J Gastrointest Surg (2008) 12:1193–1201
DOI 10.1007/s11605-008-0505-z

Cachexia Worsens Prognosis in Patients with Resectable Pancreatic Cancer

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Received: 17 October 2007 / Accepted: 13 February 2008 / Published online: 18 March 2008

Abstract
Introduction Pancreatic cancer is the fourth leading cause of cancer-related death in Western countries with a poor prognosis (5-year survival rates, 25% in patients after tumor resection with adjuvant treatment; overall, the 5-year survival rate is about 4%; Jemal et al., CA Cancer J Clin, 55:10–30, 2005). Many patients develop a cachectic status during the progression of the disease, and this syndrome accounts for up to 80% of deaths in patients with advanced pancreatic cancer. Remarkably, there are only a few data available on the impact of cachexia in patients with pancreatic cancer scheduled for tumor resection.
Material and Methods Therefore, in this study, 227 consecutive patients with ductal adenocarcinoma of the pancreas were documented over an 18-month period regarding the prevalence of cachexia and its influence on perioperative morbidity and mortality with a special interest to postoperative weight gain and survival in a prospectively designed database and followed up.
Results In 40.5% of the patients, cachexia was already present at the time of operation. The cachectic patients did present in a worse nutritional status, represented by lower protein, albumins, and hemoglobin levels. Despite no significant differences in tumor size, lymph node status, and CA19-9 levels, the resection rate in patients with cachexia was reduced (77.8% vs. 48.9%) due to a higher rate of metastatic disease in patients with cachexia. The morbidity and in-hospital mortality revealed no significant difference. However, patients with and without cachexia lost weight after operation, and the weight gain started not until 6 months after operation. The survival in patients with cachexia was significantly reduced in patients undergoing tumor resection as well as in palliative treated patients.
Conclusion Cachexia has a significant impact on survival and performance status in palliative patients as well as in patients operated for pancreatic cancer. But tumor-related cachexia is not necessarily dependent on tumor size or load and that metastatic dedifferentiation of the tumor might be a critical step in the development of tumor-associated cachexia.

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Keywords Cachexia · Pancreatic cancer · Nutritional status · Survival

Introduction

Pancreatic cancer is the fourth leading cause of cancer-related death in Western countries, and in 2006, there were about 32,000 deaths related to pancreatic cancer in the USA.[1] Ductal pancreatic adenocarcinoma is characterized by retroperitoneal and perineural infiltration, early formation of multiple distant metastases, and resistance to most

adjuvant treatment regimes.[2–7] Surgical resection is the patient's only hope for cure and offers a significantly improved prognosis, with a median survival after resection of 14–20 months and 5-year survival rates up to 25%.[6,8–12] According to recent publications, the standard treatment regime in resectable pancreatic cancer should be a potentially curative resection followed by adjuvant systemic chemotherapy.[7,13,14] However, most patients develop local or distant tumor recurrence within 2 years after resection,[2,15–17] often associated with rapid development of a cachexia syndrome.

Today, there is no definitive and consistent definition of cachexia in cancer patients. However, most authors define cachexia in tumor patients as a weight loss of 10% or more within 6 months. Severe wasting accounts for approximately 30–50% of deaths in patients with gastrointestinal cancer and up to 80% of deaths in patients with advanced pancreatic cancer.[18–21] The main physical changes in cachexia are anorexia and malnutrition resulting from changes in gastrointestinal function and loss of appetite as well as massive loss of adipose and muscle tissue because of changes in lipid and protein metabolism.[20,22–26] Increased energy expenditure in combination with decreased energy intake exacerbates the progressive disturbance of nutritional status.[26–28] In particular, because of skeletal muscle loss, many cachexia patients develop pulmonary insufficiency with dyspnea as a frequent symptom (up to 80%).[29]

Different pathways of proteolysis in cancer cachexia have been proposed, but in spite of intensive research, most of the pathophysiological mechanisms remain poorly understood.[24] The underlying mechanisms of muscle depletion also are largely unknown, but several studies have shown that an ATP/ubiquitin-dependent pathway is responsible for muscle protein catabolism.[30] Reduced oral food intake and/or increased energy expenditure can lead to a negative protein balance and weight loss in pancreatic cancer patients.[31,32] In addition, pro-inflammatory cytokines are associated with altered host energy metabolism, leading to an acute-phase reaction that results in protein degradation.[32]

