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# PEI-QUESTIONNAIRE

**A patient reported outcome questionnaire that ensures accurate & optimal treatment dosage in Pancreatic Exocrine Insufficiency.**

**Collects patient input on symptoms and impacts[1]**

**Aids treatment decisions[1]**

**Monitors disease severity in clinical practice[1]**

**Backed by rigorous scientific support[2,3]**

**Extensive literature review[2]**

**Expert physicians' interview**
(10 experts from Germany, France, and UK)[2]

**Validated through cognitive debriefing with patients**
(37 patients with PEI from Germany, France, and UK)[2]

**Assessed feasibility with physicians** (3 experts)[2]

A supportive tool to aid the diagnosis of Pancreatic Exocrine Insufficiency.

**Scan the OR code to Experience PEI Q**

**References:** 1. Joshi SR, Chowdhury S, Dharmalingam M, Bhandari S, Deshmukh V, Cruz MD, Farishta F. Prevalence of Pancreatic Exocrine Insufficiency among Patients with Diabetes Mellitus in India. The Journal of the Association of Physicians of India. 2023 Jul 1;71(7):11-2. 2. Johnson CD, Arbuckle R, Bonner N, Connett G, Dominguez-Munoz E, Levy P, Staab D, Williamson N, Lerch MM. Qualitative Assessment of the Symptoms and Impact of Pancreatic Exocrine Insufficiency (PEI) to Inform the Development of a Patient-Reported Outcome (PRO) Instrument. Patient. 2017 Oct;10(5):615-628. 3. Johnson CD, Williamson N, Janssen-van Solingen G, Arbuckle R, Johnson C, Simpson S, Staab D, Dominguez-Munoz E, Levy P, Connett G, Lerch MM. Psychometric evaluation of a patient-reported outcome measure in pancreatic exocrine insufficiency (PEI). Pancreatology. 2019 Jan;19(1):182-190

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## SUMMARY



## EDITORIAL

**Dear Reader,**
**Pancreoscopie Online editorial team is pleased to present the detailed analysis of articles dealing with pancreas disease management.**

### In terms of biomarker:

A study, published in “BMC Gastroenterology”, provides evidence for the significance of serum albumin as a prognostic biomarker in acute pancreatitis (AP), especially in predicting sustained organ failure and mortality. This insight has the potential to improve the care and outcomes of individuals with AP. Another retrospective study, published in “Immunity, inflammation and disease”, has been conducted in order to identify promising biomarkers for predicting the occurrence and survival outcome of severe AP patients. The CRP, triglycerides and glucose (TyG) index, coagulation index (Von willebrand factor antigen [vWF:Ag] and D-dimer values on admission may be potential clinical predictors of the development of severe AP. Moreover, TyG index and vWF:Ag may be helpful to predict Survival outcome, and their combination showed excellent performance in prognosis prediction.

## In terms of medical treatment:

A retrospective monocentric study, published in "Diabetology & Metabolic Syndrome", demonstrates that pancreatic enzyme replacement therapy (PERT) prescription seems associated with an improvement in gastro-intestinal disorders, but not in relevant hypoglycemia rate, with the possible exception of subjects with chronic pancreatitis (CP). In this study, if PERT prescription was safe in subjects with diabetes, PERT higher dosage tended to associate with stronger effects on gastro-intestinal disorders. Hence, exocrine pancreatic insufficiency should be sought for in subjects with diabetes and gastro-intestinal disorders, and PERT prescribed when appropriate. On the other hand, it is well known that use of immune checkpoint inhibitors (ICIs) is a substantial impact in the treatment of numerous advanced malignancies. A review of literature, published in "Alimentary Pharmacology & Therapeutics", had focused on the diagnostic and therapeutic management of gastrointestinal, pancreatic and hepatic toxicities induced by ICI use. It appears that gastrointestinal and hepatic toxicities from ICI use manifest across organ systems. Given the potential for multiple Immune-related adverse events (irAEs) to be fatal or cause significant morbidity, as multiple gastrointestinal irAEs present with overlapping symptoms, and as the oncologic indications for ICI use expand, recognition of potential toxicities with prompt evaluation and treatment are essential for clinicians.

## In terms of surgical treatment:

A study, published in "BMC Gastroenterology", shows that pancreaticoduodenectomy (PDE) and duodenum-preserving pancreatic head resection (DPPHR) are both safe methods in the treatment of CP localized in the head of the pancreas. Over-all mortality in this study was 3%, in-hospital mortality in PDE group was 5%, and mortality after DPPHR was 0%. DPPHR was also superior in the operative time. Another important multicenter randomized trial, published in "Annals of Surgery", demonstrates that postponed catheter drainage, using antibiotics, may be seen as the preferred approach when treating patients with infected necrotizing pancreatitis. On the other hand, delaying drainage seems to reduce the number of interventions and offer the opportunity to effectively treat patients with antibiotic treatment only without increased risk for adverse long-term outcomes. Finally, training for surgeons is essential and a recent study, published in "BMC Surgery", shows that to stabilize the surgical outcome of open pancreaticoduodenectomy for malignant disease, at least 20 surgeries should be performed at a certified institution during surgeon training.

We hope you enjoy reading this detailed analysis of articles dealing with pancreas disease management.

