

Article

Time to Surgery Does Not Affect Overall or Disease-Free Survival of Patients with Primary Resectable PDAC

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Abstract: (1) Background: Delay in therapy for pancreatic ductal adenocarcinoma (PDAC) may contribute to a worse outcome. The aim of this study was to investigate the prognostic value of time from diagnosis to surgery in patients undergoing upfront surgery for primarily resectable pancreatic carcinoma. (2) Methods: This retrospective single-center study included 214 patients who underwent primary resection of PDAC from January 2000 to December 2018 at University Hospital Erlangen. Using a minimum *p*-value approach, patients were stratified according to time to surgery (TtS) into two groups: TtS ≤ 23 days and TtS > 23 days. Postoperative outcome and long-term survival were compared. (3) Results: Median TtS was 25 days. The best cut-off for TtS was determined as 23 days. There were no differences regarding postoperative outcome or overall survival (OS) and disease-free survival (DFS) (OS: 23.8 vs. 20.4 months, *p* = 0.210, respectively, and DFS: 15.8 vs. 13.6 months, *p* = 0.187). Multivariate analysis revealed age, lymph node metastasis, tumor differentiation and resection status as significant independent prognostic predictors for OS and DFS. (4) Conclusions: A delay of surgery > 23 days after first diagnosis does not affect overall or disease-free survival of patients with primary resectable PDAC. However, the psychological impact of a delay to patients waiting for surgery should not be underestimated.

Keywords: pancreatic ductal adenocarcinoma; primary resection; overall survival; disease-free survival; time to surgery



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1. Introduction

Pancreatic ductal adenocarcinoma (PDAC) is a leading cause of cancer-related mortality worldwide, with a mortality rate almost as high as its incidence [1,2]. The poor prognosis is reflected in a 5-year overall survival of about 10% [3]. Nowadays, the therapy for pancreatic adenocarcinoma always includes multimodal therapy concepts. Nevertheless, surgical radical resection remains the decisive component of a potentially curative therapy. In patients with resectable pancreatic adenocarcinoma, upfront surgery is still the therapy of choice, even if current studies examine and propagate the value of neoadjuvant therapy in primarily resectable pancreatic carcinoma [4]. However, more than 70% of patients diagnosed with pancreatic cancer are not eligible for resection due to metastases or locally advanced cancer [5].

The high rate and early occurrence of metastases, the rapid progression, as well as the associated high mortality rate of pancreatic carcinoma suggest that therapy for pancreatic carcinoma may be time-critical [6]. Delays between the diagnosis of pancreatic carcinoma and the start of appropriate therapy can occur for a variety of reasons, such as the need for a biliary stenting or patient-related factors, such as processing the diagnosis or fear of

further therapy, but these delays can have a negative impact on the outcome. A prolonged time to surgery in patients with resectable pancreatic adenocarcinoma could hypothetically lead to tumor progression and, therefore, worse prognosis.

Recent investigations on the impact of time to surgery on the prognosis of patients with resectable pancreatic adenocarcinoma are inconsistent. Most studies found no impact of a time delay between diagnosis and surgery on survival [7–10]. However, there is some evidence that patients with PDAC < 20 mm benefit from surgery within 30 days after diagnosis [11]. Moreover, Sanjeevi et al. found that an interval > 32 days between diagnosis and surgery leads to a higher risk of progression to an unresectable tumor stage [12].

The aim of this study was to evaluate the impact of the time interval between first diagnostic imaging with suspected pancreatic carcinoma and surgery on overall survival and disease-free survival in patients with primarily resectable PDAC.

2. Materials and Methods

The prospectively maintained Erlangen Cancer Registry of the Department of Surgery was used to identify patients for this retrospective analysis. All adult patients with primary resectable PDAC who underwent upfront surgery at University Hospital Erlangen between 1 January 2000 and 31 December 2018 were included in this study. All patient cases were discussed in an interdisciplinary tumor board, and the pancreatic malignancy was classified as primary resectable based on the available diagnostics. Patients with tumors classified as borderline resectable according to our interdisciplinary tumor board received neoadjuvant therapy. Exclusion criteria comprehend the performance of any neoadjuvant therapy and missing data regarding the first imaging and diagnosis.

Patients' clinical data, including the date of first diagnosis, were retrieved from the clinical information system. First diagnosis was defined as the date of the first imaging with urgent suspicion of a malignant pancreatic tumor. Time to surgery (TtS) was defined as the time between first diagnosis and the date of surgery. Patients' pathological and survival data were obtained from the Erlangen Cancer Registry of the Department of Surgery. The TNM Classification of malignant tumors as presented by the Union for International Cancer Control (UICC) (according to the 8th edition from 2017) was used to describe the histopathological details [13]. Morbidity was evaluated by Clavien–Dindo classification [14]. Major morbidity was defined as Clavien–Dindo III, IV and V. Postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE) and post-pancreatectomy hemorrhage (PPH) were defined according to the definitions of the International Study Group of Pancreatic Surgery (ISGPS) [15–17]. The median follow-up time for the patients was 19.0 months (range 0–194 months).

