Impact of preoperative blood glucose levels on prognosis and postoperative complications in patients with pancreatic cancer

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Abstract. The relationship between diabetes and pancreatic cancer is well documented; however, the effect of preoperative blood glucose levels on prognosis and postoperative complications is currently unclear. The present study aimed to investigate the effect of preoperative blood glucose levels on overall survival (OS) and postoperative complications in patients with pancreatic cancer. This retrospective study included 225 patients with pancreatic cancer treated at The Fourth Hospital of Hebei Medical University from January 2015 to December 2020. Patients were grouped based on preoperative blood glucose levels (normal, ≤6.11 mmol/l; high, >6.11 mmol/l). Data on demographics, clinical history, tumor characteristics, treatment and laboratory results were collected. High preoperative blood glucose levels were associated with reduced OS time [hazard ratio (HR), 1.68; 95% confidence interval (CI), 1.15-2.45; P=0.007] and increased postoperative complications (29.2 vs. 9.8%; χ^2=13.658; P<0.001). Median OS time was significantly shorter in the high glucose group (14.2 vs. 20.5 months; HR, 1.96; 95% CI, 1.38-2.77; P<0.001). Elevated CA19-9 levels were also a predictor of poor OS (HR, 1.70; 95% CI, 1.06-2.74; P=0.029). High preoperative blood glucose and elevated CA19-9 levels were independent predictors of poor prognosis in patients with pancreatic cancer. This finding suggests that preoperative blood glucose levels have a greater impact on prognosis compared with a history of diabetes. Elevated preoperative blood glucose levels have poorer OS and a higher incidence of postoperative complications compared to those with lower preoperative glucose levels, underscoring the importance of preoperative glucose management. Effective preoperative blood glucose control may improve outcomes in patients with pancreatic cancer.

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Introduction

Pancreatic cancer, characterized by its low survival rate and late diagnosis, poses a significant challenge to oncology. Despite the advancements in treatment, the global incidence of pancreatic cancer continues to increase, with an annual incidence rate of approximately 5 per 100,000 (1). However, the five-year survival rate remains only 10%, underscoring the urgent need for innovative diagnostic and prognostic tools to improve patient outcomes (1,2). A notable area of research has been the exploration of the interplay between diabetes mellitus and pancreatic cancer. Studies have documented an increased risk of pancreatic cancer in individuals with a long-standing history of diabetes, suggesting a potential bidirectional relationship between the two conditions (3,4). In certain cases, diabetes may precede cancer development by several years, acting as an early risk or predisposing factor. Conversely, new-onset diabetes or rapidly worsening hyperglycemia can also occur as a paraneoplastic phenomenon resulting from the presence of pancreatic tumors (5,6).

The metabolic relationship between pancreatic cancer and diabetes is complex. Pancreatic cancer can impair insulin secretion owing to islet cell dysfunction or destroy insulin-producing β cells, leading to hyperglycemia. Furthermore, tumors may secrete inflammatory cytokines and tumor-derived factors that interfere with insulin action, exacerbating insulin resistance and increasing blood glucose levels (7). This hyperglycemic state often develops independent of prior diabetes and can serve as an early clinical sign of malignancy in a number of patients (8).

Preoperative glycemic control is particularly important, as hyperglycemia is associated with poor surgical outcomes, including increased infection rates, delayed wound healing and longer hospital stays (9). While blood glucose levels in patients with preexisting diabetes are often monitored during treatment, the immediate preoperative blood glucose status provides a more accurate reflection of metabolic homeostasis

at the time of surgery (10,11). Importantly, glycemic variability among patients with pancreatic cancer is influenced not only by pre-existing diabetes but also by tumor-induced metabolic disruptions, which may complicate clinical management (9). Despite the recognized importance of perioperative glycemic control, particularly in reducing surgical complications and improving patient outcomes, the specific impact of preoperative blood glucose levels on the survival of patients with pancreatic cancer remains insufficiently explored. This gap presents a critical avenue for research with the potential to inform targeted interventions aimed at optimizing preoperative glycemic control (7,9).

The present study investigated the prognostic significance of preoperative blood glucose levels in patients undergoing pancreatic cancer surgery. By delineating the relationship between preoperative glycemic status and postoperative outcomes, the present study aimed to highlight a potentially modifiable factor in the management of pancreatic cancer.

Patients and methods

Study design and patient selection. The retrospective cohort included 225 patients with histologically confirmed pancreatic cancer who were treated at The Fourth Hospital of Hebei Medical University (Shijiazhuang, China) between January 2015 and December 2020. Ethical approval was obtained from the Institutional Review Board of the Fourth Hospital of Hebei Medical University (approval no. 2023KS182), and the requirement for informed consent was waived due to the retrospective nature of the present study. Patients were eligible if they were aged ≥18 years and had complete preoperative clinical data, including fasting blood glucose levels. The exclusion criteria were as follows: i) Patients with other severe primary diseases such as respiratory, cardiovascular, cerebrovascular, liver, kidney or hematopoietic diseases; ii) those who died during the perioperative period; and iii) those with incomplete clinical data. The present study was conducted in accordance with the Declaration of Helsinki (revised in 2013).

