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Modification of BACAP score as a predictor of pancreatic carcinoma resectability at Dr. Cipto Mangunkusumo National Center Hospital Jakarta

Ahmad Ravles[1*], Agi Satria Putranto[1], Dhanasari Vidiawati Trisna[2]

[1]Digestive Surgery Division, Department of Surgery, Faculty of Medicine Universitas Indonesia – Dr. Cipto Mangunkusumo General Hospital, Jakarta 10430, Indonesia;
[2]Department of Community Medicine, Faculty of Medicine Universitas Indonesia–Dr. Cipto Mangunkusumo General Hospital, Jakarta 10430, Indonesia.

*Corresponding author:
Ahmad Ravles;
Digestive Surgery Division, Department of Surgery, Faculty of Medicine Universitas Indonesia – Dr. Cipto Mangunkusumo General Hospital, Jakarta 10430, Indonesia;
ahmadravles00@gmail.com

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ABSTRACT

Background: Surgery remains the best choice curative treatment for pancreatic cancer. Therefore, it is crucial to establish accurate diagnosis from the beginning. BACAP score and CA 19-9 have been identified as good predictors of pancreatic cancer resectability, and their accuracy is expected to increase when combined. This study aimed to determine the outcomes produced by the combination of the BACAP score and CA 19-9 tumor marker.
Methods: This was retrospective cross-sectional study involved pancreatic cancer patients who underwent surgery between January 2017 and April 2023. Logistic regression analysis was performed on all variables of the BACAP score and CA 19-9. The primary outcomes were demographic characteristics, predictive value of BACAP score, Modified BACAP score, and CA 19-9.
Results: A total 87 patients were included. BACAP score yields a sensitivity of 50.0%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 73.8%, and accuracy of 75.9% (AUC 94.6%). While modified BACAP score yielded a sensitivity of 83.1%, specificity of 85.7%, PPV of 70.5%, NPV of 92.5%, and accuracy of 83.9% (AUC 89.4%).
Conclusion: The combination of CA 19-9 and the BACAP score yields a modified score with better outcomes compared to the BACAP score alone in predicting the resectability of pancreatic carcinoma.

Keywords: pancreatic cancer, resectability, predictor, BACAP score.
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INTRODUCTION

Pancreatic cancer is a disease that continues to be a global concern. It is projected to become the second leading cause by 2030, surpassing breast, prostate, and colorectal cancers.[1] The Global Cancer Observatory (GLOBOCAN) survey in 2020 reported 495,773 new cases of pancreatic carcinoma with 466,003 deaths worldwide.[2] In Indonesia, there were 5,781 new cases with 5,690 deaths recorded. In Dr. Cipto Mangunkusumo National Center Hospital, there were 138 cases of pancreatic cancer recorded from 1995 to 2012 in various stages.[3]

The poor prognosis of this disease has not improved over the past decades. Despite performing free margin resections (R0), the five-year survival rate for pancreatic cancer remains only around seven to eight percent in all stages.[1,4,5] Only 15% of pancreatic cancer patients are eligible for resection, and among them, 30% are found to have different findings during intraoperative evaluation.[3,6-9]

Advancements in radiological technology have allowed clinicians to better establish diagnoses and predict the resectability of pancreatic cancer at an early stage. Preoperative Magnetic Resonance Imaging (MRI) has become a preferred option to overcome Abdominal Computed Tomography (CT) scan limitations in detecting small lesions, occult peritoneal carcinomatosis, and liver metastasis. It has been routinely used in France, transforming management strategies and reducing unnecessary laparotomies and pancreatic resections by ten percent in potential resectable cases of pancreatic carcinoma.[10,11]

In addition to relying on advanced radiological technology, there is still a need for alternative methods to determine the resectability of pancreatic cancer. Therefore, Maulat et al developed a predictor score for pancreatic carcinoma resectability called the National Anatomo-Clinical Database on Pancreatic Adenocarcinoma (BACAP) which consists of 6 clinical and radiological factors, with an accuracy of up to 81%.[12,13]

Many studies have used CA 19-9 as a single predictor and have shown good accuracy. However, it is expected that the accuracy will increase when combined with other tumor marker or radiological support.[14] This study aimed to determine the outcomes produced by the combination of the BACAP score and CA 19-9 tumor marker.