Although there has been some progress in elucidating the molecular mechanisms underlying the development of cancer cachexia, our knowledge of related clinical features, courses, and therapy is still limited. Physicians and surgeons often judge the cachexia syndrome as a one-way street of no return, yet to date, no detailed data on the progression of weight loss, especially in muscle or fat tissue, are available. In most cases, only the weight of the patient at the beginning of the disease is recorded; however, in cachectic patients with unresectable pancreatic cancer, nutritional interventions over an 8-week period could achieve weight stabilization and improve survival and quality of life.[18] For these reasons and to obtain more reliable data on the development and progression of cachexia in pancreatic cancer, we assessed over a period of 18 months (June 2004 through November 2005) the prevalence of cachexia in pancreatic cancer patients scheduled for tumor resection. Furthermore, the influence of cachexia on perioperative morbidity and mortality as well its impact on survival was examined in resectable pancreatic cancer patients.

Material and Methods

Patients

From June 2004 to November 2005, 227 patients with histologically confirmed ductal adenocarcinoma of the pancreas were operated in the Department of General Surgery, University of Heidelberg. Table 1 shows the characteristics of all patients in detail. Each patient was asked to give informed consent for data collection. For each patient, we performed a precise evaluation of the clinical course of the disease and the treatment until admission to our department. All data of patients who were referred for an operation were collected in a prospectively designed database. In 150 patients (66.1%), a tumor resection was performed, and in 77 patients (33.9%), a palliative operation was done because of local advanced disease or the intraoperative diagnosis of distant metastases.

Weight and Body Composition

Pre-illness stable weight, actual weight at operation, height, and duration of weight loss were registered. The body mass index for each participant was calculated [height[m]/(weight[kg] × weight[kg])]. The patients were assessed as being cachectic in cases of unintended weight loss greater than 10% of the pre-illness stable body weight. In addition, the occurrence of diabetes mellitus and related treatment were registered.

Histological Diagnosis

The histological diagnosis of ductal pancreatic cancer in each patient was established by two independent pathologists of the Department of Pathology, University of Heidelberg. In case of tumor resection, histopathological classification was made according to the TNM classification, version 2005, including examination of the resection margin and grading. Tumor staging was determined according to the Union Internationale Contre le Cancer (UICC) classification.[33,34]

Postoperative Nutritional Management

On the first postoperative day, patients were allowed to drink tea and/or water up to 500 ml/day; on the second

Table 1 Characteristics of Pancreatic Cancer Patients with and without Cachexia Scheduled for Tumor Resection

Patients with PDAC *N*=227		∅ Cachexia *N*=135 (59.5%)	Cachexia *N*=92 (40.5%)	*p* value
Gender	Male	69 (51.1)	60 (65.2)	0.036
	Female	66 (48.9)	32 (34.8)	
Age		64 (57/70)	65 (57/70)	0.380
Body mass index		24.2 (22.57/27.2)	23.01 (20.76/25.47)	0.003
Weight loss (kg)		2 (0/5)	12 (10/15)	<0.001
Weight loss (%)		2.1 (0/6.5)	14.9 (11.5/19.2)	0.001
CA19-9 (U/ml)		161 (43.25/588.65)	262.20 (46.9/1,367.0)	0.199
ASA classification	I	2 (1.5)	1 (1.1)	0.007
	II	63 (46.7)	27 (29.3)	
	III	69 (51.1)	62 (67.4)	
	IV	1 (0.7)	2 (2.2)	
Tumor resection	yes	105 (77.8)	45 (48.9)	<0.001
	no	30 (22.2)	47 (51.1)	
Distant metastases		37 (27.4)	39 (42.4)	0.019
Tumor stage	UICC II	92 (68.1)	45 (48.9)	0.005
	UICC III	6 (4.4)	8 (8.7)	
	UICC IV	37 (27.4)	39 (42.4)	
30 days mortality		5 (3.7)	6 (6.5)	0.333
Morbidity		56 (41.5)	40 (43.5)	0.765
Diabetes mellitus	Yes	27 (20)	43 (46.7)	<0.001
	No	108 (80)	49 (53.3)	

postoperative day, the patients were allowed to drink as much as they wanted, and oral food intake was routinely started on the third postoperative day. In patients with delayed gastric emptying (nausea, repeated vomiting) or patients with delayed oral food intake, we started a parenteral nutrition on the fifth postoperative day. After resection, every patient was given enzyme supplementation orally.

