

# A “TAILORED” STEP-UP APPROACH FOR MODERATE TO CRITICAL ACUTE PANCREATITIS IN LATE PHASE: A COHORT STUDY

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## Study Protocol

The Investigators retrospectively analyzed data of all patients treated at our referral Center for moderate to critical AP, as classified by Determinant-Based Classification of Acute Pancreatitis Severity (DBC). Patients treated with interventional or surgical procedures after 4 weeks (late phase) were included in the study, while patients who had undergone conservative treatment, or who has been operated within 4 weeks (early phase) were excluded from the data analysis.

The cohort sample was divided into four groups, according to the first type of the interventional or surgical management performed: percutaneous drainage group (PD), endoscopic approach group (END), surgical internal derivation of WON group (INT), and surgical necrosectomy group (NE). In all cases, the decision to intervene with an invasive procedure was taken on the basis of a clinical course not responsive to conservative management, signs of sepsis due to infected necrosis, or persistent gastric output obstruction with large fluid collections. The operative approach was chosen based on our experience and on the current Literature evidence, using a “tailored” *step-up* approach.

The acute pancreatitis severity was retrospectively graded according to the DBC, based on data drawn from clinical records.

All the procedures had been performed by surgeons, gastroenterologists/endoscopists, or interventional radiologists who composed the multidisciplinary group.

In performing primary PD, catheters up to 16 Fr were inserted using Seldinger technique, guided by ultrasound (US) or Computer Tomography (CT).

In the END approach, a lumen apposing HOT AXIOS™ (Boston Scientific, Boston, MA, USA) 15 x 10 mm metal stent was placed trans-luminally by echo-endoscopic guidance, under conscious sedation. The procedure was completed with the insertion of a naso-cystic catheter to facilitate liquefaction of debris. Further endoscopic sessions and trans-luminal necrosectomy were considered case by case.

Surgical internal derivation throughout gastric or enteric breach, adopted since 2014, was considered in the case of WON with mature walls. When the WON was not adjacent to the stomach or showed necrosis in its inferior portion, the enteric Roux-en-Y derivation was selected. However, in the vast majority of cases, trans-gastric necrosectomy and internal derivation were carried out. Firstly, a US-guided anterior gastrotomy was performed. Then, large communication up to 80 mm was created between WON and the posterior gastric wall using a mechanical stapler; finally, the necrotic debris was removed from the WON' cavity. At our Center, since 2017, a minimally invasive variant of this

approach has been performed using the da Vinci Xi robot (Intuitive Surgical Inc., Sunnyvale, CA, USA).

The NE was performed either in case of failure of endoscopic/percutaneous drainage or as a first-line treatment. It was accomplished by standard trans-peritoneal laparotomy and continuous post-operative lavage or by retroperitoneal US-guided mini-laparotomic approach, depending on the distribution of the necrotic tissue. When it was applicable, the infra-mesocolic approach was preferred. The standard trans-peritoneal NE was performed in a supine position. The retroperitoneal US-guided mini-laparotomic approach was performed in lateral decubitus: the US-guidance allowed to perform a focused right or left flank mini-laparotomy, and to obtain complete debridement using long instruments, through the retroperitoneal way.

The following variables were evaluated: sex, age, severity of inflammation according to the DBC classification, PA etiology, CT scan severity index according to Balthazar criteria, clinical prognostic score using bedside index of severity of acute pancreatitis (BISAP) score.

Total length of hospitalization, operative management, necrosis cultures, total and post-interventional Intensive Unit Care (ICU) were also recorded and analyzed together with the in-hospital morbidity, mortality and re-admissions.

Patients were checked after discharge within 14 days and followed monthly as outpatients by gastroenterologists. A CT scan was performed within 4 months, or before in case of recurrent symptoms. During the follow-up, the English Standard Short Form 36 (SF-36) questionnaire was used to evaluate the general quality of life at three and six months, one and two years. The SF-36 examines 8 areas consisting of social and physical function, physical and emotional well-being, bodily pain, vitality, mental health and overall general health perception. At the six-month follow-up, the patients also completed a specific questionnaire about the pancreatic function [10]. In particular, the total score takes in consideration abdominal pain using visual analogue pain score, diarrhea, unintentional weight loss, new onset of diabetes and use of enzyme supplementation. The score ranges between zero to five (all symptoms present).

The work has been reported in line with the STROCCS criteria.

### *Statistical analysis*

For the data analysis, the Chi-square test was used to define associations between categorical factors and surgical groups. Continuous variables with normal distribution were expressed as mean  $\pm$  standard deviation (SD) and compared using the ANOVA test. Variables with an abnormal distribution were expressed as median and compared using the Kruskal-Wallis Test. A p-value  $\leq 0.05$  was considered

statistically significant. The statistical analysis was performed using SPSS (Statistical Production and Service Solution for Windows, SPSS Inc., Chicago, IL, USA), version 24.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required