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Evaluation of the Possibility for Non-oral Enteral Feeding in Acute Pancreatitis Patients by Using PASS (Pancreatitis Activity Scoring System)

Kim Song-Hwan[1]*, Jong Nam-Hun[1], Kim Hye-Song[1], Yu Nam[1], Choe Jong-Hwa[1], Ri Un-Hui[2], Jong Sin-Hyok[1], Ri Song-Ung[1], Ri Chol-Su[2]

[1]Department of Gastroenterology, Hospital of Pyongyang University of Medical Science, Democratic People's Republic of Korea.

[2] Department of Ultrasonography, Hospital of Pyongyang University of Medical Science, Democratic People's Republic of Korea.

***Corresponding Author Email:** sb.myong@star-co.net.kp.

ABSTRACT

***Purpose**: Our purpose is to set up the new criteria for initiating NOEF(non-oral enteral feeding) safely in acute pancreatitis patients by analyzing several univariate indices and multivariate clinical scoring systems measured in the early days of NOEF. **Methods**: We involved moderately severe and severe acute pancreatitis patients who received NOEF treatment. We made a univariate and multivariate analysis of all the demographical, clinical, laboratory, radiological indices and clinical scores before NOEF, to find out the independent evaluation factors of paralytic ileus during NOEF. By analyzing ROC(receiver operating characteristics) curve, optimal cut-off points of selected independent risk factors were defined. We determined the ranges below the cut-off points as the safe ranges out of paralytic ileus during NOEF. **Results**: A total of 136 patients was involved in our study. By the univariate analysis, abdominal pain, respiratory rate, body temperature, rebound tender on physical examination, band neutrophil count, SIRS(systemic inflammatory response syndrome) score, PASS(pancreatitis activity scoring system), BISAP(bedside index of severity in acute pancreatitis), Balthazar score were associated with occurrence of paralytic ileus during NOEF($P<0.05$). By the multivariate analysis, respiratory rate and PASS were selected as the independent risk factors of paralytic ileus during NOEF($P<0.05$). Areas under ROC curves(AUROCs) of respiratory rate and PASS in predicting paralytic ileus were 0.873(0.777-0.970), 0.897(0.795-0.999), respectively. The optimal cut-off points of highest odds ratios(OR) and negative predictive values(NPV) in predicting paralytic ileus after NOEF were respiratory rate$\geqq$25bpm and PASS$\geqq$120, respectively. **Conclusion**: Safe range for NOEF during acute pancreatitis treatment is PASS<120 or respiratory rate<25bpm.*

Keywords: Acute Pancreatitis, Enteral Feeding, NOEF, Clinical Scoring System, PASS, Paralytic Ileus.

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INTRODUCTION

Acute pancreatitis is one of the emergent and long-term diseases of the gastroenterology department, of which medical course is very complicated, so establishing the correct nutrition protocol for acute pancreatitis is very important to support the prolongation of clinical course. Studies on optimal nutrition strategy have been remaining for several

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decades, and non-oral enteral feeding(NOEF) is globally accepted as the best feeding path, because it allows the main principle of acute pancreatitis management – "Resting pancreas" and also supply with enough nutrition[1-3]. Most guidelines of acute pancreatitis recommended that the moderately severe to severe patients are indicated for NOEF[4,5]. However, paralytic ileus which is sometimes repeated during the course of acute pancreatitis may disturb NOEF, leading it to be paused temporarily. This required modified definition of more detailed and real-time criteria for initiation and discontinuance of NOEF.

Clinical scoring systems for acute pancreatitis play an important role in the development of the clinical pathway to standardize of the diagnosis and treatment. Several univariate indices such as BUN(blood urea nitrogen), calcium, hemoglobin, creatinine, WBC count, blood glucose, pancreatic necrosis, peri-pancreatic fluid collection, ascites can predict the outcome and clinical course of acute pancreatitis[6-10], however, the accuracies of multivariate scoring systems such as APACHE II, CTSI, Ranson's criteria, Glasgow score, SIRS score, BISAP, PASS are exceedingly higher than those of former univariate indices[11-19]. The outcome parameters of acute pancreatitis on which most researchers mainly focus are death, complication, severity, length of hospital or ICU stay, invasive treatment, readmission, and others. Exploration of the univariate indices and multivariate scoring systems that can evaluate the patient's condition in NOEF may greatly contribute to the development of the correct clinical pathway.

