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Are There Indications for Palliative Resection in Pancreatic Cancer?

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Abstract. Controversy exists about the indication for a palliative pancreatoduodenectomy. A palliative resection for patients with a pancreatic carcinoma can be performed safely nowadays with low mortality and acceptable morbidity in centers with experience. The early results in terms of mortality and morbidity are not different from resections with curative intent or even after bypass surgery. The procedure seems effective for controlling symptoms of the disease, and the quality of life after a palliative resection is acceptable and not worse than after bypass surgery. It is, however, still doubtful whether the incidence of symptom recurrence, such as jaundice, obstruction, and pain, is lower after resection than after bypass surgery. The longer survival after palliative resection could also be due to patient selection and postoperative treatment. There are no randomized trials to prove the superiority of palliative resection over bypass surgery. The safety of pancreatic resection for cancer has already changed the policy in centers with experience, and surgeons are more willing to perform a resection because the results are better or at least the same as after bypass surgery. There are, however, no results to confirm that a palliative resection should be performed routinely or to justify resection as a debulking procedure.

Pancreatoduodenectomy in patients with pancreatic cancer is generally performed with the intention to cure these patients. Unfortunately the 5-year survival following these apparently curative resections is limited and reported to be 0% to 37% [1–5]. It has been argued by some authors that pancreatic carcinoma cannot be cured by resection, and therefore surgical treatment should be considered palliative treatment in all patients [6]. In a critical review Gudjonsson concluded that pancreatic resection has only minimal impact on survival rates in patients with carcinoma and is therefore a waste of resources [6].

It has been shown recently, however, that the overall 5-year survival rate in centers with experience is now around 20%, probably due to improved patient selection. There have also been advances in surgery, as the mortality is now less than 5% in these centers [1, 2, 4, 5, 7, 8].

The questions addressed in this paper seem even more controversial: Is there any indication for palliative resection in patients with pancreatic cancer? Should a pancreatoduodenectomy be performed routinely for palliative reasons? There are no studies in which resection has been performed as a standard procedure for palliation. Generally, a palliative resection for pancreatic cancer may be envisioned in several situations: The most common is

the situation in which a macroscopically radical resection is undertaken, but at histopathologic examination of the specimen the resection margins are microscopically involved. Although the tumor was resected with curative intention, the resection was not radical and can therefore be called palliative. Another, similar situation is that during exploration of a pancreatic tumor tumor infiltration is encountered after transection of the pancreatic neck has taken place. Transection of the pancreas is “a point of no return”; and although subsequent frozen section biopsies show tumor infiltration (e.g., in the superior mesenteric artery), one completes the operation with resection. Another situation in which resection is required is when there is bleeding from the tumor. These situations are distinct from cases in which a deliberately palliative resection is undertaken, being the equivalent of a debulking procedure; therefore the results from these studies cannot be extrapolated to routine palliative resection. Unfortunately no randomized trials are available that compare palliative resection with a surgical bypass, and only a few recent retrospective studies have been reported in which palliative results of resection and a bypass were compared.

Several aspects of palliative resection and other palliative treatments are discussed herein. First, the (early) procedure-related morbidity and mortality of palliative treatment should be considered. Second, can the various palliative treatments control symptoms by offering adequate treatment of jaundice, itching, pain relief, and gastrointestinal obstruction, resulting in an improved overall quality of life with a limited need for rehospitalization during the remaining life? Finally, what is the survival after the various palliative treatments?

Postoperative Complications and Mortality after Palliative Surgery

The results of various surgical palliative treatments during the past two decades were analyzed in a review by Watanapa and Williamson [9]. The overall results showed improvement during the decade 1981–1990, as summarized in Table 1. The mortality rates after palliative and curative resection or bypass surgery were still 9% and 14%, respectively. Recent series from centers with experience have shown that mortality after resection (most series including patients who underwent curative resection) decreased

Table 1. Operative mortality and mean survival following pancreatic resection (curative and palliative), surgical biliary bypass, and laparotomy 1971–1980 and 1981–1990.

