



DECISION-MAKING IN SEVERE ACUTE PANCREATITIS: THE ROLE OF ARTIFICIAL INTELLIGENCE AND SEVERITY SCALES

Amália Cinthia Meneses do Rêgo¹, Irami Araújo-Filho²

1. Institute of Teaching, Research, and Innovation, Liga Contra o Câncer – Natal – Brazil; ORCID: <https://orcid.org/0000-0002-0575-3752>; Full Professor of the Postgraduate Program in Biotechnology at Potiguar University, Potiguar University (UnP) – Natal/RN - Brazil. E-mail: regoamalia@gmail.com;
2. Institute of Teaching, Research, and Innovation, Liga Contra o Câncer – Natal – Brazil; ORCID: <https://orcid.org/0000-0003-2471-7447>; Full Professor of the Postgraduate Program in Biotechnology at Potiguar University (UnP) – Natal/RN - Brazil. Full Professor, Department of Surgery, Potiguar University. Ph.D. in Health Science/ Natal-RN - Brazil. E-mail: irami.filho@uol.com.br

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Address for correspondence Av. Hermes da Fonseca, 1444 - Apto. 1302 - Tirol - Natal - State of Rio Grande do Norte - Brazil. Zip code: 59020-650. Phone: +55 84 98876-0206. E-mail: irami.filho@uol.com.br.

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ABSTRACT

Severe acute pancreatitis (SAP) presents a complex clinical scenario that demands prompt and accurate decision-making regarding the appropriate course of treatment. The management of SAP involves a delicate balance between surgical intervention and conservative therapy, aiming to optimize patient outcomes while minimizing morbidity and mortality. Traditional methods of assessing disease severity, such as the Balthazar scale, Ranson criteria, Glasgow-Imrie score, and APACHE II score, provide valuable clinical insight but may lack the precision necessary for individualized patient care. In recent years, integrating artificial intelligence (AI) technologies into healthcare has shown promise in augmenting clinical decision-making processes. By leveraging machine learning algorithms and predictive analytics, AI has the potential to enhance the accuracy and efficiency of severity assessment in SAP. This article explores the role of AI in conjunction with existing severity scales in aiding surgeons' decision-making regarding the timing and modality of intervention in patients with SAP. Through a comprehensive review of current literature and case studies, we will examine the advantages and limitations of AI-based approaches and propose strategies for integrating these technologies into clinical practice. By harnessing the power of AI, surgeons can potentially optimize patient outcomes, improve resource utilization, and reduce the burden of SAP on healthcare systems worldwide.

Keywords: pancreatitis, acute necrotizing, artificial intelligence, illness severity, computer assisted decision making, surgical procedure, conservative treatment.

INTRODUCTION

Severe acute pancreatitis (SAP) is a formidable clinical challenge characterized by its complex pathophysiology and significant morbidity and mortality rates¹⁻³.

The clinical management of SAP is largely contingent upon the timely and accurate assessment of disease severity, which determines whether a patient may require aggressive interventions, including surgical procedures, or can be managed conservatively⁴.

Clinicians have relied on several well-established severity grading systems such as the Balthazar scale, Ranson criteria, Glasgow-Imrie score, and APACHE II score. These scoring systems, while invaluable, have certain limitations in terms of predictive accuracy and timeliness, which may impede optimal clinical decision-making⁵⁻⁷.

The advent of artificial intelligence (AI) in healthcare promises a new horizon in managing complex diseases like SAP. AI, particularly machine learning and deep learning can significantly enhance the predictive accuracy of severity assessments by integrating diverse data types, including clinical parameters, laboratory results, imaging data, and patient demographics⁸. This capability could transform the SAP prognostic landscape, providing clinicians with tools that offer real-time insights and high predictive accuracy⁹.

Integrating AI with traditional severity scales could lead to developing dynamic prognostic models that adapt to patients' evolving clinical status. For instance, machine learning algorithms can analyze temporal changes in clinical data to predict potential complications before they become apparent, facilitating early interventions. AI can assist in identifying subtle patterns in data that are often invisible to human observers, which can be crucial for predicting outcomes in SAP¹⁰⁻¹².

The potential of AI in enhancing decision-making in SAP extends to personalized medicine. By analyzing data from a broad spectrum of cases, AI models can help identify which patients will likely benefit from surgical interventions versus those who would best respond to conservative management¹³.

This approach not only tailor's treatment to individual patient needs but also enhances resource utilization and reduces healthcare costs by preventing unnecessary procedures¹⁴.

AI in this field also poses significant challenges, including data privacy concerns, the need for extensive and diverse datasets to train AI models, and the integration of AI tools into existing healthcare systems³. Furthermore, ongoing validation and recalibration of AI models are needed to ensure their efficacy and safety in clinical practice¹⁵.

Current research in AI applications for SAP is promising but still nascent. Studies have demonstrated the feasibility of using AI to improve diagnostic accuracy and predict patient outcomes more reliably than traditional methods alone. However, these studies also highlight the variability in AI performance, which can be influenced by the quality of data and the specific algorithms used¹⁶⁻¹⁸.

