

CLINICAL STUDY

A scoring system for preoperative assessment of resectability in periampullary neoplasms

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Abstract: *Background:* To identify the preoperative factors predicting resectability in periampullary neoplasms.

Methods: Twenty-three different parameters representing the clinical, laboratory and radiological data of 65 patients, who were operated for periampullary neoplasms, were analyzed to determine their value in assessing neoplasm resectability. Coefficients were calculated by Cox regression analysis for significant factors. A scoring system was designed for resectability. All patients were divided into 4 groups according to their scores.

Results: Twenty-six patients who had a resectable neoplasm underwent pancreatico-duodenectomy and surgical palliation was performed in the remaining 39 patients. After multivariate analysis, neoplasms larger than 4.5 cm, low leukocyte count ($<9500/\text{mm}^3$), high bilirubin levels ($>137.5 \mu\text{mol/L}$) and tomographic findings indicating neoplasm invasion were found to be independent factors predicting resectability. The score range was between 0 and 12. Patients were grouped as Group-1 (total score 0–2), Group-2 (total score 3–5), Group-3 (total score 6–8), and Group-4 (total score 9 and higher). Resectability rates were 100 % in Group 1 (n=13), 44 % in Group-2 (n=23), 21 % in Group-3 (n=14), and 0 % in Group-4 (n=15), respectively. Mean score was 3.3 in patients with resectable lesions and 7.2 in patients with unresectable lesions ($p<0.001$).

Conclusion: This simple scoring system can be a guide in the management plans of patients with periampullary neoplasms. By using this scoring system, patients with an unresectable neoplasm can be predicted and most unnecessary laparotomies can be avoided (Tab. 3, Fig. 2, Ref. 27). Full Text (Free, PDF) www.bmj.sk.

Key words: score, resectability, periampullary, and neoplasm.

Periampullary neoplasms comprise four different pathologic entities: cancers of the pancreatic head, ampulla of Vater, distal common bile duct and duodenum (1). Surgical resection by pancreatico-duodenectomy provides the only cure chance for patients with periampullary neoplasms. Therefore, an aggressive surgical management is advocated in most centers. However, depending on the origin of neoplasm, 25 % to 75 % of patients who had periampullary neoplasms and who underwent laparotomy with the surgeon's intent to perform a pancreatico-duodenectomy are found to have unresectable disease (2). Currently, palliation by nonsurgical techniques is preferred and suggested in patients found to have unresectable disease by preoperative staging (3–5).

In periampullary neoplasms, preoperative assessment of resectability has two advantages. First of all, endoscopic or transhepatic treatment of biliary obstruction may be indicated in patients whose neoplasms are proved to be unresectable by preoperative investigations. This would decrease the frequency of laparotomy without resection. Secondly, neoadjuvant chemo-radiation protocols may be appropriate for patients with unresectable

neoplasms (6). In this study, we aimed to determine the factors predicting resectability of periampullary neoplasms.

Methods

The database of Ankara Numune Hospital's 4th Department of Surgery, containing prospectively documented variables of patients treated for periampullary neoplasms was analyzed. Between January 1992 and August 2000, 138 patients with periampullary neoplasms were admitted in our clinic. Among them, 65 patients who have no metastatic disease according to radiological findings including tomography were operated on for curative intent. Mean age of the patients was 58 years (range 32 to 87). Thirty-eight patients were male and 27 patients were female. The primary neoplasms were pancreatic ductal adenocarcinomas (n=35), ampullary cancers (n=19), distal cholangiocarcinomas (n=7), and duodenal carcinomas (n=4). The standard for the assessment of resectability was surgical exploration. Neoplasms were considered unresectable during the operation if (1) neoplasm invaded the portal vein, superior mesenteric vein, superior mesenteric artery, or celiac axis, (2) there was extensive involvement of peripancreatic tissues (stomach or mesocolon), (3) there were hepatic or peritoneal metastases (7, 8). Twenty-three different parameters representing the clinical, laboratory and radiological data of 65 patients were analyzed to determine their value in predicting neoplasm resectability.

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Tab. 1. Resectability score for periampullary neoplasms.

Coefficients*	
CT	
Resectable	0
Unresectable	6
Bilirubin	
<137.5 µmol/L	0
>137.5 µmol/L	3
White blood cell count	
<9500/mm ³	2
>9500/mm ³	0
Neoplasm diameter	
<4.5 cm	0
>4.5 cm	1

* – Score is the sum of coefficients.

