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"Enteral nutrition in acute pancreatitis: earlier the better- Clinical practice considerations"

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ABSTRACT:

PURPOSE: The aim of the study was to evaluate the need of naso-jejunal feeding in severe acute pancreatitis and to compare starting of early oral feeding in Acute Pancreatitis patients with the scoring systems (RAC and mCTSI)

METHODS: This is a prospective study of 76 patients with AP over a period of 24 months admitted in a tertiary care center in Mumbai. After informed consent and ethical committee clearance, all patients with diagnosis of AP were included. Patients were classified into mild, moderate and severe AP based on RAC and mCTSI scoring. Data was entered in a predesigned proforma. Patients were observed for tolerability of oral feeds.

RESULTS: Based on mCTSI, 41% had severe, 58% had moderate, 1.3% had mild pancreatitis. All 76 patients were started on oral feeds, 80.3% tolerated oral feeds, 19.7% had to be switched to NJ feeds. Among the 61 patients tolerating oral feeds, 2 were severe, 23 moderate and 36 mild according to RAC. Among 15 patients requiring NJ feeds, 14 were severe, 1 moderate according to RAC.

CONCLUSION: There was a significant difference in severity based on RAC and mCTSI. NJ feeds should be preferred for severe of AP as per RAC, and oral feeds can be started in all patients with mild and moderate AP.

KEYWORDS: RAC, mCTSI, AP, NJ.

INTRODUCTION:

Acute pancreatitis (AP) is an acute inflammatory process of pancreas with variable involvement of other regional tissues and remote organ systems. The diagnosis is based on two of the following three criteria: (1) Abdominal pain consistent with pancreatitis; (2) A serum amylase or lipase greater than 3 times upper normal limit; and (3) Characteristic findings from abdominal imaging [1]. The two most common etiologies of AP are gallstones (40%-70%) and alcohol (25%-35%).

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Severe forms characterized by local or systemic complications, may on the other hand be very demanding and associated with severe morbidity, even death, in up to 15-20% [2].

Acute pancreatitis is hyper metabolic state marked by increased energy expenditure, proteolysis, and gluconeogenesis and insulin resistance. Nutritional supplementation in AP becomes complicated due to these diverse pathophysiologic derangements. In past, patients with AP were not given any form of enteral nutrition, because it was believed that any stimulation of the exocrine pancreas would affect the disease course negatively [3]. Now, increasing evidence suggests that enteral feeding maintains the intestinal barrier function and prevents or reduces bacterial translocation from gut [4].

Revised Atlanta classification (2012) was used to classify patients with pancreatitis into mild, moderate, and severe types. The component of organ failure in RAC is based on Modified Marshal scoring [5-7]. Conventionally, contrast-enhanced computer tomography (CECT) is used as gold standard in classifying severity of AP into mild, moderate, and severe using modified CT severity index (mCTSI). Comparison of severity status using revised Atlanta classification at 48 hrs helps in early identification of sick patients more accurately and thus Implementation of intensive treatment [8].

Studies published previously dealt with correlation between Revised Atlanta Classification (RAC) and mCTSI scoring system. [12]

AIMS & OBJECTIVES:

The aim of the study was to evaluate the need of naso-jejunal feeding in severe acute pancreatitis and to compare starting of early oral feeding in Acute Pancreatitis patients with the scoring systems (RAC and mCTSI)

MATERIALS & METHODS:

This is a prospective study of 76 patients with AP over a period of 24 months admitted in a tertiary care Centre in Mumbai. Data was collected after ethics committee approval and informed consent by participants. Patients with upper abdominal pain and tenderness of less than 24 hours duration were admitted directly to our center and after confirming the diagnosis of Acute pancreatitis, were included in our study

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

At admission, diagnosis of pancreatitis was made when two of the following three features were present:

(1) Abdominal pain consistent with AP (acute onset of a persistent, severe, epigastric pain radiating to the back).

(2) Serum amylase/lipase value, at least three times greater than the upper limit of normal.

