Original Article

Reappraisal of the current resectability criteria and optimal treatment strategies for pancreatic cancer

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Background: Recent advances in anticancer treatment and prolonged survival are the background of this study. The study aimed to reappraise the Japan Pancreas Society (JPS) resectability criteria in pancreatic cancer and to propose optimal treatment strategies.

Methods: Three hundred ninety-six consecutive patients with curative-intent surgery for pancreatic cancer from April 2011 to December 2022 were included. Overall survival based on the resectability criteria was analyzed, and Cox regression analyses were performed to identify factors associated with overall survival.

Results: The median survival times (MSTs) based on the current resectability status were 37.4, 20.1, and 26.6 months in resectable (R), in borderline resectable (BR), and unresectable (UR) disease, respectively (P<0.001), revealing an inversion phenomenon between BR and UR. Using the International Association of Pancreatology (IAP) criteria, the MST of biological BR disease was demonstrably worse than that of R disease (27.1 *vs.* 40.7 months, P=0.04), but no difference was observed between classical BR and UR locally advanced disease (18.8 *vs.* 18.7 months, P=0.97). Rather, ≤180° superior mesenteric artery (SMA) invasion was a more powerful prognostic factor than >180° SMA/celiac artery invasion in multivariate analysis (hazard ratio: 2.101, 95% confidence interval: 1.296–3.404, P=0.003). When biological BR was combined with BR, and BR with artery invasion was considered locally advanced disease as a new resectability criterion, the MSTs were 38.8, 23.5, and 18.5 months in the new R, new BR, and locally advanced groups, respectively (P<0.001).

Conclusions: The decision-making and treatment strategies based on our new classification in pancreatic cancer are considered reasonable for clinical practice.

Keywords: Neoadjuvant therapy (NAT); pancreatic cancer; prognosis; resectability criteria; treatment strategy

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Introduction

The clinical concept of "marginal resectable" in pancreatic cancer was initially proposed by Mehta *et al.* (1), and it was renamed "borderline resectable (BR)" by the National Comprehensive Cancer Network (NCCN) guidelines in 2006. Subsequently, the resectability criteria primarily based on anatomical factors have been widely applied in clinical practice because they reflect survival outcomes and facilitate treatment decision-making (2-4). Initially, these criteria were amended annually, but they have become entrenched in recent years (5,6). In 2017, the Japan Pancreas Society (JPS) also proposed the resectability criteria in pancreatic cancer

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based on the NCCN guidelines, which might be extremely distinctive compared with those for other organs (7).

Meanwhile, there has been controversy regarding the selection of these criteria based solely on anatomical factors. Thus, the International Association of Pancreatology (IAP) advocated for the use of biological and conditional factors in addition to anatomical factors in 2017 (8). The concept of incorporating biological and conditional factors into the criteria was first presented by Katz *et al.* (9). However, this strategy has not yet been adopted in the NCCN guidelines. In fact, the IAP criteria were verified in some studies, highlighting their potential clinical utility (10-13). In our clinical practice, treatment strategies, especially those involving neoadjuvant therapy (NAT), are generally based on the JPS resectability status. In particular, used regimens and duration of the NAT have been decided by this JPS resectability criteria at diagnosis. Also, even the clinical indication of conversion surgery for unresectable (UR) disease was determined by this criterion. Furthermore, recent advances in anticancer therapy have dramatically altered the environment surrounding pancreatic cancer (14,15).

Therefore, this is considered a proper time to review the resectability criteria in pancreatic cancer. In this study, we reappraised survival outcomes using our series based on the current resectability criteria with the addition of the IAP criteria and proposed optimal treatment strategies for pancreatic cancer. We present this article in accordance with the STROBE reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-102/rc).

Highlight box

Key findings

- We proposed novel resectability criteria for pancreatic cancer. The biological borderline resectable (BR) category should be combined with the BR category, and BR with arterial invasion disease was deemed locally advanced disease.

What is known and what is new?

- There has been controversy regarding the selection of the National Comprehensive Cancer Network or Japan Pancreas Society resectability criteria based solely on anatomical factors.
- We reappraised survival outcomes using our series based on the current resectability criteria with the addition of the International Association of Pancreatology criteria, which is a new endeavor.

What is the implication, and what should change now?

- Clinical decision-making and treatment strategies based on this new classification are considered reasonable for clinical practice.

Methods

Patient selection

Three hundred ninety-six consecutive patients with curative-intent surgery for pancreatic cancer at Nagoya Central Hospital from April 2011 to December 2022 were enrolled in this study. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of Nagoya Central Hospital (No. 2023-128). Written informed consent, as required by the Institutional Review Board, was obtained from all patients for use of their anonymized information.