METHOD

Study Participants

This was a retrospective cross-sectional study involved 87 pancreatic cancer patients who underwent surgery between January 2017 and April 2023. The research data was obtained from medical records.

The presence of other diseases such as biliary stones, strictures, pancreatitis, liver cirrhosis, or other pulmonary abnormalities, and prior neoadjuvant chemotherapy were excluded. The CA 19-9 value was obtained from the medical records through a blood examination at the clinical pathology laboratory using the Chemiluminescent Immunoassay method, specifically the Architect 2000. The BACAP score, comprising 6 variables (Abdominal pain, weight loss, tumor size, thrombosis, tumor location, and performance status), was applied to the entire research sample using the BACAP score calculator available at http://jdlp.fr/resectability/.

Data Analysis

Statistical analysis was conducted using IBM Statistical Package for the Social Sciences (SPSS) version 20. The data analysis consisted of descriptive statistics and inferential statistics. Descriptive statistics were used to present the obtained data in tabular form. Subsequently, bivariate and multivariate analyses were conducted. Bivariate analysis used the Chi-square test (χ^2). If the Chi-square test assumptions were not met, alternative tests such as Fisher's exact test or Mann-Whitney U test were used. Multivariate analysis was performed using logistic regression. Variables from the bivariate analysis with a p-value <0.25 or those clinically considered significant were included in the analysis using the enter method and stepwise elimination until a final model with significant p-values was obtained. An ROC curve analysis was conducted to determine the predictive value. A p-value <0.05 was considered statistically significant.

RESULTS

This study obtained a total of 87 research samples, consisting of 28 resectable patients and 59 non-resectable patients. The prevalence of pancreatic carcinoma resectability in patients from January 2017 to April 2023 was 32.2% (28 out of 87 subjects).

Age and Gender Characteristics

The normality test results indicated that the age variable was normally distributed.

Table 1. Characteristics based on age and gender

Variables	Total (N = 87)	Pancreatic Carsinoma		*p*
		Resectable (n = 28)	Non-Resectable (n = 59)	
Age, rate ± SD	54.1 ± 12.9	50.9 ± 14.5	55.6 ± 11.9	0.109
Gender, n (%)				
Male	44 (50.6%)	10 (22.7%)	34 (77.3%)	0.057
Female	43 (49.4%)	18 (41.9%)	25 (58.1%)	

Table 2. CA 19-9 as a predictor of resectability

Variable		Total (N = 87)	Pancreatic Carsinoma Resectability		*p*
			Resectable (n = 28)	Non-Resectable (n = 59)	
CA 19-9	≤140.6	31 (35.6%)	22 (71.0%)	9 (29.0%)	<0.001
	>140.6	56 (64.4%)	6 (10.7%)	50 (89.3%)	

