ORIGINAL ARTICLE

Circulating Dendritic Cells and Development of Septic Complications After Pancreatectomy for Pancreatic Cancer

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Objective: To investigate whether circulating dendritic cells in patients with pancreatic cancer is a risk factor for septic complications after pancreatectomy.

Design: Retrospective study.

Setting: University hospital.

Patients: Forty-one patients with pancreatic cancer who underwent pancreatectomy from May 2001 to July 2005. Patients were divided into 2 groups depending on whether or not they had a development of postoperative septic complications.

Main Outcome Measures: Dendritic cell, natural killer cell, and $CD4^+$ T-cell, and $CD8^+$ T-cell counts were measured preoperatively in each patient. Clinicopathologic parameters and immune parameters for each patient, operation, and tumor were compared between the 2 groups. Preoperative risk factors for postoperative septic complications were determined using logistic regression analysis.

Results: Circulating dendritic cell count before pancreatectomy in patients with septic complications postoperatively for pancreatic cancer was significantly lower than in patients without septic complications. Multivariate analysis indicated that preoperative circulating dendritic cell count was the only predictive value among the diverse clinical parameters tested in relation to the development of septic complications. Notably, when the circulating dendritic cell count was less than 10.0×10^3/mL in the peripheral blood, the risk of developing postoperative septic complications markedly increased. In such cases, the sensitivity, specificity, positive predictive value, and negative predictive value of total circulating dendritic cell count were as high as 80%.

Conclusion: In patients with pancreatic cancer, low preoperative circulating dendritic cell count ($< 10.0 \times 10^3$/mL) is a significant risk factor for the development of septic complications after pancreatectomy.

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OWING TO THE AVAILABILity of more sophisticated operative techniques and perioperative management, mortality after pancreatectomy for pancreatic malignancies has decreased in experienced institutions during the last 2 decades. However, morbidity is still relatively high.[1-5]

See Invited Critique at end of article

Several reports describing an association between preoperative immunodeficiency and increased risk of postoperative mortality and morbidity have been published.[6-8] It has also been reported that monocyte deactivation with low HLA-DR expression,[9] apoptosis of lymphocytes,[10] and depletion of dendritic cells (DCs)[11] were observed in patients with sepsis. Dendritic cells, which play a central role in helper T 1 (T_H1) cell and/or helper T 2 (T_H2) cell immune responses, are as capable of stimulating naive T cells as the most potent antigen-presenting cells[12] that initiate immune responses against pathogens.[13,14] Accordingly, we hypothesized an association between depletion of DCs and the occurrence of septic complications after pancreatectomy in patients with pancreatic cancer. This study aimed to investigate whether low numbers of circulating DCs were a risk factor for developing postpancreatectomy septic complications in patients with pancreatic cancer.

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METHODS

PATIENTS AND STUDY DESIGN

Forty-five patients with pancreatic cancer admitted consecutively for elective pancreatectomy in the surgery department at Kansai Medi-

Table 1. Postoperative Pancreatectomy Complications

Outcome	No. (%)
No complication	14 (34.1)
Nonseptic complication	9 (22.0)
Delayed gastric emptying	3
Wound infection without sepsis	3
Anastomotic stenosis	1
Anastomotic ulcer	2
Septic complication	18 (43.9)
Intraperitoneal abscess	6
Intraperitoneal infection	7
Bacteremia	3
Bacterial enterocolitis	1
Wound infection with sepsis	1

cal University from May 2001 to July 2005 were evaluated. Four patients were excluded because of liver metastasis or peritoneal dissemination found during pancreatectomy, which was diagnosed from an intraoperative frozen section. The remaining 41 patients who underwent pancreatectomy were enrolled in the study following completion of a written informed consent in accordance with the Declaration of Helsinki. The institutional review board of Kansai Medical University approved the protocol.

