



# Nil per os or Enteral Nutrition in Mild and Moderately Severe Acute Pancreatitis: A Case Series

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## Abstract

**BACKGROUND:** There are controversies regarding the treatment of mild-to-moderate pancreatitis, especially when comparing the efficacy of *nil per os* regime versus the nasogastric feeding. While some sources suggest the benefits of the nasogastric feeding, there are meager data available toward the impact of the selected treatment vis-à-vis the length of hospital stay, and as of the final outcome.

**AIM:** Authors collected data from two subgroups (treated with *nil per os* regime or nasogastric feeding, respectively) with the aim to define a safe and more efficacious regime.

**METHODS:** This case series collection was carried out in the University Hospital Center in Tirana (UHC) at the Service of Gastroenterology. The period of the study was January 1, 2018–December 31, 2019. The patients were divided into two subgroups (the control group had a *nil per os* regime and patients in the intervention group received a nasogastric feeding) according to approved inclusion and exclusion criteria.

**RESULTS:** Twenty subjects were allocated to the control group and 21 subjects were allocated to the intervention group. The length of hospital stay in the control group was 10.2 days compared with 8.4 days in the intervention group ( $p < 0.05$ ). The days' average spent with pain was 4.5 in the control group and 3.14 in the intervention group ( $p < 0.05$ ). Oral feeding begun approximately 5.45 days since the admission in the control group and 3.14 days in the intervention group ( $p < 0.05$ ). Oral food intolerance occurred in 6 patients (30%) in the control group and in one patient in the intervention group (4.8%) ( $p < 0.05$ ).

**CONCLUSIONS:** Nasogastric feeding seems to have significant benefits in the treatment of mild to moderate acute pancreatitis, when compared with the *nil per os* regime. Nasogastric feeding reduces length of stay in hospital and improves early the clinical outcomes.

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## Introduction

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas, with an increasing incidence [1].

AP has a rapid onset, ranging from mild, moderately severe, to severe AP. In 80% of cases, it is a self-limiting disease, and patients are discharged after 5–6 days. About 20% of patients have severe AP, with a significant mortality of 15% [2], [3].

Actually, there is no specific therapy for the treatment of AP. Most patients with interstitial pancreatitis recover with conservative treatment, which may include nothing by mouth status, fluid resuscitation, and pain management early adequate treatments and nutritional support have improved the outcomes [4], [5].

In 1990, total parenteral nutrition and pancreatic rest were standards of nutritional AP management, with the rationale to put the pancreas at rest, thus reducing the pancreatic exocrine secretion and meet nutritional needs [6].

Later studies demonstrated that the intestinal mucosa undergoes atrophy during oral fasting, which would induce bacteria translocation in gastrointestinal tract and cause pancreatic necrotic tissue infection [7].

There are several studies on the role of nutrition in AP; most of them are supporting the current guidelines that enteral nutrition is generally preferred over parenteral nutrition (PN), or at least enteral nutrition (EN) should be initiated first, if possible. According to the International Consensus Guidelines Committee, EN is generally preferred over PN, or at least, EN should be initiated first [8], [9], [10].

According to the American College of Gastroenterology, EN is recommended in SAP to prevent infectious complications. PN should be avoided unless the enteral route is not available, not tolerated, or not meeting caloric requirements [11]. Patients with SAP may have enteral feeding by the nasogastric (NG) or nasojejunal (NJ) tube [11].

A recent Cochrane Systematic Review on enteral nutrition versus total parenteral nutrition shows that enteral nutrition significantly reduced mortality,

multiple organ failure, systemic infections, and the need for operative interventions in patients with acute pancreatitis compared with those who had total parenteral nutrition [12], [13].

On the other hand, a recent study did not show the superiority of early nasoenteric tube feeding, as compared to an oral diet after 72 h, in reducing the rate of infection or death in patients with severe acute pancreatitis at high risk for complications [14].

The majority of studies focus on SAP, so we do not exactly know what are the modality and requirement for nutritional support in mild and moderately severe acute pancreatitis [15].

Another randomized trial, comparing nasogastric feeding (NGF) with a conventional *nil per os* regimen (NPO) in patients with mild and moderately severe acute pancreatitis, has been published [16].

The finding of this study shows that NGF commenced within 24 h of hospital admission is well tolerated in patients with mild-to-moderate acute pancreatitis. Compared with NPO, NGF significantly reduces the intensity and duration of abdominal pain, need for opiates, and risk of oral food intolerance, but not overall hospital stay [16].