The following variables were included in the univariate analysis. Age, gender, duration of symptoms, weight loss, back pain, diabetes mellitus, fever, history of cholangitis, and the length of hospital stay, hematocrit, white blood cell count, erythrocyte sedimentation rate, creatinine, bilirubin, serum transaminases (SGOT and SGPT), alkaline phosphatase, gamma glutamyl transpeptidase, albumin, and CA 19.9, ultrasonography and computerized tomography findings.

Student-t test and chi-square test were used for univariate analysis, as appropriate. Cut-off values of numeric variables were calculated by using the receiver operator characteristic (ROC) curve analysis.

Age, white blood cell count, bilirubin levels, neoplasm diameter, ultrasonography and tomography findings were significant factors predicting resectability after univariate analysis. Multivariate analysis using logistic regression was applied to these significant variables in order to determine their effect on resectability. After multivariate analysis, white blood cell count, neoplasm diameter, bilirubin level and tomography findings were found to be significant factors ($p < 0.05$). These four variables having independent effect on resectability after multivariate analysis were chosen. By using resectability as a dependent variable, another logistic regression analysis was applied to these 4 variables, and coefficients were calculated for every variable. These coefficients were rounded, and multiplied by 2 for ease of use, and formed the basis of the Resectability Score for Periampullary Neoplasm (RSPT) (Tab. 1). The minimum and maximum values of the scoring system are 0 and 12, respectively. The variables of the score were as follows (the first p value is univariate and the second p value is multivariate):

– Computerized tomography. Presence of the following parameters was considered in the determination of unresectability (9, 10): Suspicion of peritoneal metastases, vascular invasion and invasion to surrounding structures such as the celiac axis, stomach, or colon (for the effect on resectability $p = 0.003$ and 0.04). Distribution of patients: 64.8 % resectable lesion, 35.2 % unresectable lesion.

Tab. 2. Distribution of patients according to scores.

	No. of patients	Resectability* n(%)
Group 1 (score=0–2)	13	13 (100)
Group 2 (score=3–5)	23	10 (44)
Group 3 (score=6–8)	14	3 (21)
Group 4 (score>8)	15	0 (0)

* – $p < 0.001$.

– Total bilirubin level. Presence of relatively low bilirubin levels was found to be a major factor predicting resectability. The cut-off value was calculated by using ROC curve analysis as 137 µmol/L (for the effect on resectability $p = 0.01$ and 0.05). Distribution of patients: 60 % bilirubin level >137.5 µmol/L and 40 % bilirubin level <137.5 µmol/L.

– White blood cell count. An increase in the white blood cell count was found to be a determining factor for resectability. The cut-off value was calculated by ROC curve analysis as 9500/mm³ (for the effect on resectability $p = 0.03$ and 0.05). Distribution of patients: 24.6 % white blood cell count >9500/mm³, 75.4 % white blood cell count <9500/mm³.

– Neoplasm diameter. Neoplasm diameter was determined from tomographic examination. The cut-off value was calculated by ROC curve analysis as 4.5 cm. Neoplasm diameter smaller than 4.5 cm was a predictor of resectability (for the effect on resectability $p = 0.001$ and 0.02). Distribution of patients: 44.6 % neoplasm diameter >4.5 cm, 55.4 % neoplasm diameter <4.5 cm.

All patients were scored using this system. For each patient, probability of resectability according to this score was calculated as described by Hunt et al (11). They were divided into 4 groups with respect to their total scores: group 1: total score 0 to 2; group 2: total score 3 to 5; group 3: total score 6 to 8; group 4: total score >8.

SPSS version 9.0 for Windows software was used for statistical analyses and $p < 0.05$ was accepted statistically significant.

Results

Twenty-six patients had resectable neoplasms and underwent pancreaticoduodenectomy. Remaining 39 patients underwent surgical palliation for unresectable neoplasms. Causes of unresectability according to laparotomy findings were superior mesenteric vein (SMV) involvement ($n = 25$) followed by peritoneal carcinomatosis ($n = 6$), liver metastases ($n = 4$), superior mesenteric artery (SMA) involvement ($n = 2$), and portal vein (PV) involvement ($n = 2$). Surgical palliation was applied to patients with unresectable lesions.

All patients underwent computerized tomography (CT). Findings of unresectability were SMV involvement in 15 patients, SMA involvement in 2 patients, PV vein involvement in 1 patient, and peritoneal carcinomatosis in 2 patients.

