RESEARCH ARTICLE

The importance of MELD-Na and MELD 3.0 in predicting postoperative complications after pancreaticoduodenectomy

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ABSTRACT

Background: This study aims to assess whether MELD-Na and MELD 3.0 scores, commonly used for evaluating chronic liver disease severity and prioritizing transplant candidates, can predict early postoperative complications following pancreaticoduodenectomy.

Methods: Data from 102 patients who underwent elective pancreaticoduodenectomy for pancreatic head masses were analyzed. MELD-Na and MELD 3.0 scores were calculated 48 hours before surgery using preoperative blood tests. Postoperative complications, including Clavien-Dindo classifications, were recorded along with perioperative and 30-day outcomes.

Results: Higher MELD-Na and MELD 3.0 scores were significantly associated with an increased incidence of complications, including wound infections, higher Clavien-Dindo scores, and prolonged hospital stays. Notably, MELD 3.0 demonstrated superior predictive accuracy for pancreatic fistula compared to MELD-Na.

Conclusion: These findings indicate that elevated MELD-Na and MELD 3.0 scores, especially MELD 3.0, can serve as reliable predictors for postoperative complications and length of hospital stay in patients undergoing pancreaticoduodenectomy.

Key Words: *MELD-Na; MELD; Pancreaticoduodenectomy; Postoperative complications; Pancreas cancer*

INTRODUCTION

Pancreatic cancer is the fourth leading cause of cancer-related death among both men and women in the United States. 85% of these tumors are adenocarcinomas that originate from the ductal epithelium [1]. In data from the "Global burden of pancreatic cancer" study, cases peak at ages 65-69 for men and 75-79 for women [1].

In most cases, the cancer is locally advanced, and only 15 to 20 percent can be resected at the time of diagnosis [2]. Approximately 60 to 70 percent of exocrine pancreatic cancers are localized in the head of the pancreas, and 20 to 25 percent are located in the trunk/tail [3]. Pancreaticoduodenectomy is a complex, high-risk surgical procedure for tumors located in the head of the pancreas. A conventional pancreaticoduodenectomy involves the removal of the head of the pancreas, the duodenum, the first 15 cm of the jejunum, the common bile, duct, and gallbladder, and partial gastrectomy.

In experienced, high-volume centers, pancreaticoduodenectomy can be performed with postoperative mortality rates of less than 4 percent and morbidity rates between 40 and 50 percent. Twenty to thirty percent of patients completely resected survive five years [4]. Following pancreaticoduodenectomy, many complications may occur, including pancreatic fistulas, bleeding, biliary fistulas, delayed gastric emptying, and systemic complications.

The MELD score is a scoring system that includes serum bilirubin, creatinine, and INR used to estimate three-month survival, determine chronic liver disease severity, and prioritize transplantation. A higher MELD score is associated with greater severity of liver dysfunction and increased three-month mortality and morbidity risk [5]. The MELD-Na score, which is the updated version of the MELD score, is calculated by adding the serum sodium value to the MELD score. The MELD 3.0 score was created by adding albumin and gender factor to the MELD-Na score [6]. Recently, publications have suggested that the MELD-Na score can be used to predict postoperative complications in non-transplant surgeries [7].

The present study aims to determine whether MELD scoring systems, which have not been previously evaluated in the literature, are predictive of early complications following pancreaticoduodenectomy.

MATERIALS AND METHODS

Our study included patients who applied to our tertiary referral center between January 1, 2014, and August 1, 2022 and underwent elective pancreaticoduodenectomy as a result of a mass in the pancreas head. As the exclusion criteria; patients with a known diagnosis of cirrhosis, not getting results of the necessary parameters for the MELD-Na score and MELD 3.0 scoring system in preoperative blood tests, not having patient records during the follow-up of complications, having a different cancer history, or having undergone an urgent pancreaticoduodenectomy. In addition, patients receiving neoadjuvant therapy were not included in the study. By accessing the patient data *via* the hospital computer system, the demographic data of the patients, the blood tests performed within 48 hours before the operation, MELD-Na and MELD 3.0 scores, perioperative and postoperative 30-day pancreatic leaks, biliary fistulas, ileus, wound infections, intraabdominal abscess, evisceration, anastomotic leakage, pulmonary and cardiac complications, Clavien Dindo scores and hospital stay were noted and compared with complications.