*The Pancreoscopie Online editorial team*

# LONG-TERM OUTCOME OF IMMEDIATE VERSUS POSTPONED INTERVENTION IN PATIENTS WITH INFECTED NECROTIZING PANCREATITIS (POINTER): MULTICENTER RANDOMIZED TRIAL

Source : Van Veldhuisen, Charlotte L et al. Annals of Surgery 2024; 279(4): 671-8


## ABSTRACT

### Objective

To compare the long-term outcomes of immediate drainage versus the postponed-drainage approach in patients with infected necrotizing pancreatitis.

Background In the randomized POINTER trial, patients assigned to the postponed-drainage approach using antibiotic treatment required fewer interventions, as compared with immediate drainage, and over a third were treated without any intervention.

### Methods

Clinical data of those patients alive after the initial 6-month follow-up were re-evaluated. The primary outcome was a composite of death and major complications.

### Results

Out of 104 patients, 88 were re-evaluated with a median follow-up of 51 months. After the initial 6-month follow-up, the primary outcome occurred in 7 of 47 patients (15%) in the immediate-drainage group and 7 of 41 patients (17%) in the postponed-drainage group (RR 0.87, 95% CI 0.33-2.28; P=0.78). Additional drainage procedures were performed in 7 patients (15%) versus 3 patients (7%) (RR 2.03; 95% CI 0.56-7.37; P=0.34). The median number of additional interventions was 0 (IQR 0-0) in both groups (P=0.028). In the total follow-up, the median number of interventions was higher in the immediate-drainage group than in the postponed-drainage group (4 vs. 1, P=0.001). Eventually, 14 of 15 patients (93%) in the postponed-drainage group who were successfully treated in the initial 6-month follow-up with antibiotics and without any intervention remained without intervention. At the end of follow-up, pancreatic function and quality of life were similar.

### Conclusions

Also, during long-term follow-up, a postponed-drainage approach using antibiotics in patients with infected necrotizing pancreatitis results in fewer interventions as compared with immediate drainage and should therefore be the preferred approach.

## DISCUSSION

Acute pancreatitis mostly runs a mild clinical course, but 20% of patients develop severe pancreatitis with necrosis. Secondary infection of pancreatic and peripancreatic necrosis puts these patients at risk of significant morbidity and 10% to 39% mortality. Several randomized studies have attempted to optimize the treatment of patients with infected necrotizing pancreatitis. Besides antibiotic treatment, the minimally invasive step-up approach, with catheter drainage of the infected necrotic collection as the first step, followed by minimally invasive necrosectomy when needed, is the current standard treatment strategy. However, the optimal timing of drainage in infected necrotizing pancreatitis remains unknown and varies widely in current practice. The recent multicenter randomized POINTER (Postponed or Immediate Drainage of Infected Necrotizing Pancreatitis) trial compared immediate catheter drainage within 24 hours after diagnosing infected pancreatic necrosis with postponed catheter drainage. If at 6-month follow-up, immediate drainage was not superior to postponed drainage regarding complications, the question remains whether these relative benefits of the postponed-drainage approach persist after the initial 6-month follow-up. Therefore, the current study evaluates new events beyond the initial 6-month follow-up on long-term clinical outcomes of patients enrolled in the POINTER trial.

Out of the 104 patients with infected necrotizing pancreatitis enrolled in the multicenter randomized POINTER trial, 88 were re-evaluated with a median follow-up of 51 months. The primary outcome was a composite of death and major complications.
After the initial 6-month follow-up, the composite primary outcome of death and major complications occurred in 7/47 patients (15%) in the immediate-drainage group and 7/41 patients (17%) in the postponed-drainage group (RR = 0.87; 95% CI = [0.33 – 2.28]; p = 0.78). Death occurred in 4 patients (9%) in the immediate-drainage group and in 4 patients (10%) in the postponed-drainage group (RR = 0.87; 95% CI [0.23 – 3.27); p = 1.00). One or more drainage procedures were required in 7 patients (15%) in the immediate-drainage group versus 3 patients (7%) in the postponed-drainage group (RR = 2.03; 95% CI = [0.56 – 7.37]; p = 0,33) after the initial 6-month follow-up; of which 1 was initially treated with antibiotics alone. The median number of drainage procedures and necrosectomies was 0 [IQR = 0] in both groups (p = 0.28). In the total follow-up, the composite primary outcome of death and major complications occurred in 26/54 patients (48%) in the immediate-drainage group and in 21/46 patients (46%) in the postponed-drainage group (RR = 1.06; 95% CI = [0.69 – 1.60]; p = 0,80). Death occurred in 11 patients (20%) and 9 patients (20%) in the immediate-drainage group and postponed-drainage group, respectively. No differences were found in the individual components of major complications. The median number of surgical, endoscopic, and radiologic interventions (catheter drainage and necrosectomy) was 4 [IRQ = 5] in the immediate-drainage group versus 1 [IQR = 6] in the postponed-drainage group (p = 0.001). Eventually, 14 of 15 patients (93%) in the postponed-drainage group who were successfully treated in the initial 6-month follow-up with antibiotics and without any intervention remained without intervention. At the end of follow-up, pancreatic function and quality of life were similar.

In conclusion, postponed catheter drainage, using antibiotics, may be seen as the preferred approach when treating patients with infected necrotizing pancreatitis. Delaying drainage reduces the number of interventions and offers the opportunity to effectively treat patients with antibiotic treatment only without increased risk for adverse long-term outcomes. The decision to postpone intervention, however, should be individualized and based on the patient's clinical course and improvement on antibiotics. Further research in this field, including the exact role of antibiotics in the management of infected necrosis, is encouraged.