Using this dataset, a threshold analysis using a minimum *p*-value approach was performed to determine the best cut-off for time to surgery (TtS) regarding overall survival (Supplementary Table S1). Using the identified cut-off, patients with shorter TtS were compared with the group of patients with longer TtS.

This retrospective study was approved by the local ethics committee (22-165-Br).

2.1. Surgical Procedures and Postoperative Course

All surgical procedures were performed by experienced visceral surgeons with many years of practical experience in pancreatic surgery. All procedures included an adequate oncological lymphadenectomy. Depending on the tumor localization, different surgical procedures were performed. Pancreatic head resections always included an interaortocaval lymph node dissection. Interaortocaval lymph nodes do not belong to the locoregional lymph nodes of the pancreas and are therefore to be evaluated as M1 in the case of tumor involvement. Therefore, there are some patients classified as pM1 who received primary resection. In the case of intraoperative evidence of liver metastases or peritoneal carcinosis, no resection of the primary tumor was performed. Additional venous vascular resections, as well as multi-visceral resections, were performed if necessary for achieving R0 situation. Arterial vascular resection was only carried out in exceptional cases.

Adjuvant chemotherapy was generally recommended to all patients except those with a significantly reduced postoperative general condition. Some patients refused an adjuvant chemotherapy. Depending on the condition of the patient, adjuvant chemotherapy was performed with either gemcitabine or 5-FU-based chemotherapy. Regular follow-up including computer tomography (CT) of the thorax and abdomen was recommended to all patients starting quarterly and then every six months from the 3rd year.

2.2. Statistical Analysis

SPSS® Version 28 (IBM, Armonk, NY, USA) was used to analyze the data. Comparisons of metric and ordinal data were calculated with the Student's t-test or Mann–Whitney U test. The Chi-squared test was used for categorical data. The minimum p-value approach was used to determine the optimal cut-off for time to surgery (TtS). Overall survival (OS) and disease-free survival (DFS) were respectively calculated for the period between the date of surgery and the date of death, date of local or distant recurrence or date of last follow-up. For survival analysis, seven patients were excluded because of perioperative death. Possible factors related to the overall (OS) and disease-free survival (DFS) of patients were tested using univariate and multivariate analysis. Variables with a $p \leq 0.1$ in univariate analysis were used for multivariate analysis using a Cox regression model. Survival curves were plotted using the Kaplan–Meier method and compared with the log-rank test. A p -value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Dataset of Patients

A total of 214 patients underwent primary pancreatic resection because of pancreatic ductal adenocarcinoma between 1 January 2000 and 31 December 2018 at the University Hospital Erlangen. Of these, 22 patients had to be excluded because of missing data for the first imaging. Thus, 192 patients remained for this analysis.

3.2. Time to Surgery

The mean and median times between first diagnosis and surgery were 29 days (+/− 20 days) and 25 days (range 1–119 days), respectively. The distribution of patients according to time to surgery is shown in Table 1. The minimum p-value approach revealed that 23 days between first imaging and surgery was the optimum threshold to analyze the impact of a shorter (group 1) or a longer (group 2) time interval on overall survival (Supplementary Table S1). The mean time to surgery was 14 days in group 1 compared to 43 days in group 2. Analysis of delay reasons especially revealed an eight-fold time interval between first diagnosis and first presentation in our hospital in group 2 (TtS > 23 days) compared to group 1 (Figure 1).

Table 1. Distribution of patients undergoing pancreatic resection for pancreatic ductal adenocarcinoma according to time to surgery (TtS) (days) ($n = 192$).

	Number (n)	% of All Patients
TtS ≤ 10 days	26	13.5
TtS > 10 and ≤ 20 days	51	26.6
TtS > 20 and ≤ 30 days	49	25.5
TtS > 30 and ≤ 40 days	29	15.1
TtS > 40 and ≤ 50 days	17	8.9
TtS > 50 and ≤ 60 days	4	2.1
TtS > 60 and ≤ 90 days	11	5.7
TtS > 90 and ≤ 120 days	5	2.6