Morbidity

For in-hospital morbidity, every sign or symptom that prolonged the in-hospital stay and/or had to be treated by surgical therapy, interventional drainage, or non-invasive therapy was registered. The prevalence of wound infection, postoperative bleeding, and cholangitis, pancreatic fistula, intra-abdominal abscesses, delayed gastric emptying, pneumonia, urinary tract infection, myocardial infarction, and pulmonary embolism were evaluated.[35,36]

Follow-up

For follow-up, we saw patients every 6 months in our outpatient clinic or performed a telephone interview. Patients were asked if any treatments were necessary after discharge from the Department of Surgery. In addition, we asked whether they had developed diabetes, whether body weight was stable after the operation, and whether they had completed planned adjuvant or palliative oncological treatment.

Statistical Analysis

Statistical analysis, including multivariate analysis, was performed using SPSS software, version 14 (SPSS Inc., Chicago, IL., USA). Survival curves were calculated using Kaplan–Meier analysis and the log-rank test. For testing significant differences between the examined groups, we

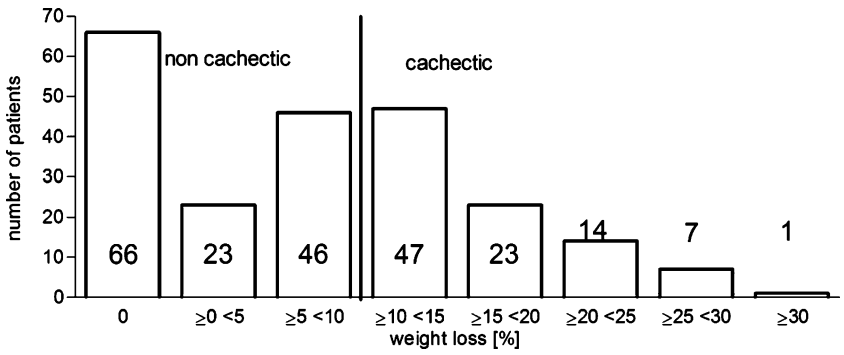


Figure 1 Preoperative weight loss in 227 consecutive patients scheduled for tumor resection: shows the distribution of weight loss (%) in patients divided in patients with and without cachexia.

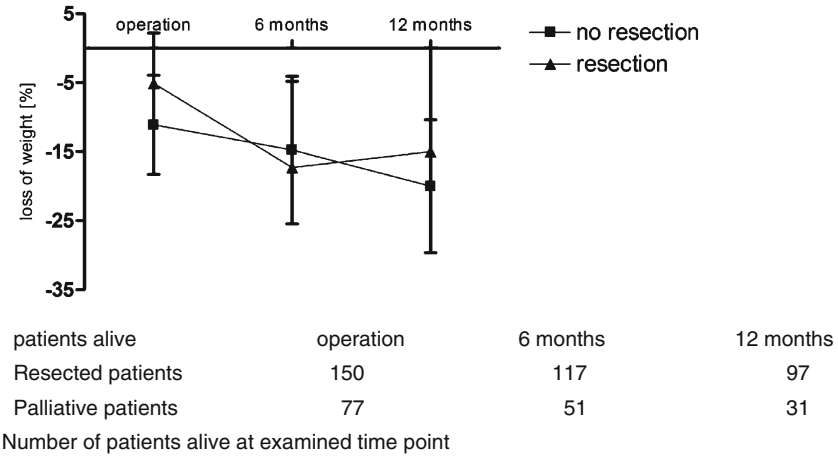


Figure 2 Postoperative weight course of pancreatic cancer patients with tumor resection or with palliative operations.

used the Student's *t* test and the Mann–Whitney *U* test. Significance level was defined as $p<0.05$. Results are reported as median [lower/upper quartile].