# PANCREATIC ENZYME REPLACEMENT THERAPY IN SUBJECTS WITH EXOCRINE PANCREATIC INSUFFICIENCY AND DIABETES MELLITUS: A REAL-LIFE, CASE–CONTROL STUDY

Source : Alexandre-Heymann Laure et al. Diabetology & Metabolic Syndrome 2024; 16(1): 39


## ABSTRACT

### Background

Exocrine pancreatic insufficiency (EPI) can be associated with all types of diabetes. Pancreatic enzyme replacement therapy (PERT) has short and long-term benefits in subjects with EPI, but its effects on diabetes control are uncertain. We aimed to study the effects of PERT initiation on glycemic control in subjects with diabetes and EPI from any cause.

### Methods

In this retrospective study, we compared subjects with EPI and diabetes who were prescribed PERT with subjects with diabetes who had a fecal elastase-1 concentration dosage, but did not receive PERT. The primary outcome was the effect of PERT on hypoglycemia frequency and severity. The secondary outcomes were the effects of PERT on gastro-intestinal disorders, HbA1c and body mass index (BMI).

### Results

48 subjects were included in each group. Overall, PERT did not have any significant effect on hypoglycemia frequency or severity, but hypoglycemia frequency tended to decrease in subjects with chronic pancreatitis. While 19% of subjects experienced mild hyperglycemia after PERT initiation, we did not report any keto-acidosis or any other severe adverse event. Gastro-intestinal disorders improved in 80% of subjects treated with PERT, versus in 20% of control subjects ($p = 0.02$). Gastro-intestinal disorders improved in 87% of subjects with recommended dosage of PERT, versus in 50% of subjects with underdosage (NS). HbA1c and BMI evolution did not differ between the groups.

### Conclusions

PERT initiation is safe in subjects with diabetes and EPI. It does not globally decrease hypoglycemia severity of frequency, but is associated with a decrease in gastro-intestinal disorders.

Trial registration Retrospectively registered. The database was registered with the Commission Nationale Informatique et Libertés (CNIL), registration number: 2203351v0. The study was approved by the local ethics committee CLEP, registration number: AAA-2023-09047


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## DISCUSSION

Exocrine pancreatic insufficiency (EPI) is a hallmark of diabetes mellitus secondary to pancreatic diseases, also known as pancreatogenic diabetes. Many studies have shown that treating EPI with pancreatic enzyme replacement therapy (PERT) has both short- and long-term benefits. However, only a few studies have been conducted on the effects of PERT on glycemic control. Therefore, the present retrospective monocentric study has been conducted in order to evaluate the real-life effects of PERT initiation on glycemic control in subjects with diabetes and EPI from any cause.

Subjects with EPI and diabetes who were prescribed PERT have been compared with subjects with diabetes who had a relatively low fecal elastase-1 concentration dosage, but did not receive PERT. In total, 48 subjects were included in each group. The primary outcome was the effect of PERT on hypoglycemia frequency and severity. The secondary outcomes were the effects of PERT on gastro-intestinal disorders, HbA1c, body mass index (BMI), and on overall diabetes management.

Overall, PERT did not have any significant effect on hypoglycemia frequency or severity, but hypoglycemia frequency tended to decrease in subjects with chronic pancreatitis. While 19% of subjects experienced mild hyperglycemia after PERT initiation, no keto-acidosis or other severe adverse event have been reported. On the other hand, gastro-intestinal disorders improved in 80% of subjects treated with PERT, versus in 20% of control subjects ($p = 0,02$). Als, gastro-intestinal disorders improved in 87% of subjects with recommended dosage of PERT, versus in 50% of subjects with underdosage (NS). Finally, HbA1c and BMI evolution did not differ between the groups.

In conclusion, PERT prescription seems associated with an improvement in gastro-intestinal disorders, but not in relevant hypoglycemia rate, with the possible exception of subjects with chronic pancreatitis. In this study, PERT prescription was safe in subjects with diabetes, even though diabetes medication had to be mildly intensified in about one-fifth of the subjects after PERT initiation. Also, PERT higher dosage tended to associate with stronger effects on gastro-intestinal disorders. Hence, EPI should be sought for in subjects with diabetes and gastro-intestinal disorders, and PERT prescribed when appropriate. Prospective studies on PERT effects in subjects with diabetes would be useful to better understand its long-term effects in this population, and to confirm or infirm its beneficial effects on hypoglycemia rate and weight gain.

# CONTEMPORARY MANAGEMENT OF GASTROINTESTINAL, PANCREATIC AND HEPATIC TOXICITIES OF IMMUNE CHECKPOINT INHIBITORS

Source: Matthew J. Townsend et al. Alimentary Pharmacology & Therapeutics 2024; 59(11): 1350-65


## ABSTRACT

### Background

Immune checkpoint inhibitors (ICIs) are effective oncologic agents which frequently cause immune-related adverse events (irAEs) which can impact multiple organ systems. Onco-Gastroenterology is a novel and emerging subspecialty within gastroenterology focused on cancer treatment-related complications. Gastroenterologists must be prepared to identify and manage diverse immune-mediated toxicities including enterocolitis, hepatitis, pancreatitis and other ICI-induced toxicities.

### Aim

To provide a narrative review of the epidemiology, diagnostic evaluation and management of checkpoint inhibitor-induced gastrointestinal and hepatic toxicities.

### Methods

We searched Cochrane and PubMed databases for articles published through August 2023.