We performed bile duct decompression preoperatively for any patient experiencing obstructive jaundice due to tumor invasion of the bile duct. None of the patients had any severe organ dysfunction, acute biliary tract infection, or other acute inflammation at the time of operation or blood sampling. Several days preoperatively, blood samples were taken from each patient in the morning after fasting overnight, and DC, natural killer (NK) cell, $CD4^+$ T-cell, and $CD8^+$ T-cell counts were performed. All data, including occurrence of postoperative complications, were collected retrospectively from the pancreas database at Kansai Medical University. Patients were classified into 1 of 2 groups: those who experienced postoperative septic complications and those who did not. To examine presumed risk factors for postoperative complications, clinicopathologic factors, blood examination results (including preoperative C-reactive protein [CRP] level and immune parameters), operation, and tumor were compared between the 2 groups. Preoperative risk factors for postoperative septic complications were also analyzed using logistic regression analysis.

A potentially curative pancreatectomy was scheduled for each patient. Patients were preoperatively classified according to the recommendations of the American Society of Anesthesiologists for more accurate evaluation of anesthetic risks.[15] Surgical procedures for pancreatectomy were performed as previously described[16]; 7 patients underwent additional reconstruction of the portal vein. Each operation was either performed or supervised by 2 senior surgeons experienced in pancreatic operations. Pathologic staging was performed in accordance with *TNM Classification of Malignant Tumors, Sixth Edition*.[17] After pancreatectomy, each patient was discharged when all signs of acute inflammation (high-grade fever, elevated leukocyte count or CRP levels) resolved and sufficient oral intake was attained.

DEFINITION OF POSTOPERATIVE COMPLICATIONS

Each postoperative day when patients demonstrated clinical symptoms of systemic inflammatory response syndrome was prospectively recorded.[18] However, clinical symptoms of systemic inflammatory response syndrome within the first 4 postoperative days were excluded as systemic responses to surgical stress. After the fourth day, any patient's complication that involved clinical symptoms of infection-induced systemic inflammatory response syndrome that continued for more than 2 days of the in-hospital stay was considered a septic complication.[5]

Intra-abdominal abscess was defined by a collection of purulent matter confirmed by ultrasound or computed tomography–guided aspiration and fluid culture. Intra-abdominal infection was regarded as the presence of pus or microbiologic findings of bacteria in the drainage tubes without any radiologic findings. Bacteremia was identified by the isolation of microbes from peripheral blood culture. Bacterial enterocolitis was defined by reiterative diarrhea, inflammatory indications from blood tests, and the presence of pathogenic bacteria in the stool culture.

Surgical wounds were observed daily and, upon appearance of any sign of infection (such as local heat, rubor, swelling and/or fever), the wound was opened for drainage. Wound infection was identified by purulent discharge from a disrupted wound. Delayed gastric emptying was defined as either the need for nasogastric intubation for 10 or more days or the inability to tolerate regular food on the 14th postoperative day.[2] Anastomotic stenosis was diagnosed by the poor passage of contrast agents through the anastomosis. When a patient showed lack of appetite, epigastlargia, or bloody discharge from a nasogastric tube or in the stool, upper gastrointestinal fiberscopy was used to detect anastomotic ulcers.

ESTIMATION OF PHYSIOLOGIC ABILITY AND SURGICAL STRESS SCORES

The Estimation of Physiologic Ability and Surgical Stress (E-PASS) is a scoring system used to predict the risk of complication after an elective digestive operation using multiple regression analysis.[19] This system comprises a preoperative risk score, a surgical stress score, and a comprehensive risk score, the latter determined by combining the 2 former scores. A previous prospective multi-center study conducted by Haga et al[20] revealed that postoperative morbidity and mortality increased reproducibly as the comprehensive risk score increased; E-PASS scores were compared between patients with and without septic complications.

FLOW CYTOMETRIC ANALYSIS

Circulating dendritic cell count was measured by flow cytometry assay using FACScan (Becton Dickinson, Sunnyvale, California) as described previously.[21] Counts of NK cell, $CD4^+$ T-cell, and $CD8^+$ T-cell immunoeffectors were similarly measured.

STATISTICAL ANALYSIS

Data relating to clinical characteristics, preoperative laboratory results, flow cytometry values, and the operation were statistically analyzed. Continuous variables were compared using the Mann-Whitney test. Based on preoperative DC, NK, $CD4^+$ T-cell, and $CD8^+$ T-cell counts, patients were grouped into low-count or high-count subgroups, with the cutoff defined by the median value of all patients.