(3) Characteristic findings of gallstone pancreatitis on ultrasound. [8]

Patients were grouped based on Revised Atlanta Classification. The component of organ failure was according to Modified Marshal Scoring [9]

Patients were classified into mild, moderate and severe acute pancreatitis based on Revised Atlanta Classification (Table 2)

Table 1- Revised Atlanta classification

Class	Definition
Mild acute pancreatitis	i. No organ failure ii. No local or systemic complications
Moderate acute pancreatitis	i. Organ failure that resolves in 48hours and/or ii. Local or systemic complication without persistent organ failure
Severe acute pancreatitis	Persistent organ failure i. Single organ failure ii. Multiple organ failure

As per protocol, patients underwent CT scan after 48hrs of admission and modified CTSI was calculated. [10]

Table 2- Modified CT severity index:

Category		
Pancreatic inflammation	0	Normal pancreas
	2	Intrinsic pancreatic abnormality with or without inflammatory changes in peri pancreatic fat

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

	4	Pancreatic or peri pancreatic fluid collection or peri pancreatic fat necrosis
Pancreatic necrosis	0	None
	2	30% or less
	4	More than 30%
Extra pancreatic complications	2	One or more of pleural effusion, ascites, vascular complications, parenchymal complications, gastrointestinal involvement

Total score is given out of 10 to determine the grade of pancreatitis

• 0-2: mild • 4-6: moderate • 8-10: severe

Patients were classified as mild, moderate and severe based on the mCTSI score (Table 3)

All patients were kept NBM for 24 hours. IV hydration was given during this period. Later all were started on oral sips of clear water. Patients who tolerated oral sips for 24 hours were given oral feeds comprising of coconut water/ fresh fruit juice etc. whereas, those who were unable to tolerate oral nutrition as they experienced increase in abdominal pain and /or vomiting [11], they were started on NJ feeds. Supplemental IV hydration was continued in all the patients till they tolerated full-fledged oral feeds. Trial of oral was given after 3-6 days, depending on improvement in clinical and biochemical parameters.

Patients were observed for any complications, symptomatic relief and mortality till the duration of the hospital stay. Over a period of 24 months, 76 patients who fulfilled our inclusion criteria were included in the study.

Sample Size Calculation

With z of 1.96 and precision of 0.12, using prevalence of 55.8% of Acute Pancreatitis Patients starting successfully on Oral Feeds® [23] using below mentioned formula, the sample size calculated was 65.80.

Thus, it is planned to enroll minimum of 66 cases for the present study, exceeding the number, depending on time frame of the Study.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

$$n = p\left(1 - p\right)\left(\frac{Z}{E}\right)^2$$

Where-

Z: z-statistics for desired level of confidence (i.e., *0.05) (1.96 for 95% CI)*

p: The estimate of Expected proportion with variable of interest in population *(0.558)*

E: The precision level *(0.12)*

Calculations: -

Z	**1.96**	**Z-square**	**3.8416**
P (Proportion)	**0.558**		
1-P	**0.442**		
E	**0.120**	**E-square**	**0.0144**
P X (1-P)	**0.246**		
Z^2 X [P X (1-P)]	**0.95**		
Sample Size (n)=	**65.80**		

(http://sphweb.bumc.bu.edu/otlt/MPH-Modules/BS/BS704_Power/BS704_Power4.html)

Statistical Analysis:

Qualitative data was represented in form of frequency and percentage. Among Qualitative data, **Nominal data** included *Gender of Cases enrolled, Comorbidities, Type of Feed (Oral, NJ Tube), etc.* Among Qualitative data, **Ordinal data** included *Clinical Severity Score (Revised Atlanta Classification) and Radiology Score (mCTSI) and* was represented using in form of frequency and percentage. Quantitative data was represented using Mean ± SD and Median & IQR (Interquartile range). Quantitative data included *age and day of starting Oral Feeds in Acute Pancreatitis or insertion of NJ tube*.

Comparison of Quantitative data measured between qualitative variable with **more than two sub-groups** was done using One Way Analysis of Variance, if the data passes 'Shapiro–Wilk test

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Normality test' or by Kruskal-Wallis One Way Analysis of Variance on Ranks if the data fails 'Shapiro–Wilk test Normality' test. If p-value of One-Way Analysis of Variance or Kruskal-Wallis One Way Analysis of Variance on Ranks was statistically significant, Tukey HSD test or Dunn's post hoc test for pair-wise comparison was applied for ANOVA and Kruskal-Wallis ANOVA respectively **(e.g., Comparison of day of starting Oral Feeds by Clinical Severity of Acute Pancreatitis (Mild, Moderate, Severe)).**

Correlation between Quantitative data was done by using Pearson product-moment correlation, if the data passed 'Shapiro–Wilk test Normality test' or by Spearman's rank correlation, if the data failed 'Shapiro–Wilk test Normality' test **(Correlation between day of starting Oral Feeds by Clinical Severity of Acute Pancreatitis (mild,moderate,severe).**

Results were graphically represented where deemed necessary.