### Results

Gastrointestinal and hepatic irAEs include most commonly enterocolitis and hepatitis, but also pancreatitis, oesophagitis, gastritis, motility disorders (gastroparesis) and other rarer toxicities. Guidelines from the National Comprehensive Cancer Network, American Society of Clinical Oncology and European Society for Medical Oncology, in combination with emerging cohort and clinical trial data, offer strategies for management of ICI toxicities. Evaluation of irAEs severity by formal classification and clinical stability, and a thorough workup for alternative etiologies which may clinically mimic irAEs underlie initial management. Treatments include corticosteroids, biologics and other immunosuppressive agents plus supportive care; decisions on dosing, timing and choice of steroid adjuncts and potential for subsequent checkpoint inhibitor dosing are nuanced and toxicity-specific.

### Conclusions

Expanding clinical trial and cohort data have clarified the epidemiology and clinical characteristics of gastrointestinal, pancreatic and hepatic toxicities of ICIs. Guidelines, though valuable, remain based principally on retrospective cohort data. Quality prospective, controlled studies may refine algorithms for treatment and potential immunotherapy rechallenge.


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## DISCUSSION

The use of immune checkpoint inhibitors (ICIs) has made a substantial impact in the treatment of numerous advanced malignancies. ICIs are monoclonal antibodies which block the immune "checkpoint" receptors cytotoxic T-lymphocyte associated protein-4 (CTLA-4), programmed cell death-1 (PD-1) or PD-1 ligand (PD- L1). Immune-related adverse events (irAEs) from these effective therapies are also common as an "off-target" effect from cytotoxic T-lymphocyte-mediated immune response, most frequently involving barrier tissues (skin, gastrointestinal tract, liver and respiratory epithelium) and endocrine organs. They have the potential to impact any organ throughout the ICI treatment course and months to years after discontinuation. As such, an understanding of key clinical features and treatment strategies is relevant not only to oncologists and hospitalists but also to the subspecialists who help diagnose and co-manage these irAEs.

This narrative review focuses on the diagnostic and therapeutic management of gastrointestinal, pancreatic and hepatic toxicities induced by ICI use. PubMed and Cochrane databases were searched for literature published between January 2005 and August 2023.

In addition to pancreatitis, oesophagitis, gastritis, motility difficulties (gastroparesis), and other less prevalent toxicities, the most common gastrointestinal and hepatic adverse events are enterocolitis and hepatitis. Strategies for managing ICI toxicities are provided by the National Comprehensive Cancer Network, American Society of Clinical Oncology, and European Society for Medical Oncology guidelines, as well as by new data from clinical trials and cohort studies. Initial care is based on a comprehensive workup for other etiologies that may clinically mimic irAEs, as well as an assessment of the severity of irAEs by formal classification and clinical stability. Treatment options include corticosteroids, biologics, and other immunosuppressive drugs in addition to supportive treatment; dosage, timing, and steroid adjunct selection are complex and toxicity-specific decisions.

In conclusion, gastrointestinal and hepatic toxicities from ICI use manifest across organ systems. Given the potential for multiple irAEs to be fatal or cause significant morbidity, as multiple gastrointestinal irAEs present with overlapping symptoms, and as the oncologic indications for ICI use expand, recognition of potential toxicities with prompt evaluation and treatment are essential for clinicians across specialities. Future prospective, controlled trials may help clarify management strategies, including refined risk stratification for re-challenge of immunotherapy and the optimal use of steroid-sparing biologic therapies in the treatment of severe toxicities.

# ANALYSIS OF FACTORS INFLUENCING ONSET AND SURVIVAL OF PATIENTS WITH SEVERE ACUTE PANCREATITIS: A CLINICAL STUDY

Source: Xiaoli Qin et al. Immunity, inflammation and disease 2024; 12(6): 1267


## ABSTRACT

### Objective

Acute pancreatitis (AP) is an inflammatory disease of the pancreas, and the prognosis of severe AP (SAP) is poor. The study aimed to identify promising biomarkers for predicting the occurrence and survival outcome of SAP patients.

### Materials and Methods

Two hundred and forty AP patients were retrospectively recruited, in which 72 cases with SAP. Blood test was done for collection of laboratory indicators. After treatment, the mortality of patients was recorded.

Results Patients in the SAP group had higher intensive care unit admissions and longer hospital stays ($p < .001$). Among laboratory parameters, significantly high values of C-reactive protein (CRP), triglycerides and glucose (TyG) index, Von willebrand factor antigen (vWF:Ag) and D-dimer were found in SAP groups relative to non-SAP ones. Receiver operating characteristic curve indicated the good performance of CRP, TyG index, vWF:Ag and D-dimer in SAP diagnosis. Among all SAP cases, 51 survived while 21 died. TyG index (odds ratio [OR] = 6.914, 95% confidence interval [CI] = 1.193–40.068, $p = .028$), vWF:Ag (OR = 7.441, 95% CI = 1.236–244.815, $p = .028$), and D-dimer (OR = 7.987, 95% CI = 1.251–50.997, $p = .028$) were significantly related to survival outcome of SAP patients by multiple logistic regression analysis. Both TyG index and vWF showed favorable efficiency in predicting overall prognosis. The area under the curve for the multivariate model (PRE = −35.908 + 2.764 × TyG + 0.021 × vWF:Ag) was 0.909 which was greater than 0.9, indicating its excellent performance in prognosis prediction.

### Conclusion

CRP, TyG index, vWF:Ag, and D-dimer values on admission may be potential clinical predictors of the development of SAP. Moreover, TyG index and vWF:Ag may be helpful to predict survival outcome.Is serum albumin a pivotal biomarker in anticipating acute pancreatitis outcomes?