Patient management and evaluation

Preoperative blood examination was performed 1 or 2 days prior to the initial treatment. Treatment was performed on the patients' resectability status, which was determined by the JPS (7). Patients with resectable (R) cancer or those with cancer abutment to the portal vein (R-PV) underwent upfront surgery or received NAT. Conversely, patients with cancers classified as either borderline resectable with portal vein invasion (BR-PV) or borderline resectable with arterial invasion (BR-A) received NAT for 2 or 3 months. Patients with unresectable locally advanced (UR-LA) cancer or distant metastasis (UR-M) received induction chemotherapy or chemoradiotherapy. When patients with UR cancer could continue treatment with the maintenance of radiologically stable disease and mostly normalized tumor markers, conversion surgery was performed (16). The neoadjuvant regimens included gemcitabine + S-1 (tegafur + oteracil + gimeracil), S-1 + radiotherapy, gemcitabine + nab-paclitaxel, and FOLFIRINOX (fluorouracil + levofolinate calcium + irinotecan hydrochloride + oxaliplatin). In all patients, gemcitabine or S-1 was administered postoperatively as adjuvant chemotherapy unless contraindicated by the patient's condition or other reasons.

Pancreatic cancer surgery was performed mainly using a mesenteric approach (17,18). D2 lymphadenectomy was routinely performed when macroscopic liver or peritoneal metastases were absent.

Tumor staging was performed using the JPS's classification of pancreatic carcinoma, fourth English edition (7). In the current study, zero mm rule was utilized to evaluate the residual tumor (R) status. Postoperative complications were defined as Clavien-Dindo grade IIIa or higher complications (19). Postoperative pancreatic fistula was defined by the International Study Group

Table 1 Patient backgrounds based on resectability status

Variables	Resectable (n=187)		Borderline resectable (n=114)		Unresectable (n=95)		P
	R (n=126)	R-PV (n=61)	BR-PV (n=64)	BR-A (n=50)	UR-LA (n=80)	UR-M (n=15)	
Age (years)	70.4±9.3	70.3±8.7	66.9±7.4	67.4±10.5	66.4±9.3	67.7±7.2	0.002*
Sex (male/female)	71/55	34/27	36/28	33/17	45/35	8/7	0.79
BMI (kg/m^2)	22.5±3.4	21.8±3.1	22.1±3.0	22.9±2.8	21.9±3.2	20.8±3.0	0.12
ASA-PS (1/2/3)	24/92/10	12/44/5	15/45/4	13/35/2	20/56/4	4/11/0	0.94
Tumor location (head/body and tail)	61/65	55/6	57/7	39/11	59/21	10/5	<0.001*
Biliary drainage	37 (29.6)	32 (53.3)	21 (32.8)	36 (72.0)	35 (43.8)	5 (33.3)	0.005*
Pre-ope CEA (ng/mL)	4.0±3.5	8.9±29.5	6.5±12.1	4.8±6.5	3.7±2.5	3.8±3.2	0.72
Pre-ope CA19-9 (U/mL)	881±1,981	1,142±4,764	1,894±5,285	1,182±2,531	1,808±6,563	349±632	0.11
Pre-ope DUPAN-2 (U/mL)	334±644	972±2,982	1,344±6,531	656±2,168	248±483	136±194	0.008*
Neoadjuvant therapy	14 (11.1)	6 (9.8)	14 (21.9)	22 (44.0)	56 (70.0)	8 (53.3)	<0.001*
GnP	5 (4.0)	4 (6.6)	10 (15.6)	13 (26.0)	27 (33.8)	4 (26.7)	
FOLFIRINOX	0	0	1 (1.6)	2 (4.0)	12 (15.0)	0	
GS	9 (7.1)	2 (3.3)	2 (3.1)	0	1 (1.3)	1 (6.7)	
Multiple regimen	0	0	1 (1.6)	4 (8.0)	14 (17.5)	3 (20.0)	
RT	1 (0.8)	0	0	3 (6.0)	2 (2.5)	0	

Data are presented as mean ± standard deviation, number, or n (%). *, statistically significant. R, resectable; R-PV, resectable with portal vein abutment; BR-PV, borderline resectable with portal vein invasion; BR-A, borderline resectable with arterial invasion; UR-LA, unresectable with locally advanced; UR-M, unresectable with distant metastasis; BMI, body mass index; ASA-PS, American Society of Anesthesiologists-physical status; ope, operative; CEA, carcinoembryonic antigen; CA19-9, carbohydrate antigen 19-9; DUPAN-2, duke pancreatic monoclonal antigen type 2; GnP, gemcitabine + nab-paclitaxel; GS, gemcitabine + S-1; RT, radiation therapy.

of Pancreatic Surgeons classification (20).

As the IAP proposed for the use of biological and conditional factors in addition to anatomical factors in 2017, patients with R or R-PV disease and high carbohydrate antigen 19-9 (CA19-9) levels (≥500 U/mL) were considered to be the biological BR disease (8).