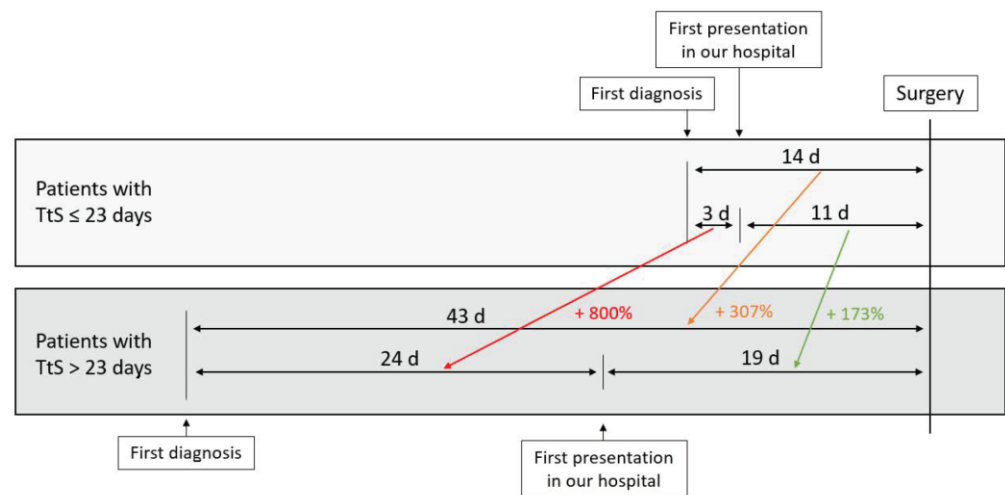


Figure 1. Mean time (in days (d)) between first imaging and surgery, and first admission in our hospital and surgery, stratified for patients with time to surgery (TtS) \leq 23 days vs. $>$ 23 days.

3.3. Patient Characteristics

Of the 192 included patients (median age: 68 years, 49% female), 90 patients had a TtS \leq 23 days (group 1), whereas 102 patients underwent surgery 24 days or later after first diagnosis (group 2). Patient characteristics including ASA score, comorbidities, preoperative biliary stenting and preoperative laboratory did not differ between the two groups (Table 2).

Table 2. Characteristics of patients undergoing pancreatic resection for pancreatic ductal adenocarcinoma stratified to time to surgery (TtS) (\leq 23 days vs. $>$ 23 days).

	TtS \leq 23 Days	TtS $>$ 23 Days	p-Value
Number	90	102	
Age (years), median (IQR)	68 (15)	69 (14)	0.433
Gender, n (%)			1.000
Female	44 (49)	50 (49)	
Male	46 (51)	52 (51)	
ASA (n = 180) *, n (%)			0.769
I	2 (2)	1 (1)	
II	51 (61)	61 (64)	
III	31 (37)	34 (35)	
BMI (kg/m²), median (IQR)	25.5 (4.4)	25.6 (6.4)	0.965
Alcohol abuse (n = 169) *, n (%)	44 (56)	43 (47)	0.280
Nicotine abuse (n = 189) *, n (%)	19 (22)	23 (23)	0.863
Comorbidity, n (%)			
Hypertension	48 (53)	62 (61)	0.310
Diabetes	20 (22)	34 (33)	0.108
Cardiovascular	10 (11)	14 (14)	0.665
Pulmonary	8 (9)	9 (9)	1.000
Cerebrovascular	4 (4)	7 (7)	0.546
Liver disease	7 (8)	9 (9)	1.000
Preoperative biliary stenting, n (%)	45 (50)	56 (55)	0.561
Preoperative hemoglobin (g/dL), median (IQR)	12.9 (2.4)	12.7 (2.3)	0.587
Preoperative WBC (10⁹/L), median (IQR)	6.8 (3.2)	7.2 (3.6)	0.402
Preoperative albumin (g/L), median (IQR)	40.4 (6.6)	40.1 (7.8)	0.954
Preoperative CRP (mg/L), median (IQR)	8 (20)	5 (15)	0.140
Preoperative CA19-9 (U/mL) (n = 174) *, median (IQR)	118 (619)	88 (213)	0.265
Preoperative CEA (ng/mL) (n = 137) *, median (IQR)	3.0 (3.9)	2.3 (3.3)	0.197

IQR = interquartile range; ASA = American Society of Anesthesiologists classification; BMI = body mass index; WBC = white blood cells; CRP = C-reactive protein. * Missing data.

3.4. Surgical and Histopathological Details

Pancreatic head resection was performed most frequently (75%), followed by distal pancreatectomy (21%) and total pancreatectomy (4%). Additional vascular and multi-visceral resection was required in 30% and 18% of patients, respectively. R0 resection was achieved in 88% of the patients.

The surgical and histopathological details, including the TNM stage and the R-status of the patients, were similar among the two groups (Table 3).

Table 3. Surgical and histopathological details of patients undergoing pancreatic resection for pancreatic ductal adenocarcinoma stratified to time to surgery (TtS) (≤ 23 days vs. > 23 days).