Results

All Patients

Of the 227 patients with histologically proven ductal adenocarcinoma, 40.5% ($N=92$) were cachectic and 59.5% ($N=135$) were non-cachectic (Table 1). Figure 1 presents the distribution of weight loss in the patients who presented in the department of surgery for an operative treatment. Regarding the body mass index, there was a significant difference between cachectic and non-cachectic patients ($p=0.003$, Table 1). Median weight loss in cachectic patients was 12 kg (10/15 kg); median relative weight loss was 14.9% (11.5/19.2). In the non-cachectic patients, median weight loss and relative weight loss was 2 kg (0/5) and 2.1% (0/6.5), respectively ($p<0.001$). Figure 2 shows the postoperative course of weight loss and weight gain in patients with pancreatic cancer after tumor resection or palliative operation. There was no significant difference in preoperative CA19-9 levels as a marker of tumor load [non-cachectic: median=161 U/l (43.25/588.65) vs. 262.20 (46.9/1367.0) in cachectic patients] ($p=0.199$).

We identified a significant difference in resection rate between patients with and without cachexia: in 77.8% of patients without cachexia and in only 48.9% of patients with cachexia, tumor resection was possible ($p=<0.001$). In 150 patients, the tumor could be resected, and in 77 patients, a palliative bypass operation or an exploratory laparotomy was performed. Stage UICC II was diagnosed in 68.1% ($N=92$) of patients without cachexia versus 48.9% ($N=45$) of patients with cachexia. During the operation, significantly more UICC IV stages (metastatic disease) were diagnosed in patients with cachexia (42.4%, $N=39$) than in patients without cachexia (27.4%, $N=37$; $p=0.005$). In regard to perioperative morbidity and in-hospital mortality, there was no significant difference between patients with and without cachexia (perioperative morbidity $p=0.765$, in hospital mortality $p=0.333$). In contrast, there was a significant difference in endocrine pancreatic function between the groups. A total of 20% ($N=27$) of patients without cachexia had diabetes mellitus, but in the group of patients with cachexia, 46.7%, ($N=43$) were diabetic ($p=<0.001$). There was no significant difference in the treatment of diabetes mellitus between patients with and without cachexia ($p=0.557$) regarding the need of insulin, oral medication, or a glucose-reduced diet. Table 2 shows

Table 2 Laboratory Tests of Pancreatic Cancer Patients with and without Cachexia Scheduled for Tumor Resection

Patients with PDAC $N=227$	∅ Cachexia $N=135$ (59.5%)	Cachexia $N=92$ (40.5%)	p value
CrP (g/l)	4.4 (1.0/10.1)	8.3 (2.3/30.9)	0.003
Protein (g/l)	73.9 (71.15/77.2)	71.9 (68.18/75.6)	0.007
Albumin (g/l)	44.1 (41.3/46.1)	41.35 (39.43/43.9)	<0.001
Glucose (mg/dl)	111.5 (98.0/141.0)	141.0 (104.25/175.25)	0.002
Haemoglobin (g/dl)	13.1 (12.15/14.3)	12.6 (11.53/13.7)	0.019
Bilirubin (mg/dl)	0.8 (0.45/2.05)	0.9 (0.5/3.7)	0.301

Table 3 Characteristics of Patients with and without Cachexia Undergoing Tumor Resection

Resected patients N=150		∅ Cachexia N=105 (70%)	Cachexia N=45 (30%)	p value
Gender	Male	52 (49.5)	29 (64.4)	0.094
	Female	53 (50.5)	16 (35.6)	
Age		64 (57/ 70)	66 (61/72)	0.245
Body mass index		24.22 (22.54/27.37)	23.67 (21.88/26.16)	0.189
Weight loss (kg)		0 (0/ 4.5)	12 (10.0/16.5)	<0.001
Weight loss (%)		0 (0/ 5.7)	15.3 (12.3/20)	<0.001
CA19-9 (U/ml)		148.85 (36.39/419.5)	137.45 (20.73/658.93)	0.980
ASA classification	I	2 (1.9)	0 (0)	0.198
	II	49 (46.7)	17 (37.8)	
	III	54 (51.4)	28 (62.2)	
Tumor size	T1	1 (1.0)	0 (0)	0.508
	T2	0 (0)	0 (0)	
	T3	101 (96.2)	45 (100)	
	T4	3 (2.8)	0 (0)	
Lymph node status	Negative	23 (21.9)	9 (20)	0.795
	Positive	82 (78.1)	36 (80)	
Distant metastases		11 (10.5)	1 (2.2)	0.089
Grading	G1	4 (3.9)	6 (14.3)	0.076
	G2	64 (62.7)	26 (61.9)	
	G3	34 (33.3)	10 (23.8)	
Resection margin	R0	58 (55.8)	18 (40)	0.062
	R1	43 (41.3)	24 (53.3)	
	R2	3 (2.9)	3 (6.7)	
Tumor stage	UICC II	91 (86.6)	44 (97.8)	0.040
	UICC III	3 (2.9)	0 (0)	
	UICC IV	11 (10.5)	1 (2.2)	
Type of resection	Whipple	78 (74.3)	39 (86.7)	0.076
	Total DP	8 (7.6)	4 (8.9)	
	Left res.	19 (18.1)	2 (4.4)	
30 days mortality		3 (2.9)	2 (4.4)	0.621
Morbidity		45 (42.9)	25 (55.6)	0.155
Diabetes mellitus	Yes	22 (21)	22 (48.9)	0.001
	No	83 (79)	23 (51.1)	