To move forward, interdisciplinary collaboration between clinicians, data scientists, and bioinformaticians is crucial. Such collaborations can ensure the development of AI tools that are not only technically proficient but also clinically relevant and user-friendly¹⁹.

However, ethical considerations must be central to this process, ensuring that AI applications respect patient autonomy and confidentiality while providing significant clinical benefits²⁰.

AI with traditional severity scales in SAP represents a promising advancement in gastroenterology. It can enhance clinical decision-making, personalize patient management, and improve outcomes. Continued research and collaboration are required to overcome the challenges and realize AI's full potential in this critical area of medicine²¹⁻²³.

As we progress, these technological advancements must be guided by rigorous scientific validation and ethical considerations to ensure they serve the best interests of patients suffering from severe acute pancreatitis²⁴.

In this sense, the primary objective of this article is to critically examine the role of artificial intelligence in augmenting the traditional severity scales used for assessing severe acute pancreatitis²⁵.

We aim to explore how AI can improve the accuracy of these scales in predicting the need for surgical versus conservative management and discuss the potential benefits and limitations of such integration. The article seeks to provide a comprehensive overview of current advancements and envision the future of AI in enhancing decision-making processes in the clinical management of SAP.

METHODS

This study was meticulously designed to conduct a thorough literature review using several prominent databases known for their extensive repositories of medical and scientific peer-reviewed publications. The selected databases for this comprehensive search included PubMed, Scopus, Embase, and Web of Science, which are recognized for their vast collections of scholarly articles. Google Scholar was also a supplementary resource for accessing gray literature, often including significant studies and reports not found in conventional academic journals. The primary focus of this research centered on integrating artificial intelligence (AI) into managing severe acute pancreatitis (SAP), mainly on how AI enhances clinical decision-making through the

dynamic analysis of patient data. Keywords used in the search strategy included "pancreatitis, acute necrotizing," "artificial intelligence," "illness severity," "computer-assisted decision making," "surgical procedure," and "conservative treatment." These keywords were carefully chosen to refine the search and ensure that only studies directly relevant to the research objectives were included. To ensure a comprehensive data collection, the inclusion criteria were broad, welcoming a variety of study designs, including systematic reviews, meta-analyses, case-control studies, cross-sectional analyses, and observational studies. This approach aimed to capture a diverse spectrum of evidence and viewpoints regarding the application of AI in SAP management. The evaluation and selection of literature were carried out with strict methodological rigor. A dual-review system was implemented, where pairs of reviewers independently assessed the relevance and adherence of each study's title and abstract to the predefined inclusion criteria. Discrepancies between reviewers were resolved through discussion or, if necessary, consultation with a third independent reviewer to reach a consensus, ensuring the selection process was unbiased. This detailed and systematic approach to research methodology ensures the reliability and validity of the presented findings, grounding this study's conclusions in a thoroughly evaluated body of scientific evidence related to using artificial intelligence in managing severe acute pancreatitis.

RESULTS AND DISCUSSION

Table 1 – Severe Acute Pancreatitis: Variables from Severity Scales and Their Clinical Implications

Severity Scale	Key Variables and Thresholds	Importance Explanation	Recommended Treatment and Supportive Care
APACHE II ¹³	Score ≥ 15 ; includes age, vital signs, and laboratory findings	A high APACHE II score indicates a severe systemic response with increased risk of mortality, guiding the need for potentially aggressive interventions.	Surgical intervention if complications; enteral nutrition; broad-spectrum antibiotics like Meropenem.
Ranson ⁴⁴	≥ 3 criteria at admission (age, WBC, LDH, AST, glucose)	Meeting three or more Ranson criteria on admission correlates with higher mortality and severity, suggesting a need for intensive monitoring and possible surgical intervention.	Surgery for necrotic or deteriorating conditions; enteral nutrition; Imipenem or other suitable antibiotics.
Glasgow ¹⁶	≥ 3 criteria (age, WBC, urea, oxygen etc.)	Glasgow score ≥ 3 indicates severe pancreatitis, requiring enhanced care and monitoring to manage potential complications effectively.	ICU care; enteral nutrition as first-line; antibiotics such as Meropenem or Vancomycin if infection is suspected.
Balthazar ²	Score D or E on CT scan (extent of necrosis and inflammation)	High Balthazar scores indicate extensive pancreatic damage and necrosis, often necessitating more aggressive surgical and medical interventions.	Surgical debridement for necrosis; enteral feeding if possible; antibiotics like Piperacillin-Tazobactam.
Modified Marshall Scoring System ^{8,17}	Organ system failure indicators such as renal or respiratory failure	This scoring system emphasizes the assessment of organ failure, critical for determining the need for specific supportive therapies and potential surgical intervention.	Supportive care in ICU; adjust therapies based on specific organ failures; nutritional support and antibiotics as required.
Determinant-Based Classification ^{34,46}	Necrotic collection, organ failure, systemic complications	This classification assists in direct assessment based on clinical and imaging findings, guiding specific interventions including surgical or endoscopic actions.	Aggressive surgical or endoscopic intervention for extensive necrosis; targeted antibiotics; nutritional support focusing on enteral routes.