	TtS ≤ 23 Days (n = 90)	TtS > 23 Days (n = 102)	p-Value
Kind of surgery			0.743
Pancreatic head resection	69 (77)	76 (74)	
Distal pancreatectomy	17 (19)	23 (23)	
Total pancreatectomy	4 (4)	3 (3)	
Portal vein resection, n (%)	26 (29)	30 (29)	1.000
Arterial resection, n (%)	3 (3)	1 (1)	0.342
Multi-visceral resection, n (%)	19 (21)	15 (15)	0.262
Operative time (min), median (IQR)	280 (101)	278 (108)	0.494
Intraoperative blood loss (mL), median (IQR)	600 (575)	500 (700)	0.809
Intraoperative blood transfusion, n (%)	23 (26)	31 (30)	0.521
T category			0.664
pT1	4 (4)	8 (8)	
pT2	16 (18)	20 (20)	
pT3	68 (76)	73 (72)	
pT4	2 (2)	1 (1)	
n category			0.662
pN0	35 (39)	43 (42)	
pN+	55 (61)	59 (58)	
M category			0.621
pM0	83 (92)	91 (89)	
pM1	7 (8)	11 (11)	
R-status			0.687
R0	78 (87)	90 (88)	
R1	8 (9)	10 (10)	
R2	4 (4)	2 (2)	
Differentiation			0.550
G1	3 (3)	1 (1)	
G2	30 (33)	35 (34)	
G3	57 (63)	66 (65)	

3.5. Short-Term Postoperative Outcome Parameters

The postoperative outcome parameters are shown in Table 4. Regarding in-hospital morbidity, including POPF, DGE and PPH as well as re-operation rate and in-hospital mortality, there was no significant difference between the two groups. Both groups had a median length of postoperative stay of 18 days ($p = 0.366$). In total, 55% of the patients received an adjuvant chemotherapy, with a slightly higher rate in group 2 (57% vs. 52%, $p = 0.534$) (Table 4).

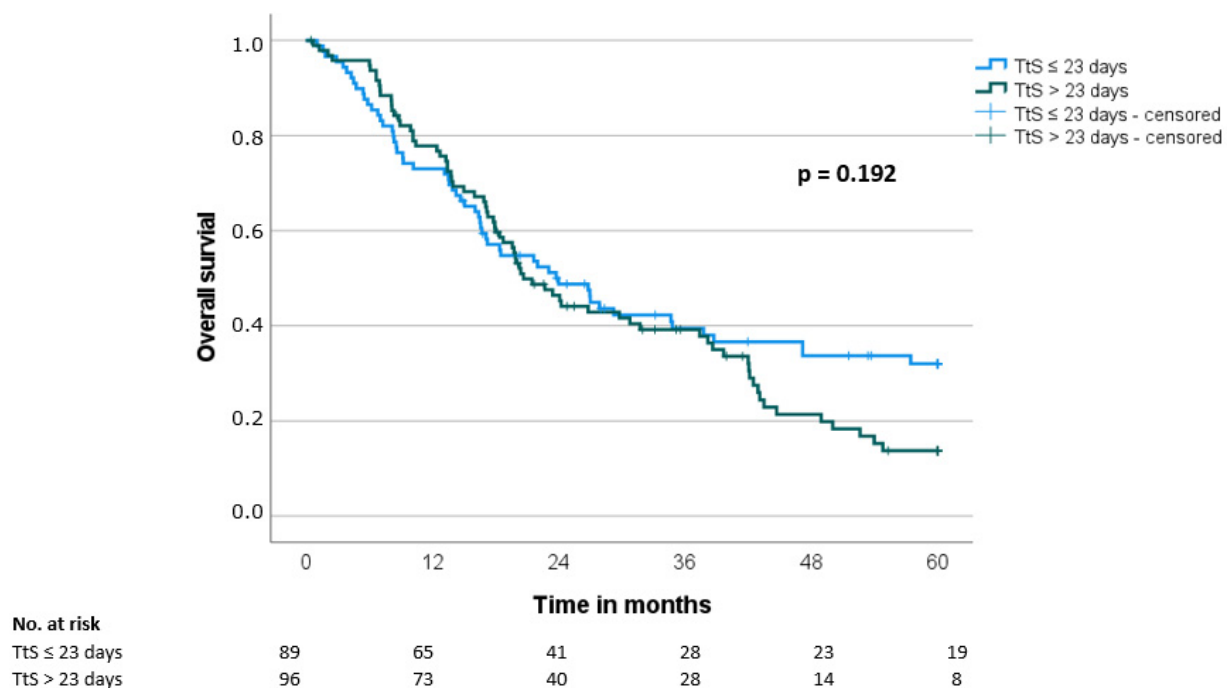
Table 4. Outcome parameter of patients undergoing pancreatic resection for pancreatic ductal adenocarcinoma stratified to time to surgery (TtS) (≤ 23 days vs. >23 days).