Therefore, we aimed to define the initiation criteria for safe NOEF in acute pancreatitis patients by multivariate study of the several real-time acting univariate indices and clinical scoring systems(SIRS, BISAP, PASS, Balthazar grade) which can possibly affect on NOEF.

METHODS

Study Cohort and Data Collection

We retrospectively studied all moderately severe and severe acute pancreatitis patients who admitted and were given NOEF in Gastroenterology Department, Hospital of Pyongyang University of Medical Science between January 2021 and December 2023. Diagnosis and severity classification were defined by modified Atlanta classification in 2013[20].

Management of all patients were based on the National Practical Guideline of Acute Pancreatitis. All patients in our study started to be given NOEF through the naso-jejunal tube 2-5 days after admission. We have used the standard semi-elemental feeding formulas which were made in Nutrition Department of our hospital.

Table 1. Assessment of several scoring systems

Scores	Parameter	Weights
SIRS score[21]	Body temperature>38.3°C or <36.0°C	+1
	Heartbeat>90bpm	+1
	Respiratory rate>20/minute	+1
	WBC count>12,000/mL or <4000/mL	+1
PASS[22]	Organ failure	×100 for each system
	Tolerating solid diet (yes=0, no=1)	×40
	SIRS	×25 for each criterion
	Abdominal pain (0-10)	×5
	Morphine equivalent dose (mg)	×5

Scores	Parameter	Weights
BISAP[23]	BUN>25 ㎎/dL	+1
	Glasgow coma scale<15	+1
	SIRS	+1
	Age>60	+1
	Pleural effusion	+1
Balthazar grade[24]	Normal pancreas	A(0)
	Focal or diffuse enlargement of the pancreas	B(1)
	Peripancreatic inflammation with intrinsic pancreatic abnormalities	C(2)
	Intrapancreatic or extrapancreatic fluid collections	D(3)
	Two or more large collections of gas in the pancreas or retroperitoneum	E(4)

Demographic and clinical parameters, laboratorial and instrumental results of all patients were collected everyday since the admission days.

Scoring Systems for Acute Pancreatitis

Based on the collected data, clinical and radiological scores as SIRS score, PASS, BISAP, and Balthazar grade were calculated at the point of NOEF initiation(2-5 days after admission)(Table 1).

Definition of Clinical Outcome-Paralytic Ileus

One or more of following criteria were defined as paralytic ileus[25].

- Abdominal distention.
- Diffuse, persistent abdominal pain(VAS increase).
- Nausea and/or vomiting.
- Delayed passage of or inability to pass flatus for more than 24 hours.

Statistical Analysis

IBM SPSS Statistics version 20.0 was used for statistical analysis. By univariate analysis, all the demographic, clinical, laboratorial, radiological and therapeutic parameters were compared between two groups(ileus-positive group and ileus-negative group after NOEF) at the point of the NOEF initiation to identify the relative factors of paralytic ileus. We have obtained multivariate logistic regression model based on the selected variables by univariate analysis to select the independent risk factors of paralytic ileus. ROC(receiver operating characteristic) curves of selected risk factors for paralytic ileus were produced and AUC(area under curve) of every parameter was analyzed to evaluate optimal cut-off points.

Table 2. Univariate analysis result of study cohort, n=136, $\overline{X}$ ±SD, n(%).