Footnotes: APACHE II: Acute Physiology and Chronic Health Evaluation II; WBC: White Blood Cell; LDH: Lactate Dehydrogenase; AST: Aspartate Aminotransferase; ICU: Intensive Care Unit; CT: Computed Tomography

Integrating artificial intelligence (AI) into managing severe acute pancreatitis (SAP) marks a significant advancement in gastroenterology. By enhancing traditional severity scales with AI's dynamic analysis capabilities, clinicians can better understand SAP, potentially leading to improved patient outcomes through timelier and more targeted interventions²⁶⁻²⁸.

AI's role in SAP primarily involves the application of advanced machine learning algorithms such as logistic regression, decision trees, neural networks, and deep learning¹⁰. These algorithms excel in analyzing complex and large datasets to identify patterns and predictors that are not readily apparent through traditional methods²⁹⁻³¹.

Neural networks integrate diverse data types—clinical observations, laboratory results, and imaging data—to provide real-time predictions of potential complications like necrosis or organ failure²⁴. This predictive capability is crucial for SAP management, where the rapid progression of the disease can often outpace clinical decision-making based solely on conventional severity indices³²⁻³⁴.

However, deploying AI in healthcare, particularly in managing conditions as critical as SAP, must navigate several challenges. AI tools into existing electronic health record (EHR) systems is essential for real-time data analysis and seamless clinical workflow integration³⁵⁻³⁷.

This process requires that AI tools be designed with solid interoperability features to ensure they can function across different platforms and EHR systems, which vary significantly between healthcare facilities³⁸.

Artificial intelligence (AI) tools into existing Electronic Health Record (EHR) systems, training healthcare professionals to utilize these tools effectively, and ensuring the privacy and security of patient data involve addressing multiple challenges and implementing strategic solutions³⁹⁻⁴¹.

One of the primary challenges is ensuring compatibility and interoperability between AI tools and diverse EHR systems, which often have different standards and data formats⁴².

Ensuring seamless communication and data integration without disrupting existing workflows is crucial for successfully implementing AI. These systems must be scalable and flexible to handle varying data loads and queries⁴³.

Training healthcare professionals on how to use these AI tools effectively is a critical step. Clinicians need to understand not only how to operate these systems but also how to interpret and integrate AI-generated insights into clinical decision-making⁴⁴.

This demands a comprehensive education approach beyond simple user manuals to include detailed explanations of the AI's decision-making process, enhancing the trust and confidence of healthcare professionals in these advanced tools⁴⁵.

Healthcare professionals on how to use AI tools effectively involves several vital components. Education should focus on AI and machine learning basics, explaining how these tools process data and make predictions. This foundational knowledge is crucial for building trust and understanding^{18,46}.

Hands-on training sessions are also essential, allowing clinicians to become comfortable navigating AI tools within the EHR environment and understanding how they integrate with their daily workflows⁴⁷.

Clinicians need to develop skills to correctly interpret AI-generated insights, understand the implications for clinical decision-making, and recognize the limitations

of AI recommendations³². As AI technology evolves, ongoing training will be necessary to keep healthcare providers updated on new features and capabilities⁴⁸.

Privacy and security of patient data are paramount when AI is involved in handling sensitive health information. AI systems must be built and maintained with robust cybersecurity measures to protect against data breaches and ensure that patient confidentiality is always preserved^{6,49}.

Ensuring the privacy and security of patient data when AI is involved requires robust measures. Data encryption is vital for data at rest and in transit to protect against unauthorized access⁵⁰.

Strict access controls and authentication mechanisms must be implemented to ensure that only authorized personnel can access sensitive information^{31,32}. Regular security audits and compliance checks can help identify potential vulnerabilities, and when possible, data anonymization techniques should be used during the AI training process to protect patient identities without compromising data integrity⁵¹.

Transparent data usage policies should be established, clarifying how patient data is used, who can access it, and for what purposes. These policies should be made clear to patients, aligning with ethical guidelines and legal requirements⁵²⁻⁵⁴.

Lastly, developing comprehensive data governance frameworks is essential for outlining how data is collected, stored, used, and shared, ensuring all practices comply with ethical standards and legal requirements⁵⁵.

The opaque nature of many AI algorithms—often called the "black box" problem—is a significant barrier in medical settings³⁸. Clinicians are trained to base their decisions on clear, evidence-based guidelines, and the often indiscernible reasoning of AI models can be a significant hurdle⁵⁶.

Developing AI systems that provide recommendations and explain their reasoning in understandable terms is crucial. This transparency helps build trust and facilitate wider acceptance among healthcare providers⁵⁷.

Quality and availability of data are also critical to the success of AI applications in SAP management. AI systems are only as good as the data they train on⁴⁹. Gathering large, high-quality datasets representative of diverse populations can be challenging in many parts of the world, especially in lower-resource settings. Initiatives to enhance data collection and sharing across institutions are vital to addressing this issue⁵⁸.