Diagnostic criteria. Pancreatic cancer was diagnosed based on the Chinese Guidelines for Diagnosis and Treatment of Pancreatic Cancer (2020 Edition) (12) using enhanced computed tomography and/or magnetic resonance imaging. The pathological diagnosis followed the 5th Edition of the World Health Organization Classification of Tumors of the Digestive System (13), which includes ductal adenocarcinoma and its variants.

Grouping and treatments. The preoperative blood glucose level was defined as the fasting blood glucose level measured from venous blood samples collected in the morning before food intake. Patients were categorized into two groups based on blood glucose levels: Normal blood glucose (≤6.11 mmol/l) and high blood glucose (>6.11 mmol/l). Additionally, the patients were grouped based on diabetic status into those with and without diabetes. Treatment regimens, including surgical resection and adjuvant chemotherapy, followed the current clinical guidelines. All patients underwent perioperative management according to the Chinese Guidelines for Perioperative Management of Pancreatic Cancer (12).

Data collection and outcomes. Demographic characteristics, clinical history, tumor characteristics, treatment details and laboratory results were collected. The primary outcome was overall survival (OS), which was defined as the time from diagnosis to death from pancreatic cancer. Secondary outcomes included postoperative complications requiring clinical intervention such as infection, bleeding (arterial or gastrointestinal), wound disruption and pancreatic fistula, all of which were documented and analyzed.

Follow-up. Patients were followed up regularly through outpatient visits, telephone interviews and medical record reviews. The follow-up period was conducted until December 2023. The survival status was documented during each follow-up period.

Statistical analysis. Data analysis was performed using SPSS software (version 26.0; IBM Corp.). Continuous variables are presented as the mean ± standard deviation or median with interquartile range, and compared using unpaired Student's t-test or Mann-Whitney U test, as appropriate. Categorical variables were expressed as frequencies and percentages, and compared using χ^2 or Fisher's exact tests. Survival analysis was conducted using the Kaplan-Meier method, and differences were assessed using the log-rank test. Factors associated with OS were identified using univariate and multivariate Cox proportional hazard regression models. $P<0.05$ was considered to indicate a statistically significant difference.

Results

Patient characteristics. A total of 225 patients were included in the present study. The median age was 62 years (range 31-83 years), with a higher prevalence in men (66.7%) than in women (33.3%). 153 in the normal blood glucose group and 72 in the high blood glucose group (Table I).

No significant differences were observed between the normal and high blood glucose groups in terms of age, sex distribution, smoking history, weight loss, albumin levels, total bilirubin, CA19-9 levels, neutrophil-to-lymphocyte ratio (NLR), tumor size, tumor location, lymph node involvement, lymphovascular invasion, perineural invasion, tumor grade, TNM stage or adjuvant chemotherapy. However, the platelet-to-lymphocyte ratio (PLR) and postoperative complications were significantly different between the normal and high blood glucose groups.

A total of 192 patients had no history of diabetes, whereas 33 patients had a history of diabetes. When grouped by diabetes history, no significant differences were observed in terms of age, sex, smoking history, weight loss, albumin levels, total bilirubin, CA19-9 levels, NLR, PLR, tumor size, location, lymph node involvement, lymphovascular invasion, perineural invasion, tumor grade, TNM stage, adjuvant chemotherapy and postoperative complications between the normal and high blood glucose groups (Table II).

The baseline characteristics of diabetic patients divided into normal and high blood glucose groups were analyzed (Table SI). No significant differences were noted between

Table I. Patient demographics and baseline characteristics based on blood glucose levels.