The effect of potential risk factors on the development of septic complications after pancreatectomy was analyzed using the χ^2 test, except when the expected frequency of patients with septic complications was less than 5, in which case the Fisher exact test was used. Because this was a multivariate analysis, logistic regression was used to determine independent risk factors for septic complication. All statistical analyses were per-

Table 2. Clinical Characteristics and E-PASS Scores of Patients With and Without Septic Complications (SCs)

Characteristic	Patients With SCs	Patients Without SCs	*P* Value
No. of patients	18	23	
Sex, No. (%)			
M	8 (44)	14 (61)	.30
F	10 (56)	9 (39)	
Median age (range), y	67 (52-71)	64 (47-83)	.48
Preoperative jaundice, No. (%)			
Yes	7 (39)	11 (48)	.57
No	11 (61)	12 (52)	
Preoperative diabetes mellitus, No. (%)			
Yes	8 (44)	12 (52)	.62
No	10 (56)	11 (48)	
Preoperative chemoradiotherapy, No. (%)			
Yes	9 (50)	13 (57)	.68
No	9 (50)	10 (43)	
Median E-PASS score (range)			
Preoperative risk score	0.46 (0.28-0.66)	0.44 (0.25-0.87)	.43
Surgical stress score	0.77 (0.39-2.64)	0.73 (0.42-2.71)	.26
Comprehensive risk score	0.99 (0.47-2.55)	0.83 (0.30-2.94)	.16

Abbreviation: E-PASS, Estimation of Physiologic Ability and Surgical Stress.

Table 3. Surgical Characteristics of Patients With and Without Septic Complications (SCs)

Characteristic	Patients With SCs	Patients Without SCs	*P* Value
ASA classification, No. (%)			
I or II	17 (94)	19 (83)	.36
III	1 (6)	4 (17)	
Type of operation, No. (%)			
Distal pancreatectomy	6 (33)	4 (17)	.29
Pancreatoduodenectomy or pylorus-preserving pancreatoduodenectomy	10 (56)	18 (78)	
Total pancreatectomy	2 (11)	1 (4)	
Reconstruction of portal vein, No. (%)	3 (17)	4 (17)	.65
Median duration of operation (range), min	593 (265-900)	565 (330-870)	.45
Median blood loss (range), mL	1570 (560-7250)	1390 (285-7885)	.13
Blood transfusion, No. (%)			
Allogeneic	12 (67)	12 (52)	.10
Autologous	2 (11)	9 (39)	
None	4 (22)	2 (9)	
Median postoperative hospitalization (range), d	49 (29-93)	36 (12-74)	.04

Abbreviation: ASA, American Society of Anesthesiologists.

formed using StatView, version 5.0 (Abacus Concepts, Berkeley, California). $P < .05$ was defined as significant.

RESULTS

CLINICAL CHARACTERISTICS AND PARAMETERS

Forty-one patients (22 men and 19 women) were assessed in this study. The median age of the patients was 65 years (range, 47-83). Twenty patients (49%) had diabetes mellitus before the operation. Eighteen patients (44%) had obstructive jaundice and underwent bile duct decompression before the operation. Preoperative chemoradiotherapy was performed in 22 patients (54%). Ten patients underwent distal pancreatectomy, 25 underwent pancreatoduodenectomy, 3 underwent pylorus-preserving pancreatoduodenectomy, and 3 underwent total pancreatectomy. Median operation time was 590 minutes (range, 265-900). Median intraoperative blood loss was 1390 mL (range, 285-7890). Twenty-four patients (58%) required allogeneic blood transfusion, 11 (27%) underwent autologous transfusion, and 6 (15%) did not require transfusion. The median postoperative hospitalization period was 40 days (range, 12-93). There was no in-hospital death postoperatively.