	TtS ≤ 23 Days (n = 90)	TtS > 23 Days (n = 102)	p-Value
Morbidity, n (%)	56 (62)	62 (61)	0.882
Major morbidity, n (%)	22 (24)	32 (31)	0.336
Mortality, n (%)	1 (1)	6 (6)	0.123
Re-operation, n (%)	8 (9)	10 (10)	1.000
POPF, n (%)	13 (14)	21 (21)	0.344
DGE, n (%)	32 (36)	29 (28)	0.352
PPH, n (%)	1 (1)	0 (0)	0.469
Surgical site infection, n (%)	8 (9)	4 (4)	0.232
Length of postoperative stay (days), median (IQR)	18 (15)	18 (12)	0.366
Adjuvant chemotherapy, n (%)	47 (52)	58 (57)	0.534
Overall survival (months) *, median (SD)	24.0 (4.2)	20.7 (2.1)	0.192
Disease-free survival (months) *, median (SD)	15.2 (2.4)	13.6 (1.5)	0.187

POPF = postoperative pancreatic fistula; DGE = delayed gastric emptying; PPH = post-pancreatectomy hemorrhage; IQR = interquartile range; SD = standard deviation. * Seven patients were not included in the survival analysis because of perioperative death.

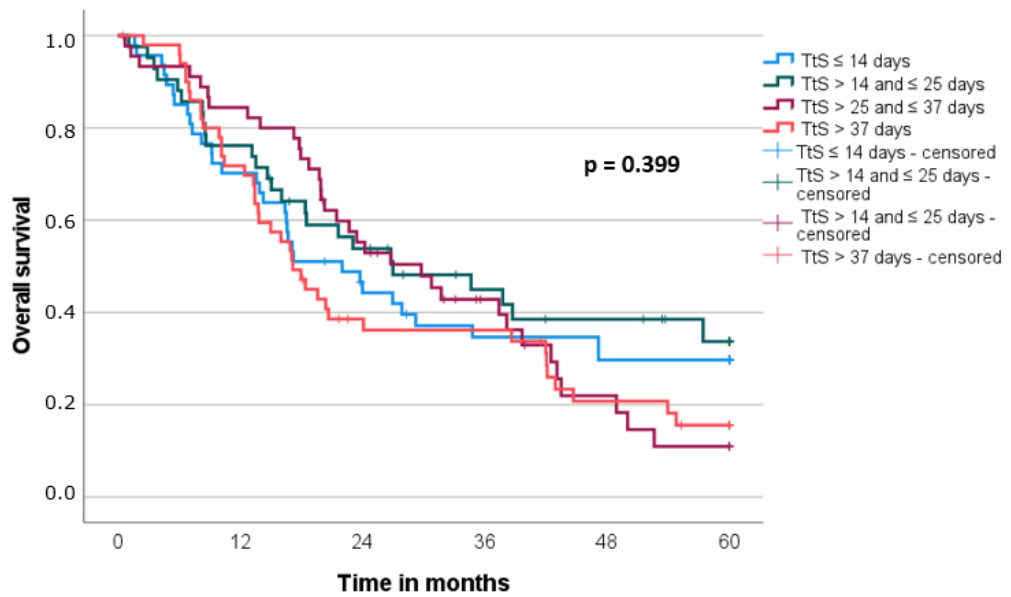
3.6. Overall and Disease-Free Survival

The median overall survival (OS) and disease-free survival (DFS) were 21.5 ± 2.0 months and 13.7 ± 1.5 months, respectively. Both the overall survival and the disease-free survival showed no significant difference between the groups (OS: 24.0 months vs. 20.7 months, $p = 0.192$; DFS: 15.2 months vs. 13.6 months, $p = 0.187$) (Table 4, Figures 2a and 3a). Using stratification of patients in quartiles of time to surgery, there was again no difference between the groups (OS: $p = 0.399$; DFS: $p = 0.427$) (Figures 2b and 3b).