DP duodenopancreatectomy, *Left res* left resection

the differences in laboratory results between patients with and without cachexia. In patients with cachexia, total protein (p=0.007), albumin (p=<0.001), and hemoglobin levels (p=0.019) were significantly reduced. In contrast, C-reactive protein (CrP; p=0.003) and glucose levels (p= 0.002) were significantly elevated in these patients. There was no difference in bilirubin levels between the patients with and without cachexia (p=0.301).

To evaluate the impact of cachexia on the postoperative course, patients were separated into a resected and a palliative-operated group.

Patients Undergoing Tumor Resection

In patients undergoing tumor resection (N=150), there was no significant difference in age, gender, body mass index or American Society of Anesthesiologists (ASA) classification. Table 3 highlights that the distribution of the type of resections is not significantly different between patients with and without cachexia. Furthermore, a difference in tumor location between patients with and without was not present, and the preoperative documented weight loss was independent of the tumor location. The CA19-9 levels were

Table 4 Laboratory Results in Patients with and without Cachexia Undergoing Tumor Resection

Patients with PDAC N=150	∅ Cachexia N=105 (70%)	Cachexia N=45 (30%)	p value
CrP (g/l)	4.1 (1.0/9.2)	6.3 (1.0/11.7)	0.317
Protein (g/l)	73.5 (70.73/77.2)	70.85 (68.33/75.8)	0.040
Albumin (g/l)	43.9 (40.98/45.90)	41.7 (39.6/43.9)	0.016
Glucose (mg/dl)	113.0 (98.75/142.5)	124.0 (98.0/169.5)	0.252
Haemoglobin (g/dl)	13.0 (12.05/14.25)	13 (11.7/13.7)	0.316
Bilirubin (mg/dl)	0.8 (0.4/1.85)	1.45 (0.6/6.28)	0.078

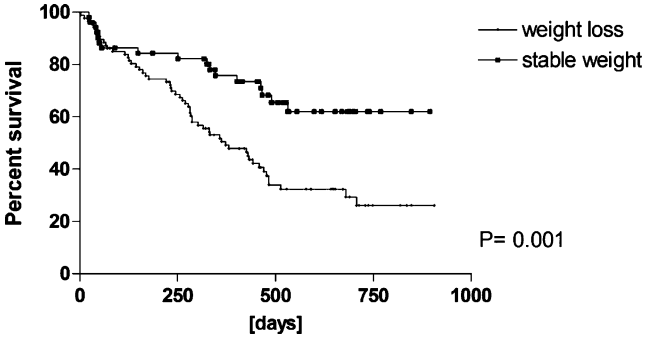


Figure 3 Kaplan–Meier survival curves in resectable pancreatic cancer patients with preoperative weight loss and resectable pancreatic cancer patients with stable weight.

not significantly different between patients, in whom a tumor resection was performed, with and without cachexia as well as tumor size and lymph node metastases as an index for similar tumor load in these groups. The median relative weight loss in patients after tumor resection at the time of operation was 0% (0/5.7) in patients without cachexia and 15.3% (12.3/20) in patients with cachexia (p=<0.001). However, although CA 19-9 levels, tumor size, lymph node invasion, and tumor stage were comparable, patients with cachexia had a tendency to a higher rate of R1 resections than patients without cachexia (p=0.062). Furthermore, more patients with cachexia and pancreatic cancer developed diabetes mellitus (p=0.001, Table 3); patients undergoing tumor resection with cachexia had significantly reduced protein (p=0.040) and albumin levels (p=0.016, Table 4). There was a non-significant tendency to longer survival in patients without cachexia (p=0.240). Median survival was 483 days for patients without cachexia compared to 426 days for patients with cachexia.