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## DISCUSSION

Acute pancreatitis (AP) is a disorder characterized by parenchymal injury of the pancreas controlled by immune cell-mediated inflammation. The prognosis of mild AP (MAP) is generally good after short-term treatment. However, severe acute pancreatitis (SAP) is often accompanied by organ dysfunction, systemic or local complications, and the prognosis is poor. Patients with SAP have variable and extremely rapid progression. If the treatment is not timely, SAP patients can be complicated by various diseases or infections, which greatly increases the risk of death. Therefore, early correct prediction of the severity and prognosis of SAP patients has guiding effects on the timely targeted intervention. So, the present retrospective study has been conducted in order to identify promising biomarkers for predicting the occurrence and survival outcome of SAP patients.

In total, 240 AP patients, of which 72 cases with SAP, were retrospectively included in the analysis, and their clinical laboratory indicators were recorded to explore their prognostic value in the development and clinical outcome of SAP patients. Specially, triglycerides and glucose (TyG) index and coagulation index (Von willebrand factor antigen [vWF:Ag] and D-dimer were of significant concern. The diagnostic significance was determined by plotting the receiver operating characteristic (ROC) curve, and after treatment, the mortality of patients was recorded.

Patients in the SAP group had higher intensive care unit (ICU) admissions and longer hospital stays ($p < 0.001$). Among laboratory parameters, significantly high values of WBC, CRP, BUN, creatinine, Ca, PaO2 /FiO2, FBG, TG, TyG index, vWF:Ag, and D-dimer were found in SAP groups relative to non-SAP ones, while significantly low values of albumin and PaO2/FiO2 were detected ($p < 0.001$). If the ROC curve indicated the high diagnostic value of CRP (area under the curve [AUC] = 0.891), TyG index (AUC = 0.826) and vWF (AUC = 0.801); D-dimer had the best diagnostic value (AUC = 0.925) with a sensitivity of 88,89%, and a specificity of 94.05%. Out of all SAP cases, 21 people died and 51 people survived. Multiple logistic regression analysis revealed a significant relationship between the survival outcome of SAP patients and the TyG index (OR = 6.914; 95% CI = [1.193 - 20.068]; p =0,028), vWF:Ag (OR = 7.441; 95% CI = [1.236 – 244.815]; p =0,028), and D-dimer (OR = 7.987 95% CI = [1.251 – 250.997]; p =0.028). In terms of determining overall prognosis, both the TyG index and vWF demonstrated favorable efficiency. The multivariate model (PRE = -35.908 + 2.764 × TyG + 0.021 × vWF:Ag) performed exceptionally well in prognosis prediction, as evidenced by its area under the curve of 0.909, which was more than 0.9.

In conclusion, CRP, TyG index, vWF:Ag, and D-dimer values on admission appear to be potential clinical predictors of the development of SAP. Moreover, TyG index and vWF:Ag may be useful in predicting survival outcome, and their combination showed excellent performance in prognosis prediction.

# IS SERUM ALBUMIN A PIVOTAL BIOMARKER IN ANTICIPATING ACUTE PANCREATITIS OUTCOMES?


## ABSTRACT

### Aim

This study aimed to assess the significance of serum albumin levels within 24 h of patient admission in correlation with the incidence of outcomes and mortality in patients diagnosed with acute pancreatitis.

### Methods

A retrospective study was conducted over a 5-year period, from January 2018 to December 2023, at the Mohammed VI University Hospital in Oujda, Morocco. The study included 371 patients diagnosed with acute pancreatitis.

Hypoalbuminemia (≤ 30 g/L) was observed in 124 patients (33.4% of cases), and these patients had a higher mean age compared to those with normal albumin levels (P = 0.003).

### Results

Hypoalbuminemia was significantly associated with persistent Systemic Inflammatory Response Syndrome (SIRS) (70.8% vs. 29.2%, P = 0.000), a higher BISAP score (66.7% vs. 33.3%, P = 0.000), and a higher CTSI score (51.7% vs. 48.3%, P = 0.000).

Hypoalbuminemia was also associated with the presence of pleural effusion (P = 0.000). The mortality in the sample was 4.6%, and it was significantly associated with hypoalbuminemia (76.5%, P = 0.000).

### Conclusion

Serum albumin levels within 24 h of patient admission appear to be a significant prognostic biomarker in acute pancreatitis, particularly in anticipating persistent organ failure and mortality.

## DISCUSSION

Albumin is the most abundant protein in the body and serves a variety of essential functions (regulation of oncotic pressure, binding and transportation of both endogenous and exogenous substances, anti-oxidant functions). Hypoalbuminemia is frequently observed in various clinical conditions (sepsis, kidney failure, nephrotic syndrome, cancer, decompensated liver cirrhosis, surgical procedures). Acute pancreatitis (AP), especially in situations of severe AP, can also exhibit hypoalbuminemia. Some studies have shown that low serum albumin levels in AP are significantly related to poor prognosis, and could be an important tool for predicting adverse outcomes, especially in anticipating persistent organ failure and mortality. Some studies have shown that low serum albumin levels in AP are significantly related to poor prognosis, and could be an important tool for predicting adverse outcomes, especially in anticipating persistent organ failure and mortality. So, the present retrospective study aimed to assess the significance of serum albumin levels within 24 h of patient admission in correlation with the incidence of outcomes and mortality in AP.