Calculation of MELD scoring systems

MELD score=3.8 × $\log_e$ (serum bilirubin (mg/dL))+11.2 × $\log_e$(INR) + 9.6 × $\log_e$(serum creatinine (mg/dL))+6.4

MELD-Na score=MELD score+1.32 × (137-Na)–[0.033 × MELD Skoru × (137-Na)]

MELD 3.0 score=1.33 (if female)+[4.56 × $\log_e$ (bilirubin)]+[0.82 × (137–Na)]–[0.24 × (137–Na) × $\log_e$ (bilirubin)]+[9.09 × $\log_e$ (INR)]+[11.14 × $\log_e$ (creatinine)]+[1.85 × (3.5–albumin)]–[1.83 × (3.5–albumin) × $\log_e$ (creatinine)]+6

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Statistical analysis

SPSS 26.0 for Windows program was used for statistical analysis. Descriptive statistics; numbers and percentages for categorical variables, mean, standard deviation, median, minimum and maximum for numerical variables were given. Comparisons of numerical variables in two independent groups were made with Student's T test for the variable satisfying the normal distribution condition, and with the Mann-Whitney U test when the normal distribution condition was not met. A *Chi-square* test was used to analyze the ratios in the groups. A ROC analysis was used to determine the specificity and sensitivity of the tests. The statistical alpha significance level was accepted as $p<0.05$.

Ethics committee approval

The study started with the approval of the Ethics Committee of Health Sciences University Istanbul Training and Research Hospital with decision number 254 on 19.08.2022. Informed consent forms were signed by all patients who were included in the study.

RESULTS

The study includes data from 102 patients. Of these patients, 69 were male and 33 were female, with a mean age (± SD) of 62.6 (± 10.5) and a mean body mass index (± SD) of 24.3 (± 4.4). MELD-Na and MELD 3.0 scores of the patients were calculated according to the blood results taken within 48 hours before the operation.

Any complication was detected in 44 patients, and there was a significant increase in MELD-Na and MELD 3.0 values in patients who developed complications (p:0.001, p:0.003, respectively). In our study, no significant relationship was found between other parameters such as age, Body Mass Index (BMI), tumor localization, pancreatic duct diameter, pancreatic tissue characteristics, type of operation, preoperative ASA score, smoking, comorbidity, perioperative blood replacement, and postoperative complications. As shown in Table 1, the data for patients with and without postoperative complications are presented. The highest sensitivity and specificity values were accepted as cut-off values in ROC analyses based on complications for MELD-Na and MELD 3.0. According to the ROC curve analysis for MELD 3.0, the sensitivity was 52% and the specificity was 78% at the cutoff value of ≥ 10.5, while the sensitivity was 48% and the specificity was calculated as 86% at the cutoff value of ≥ 11.5 for MELD-Na.

Table 1) General characteristics of patients with complications

Complication		No (n:58)	Yes (n:44)	P-value
Age		61.91 ± 11.43	63.52 ± 9.385	0.45
BMI (kg/m^2) (mean ± SD)		24.53 ± 4.3	23.64 ± 4.54	0.348
Gender (n,%)	Female (n,%)	20 (34.5%)	13 (29.5%)	0.598
	Male (n,%)	38 (65.5%)	31 (70.5%)	
Meld-Na (median- IQR)		8-4	10-7	0.001
Meld-3.0 (median- IQR)		8-6	11-6	0.003
Tumor localization (n,%)	Head of pancreas	31 (53.4%)	22 (50%)	0.877
	Ampulla of vater	17 (29.3%)	12 (27.3%)	
	Common bile duct	5 (8.6%)	6 (13.6%)	
	Duodenum	5 (8.6%)	4 (9.1%)	
Pancreatic duct diameter (n,%)	<3 mm	18 (31%)	16 (36.4%)	0.376
	3-6 mm	24 (41.4%)	21 (47.7%)	
	>6 mm	16 (27.6%)	7 (15.9%)	
ASA scores (n,%)	ASA-1	2 (3.4%)	1 (2.3%)	0.869
	ASA-2	41 (70.7%)	33 (75%)	
	ASA-3	15 (25.9%)	10 (22.7%)	
	ASA-4	0 (0%)	0 (0%)	
Smoking status (n,%)	No	33 (56.9%)	31 (70.5%)	0.373
	Ex-smoker	8 (13.8%)	4 (9.1%)	
	Yes	17 (29.3%)	9 (20.5%)	
Comorbidity (n,%)	No	29 (50%)	14 (31.8%)	0.066
	Yes	29 (50%)	30 (68.2%)	
Perioperative ES replacement (n,%)	No	46 (79.3%)	30 (68.2%)	0.202
	Yes	12 (20.7%)	14 (31.8%)	
Operation type (n,%)	Standard whipple	23 (39.7%)	13 (29.5%)	0.29