Postoperative follow-up

Patients underwent follow-up once per month for 6 months and every 3 months thereafter. Blood test, including serum tumor markers, was performed at every follow-up visit. Dynamic computed tomography (CT) or magnetic resonance imaging was performed every 3 months, and initial recurrence pattern was evaluated by these images.

Statistical analysis

Statistical analyses were performed by using JMP Pro version 16.0.0 (SAS Institute, Cary, NC, USA). Continuous variables were compared by using the two-sample *t*-test. Categorical variables were compared by using Fisher's exact test or the χ^2 test as appropriate. Overall survival was defined as the time from initial treatment or surgery to death from any cause, which was both oncologic and non-oncologic. Survival curves were depicted using the Kaplan-Meier method and compared by using the log-rank test. Univariate and multivariate Cox regression analyses were conducted to determine factors associated with overall survival. P<0.05 was considered significant.

Results

Clinical features based on the current resectability status

Patients' backgrounds based on their resectability status are presented in *Table 1*. Younger patients tended to have BR or UR disease. The median levels of preoperative tumor

Table 2 Peri- and postoperative outcomes based on resectability status

Variables	Resectable (n=187)		Borderline resectable (n=114)		Unresectable (n=95)		P
	R (n=126)	R-PV (n=61)	BR-PV (n=64)	BR-A (n=50)	UR-LA (n=80)	UR-M (n=15)	
Operative procedure							<0.001*
SSPPD	63 (50.0)	57 (93.4)	62 (96.9)	38 (76.0)	56 (70.0)	10 (66.7)	
DP	62 (49.2)	4 (6.6)	1 (1.6)	11 (22.0)	21 (26.3)	5 (33.3)	
TP	1 (0.8)	0	1 (1.6)	1 (2.0)	3 (3.8)	0	
Portal vein resection	4 (3.2)	40 (65.6)	59 (92.2)	37 (74.0)	59 (73.8)	6 (40.0)	<0.001*
Arterial resection	2 (1.6)	0	0	2 (4.0)	12 (15.0)	1 (6.7)	<0.001*
Blood transfusion	8 (6.3)	9 (14.8)	18 (28.1)	9 (18.0)	19 (23.8)	3 (20.0)	0.002*
Clavien-Dindo (≥IIIa)	73 (57.9)	13 (21.3)	8 (12.5)	18 (36.0)	25 (31.3)	8 (53.3)	<0.001*
POPF (≥ Grade B)	46 (36.5)	9 (14.8)	3 (4.7)	14 (28.0)	16 (20.0)	5 (33.3)	<0.001*
R0 resection	116 (92.1)	58 (95.1)	60 (93.8)	46 (92.0)	74 (92.5)	10 (66.7)	<0.001*
Lymph node metastasis	64 (50.8)	37 (60.7)	52 (81.3)	31 (62.0)	39 (48.8)	9 (60.0)	0.001*
Mortality	0	1 (1.6)	1 (1.6)	0	0	0	0.50
Adjuvant chemotherapy	101 (80.2)	49 (80.3)	56 (87.5)	36 (72.0)	62 (77.5)	10 (66.7)	0.31
Initial recurrence patterns							
Local	20 (15.9)	16 (26.2)	22 (34.4)	18 (36.0)	28 (35.0)	4 (26.7)	0.01*
Liver	27 (21.4)	17 (27.9)	14 (21.9)	14 (28.0)	16 (20.0)	8 (53.3)	0.10
Peritoneum	19 (15.1)	6 (9.8)	13 (20.3)	13 (26.0)	19 (23.8)	5 (33.3)	0.09
Lung	6 (4.8)	7 (11.5)	1 (1.6)	7 (14.0)	11 (13.8)	4 (26.7)	0.005*

Data are presented as number (%). *, statistically significant. R, resectable; R-PV, resectable with portal vein abutment; BR-PV, borderline resectable with portal vein invasion; BR-A, borderline resectable with arterial invasion; UR-LA, unresectable with locally advanced; UR-M, unresectable with distant metastasis; SSPPD, subtotal stomach-preserving pancreatoduodenectomy; DP, distal pancreatectomy; TP, total pancreatectomy; POPF, postoperative pancreatic fistula.

markers, especially CA19-9 and duke pancreatic monoclonal antigen type 2 (DUPAN-2), tended to increase with worsening of the resectability status. Similarly, the frequency of NAT administration increased with disease progression.

When peri- and postoperative outcomes were examined, the frequencies of portal vein resection, arterial resection, and blood transfusion significantly increased with worsening of the resectability status, but the R0 resection rates were similar among the groups. Concerning the initial recurrence patterns, the local recurrence rate was significantly higher in advanced disease, but there was no certain trend for the distant metastasis patterns (*Table 2*).

Survival outcomes based on the current resectability status

Overall survival outcomes were analyzed according to the current resectability status, as presented in *Figure 1*. The median survival times (MSTs) were 40.7, 30.6, 21.1, 19.8, 26.6, and 21.3 months in the R, R-PV, BR-PV, BR-A, UR-LA, and UR-M groups, respectively (P<0.001). When the status was simplified, the MSTs were 37.4, 20.1, and 26.6 months in the R, BR, and UR groups, respectively (P<0.001), revealing an inversion phenomenon between BR and UR disease.