Operation	1971–1980			1981–1990		
	No.	Mortality (%)	Survival (months)	No.	Mortality (%)	Survival (months)
Resection	386	17	12.7	481	9	17.0
Bypass	1654	17	5.4	1144	14	6.6
Laparotomy only	1039	36	2.6	643	18	3.1

Modified from Watanapa and Williamson [9], with permission from Blackwell Science Ltd.

below 5% during the 1990s, and it has even been reported to be 0% to 2% in some series [1, 10–12]. Postoperative complications are still substantial, reported at 20% to 50%. A reduction in mortality and morbidity has also been reported in recent series of bypass surgery with an in-hospital mortality of 2.5% [13–15].

In two recent studies, one from The Johns Hopkins Hospital, Baltimore (USA) and the other from our institution (Academic Medical Center, Amsterdam, The Netherlands), surgical bypass and palliative resection were compared [16, 17]. Both studies are retrospective and therefore suffer from methodologic flaws. In the study from The Netherlands patients were matched for tumor size. In both studies local resection of the primary tumor was not possible in patients who underwent a bypass, whereas many of the patients with a palliative resection underwent this intervention in a curative attempt but unfortunately histologic positive resection margins were found. The lymph node status may also be different in the two groups and is obviously unknown after bypass surgery. In the study from Johns Hopkins only patients with pancreatic carcinoma were included, whereas a few patients with other types of tumors (ampullary) were included in the other study. Patients' characteristics and symptoms of the two groups are comparable for the two studies (Table 2). Postoperative complications after resection and bypass—respectively, 42% versus 32% and 44% versus 33%—were not significantly different for the two procedures, nor was the in-hospital mortality (Table 2). The postoperative hospital stay was significantly shorter after the bypass procedure.

Significantly more patients underwent postoperative chemotherapy or radiotherapy after palliative resection: 78% versus 48% after bypass in one series [16]. This is another important factor that could influence survival. From these two studies it was concluded that the perioperative morbidity and mortality after palliative resection were acceptable, and therefore a more aggressive approach should be offered to patients with pancreatic cancer [16, 17].

It could be hypothesized that this approach could lead to an increase of palliative or nonradical resections with probably a related increase of postoperative complications by negative selection of the patients. The results of one study were analyzed at the beginning of 1993. A recent evaluation of the results of the 206 patients who underwent a resection after that period was performed to determine if a possible change in attitude led to an increase in palliative resections. The results are summarized in Table 3. About 30% of the patients underwent a palliative resection, a percentage not different from the previous period in this institution and from the literature [1, 5, 6, 10, 11]. In a recent series of 650 consecutive resections from Johns Hopkins positive margins were found in 29% of the 282 patients with a pancreatic carcinoma [12]. As shown in Table 3, the postoperative complications, mortality, and hospital stay after palliative resection were no higher than after radical resection.

Table 2. Patient characteristics, symptoms, postoperative complications, and hospital stay from two series in the literature in which palliative resection and bypass surgery were compared.

Parameter	Johns Hopkins [16]		Amsterdam [17]	
	Resection (n = 64)	Bypass (n = 62)	Resection (n = 36) ^a	Bypass (n = 24)
Age (range)	65 (37–85)	65 (41–81)	62 (37–74)	61 (40–83)
Jaundice (%)	77	66	89	88
Pruritus (%)			75	63
Pain (%)	50	65	58	58
Median tumor size (cm)	3.6	—	4.30	4.25
Complications (%)	42	32	44	33
Hospital mortality	2 (1.6%)	2 (1.6%)	1 (3.0%)	0
Postoperative stay (days)	18.4	15*	25	18*
Postoperative therapy (%) ^b	78	48	17	16

^aPatients (n = 36) were matched for tumor size and were selected from a group of 56 patients.

^bPostoperative therapy included chemotherapy (5-fluorouracil), and radiation therapy.

*p < 0.05, bypass versus resection.

Table 3. Patient characteristics, postoperative complications, mortality, and hospital stay in 178 patients with malignant disease of the 206 who underwent pancreatic resection from September 1992 to October 1997 in the Academic Medical Center/Amsterdam.