	Pylorus preserving whipple	35 (60.3%)	31 (70.5%)	
Pancreatic tissue	Soft	22 (37.9%)	20 (45.5%)	0.33
	Medium	12 (20.7%)	12 (27.3%)	
	Hard	24 (41.4%)	12 (27.3%)	

Complications in patients were analyzed according to cut-off values. Wound infection, Clavien Dindo score, hospital stay, and general complication values were found to be significant in both groups. When the patients were evaluated in terms of pancreatic fistula, it was seen that the high MELD 3.0 score was significantly associated with fistula, but no significant correlation could be determined for the MELD-Na score (p:0.020 *vs.* p:0.596). Similarly, while a significant relationship was observed in MELD 3.0 in postoperative pulmonary complications, this relationship was not found in MELD-Na (p:0.030 *vs.* p:0.090). In addition, no significant correlation was found between mortality rates, complications such as intra-abdominal abscess, evisceration, ileus, biliary fistula, and MELD-Na score and MELD 3.0 score. Details of the table in which we examined the relationship between MELD-Na and MELD 3.0 scores and complications are given in Tables 2 and 3.

Table 2) Patient demographics and hospital data compared to MELD-Na and MELD-3.0

		MELD-Na ≤ 11.5, n (%)	**MELD-Na >11.5, n (%)**	**P**	**MELD-3.0 ≤ 1 0.5, n (%)**	**MELD-3.0 >10.5, n (%)**	**P-value**
Gender	Male	44 (63.8%)	25 (36.2%)	0.012	42 (60.9%)	27 (39.1%)	0.241
	Female	29 (87.9%)	4 (12.1%)		24 (72.7%)	9 (27.3%)	
Operation type	Standard whipple	26 (72.2%)	10 (27.8%)	0.914	24 (66.77%)	12 (33.33%)	0.76
	Pylorus preserving whipple	47 (71.2%)	19 (28.8%)		42 (63.60%)	24 (36.40%)	
Comorbidity	No	36 (83.7%)	7 (16.3%)	0.02	32 (74.4%)	11 (25.6%)	0.08
	Yes	37 (62.7%)	22 (37.3%)		34 (57.6%)	25 (42.4%)	
Smoking status	No	45 (70.3%)	19 (29.7%)	0.626	42 (65.6%)	22 (34.4)	0.203
	Ex-smoker	18 (69.2%)	8 (30.8%)		14 (53.8%)	12 (46.2%)	
	Yes	10 (83.3%)	2 (16.7%)		10 (83.3%)	2 (16.7%)	
ASA score	1-2	58 (75.3%)	19 (24.7%)	0.318	53 (69.9%)	24 (31.1%)	0.309
	3-4	15 (60%)	10 (40%)		13 (52%)	12 (48%)	
Mortality	No	71 (73.2%)	26 (26.8%)	0.138	64 (66.00%)	33 (34.00%)	0,342
	Yes	2 (40.0%)	3 (60.0%)		2 (40.00%)	3 (60.00%)	
TNM classification	Stage 0-1-2	67 (73.6%)	24 (26.4%)	0.185	61 (67%)	30 (33%)	0,157
	Stages 3-4	6 (54.50%)	5 (45.50%)		5 (45.50%)	6 (54.50%)	
Length of stay in hospital (mean ± SD)		13.37 ± 7.84	15.92 ± 10.62	0.02	13.33 ± 8.3	15.45 ± 9.82	0.019

Table 3) Evaluation of complication subgroups according to MELD-Na and MELD-3.0 score