Table 3. CA19-9 Prediction Values

Sensitivity	Specificity	PPV	NPV	Accuracy
78.6%	84.7%	70.9%	89.3%	82.8%

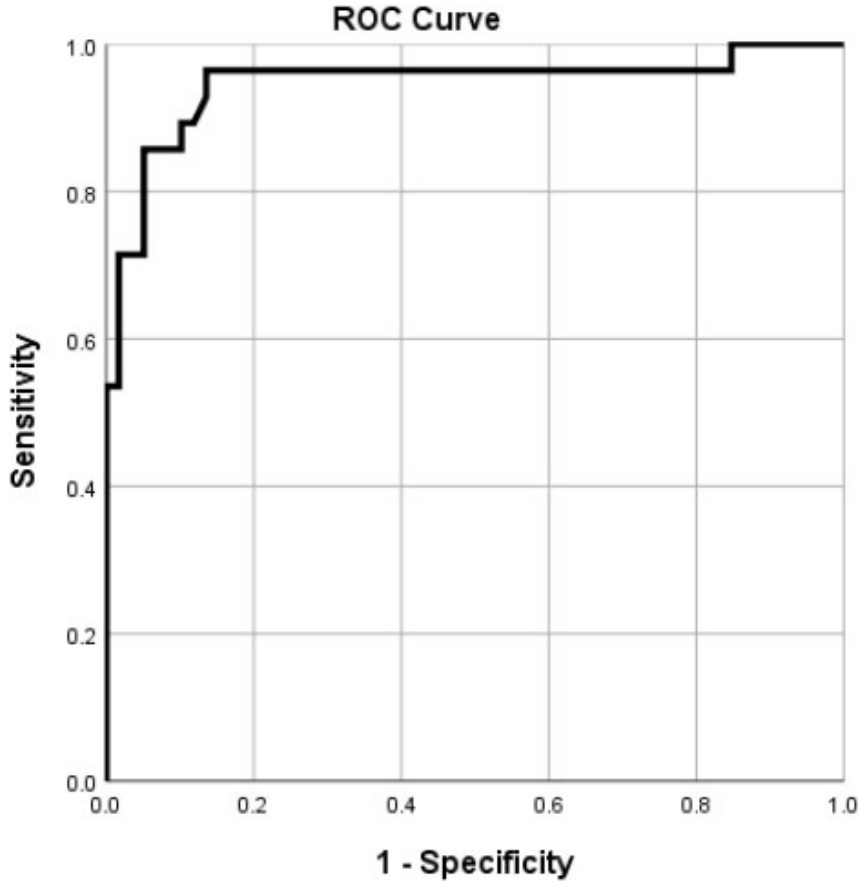

Figure 1. ROC curve for CA19-9 values (AUC 94.6%, 95% CI: 88.5% - 100%, p <0.001).

In this study, the overall mean age of the patients was 54.1 ± 12.9 years, with the resectable group having a mean age of 50.9 ± 14.5 years, and the non-resectable group had a mean age of 55.64 ± 11.87 years. Bivariate analysis using the independent t-test showed that there was no significant difference in the mean age and gender of patients with pancreatic carcinoma resectability (p > 0.05) (Table 1).

CA 19-9 as a Predictor of Resectability

In the resectable pancreatic carcinoma patient group, 22 out of 31 subjects

Table 4. Characteristics of the BACAP score

Characteristics	Pancreatic Carsinoma		*p*
	Resectable (n=28)	Non-Resectable (n=59)	
Abdominal pain, n (%)			
No	24 (80.0)	6 (20.0)	
Yes	4 (7.0)	53 (93.0)	<0.001*
Weight loss, n (%)			
< 8%	19 (90.5)	2 (9.5)	
≥ 8%	9 (13.6)	57 (86.4)	<0.001*
Tumor size, n (%)			
<2 cm	1 (50.0)	1 (50.0)	
2–3.3 cm	12 (75.0)	4 (25.0)	
>3.3 cm	15 (21.7)	54 (78.3)	<0.001*
Thrombosis, n (%)			
No	24 (61.5)	15 (38.5)	
Yes	4 (8.3)	44 (91.7)	<0.001*
Location, n (%)			
Caput	23 (38.3)	37 (61.7)	
Corpus & Tail	5 (18.5)	22 (81.5)	0.067
ECOG			
0	10 (90.9)	1 (9.1)	
1	17 (54.8)	14 (45.2)	
2	1 (2.2)	44 (97.8)	<0.001*