Survival outcomes based on the modified resectability status

In *Figure 2*, the biological BR status proposed by IAP, which consisted of patients with R disease and high CA19-9 levels (≥500 U/mL), was adopted in this analysis (8). When overall survival was analyzed from initial treatment, the MSTs were

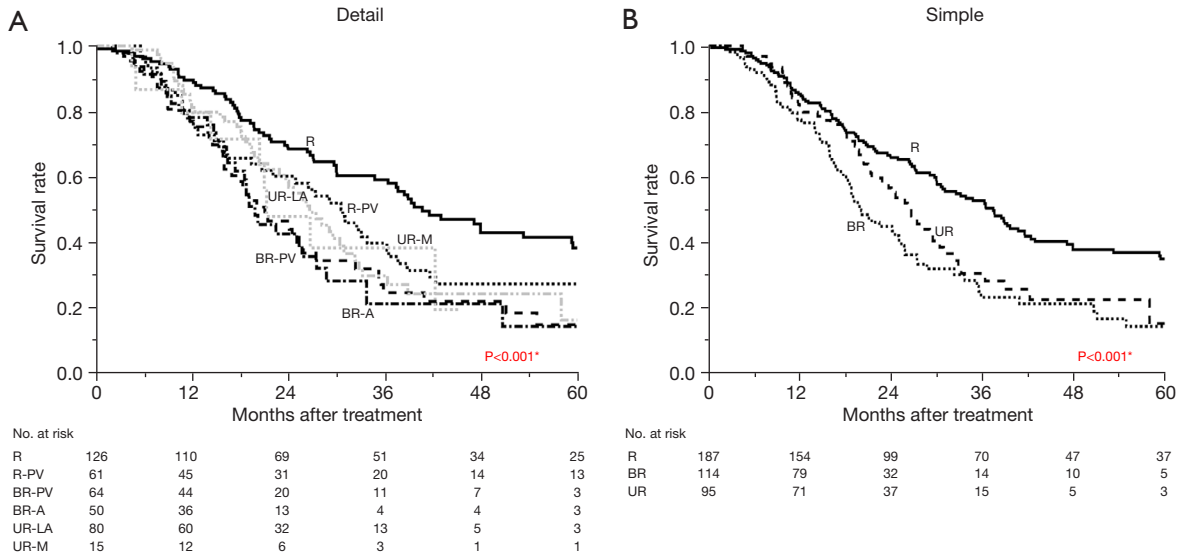

Figure 1 Overall survival outcomes based on the current resectability status. (A) The median survival times were 40.7, 30.6, 21.1, 19.8, 26.6, and 21.3 months in the R, R-PV, BR-PV, BR-A, UR-LA, and UR-M groups, respectively. (B) The median survival times using the simplified resectability criteria were 37.4, 20.1, and 26.6 months in the R, BR, and UR groups, respectively. *, statistically significant. R, resectable; R-PV, resectable with portal vein abutment; BR-PV, borderline resectable with portal vein invasion; BR-A, borderline resectable with arterial invasion; UR-LA, unresectable with locally advanced disease; UR-M, unresectable with distant metastasis.