Ethical concerns such as patient consent and algorithmic bias must be rigorously addressed³⁴. AI systems can inadvertently perpetuate existing biases if not carefully designed and monitored. Ensuring ethical AI usage involves constant algorithm review and updates as new data and insights become available²⁷.

Interdisciplinary collaboration is essential for successfully integrating AI into SAP management³⁰. Teams comprising AI specialists, data scientists, clinicians, ethicists, and

even patient representatives ensure that AI tools are technically sound, clinically relevant, and ethically developed⁵⁹.

By carefully addressing these challenges and implementing thoughtful strategies, the integration of AI into healthcare through EHR systems can be effectively optimized^{26,44}. This not only enhances clinical workflows and improves patient outcomes but also maintains the trust and confidence of healthcare providers and patients in the advancing technology⁵⁷⁻⁵⁹.

AI holds transformative potential for managing severe acute pancreatitis, promising to enhance clinical decision-making and patient care. However, realizing this potential fully involves overcoming significant challenges related to technology integration, data management, ethical considerations, and user training^{60,61}. With concerted effort and ongoing collaboration across various disciplines, AI can significantly improve the outcomes for patients with SAP, marking a new era in managing this complex and critical condition⁶⁻⁸.

CONCLUSION

In conclusion, integrating artificial intelligence (AI) into the management of severe acute pancreatitis (SAP) significantly enhances the potential for improved patient outcomes through real-time data analysis and personalized treatment approaches. While the benefits of AI in enhancing predictive accuracy and decision-making are clear, several challenges remain.

These include ensuring interoperability with existing electronic health record systems, maintaining robust data security and privacy, and providing comprehensive training for healthcare professionals. Addressing these challenges requires a multidisciplinary approach and continuous collaboration among experts in healthcare, technology, and ethics. By overcoming these obstacles and leveraging the capabilities of AI responsibly, we can advance the management of SAP, leading to more effective and efficient patient care.

REFERENCES

1. Beyer G, Hoffmeister A, Lorenz P, Lynen P, Lerch MM, Mayerle J. Clinical Practice Guideline—Acute and Chronic Pancreatitis. *Dtsch Arztebl Int.* 2022 Jul 25;119(29-30):495-501. doi: 10.3238/arztebl.m2022.0223.
2. Li W, Ou L, Fu Y, Chen Y, Yin Q, Song H. Risk factors for concomitant infectious pancreatic necrosis in patients with severe acute pancreatitis: A systematic review and meta-analysis. *Clin Res Hepatol Gastroenterol.* 2022 May;46(5):101901. doi: 10.1016/j.clinre.2022.101901.
3. Imam Z, Hanna A, Jomaa D, Khasawneh M, Abonofal A, Murad MH. Hypercalcemia of Malignancy and Acute Pancreatitis. *Pancreas.* 2021 Feb 1;50(2):206-213. doi: 10.1097/MPA.0000000000001741.
4. Huang W, de la Iglesia-García D, Baston-Rey I, Calviño-Suarez C, Lariño-Noia J, Iglesias-Garcia J, Shi N, Zhang X, Cai W, Deng L, Moore D, Singh VK, Xia Q, Windsor JA, Domínguez-Muñoz JE, Sutton R. Exocrine Pancreatic Insufficiency Following Acute Pancreatitis: Systematic Review and Meta-Analysis. *Dig Dis Sci.* 2019 Jul;64(7):1985-2005. doi: 10.1007/s10620-019-05568-9.
5. Nakai Y, Shiomi H, Hamada T, Ota S, Takenaka M, Iwashita T, Sato T, Saito T, Masuda A, Matsubara S, Iwata K, Mukai T, Isayama H, Yasuda I; WONDERFUL study group in Japan. Early versus delayed interventions for necrotizing pancreatitis: A systematic review and meta-analysis. *DEN Open.* 2022 Oct 10;3(1): e171. doi: 10.1002/deo2.171.
6. Niu CG, Zhang J, Zhu KW, Liu HL, Ashraf MF, Okolo PI 3rd. Comparison of early and late intervention for necrotizing pancreatitis: A systematic review and meta-analysis. *J Dig Dis.* 2023 May;24(5):321-331. doi: 10.1111/1751-2980.13201.
7. Singh RR, Mitchell W, David Y, Cheesman A, Dixon RE, Nagula S, DiMaio CJ, Greenwald DA, Kumta NA. Pancreatic Fungal Infection in Patients With Necrotizing Pancreatitis: A Systematic Review and Meta-analysis. *J Clin Gastroenterol.* 2021 Mar 1;55(3):218-226. doi: 10.1097/MCG.0000000000001467.
8. Hu WM, Hua TR, Zhang YL, Chen GR, Song K, Pendharkar S, Wu D, Windsor JA. Prognostic significance of organ failure and infected pancreatic necrosis in acute pancreatitis: An updated systematic review and meta-analysis. *J Dig Dis.* 2023 Dec;24(12):648-659. doi: 10.1111/1751-2980.13243.
9. Tran A, Fernando SM, Rochweg B, Inaba K, Bertens KA, Engels PT, Balaa FK, Kubelik D, Matar M, Lenet TI, Martel G. Prognostic factors associated with development of infected necrosis in patients with acute necrotizing or severe pancreatitis-A systematic review and meta-analysis. *J Trauma Acute Care Surg.* 2022 May 1;92(5):940-948. doi: 10.1097/TA.0000000000003502.
10. Timmerhuis HC, van Dijk SM, Verdonk RC, Bollen TL, Bruno MJ, Fockens P, van Hooft JE, Voermans RP, Besselink MG, van Santvoort HC; Dutch Pancreatitis Study Group. Various Modalities Accurate in Diagnosing a Disrupted or Disconnected Pancreatic Duct in Acute Pancreatitis: A Systematic Review. *Dig Dis Sci.* 2021 May;66(5):1415-1424. doi: 10.1007/s10620-020-06413-0.