SEPTIC COMPLICATIONS

Eighteen patients (44%) developed septic complications, while 23 (56%) had relatively uneventful postoperative recoveries (no complication, 14 patients; nonseptic complication, 9 patients) (**Table 1**). Septic complications were often diagnosed on days 9 to 12 post-

Table 4. Tumor Characteristics of Patients With and Without Septic Complications (SCs)[a]

Characteristics	No. of Patients With SCs	No. of Patients Without SCs	*P* Value
Median tumor size (range), mm	32 (16-110)	30 (22-80)	.94
Tumor status			
T1 or T2	3	1	.16
T3	11	20	
T4	4	2	
Nodal status			
N0	9	9	.49
N1	9	14	
pTNM stage			
IA or IB	3	1	.27
IIA	3	7	
IIB	8	13	
III	4	2	
Residual tumor			
R0	5	6	.23
R1	8	15	
R2	5	2	

[a] No patients had distant metastasis at the time of operation.

Table 5. Blood Examinations of Patients With and Without Septic Complications (SCs)

Analyte	Median (Range)		*P* Value[a]
	Patients With SCs	Patients Without SCs	
Hemoglobin, g/dL	11.1 (8.7-13.8)	11.5 (8.5-14.6)	.77
Leukocytes, /μL	5200 (2400-7500)	5000 (3100-7500)	.81
Monocytes, /μL	290 (180-610)	290 (70-650)	.56
Lymphocytes, /μL	1200 (200-2600)	1200 (500-1800)	.81
Creatinine, mg/dL	0.6 (0.3-0.9)	0.7 (0.4-1.0)	.43
Albumin, g/dL	3.7 (2.5-4.5)	3.8 (2.3-4.2)	.62
Total bilirubin, mg/dL	0.6 (0.3-2.7)	0.7 (0.2-3.2)	.42
AST, U/L	25 (15-72)	23 (16-87)	.45
ALT, U/L	27 (11-152)	20 (11-237)	.45
CRP, mg/L	3 (0-59)	1 (0.0-26)	.047
Amylase, U/L	47 (19-207)	53 (8-399)	.31
CA 19-9, U/mL	38 (1-26419)	100 (1-9116)	.23

Abbreviations: ALT, alanine aminotransaminase; AST, aspirate aminotransaminase; CA, carbohydrate antigen; CRP, C-reactive protein.

[a] Statistical significance was determined using the Mann-Whitney test.

SI conversion factors: To convert ALT, amylase, and AST to microkatal per liter, multiply by 0.01667; albumin and hemoglobin to grams per liter, multiply by 10.0; CRP to nanomoles per liter, multiply by 9.524; creatinine to micromoles per liter, multiply by 88.4; leukocytes, lymphocytes, and monocytes to $\times 10^9$/L, multiply by 0.001; and total bilirubin to micromoles per liter, multiply by 17.104.

operatively (range, 5-26). Patients were divided into 2 groups depending on if they had a postoperative septic complication (n=18) or did not (n=23).

CLINICOPATHOLOGIC PARAMETERS

Patient-related parameters and the E-PASS scores were distributed similarly between patient groups with and without septic complications (**Table 2**). There were no statistically significant differences between groups for parameters related to the operation or the tumor (**Table 3** and **Table 4**). As a matter of course, the mean duration of postoperative hospital stay was significantly longer in patients who developed septic complications (49 days; range, 29-93) than in those who did not (36 days; range, 12-74; *P*=.04) (Table 3).

Although the median CRP level was significantly higher in patients with septic complications than in those without, it was within normal reference range in both groups. There were no statistically significant differences in preoperative levels of leukocytes, hemoglobin, albumin, amylase, aspartate aminotransferase, alanine aminotransferase, total bilirubin, or carbohydrate antigen 19-9 between the patients with and patients without septic complications (**Table 5**).

IMMUNOLOGIC PARAMETERS

As shown in the **Figure**, DC counts (circulating DC type 1 [DC1], circulating DC type 2 [DC2], and total circulating DCs) in patients with septic complications were significantly lower than those without septic complications (*P*=.02, *P*=.008, and *P*=.003, respectively). However, there were no significant differences in NK cell, $CD4^+$ T-cell, or $CD8^+$ T-cell counts between the 2 groups (**Table 6**).