Chi-square test
** Indicates statistical significance, p < 0.05*

Table 5. BACAP prediction values

Sensitivity	Specificity	PPV	NPV	Accuracy
50.0%	100%	100%	73.8%	75.9%

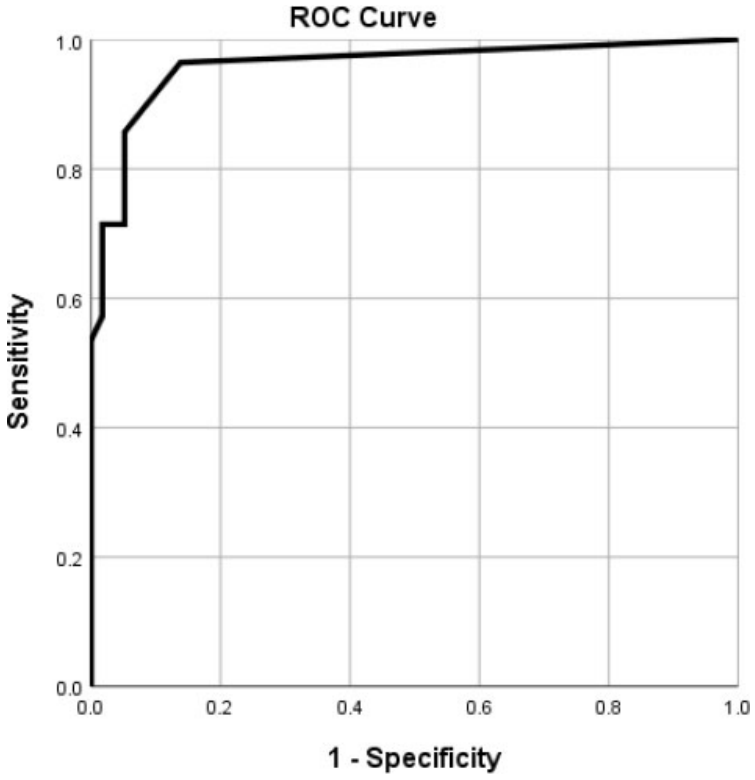

Figure 2. ROC curve for the BACAP score (AUC 94.6%, 95% CI: 88.5% - 100%), *p* <0.001).

(71.0%) had CA19-9 levels ≤ 140.6, while in the non-resectable group, 6 out of 56 patients (10.7%) had the same levels. Bivariate analysis using the chi-square test showed that the resectability of pancreatic carcinoma was influenced by CA 19-9 levels ($p < 0.001$) (Table 2).

Based on Receiver Operating Characteristic (ROC) analysis, the predictive value of CA 19-9 as a predictor of pancreatic carcinoma resectability was obtained, as shown in Table 3. At a cut-off value of 140.6, the sensitivity was 78.6%, specificity was 84.7%, positive predictive value (PPV) was 70.9%, negative predictive value (NPV) was 82.8%, and accuracy was 82.8%. The area under the curve (AUC) value of 94.6% in this study was considered excellent in indicating the level of accuracy. The ROC curve depicted in Figure 1.

Characteristics of the BACAP score

In this stage, the BACAP score was applied to the entire research sample. Based on the results of the proportion difference test using the Chi-square test, there were five variables (abdominal pain, weight loss, tumor size, presence of thrombosis, and CA 19-9 level) that showed significant p-values (<0.05), indicating that these five variables influenced resectability. However, the location of the tumor did not significantly affect resectability ($p = 0.067$) (Table 4).

Prediction Value of the BACAP Score as a Predictor of Resectability

Analysis using the Receiver Operating Characteristic (ROC) curve was conducted to determine the ability of the BACAP score to predict pancreatic carcinoma resectability. Using a cutoff value of 0.5 for the BACAP score in this study resulted in a sensitivity of 50.0%, specificity of 100%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 73.8%, and accuracy of 75.9% (AUC 94.6%), as shown in Table 5 and Figure 2.

Modification of the BACAP Score as a Predictor of Resectability

The modification of the score was done by logistic regression analysis. Subsequently, a stepwise elimination method was applied multiple times, removing variables with

the highest p-values to obtain a final model with significant variables. Eventually, out of the seven variables, a final model was obtained consist of three variables with significant p-values ($p < 0.05$). The weightage grouping of each score is shown in Table 6.

The analysis using the ROC curve is presented in Table 7 and Figure 3. The best cutoff point is ≥3. The larger the total score obtained in the modified BACAP score, the higher the prediction of tumor resectability.

The results of the comparison between the prediction values of the BACAP score and the modified BACAP score as predictors of pancreatic carcinoma resectability indicate that the outcomes generated by the modified BACAP score appear to be better, as shown in Table 8.