Over a 5-year period, from January 2018 to December 2023, 371 patients diagnosed with AP at the Mohammed VI University Hospital in Oujda (Morocco) have been included in the analysis.
Hypoalbuminemia (≤ 30 g/L) observed in 124 patients, constituting 33.4% of cases. Patients with hypoalbuminemia had a higher mean age (59,62 years) compared to those with normal albumin levels (53,54 years, p = 0,003). However, no significant differences were found regarding gender, BMI and the duration between symptoms onset and consultation. Regarding severity scores: a significant association was found between hypoalbuminemia, systemic inflammatory response syndrome (SIRS), bedside index of severity in AP (BISAP score), and computed tomography severity index (CTSI).

Among patients with persistent SIRS after 48 h, 70.8% had hypoalbuminemia, and 29.2% had normal albumin levels ($p < 0.001$). 66.7% of patients with a BISAP score ≥ 3 had hypoalbuminemia compared to 33.3% with normal albumin levels ($p < 0,001$). Among patients with a CTSI score > 3, 51.7% had hypoalbuminemia ($p < 0,001$). Hypoalbuminemia was also associated with the presence of pleural effusion ($p < 0,001$) and ascites ($p < 0,001$). The mortality in our sample was 4,6%, and it was significantly associated with hypoalbuminemia (76,5%; $p < 0,001$). Finally, the mean albumin level in deceased patients was significantly lower compared to living patients (29,6 g/l vs. 36,4 g/l; $p < 0.001$).

In conclusion, this study provides evidence for the significance of serum albumin as a prognostic biomarker in AP, especially in predicting sustained organ failure and mortality. This insight has the potential to improve the care and outcomes of individuals with AP. Nevertheless, further researches are crucial to validate these findings and investigate the potential advantages of incorporating serum albumin levels into clinical decision-making for AP.

# STEP-UP APPROACH FOR THE TREATMENT OF INFECTED NECROTISING PANCREATITIS: REAL LIFE DATA FROM A SINGLE-CENTRE EXPERIENCE WITH LONG-TERM FOLLOW-UP

Source: Valentin Claire et al. BMC Gastroenterology 2024; 24(1): 213


## ABSTRACT

### Background

About 20% of patients with acute pancreatitis develop a necrotising form with a worse prognosis due to frequent appearance of organ failure(s) and/or infection of necrosis. Aims of the present study was to evaluate the "step up" approach treatment of infected necrosis in terms of: feasibility, success in resolving infection, morbidity of procedures, risk factors associated with death and long-term sequels.

### Methods

In this observational retrospective monocentric study in the real life, necrotizing acute pancreatitis at the stage of infected walled-off necrosis were treated as follow: first step with drainage (radiologic and/or endoscopic-ultrasound-guided with lumen apposing metal stent); in case of failure, minimally invasive necrosectomy sessions(s) by endoscopy through the stent and/or via retroperitoneal surgery (step 2); If necessary open surgery as a third step. Efficacy was assessed upon to a composite clinical-biological criterion: resolution of organ failure(s), decrease of at least two of clinico-biological criteria among fever, CRP serum level, and leucocytes count).

### Results

Forty-one consecutive patients were treated. The step-up strategy: (i) was feasible in 100% of cases; (ii) allowed the infection to be resolved in 33 patients (80.5%); (iii) Morbidity was mild and rapidly resolutive; (iv) the mortality rate at 6 months was of 19.5% (significant factors: SIRS and one or more organ failure(s) at admission, fungal infection, size of the largest collection ≥ 16 cm). During the follow-up (median 72 months): 27% of patients developed an exocrine pancreatic insufficiency, 45% developed or worsened a previous diabetes, 24% had pancreatic fistula and one parietal hernia.

### Conclusions

Beside a very good feasibility, the step-up approach for treatment of infected necrotizing pancreatitis in the real life displays a clinico-biological efficacy in 80% of cases with acceptable morbidity, mortality and long-term sequels regarding the severity of the disease.


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## DISCUSSION

Acute pancreatitis (AP) is a common disease, with an increasing incidence. Mortality depends on the severity of AP with two main prognostic factors: organ failure and the presence of necrosis. Necrotising AP mortality is estimated at around 15% and increases up to 35% in case of infection. An interventional procedure is most often necessary in case of infected necrosis. Previously, the standard treatment for severe post-AP necrosis infection was open laparotomy surgery for necrosectomy. Nevertheless, it was associated with high mortality. Then, minimally invasive radiological, endoscopic and surgical techniques were developed that can be included in the step-up approach and appeared finally superior to open surgery with significantly lower new-onset of organ failure and mortality as well as shorter hospital stay. Moreover, the endoscopic approach (when possible) may be superior to minimally invasive surgical ones in term of mortality, major complications and sequels. Considering these results, the "step up" approach was validated by an inter- national consensus in 2012 and by other nationals and European consensus. Thus, this present observational retrospective monocentric study, in the real life, has been conducted in order to evaluate the "step up" approach treatment of infected necrosis in terms of: feasibility, success in resolving infection, morbidity of procedures, risk factors associated with death and long-term sequels.

Initially, drainage (radiologic and/or endoscopic-ultrasound-guided with lumen apposing metal stent) was used to treat necrotizing acute pancreatitis at the stage of infected walled-off necrosis. If this failed, minimally invasive necrosectomy sessions were performed using endoscopy through the stent and/or retroperitoneal surgery (step 2); if open surgery was required, it was the third step. A composite clinical-biological criterion was used to evaluate efficacy: the remission of organ failure or failures, and the reduction of at least two clinical-biological criteria, such as fever, CRP serum level, and leucocyte count. In total, 41 consecutive patients were treated and analyzed.