MULTIVARIATE ANALYSIS

Multivariate analysis using logistic regression analysis identified lower circulating DC count as an independent risk factor for the occurrence of postoperative septic complication (**Table 7**). When patients were divided into 2 groups by the median value for total circulating DC count, circulating DC counts less than 10.0×10^3/mL functioned as an indicator for the occurrence of postoperative septic complications with sensitivity, specificity, positive predictive value, and negative predictive value of around 80% (**Table 8**).

COMMENT

In this study, we demonstrated that patients with septic complications after pancreatectomy for pancreatic cancer had a significantly lower number of circulating DCs before pancreatectomy, compared with those without septic complications. Among the diverse clinical parameters examined, multivariate analysis indicated preoperative circulating DC count as the only predictive value for septic complication. In particular, when the circulating DC count was less than 10.0×10^3/mL in peripheral blood, the risk of developing postoperative septic complications increased markedly, and the sensitivity, specificity, positive predictive value, and negative predictive value of total circulating DC counts less than 10.0×10^3/mL were as high as 80%.

Dendritic cells display a strong capacity to stimulate naive T cells and initiate an effective immune response against various pathogens with concentrations of surface major histocompatibility complex–peptide complexes, which are much higher than other antigen-

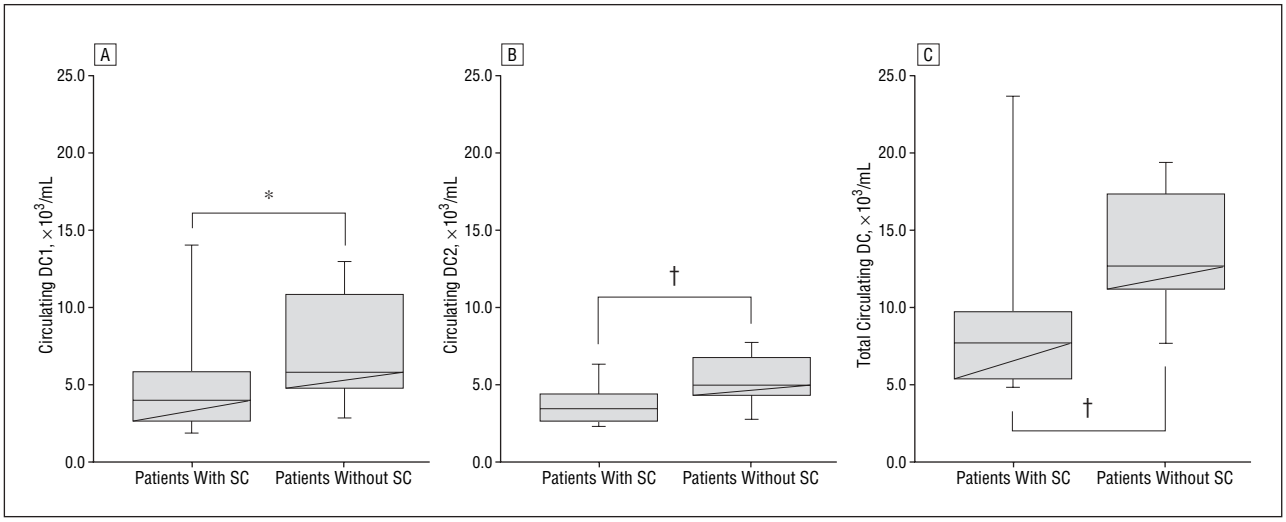

Figure. Comparison of preoperative circulating dendritic cell (DC) counts (A, circulating DC type 1 [DC1]; B, circulating DC type 2 [DC2]; C, total circulating DC) between patients with and without septic complications (SCs). Blood samples were collected a few days preoperatively from each patient, and the number of circulating DCs was assayed using flow cytometry. Asterisk indicates $P < .03$ (patients with SCs vs those without). Dagger indicates $P < .01$ (patients with SCs vs those without). Horizontal lines show the median value. Diagonal lines show the 25th and 75th percentiles. Error bars show minimum and maximum values.