Table 6. BACAP score modified

Variables	Coefisien B	OR	IK95%	*p*	Score
Weight loss <8%	-3.469	0.031	0.003-0.370	0.006	1
ECOG					
<2	-6.777	0.001	0.000-0.086	0.002	2
≥2	-5.503	0.004	0.000-0.151	0.003	1
CA 19-9 <140.6	-3.843	0.021	0.002-0.267	0.003	1
Total score					5

Table 7. Prediction values of the modified BACAP score

Cut-off point	Sensitivity	Specificity	PPV	NPV	Accuracy
≥3	83,1%	85,7%	70,5%	92,5%	83,9%

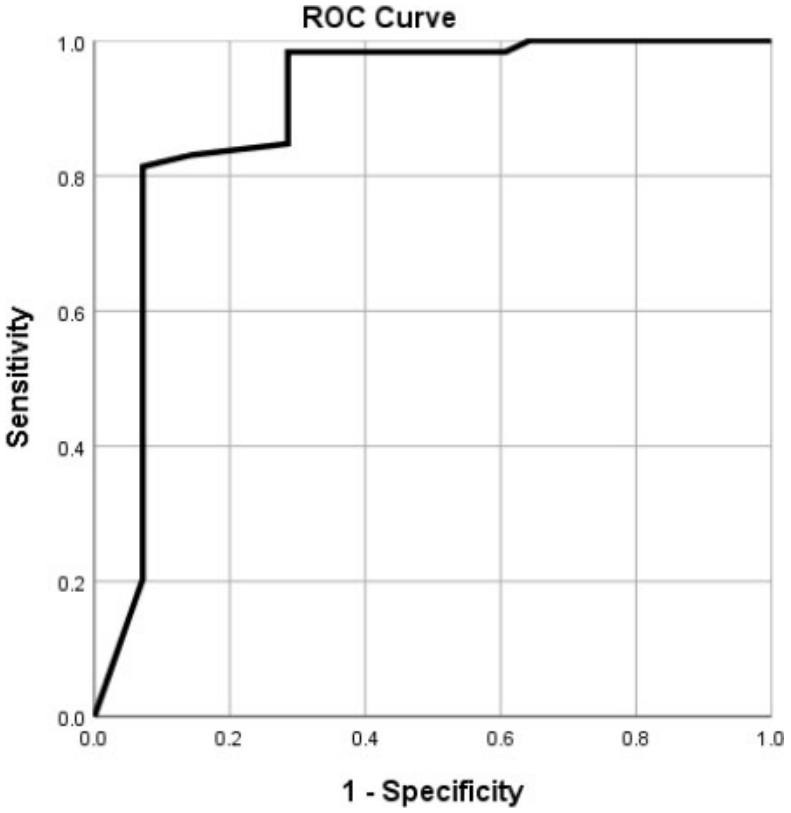

Figure 3. ROC curve for the modified BACAP score (AUC 89.4%, 95% CI: 80.5% - 98.4%, $p < 0.001$).

Table 8. Comparison of resectability prediction values

Parameters	*Cut-off*	Sensitivity	Specificity	PPV	NPV	Accuracy
BACAP score	>50%	50%	100%	73.8%	75.9%	75.9%
modified BACAP score	≥3	83.1%	85.7%	70.5%	92.5%	83.9%

DISCUSSION

The prevalence of resectable pancreatic carcinoma in this study was 32.2%. The overall average age obtained in this study was 54.1 ± 12.9 years. There was no statistically significant difference in the mean age and gender between patients with resectable pancreatic carcinoma ($p = 0.056$). These findings are consistent with the studies conducted by Pasihulizan et al ($p = 0.625$) and Gaddam et al, which also did not find any significant differences in resectability of pancreatic carcinoma based on gender distribution and mean age.[3,15,16]