Resectability rates according to score groups were shown in Table 2. Resectability data according to score groups showed a statistically significant decrease in resectability with increasing

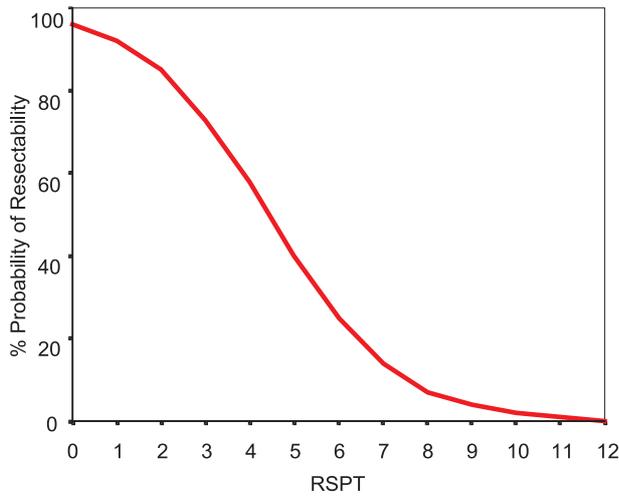


Fig. 1. Calculated probabilities of resectability according to RSPT.

scores. Calculated probabilities of resectability rates according to scores are presented in Figure 1. Mean score was 3.3 in patients with resectable lesion and 7.2 in patients with unresectable lesion ($p < 0.001$, student's t test).

Resectability rates according to histopathologic type of neoplasm were 89.5 % for ampullary neoplasms, 75 % for duodenal cancer, 14.7 % for pancreatic cancer, and 14.3 % for distal cholangiocarcinoma ($p < 0.001$). Score groups and resectability rates according to histopathologic type of neoplasm were given in Table 3. Resectability rates according to score groups were also showed significant relationship with the histopathologic type of neoplasm.

Discussion

Surgery has offered the primary means for cure and palliation for periampullary neoplasms. Together with the advances and improvements in surgical therapy, a number of advances have

Tab. 3. Score groups and resectability rates according to histopathologic type of neoplasm.

Histopatologic type	Score groups				
	Group 1 n (%)	Group2 n (%)	Group 3 n (%)	Group 4 n (%)	Total n (%)
Pancreas*	4(11)	9(26)	9(26)	13(37)	35
Resectable	4(11)	1(3)	0(0)	0(0)	5(14)
Unresectable	0(0)	8(23)	9(26)	13(37)	30(86)
Ampullary*	8(42)	7(37)	3(16)	1(6)	19
Resectable	8(42)	7(37)	2(10)	0(0)	17(89)
Unresectable	0(0)	0(0)	1(6)	1(6)	2(11)
Cholangiocarcinoma		6(86)		1(14)	7
Resectable		1(14)		0(0)	1(14)
Unresectable		5(72)		1(14)	6(86)
Duodenum	1(25)	1(25)	2(50)		4
Resectable	1(25)	1(25)	1(25)		3(75)
unresectable	0(0)	0(0)	1(25)		1(25)
Total	13	23	14	15	65
Resectable	13(100)	10(44)	3(21)	0(0)	26(40)
unresectable	0(0)	13(56)	11(79)	15(100)	39(60)

* - $p < 0.05$

been made in endoscopic and radiological interventions. Prior reports of exceedingly higher morbidity and mortality rates associating operative palliation have further encouraged the use of non-operative techniques for definitive palliation. More recently, minimally invasive techniques have also been promoted as alternatives to traditional surgical management (1, 2). For these reasons, preoperative assessment of resectability in periampullary neoplasms has become an important subject. Thus, the frequency of laparotomy without resection can be decreased. Also, neo-adjuvant chemo-radiation protocols can be considered for these patients (6, 12).

There are numerous articles in the literature evaluating the resectability in periampullary neoplasms by different variables including imaging techniques (6–10, 13, 14), but they are not being used in a scoring system for the prediction of resectability and there is no definitive criteria addressing the use of advanced imaging techniques rather than tomography for the determination of resectability. RSPT combines only tomographic findings as an imaging technique and laboratory variables. Results of RSPT can be useful in addressing the use of advanced imaging techniques for periampullary neoplasms.

CT scanning was found to be the major parameter of RSPT. In our study, 84.2 % of patients who were predicted to have unresectable neoplasms according to CT findings, had unresectable neoplasms at surgery, and 51.1 % of patients who were predicted to have resectable neoplasms according to CT findings had resectable neoplasms at surgery. These findings reinforce those reported by other researchers, suggesting that CT findings predicting unresectability are more reliable than the prediction of resectability (9, 10, 14–16). Also it was stated in the literature that CT is inadequate for the preoperative assessment of potentially resectable pancreatic and periampullary neoplasms (17–19).

High bilirubin levels were the second important component of RSPT. Jaundice is a common symptom of periampullary neoplasms. Moreover, bilirubin levels can be used to estimate the progression of disease (20, 21). High bilirubin levels may suggest the existence of an advanced neoplasm.