presenting cells, such as B cells and monocytes.[22-24] Microbial structures, such as peptidoglycan, flagellin, lipopolysaccharide, and unmethylated cytosine-guanine motifs (prevalent in bacterial DNA, viruses, and the yeast form of *Candida albicans*), are recognized through the Toll-like receptor family expressed on DCs, which then induce T_H1 or T_H2 immune responses.[25] Thus, DCs are also important for inducing a potent immune response against microorganism infection and contribute to the prevention of infection. It has been reported that the patients with common variable immunodeficiency have lower DC counts as well as impaired DC function.[26] It is likely that the deterioration of circulating DCs documented in patients who experience postpancreatectomy septic complications is one sign of weakened host immunity, which allows pathogens to multiply.

Human DCs are divided into 2 subset populations that are functionally and phenotypically heterogeneous: DC1 (myeloid DC population), which stimulates $CD4^+$ T cells to differentiate into T_H1 cells, and DC2 (lymphoid DC population), which induces differentiation into T_H2 cells or the generation of regulatory T cells.[12,27,28] Differentiation of naive T cells into T_H1 or T_H2 effectors is determined not only by cytokine environment (IL-12 [interleukin 12] vs IL-4), the nature and strength of T-cell receptor–mediated signals, and genetic background, but also by the type and activation state of the DCs.[29-31]

Type 1 DCs play a central role in promoting immune responses against malignancies, and we have previously reported that in patients with pancreatic cancer, circulating DC1 count and function are impaired relative to healthy individuals.[21,32] Alternatively, circulating DC2 is considered important for the tolerance induction in organ transplantation.[33] Recent reports also suggest that DC2 is capable of inducing a T_H1 response to several kinds of microbes.[34-37] Significantly lower circulating DC1 ($P < .05$) and circulating DC2 ($P < .01$) levels in patients with septic complications than in those without suggest that decreased numbers of circulating DC1 and circulating DC2 may both be associated with the occurrence of septic complications after pancreatectomy.

Table 6. Flow Cytometric Assays of Patients With and Without Septic Complications (SCs)

Parameter	Median (Range)		*P* Value
	Patients With SCs	Patients Without SCs	
PBMCs, $\times 10^6$/mL	2.3 (1.3-4.2)	2.2 (0.9-4.9)	.92
NK cells, $\times 10^5$/mL	2.0 (0.6-5.2)	2.2 (0.5-6.5)	.73
$CD4^+$ T cells, $\times 10^5$/mL	5.3 (2.0-11.5)	4.2 (0.4-12.0)	.15
$CD8^+$ T cells, $\times 10^5$/mL	2.6 (1.2-6.2)	2.0 (0.6-4.7)	.43

Abbreviations: PBMC, peripheral blood mononuclear cell; NK, natural killer.

Preoperative CRP levels, which were significantly higher in patients with septic complications than in those without, did not demonstrate any statistical correlation with the occurrence of the septic complications (data not shown). Therefore, preoperative CRP levels are unlikely to be a principal factor in the development of postpancreatectomy septic complications.

Additional risk factors that have been reported for the development of postoperative septic complications include lack of surgical skills.[3,7] To control for surgical variables in this study, all operations were performed or supervised by 2 senior surgeons experienced in pancreatic surgery; the in-hospital mortality rate was 0%. There were no significant differences in other operation-related factors, such as type of operation, duration of operation, intraoperative blood loss, or requirement for blood transfusion between patients with and without septic complications. Thus, we conclude that surgical technique was maintained at a high level and would not substantially affect the occurrence of postoperative complications.

