

CHALLENGES IN ACUTE PANCREATITIS MANAGEMENT

Ph.D. Thesis Booklet

Dorottya Tarján M.D.

SEMMELWEIS UNIVERSITY

Translational Medicine Program

Pharmaceutical Sciences and Health Technologies Division



Supervisors:

Prof. Péter Hegyi, M.D., Ph.D.

Alexandra Mikó, M.D., Ph.D.

Official reviewers:

Petra Golovics, M.D., Ph.D.

Zoltán Szepes, M.D., Ph.D.

Head of the Complex
Examination Committee:

Prof. Gábor Varga, Ph.D., D.Sc.

Members of the Complex
Examination Committee

Prof. Áron Vincze, M.D., Ph.D.

Prof. Karl J. Oldhafer, M.D., Ph.D.

Roland Molontay, B.Sc., M.Sc., Ph.D.

Zoltán Zádori, M.D., Ph.D.

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1. Introduction

1.1. Overview of the topic

1.1.1. What is the topic?

Acute Pancreatitis (AP) is the leading gastrointestinal disease necessitating emergency hospitalization. Infected necrosis occurs in approximately 30% of patients with acute necrotizing pancreatitis and, when complicated by sepsis, is associated with increased mortality rates of up to 40%.

Acute biliary pancreatitis during pregnancy is a rare condition but poses significant clinical challenges. Symptomatic gallstone disease is a leading cause of non-obstetric hospitalizations and surgical interventions in pregnant women and is associated with an increased risk of preterm birth.

1.1.2. What is the problem to solve?

The diagnosis of Infected Necrotizing Pancreatitis (INP) is challenging because AP itself causes systemic inflammatory features that overlap with signs of infection, often leading to the overuse of antibiotics.

Early cholecystectomy following mild biliary pancreatitis is recommended in nonpregnant patients to reduce the risk of recurrence; however, the optimal management approach in pregnant women remains uncertain. Pregnancy itself has been identified as an independent risk factor for increased readmission and recurrence of AP. Despite this, pregnant patients are substantially less likely to undergo cholecystectomy or Endoscopic Retrograde Cholangiopancreatography (ERCP) compared with nonpregnant patients.

1.1.3. What is the importance of the topic?

Although multiple scoring systems are used to evaluate the severity of AP, none have been validated to reliably predict the presence of infection.

Biliary pancreatitis during pregnancy carries distinct maternal and fetal risks, with reported recurrence rates of up to 50% in the first trimester and substantially higher readmission rates compared with nonpregnant women. While current guidelines support laparoscopic cholecystectomy for symptomatic biliary disease and ERCP for urgent conditions such as choledocholithiasis or

cholangitis, ongoing concerns regarding procedural safety - particularly related to timing during pregnancy - continue to contribute to clinical hesitation.

1.1.4. What would be the impact of our research results?

Early detection of infection is critical for timely intervention and optimal management, especially in high-risk patients who may benefit from prompt antibiotic therapy.

Our second study supports more informed and confident decision-making regarding cholecystectomy and ERCP in pregnant patients with biliary pancreatitis. By clarifying safety, complication rates, and recurrence risk, these findings may help refine clinical guidelines, reduce practice variability, and promote timely intervention, ultimately improving maternal and fetal outcomes.

2. Objectives

2.1. Study I – Persistently High Procalcitonin and C-Reactive Protein Are Good Predictors of Infection in

Acute Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis

The objective of this study was to perform a comprehensive meta-analysis evaluating laboratory markers as early predictors of INP.

2.2. Study II. – Safety and Effectiveness of Cholecystectomy and Endoscopic Retrograde Cholangiopancreatography in Biliary Pancreatitis During Pregnancy: BORN Study

This international retrospective cohort study aimed to analyze current practices and outcomes of managing biliary AP in pregnant patients, focusing on the role of cholecystectomy and ERCP.

3. Methods

3.1. Study I

This study was performed in accordance with the Cochrane Handbook and the PRISMA 2020 guidelines, with the study protocol prospectively registered in PROSPERO (no.: CRD42022370672). A systematic search was conducted in Medline (via PubMed), Embase,

and Central databases on 27 October 2022. Study selection, data extraction, and assessment of agreement were independently performed by two reviewers, with disagreements resolved by discussion. In the eligible studies, the presence of infection in necrotizing pancreatitis was confirmed using a reference test, which involved detecting gas within the necrotic collection through computed tomography imaging or analyzing collected samples, which tested positive on Gram staining or culture. Laboratory biomarkers used to differentiate sterile necrotizing pancreatitis from INP served as the index test. Our outcome measures included sensitivity, specificity, the receiver operating characteristic (ROC) curve, and area under the ROC curve (AUC).

3.2. Study II.

This international retrospective multicenter cohort study collected data on demographics, clinical presentation, management strategies, timing and type of cholecystectomy, procedural approaches, complications, and outcomes. Continuous variables were reported as medians with interquartile ranges, while categorical

variables were presented as frequencies and percentages. Group comparisons were performed using Welch's t-test, Pearson's chi-squared test, or Fisher's exact test.

4. Results

4.1. Study I.

Eight of the thirteen included studies were eligible for meta-analysis, with the remaining five contributing to the systematic review only. Within the first 72 hours after admission, the AUC of C-Reactive Protein (CRP) was 0.69 (CI: 0.62–0.76), for Procalcitonin (PCT) it was 0.69 (CI: 0.60–0.78), and for white blood cell count it was 0.61 (CI: 0.47–0.75). After the first 72 h, the pooled AUC of CRP showed an elevated level of 0.88 (CI: 0.75–1.00), and for PCT, it was 0.86 (CI: 0.60–1.11).

4.2. Study II.

A total of 101 cases from 14 countries and 19 centers were included. Following mild AP during pregnancy, cholecystectomy was associated with a lower readmission rate due to recurrent AP or other gallstone-related complications compared with conservative management

(0% vs 24%; n=0/17 vs n=12/49; p=0.027). Cholecystectomy during pregnancy had a low complication rate, comparable to postpartum surgery (12% vs 10%; n=2/17 vs n=3/30; p>0.999). Preterm birth occurred in 7.1% (n=1/14) of patients who underwent cholecystectomy versus 11% (n=5/45) without surgery. Fetal loss after surgery was observed only during the first trimester (n=3/17 vs n=1/49).

Regarding ERCP, no significant differences were observed between the surgical and ERCP groups in rates of readmission (5%, n=1/21 vs 27%, n=4/15; p=0.138), fetal loss (5%, n=1/21 vs 27%, n=4/15; p=0.138), or preterm birth (6%, n=1/17 vs 8%, n=1/12; p>0.999). Likewise, among patients who underwent ERCP versus those who did not, fetal loss (9.1%, n=2/22 vs 5.4%, n=4/74; p=0.618) and preterm birth rates (5.9%, n=1/17 vs 12%, n=8/65; p=0.677) did not differ significantly.

5. Conclusions

5.1. Study I.

During the first 72 hours after hospital admission CRP and PCT perform poorly as predictors of infection; however, their predictive accuracy improves substantially after this period, reaching levels suitable for clinical application.

5.2. Study II.

Cholecystectomy performed during the second or third trimester is a safe and effective intervention to prevent recurrent biliary events in pregnant patients with mild biliary pancreatitis. In contrast, its safety in the first trimester remains unclear due to limited evidence and a possible increased risk of fetal loss. ERCP is safe throughout pregnancy.

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