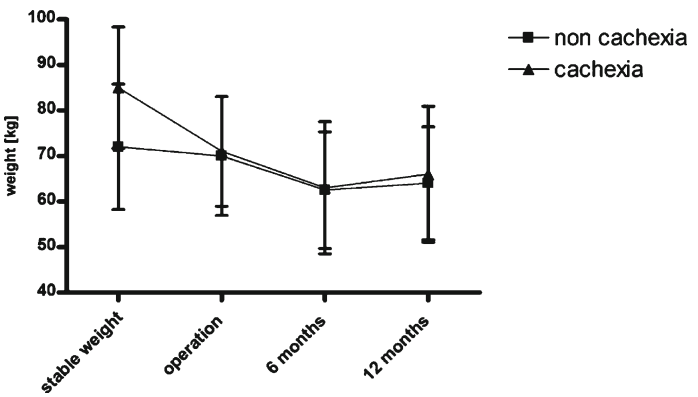
In contrast, when patients are divided into groups with and without weight loss, a significant survival difference was found. Patients without weight loss had a mean survival of 654 days, whereas survival for patients with weight loss was 451 days after resection (p=0.001, Fig. 3). Furthermore, in the multivariate analysis, weight loss emerged as an independent prognostic factor. At the end of the follow-up period [median follow-up 406 days (221/; 532)] 59.3% (N=80) of patients without cachexia were still alive; 44.4% (N=40) of patients with cachexia were alive.

In this study, the natural course of postoperative weight loss/gain of the patients was evaluated every 6 months. Figure 4 shows the pre-illness stable weight as well as the median body weight at operation and the postoperative course at 6 and 12 months after the operation. Interestingly, patients with and without cachexia exhibited weight loss after tumor resection. At 6 months after the operation, patients with cachexia had lost 23.4% of their pre-illness stable weight, and patients without cachexia had lost 14.8%. Weight gain began at the earliest at 6–12 months after the operation (Fig. 4).

Palliative Surgery

In 77 patients, a palliative surgical procedure—either exploratory laparotomy, gastrojejunostomy, and/or a choledochojejunostomy—was performed. A total of 38.9% (N=30) of the palliative operated patients had no cachexia; the remaining 61.03% (N=47) did. Between the two groups, there were no significant differences in age, gender, ASA classification, occurrence of distant metastases, or tumor stage (Table 5).

Survival did not differ between the two groups. Median survival was 287 days in patients without cachexia compared to 227 days for patients with cachexia (Fig. 5). After the palliative surgery, patients continued to lose body



patients alive	operation	6 months	12 months
Non cachexia	105	74	51
Cachexia	45	32	22

Number of patients alive at examined time points

Figure 4 Median weight in patients with resectable pancreatic cancer patients: 6 months before tumor diagnosis (stable weight), 1 day before tumor resection (operation), 6 months postoperatively, and 12 months postoperatively.

Table 5 Characteristics of Patients with and without Cachexia Undergoing Palliative Surgery

Palliative surgery N=77		∅ Cachexia N=30 (38.9%)	Cachexia N=47 (61.03%)	p value
Gender	Male	17 (56.7)	31 (66.0)	0.415
	Female	13 (43.3)	16 (34.0)	
Age		63 (55/70)	64 (55/70)	0.597
Body mass index		24.81(22.55/27.29)	22.59 (19.93/24.93)	0.017
Weight loss (kg)		3.5 (1.5/6)	12 (10/15)	<0.001
Weight loss (%)		5.8 (1.7/7.9)	14.9 (11.4/18.6)	<0.001
Ca19-9 (U/l)		435.00 (66.1/2711.0)	359.0 (79.9/2483.0)	0.771
ASA classification	I	0 (0)	1 (2.1)	0.055
	II	14 (46.7)	10 (21.3)	
	III	15 (50.0)	34 (72.3)	
	IV	1 (3.3)	2 (4.3)	
Distant metastases		26 (86.7)	38 (80.8)	0.509
Tumor stage	UICC II	1 (3.3)	1 (2.1)	0.536
	UICC III	3 (10.0)	8 (17.0)	
	UICC IV	26 (86.7)	38 (80.9)	
30 days mortality		21 (6.7)	4 (8.5)	0.770
Morbidity		11 (36.7)	15 (31.9)	0.669
Diabetes mellitus	Yes	5 (16.7)	21 (44.7)	0.012
	No	25 (83.3)	26 (55.3)	