The step-up strategy was feasible in 100% of cases and allowed the infection to be resolved in 33 patients (80.5%). At 6 months, the mortality rate was 19.5%, and the morbidity was minor and quickly resolved. The presence of a fungal infection, the size of the largest collection exceeding 16 cm, and systemic inflammatory response syndrome (SIRS) linked to one or more organ failures at hospital admission were the important factors that explained the mortality rate. Lastly, during the follow-up period (median = 72 months), 24% of patients experienced a pancreatic fistula and one parietal hernia, 45% developed or exacerbated a prior diabetes, and 27% developed an exocrine pancreatic insufficiency.

In conclusion, the "step up" strategy is nowadays the strategy validated by several consensus conferences for the treatment of necrosis infection occurring in severe acute pancreatitis. While most studies have studied or compared the different techniques, the present work is original because it evaluates the "step up" approach as a whole and in the real life. Multidisciplinary "step up" approach appears to be feasible with a clinico-biological efficacy on infection in 80% of cases and with an acceptable morbidity, mortality and long-term sequels. Nevertheless, some points of the strategy should be clarified to establish a clearer management algorithm. To date, there are no consensual clinical or biological or radiological criteria defining failure and leading to the next step in the step-up strategy as well as timing, sequence and number of necrosectomy sessions. In this sense, it would be interesting to establish a composite score or precise criteria for response or non-response.

# SURGICAL TREATMENT OF CHRONIC PANCREATITIS WITH AN INFLAMMATORY PANCREATIC HEAD MASS: A RETROSPECTIVE STUDY

Source: Rousek Michael et al. BMC Gastroenterology 2024; 24(1): 345


## ABSTRACT

### Background

Conservative treatment of chronic pancreatitis has only a limited effect in most patients. Surgery offers very good long-term results, even in the early stages of the disease. Unfortunately, only a minority of patients undergo surgical treatment. The aim of this work was to summarise the current treatment options for patients with an inflammatory mass of the pancreatic head. Data from patients in our study demonstrates that the surgery is a safe method, and here we compare the perioperative and early postoperative outcomes of patients who underwent a pancreatoduodenectomy and duodenum-preserving pancreatic head resection for chronic pancreatitis.

### Methods

All patients who underwent a pancreaticoduodenectomy or a duodenum-preserving pancreatic head resection in our department between 2014 and 2022 were included in this study. Perioperative and early postoperative results were statistically analysed and compared.

### Results

Thirty-eight pancreaticoduodenectomies and 23 duodenum-preserving pancreatic head resections were performed. The overall mortality was 3%, whereas the in-hospital mortality after pancreaticoduodenectomy was 5%. The mortality after duodenum-preserving pancreatic head resection was 0%. No statistically significant differences in the hospital stay, blood loss, and serious morbidity were found in either surgery. Operative time was significantly shorter in the duodenum-preserving pancreatic head resection group.

### Conclusions

Both pancreatoduodenectomy and duodenum-preserving pancreatic head resection are safe treatment options. Duodenum-preserving pancreatic head resection showed a statistically significant superiority in the operative time compared to pancreaticoduodenectomy. Although other monitored parameters did not show a statistically significant difference, the high risk of complications after pancreaticoduodenectomy with a mortality of 5%; maintenance of the duodenum and upper loop of jejunum, and lower risk of metabolic dysfunctions after duodenum-preserving pancreatic head resection may favour duodenum-preserving pancreatic head resection in recommended diagnoses. Attending physicians should be more encouraged to use a multidisciplinary approach to assess the suitability of surgical treatment in patients with chronic pancreatitis.


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## DISCUSSION

Pain is the most common symptom in patients with chronic pancreatitis (CP) and occurs in 80–90% of cases. Conservative management is always the first step of treatment (alcohol abstinence, quitting cigarette smoking, and pharmacological management of pain). In patients with CP localized predominantly in the head of the pancreas, a surgical resection is a treatment option. Pancreaticoduodenectomy (PDE) and duodenum-preserving pancreatic head resection (DPPHR) are both commonly performed in these situations. The aim of the present study was to provide a clear review of the current treatment options for CP localized in the head of the pancreas. A comparison of the perioperative and postoperative outcomes of the 2 most widely-used pancreatic head resections is also presented.

Between 2014 and 2022, a total of 61 resections for CP localized in the pancreatic head were performed at the Department of Surgery, Military University Hospital in Prague (Czech Republic) and The Second Faculty of Medicine of Charles University: 38 patients after PDE and 23 patients after DPPHR were included into the study. From the PDE group, the standard Whipple procedure was performed in 20 patients, whereas 18 patients underwent a pylorus-preserving PDE. Perioperative and early postoperative results were statistically analyzed and compared.

The in-hospital mortality following PDE was 5%, whereas the total mortality was 3%. Following pancreatic head excision with duodenum preservation, there was no mortality. There were no statistically significant differences between the two surgeries in terms of major morbidity, blood loss, or hospital stay. The DPPHR group saw a considerably reduced operating time and mortality after DPPHR was 0%. DPPHR was also superior in the operative time. Other monitored parameters did not show a statistically significant difference. Finally, maintenance of the duodenum and upper loop of jejunum, and lower risk of metabolic dysfunctions after DPPHR may encourage the preference DPPHR in recommended diagnoses.

In conclusion, PDE and DPPHR are both safe methods in the treatment of CP localized in the head of the pancreas. The over-all mortality in our pool of patients was 3%, in-hospital mortality in the PDE group was 5%, and mortality after DPPHR was 0%. DPPHR was also superior in the operative time.