		MELD-Na ≤ 11.5, n (%)	**MELD-Na >11.5, n (%)**	**P**	**MELD-3.0 ≤ 10.5, n (%)**	**MELD-3.0 >10.5, n (%)**	**p**
Wound infection	No	66 (77.60%)	19 (22.40%)	0.002	61 (71.80%)	24 (28.20%)	0.001
	Yes	7 (41.20%)	10 (58.80%)		5 (29.40%)	12 (70.60%)	
Intra-abdominal abscess	No	67 (73.6%)	24 (26.4%)	0.185	60 (65.90%)	31 (34.10%)	0.455
	Yes	6 (54.50%)	5 (45.50%)		6 (54.50%)	5 (45.50%)	
Evisceration	No	71 (72.40%)	27 (27.60%)	0.319	64 (65.30%)	34 (34.70%)	0.553
	Yes	2 (50.00%)	2 (50.00%)		2 (50.00%)	2 (50.00%)	
Bile fistula	No	69 (71.10%)	28 (28.90%)	0.664	62 (63.90%)	35 (36.10%)	0.654

	Yes	4 (80.00%)	1 (20.00%)		4 (80.00%)	1 (20.00%)	
Pancreatic fistula	No	40 (72.70%)	15 (27.30%)	0.596	38 (69.10%)	17 (30.90%)	0.02
	Grade A	24 (72.70%)	9 (27.30%)		24 (72.70%)	9 (27.30%)	
	Grade B	7 (58.30%)	5 (41.70%)		3 (25.00%)	9 (75.00%)	
	Grade C	2 (100.00%)	0 (0.00%)		1 (50.00%)	1 (50.00%)	
Postoperative bleeding	No	72 (74.20%)	25 (25.80%)	0.022	65 (67.00%)	32 (33.00%)	0.051
	Yes	1 (20.00%)	4 (80.00%)		1 (20.00%)	4 (80.00%)	
Pulmonary complication	No	65 (74.70%)	22 (25.30%)	0.09	60 (69.00%)	27 (31.00%)	0.03
	Yes	8 (53.30%)	7 (46.70%)		6 (40.00%)	9 (60.00%)	
Any Complications	No	50 (86.20%)	8 (13.80%)	0	45 (77.60%)	13 (22.40%)	0.002
	Yes	23 (52.30%)	21 (47.70%)		21 (47.70%)	23 (52.30%)	
Clavien Dindo score	0	36 (83.70%)	7 (16.30%)	0.025	33 (76.70%)	10 (23.30%)	0.046
	1	11 (84.60%)	2 (15.40%)		10 (76.90%)	3 (23.10%)	
	2	14 (58.30%)	10 (41.70%)		11 (45.80%)	13 (54.20%)	
	3a	7 (53.80%)	6 (46.20%)		7 (53.80%)	6 (46.20%)	
	3b	3 (100.00%)	0 (0.00%)		3 (100.00%)	0 (0.00%)	
	4-5	2 (33.30%)	4 (66.70%)		2 (33.33%)	4 (66.67%)	

Based on the pathology results of the patients, it was determined that 10 (9.8%) had benign pathologies.

DISCUSSION

It has been shown that the MELD score and the later revised MELD-Na score are used to determine organ allocation priorities for liver transplantation and are valuable in predicting postoperative complications in non-transplant surgeries [7-9]. Postoperative complications are quite common in patients who underwent pancreaticoduodenectomy for pancreatic cancer. It has been demonstrated in many previous studies that early detection of these complications can significantly reduce postoperative mortality and morbidity [9]. In our study, it was shown that MELD-Na and MELD 3.0 scores can be very successful in predicting postoperative complications, especially wound infection, pancreatic fistula, pulmonary complications, and postoperative bleeding.

Al abbas et al., in which patients who underwent distal pancreatectomy and Whipple operation were examined, a positive correlation was found between a MELD score above 11 and mortality, length of hospital stay, and transfusion requirements. In a study examining 1096 patients who underwent elective gastrectomy, it was found that mortality and complication rates increased significantly in patients with a MELD score above 11 compared to patients with a MELD score below 11.