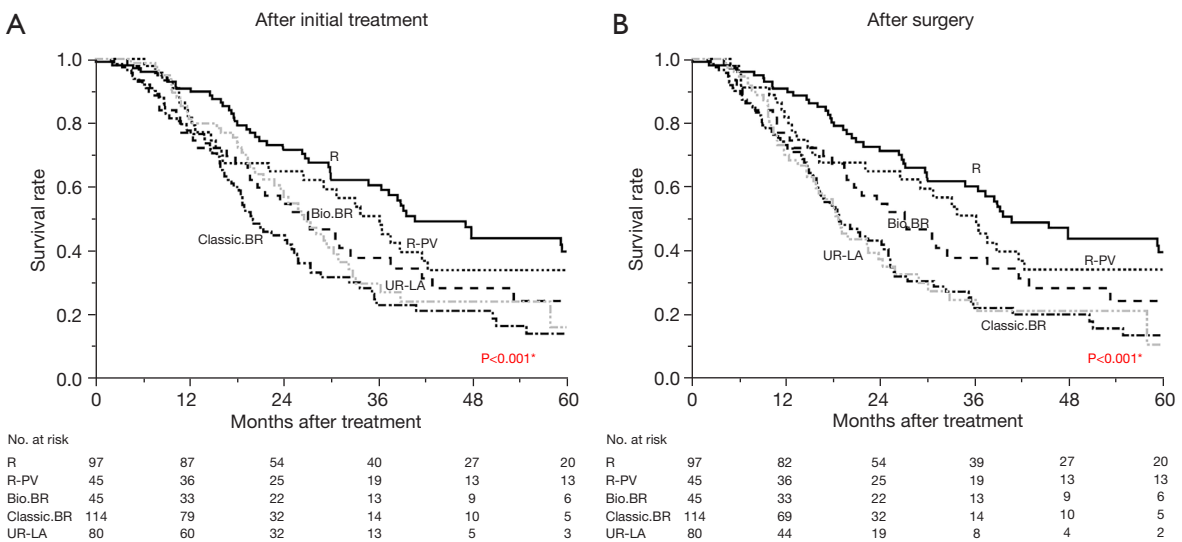

Figure 2 Overall survival outcomes based on biological factors. (A) Overall survival outcomes after initial treatment were analyzed, and the median survival times were 40.7, 36.2, 27.1, 20.1, and 26.6 months in the R, R-PV, biological BR, classical BR, and UR-LA groups, respectively. (B) The median survival times after surgery were 40.7, 36.2, 27.1, 18.8, and 18.7 months in the R, R-PV, biological BR, classical BR, and UR-LA groups, respectively. *, statistically significant. R, resectable; R-PV, resectable with portal vein abutment; biological BR, biological borderline resectable; classical BR, classical borderline resectable; Bio., biological; Classic., classical; UR-LA, unresectable with locally advanced disease.

Table 3 Univariate and multivariate analysis of prognostic factors concerning resectability status for overall survival

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	P	HR	95% CI	P
PV/SMV ≤180° contact	1.014	0.729–1.409	0.94			
PV/SMV >180° contact or contour irregularity	1.633	1.249–2.134	<0.001*	1.133	0.768–1.671	0.53
CHA contact between CA and hepatic artery bifurcation	0.581	0.216–1.564	0.28			
SMA ≤180° contact	2.438	1.524–3.899	<0.001*	2.101	1.296–3.404	0.003*
CA ≤180° contact	0.685	0.219–2.140	0.51			
SMA/CA >180° contact	1.001	0.694–1.444	>0.99			
Unreconstructible PV/SMV	1.573	0.857–2.887	0.14			
CA19-9 (≥500 U/mL)	1.722	1.304–2.275	<0.001*	1.645	1.238–2.185	<0.001*
PV invasion						
Type A		Ref			Ref	
Type B	1.431	1.053–1.945	0.02*	1.305	0.910–1.872	0.15
Type C	2.086	1.427–3.048	<0.001*	1.550	0.916–2.621	0.10
Type D	1.775	1.134–2.777	0.01*	1.598	0.942–2.709	0.08

*, statistically significant. HR, hazard ratio; CI, confidence interval; PV, portal vein; SMV, superior mesenteric vein; CHA, common hepatic artery; CA, celiac artery; SMA, superior mesenteric artery; CA19-9, carbohydrate antigen 19-9.

40.7, 36.2, 27.1, 20.1, and 26.6 months in the R, R-PV, biological BR, classical BR, and UR-LA groups, respectively (P<0.001) (*Figure 2A*). Conversely, the MSTs after surgery were 40.7, 36.2, 27.1, 18.8, and 18.7 months in the R, R-PV, biological BR, classical BR, and UR-LA groups, respectively (P<0.001) (*Figure 2B*). Thus, the outcome for biological BR disease was demonstrably worse than that of R disease (P=0.04), but no survival difference was found between classical BR and UR-LA disease (P=0.97).

Multivariate analysis of prognostic factors concerning the resectability status

The results of univariate and multivariate analyses of prognostic factors concerning the resectability status, including our classification of portal vein invasion (Nakao classification) (21,22), for overall survival are presented in *Table 3*. In this analysis, each factor was based on preoperative radiologic finding, and the images before NAT was adopted. In univariate analysis, >180° portal vein/superior mesenteric vein invasion or contour irregularity, ≤180° superior mesenteric artery (SMA) invasion, high CA19-9 levels (≥500 U/mL), and portal vein invasion (type B/C/D) were identified as prognostic factors. Multivariate analysis identified ≤180° SMA invasion and high CA19-9 levels (≥500 U/mL) as independent prognostic factors. Specifically, ≤180° SMA invasion was a more powerful prognostic factor than >180° SMA/celiac artery invasion (hazard ratio: 2.101, 95% confidence interval: 1.296–3.404, P=0.003).

Discussion

In this study, overall survival was surprisingly better in UR disease than in BR disease when analyzed using the current resectability criteria, revealing an inversion phenomenon. Considering the IAP criteria, the outcome for biological BR disease was demonstrably worse than that of R disease, and no survival difference was detected between classical BR and UR-LA disease. Rather, ≤180° SMA invasion was a more powerful prognostic factor than >180° SMA/celiac artery invasion.