Characteristic	Blood glucose		P-value
	Normal (n=153)	Hyperglycemia (n=72)	
Median age, years (range)	61 (31-83)	64 (35-81)	0.066
Sex, n (%)			0.064
Female	71 (46.4)	24 (33.3)	
Male	82 (53.6)	48 (66.7)	
Smoking history, n (%)			0.531
No	98 (64.1)	43 (59.7)	
Yes	55 (35.9)	29 (40.3)	
Weight loss, n (%)			0.459
No	103 (67.3)	52 (72.2)	
Yes	50 (32.7)	20 (27.8)	
Median albumin level (range), g/l	44.0 (35.8-48.6)	43.6 (28.0-48.6)	0.804
Median total bilirubin (range), mmol/l	14 (5-281)	15 (5-281)	0.087
CA19-9, n (%)			0.093
<37 U/ml	36 (23.5)	10 (13.9)	
37-1,000 U/ml	92 (60.1)	43 (59.7)	
>1,000 U/ml	25 (16.3)	19 (26.4)	
Median neutrophil-to-lymphocyte ratio (range)	2.89 (0.70-18.07)	2.93 (0.94-98.09)	0.237
Median platelet-to-lymphocyte ratio (range)	223 (150-299)	211 (151-298)	0.044
Median tumor size (range), cm	3.50 (0.80-10.51)	3.69 (1.80-11.00)	0.283
Location, n (%)			0.469
Tail of pancreas	63 (41.2)	26 (36.1)	
Head of pancreas	90 (58.8)	46 (63.9)	
Lymph node involvement, n (%)			0.058
No	86 (56.2)	50 (69.4)	
Yes	67 (43.8)	22 (30.6)	
Lymphovascular invasion, n (%)			0.625
No	110 (71.9)	54 (75.0)	
Yes	43 (28.1)	18 (25.0)	
Perineural invasion, n (%)			0.912
No	50 (32.7)	23 (31.9)	
Yes	103 (67.3)	49 (68.1)	
Grade, n (%)			0.740
I	19 (12.4)	7 (9.7)	
II	88 (57.5)	45 (62.5)	
III	46 (30.1)	20 (27.8)	
TNM stage, n (%)			0.564
I	60 (39.2)	32 (44.4)	
II	79 (51.6)	36 (50.0)	
III	14 (9.2)	4 (5.6)	
Adjuvant chemotherapy, n (%)			0.750
No	50 (32.7)	22 (30.6)	
Yes	103 (67.3)	50 (69.4)	
Postoperative complications, n (%)			<0.001
No	138 (90.2)	51 (70.8)	
Yes	15 (9.8)	21 (29.2)	

Table II. Patient demographics and baseline characteristics based on diabetes history.

Characteristic	Diabetes history		P-value
	No (n=192)	Yes (n=33)	
Median age (range), years	62 (55-67)	64 (59-70)	0.175
Sex, n (%)			0.461
Female	83 (43.2)	12 (36.4)	
Male	109 (56.8)	21 (63.6)	
Smoking history, n (%)			0.296
No	123 (64.1)	18 (54.5)	
Yes	69 (35.9)	15 (45.5)	
Weight loss, n (%)			0.606
No	131 (68.2)	24 (72.7)	
Yes	61 (31.8)	9 (27.3)	
Median albumin (range), g/l	43.7 (40.7-45.6)	44.1 (41.3-45.2)	0.721
Median total bilirubin (range), mmol/l	14 (10-68)	14 (10-21)	0.573
CA19-9, n (%)			0.418
<37 U/ml	41 (21.4)	5 (15.2)	
37-1,000 U/ml	116 (60.4)	19 (57.6)	
>1,000 U/ml	35 (18.2)	9 (27.3)	
Median neutrophil-to-lymphocyte ratio (range)	2.93 (2.19-3.88)	2.89 (2.31-4.00)	0.554
Median platelet-to-lymphocyte ratio (range)	221 (191-261)	211 (174-263)	0.158
Median tumor size (range), cm	3.50 (3.00-5.00)	3.50 (3.00-5.52)	0.864
Location, n (%)			0.429
Tail of pancreas	78 (40.6)	11 (33.3)	
Head of pancreas	114 (59.4)	22 (66.7)	
Lymph node involvement, n (%)			0.429
No	114 (59.4)	22 (66.7)	
Yes	78 (40.6)	11 (33.3)	
Perineural invasion, n (%)			0.776
No	63 (32.8)	10 (30.3)	
Yes	129 (67.2)	23 (69.7)	
Lymphovascular invasion, n (%)			0.982
No	140 (72.9)	24 (72.7)	
Yes	52 (27.1)	9 (27.3)	
Grade, n (%)			0.450
I	23 (12.0)	3 (9.1)	
II	110 (57.3)	23 (69.7)	
III	59 (30.7)	7 (21.2)	
TNM stage, n (%)			0.806
I	77 (40.1)	15 (45.5)	
II	99 (51.6)	16 (48.5)	
III	16 (8.3)	2 (6.0)	
Adjuvant chemotherapy, n (%)			0.821
No	62 (32.3)	10 (30.3)	
Yes	130 (67.7)	23 (69.7)	
Postoperative complications, n (%)			0.056
No	165 (85.9)	24 (72.7)	
Yes	27 (14.1)	9 (27.3)	

these groups in terms of demographic, clinical or tumor characteristics, such as age, sex, CA19-9 levels, tumor size and postoperative complications. This balanced distribution supports the analysis by minimizing the potential confounding effects related to baseline characteristics.

A comparison of the prevalence of hyperglycemia between the diabetic and non-diabetic groups was conducted, which demonstrated a significantly higher proportion of hyperglycemia in patients with diabetes (54.5%) compared with that in patients without diabetes (28.1%) (P=0.005; Table SII).