White blood cell count is a test, which is very commonly used in medicine. Immunity against malignant cells is accomplished primarily by leukocytes (22). In our study, low white blood cell count was found to be an independent factor predicting unresectability. This may be due to insufficient immune response to neoplasm. The importance of immune response to neoplasm cells was shown in many neoplasms including colon cancers and melanoma (23); but was not well known in periampullary neoplasms.

The last component of RSPT was neoplasm diameter. This parameter was taken separately from other CT findings because of the controversies in its cut-off value for respectability (24–26). Periampullary neoplasms larger than 4.5 cm had a low rate of resectability according to our study.

Our scoring system, by adding 3 simple criteria to CT findings, may determine the patients who need advanced diagnostic techniques. According to RSPT, patients in group 1 and group 4

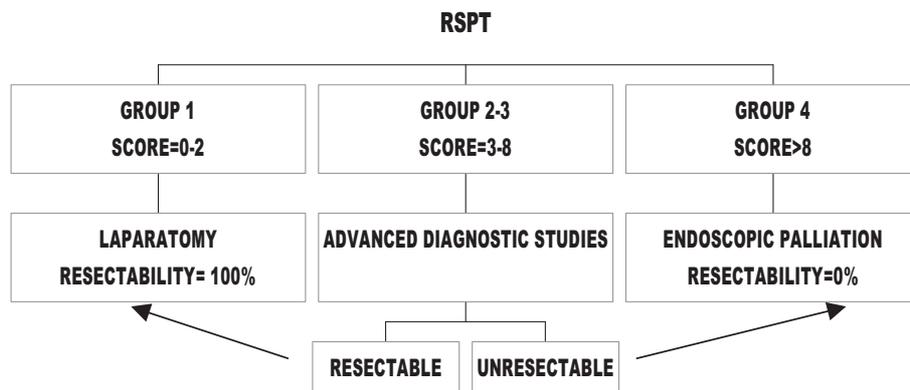


Fig. 2. Algorithm for the management of periampullary neoplasms according to RSPT.

did not need any other diagnostic modality. All patients in group 1 had resectable neoplasms and all patients in group 4 had unresectable neoplasms. Patients having a total score between 3 and 8 seem to require advanced techniques according to RSPT. By this way, resectability can be predicted correctly in approximately 43 % of patients with periampullary neoplasms.

Histopathologic type of neoplasm was not evaluated as a preoperative factor predicting resectability in our study, because it was not possible to determine it in the preoperative period. However, results of laparotomy and histopathological examination revealed histopathologic types of neoplasm. Our scoring system was also useful for prediction of resectability in all type of periampullary neoplasms including pancreas and ampullary neoplasms.

Scoring systems are useful in identifying the patients with high and low risk. They are also useful for standardizing the results and selection of homogenous groups for proper comparisons between different patient populations. These data can be used as inclusion or exclusion criteria (11). A scoring system decreases some of our clinical problems, reducing the number of possible relevant variables to absolute numbers. With the help of this information, patients may be selected for endoscopic palliations or radical resections and some decisions regarding necessity of advanced laboratory and imaging techniques.

In intensive care units and less frequently in other areas of clinical practice, scoring systems are frequently used to predict prognosis of the critically ill (11) and other types of patients, respectively. Scoring systems are not frequently used for the prediction of resectability in malignancies. These systems are generally designed by applying multivariate analyses to different variables. For the analysis of resectability, logistic regression model can be used with sufficient accuracy (27). In our study, we used the logistic regression model to calculate the coefficients of variables.

An ideal scoring system should be objective, reliable, and practical, in order to be used in clinical practice (11). The variables in RSPT are all objective and easily available. The score is practical and easy to calculate.

Results of this study have shown that RSPT is a useful scoring system in the management of patients with periampullary neoplasms (Fig. 2). Total scores less than 3 indicate resectable neoplasms and these patients can be operated directly without any further diagnostic evaluations. Total scores greater than 8 represent unresectable neoplasms. Non-surgical palliation and/or neoadjuvant chemotherapy can be planned in these cases, but some patients with significant duodenal obstruction may require surgical palliation. Patients with scores between 3 and 8 seemed to need further diagnostic studies such as MRI, MRCP, visceral angiography or diagnostic laparoscopy to determine the resectability of their neoplasms.

We aimed to design a resectability score that can be used in different patient populations. Of course, this system can be modified and improved. We hope that RSPT will help surgeons to evaluate and plan the management of their patients with periampullary neoplasms, thus our suggestions will have to be confirmed by other researchers.

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