Because the resectability criteria in pancreatic cancer were newly proposed in the NCCN guidelines in 2006, they are well established in clinical practice. Furthermore, this clinical concept is reflected in general rules for the study of pancreatic cancer by the JPS (7). To date, we have verified survival outcomes based on these criteria and demonstrated

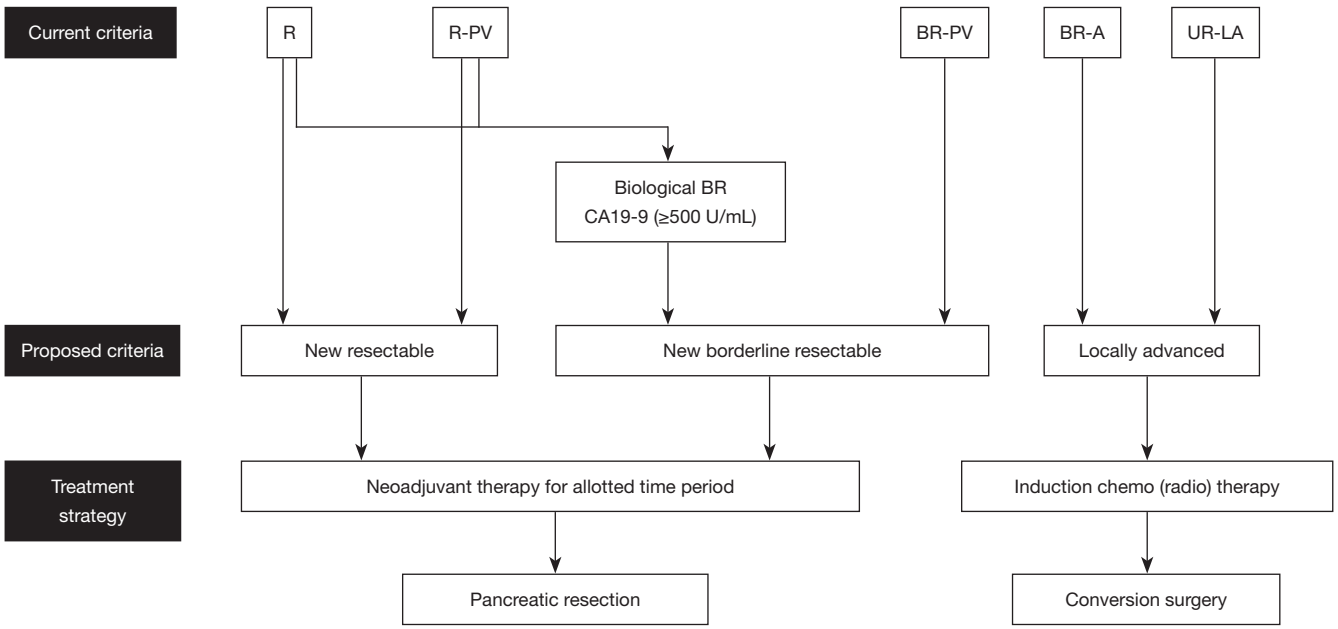

Figure 3 Proposal of new resectability criteria and treatment strategies in pancreatic cancer. R, resectable; R-PV, resectable with portal vein abutment; BR-PV, borderline resectable with portal vein invasion; BR-A, borderline resectable with arterial invasion; UR-LA, unresectable with locally advanced disease; biological BR, biological borderline resectable; CA19-9, carbohydrate antigen 19-9.

their clinical utility in pancreatic cancer (3,4). The survival outcomes were distinctly classified, and they worsened as the resectability status worsened. However, these criteria have been debated in recent years because of certain challenges (23). Surprisingly, our current study revealed that survival was better in UR disease than in BR disease. This might be attributable to recent long-term induction chemotherapy or chemoradiotherapy before surgery in UR disease because 8 months of NAT have been recommended before conversion surgery in our country (16,24). Overall survival in UR disease was prolonged by approximately 8 months, which might be attributable to long-term NAT. In other words, the survival outcomes in BR disease have not been improved by present treatment strategies, such as 2–3 months of NAT (6). These results highlight the need to reappraise and propose new resectability criteria.

As frequently noted, the current NCCN resectability criteria are based solely on anatomical features; thus, it is natural that patients with various pathological stages were included in the same resectability category. This point was previously raised, and the clinical importance of biological factors has grown considerably (10,11,25,26). High CA19-9 levels (≥500 U/mL) and regional lymph node metastasis [biopsy or positron emission tomography-CT (PET-CT)] as proposed by the IAP (8), other tumor markers, circulating tumor cells, and circulating tumor DNA are considered candidate biological factors (23). However, CA19-9 levels could be the most promising factor under these circumstances. In fact, biological BR disease, namely R disease in patients with high CA19-9 levels (≥500 U/mL), was associated with significantly worse survival in our study, indicating that this status should be combined with the BR category.