Factors associated with OS. Univariate analysis identified high blood glucose levels as significantly associated with decreased OS [hazard ratio (HR), 1.96; 95% CI, 1.38-2.77]. In the multivariate Cox regression model, high blood glucose level was an independent predictor of poor OS (HR 1.68; 95% CI, 1.15-2.45), along with CA19-9 >1,000 U/ml (HR 1.70; 95% CI, 1.06-2.74). Diabetes history was also associated with decreased OS in the univariate analysis (HR 1.70; 95% CI, 1.13-2.58), but not in the multivariate analysis (HR 1.35; 95% CI, 0.87-2.10). Similarly, grade III was associated with decreased OS in univariate analysis (HR 1.92; 95% CI, 1.01-3.66), but showed no significant impact in multivariate analysis (HR 1.13; 95% CI, 0.77-1.65; Table III).

Survival analysis. Kaplan-Meier analysis indicated a significantly shorter median OS time in the high blood glucose group (10.0 months) compared with that in the normal blood glucose group (23.0 months) (P<0.001). Additionally, the 1- and 2-year survival rates were markedly lower in patients with high blood glucose levels, at 45 and 20%, respectively, compared with 65 and 35% in the normal glucose group (Fig. 1).

For patients with CA19-9 levels >1,000 U/ml, the median OS was significantly reduced (10.0 months), compared with those with CA19-9 levels between 37 and 1,000 U/ml (22.0 months) and those with CA19-9 levels <37 U/ml (23.0 months) (Fig. 2). Multivariate Cox regression analysis further validated CA19-9 levels >1,000 U/ml as an independent predictor of poor OS (HR 1.70; 95% CI, 1.06-2.74), along with high blood glucose levels (HR 1.68; 95% CI, 1.15-2.45). Although diabetes history was associated with significantly decreased OS in univariate analysis (HR 1.70; 95% CI, 1.13-2.58), this association did not hold in the multivariate model (HR 1.35; 95% CI, 0.87-2.10) (Table III), suggesting that immediate metabolic status, rather than diabetes history, serves a critical role in prognosis.

Postoperative complications. Postoperative complications were more common in the high blood glucose group compared with the normal glucose group (29.2 vs. 9.8%; (Table I). The most frequent complications were infection, delayed wound healing and anastomotic leakage. Postoperative complications were more frequent in patients with a history of diabetes than in those without diabetes; however, the difference was not significant (27.3 vs. 14.1%; Table II).

Discussion

Pancreatic cancer is a highly malignant tumor with a poor prognosis. Despite significant advancements in diagnostic and therapeutic approaches in recent years, the OS rate remains low (1). The aggressive nature of pancreatic cancer, combined with its often asymptomatic early stages, results in numerous patients being diagnosed at an advanced stage, which negatively affects treatment outcomes and survival rates (7). Among the numerous factors that influence prognosis, preoperative metabolic status and tumor markers are considered to be key predictive factors (8). Diabetes mellitus, a common metabolic disorder, has been extensively studied and linked to the incidence and prognosis of various malignancies, including renal and prostate cancer (14,15). Additionally, preoperative blood glucose levels and tumor markers such as CA19-9 are suggested to serve important roles in cancer prognosis (16). However, the specific effects of these factors on patients with pancreatic cancer remain controversial. The present study aimed to systematically evaluate the effects of a preoperative history of diabetes and preoperative blood glucose and CA19-9 levels on the prognosis of patients with pancreatic cancer to provide insights for clinical decision-making (17).

The present study included clinical data from >200 patients with pancreatic cancer and performed Kaplan-Meier survival, Cox's regression, and univariate and multivariate analyses. The baseline characteristics of the patients with diabetes were similar between the normal and high blood glucose groups, which reduced the potential effects of confounding factors in the outcome analysis. The prevalence of hyperglycemia was significantly higher in the diabetic group compared with that in the non-diabetic group, which indicated distinct differences in blood glucose control between these populations. Patients with diabetes often face challenges in maintaining normoglycemia due to factors such as insulin resistance and impaired pancreatic function (11). This result underscores the importance of intensified blood glucose management in patients with diabetes to reduce the risk of hyperglycemia-related complications.

After adjusting for other potential confounding factors, preoperative blood glucose level was an independent prognostic factor in patients with pancreatic cancer. High blood glucose levels were significantly associated with poor survival rates. Secondly, CA19-9 levels >1,000 U/ml were an independent prognostic factor, which indicated that patients with elevated CA19-9 levels had significantly worse survival outcomes. Finally, while preoperative diabetes history was associated with worse survival rates in the univariate analysis, it did not remain significant in the multivariate analysis, suggesting that its impact might be mediated through other factors, such as blood glucose levels and inflammatory status.

The present study demonstrated a significantly higher incidence of postoperative complications, including infections, delayed wound healing and anastomotic leaks in the high blood glucose group compared with that in the normoglycemic group. This finding aligns with previous research indicating that elevated blood glucose levels markedly increase the risk of postoperative complications, particularly those related to infection and delayed healing (18). Compared with analyzing individual complications separately, combining complications into a single composite measure offers a more comprehensive perspective and reduces statistical variability, especially given the lower incidence of individual events (19).