Based on the application of CA 19-9 in this study, the final sensitivity was determined to be 78.6%, with a specificity of 84.7%. The positive predictive value (PPV) was found to be 70.9%, the negative predictive value (NPV) was 89.3%, and the accuracy was 82.8% (AUC 94.6%). These results indicate that CA 19-9 can be considered a reliable instrument for predicting the resectability of pancreatic cancer. These findings are consistent with previous studies conducted by Pasihulizan et al, Killic et al, and the NCCN guidelines, which all recognize CA 19-9 as a valuable diagnostic marker for pancreatic carcinoma.[3,17-20]

The application of the BACAP score in the study population resulted in a sensitivity of 50.0%, specificity of 100.0%, positive predictive value (PPV) of 100%, negative predictive value (NPV) of 73.8%, and accuracy of 75.9% (AUC 94.6%). These results are lower compared to the study conducted by Maulat et al. This discrepancy could be attributed to the different characteristics of the study population. Factors such as the conservative mindset towards disease complaints, socio-cultural influences, and low awareness of early medical consultation contribute to patients seeking treatment at more advanced stages of the disease, with larger lesions, significant weight loss, and poorer performance status. As a result, these predictive values indicate that the BACAP score is not

sufficiently accurate as a diagnostic tool in this particular study population.[12]

The aim of this study was to determine whether the modification of the BACAP score by adding the CA 19-9 tumor marker variable would result in better outcomes. CA 19-9 tumor marker became the seventh variable component and underwent logistic regression to obtain a final model with significant values ($p < 0.05$). Although the initial regression model showed non-significant p-values for all variables (due to interactions between variables), after several elimination processes, the final modified BACAP score model was obtained with significant values, consisting of three variables: weight loss, ECOG, and CA 19-9, with a total score weight of 5. Using a cutoff value of three or higher, this modified BACAP score resulted in a sensitivity of 83.1%, specificity of 85.7%, positive predictive value (PPV) of 70.5%, negative predictive value (NPV) of 92.5%, and accuracy of 83.9% (AUC 89.4%). This modification yielded better outcomes than the original BACAP score. To the best of the researchers' knowledge, only the BACAP score formulates multiple factors in predicting the resectability of pancreatic cancer, and there have been no other studies modifying or combining these factors. Therefore, the results of this study can only be compared with the original BACAP score.

While this study has demonstrated that the outcomes produced by the modified BACAP score are better than the previous score and are suitable for use as a diagnostic tool in predicting resectability accurately, it does not mean that radiological examinations should be disregarded. The modified BACAP score serves as an additional instrument that strengthens the existing radiological assessments in determining the appropriate course of action.

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CONCLUSION

The modified BACAP score shows promising results as a diagnostic tool for predicting the resectability of pancreatic cancer, with improved outcomes compared to the original BACAP score. However, it should be used in conjunction with radiological assessments to ensure comprehensive decision-making. Further research with larger sample sizes and multi-center studies would be valuable to validate the findings and enhance the applicability of the modified BACAP score in different populations.

CONFLICT OF INTEREST

All researchers declare no conflict of interest.

FUNDING

This research received no funding from any specific commercial or institutional sources.

ETHICAL APPROVAL

This study obtained ethical approval from the Research Ethics Committee of the Faculty of Medicine, University of Indonesia / Dr. Cipto Mangunkusumo National General Hospital (RSCM) Jakarta with approval number KET- 384/UN2.F1/ETIK/PPM.00.02/2023.

AUTHOR CONTRIBUTION

All authors contributed equally with regards to this research.