In Albania, the modality for putting the pancreatic rest is either *nil per os* or nasogastric feeding and still there is not any clinical trial to compare this regime in the medical and patient perspective in the mild and moderately severe acute pancreatitis.

Thus, the aim of our study is to determine the effect of NGF versus NPO on the patient with mild and moderately severe acute pancreatitis in the length of stay on hospital, pain reduction, need for opiates, and tolerance on oral feeding.

## Materials and Methods

### Study aim and design

We collected data from two subgroups (treated with *nil per os* regime or nasogastric feeding, respectively) with the aim to define a safe and more efficacious regime.

The study was designed as a case series collection and it has been carried out in the University Hospital Center in Tirana (UHC) at the Service of Gastroenterology. The period of the study was January 1, 2018–December 31, 2019.

The inclusion criteria were:

- Diagnosis of mild and moderately severe acute pancreatitis based on Atlanta revised criteria [17]
- A written informed consent

The exclusion criteria

- Age < 18 years
- Pregnant women or breastfeeding
- Malignancy
- Post-ERCP pancreatitis
- Symptoms for more than 96 h

Patients were randomly assigned into 1:1 ratio either to *nil per os* regime or to nasogastric feeding regime initiated within 24 h after the randomization. The study coordinator, with the use of sealed number envelopes, performed the randomization. To blind the allocation process, we used a block of four and six, generated by computer. The patient or their legal representatives provided the written informed consent.

### Study protocol

The management of patients in the trial and the clinical decision was responsibility of treating team, which was independent from the principal investigator.

The patients assigned to the *nil per os* did not receive nutrition other than intravenous fluids during the first 72 h. The patients who had been assigned to nasogastric feeding received a nasogastric feeding which initiated within 24 h of randomization. The nasogastric feeding started with 20 ml/h and increased gradually up to 100 ml/h within 48 h. The duration of the nasogastric feeding and the beginning of the oral feeding were decided by treating team. Therefore, the treating team was responsible for the defining the cases with progress toward the severe acute pancreatitis.

### Outcomes

The primary outcome is the length of stay at hospital. In addition, the secondary outcomes included:

- Need for opiates.
- Progression disease severity (mild acute pancreatitis to moderately severe acute pancreatitis, and progression of moderately severe acute pancreatitis to severe acute pancreatitis according to Atlanta revised criteria).
- Time (in days) from admission until the day without pain (visual analog scale: VAS  $\leq 2$ ) (intensity of pain was assessed using VAS score at rest).
- Intolerance during the beginning of the oral feeding (relapse of pain, nausea, and vomiting)
- Time (in days) from the admission to the beginning of the oral feeding

### Statistical analysis

All data were analyzed with the SPSS. Continuous variables were expressed as mean  $\pm$  SD if

they were normally distributed or median and interquartile range if they were not normally distributed (as it was investigated at Kolmogorov–Smirnov test). Categorical variable was expressed as frequency. It is used Mann–Whitney, t-test, or Chi-square test for comparing the groups regarding the baseline characteristic and the interested outcomes. The survival analysis (Kaplan–Meier technique) is used to assess the effect of the each regime on duration of the pain.  $p < 0.05$  was considered statistically significant.

## Results

During the study period, 87 patients were admitted to the Service of Gastroenterology, UHC of Tirana. Of these, only 41 subjects had fulfilled the criteria regarding the participation in the study and had given the written informed consent.

After the randomization, we allocated 20 subjects to the control group (NPO) and 21 subjects to the intervention group (NGF). None of the participants left the study (Figure 1).

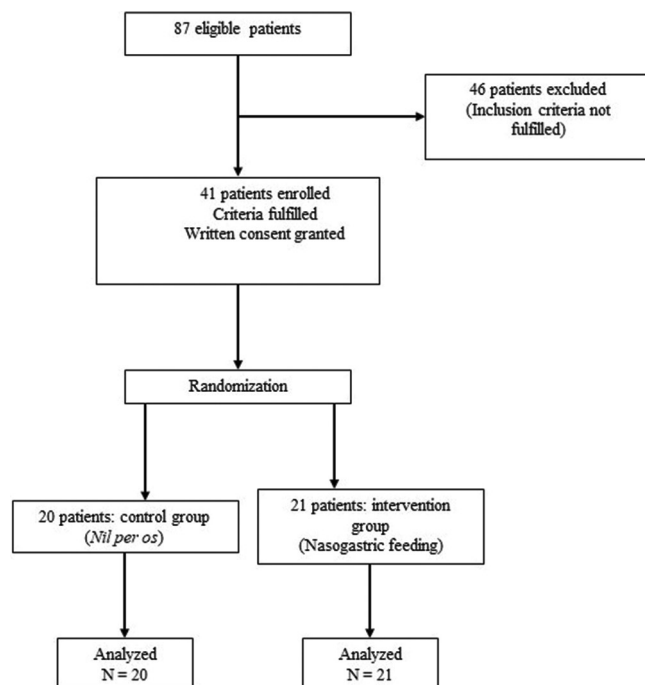


Figure 1: Patients allocated into two groups (nil per os and NGF).