Microsoft Excel, included in Office 365 package, was used for data entry, compilation, grouping of quantitative data and rectification of typographic errors and PSPP version 1.6.2 (1st July 2022 release) was used for statistical analysis. Graphical representation was done in Microsoft Excel. An alpha value (p-value) of <=0.05 was used as the cut-off for statistical significance.

RESULTS:

The mean age of the patients was 41 years (ranging between 22 and 71) and majority (35.5%) of patients were in age range of 42-51 yrs.

In our study 64.5 % patients were females.

Patients were classified based on the Revised Atlanta Classification into mild, moderate and severe.

According to the RAC, out of 76 patients 36 were mild (47.4%), 24 were moderate (31.6%) and 16 of them were severe (21.1%). (Table 3)

Based on the mCTSI grading (Table 4) 31 of 76 patients had severe pancreatitis (41%), 44 out of 76 had moderate pancreatitis (58%).1 out of 76 had mild pancreatitis (1.3%).

Table 3: RAC and mCTSI scoring of the patients

RAC	Frequency
Mild	36 (47.4%)

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Moderate	24 (31.6%)
Severe	16 (21.1%)
Total	76 (100%)
mCTSI	
Mild	1 (1.3%)
Moderate	44 (57.9%)
Severe	31 40.8%)
Total	76 (100%)

Table 4: Oral feeds tolerated in AP patients

Oral feeds tolerated	Frequency
Yes	61 (80.3%)
No	15 (19.7%)
Total	76 (100%)

All patients were started on oral feeds. Of them, 61 out of 76 (80.3%) tolerated oral feeds within 24 hours and 15 (19.7 %) had to be started on NJ feeds. (Table 2)

Table 5: Feeding tolerated according to Revised Atlanta Classification

RAC/Oral feeds tolerated	Yes	No	Total
Mild	36	0	36
Moderate	23	1	24
Severe	2	14	16
Total	61	15	76

Among 61 patients who tolerated oral feeds, 2 were severe, 23 were moderate and 36 were mild according to RAC.

Among 15 requiring NJ feeds, 14 were severe according to RAC (93%), 1 was moderate (7%).

Table 6: No. of days NJ feeds were given (total 15 patients)

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Atlanta score/ No. of days	<7days	7-14days	>14days	Death	Total patients
Moderate	1	0	0	0	1
Severe	2	8	2	2	14
Total patients	3	8	2	2	15

Among the 15 patients requiring NJ feeds, 3 (20%) patients were able to tolerate oral feeds by 7th day, 8 tolerated oral feeds by 14th day (53%). 2 (13%) succumbed to pancreatitis on NJ feeds after being kept on mechanical ventilation (Table 6). Among severe AP patients, those who were in transient organ failure were treated accordingly, 2 who had persistent organ failure had to be kept on mechanical ventilation.

Table 7: Comparison of Revised Atlanta Classification vs modified CT severity score

mCTSI * Revised Atlanta Classification Crosstabulation						
			Revised Atlanta Classification			**Total**
			1)Mild	**2)Moderate**	**3)Severe**	
mCTSI	**1)Mild**	**Count**	1	0	0	1
		% within CTSI	100.0%	.0%	.0%	100.0%
	2)Moderate	**Count**	35	9	0	44
		% within CTSI	79.5%	20.5%	.0%	100.0%
	3)Severe	**Count**	0	15	16	31
		% within CTSI	.0%	48.4%	51.6%	100.0%
Total		**Count**	36	24	16	76
		% within CTSI	47.4%	31.6%	21.1%	100.0%

Of the 60 patients that were clinically mild and moderate based on the Revised Atlanta Classification, 45 patients were Mild & Moderate pancreatitis according to modified CTSI and 15 were severe. Of the 31 patients who were classified as severe according to mCTSI, only 16 of them were clinically severe as per RAC and the rest 15 were clinically moderate.

Mc Nemar-Bowkers Test applied to the above table gives a significant value of 1.39E-011 which suggests that the two scoring systems are significantly discordant with each other.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

Table 8: Tolerability of oral feeds according to Revised Atlanta Classification

mCTSI * Revised Atlanta Classification * Oral feeds tolerated Cross tabulation							
Oral feeds tolerated				**Revised Atlanta Classification**			**Total**
				1)Mild	**2)Moderate**	**3)Severe**	
1)YES	**mCTSI**	**1)Mild**	**Count**	1	0	0	1
			% within CTSI	100.0%	.0%	.0%	100.0%
		2)Moderate	**Count**	35	9	0	44
			% within CTSI	79.5%	20.5%	.0%	100.0%
		3)Severe	**Count**	0	14	2	16
			% within CTSI	.0%	87.5%	12.5%	100.0%
	Total		**Count**	36	23	2	61
			% within CTSI	59.0%	37.7%	3.3%	100.0%
2)NO	**mCTSI**	**3)Severe**	**Count**		1	14	15
			% within CTSI		6.7%	93.3%	100.0%
	Total		**Count**		1	14	15
			% within CTSI		6.7%	93.3%	100.0%