(a)

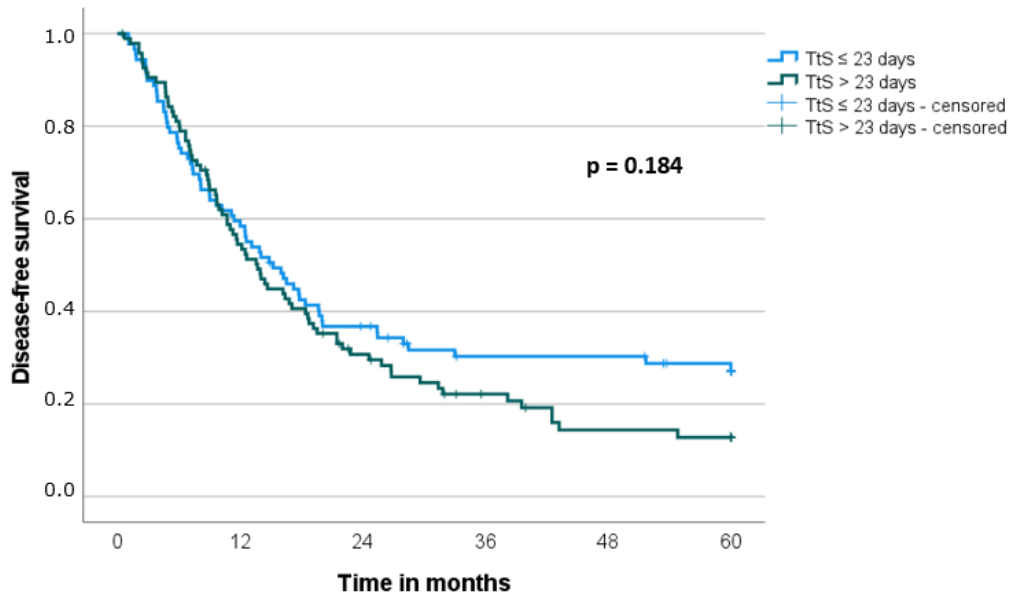
Figure 2. Cont.



No. at risk	0	12	24	36	48	60
TtS ≤ 14 days	47	33	20	14	12	12
TtS > 14 and ≤ 25 days	42	32	21	14	11	7
TtS > 25 and ≤ 37 days	45	38	24	13	6	3
TtS > 37 days	51	35	16	15	8	5

(b)

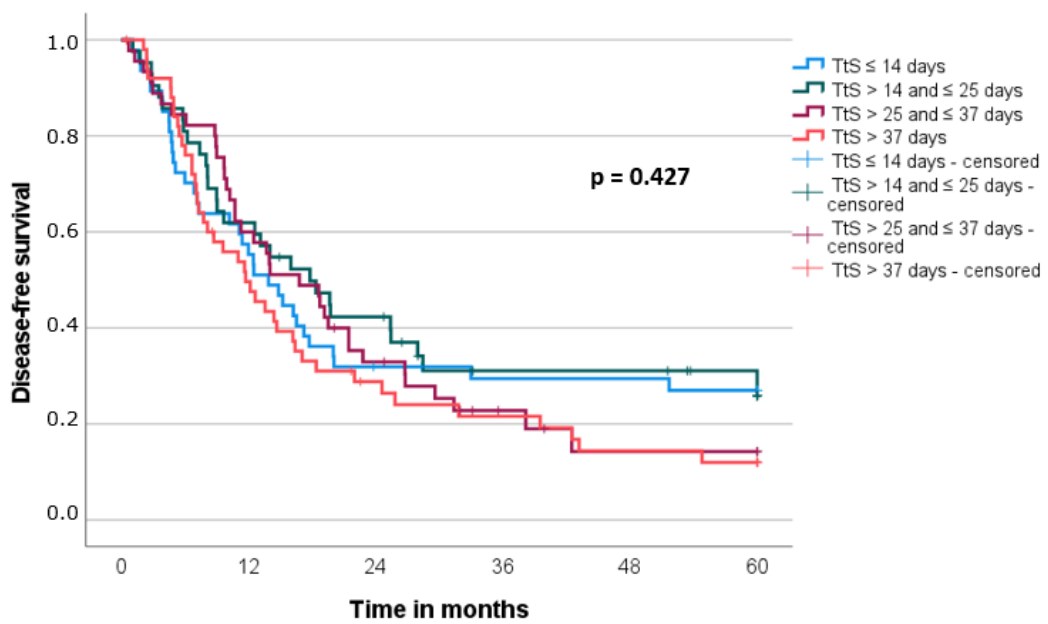
Figure 2. (a) Overall survival (OS) according to time to surgery (TtS) (≤23 days vs. >23 days). (b) Overall survival (OS) according to time to surgery (TtS) (≤14 days (first 25% quartile) vs. >14 and ≤25 days (second 25% quartile) vs. >25 and ≤37 days (third 25% quartile) vs. >37 days (fourth 25% quartile)). Seven patients were not included in the survival analysis because of perioperative death.



No. at risk	0	12	24	36	48	60
TtS ≤ 23 days	89	53	31	28	21	17
TtS > 23 days	96	51	26	15	9	8

(a)

Figure 3. Cont.



