedrazzoli S. Survival after resection for ductal adenocarcinoma of the pancreas. *Br J Surg* 1996; 83:625-31. [96296238]

11. Praderi RC. History of pancreatic surgery. In: *Surgery of the Pancreas*. Trede M, Carter DC, Longmire WP Jr, eds. Edinburgh: Churchill Livingstone, 1997.

12. Halsted WS. Contribution to the surgery of the bile passages, especially of the bile duct. *Boston Med Surg J* 1899; 141:645-52.

13. Codivilla A. Rendiconto statistico della sezione chirurgica dell'ospedale di Imola 1898.

14. Kausch W. Das Carcinom der Papilla duodeni und seine radikale Entfernung. *Beitr Klin Chir* 1912; 78:439-51.

15. Brunschwig A. Resection of the head of the pancreas and duodenum for carcinoma. Pancreatoduodenectomy. *Surg Gynecol Obstet* 1937; 65:681-4.

16. Traverso LW, Longmire WP. Preservation of the pylorus in pancreatico-duodenectomy. *Surg Gynecol Obstet* 1978; 46:959-63.

17. Flautner L, Tihanyi T, Szécsény A. Pancreatogastrostomy; an ideal complement to pancreatic head resection with preservation of the pylorus in the treatment of chronic pancreatitis. *Am J Surg* 1985; 150:608-10.

18. Cameron JL, Pitt HA, Yeo CJ, Lillemoe KD, Kaufman HS, Coleman J. One hundred and forty-five consecutive pancreatoduodenectomies without mortality. *Ann Surg* 1993; 217:430-8. [93256635]

19. Trede M. The surgical options. In: *Trede M, Carter DC, Longmire WP Jr, eds. Surgery of the Pancreas*. Edinburgh: Churchill Livingstone, 1997.

20. Gudjonsson B. Cancer of the pancreas – 50 years of surgery. *Cancer* 1987; 60:2284-303.

21. Bramhall SR, Allum WH, Jones AG, Allwood A, Cummins C, Neoptolemos JP. Treatment and survival in 13,560 patients with pancreatic cancer, and incidence of the disease, in the West Midlands: an epidemiological study. *Br J Surg* 1995; 82:111-5.

22. Tsuchiya R, Noda T, Harada N, Miyamoto T, Tomioka T, Yamamoto K, et al. Collective review of small carcinomas of the pancreas. *Ann Surg* 1986; 203:77-81. [86102281]

23. Warshaw AL, Tepper JE, Shipley WU. Laparoscopy in the staging and planning of therapy for pancreatic cancer. *Am J Surg* 1986; 151:76-9.

24. John TG, Greig JD, Carter DC, Garden OJ. Carcinoma of the pancreatic head and periaampullary region: tumour staging with laparoscopy and laparoscopic ultrasonography. *Ann Surg* 1995; 221:136-46.

25. Rösch T, Braig C, Gain T, Feuerbach S, Siewert JR, Schusdzarra V, Classen M. Staging of pancreatic and ampullary carcinoma by endoscopic ultrasonography. *Gastroenterology* 1992; 102:188-99. [92090624]

26. Livingston EH, Welton ML, Reber HA. Surgical treatment of pancreatic cancer: the United States experience. *Int J Pancreatol* 1991; 9:153-62.

27. Tangoku A, Nishikawa M, Adachi A, Suzuki T. Plasma gastrin and cholecystokinin response after pylorus preserving pancreatoduodenectomy with Billroth-I type of reconstruction. *Ann Surg* 1991; 214:56-60. [91290940]

28. Grace PA, Pitt HA, Longmire WP. Pylorus preserving pancreatoduodenectomy: an overview. *Br J Surg* 1990; 77:968-74.

29. Kozuschek W, Reith HB, Waleczek H, Haarmann W, Edelmann M, Sonntag D. A comparison of long term results of the standard Whipple procedure and the pylorus

preserving pancreatoduodenectomy. J Am Coll Surg 1994; 178:443-58.

30. Wenger FA, Jacobi CA, Haubold K, Zieren HU, Müller JM. Gastrointestinale Lebensqualität nach Duodenopankreatektomie beim Pankreaskarzinom. Vorläufige Ergebnisse einer prospektiv-randomisierten Studie: PD vs PPPD. Chirurg 1999; 70:1454-9.