As shown in Table 1, the study groups do not have significant difference regarding the baseline demographic characteristics (age and sex) and etiology and clinical characteristic. The median of age for the control group (NPO) is 50 years old, meanwhile, the median of the other group is 47 and the difference was not significant as it was investigated in Mann–Whitney U-test. In addition, both groups had the same model of sex and etiology of acute pancreatitis distribution. The most frequently etiology of acute pancreatitis in

both groups was the alcoholic etiology. At the baseline, the two groups did not have any significant difference regarding the intensity of the pain assessed using the VAS score at rest.

Table 1: Baseline characteristics of the two groups

Characteristics in baseline	NPO	NGF	p
Sex, n (%)			
Male	14 (70)	15 (71.5)	>0.05*
Female	6 (30)	6 (28.5)	
Etiology of pancreatitis, n (%)			
Biliary	7 (35)	8 (38.1)	>0.05*
Alcohol	9 (45)	9 (42.9)	
Other	4 (20)	4 (19)	
Age (years), median (IQR)	50 (16)	45 (17)	>0.05 <sup>^</sup>
VAS (score), median (IQR)	8 (2)	8 (2)	>0.05 <sup>^</sup>

\*Chi-square, <sup>^</sup>Mann–Whitney U-test. NPO: Nil per os, NGF: Nasogastric feeding, VAS: Visual analog scale, IQR: Interquartile range.

The length of hospital stay in NPO was 10.2 days compared with 8.4 days in NGF group (in t-test,  $p < 0.05$ ). The average of days spent with pain was 4.5 days in the control group and 3.14 days in the intervention group (t-test,  $p < 0.05$ ). Oral feeding was introduced approximately 5.45 days after the admission in the NPO group and after 3.14 days in the NGF groups (t-test,  $p < 0.05$ ). Oral food intolerance presented with pain, nausea/vomiting occurred in 6 patients (30%) among the NPO group, but only in one patient in the intervention group (4.8%) ( $p < 0.05$ ) (Table 2).

Table 2: The interested outcomes according to the group

Interested outcomes	NPO (mean)	NGF (mean)	p*
Length of stay at hospital (days)	10.2	8.4	<0.05
Time until pain free (VAS $\leq 2$ ) (days)	4.5	3.14	<0.05
Time until to oral feeding (days)	5.45	3.8	<0.05

\*t-test. NPO: Nil per os, NGF: Nasogastric feeding, VAS: Visual analog scale.

The use of the NGF decreased significantly the need for opiates after 72 h of randomization. Only two patients had been in need for opiates among the NGF groups compared with 7 (35%) patients of the NPO group. The progression toward the severe acute pancreatitis occurred in one patient in the NGF group and two patients in the NPO group but this difference in frequency was not significant ( $p > 0.05$ ) (Table 3).

Table 3: The interested outcome according to the group

Interested outcomes	NPO, n(%)	NGF, n (%)	p*
Need for opiates after 72 h	7 (35)	2 (9.5)	<0.05
Intolerance food	6 (30)	1 (4.8)	<0.05
Progression toward severe pancreatitis	2 (10)	1 (4.8)	>0.05

\*Chi-square. NGF: Nasogastric feeding, NLP: NPO: nil-per-os regime.

In Figure 2, we show the graphic presentation of the effect of type of the nutrition regime on the time until minimal or no pain. The Kaplan–Meier analysis indicated that all patients belonged to NGF group had minimal or no pain within 5 days and the patients belonged to the NPO had minimal or no pain at all within 8 days. This time for each group differ significantly (log rank  $p < 0.05$ ).

## Discussion

To the best of our knowledge, this study is the first attempt to compare the effect of the nutrition

regimes on the mild and moderately severe pancreatitis in Albanian hospital setting. Design of the study as a proper randomized clinical trial adds more value to the finding of the study.