Hyperglycemia is considered to increase the complication rates through several mechanisms. First, elevated blood glucose levels have been shown to suppress immune function,

Table III. Univariate and multivariate analysis of influencing factors using Cox's regression.

	Univariate analysis					Multivariate analysis				
Characteristic	No. of patients	Patient deaths	HR	95% CI	P-value	No. of patients	Patient deaths	HR	95% CI	P-value
Age	225	153	1.00	0.99-1.02	0.736					
Sex										
Female	95	64	-	-						
Male	130	89	1.12	0.81-1.55	0.506					
Blood glucose										
Normal blood glucose	153	101	-	-		153	101	-	-	
Hyperglycemia	72	52	1.96	1.38-2.77	<0.001	72	52	1.68	1.15-2.45	0.007
Diabetes history										
No	192	125	-	-		192	125	-	-	
Yes	33	28	1.70	1.13-2.58	0.011	33	28	1.35	0.87-2.10	0.184
Smoking history										
No	141	96	-	-						
Yes	84	57	0.99	0.71-1.37	0.935					
CA199, U/ml										
<37	46	32	-	-		46	32	-	-	
37-1,000	135	77	0.78	0.51-1.18	0.237	135	77	0.73	0.48-1.11	0.136
>1,000	44	44	1.91	1.21-3.04	0.006	44	44	1.70	1.06-2.74	0.029
Weight loss										
No	155	107	-	-						
Yes	70	46	1.01	0.71-1.44	0.940					
Albumin	225	153	1.02	0.97-1.07	0.496					
Total bilirubin	225	153	1.00	1.00-1.00	0.981					
Neutrophil-to-lymphocyte ratio	225	153	1.02	1.00-1.03	0.084	225	153	1.02	1.00-1.04	0.081
Platelet-to-lymphocyte ratio	225	153	1.00	1.00-1.00	0.960	225	153	1.00	1.00-1.01	0.220
Location										
Tail of pancreas	89	57	-	-						
Head of pancreas	136	96	1.13	0.81-1.57	0.468					
Size	225	153	1.07	0.98-1.16	0.130					
Lymph node involvement										
No	136	90	-	-						
Yes	89	63	1.07	0.77-1.48	0.693					

Table III. Continued.

Characteristic	Univariate analysis					Multivariate analysis				
	No. of patients	Patient deaths	HR	95% CI	P-value	No. of patients	Patient deaths	HR	95% CI	P-value
Perineural invasion										
No	73	55	-	-						
Yes	152	98	0.95	0.68-1.32	0.746					
Lymphovascular invasion										
No	164	109	-	-						
Yes	61	44	1.14	0.80-1.62	0.474					
Grade										
I	26	13	-	-		26	13	-	-	
II	133	94	2.15	1.17-3.96	0.013	133	94	1.03	0.69-1.30	0.093
III	66	46	1.92	1.01-3.66	0.046	66	46	1.13	0.77-1.65	0.089
Adjuvant chemotherapy										
No	72	44	-	-						
Yes	153	109	1.19	0.84-1.70	0.325					
Postoperative complications										
No	189	128	-	-						
Yes	36	25	1.04	0.67-1.60	0.871					

HR, hazard ratio; CI, confidence interval.