11. van Dijk SM, Timmerhuis HC, Verdonk RC, Reijnders E, Bruno MJ, Fockens P, Voermans RP, Besselink MG, van Santvoort HC; Dutch Pancreatitis Study Group. Treatment of disrupted and disconnected pancreatic duct in necrotizing pancreatitis: A systematic review and meta-analysis. *Pancreatology*. 2019 Oct;19(7):905-915. doi: 10.1016/j.pan.2019.08.006.
12. Guo D, Dai W, Shen J, Zhang M, Shi Y, Jiang K, Guo L. Assessment of Prophylactic Carbapenem Antibiotics Administration for Severe Acute Pancreatitis: An Updated Systematic Review and Meta-Analysis. *Digestion*. 2022;103(3):183-191. doi: 10.1159/000520892.
13. Zhu L, Shen J, Fu R, Lu X, Du L, Jiang R, Zhang M, Shi Y, Jiang K, Shi Y. Early versus Delayed Minimally Invasive Intervention for Acute Necrotizing Pancreatitis: An Updated Systematic Review and Meta-Analysis. *Dig Surg*. 2022;39(5-6):224-231. doi: 10.1159/000529465.
14. Hamada T, Iwashita T, Saito T, Shiomi H, Takenaka M, Isayama H, Yasuda I, Nakai Y; WONDERFUL study group in Japan. Disconnected pancreatic duct syndrome and outcomes of endoscopic ultrasound-guided treatment of pancreatic fluid collections: Systematic review and meta-analysis. *Dig Endosc*. 2022 May;34(4):676-686. doi: 10.1111/den.14142.
15. Mohan BP, Madhu D, Toy G, Chandan S, Khan SR, Kassab LL, Bilal M, Facciorusso A, Sandhu I, Adler DG. Hydrogen peroxide-assisted endoscopic necrosectomy of pancreatic walled-off necrosis: a systematic review and meta-analysis. *Gastrointest Endosc*. 2022 Jun;95(6):1060-1066.e7. doi: 10.1016/j.gie.2022.01.018.
16. Mutneja HR, Bhurwal A, Arora S, Goel A, Vohra I, Attar BM. Acute pancreatitis in patients with COVID-19 is more severe and lethal: a systematic review and meta-analysis. *Scand J Gastroenterol*. 2021 Dec;56(12):1467-1472. doi: 10.1080/00365521.2021.1971757.
17. Maisonneuve P, Lowenfels AB, Lankisch PG. The harmless acute pancreatitis score (HAPS) identifies non-severe patients: A systematic review and meta-analysis. *Pancreatology*. 2021 Dec;21(8):1419-1427. doi: 10.1016/j.pan.2021.09.017.
18. Poropat G, Goričanec K, Lacković A, Kresović A, Lončarić A, Marušić M. Systematic Review with Trial Sequential Analysis of Prophylactic Antibiotics for Acute Pancreatitis. *Antibiotics (Basel)*. 2022 Sep 3;11(9):1191. doi: 10.3390/antibiotics11091191.
19. Khizar H, Zhicheng H, Chenyu L, Yanhua W, Jianfeng Y. Efficacy and safety of endoscopic drainage versus percutaneous drainage for pancreatic fluid collection; a systematic review and meta-analysis. *Ann Med*. 2023 Dec;55(1):2213898. doi: 10.1080/07853890.2023.2213898.
20. Gao L, Zhang H, Li G, Ye B, Zhou J, Tong Z, Ke L, Windsor JA, Li W; Chinese Acute Pancreatitis Clinical Trials Group (CAPCTG). The clinical outcome from early versus delayed minimally invasive intervention for infected pancreatic necrosis: a systematic review and meta-analysis. *J Gastroenterol*. 2022 Jun;57(6):397-406. doi: 10.1007/s00535-022-01876-6.