Parameter	Radical resection (n = 121)	Palliative resection (n = 57)	Malignant tumor (n = 178)
Age (range)	65 (37–79)	63 (42–83)	
Male/female	65/56	23/34	
Complications	66 (55%)	30 (53%)	96 (54%)
Hospital mortality	3 (2.5%)	0	3 (1.7%)
Hospital stay (days)	16 (6–167)	17 (9–222)	

It is evident that these results, as most results from the literature, are generally reported from centers with experience. The policy of performing nonradical resections as an (adequate) palliative treatment should be followed only when the morbidity and mortality are known to be acceptable. An analysis of the results after pancreatic resection in The Netherlands in 1994 and 1995 showed that overall hospital mortality was 11% (Table 4). The mortality in small-volume centers (fewer than five resections per year) was 16.5%; it was 1.5% in high-volume centers (more than 24 resections annually) [18, 19]. A similar relation between hospital volume and mortality has been

Table 4. In-hospital mortality in 1994–1995 in The Netherlands divided into four categories based on hospital volume (number of resections).

No. resections per year	Total patients	Discharge		Mortality	
		Home	Other	No.	%
<5	195	151	13	31	16.5
5–9	87	79	0	8	9.2
10–24	80	68	5	7	8.8
>24	66	63	2	1	1.5
Total	428	361	20	47	11

From Gouma et al. [19], with permission.

found in Maryland (USA), New York State (USA), and the United Kingdom [20–22]. An aggressive approach toward pancreatic resection can therefore not be advocated for all centers, particularly not those with limited experience.

Relief of Symptoms

Jaundice

Jaundice and severe itching, associated with cholangitis in about 20%, are symptoms that should be relieved as soon as possible. Early relief of jaundice can be obtained adequately in most patients by all palliative methods: endoscopic stenting (success rate 82–100%), bypass surgery (success rate 75–100%), and palliative resection (success rate > 95%). However, recurrence of jaundice with or without cholangitis is more frequently reported after the use of stents. Four prospective randomized trials have shown that recurrent jaundice/cholangitis was more frequent after stenting (up to 38%) than after bypass surgery (3–10%) [23–26]. Whether these short periods of recurrent jaundice/cholangitis and subsequent stent changes have any effects on the quality of life of these patients remains to be analyzed. Recurrent jaundice after palliative bypass (Fig. 1) in more recently published series occurred in 0% to 10% (Table 5) [13–15].

It has been reported that recurrence of jaundice is uncommon after palliative resection. Recurrent jaundice occurred in 9% of 157 patients who underwent a pancreatic resection (30% for palliation) at our institution after a mean interval of 37 weeks (range 6–73 weeks). Jaundice was incidentally caused by liver metastases, but in most patients it was due to obstruction of the hepatojejunostomy by local tumor growth in the pancreatic head area (Fig. 2).

Gastrointestinal or Duodenal Obstruction

Reviews from the literature have shown that late duodenal obstruction occurs in 0% to 20% of patients after endoscopic palliation and in around 17% after a surgical bypass without a (prophylactic) gastrojejunostomy [23–27]. In a consecutive series of 691 patients treated by endoscopic stenting in our Department of Gastroenterology (AMC), the overall incidence of duodenal obstruction until death was 11%; 9% in patients with a pancreatic carcinoma, 14% for patients with bile duct carcinoma, and 23% for patients with an ampullary tumor [28]. The incidence of duodenal obstruction correlated with the survival time (Table 6). Of the 75 patients with obstruction, 68 (90%) required a gastrojejunostomy after a mean period of 8.5 months. In a series of

Fig. 1. Percutaneous insertion of a wall stent for biliary obstruction caused by progression and local tumor growth: 6 months after a palliative biliary bypass procedure.

surgical bypasses with prophylactic gastrojejunostomy, recurrent symptoms of obstruction were found in 7%; a few patients were treated with a second bypass [14].

In a series of 157 patients who underwent a pancreatic resection (30% not radical) in our institution, 22 patients developed symptoms of gastrointestinal (GI) obstruction during follow-up, and a stenosis was found in 9 patients by a radiologic GI series (6%). It can be concluded that late obstruction has been reported to occur after all palliative procedures in 6% to 9% of patients.