weight regardless of their preoperative weight loss (Fig. 6). In the lab work results, there were significant differences between patients with and without cachexia. The CrP levels were doubled in patients with cachexia (p=0.019) compared to patients without cachexia. Albumin (p=<0.001) and protein levels (p=0.051) were reduced in patients with cachexia. The glucose levels were significantly elevated in patients with cachexia (p=0.003); hemoglobin was also significantly reduced in patients with cachexia (p=0.007). In bilirubin levels, there was no significant difference between the examined groups (Table 6).

Discussion

This study examined 227 consecutive patients, 150 of these underwent resection for ductal adenocarcinoma of the pancreas. The prevalence of cachexia in this study was 40.5%, demonstrating that even in selected patients with an early stage of pancreatic cancer who are scheduled for pancreatic cancer resection, almost half of the patients had significant preoperative weight loss. We can assume that the occurrence of a dramatic weight loss is a symptom of a progressed tumor stage (Table 1). Additionally, the weight loss of patients with cachexia had significant impact on the nutritional status, with reduced protein, albumin, and hemoglobin levels. Furthermore, patients with cachexia had significantly higher CrP levels, which underlines the chronic and systemic inflammatory reaction of these patients and supports the proposal of Fearon et al.[32] to include CrP values in the diagnosis of cachexia (Table 2). This emphasizes that pancreatic cancer even in non-metastatic stages causes a systemic process, and there are hints that pro-inflammatory reactions can induce hypermetabolism resulting in weight loss and cachexia.[37] In addition, it is well known that pancreatic cancer can induce diabetes, and this is especially true in patients with cachexia which had a significant higher rate of diabetes with an altered glucose metabolism represented by higher glucose levels, which may highlight the underestimated systemic effects of the tumor.[38]

For further analysis, the patients were separated into a resected and a palliative-treated group. In patients with

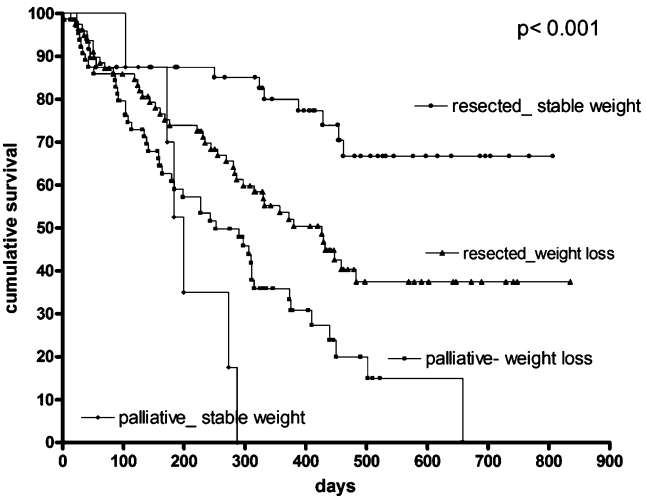
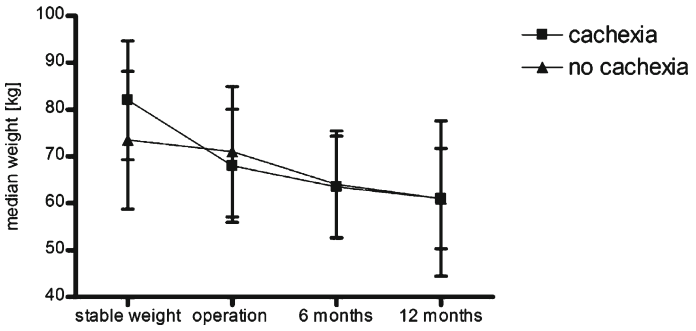