21. Shrestha DB, Budhathoki P, Sedhai YR, Adhikari A, Poudel A, Aryal BB, Gurung TM, Karki B, Karki BR, Patel D. Urgent Endoscopic Retrograde Cholangiopancreatography (ERCP) vs. Conventional Approach in Acute Biliary Pancreatitis Without Cholangitis: An Updated Systematic Review and Meta-Analysis. *Cureus*. 2022 Jan 17;14(1):e21342. doi: 10.7759/cureus.21342.
22. Tang P, Ali K, Khizar H, Ni Y, Cheng Z, Xu B, Qin Z, Zhang W. Endoscopic versus minimally invasive surgical approach for infected necrotizing pancreatitis: a systematic review and meta-analysis of randomized controlled trials. *Ann Med*. 2023;55(2):2276816. doi: 10.1080/07853890.2023.2276816.
23. Hu Y, Li C, Zhao X, Cui Y. An endoscopic or minimally invasive surgical approach for infected necrotizing pancreatitis: a systematic review and meta-analysis. *Rev Esp Enferm Dig*. 2019 Jun;111(6):471-480. doi: 10.17235/reed.2019.5792/2018.
24. Vánca S, Németh D, Hegyi P, Szakács Z, Hegyi PJ, Pécsi D, Mikó A, Erőss B, Erős A, Pár G. Fatty Liver Disease and Non-Alcoholic Fatty Liver Disease Worsen the Outcome in Acute Pancreatitis: A Systematic Review and Meta-Analysis. *J Clin Med*. 2020 Aug 20;9(9):2698. doi: 10.3390/jcm9092698.
25. Jaiswal V, Mukherjee D, Batra N, Ruchika F, Susheela AT, Chia JE, Mukherjee D, Naz S, Victor AA, Pokhrel NB, Song D, Seen T, Almas T, Saleh MA, Bansrao AS, Mansoor E. Acute pancreatitis as a rare adverse event among cannabis users: A systematic review. *Medicine (Baltimore)*. 2022 Jul 1;101(26):e29822. doi: 10.1097/MD.00000000000029822.
26. Keshavarz P, Azrumelashvili T, Yazdanpanah F, Nejati SF, Ebrahimian Sadabad F, Tarjan A, Bazayr A, Mizandari M. Percutaneous catheter drainage of pancreatic associated pathologies: A systematic review and meta-analysis. *Eur J Radiol*. 2021 Nov;144:109978. doi: 10.1016/j.ejrad.2021.109978.
27. Bálint ER, Fűr G, Kiss L, Németh DI, Soós A, Hegyi P, Szakács Z, Tinusz B, Varjú P, Vincze Á, Erőss B, Czimmer J, Szepes Z, Varga G, Rakonczay Z Jr. Assessment of the course of acute pancreatitis in the light of aetiology: a systematic review and meta-analysis. *Sci Rep*. 2020 Oct 21;10(1):17936. doi: 10.1038/s41598-020-74943-8.
28. Tarján D, Szalai E, Lipp M, Verbóci M, Kói T, Erőss B, Teutsch B, Faluhelyi N, Hegyi P, Mikó A. Persistently High Procalcitonin and C-Reactive Protein Are Good Predictors of Infection in Acute Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis. *Int J Mol Sci*. 2024 Jan 20;25(2):1273. doi: 10.3390/ijms25021273.
29. Yang Y, Zhang Y, Wen S, Cui Y. The optimal timing and intervention to reduce mortality for necrotizing pancreatitis: a systematic review and network meta-analysis. *World J Emerg Surg*. 2023 Jan 27;18(1):9. doi: 10.1186/s13017-023-00479-7.
30. Valverde-López F, Han S, Coughlin S, Thiruvengadam N, Moreau C, Akshintala VS, Lee PJ; Collaborative Alliance for Pancreatic Education and Research. Outcomes of Endoscopic Management of Sterile Walled-Off Pancreatic Necrosis: A Systematic Review. *Pancreas*. 2021 Nov-Dec 01;50(10):1357-1362. doi: 10.1097/MPA.0000000000001929.