Pain Relief

Many patients suffering from pancreatic carcinoma have abdominal or back pain as the presenting symptom, or they develop pain during the course of the disease. No studies have compared the effect of palliative resection and bypass surgery on pain relief. A prospective randomized study in patients who underwent bypass surgery with or without chemical splanchnicectomy showed that

Table 5. Late complications and survival in recent studies on biliary bypass procedures for pancreatic (and periampullary) carcinoma.

Study	Year	No. of patients	Biliary bypass (no.)	GI bypass (no.)	Early complications (%)	Late complications (%)			Hospital stay (days)	Survival (months)
						Jaundice	GI obstruction	Morbidity (%)		
Lillemoe [15]	1993	118	110	107 (91%)	37	3	4	2.5	14	7.7
Parks [13]	1997	61	61	—	21	8	8	8.0	10	6.5
Wagensveld [14]	1997	126	124	118 (94%)	30	—	7	2.5	17	7.5

Fig. 2. Percutaneous transhepatic cholangiography and subsequent biliary drainage in a patient 34 weeks after a palliative pylorus-preserving Whipple procedure. Note the dilatation of the hepatojejunostomy and the jejunal Roux limb caused by local tumor ingrowth into the jejunal limb more distally at the site of the mesocolon due to the recurrence.**Table 6.** Duodenal obstruction after palliative endoscopic treatment of 691 patients with obstructive jaundice due to a pancreatic head region tumor.

Parameter	Pancreatic tumor	Bile duct tumor	Ampullary tumor
No. of patients	581	29	81
Duodenal obstruction (%)	9	14	23
Onset (days)	206	293	419
Survival (months)	5.0	6.5	13.5

Adapted from Coene et al. [28].

reduction of pain after surgery in combination with intraoperative chemical splanchnicectomy was greater than in patients without alcohol injection [29]. Pain relief was limited to approximately 3 to 4 months. It is unknown whether chemical splanchnicectomy should also be performed during palliative resection. From personal experience in the outpatient clinic we know that a substantial number of patients after palliative resection suffer from both abdominal and back pain during their disease, but that pain relief by medication can be obtained in most patients. Percutaneous

celiac nerve blocks or transthoracic splanchnicectomy can be successfully performed in a small subgroup of patients [30–32].

Quality of Life

Some pessimists suggest that patients who survive pancreatic resection are gastrointestinal cripples. Quality of life assessment of these patients is therefore important. Especially, studies on palliative treatment should encompass quality of life measurements, as standard measures of outcome are not sensitive enough to determine treatment strategies. In addition to morbidity, mortality, and survival, quality of life should be a primary endpoint of clinical studies.

McLeod et al. described quality of life in patients after a Whipple procedure without signs of recurrent or residual disease [33]. In 25 patients with curative Whipple procedures the quality of life 6 months after resection was no different from a matched control group of cholecystectomy patients. Quality of life after a palliative pylorus-preserving pancreatoduodenectomy has not yet been studied.

In an ongoing study in our hospital, quality of life is assessed in patients undergoing surgical exploration for periampullary carcinoma. Questionnaires comprising the generic MOS (Medical Outcome Studies) are used before exploration, at 2 weeks, and at 3, 6, 9, and 12 months after discharge. The MOS is recorded and transformed into seven subscales as described, with higher scores indicating better quality of life [34]. Patients who underwent a palliative pylorus-preserving resection were followed for 1 year. The values of the reference population and available questionnaires of the first 15 patients are shown in Table 7.

A significant decrease in all quality of life subscales is visible 2 weeks after discharge compared to preoperative values. Three months after discharge the mean quality of life is comparable or even better than the preoperative quality of life. At 9 and 12 months a slow decrease in quality of life becomes apparent, which can be explained by progressive tumor growth. Results from our study and the literature suggest that quality of life can be reasonable even after a palliative resection [33–35].

Survival

It is remarkable that both studies reported previously found a longer survival in patients after a palliative resection than after bypass surgery [17, 18]. The actuarial survival curves (Kaplan-Meier) for both studies are shown in Figure 3. In the Johns Hopkins study the 2-year survivals were, respectively, 16% versus 8% and in the AMC study 24% versus 2% [17, 18]. It has been suggested that this longer survival might be due to patient selection. It has been mentioned before that lymph node status, local tumor invasion, and exact tumor size could not be evaluated in

Table 7. Quality of life scores during 12 months after palliative pancreatic resection ($n = 15$).