31. Sharp KW, Ross CHB, Halter SA, Morrison JG, Richards WO, Williams LF, Sawyers JL. Pancreatoduodenectomy with pylorus preservation for carcinoma of the pancreas: A cautionary note. Surgery 1989; 105:645-53.

32. Roder JD, Stein HJ, Hüttel W, Siewert JR. Pylorus preserving versus standard pancreaticoduodenectomy: an analysis of 110 pancreatic and periampullary carcinomas. Br J Surg 1992; 79:152-5.

33. Klinkenbijl JHG, van der Schelling GP, Hop WCJ, van Pel R, Bruining HA, Jeekel J. The advantages of pylorus-preserving pancreatoduodenectomy in malignant disease of the pancreas and periampullary region. Ann Surg 1992; 216:142-5.

34. Heise JW, Becker H, Borchard F, Röher HD. Zum Radikalitätsrisiko der pyloruserhaltenden Duodenopankreatektomie beim duktaalen Carcinom. Chirurg 1994; 65:780-4.

35. Tsao JJ, Rossi RL, Lowell JA. Pylorus-preserving pancreatoduodenectomy. Is it an adequate cancer operation? Arch Surg 1994; 129:405-12.

36. Takao S, Aikou T, Shintchi H, Uchikura K, Kubo M, Imamura H, Maenohara SH. Comparison of relaps and long-term survival between pylorus-preserving and Whipple pancreaticoduodenectomy in periampullary cancer. Am J Surg 1998; 176:467-70.

37. Braasch JW, Rossi RL, Watkins E, Winter PF, Deziel DJ. Pyloric and gastric preserving pancreatic resection. Experience with 87 patients. Ann Surg 1986; 204:411-417.

38. Yeo CJ, Cameron JL. The alternative techniques for performing the Whipple operation. Adv Surg 1996; 30:293-310.

39. Bassi C, Falconi M, Tihanyi TF, Salvia R, Valerio A, Caldiron E, et al. Resection in chronic pancreatitis: Anastomosis with the jejunum or with the stomach? Ann Ital Chir 2000; 71:51-5.

40. Tihanyi TF, Flautner LE. Management of the pancreatic remnant: Pancreaticogastrostomy. In Pancreatic Tumors: Achievements and Perspectives. Dervenis C, Bassi C, eds. Stuttgart: Georg Thieme Verlag, 2000: 187-94.

41. Fortner JG. Regional resection of cancer of the pancreas. A new surgical approach. Surgery 1973; 73:307-20.

42. Cubilla AL, Fortner J, Fitzgerald PJ. Lymph node involvement in carcinoma of the pancreas area. Cancer 1978; 41:880-7.

43. Ishikawa O, Ohhigashi H, Sasaki Y, Kabuto T, Fukuda I, Furukawa H, et al.: Practical usefulness of lymphatic and connective tissue clearance for the carcinoma of the pancreas head. Ann Surg 1988; 208:215-20. [88293062]

44. Manabe T, Ohshio G, Baba N, Miyashita T, Asano N, Tamura K, et al.: Radical pancreatectomy for ductal cell carcinoma of the head of the pancreas. Cancer 1989; 64:1132-7. [89336643]

45. Satake K, Nishiwaki H, Yokomatsu H, Kawazoe Y, Kim K, Haku A, et al.: Surgical curability and prognosis for standard versus extended resection for T1 carcinoma of the pancreas. Surg Gynecol Obstet 1992; 175:259-65. [92383665]

46. Naganuma T, Isaji S, Kawarada Y. Staging and extended resection for pancreatic cancer. Pancreas 1998; 16:355-62. [98208460]

47. Pedrazzoli S, DiCarlo V, Dionigi R, Mosca F, Pederzoli P, Pasquali C, et al.: Standard versus extended lymphadenectomy associated with pancreatoduodenectomy in the surgical treatment of adenocarcinoma of the head of the pancreas: a multicenter,

prospective, randomized study.
Lymphadenectomy Study Group. *Ann Surg*
1998; 228:508-17. [99005000]

48. Pedrazzoli S, Begler HG, Obertop H,

Andren-Sandberg A., Fernandez-Cruz L,
Henne-Bruns D, et al. A surgical and
pathological based classification of resective
treatment of pancreatic cancer. *Dig Surg*
1999; 16:337-45. [99380779]