Variables	Ileus-positive (n=20)	Ileus-negative (n=116)	Total(n=136)	P
Age(years)	54.60±14.20	51.46±13.55	51.92±13.65	0.343
Male	8(40.0)	50(43.1)	58(42.6)	0.796
Clinical features				
Abdominal pain(VAS)	2.80±2.69	1.35±1.17	1.57±1.56	0.000
GCS	14.95±0.22	14.94±0.65	14.94±0.61	0.944
SBP, mmHg	134.50±20.38	128.88±23.12	129.71±22.75	0.309
Heartbeat, bpm	81.10±16.89	76.84±9.28	77.47±10.76	0.103
Respiratory rate, /min	23.70±2.96	19.52±2.10	20.13±2.68	0.000
Body temperature, ℃	37.12±0.74	36.79±0.62	36.84±0.65	0.039

Variables	Ileus-positive (n=20)	Ileus-negative (n=116)	Total(n=136)	P
BMI, kg/m^2	22.96±2.50	23.93±3.53	23.85±3.45	0.481
Abdominal distention	18(90.0)	100(86.2)	118(86.8)	0.916
Rebound tender	15(75.0)	46(39.7)	61(44.9)	0.003
Laboratory results				
RBC count, T/L	3.83±0.81	3.78±0.64	3.80±0.67	0.783
WBC count, G/L	13.02±4.67	10.46±2.19	11.07±3.04	0.100
Band cell, %	7.75±11.21	3.04±5.98	3.74±7.13	0.006
PLT count, G/L	163.13±75.37	177.69±67.34	174.78±68.77	0.452
ALT, U/L	51.11±29.04	42.21±31.27	43.47±31.01	0.248
AST, U/L	62.11±37.59	55.77±34.58	56.66±34.94	0.466
TP, g/L	59.60±6.02	62.65±7.27	62.19±7.16	0.079
SCr, mg/dL	1.36±1.11	1.65±1.58	1.57±1.47	0.474
Image studies				
Pleural effusion	12(60.0)	61(52.6)	73(53.7)	0.539
Pancreatic enlargement	5(25.0)	38(32.8)	43(31.6)	0.491
Local complications	7(35.0)	47(40.5)	54(39.7)	0.641

Table 2. (Continued).

Variables	Ileus-positive (n=20)	Ileus-negative (n=116)	Total(n=136)	P
Clinical scores				
SAP(RAC)	9(45.0)	3(2.6)	12(8.8)	0.000
SIRS score	1.70±0.86	0.82±0.71	0.95±0.79	0.000
PASS	179.50±73.64	86.55±39.55	100.22±56.46	0.000
BISAP	1.65±0.75	0.99±0.73	1.09±0.76	0.000
Balthazar grade	2.42±1.17	2.35±0.87	2.36±0.91	0.768

VAS: visual analogue scale, GCS: Glasgow coma scale, SBP: systemic blood pressure, bpm: beat per minute, BMI: body mass index, RBC: red blood cell, WBC: white blood cell, PLT: platelet, ALT: alanine transaminase, AST: aspartate transaminase, TP: total protein, SCr: serum creatinine, SAP: severe acute pancreatitis, RAC: revised Atlanta classification, SIRS: systemic inflammatory response syndrome, PASS: pancreatitis activity scoring system, BISAP: bedside index of severe acute pancreatitis.

Table 3. Multivariate logistic regression analysis result of selected variables for paralytic ileus prediction, n=136.

Selected variables	B	S.E	Wald	df	P
VAS	0.139	0.261	0.283	1	0.595
Respiratory rate	1.093	0.295	13.735	1	0.000
Body temperature	0.163	0.618	0.007	1	0.792
Abdominal distention(yes=1, no=0)	0.330	0.921	0.129	1	0.720
Band cell	-0.015	0.050	0.091	1	0.762
RAC(SAP=1, MSAP=0)	-0.172	1.994	0.007	1	0.931
SIRS score	-1.610	0.993	2.629	1	0.105
PASS	0.038	0.018	4.644	1	0.031
BISAP	0.550	0.617	0.793	1	0.373
Constant	-34.896	24.908	1.963	1	0.161

VAS: visual analogue scale, RAC: revised Atlanta classification, SAP: severe acute pancreatitis, MSAP: moderately severe acute pancreatitis, SIRS: systemic inflammatory response syndrome, PASS: pancreatitis activity scoring system, BISAP: bedside index of severe acute pancreatitis.