On cross tabulation of the RAC and mCTSI and tolerability of oral feeds it was found that 15 patients who were severe on CTSI did not tolerate oral feeds, whereas other 16 classified as severe on mCTSI could tolerate oral feeds. 2 who were severe as per RAC could tolerate oral feed whereas 14 patients who were severe on RAC did not tolerate oral feeds.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

McNemars test applied to the above table gives a value of 2.29E-011 which is statistically significant. The above table suggests that oral feeding can be started based on the RAC as 35 who were moderate on mCTSI but mild on RAC tolerated oral feeds after admission and 14 who were severe on mCTSI and moderate on RAC also tolerated oral feeds. So RAC is a better predictor of the status and management of the patient as compared to mCTSI.

DISCUSSION:

The patients in the present study were in the age range of 22-71 and mean age of 41yrs. A similar Study by Padu et al [12] has age range of 23 to70 years. Mean age was 44.73 ± 11.61 years. The mean age was 42.9 ± 15.9 years (range: 18–80 years) in a study by Raghu et al [13], that correlates best with our study.

In our study female: male ratio was 1.8:1 which is similar to Padu et al [12] and Malik et al [14].

Also our study correlates well with the Espen recommendations which are as follows [15]

1- Patients with AP should be considered at moderate to high nutritional risk, because of the catabolic nature of the disease and because of the impact of the nutritional status for disease development.

2.Oral feeds should be offered as soon as clinically tolerated and independent of serum lipase concentrations in patients with predicted mild AP. [Grade of Recommendation A]

In accordance with the same in our study all patients were started on oral feeds. Of them, 61 out of 76 (80%) tolerated oral feeds. Remaining 15 were switched to NJ feeds (20%).

AP is graded as mild, moderate and severe based on Revised Atlanta Classification. Various studies comparing enteral nutrition (EN) with parenteral nutrition (PN) have shown that enteral feeding is better than PN or equally effective, is cheaper, and has fewer complications. Enteral nutrition is important in restoring and, if provided early, probably preventing morphologic changes in the intestine. [2] This may significantly reduce the development of late complications. This prospective study evaluates whether there is need of NJ feeds in all cases of severe AP and intends to establish the association between RAC and mCTSI and the days to start oral feeds.

In our study of 76 patients, we observed that despite mCTSI being severe, RAC was moderate in 15 patients. mCTSI is an objective score based solely on radiology, whereas RAC is an objective classification taking into consideration clinical, radiological and biochemical parameters. So, RAC appeared more relevant compared to mCTSI.

ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

In our study 78.9% of the patients were mild/moderate pancreatitis as per RAC and only 21.1% were severe pancreatitis. This is in accordance with the fact that several studies of acute pancreatitis have reported that most patients (70 to 80%) have mild/moderate disease. [16].

These findings are similar to the study by Pongprasobchai *et al* [17] who also found the distribution of AP as 72%, 16%, and 12% as mild, moderate, and severe AP, respectively, as per RAC.

RAC can be used as a basis for this clinico-radiological-biochemical classification. Giving oral feed trial to all the patients and introducing NJ tube in only those who could not tolerate oral feeds, would reduce the need for an invasive procedure and reduce the complications associated with the insertion of tubes; thus, reducing the hospital stay and early return to work. For severe AP patients as per RAC, NJ feeds should be preferred upfront.

CONCLUSION:

1. There was a statistically significant difference in the severity based on RAC and mCTSI.
2. NJ feeds should be preferred over oral feeds for patients who were severe as per RAC.
3. There is moderate linear correlation between severity of acute pancreatitis and the number of days to resume oral feeds.
4. Patients tolerating oral feeds are less likely turn severe, and vice versa and the results are statistically significant.

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ISSN: 0975-3583,0976-2833 VOL14, ISSUE 08, 2023

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ABBREVIATIONS:

NJ- NASOJEJUNAL

AP- ACUTE PANCREATITIS

RAC- REVISED ATLANTA CLASSIFICATION

mCTSI- MODIFIED CT SEVERITY INDEX

CT- COMPUTERISED TOMOGRAPHY

EN- ENTERAL NUTRITION

PN- PARENTERAL NUTRITION

NBM- NIL BY MOUTH

IV- INTRAVENOUS