(b)

Figure 3. (a). Disease-free survival (DFS) according to time to surgery (TtS) (≤ 23 days vs. > 23 days). (b) Disease-free survival (DFS) according to time to surgery (TtS) (≤ 14 days (first 25% quartile) vs. > 14 and ≤ 25 days (second 25% quartile) vs. > 25 and ≤ 37 days (third 25% quartile) vs. > 37 days (fourth 25% quartile)). Seven patients were not included in the survival analysis because of perioperative death.

3.7. Prognostic Factors for Overall and Disease-Free Survival

Potentially prognostic factors of patients with resected pancreatic carcinoma regarding OS and DFS are presented in Table 5. Multivariate analysis revealed that age (OS: hazard ratio (HR) 2.39, $p < 0.001$; DFS: HR 1.51, $p = 0.032$), lymph node metastasis (OS: HR 2.00, $p < 0.001$; DFS: HR 1.78, $p = 0.005$), R-status 1 or 2 (OS: HR 2.69, $p = 0.001$; DFS: HR 1.74, $p = 0.050$) and differentiation with a grading of 3 (OS: HR 1.84, $p = 0.003$; DFS: HR 1.62, $p = 0.017$) were significant independent prognostic factors regarding OS as well as DFS (Table 5).

Table 5. Prognostic factors of patients with resected pancreatic ductal adenocarcinoma for overall survival (OS) and disease-free survival (DFS).

	Overall Survival (OS) *						Disease-Free Survival (DFS) *				
	n	Univariate		Multivariate			Univariate		Multivariate		
		Median OS	p	HR	95% CI	p-Value	Median DFS	p	HR	95% CI	p-Value
Age											
≤70 years	108	37.4	0.002	2.39	1.63–3.49	<0.001	16.5	0.054	1.51	1.04–2.19	0.032
>70 years	77	17.9					11.0				
Gender											
Female	92	26.8	0.505				13.7	0.764			
Male	93	21.5					14.4				

Table 5. Cont.

	n	Overall Survival (OS) *					Disease-Free Survival (DFS) *				
		Univariate		Multivariate			Univariate		Multivariate		
		Median OS	p	HR	95% CI	p-Value	Median DFS	p	HR	95% CI	p-Value
ASA (n = 174) **											
I/II	112	26.8	0.035	1.27	0.87–1.86	0.210	15.2	0.053	1.16	0.79–1.70	0.444
III	62	16.9					11.1				
Ca19-9 (n = 170) **											
<50 U/mL	64	24.2	0.197				16.8	0.070	1.01	0.69–1.50	0.945
≥50 U/mL	106	22.7					12.5				
Interval to surgery											
≤23 days	89	24.0	0.192				15.2	0.184			
>23 days	96	20.7					13.7				
Kind of surgery											
Pancreatic head resection	141	24.1	0.333				16.2	0.395			
Distal pancreatectomy	38	18.0					10.7				
Total pancreatectomy	6	6.7					6.7				
Vascular resection											
Yes	54	17.2	0.190				9.7	0.260			
No	131	23.7					15.2				
Multi-visceral resection											
Yes	30	18.0	0.329				9.7	0.316			
No	155	24.0					14.7				
T category											
pT1/pT2	47	37.8	0.011	1.36	0.83–2.15	0.234	22.8	0.004	1.32	0.83–2.09	0.243
pT3/pT4	138	19.9					12.5				
N category											
pN0	77	39.7	<0.001	2.00	1.34–3.00	<0.001	19.2	<0.001	1.78	1.19–2.67	0.005
pN+	108	18.4					12.5				
M category											
M0	168	24.0	0.032	0.74	0.37–1.50	0.405	14.8	0.158			
pM1	17	12.7					9.6				
R-status											
R0	162	24.2	<0.001	2.69	1.48–4.89	0.001	16.0	0.013	1.74	1.00–3.02	0.050
R1/R2	23	10.2					8.8				
Differentiation											
G1/G2	68	38.2	<0.001	1.84	1.23–2.76	0.003	20.0	<0.001	1.62	1.09–2.40	0.017
G3	117	17.2					12.2				
Morbidity											
Yes	111	20.4	0.323				14.0	0.737			
No	74	31.7					14.0				
Re-operation											
Yes	16	17.2	0.334				14.0	0.683			
No	167	23.4					14.0				
Adjuvant chemotherapy											
Yes	105	23.8	0.721				14.8	0.981			
No	80	18.5					12.2				

ASA = American Society of Anesthesiologists classification. * Seven patients were not included in the survival analysis because of perioperative death. ** Missing data.

4. Discussion

A delay in treatment of pancreatic ductal adenocarcinoma may contribute to poor prognosis. In our single-center retrospective study including 192 patients who underwent primary surgery for pancreatic ductal adenocarcinoma, the time interval between first diagnostic imaging and surgery did not affect overall survival and disease-free survival.