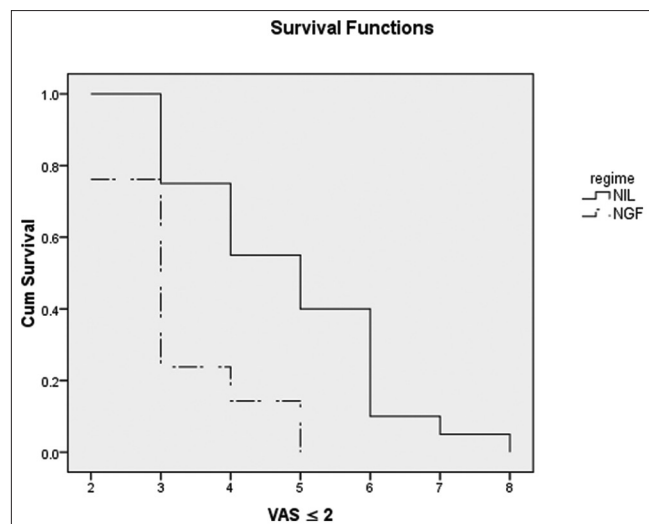


Figure 2: Kaplan-Meier analysis for the effect of regime the time to minimal or no pain in two groups

It is important to mention from the beginning of the discussion session that the vast majority of the available studies are focused on severe acute pancreatitis, which make more difficult to compare our finding with other studies.

The study indicates that use of the NGF since from the admission reduces significantly the length of hospital stay among the patients with mild and moderately severe pancreatitis. Sources suggest that enteral nutrition, when started 24 h after hospital admission, will reduce complications, the length of stay, as well as the mortality among patients presenting with acute pancreatitis [18].

This trial shows that the use of NGF reduces significantly the rate of the need for opiates in patients and number of the day with pain (VAS >2) when it is compared with NPO regime. This is consistent with the finding of the other studies that putting the pancreatic to rest promotes decreasing of pain level and accelerates healing [16], [19].

Further, the NGF reduces the days when patient are restricted from *per os* feeding, and even more reduce the risk for oral food intolerance. This finding is consistent with the conclusions of other reports, suggesting that NGF decreases the risk for oral food intolerance [16]. As shown, the intestinal mucosa undergoes atrophy during oral fasting, which would induce bacteria translocation in gastrointestinal tract and cause pancreatic necrotic tissue infection [12]. Thus, the principle of nutritional support is that pancreatic stimulation should be reduced to basal rates, but the gut integrity should be maintained and that the stress response should be contained to reduce the likelihood of the multiorgan failure, nosocomial infections [16], [19].

Thus, early introduction of the oral feeding will prevent the bacteria translocation and furthermore the systemic infections which are considered the major complication of the acute pancreatitis [6].

The type of nutrition does not affect the progression of the mild acute pancreatitis to moderately severe acute pancreatitis and severe acute pancreatitis as the percentage of progression is not different among the groups. These data are consistent with some of the conclusions found in the literature review process [16], [18], [19], [20]. Overall, there is still controversy and debates remain open, with some authors denoting a clear supremacy of the enteral route of nutrition [21], [22]. Other sources found enteral nutrition and total parental nutrition as comparable toward efficacy: Here again, we are dealing with an acute condition and of particular severity [23].

The above findings have an important practical implication from both perspectives. From the patient perspective, it affects and improves the quality of life as the patients have a shorter time under pain and restricted on oral feeding.

From the medical perspective, NGF regime reduces significantly the length of hospital stay and need of the opiates, which means the reducing of the financial cost for the each inpatient. In addition, the shorter time of the restricted no oral feeding implicates both perspectives. From the patient perspective, early oral feeding improves the patient's quality of live and from the medical perspective; the early oral feeding prevents the development of short time complication of long restriction of oral feeding.

## Conclusions

When compared with *nil per os*, the use of nasogastric feeding among the patients with mild and moderately severe acute pancreatitis after admission is well tolerated, improves their quality of life, and reduces the length of hospital stay. Both types of nutrition do not affect the progression to severe form of diseases. However, the results of our study need confirmation with larger studies, focused on the issue of the nutrition on the management of the mild and moderately severe pancreatitis.

## Ethical Statement

Service of Gastrohepatology, UHC of Tirana, has approved the study in accordance with institutional regulations in place.

## Authors' Contribution

FK and SX wrote the initial draft of the manuscript and conceived the study. AB mentored the study and the manuscript preparation. GV edited the final version. All authors have seen and approved the submitted manuscript.

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