Figure 5 Kaplan–Meier survival curves in pancreatic cancer patients with tumor resection and preoperative weight loss, pancreatic cancer patients with tumor resection and preoperative stable weight, pancreatic cancer patients with palliative surgery and preoperative weight loss and stable weight, and pancreatic cancer patients with palliative surgery with stable weight.



patients alive	operation	6 months	12 months
Non cachexia	30	18	10
Cachexia	47	25	9

Number of patients alive at examined time points

Figure 6 Median weight in patients with non-resectable pancreatic cancer patients: 6 months before tumor diagnosis (stable weight), 1 day before tumor resection (operation), 6 months postoperatively, and 12 months postoperatively.

tumor resection, no differences in tumor size, resection margins, or lymph node invasion were present between patients with and without cachexia. These results agree with those of recent studies which found that tumor-related cachexia is not necessarily dependent on tumor size or load.[39–41] Further support comes from the finding that preoperative CA 19-9 levels in patients with and without cachexia (in the resection as well as in the palliative groups) was not significantly different. Moreover, the occurrence of distant metastasis was significantly higher in patients with cachexia, leading to a reduced resection rate and a worse UICC Stadium in these patients. The earlier metastatic occurrence in patients with cachexia suggest that dedifferentiation of the tumor is a critical step in the development of tumor-associated cachexia. A recent study has found that certain tumors may create an environment that predetermines metastasis by tumor-mediated upregulation of chemoattractants; thus, metastatic dedifferentiation of the tumor might play a key role in the systemic effects of malignant diseases.[38]

We also found that weight loss in the context of cachexia is an important factor in the prognosis of patients with pancreatic cancer. In this study, survival was significantly better in patients who exhibited no weight loss compared to patients who did, especially in the resected group. Additionally, this observation was verified by multivariate analysis in which weight loss was identified as an independent prognostic factor for survival in patients with pancreatic cancer. Davidson et al.[18] demonstrated recently a longer survival in weight-stable pancreatic cancer with palliative treatment. The current study has now shown that this is also the case for patients who undergo resection for pancreatic cancer.

In addition, there was no difference in the preoperative performance status of the patients. Remarkably, all patients, regardless of group, lost up to 23% of their stable weight as far as 6 months after the operation. Quite surprisingly, initial weight gain started no earlier than 6–12 months after resection, and no differences in the postoperative course of weight gain between patients after tumor resection with and without cachexia were found, whereas the postoperative course of weight in palliative patients is difficult to explain because only very few patients survived for 12 months in this group. This outcome may mean that progressive weight loss of patients with cachexia could be moderated by tumor resection, thereby removing the trigger for wasting in tumor-associated cachexia.

Conclusion

In conclusion, patients with cachexia undergoing tumor resection do not exhibit a worse preoperative performance condition and do not have larger tumors or a worse tumor

Table 6 Differences in Laboratory Tests in Palliative Operated Patients with and without Cachexia

Patients with PDAC *N*=77	∅ Cachexia *N*=30 (38.9%)	Cachexia *N*=47 (61.03%)	*p* value
CrP (g/l)	7.2 (1.8/11.6)	14.7 (5.1/37.9)	0.019
Protein (g/l)	75.1 (71.93/77.23)	72.2 (67.85/75.58)	0.051
Albumin (g/l)	44.7 (42.75/47.1)	41.15 (38.53/ 43.55)	<0.001
Glucose (mg/ dl)	105.5 (97,25/135.25)	149.0 (107.0/191.0)	0.003
Haemoglobin (g/ dl)	13.75 (12.65/14.58)	12.60 (11.2/13.6)	0.007
Bilirubin (mg/dl)	1.0 (0.5/3.0)	0.8 (0.5/2.45)	0.705

grade; however, preoperative weight loss may predict a shorter survival. Because more cachectic patients are in a metastasized tumor stage, this status is associated with more progressed tumor disease. Therefore, weight loss may indicate a switch of pancreatic cancer to systemic disease. More efforts should target minimizing pre- and postoperative weight loss because even stabilization of weight can prolong survival.[18] We suggest that in further studies of pancreatic cancer treatment, more attention should be focused on the development of cachexia and ongoing weight loss.

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