REFERENCES

1. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas cancers in the United States. Cancer Res. 2014;74(11):2913-2921.
2. Globocan. Incidence, mortality, and prevalence by cancer site in Indonesia [Internet]. 2020. Available from: https://gco.iarc.fr/today/data/factsheets/populations/360-indonesia-fact-sheets.pdf.
3. Pasihulizan. Hubungan CA 19-9 Praoperasi terhadap Resektabilitas Adenokarsinoma Kaput Pankreas [Tesis]. Jakarta: Fakultas Kedokteran Universitas Indonesia; 2020.
4. Neuzillet C, Gaujoux S, Williet N, Bachet JB, Bauguion L, Colson Durand L, et al. Pancreatic cancer: French clinical practice guidelines for diagnosis, treatment and follow-up (SNFGE, FFCD, GERCOR, UNICANCER, SFCD, SFED, SFRO, ACHBT, AFC). Dig Liver Dis. 2018;50(12):1257-1271.
5. Bouvier AM, Uhry Z, Jooste V, Drouillard A, Remontet L, Launoy G, et al; French Network of Cancer Registries (FRANCIM). Focus on an unusual rise in pancreatic cancer incidence in France. Int J Epidemiol. 2017;46(6):1764-1772.
6. Kommalapati A, Tella SH, Goyal G, Ma WW, Mahipal A. Contemporary management of localized resectable pancreatic cancer. Cancers. 2018;10(1):24.
7. Rawla P, Sunkara T, Gaduputi V. Epidemiology of pancreatic cancer: global trends, etiology and risk factors. World J Oncol. 2020;10(1):10–27.
8. Winter JM, Brennan MF, Tang LH, D'Angelica MI, Dematteo RP, Fong Y, et al. Survival after resection of pancreatic adenocarcinoma: results from a single institution over three decades. Ann Surg Oncol. 2012;19(1):169-175.
9. Kneuertz PJ, Cunningham SC, Cameron JL, Torrez S, Tapazoglou N, Herman JM, et al. Palliative surgical management of patients with unresectable pancreatic adenocarcinoma: trends and lessons learned from a large, single institution experience. J Gastrointest Surg. 2011;15(11):1917-1927.
10. Costache MI, Costache CA, Dumitrescu CI, Tica AA, Popescu M, Baluta EA, et al. Which is the best imaging method in pancreatic adenocarcinoma diagnosis and staging-CT, MRI or EUS?. Curr Health Sci J. 2017;43(2):132-136.
11. Deng Y, Ming B, Wu JL, Zhou T, Zhang SY, Chen Y, et al. Magnetic resonance imaging for preoperative staging of pancreatic cancer based on the 8th edition of AJCC guidelines. J Gastrointest Oncol. 2020;11(2):329-336.
12. Schima W, Ba-Ssalamah A, Goetzinger P, Scharitzer M, Koelblinger C. State-of-the-art magnetic resonance imaging of pancreatic cancer. Top Magn Reson Imaging. 2007;18(6):421-429.
13. Maulat C, Canivet C, Touraine C, Gourgou S, Napoleon B, Palazzo L, et al. A new score to predict the resectability of pancreatic adenocarcinoma: The BACAP score. Cancers. 2020;12(4):783.
14. Marion-Audibert AM, Vullierme MP, Ronot M, Mabrut JY, Sauvanet A, Zins M, et al. Routine MRI with DWI sequences to detect liver metastases in patients with potentially resectable pancreatic ductal carcinoma and normal liver CT: a prospective multicenter study. AJR Am J Roentgenol. 2018;211(5):W217-W225.
15. Coppola A, Farolfi T, La Vaccara V, Cammarata R, Caputo D. Role of neoplastic markers in pancreatic adenocarcinoma. J Clin Med. 2022;11(21):6509.
16. Gaddam S, Abboud Y, Oh J, Samaan J, Nissen NN, Lu SC, et al. Incidence of pancreatic cancer by age and sex in the US, 2000-2018. JAMA. 2021;326(20):2075-2077.
17. Killic M, Göçmen E, Tez M, Ertan T, Keskek M, Koç M. Value of preoperative serum CA 19-9

levels in predicting resectability for pancreatic cancer. Can J Surg. 2006;49(4):241.
18. Tempero MA. NCCN guidelines updates: pancreatic cancer. J Natl Compr Canc Netw. 2019;17(5.5):603-605.
19. Springfeld C, Jäger D, Büchler MW, Strobel O, Hackert T, Palmer DH, et al. Chemotherapy for pancreatic cancer. La Presse Medicale. 2019;48(3):e159-e174.
20. Wang H, Liu J, Xia G, Lei S, Huang X. Survival of pancreatic cancer patients is negatively correlated with age at diagnosis: a population-based retrospective study. Scientific Reports. 2020;10(1):7048.

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