In light of these findings, we would like to propose new resectability criteria and subsequent treatment strategies in pancreatic cancer (*Figure 3*). Considering that survival in the biological BR group was evidently worse than that in the R group, this category should be combined with the BR category, and NAT should be provided for a longer period until the CA19-9 level reaches a certain threshold. Conversely, >180° SMA/celiac artery invasion was originally assumed to be a more powerful prognostic factor than ≤180° SMA/celiac artery invasion, but the opposite effect was observed. Instead, ≤180° SMA invasion was identified as an independent prognostic factor in our series, indicating that BR-A disease is a form of locally advanced disease. In short, induction treatment followed by conversion surgery should be considered for BR-A disease.

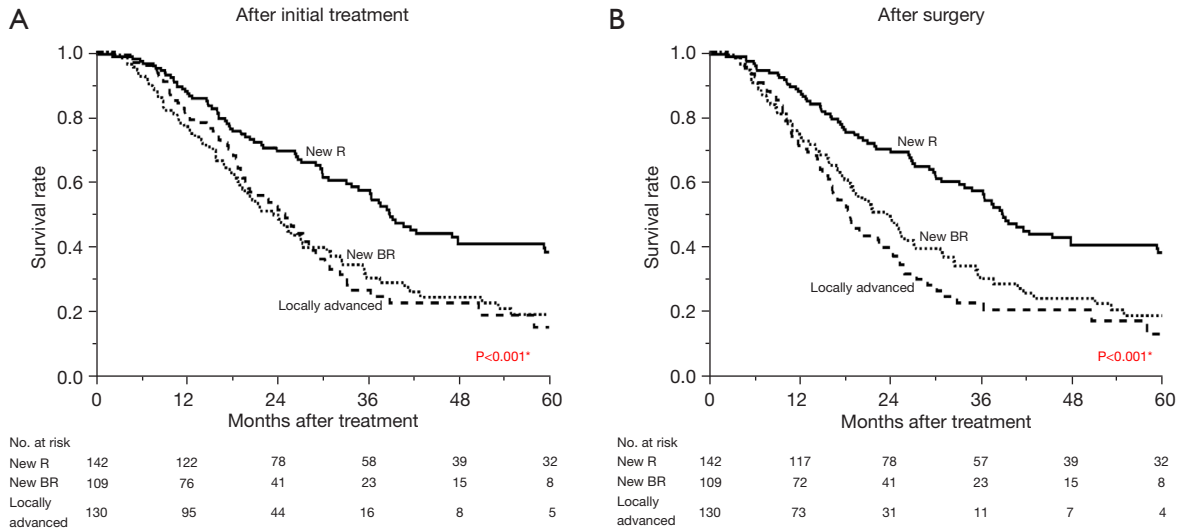

Figure 4 Overall survival outcomes based on the new resectability criteria. (A) Overall survival initial treatment was analyzed, and the median survival times were 38.9, 23.5, and 24.4 months in the new R, new BR, and locally advanced groups, respectively. (B) The median survival times after surgery were 38.8, 23.5, and 18.5 months in the new resectable, new BR, and locally advanced groups, respectively. *, statistically significant. New R, new resectable; new BR, new borderline resectable.

Figure 4 presents the survival outcomes based on the new resectability criteria. The MSTs after initial treatment were 38.9, 23.5, and 24.4 months in the new R, new BR, and locally advanced groups, respectively, and the MSTs after surgery in these groups were 38.8, 23.5, and 18.5 months, respectively. Thus, the survival outcomes were clearly categorized, and this classification appears reasonable for clinical practice. Although the survival outcomes of new BR and locally advanced after initial treatment were comparable (MST; 23.5 *vs.* 24.6 months, P=0.94), the new BR showed a tendency of better survival than locally advanced after surgery (MST; 23.5 *vs.* 18.5 months, P=0.21). These results could attribute to the long-term NAT (basically more than 8 months) for the locally advanced disease, and further study is necessary, including positioning the biological BR disease.

Our study had several limitations. First, it was retrospective in design. Second, the study cohort consisted only of patients who underwent pancreatic cancer resection in our institution, and the operative indications were at the treating surgeon's discretion. Therefore, selection bias might have been introduced. In fact, some patients who underwent resection were included in the UR category. Finally, the cohort combined patients who underwent upfront surgery with those who underwent NAT, and this heterogeneity decreases the analysis of the accuracy. Clinical indication of NAT has changed with the times, and dose intensity of NAT and adjuvant chemotherapy were unfortunately unclear in this study.

Conclusions

In conclusion, we proposed novel resectability criteria for pancreatic cancer. The biological BR category should be combined with the BR category, and BR-A disease was deemed locally advanced disease. Clinical decision-making and treatment strategies based on this new classification are considered reasonable for clinical practice.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-102/rc

Data Sharing Statement: Available at https://jgo.amegroups.

com/article/view/10.21037/jgo-24-102/dss

Peer Review File: Available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-102/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-24-102/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Institutional Review Board of Nagoya Central Hospital (No. 2023-128). Written informed consent, as required by the Institutional Review Board, was obtained from all patients for use of their anonymized information.