The influence of time delays between diagnosis and treatment of pancreatic cancer was the topic of research in a few studies. The results of the present study are consistent with those of most others, which found no impact of a time delay to surgery on overall survival [7–11,18–20]. However, there are some studies that have shown higher resectability rates in patients with pancreatic cancer when the time delay to surgery is reduced. Glant et al. described a higher risk of unknown metastases encountered during surgery in patients with proximally located PDAC and longer intervals between the last diagnostic imaging

and surgery [21]. Roberts et al. showed that avoiding preoperative biliary drainage in PDAC patients leads to shorter time intervals between diagnostic imaging and surgery and to more potentially curative resections [22]. In addition, Sanjeevi et al. reported a doubled risk for an unresectable tumor when the time to surgery exceeded 32 days [12]. However, none of these studies analyzed survival rates. Thus, it remains unclear whether the findings of these mentioned studies were also reflected in a better oncological outcome.

However, there are several aspects to consider concerning the time to surgery: First, in addition to the time interval for surgery itself, the reason for the delay may also play a decisive role. One of the most important reasons for delaying surgery is performing preoperative biliary drainage, although some recent studies have shown that this can increase the postoperative complication rate and that early surgery is safe in the presence of jaundice up to a bilirubin of 250 $\mu\text{mol/L}$ [23–25]. However, the rate of patients with preoperative biliary stenting did not differ in our cohort. In the group of delayed surgery, our analysis showed, in particular, a delay in the time interval between initial diagnosis and presentation in our hospital, which could have different explanations: Either uncertainty in diagnostics led to further investigations that required more time, or there was a delay of patient referral to the pancreas center, or patient-related aspects such as processing of the diagnosis or respect for further therapy led to a delayed admission. On the other hand, there may also be patients who can benefit from the delay to surgery: Patients with a poor general condition at the time of diagnosis could be brought to an operable status by intensified prehabilitation, including nutritional therapy. Moreover, a delay caused by additional diagnostic measurements such as liver-MRI can lead to a better selection of patients who may benefit from surgical exploration.

Second, there is likely to be a selection bias when determining the time to surgery since, for example, patients with a larger tumor appear more urgent and are therefore operated on earlier but have a poorer prognosis due to the advanced tumor. However, TNM classification did not differ between groups.

Third, the question is raised whether patients who develop metastasis or a progression to local irresectability within some days would really benefit from resection. Using a longer time interval between diagnosis and resection may give the chance to select these patients before undergoing surgery, as even R0 resection would not improve their survival but carries the risk of possible postoperative complications, which in turn delays the necessary chemotherapy.

Fourth, there is a relevant psychological impact of delayed surgery on cancer patients that may lead to a seriously impaired quality of life by waiting for surgery [26].

Fifth, patients with delayed surgery need to be re-differentiated based on the exact time interval of delay, since a delay in the range of 25–50 days could have a different impact compared to a delay of 90–120 days. However, due to the limited number of patients in the group with the longest delays to surgery, a possible effect cannot be meaningfully investigated in our collective. Using stratification in quartiles (Figures 2b and 3b), there is no significant difference in survival for the quartile with a time to surgery > 37 days compared to the other quartiles.

Moreover, upfront surgery for primarily resectable pancreatic carcinoma is currently under scrutiny, as recent studies show improved survival through neoadjuvant chemotherapy even in the case of primarily resectable tumors [4]. Our results cannot be extrapolated to patients with neoadjuvant therapy. Therefore, if neoadjuvant therapy becomes the standard of care for patients with primarily resectable pancreatic carcinoma in the future, the current data will lose their value.

The present study has several limitations. First, it is a single-center study that has the advantage of a homogeneous therapy concept but makes it difficult to generalize the results. Second, the retrospective analysis of prospective recorded data may have incurred some bias. Third, the number of patients is limited and was collected over a long period of 18 years. Therapy of pancreatic carcinoma changed over the years, especially concerning

adjuvant chemotherapy. However, there was no significant difference between the groups regarding the year of surgery.

5. Conclusions

The present study confirms current data that the time to surgery does not affect overall or disease-free survival of patients with primary resectable PDAC. However, the psychological impact of delayed surgery should also be considered, as the quality of life of cancer patients is seriously impaired by waiting for surgery.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/jcm11154433/s1>. Table S1: Minimum *p*-value approach for influence of the time interval between first imaging, where a suspicious pancreatic lesion was observed, to surgery on overall survival (OS) (*n* = 192).

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Informed Consent Statement: Because of the retrospective design without identifying patient information, informed consent was not obtained.

Data Availability Statement: All data generated or analyzed during this study are included in this published article. The publication contains one supplemental table.

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