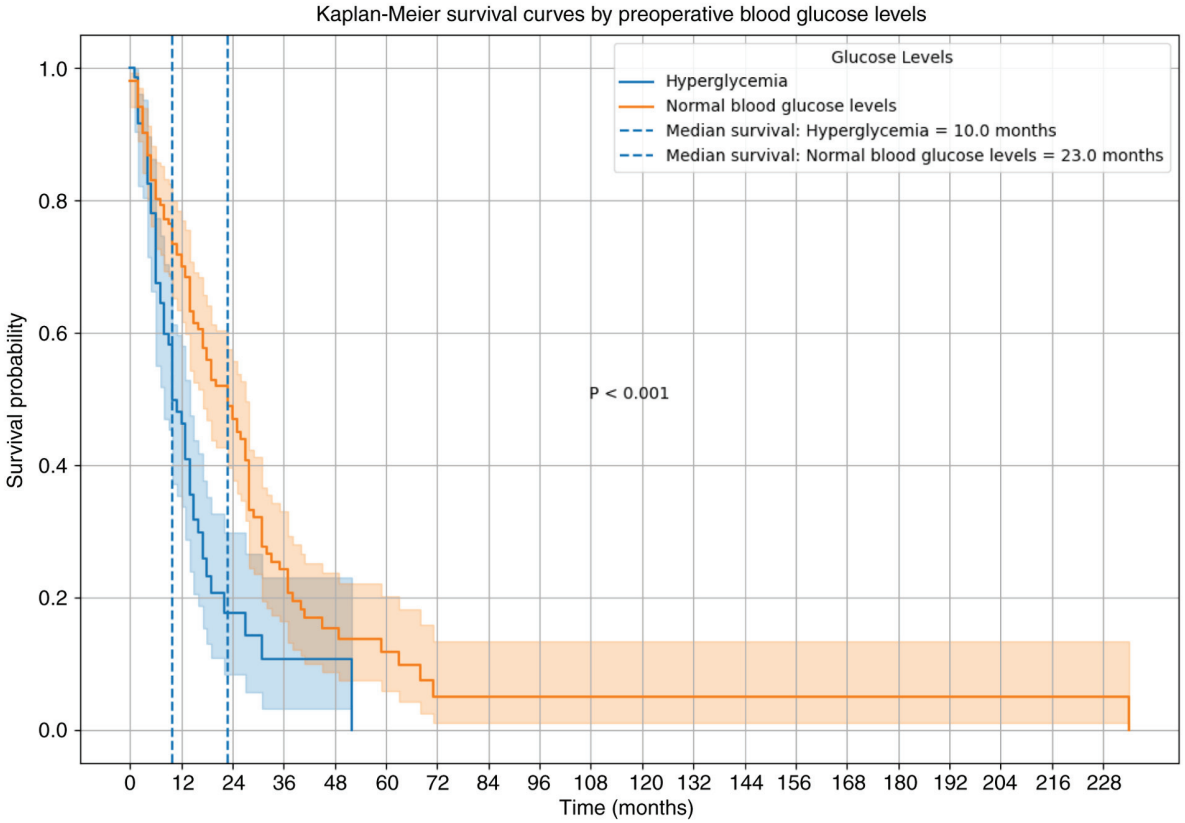

Figure 1. Kaplan-Meier survival curves by preoperative blood glucose levels. The survival curves of patients with normal blood glucose levels compared with those with hyperglycemia are shown. The median overall survival time was significantly shorter in the high blood glucose group (10.0 months) compared with the normal blood glucose group (23.0 months) (P<0.001).

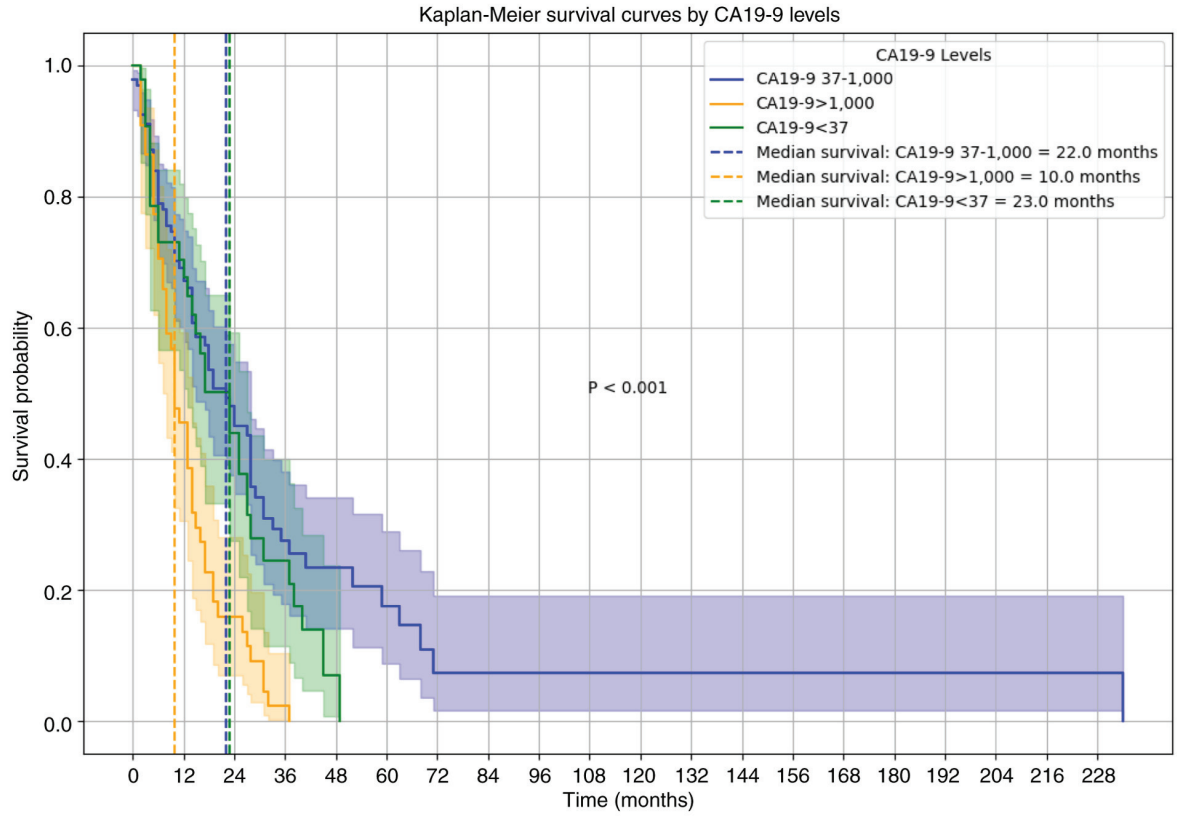

Figure 2. Kaplan-Meier survival curves by CA19-9 levels. The survival curves stratified by CA19-9 levels are shown. Patients with CA19-9 levels >1,000 U/ml had a significantly shorter median overall survival time (10.0 months) compared with those patients with CA19-9 levels between 37 and 1,000 U/ml (22.0 months) and those patients with CA19-9 levels <37 U/ml (23.0 months) (P<0.001).