Parameter	Quality of life mean score						
	Reference population	Preoperative	2 Weeks	3 Months	6 Months	9 Months	12 Months
Missing/died		—/—	1/—	1/1	1/2	2/3	1/5
Questionnaires		15	14	13	12	10	9
Energy	—	57	53	63	66	62	39
Health perception	72	43	44	58	55	45	32
Physical condition	86	55	33	56	65	59	57
Bodily pain	74	64	54	68	63	61	61
Mental function	77	63	66	76	80	74	58
Role function	87	36	29	64	65	44	21
Social function	92	70	46	69	76	62	43

Fig. 3. Actuarial survival curves (Kaplan-Meier) for patients undergoing palliative resection and palliative bypass surgery in the Johns Hopkins study (A) and the Amsterdam study (B). A: From Lillimoe et al. [16], with

permission from Lippincott Williams and Wilkins. B: From Reinders et al. [17], with permission.

patients after bypass surgery. The difference in survival could also be due to differences in postoperative chemotherapy and the chemotherapy and radiotherapy in these series. The survival after bypass surgery (mean survival 11 months) seems to be much better than survival after treatment with an endoprosthesis (5.5 months) or in other surgical bypass studies, which could also be related to patient selection and the referral pattern to these centers.

Résumé

Les indications de la duodénopancréatectomie à titre palliatif restent discutées. La duodénopancréatectomie peut être effectuée pour cancer avec sûreté, avec une mortalité basse et une morbidité acceptable dans les centres d'excellence. Les résultats précoces en terme de mortalité et de morbidité ne sont pas différents des résections avec intention de cure ou même de la chirurgie de dérivation. Cette chirurgie contrôle efficacement les symptômes de la maladie. La qualité de vie après résection palliative est acceptable, pas très différente de celle après la chirurgie de dérivation. Cependant, on ne sait toujours pas si le taux de récurrence des symptômes comme l'ictère, l'obstruction ou la douleur est réduit après résection palliative par rapport à la dérivation. La survie

supérieure après résection palliative pourrait en fait être en rapport avec la sélection des patients et le traitement postopératoire. Aucune étude randomisée n'existe pour prouver la supériorité de la résection palliative sur la chirurgie de dérivation. Comme les résultats de la résection palliative sont meilleurs ou au moins équivalents à la chirurgie de dérivation, les chirurgiens ayant une certaine expérience avec cette chirurgie la préfèrent. Il n'existe, cependant, aucune preuve qu'il faut la pratiquer de façon systématique ou comme chirurgie de réduction tumorale.

Resumen

En la actualidad, los pacientes con cáncer de páncreas pueden ser tratados, en centros especializados, mediante resecciones paliativas, que cursa con una morbilidad aceptable y una escasa mortalidad. Los resultados precoces, por lo que a la morbi-mortalidad se refiere, no son diferentes a los obtenidos en resecciones con propósito curativo e incluso, a los observados tras operaciones derivativas. La resección paliativa, parece ser eficaz en el control de los síntomas de la enfermedad y, la calidad de vida es aceptable, similar a la que proporciona la cirugía derivativa. Sin embargo, la recidiva de la ictericia, obstrucción y dolor no parecen ser menos frecuentes tras la resección que tras

cirugía derivativa. La supervivencia mas prolongada, tras cirugía paliativa, puede ser debida no solo a la selección de los pacientes, sino también al tratamiento postoperatorio. No existen estudios randomizados que demuestren la superioridad de la resección paliativa frente a la cirugía derivativa. Las garantías que ofrece la resección pancreática han determinado un cambio en la política de centros especializados; los cirujanos prefieren realizar resecciones, ya que los resultados son mejores o por lo menos iguales a los que se obtienen con cirugía derivativa. No obstante, los resultados obtenidos, no permiten la indicación de forma rutinaria de la resección paliativa, ni justifican dicha operación como proceso reductor de masa tumoral.

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