Although there are several types of immunologic examinations available for predicting the risk of develop-

Table 7. Multivariate Analysis of Preoperative Risk Factors for Postoperative Septic Complications (SCs)[a]

Risk Factor	No. of Patients With SCs	No. of Patients Without SCs	OR (95% CI)	*P* Value
Preoperative circulating DC type 1, $\times 10^3$/mL				
< 5.5	13	7	0.71 (0.03-5.96)	.78
≥ 5.5	5	16		
Preoperative circulating DC type 2, $\times 10^3$/mL				
< 4.5	14	7	0.93 (0.04-8.30)	.95
≥ 4.5	4	16		
Preoperative total circulating DC, $\times 10^3$/mL				
< 10.0	15	4	31.24 (2.09-1395.82)	.03
≥ 10.0	3	19		
CRP, mg/L				
> 3	8	7	0.56 (0.09-3.17)	.51
≤ 3	10	16		

Abbreviations: CI, confidence interval; CRP, C-reactive protein; DC, dendritic cell; OR, odds ratio.
[a]Subgroups of patients with low or high preoperative levels of circulating DC type 1, circulating DC type 2, and total circulating DC are defined using the median as a cutoff value. Subgroups of patients with high preoperative CRP levels were defined using the upper rather than the normal reference of our laboratory.

Table 8. Predictive Values of Circulating Dendritic Cells (cDCs) for Septic Complication After Pancreatectomy for Pancreatic Cancer[a]

Measure	cDC Type 1, %	cDC Type 2, %	Total cDC, %
Sensitivity	72	78	83
Specificity	70	70	83
Positive predictive value	65	67	79
Negative predictive value	76	80	86

[a]The data were calculated by dividing patients into 2 subgroups that display cDC values either lower or higher than the median (10.0×10^3/mL) cDC count.

ing postoperative septic complications,[6-8] most examinations are technically complex and require a relatively long period to generate results. In contrast, circulating DC count can be easily measured in a few hours using flow cytometry and therefore can be practically introduced in daily clinical evaluations. Moreover, the sensitivity, specificity, positive predictive value, and negative predictive value of circulating DC counts less than 10.0×10^3/mL as they relate to postoperative septic complications were quite high, at approximately 80%. Therefore, we strongly support the use of circulating DC count as a measure to predict whether postoperative septic complications are likely to develop in patients with pancreatic cancer.

In conclusion, low preoperative circulating DC count ($< 10.0 \times 10^3$/mL) can be a risk factor for patients with pancreatic cancer to develop postoperative septic complications after pancreatectomy. Accurate estimation of patients who are at high risk for septic complication is crucial for planning preventive and therapeutic strategies.

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INVITED CRITIQUE

Septic complications are an important determinant of postoperative outcomes in patients with pancreatic cancer. However, preoperative risk stratification is not routinely available, and therefore the onset of treatment is usually late. In this elegant study, Takahashi and his colleagues suggested that low numbers of circulating DCs, which are important for immune surveillance, was a risk factor for developing septic complications after pancreatectomy. The availability of this method provides us with a relatively easy way to preoperatively anticipate the occurrence of postoperative infectious complications, which may allow for the development of novel therapeutic strategies designed to stimulate host defense mechanisms and to reduce the incidence and severity of septic complications.

While the conclusion is provocative, several questions remain. It is unclear what causes the preoperative immunodeficiency. In a previous study,[1] the authors reported that the number and activity of circulating myeloid DCs (DC1) in pancreatic cancer patients were significantly lower than those in healthy controls, and surgical resection was beneficial for restoring the impaired immunity by improving DC function. It seems that preoperative immunodeficiency is caused by malignancy. Therefore, it would be interesting to study the relationship between TNM classification and preoperative circulating DC count. In addition, it is still unclear whether the early postoperative immune functions play a role in predicting infectious complications, because surgical trauma can also influence immune responses. Another question is how to improve immune function in patients with pancreatic cancer. Immunonutrition with a supplemented enteral formula is a new and interesting topic. Further insights into the mechanisms of modification of immune-effector cells might pave the way for efficient treatment strategies.

A more profound study of immunologic dynamics in pancreatic cancer patients may lead to immunologic therapeutic approaches for improving immune function and clinical outcome. However, the authors should be congratulated for providing the much-needed starting point from which future studies will be performed.

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1. Takahashi K, Toyokawa H, Takai S, et al. Surgical influence of pancreatectomy on the function and count of circulating dendritic cells in patients with pancreatic cancer. *Cancer Immunol Immunother*. 2006;55(7):775-784.