In the study by Shannon et al., in which patients who underwent inguinal hernia, umbilical hernia, and colon resection were examined, it was observed that for each 1-point increase in the mean MELD score, there was an increase of 7.8%, 13.8% and 11.6% in any postoperative complication, respectively. Complication rates were found to increase with the increase in MELD score. Similarly, in a study investigating bleeding and mortality after cholecystectomy, it was found that each 1-point increase in the MELD score causes a 7% increase in mortality, and the high score is significantly associated with postoperative bleeding, In a study examining 10,842 patients who underwent elective surgery for colon cancer, it was seen that the risk of postoperative complications increased 1.3 times in patients with a MELD-Na score above 9, and the risk of mortality increased 2.7 times in patients with a score above 8, Similarly, in our study, a significant relationship was found between high MELD-Na and MELD 3.0 scores and complications and postoperative bleeding, but no significant relationship was found between mortality and high score.

According to Cookley et al., in which 44,540 patients undergoing elective colorectal surgery were evaluated, the MELD-Na score was a significant independent risk factor for anastomotic leakage. Additionally, when MELD-Na scores are above 20, 10% of rectal resections result in anastomotic leakage. Schlosser et al., in which 304,277 patients were evaluated retrospectively, a significant correlation was observed between a high MELD-Na score and postoperative complications, length of hospital stay, reoperation, and mortality. In a different study examining 85 patients who underwent emergency surgery, high MELD-Na scores were found to be associated with postoperative complications and prolonged discharge time, in our study, results were obtained supporting the literature studies. Wound infection, any complications, postoperative bleeding, and hospital stay were found to be higher in patients with a MELD-Na score above 11.5. Additionally, a significant correlation was found between the Clavien Dindo score, which is used to assess postoperative complications, and the high MELD-Na score.

In many studies, high body mass index, soft pancreatic tissue, and narrow pancreatic duct diameter have been associated with pancreatic fistula and postoperative complications, In a study comparing pylorus-preserving whipple and standard whipple surgery, no difference was found between the two types of operation in complication rates, except for the increased rate of delayed gastric emptying, Our study found that BMI, pancreatic tissue characteristics, duct diameter, and operation type were not significantly associated with complications.

In a study describing the MELD 3.0 scoring system and comparing the status of MELD-Na and MELD 3.0 in end-stage liver disease, MELD 3.0 was found to be more significant in predicting mortality [6]. In a comment written on this study, this study was seen as positive in terms of reducing gender-based inequalities, but they stated that more information is required regarding transgender individuals or women taller than 175 cm, and adding muscle mass measurement to this scoring may yield healthier results. In another comment published in response to the clinical study on MELD 3.0, the effort put forth in this regard is appreciated, but the authors conclude that MELD 3.0 has been presented without adequate evidence and there is not yet a ready scoring system for clinical use.

To the best of our knowledge, we were unable to find any study comparing MELD-Na and MELD 3.0 scores in pancreatectomy patients. Our study demonstrated that MELD 3.0 was more effective in predicting pancreatic fistulas and pulmonary complications, despite the similarity in overall complication rates between the two scoring systems.

There are some limitations. One of the most important limitations of our study is that it is a retrospective study. The cases in the study were not standardized in terms of surgical experience, which can be seen as another limitation. In addition, not all patients included in the study were diagnosed with malignancy, and we think that it may be important in terms of complications. Finally, although these scoring systems give an idea about early postoperative mortality and morbidity, they do not provide information about long-term outcomes.

CONCLUSION

In conclusion, a first-of-its-kind study has examined the relationship between early complications after pancreatic cancer and MELD-Na and MELD 3.0 scores. Based on the results of our study, high MELD-Na and MELD 3.0 scores were directly related to an increase in postoperative complications, and we believe that these scores can be used clinically as a predictor of complications due to their accessibility and low cost. The MELD 3.0 score system also demonstrated better results in terms of pancreatic fistulas and pulmonary complications than the MELD-Na score. It is our belief that more research comparing these two scoring systems will facilitate the introduction of these scoring systems into everyday practice.

CONFLICT OF INTEREST

All authors are in agreement with the contents of a manuscript and confirm that the paper is not being published or under consideration elsewhere.

There is no conflict of interest in our article.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

AUTHOR CONTRIBUTIONS

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