References

1. Mehta VK, Fisher G, Ford JA, et al. Preoperative chemoradiation for marginally resectable adenocarcinoma of the pancreas. J Gastrointest Surg 2001;5:27-35.
2. Kato H, Usui M, Isaji S, et al. Clinical features and treatment outcome of borderline resectable pancreatic head/body cancer: a multi-institutional survey by the Japanese Society of Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2013;20:601-10.
3. Yamada S, Fujii T, Sugimoto H, et al. Aggressive surgery for borderline resectable pancreatic cancer: evaluation of National Comprehensive Cancer Network guidelines. Pancreas 2013;42:1004-10.
4. Yamada S, Fujii T, Takami H, et al. Evaluation and proposal of novel resectability criteria for pancreatic cancer established by the Japan Pancreas Society. Surgery 2017;162:784-91.
5. Katz MH, Marsh R, Herman JM, et al. Borderline resectable pancreatic cancer: need for standardization and methods for optimal clinical trial design. Ann Surg Oncol 2013;20:2787-95.
6. Network NCC. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Version 2 2023 ed.: NCCN; 2023.
7. Japan Pancreas Society. Classification of Pancreatic Carcinoma. Fourth English ed. Tokyo: Kanehara & Co., Ltd.; 2017.
8. Isaji S, Mizuno S, Windsor JA, et al. International consensus on definition and criteria of borderline resectable pancreatic ductal adenocarcinoma 2017. Pancreatology 2018;18:2-11.
9. Katz MH, Pisters PW, Evans DB, et al. Borderline resectable pancreatic cancer: the importance of this emerging stage of disease. J Am Coll Surg 2008;206:833-46; discussion 846-8.
10. Hayasaki A, Isaji S, Kishiwada M, et al. Survival Analysis in Patients with Pancreatic Ductal Adenocarcinoma Undergoing Chemoradiotherapy Followed by Surgery According to the International Consensus on the 2017 Definition of Borderline Resectable Cancer. Cancers (Basel) 2018;10:65.
11. Kato Y, Yamada S, Tashiro M, et al. Biological and conditional factors should be included when defining criteria for resectability for patients with pancreatic cancer. HPB (Oxford) 2019;21:1211-8.
12. Medrano J, Garnier J, Ewald J, et al. Patient outcome according to the 2017 international consensus on the definition of borderline resectable pancreatic ductal adenocarcinoma. Pancreatology 2020;20:223-8.
13. Anger F, Döring A, van Dam J, et al. Impact of Borderline Resectability in Pancreatic Head Cancer on Patient Survival: Biology Matters According to the New International Consensus Criteria. Ann Surg Oncol 2021;28:2325-36.
14. Conroy T, Desseigne F, Ychou M, et al. FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011;364:1817-25.
15. Von Hoff DD, Ervin T, Arena FP, et al. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. N Engl J Med 2013;369:1691-703.
16. Satoi S, Yamaue H, Kato K, et al. Role of adjuvant surgery for patients with initially unresectable pancreatic cancer with a long-term favorable response to non-surgical anti-cancer treatments: results of a project study for

pancreatic surgery by the Japanese Society of Hepato-Biliary-Pancreatic Surgery. J Hepatobiliary Pancreat Sci 2013;20:590-600.
17. Nakao A, Takagi H. Isolated pancreatectomy for pancreatic head carcinoma using catheter bypass of the portal vein. Hepatogastroenterology 1993;40:426-9.
18. Nakao A. Isolated pancreatectomy using mesenteric approach. J Hepatobiliary Pancreat Sci 2022;29:293-300.
19. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 2004;240:205-13.
20. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery 2017;161:584-91.
21. Nakao A, Harada A, Nonami T, et al. Clinical significance of portal invasion by pancreatic head carcinoma. Surgery 1995;117:50-5.
22. Nakao A, Kanzaki A, Fujii T, et al. Correlation between radiographic classification and pathological grade of portal vein wall invasion in pancreatic head cancer. Ann Surg 2012;255:103-8.
23. Oba A, Del Chiaro M, Satoi S, et al. New criteria of resectability for pancreatic cancer: A position paper by the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS). J Hepatobiliary Pancreat Sci 2022;29:725-31.
24. Satoi S, Yamamoto T, Yamaki S, et al. Surgical indication for and desirable outcomes of conversion surgery in patients with initially unresectable pancreatic ductal adenocarcinoma. Ann Gastroenterol Surg 2019;4:6-13.
25. Gemenetzis G, Blair AB, Nagai M, et al. Anatomic Criteria Determine Resectability in Locally Advanced Pancreatic Cancer. Ann Surg Oncol 2022;29:401-14.
26. Huang B, Geng H, Jin Y, et al. Is it justified to assess the resectability of pancreatic cancer combined with biological and conditional factors? Transl Cancer Res 2022;11:3458-70.

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