particularly by inhibiting neutrophil chemotaxis and phagocytosis, which lowers the body's defense against pathogens and increases infection risks, such as wound infections and anastomotic leaks (20). Additionally, hyperglycemia delays wound healing by reducing collagen synthesis, impairing fibroblast activity and restricting blood flow, thereby hindering tissue access to the oxygen and nutrients that are essential for healing. This delayed healing effect likely contributes to an increased risk of wound dehiscence and anastomotic leakage (18). Moreover, hyperglycemia amplifies the inflammatory response, promoting the release of pro-inflammatory cytokines such as TNF-α and IL-6, which exacerbate tissue damage and elevate the risk of complications. The accumulation of advanced glycation end products (AGEs) further exacerbates tissue injury and impedes normal repair processes, making patients more vulnerable to postoperative complications (21).

Although combining complications provides a broader view and increased statistical power, this approach may obscure the unique effects of hyperglycemia on each type of complication. A previous study has highlighted the advantages of such combined analyses, particularly in patients with diabetes or preoperative hyperglycemia, as the interrelated nature of complications such as cardiovascular events and infections enhances the statistical reliability and clinical interpretability of the findings (22). For example, when assessing the impact of hyperglycemia on infection risk, combining complications assists in identifying high-risk patients and underscores the importance of rigorous preoperative glucose management (21). Despite these benefits, future studies should explore individual complications to evaluate the distinct effects of hyperglycemia on various postoperative outcomes, which may aid in creating personalized glucose management strategies for high-risk patients (20). Overall, these findings support the need for stringent preoperative glucose control to reduce infection risk and delay wound healing and anastomotic leaks, thus improving surgical outcomes.

High preoperative blood glucose levels have been associated with a poor prognosis in various types of cancer, including pancreatic cancer. Balzano *et al* (23) found that elevated blood glucose levels were significantly associated with an increased incidence and mortality of pancreatic cancer. Huxley *et al* (24) also reported that preoperative hyperglycemia was significantly correlated with reduced OS in patients with pancreatic cancer. In the present study, preoperative blood glucose level emerged as an independent prognostic factor, even after adjusting for other potential confounding factors. This suggested that glycemic control has a direct impact on patient outcomes, independent of other metabolic disorders or comorbidities. Hyperglycemia may promote tumor cell proliferation, inhibit apoptosis and affect the tumor microenvironment, thereby influencing the prognosis (25). These findings highlighted the critical role of preoperative metabolic control in the management of patients with pancreatic cancer.

The relationship between preoperative blood glucose levels and a history of diabetes is complex. Previous studies have shown that history of diabetes is generally associated with a worse cancer prognosis (6,14,15). Meyerhardt *et al* (26) conducted a meta-analysis and found that diabetes was linked to poor outcomes in various types of cancer, including pancreatic cancer. However, in the present study, although a preoperative history of diabetes was significant in the univariate analysis, it did not remain significant in the multivariate analysis. This discrepancy may be explained by the fact that the impact of a history of diabetes on prognosis may be mediated by current blood glucose levels and related metabolic disturbances (26). Chronic hyperglycemia and associated metabolic abnormalities, such as insulin resistance and chronic inflammation, may contribute to poor outcomes in patients with diabetes (27). Therefore, the immediate preoperative metabolic state, as reflected by blood glucose levels, may be more critical in predicting outcomes compared with presence of a history of diabetes.

The non-significance of a history of preoperative diabetes in the multivariate analysis could be due to several factors. First, while a history of diabetes indicates long-term metabolic dysregulation, preoperative blood glucose levels may have a more direct impact on surgical and oncological outcomes. Kleeff *et al* (28) suggested that, although a history of diabetes is related to prognosis, pre-and postoperative glycemic controls are more significant factors affecting outcomes. Second, a history of diabetes may indirectly influence the prognosis through blood glucose levels and other metabolic parameters. Patients with diabetes often exhibit insulin resistance, chronic inflammation and other metabolic issues that affect their prognosis through various pathways (28). Additionally, a history of diabetes may be associated with other comorbidities and risk factors that were accounted for in the multivariate analysis, reducing its independent significance.