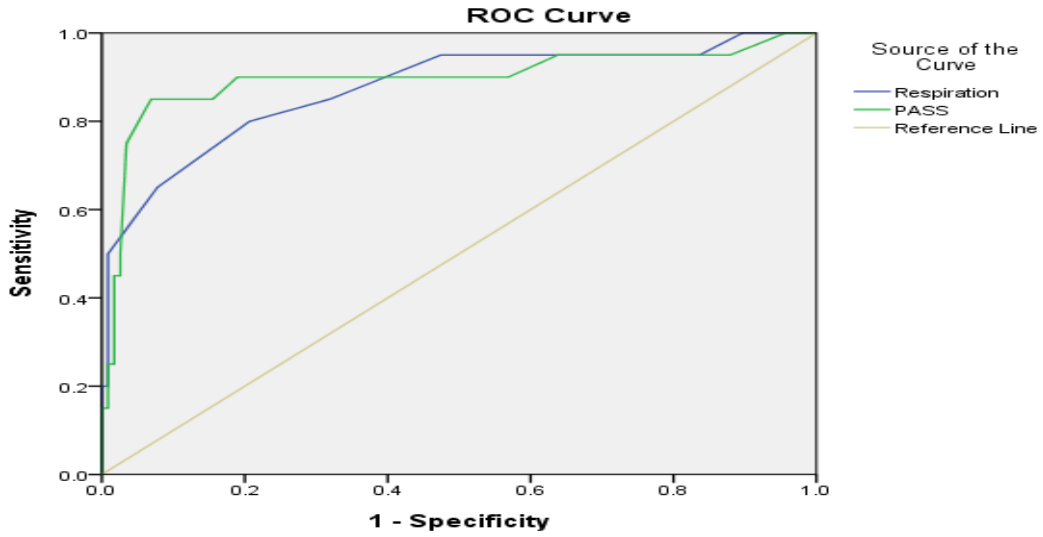

Figure 1. Receiver operating characteristic curves of respiratory rate and non-oral enteral feeding for the prediction of paralytic ileus after non-oral enteral feeding.

RESULTS

A total of 136 patients with moderately severe to severe acute pancreatitis patients were given NOEF treatment between January 2021 and December 2023. As seen in Table 2, average age of the study cohort were 50.92±13.65 and 58 patients(42.6%) were males.

As the univariate analysis result, abdominal pain(VAS), respiratory rate, body temperature, rebound tender, band cell count were of high relation with paralytic ileus(P<0.05). SIRS score, PASS, BISAP were highly correlated to paralytic ileus(P<0.0001), but Balthazar grade had no discriminative value(P=0.768)(Table 2). After the multivariate logistic regression analysis, respiratory rate and PASS were selected as the independent risk factors of paralytic ileus(P<0.05)(Table 3). For paralytic ileus evaluation, ROC curves of selected parameters after multivariate logistic regression indicated that AUCs of PASS and respiratory rate were 0.897(0.795-0.999), 0.873(0.777-9.970), respectively(Figure 1, Table 4). Optimal cut-off points of the parameters were respiratory rate>25/min and PASS>120(Table 5).

Table 4. AUCs of respiratory rate and non-oral enteral feeding for the prediction of paralytic ileus after non-oral enteral feeding.

Selected variables	AUC	S.E	P	95% CI
Respiratory rate	0.873	0.049	<0.0001	0.777-0.970
PASS	0.897	0.052	<0.0001	0.795-0.999

AUC: area under curve.

Table 5. Optimal cut-off points of selected variables for the prediction of paralytic ileus after non-oral enteral feeding.

Selected variables	Sen(%)	Spe(%)	PPV(%)	NPV(%)	OR
Respiratory rate≧25/min	85.0	99.1	94.4	97.4	651.7
PASS≧120	90.0	81.0	45.0	97.9	38.5

Sen: sensitivity, Spe: specificity, PPV: positive prediction value, NPV: negative prediction value, OR: Odds ratio, PASS: pancreatitis activity scoring system.