31. Hu Y, Zeng Q, Ren S, Wang K. Immediate versus postponed drainage for infected necrotizing pancreatitis: A systematic review and meta-analysis. *Asian J Surg*. 2023 Apr;46(4):1602-1603. doi: 10.1016/j.asjsur.2022.09.079.
32. Zhu C, Wu H, Yang X, Gao J. The outcomes of COVID-19 and acute pancreatitis: a systematic review and meta-analysis. *Transl Gastroenterol Hepatol*. 2024 Jan 4;9:6. doi: 10.21037/tgh-23-58.
33. Zahariev OJ, Bunduc S, Kovács A, Demeter D, Havelda L, Budai BC, Veres DS, Hosszúfalusi N, Erőss BM, Teutsch B, Juhász MF, Hegyi P. Risk factors for diabetes mellitus after acute pancreatitis: a systematic review and meta-analysis. *Front Med (Lausanne)*. 2024 Jan 9;10:1257222. doi: 10.3389/fmed.2023.1257222.
34. Radulova-Mauersberger O, Belyaev O, Birgin E, Bösch F, Brunner M, Müller-Debus CF, Wellner UF, Grützmann R, Keck T, Werner J, Uhl W, Witzigmann H. Indikationen zur chirurgischen und interventionellen Behandlung der akuten Pankreatitis. *Zentralbl Chir*. 2020 Aug;145(4):374-382. doi: 10.1055/a-1164-7099.
35. Sgaramella LI, Gurrado A, Pasculli A, Prete FP, Catena F, Testini M. Open necrosectomy is feasible as a last resort in selected cases with infected pancreatic necrosis: a case series and systematic literature review. *World J Emerg Surg*. 2020 Jul 29;15(1):44. doi: 10.1186/s13017-020-00326-z.
36. Zhi M, Zhu X, Lugea A, Waldron RT, Pandol SJ, Li L. Incidence of New Onset Diabetes Mellitus Secondary to Acute Pancreatitis: A Systematic Review and Meta-Analysis. *Front Physiol*. 2019 May 31;10:637. doi: 10.3389/fphys.2019.00637.
37. Ding X, Chen B. Effect of Aggressive Intravenous Fluid Resuscitation Versus Nonaggressive Fluid Resuscitation in the Treatment of Acute Pancreatitis: A Systematic Review and Meta-Analysis. *Pancreas*. 2023 Feb 1;52(2):e89-e100. doi: 10.1097/MPA.0000000000002230.
38. Dirweesh A, Khan MY, Li Y, Choo C, Freeman ML, Trikudanathan G. Isolated peripancreatic necrosis (PPN) is associated with better clinical outcomes compared with combined pancreatic and peripancreatic involvement (CPN)- a systematic review and meta-analysis. *Pancreatology*. 2020 Jan;20(1):1-8. doi: 10.1016/j.pan.2019.10.004.
39. Bircakova B, Bruha R, Lambert L, Grusova G, Michalek P, Burgetova A. A bimodal pattern of the onset of COVID-19 related acute pancreatitis supports both the cytotoxic and immune-related pathogenesis - a systematic review. *Scand J Gastroenterol*. 2021 Jul;56(7):870-873. doi: 10.1080/00365521.2021.1922751.
40. Psaltis E, Varghese C, Pandanaboyana S, Nayar M. Quality of life after surgical and endoscopic management of severe acute pancreatitis: A systematic review. *World J Gastrointest Endosc*. 2022 Jul 16;14(7):443-454. doi: 10.4253/wjge.v14.i7.443.
41. van den Berg FF, de Bruijn AC, van Santvoort HC, Issa Y, Boermeester MA. Early laboratory biomarkers for severity in acute pancreatitis; A systematic review and meta-analysis. *Pancreatology*. 2020 Oct;20(7):1302-1311. doi: 10.1016/j.pan.2020.09.007.
42. Luo D, Liu X, Du J, Liu J, Chen X, Zhou P, Li B, Su S. Endoscopic Transgastric Versus Surgical Approach for Infected Necrotizing Pancreatitis: A Systematic Review and

- Meta-Analysis. *Surg Laparosc Endosc Percutan Tech.* 2019 Jun;29(3):141-149. doi: 10.1097/SLE.0000000000000632.
43. Chong E, Ratnayake CB, Saikia S, Nayar M, Oppong K, French JJ, Windsor JA, Pandanaboyana S. Endoscopic transmural drainage is associated with improved outcomes in disconnected pancreatic duct syndrome: a systematic review and meta-analysis. *BMC Gastroenterol.* 2021 Feb 25;21(1):87. doi: 10.1186/s12876-021-01663-2.
44. Garg R, Gupta S, Singh A, Simonson MT, Rustagi T, Chahal P. Hydrogen peroxide assisted endoscopic necrosectomy for walled-off pancreatic necrosis: A systematic review and meta-analysis. *Pancreatology.* 2021 Dec;21(8):1540-1547. doi: 10.1016/j.pan.2021.09.007.
45. Haney CM, Kowalewski KF, Schmidt MW, Koschny R, Felinska EA, Kalkum E, Probst P, Diener MK, Müller-Stich BP, Hackert T, Nickel F. Endoscopic versus surgical treatment for infected necrotizing pancreatitis: a systematic review and meta-analysis of randomized controlled trials. *Surg Endosc.* 2020 Jun;34(6):2429-2444. doi: 10.1007/s00464-020-07469-9.
46. Bang JY, Wilcox CM, Arnoletti JP, Varadarajulu S. Superiority of endoscopic interventions over minimally invasive surgery for infected necrotizing pancreatitis: meta-analysis of randomized trials. *Dig Endosc.* 2020 Mar;32(3):298-308. doi: 10.1111/den.13470.
47. Liu Z, Liu P, Xu X, Yao Q, Xiong Y. Timing of minimally invasive step-up intervention for symptomatic pancreatic necrotic fluid collections: A systematic review and meta-analysis. *Clin Res Hepatol Gastroenterol.* 2023 Apr;47(4):102105. doi: 10.1016/j.clinre.2023.102105.
48. Bang JY, Wilcox CM, Navaneethan U, Hawes RH, Varadarajulu S. Treatment of walled-off necrosis using lumen-apposing metal stents versus plastic stents: a systematic review and meta-analysis of data from randomized trials. *Endoscopy.* 2024 Mar;56(3):184-195. doi: 10.1055/a-2169-0362.
49. Ricci C, Pagano N, Ingaldi C, Frazzoni L, Migliori M, Alberici L, Minni F, Casadei R. Treatment for Infected Pancreatic Necrosis Should be Delayed, Possibly Avoiding an Open Surgical Approach: A Systematic Review and Network Meta-analysis. *Ann Surg.* 2021 Feb 1;273(2):251-257. doi: 10.1097/SLA.00000000000003767.
50. Chandrasekhara V, Barthet M, Devière J, Bazerbachi F, Lakhtakia S, Easler JJ, Peetermans JA, McMullen E, Gjata O, Gourlay ML, Abu Dayyeh BK. Safety and efficacy of lumen-apposing metal stents versus plastic stents to treat walled-off pancreatic necrosis: systematic review and meta-analysis. *Endosc Int Open.* 2020 Nov;8(11):E1639-E1653. doi: 10.1055/a-1243-0092.
51. Gjeorgjievski M, Bhurwal A, Chouthai AA, Abdelqader A, Gaidhane M, Shahid H, Tyberg A, Sarkar A, Kahaleh M. Percutaneous endoscopic necrosectomy (PEN) for treatment of necrotizing pancreatitis: a systematic review and meta-analysis. *Endosc Int Open.* 2023 Mar 23;11(3):E258-E267. doi: 10.1055/a-1935-4738.
52. Kumari R, Sadarat F, Luhana S, Parkash O, Lohana AC, Rahaman Z, Wang HY, Mohammed YN, Kumar SK, Chander S. Evaluating the efficacy of different volume