CA19-9 is one of the most commonly used tumor markers for pancreatic cancer. Several studies have confirmed its prognostic value. Duffy *et al* (29) reported that elevated CA19-9 levels were significantly associated with tumor burden and poor prognosis in patients with pancreatic cancer. Ballehani nna and Chamberlain (30) provided a comprehensive review of CA19-9 as a pancreatic cancer biomarker, highlighting its potential for risk stratification and prognosis. In the present study, CA19-9 levels >1,000 U/ml were identified as an independent prognostic factor, which is consistent with previous research (29,30). Elevated CA19-9 levels indicate higher tumor burden and more aggressive disease, thus contributing to worse survival outcomes (31). This finding supports the clinical utility of CA19-9 in stratifying patients with pancreatic cancer and guiding therapeutic decisions such as more aggressive treatment approaches for patients with high CA19-9 levels (32).

Hyperglycemia may affect the prognosis of pancreatic cancer through several mechanisms. Firstly, hyperglycemia promotes cancer cell proliferation and inhibits apoptosis. Previous research has shown that high glucose levels can enhance the glycolytic pathway in cancer cells by providing them with the energy required for rapid growth and division (33). Second, hyperglycemia can create a pro-inflammatory environment by increasing the levels of pro-inflammatory cytokines, such as TNF-α and IL-6, which can support tumor progression and metastasis (34). Third, chronic hyperglycemia can lead to insulin resistance, which in turn can result in higher insulin and insulin-like growth factor levels. These factors promote cell proliferation and inhibit apoptosis, further contributing to tumor growth and poor prognosis (26). Additionally, hyperglycemia alters the composition of the

tumor microenvironment to promote cancer cell proliferation. For example, the inflammatory environment in hyperglycemia promotes the accumulation of immunosuppressive cells that suppress antitumor immune responses (35). High glucose levels may encourage angiogenesis, provide more nutrients and oxygen to cancer cells, and accelerate tumor growth and spread (6). In the present study, no significant differences were observed in the baseline characteristics between the normal and high blood glucose groups, suggesting that blood glucose levels do not influence pancreatic cancer prognosis through these clinicopathological factors. This finding further supports the results of Cox's regression analysis, which indicated that a high blood glucose level is an independent risk factor affecting patient prognosis.

Inflammation serves an important bridging role in the relationship between hyperglycemia, diabetes and cancer prognosis (35). Both hyperglycemia and diabetes are closely associated with chronic low-grade inflammation, which is a key factor in cancer progression and worsening outcomes (35,36). Inflammatory markers, such as C-reactive protein and fibrinogen, have been shown to be elevated in diabetes patients and are associated with worse outcomes in various types of cancer, including pancreatic cancer (37). In patients with diabetes, persistent hyperglycemia induces oxidative stress and promotes the formation of AGEs that activate multiple inflammatory pathways, thereby enhancing the invasiveness and metastatic potential of cancer cells (6). An inflammatory environment can promote angiogenesis, tissue remodeling and immune evasion, all of which are conducive to cancer progression. This highlights the importance of managing not only blood glucose levels but also the inflammatory status in patients with diabetes to improve outcomes.

Although the present study provides valuable insights into the prognostic factors of pancreatic cancer, it has numerous limitations. First, the retrospective nature of the present study may have introduced a selection bias. Second, the single-center design limits the generalizability of the present findings. Future multicenter prospective studies are required to validate these findings. Additionally, further research should explore the underlying biological mechanisms linking hyperglycemia, diabetes and pancreatic cancer prognosis, as well as potential interventions to optimize metabolic control in patients with pancreatic cancer. Notably, owing to the retrospective nature of data collection, certain important prognostic factors, such as venous invasion, arterial invasion and neoadjuvant chemotherapy, were not consistently available for all included patients. These factors are known to influence survival in pancreatic cancer (38,39), and their absence may limit the robustness of the survival analysis, potentially introducing a bias in evaluating the impact of preoperative blood glucose levels and CA19-9 on OS.

In conclusion, the present study emphasizes the significant impact of the preoperative metabolic status on the prognosis of patients with pancreatic cancer. High preoperative blood glucose levels and elevated CA19-9 levels were identified as independent prognostic factors, whereas the impact of a history of preoperative diabetes may be mediated through blood glucose levels and related metabolic disturbances. These findings highlight the importance of comprehensive preoperative metabolic evaluation and control to improve patient outcomes. Future research should focus on elucidating the mechanisms underlying these associations and on developing strategies to optimize metabolic management in patients with pancreatic cancer.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

SBW, LP and WY conceptualized and designed the study. SBW and TP performed the data analyses. XZ and SYW collected the clinical samples. LP interpreted the data. SBW drafted the manuscript, which was revised by WY and LP. SBW, TP, SYW, XZ, LP and WY confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

The present study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The present study was approved by the Institutional Research Ethics Committee at the Fourth Hospital of Hebei Medical University (Shijiazhuang, China; approval no. 2023KS182) and all patients provided written consent for participation in the present study.

Patient consent for publication

Written informed consent for publication was obtained from all individuals involved in the present study.

Competing interests

The authors declare that they have no competing interests.

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