DISCUSSION

Setting up the common and optimal criteria for the initiation and pause of the enteral feeding during the management of acute pancreatitis may be the great approach not only to supply with the nutrition for the long- term management of the disease and also to prevent the iatrogenic complication by the procedure. As the heart failure may be exacerbated after overload of much fluid infusion, the gastrointestinal failure(i.e paralytic ileus) by acute pancreatitis may also be exacerbated after overload of much food. Because the standard measures are relatively established for the heart failure, most of the clinicians rarely make mistakes for the management of disease. But the gastrointestinal tracts have higher compliance than cardiovascular system, so they underestimate the gastrointestinal failure which may be followed by the exacerbation of the disease(i.e intra-abdominal hypertension or abdominal compartment syndrome). ESPEN guideline recommended to determine the absolute and relative criteria of EN(enteral nutrition, meaning NOEF) initiation on the base of measuring IAP(intra-abdominal pressure)[26]. To our regrets, all the methods for measuring IAP are too invasive to generally apply in clinical practice, that is why it is important to newly establish the non-invasive and accurate criteria for NOEF initiation.

Predominance of PASS as the real-time activity assessment tool for the prediction of acute pancreatitis was again proved. We thought that following two conditions were essential for the clinical scoring systems to be used as the real-time assessment tools. First is the positive co-relationship between a scoring system and every event(every adverse outcome parameter like) during the clinical course of the disease. Second is the possibility of quick calculation of the scoring system. Several scoring systems like Ranson's criteria and APACHE-II have high co-relationship with adverse outcomes of acute pancreatitis, but they need long time to be calculated. On the other hand, SIRS score has a real-time variability by quick calculation, but it can not predict all the adverse events during the disease. So, these scores could not be widely used as real-time assessment tools in clinical practice.

Although PASS has not been widely investigated globally, several studies[27,28] and our late practice proved that this real-time scoring system reached or passed the standards of former scoring systems in the prediction of outcomes as death, severity and readmission. But we could not find the studies evaluating the relationship between PASS and nutrition. By the result of our study, PASS has a high co-relationship with the paralytic ileus which is the most important adverse event disturbing enteral nutrition. Most of the indices in PASS seemed to be the main causes or the symptoms of paralytic ileus. Abdominal pain, several SIRS parameters and possibility of oral diet are the direct symptoms and conditions of ileus, whereas organ failure indirectly reflects the ACS(abdominal compartment syndrome) which is the complication of paralytic ileus. The use of Morphine is one of the main causes of intestinal paralysis. These are why PASS necessarily had superior value in the prediction of paralytic ileus.

As not expected, we resulted that respiratory rate had nearly same predictive value with PASS-the assessment tool containing several risk factors. The reason why respiratory rate could be selected as the independent risk factor despite it is involved in several multivariate scores like SIRS, PASS, and BISAP is that we declared paralytic ileus with two parameters(abdominal distention, delayed passage of or inability to pass flatus for more than 24 hours), which shows the condition of lung oppression by intraabdominal hypertension. However, in our opinion, rapid respiration in the early periods of acute

pancreatitis is mostly due to intraabdominal hypertension, whereas rapid respiration in the late periods may be followed by the compensatory response to the ventilation disorder due to pneumonia or pleural effusion so that it should not be simply regarded as the indicator of paralytic ileus.

Our study has several limitations. First, we didn't attempt overload nutrition after intestinal paralysis. Some studies claimed remaining of enteral nutrition even with the signs of paralytic ileus during the clinical course[29]. Most of the patients we treated denied to remain enteral feeding after the presentation of ileus. So it is not enough to deny the former theories which emphasized to remain NOEF even after intestinal paralysis. But our trial may be helpful to set safer criteria for enteral feeding. Second problem is that our study contained not enough cohort than needed. We expect larger studies to validate our result.

CONCLUSION

Safe range for NOEF during acute pancreatitis treatment is PASS<120 or respiratory rate<25bpm.

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Conflict of Interest

The authors declare that there is no conflict of interest.

Author Contributions

Kim Song Hwan: study concept and design, acquisition of data, analysis and interpretation of data, drafting of manuscript, and statistical analysis, **Jong Nam Hun:** study concept and design, analysis and interpretation of data, **Kim Hye Song and Yu Nam:** acquisition of data, statistical analysis, **Choe Jong Hwa:** study concept and design, acquisition and interpretation of data, **Ri Un Hui:** acquisition and analysis of data, **Jong Sin Hyok:** critical revision of the manuscript for important intellectual content, **Ri Song Ung:** Administrative and drafting of manuscript, **Ri Chol Su:** acquisition and analysis of data.

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