# THE REQUIRED EXPERIENCE OF OPEN PANCREATICODUODENECTOMY BEFORE BECOMING A SPECIALIST IN HEPATOBILIARY AND PANCREATIC SURGEONS: A MULTICENTER, COHORT STUDY OF 334 OPEN PANCREATICODUODENECTOMIES

Source: Fuji Tomokazu et al. BMC Surgery 2024; 24(1): 366


## ABSTRACT

### Background

Open pancreaticoduodenectomy (OPD) is an essential surgical procedure for expert hepato-biliary-pancreatic (HBP) surgeons. However, there is no standard for how many surgeries must be performed by a surgeon in training before they are considered to have enough experience to ensure surgical safety.

### Methods

Cumulative Sum (CUSUM) analysis was performed using the surgical data of OPDs performed during the training period of board-certified expert surgeons of the Japanese Society of Hepato-Biliary-Pancreatic Surgery.

### Results

Fourteen HBP surgeons participated in this study and performed 334 OPDs during their training period. The median (interquartile range) values for operative time, blood loss, and length of hospital stay were 455 (397–519) minutes, 450 (234-–716) ml, and 28 (21–38) days, respectively. CUSUM analysis showed inflection points at 20 surgeries performed for operative time. After 20 procedures, operative time was significantly shorter (461 min vs. 425 min, $p = 0.021$) and blood loss was significantly lower (470 ml vs. 340 ml, $p = 0.038$). No significant differences between within 20 and after 21 procedures were found in the complication rate (53% vs. 48%, $p = 0.424$) and rate of in-hospital deaths (1.5% vs.1.4%. $p = 0.945$). Up to 20 surgeries, PDAC and another malignant tumor had longer operative time than benign/low malignant diseases (486 min vs. 472 min vs. 429 min, $p < 0.001$), and higher blood loss (500 ml vs. 502 ml vs. 355 ml, $p < 0.001$). Mortality rate was higher at PDAC cases (5% vs. 0% vs. 0%, $p = 0.01$). After the 21 procedures, these outcomes were improved and no differences in by primary disease were observed. Multivariable analysis showed that within 20 surgeries were independent risk factors of longer operative time (HR2.6, $p = 0.013$) and higher blood loss (HR2.0, $p = 0.049$).

### Conclusions

To stabilize the surgical outcome of OPD for malignant disease, at least 20 surgeries should be performed at a certified institution during surgeon training.


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## DISCUSSION

Pancreaticoduodenectomy (PD) is one of the challenging procedures characterized by high complication and mortality rates that requires advanced skills and specialized anatomical knowledge of hepato-biliary-pancreatic (HBP) surgeons. While it is crucial that HBP surgeons perform open PD (OPD) safely and certainly, the number of surgeries that should be performed during the surgeon training period remains uncertain. This multicenter, cohort study aimed to investigate the learning curve of OPDs performed by board-certified HBP surgeons during their training periods at board-certified institutions of the board certification system of the Japanese Society of Hepato-Biliary-Pancreatic Surgery (JSHBPS).

A total of 334 adult patients who underwent OPD by 14 surgeons between January 2008 and December 2022 from 5 medical hospitals in Japan have been included in the analysis. The primary endpoint was operative time, and the secondary endpoints were, blood loss, hospital stay, mortality rate, and surgical complications. Cumulative Sum (CUSUM) analysis was performed to assess the change by number of experiences for operative time and to identify the number of procedures necessary to reach optimal performance.

The median (interquartile range) values for operative time, blood loss, and length of hospital stay were 455 (397–519) minutes, 450 (234–-716) ml, and 28 (21–38) days, respectively. For operative time, CUSUM analysis revealed inflection points at 20 operations. In CUSUM analysis of operation time including all trainees, the flection point was found after the 20 procedures. Cases and outcomes were compared before and after the 20 cases. After 20 procedures, the PDAC rate was significantly higher (31% vs. 45%; p = 0.024), operative time was significantly shorter (461 min vs. 425 min; p = 0.021), and blood loss was significantly lower (470 ml vs. 340 ml; p = 0038). On the other hand, no differences in these outcomes by before and after 10 procedures were observed. (supplemental Table e1). No significant differences between within 20 and after 21 procedures were found in the complication rate (53% vs. 48%; p = 0.424) or rate of in-hospital deaths (1.5% vs. 1.4%; p = 0.945). Up to 20 surgeries, PDAC and another malignant tumor had longer operative time than benign/low malignant diseases (486 min vs. 472 min vs. 429 min; p < 0.001), and higher blood loss (500 ml vs. 502 ml vs. 355 ml; p < 0.001). Mortality rate was higher at PDAC cases (5% vs. 0% vs. 0%; p = 0.01) and all complication rates were higher at another malignant tumor (35% vs. 62% vs. 52%; p = 0.04). After the 21 procedures, operative time and blood loss were improved and no differences in by primary disease were observed: (430 min vs. 445 min vs. 410 min; p = 0.328), (345 ml vs. 400 ml vs. 315 ml; p = 0.642). Finally, multivariable analysis showed that within 20 surgeries were independent risk factors of longer operative time (HR = 2.6; p = 0.013) and higher blood loss (HR = 2.0; p = 0.049).

In conclusion, the hepato-biliary-pancreatic surgery training at certified institutions was done safely. To stabilize the surgical outcome of OPD, at least 20 surgeries should be per- formed at certified institutions during surgeon training. In addition, difficult cases should be experienced step by step.

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