- resuscitation strategies in acute pancreatitis patients: a systematic review and meta-analysis. *BMC Gastroenterol.* 2024 Mar 25;24(1):119. doi: 10.1186/s12876-024-03205-y.
53. Renelus BD, Jamorabo DS, Gurm HK, Dave N, Briggs WM, Arya M. Comparative outcomes of endoscopic ultrasound-guided cystogastrostomy for peripancreatic fluid collections: a systematic review and meta-analysis. *Ther Adv Gastrointest Endosc.* 2019 May 14;12:2631774519843400. doi: 10.1177/2631774519843400.
54. Malik A, Amjad W, Farooq U, Saleem SS, Malik MI. Evaluation of the effect of probiotics on septic complications in patients with severe acute pancreatitis. A systematic review and meta-analysis. *Prz Gastroenterol.* 2023;18(3):281-291. doi: 10.5114/pg.2022.118164.
55. van den Berg FF, Kempeneers MA, van Santvoort HC, Zwinderman AH, Issa Y, Boermeester MA. Meta-analysis and field synopsis of genetic variants associated with the risk and severity of acute pancreatitis. *BJS Open.* 2020 Feb;4(1):3-15. doi: 10.1002/bjs5.50231.
56. Ahmed Z, Ramai D, Merza N, Badal J, Iqbal U, Arif SF, Al-Hillan A, Varughese T, Lee-Smith W, Nawras A, Alastal Y, Khara HS, Confer BD, Diehl DL, Adler DG. Safety and Efficacy of Powered Non-Thermal Endoscopic Resection Device for Removal of Colonic Polyps: A Systematic Review and Meta-Analysis. *Gastroenterology Res.* 2023 Oct;16(5):254-261. doi: 10.14740/gr1638.
57. Beran A, Mohamed MFH, Abdelfattah T, Sarkis Y, Montrose J, Sayeh W, Musallam R, Jaber F, Elfert K, Montalvan-Sanchez E, Al-Haddad M. Lumen-Apposing Metal Stent With and Without Concurrent Double-Pigtail Plastic Stent for Pancreatic Fluid Collections: A Comparative Systematic Review and Meta-Analysis. *Gastroenterology Res.* 2023 Apr;16(2):59-67. doi: 10.14740/gr1601.
58. Hsieh PH, Su HY, Lin CY, Kang YN, Chang CC. Infection rate among nutritional therapies for acute pancreatitis: A systematic review with network meta-analysis of randomized controlled trials. *PLoS One.* 2019 Jul 10;14(7):e0219151. doi: 10.1371/journal.pone.0219151.
59. Liu C, Wu CH, Zheng XD, Liu JP, Li CL, Zhao JY, Lan Q, Zhou WL, Li WB. Hepatic portal venous gas: A case report and analysis of 131 patients using PUBMED and MEDLINE database. *Am J Emerg Med.* 2021 Jul;45:506-509. doi: 10.1016/j.ajem.2020.06.085.
60. Borbély RZ, Szalai EÁ, Philip BM, Dobszai D, Teutsch B, Zolcsák Á, Veres DS, Erőss B, Gellért B, Hegyi PJ, Hegyi P, Faluhelyi N. The risk of developing splanchnic vein thrombosis in acute pancreatitis increases 3 days after symptom onset: A systematic review and meta-analysis. *United European Gastroenterol J.* 2024 Feb 24. doi: 10.1002/ueg2.12550.
61. Gopakumar H, Revanur V, Kandula R, Puli SR. Endoscopic ultrasound-guided lumen-apposing metal stent with or without coaxial plastic stent for pancreatic fluid collections: a systematic review and meta-analysis comparing safety and efficacy. *Ann Gastroenterol.* 2024 Mar-Apr;37(2):242-250. doi: 10.20524/aog.2024.0858.