Chirurgia (2026) 121: 321-327
No. 3, May - June

http://dx.doi.org/10.21614/chirurgia.3194

Risk Factors for Acute on Chronic Pancreatitis – A Multicentric Case-Control Study

Alina Florentina Pistriţu[1,2], Mihai Radu Pahomeanu[1,2]*, Andreea Irina Ghiţă[1], Irina Ştefania Diaconu[1], Hosein Nayyerani[1], Andreea Daniela Bota[1,3], Deniz Günşahin[1,4], Cristian George Ţieranu[1,3], Vasile Şandru[1,4], Carmen Monica Preda[1,5], Bogdan Silviu Ungureanu[6,7], Lucian Negreanu[1,2]

[1]Faculty of Medicine, Carol Davila University of Medicine and Pharmacy. Bucharest, Romania
[2]Internal Medicine and Gastroenterology Department, University Emergency Hospital of Bucharest, Romania
[3]Gastroenterology Department, Elias Emergency University Hospital, Bucharest, Romania
[4]Gastroenterology Department, Clinical Emergency Hospital of Bucharest, Romania
[5]Gastroenterology Department, Fundeni Clinical Institute, Bucharest, Romania
[6]Faculty of Medicine, Craiova University of Medicine and Pharmacy, Craiova, Romania
[7]Gastroenterology Department, Dolj County Emergency Hospital, Craiova, Romania

***Corresponding author:**
Mihai Radu Pahomeanu, MD
Internal Medicine and Gastroenterology Department, University Emergency Hospital of Bucharest, Romania
E-mail: mihairadu.pahomeanu@gmail.com

Rezumat

Factori de risc pentru pancreatita cronică acutizată – un studiu multicentric de tip caz-control

Obiective: Pancreatita cronică acutizată (PCA) este definită ca agravarea acută a procesului inflamator asociat pancreatitei cronice (PC) şi determină, de regulă, deteriorarea stării clinice şi accentuarea durerii pancreatice. Heterogenitatea acestei afecţiuni îngreunează înţelegerea detaliilor din spatele unor date clinice importante, precum diferenţele legate de sex, etiologia sau evoluţia la externare. Ne-am propus să stabilim dacă anomaliile pancreatice congenitale reprezintă un factor pentru dezvoltarea PCA.
Metode: În acest studiu multicentric de tip caz-control, 181 de cazuri de PCA au fost comparate cu 1754 de controale cu pancreatită acută (PA) provenind din patru centre. Pacienţii au fost spitalizaţi consecutiv între 1 ianuarie 2015 şi 31 decembrie 2023. În analiza statistică au fost utilizate frecvenţe, regresie logistică, precum şi testele chi-pătrat Pearson, Shapiro–Wilk şi Mann–Whitney U. Cazurile au fost extrase din registrul BUC-API, actual redenumit RO-API.
Rezultate: Bărbaţii au prezentat o probabilitate de 2,6 ori mai mare de a suferi de PCA ($p < 0,01$). Pacienţii cu anomalii pancreatice au avut o probabilitate de 51,2 ori mai mare de a dezvolta PCA ($p < 0,01$). S-a observat o şansă cu 70% mai mică de deces în timpul spitalizării în cazul pacienţilor cu PCA comparativ cu cei cu PA ($p < 0,01$).
Concluzie: Bărbaţii cu anomalii pancreatice prezintă un risc mai mare de a dezvolta PCA.

Cuvinte cheie: pancreatită cronică acutizată, sex, pancreas, anomalii pancreatice, pancreatită, factori de risc

Received: 10.08.2025
Accepted: 15.12.2026

Abstract

Background/Objectives: Acute on chronic pancreatitis (ACP) is defined as acute worsening of the inflammatory process associated with chronic pancreatitis (CP) and typically results in deteriorating clinical condition and increased pancreatic pain. The heterogeneity of this disease hinders understanding the details behind important clinical data, such as sex differences, etiology, or outcome at discharge. We aim to find if congenital pancreatic abnormalities are a factor for ACP development.

Methods: In this multicentric case-control study, 181 cases of acute on chronic pancreatitis (ACP) were compared with 1754 controls with acute pancreatitis (AP) from four centers. The patients were consecutively hospitalized between January 1, 2015 and December 31, 2023. Frequencies, logistic regression, and the Pearson chi-square, Shapiro–Wilk, and Mann–Whitney U tests were deployed in the statistical analysis.

Results: The males had a 2.6 times higher likelihood of suffering from ACP ($p < 0.01$). If the patients had pancreatic abnormalities, they had a 51.2 times higher probability of developing ACP ($p < 0.01$). A 70% lower chance of dying during hospitalization if a patient suffered from ACP rather than AP was observed ($p < 0.01$).

Conclusion: Males with pancreatic abnormalities have a higher risk of developing ACP.

Keywords: acute on chronic pancreatitis, sex, pancreas, pancreatic abnormalities, pancreatitis, risk factors

Introduction

Acute on chronic pancreatitis (ACP) represents "acute worsening of the inflammatory process associated with chronic pancreatitis (CP), resulting in a deterioration of the patient's clinical condition, typically resulting in increased pancreatic pain" (1). The distinction between ACP and acute pancreatitis (AP) is that a prior diagnosis of CP is needed to diagnose ACP. Less frequently, ACP might be accompanied by worsening jaundice, vomiting, panniculitis (2,3), or complications such as malabsorption or mediastinal pseudocysts (4,5). Regarding other important clinical factors, there are not enough reliable data published to date to quantify the magnitude of sex stratification, etiology, or incidence (1,6).

The literature on ACP is quite scarce because a clear definition of this condition has only recently been proposed (1,7). Nevertheless, in the literature, there have been several attempts to describe this disease. Although ACP is a pathology that occurs in a pancreas altered by chronic fibroinflammatory destruction seen in CP, most of the literature links ACP more with AP (7) because the clinical, biological, and radiological presentation of both are strikingly similar. The group of cases included in this research fits the above-mentioned proposed ACP definition. Previously to the proposed definition of ACP, some authors found a predominance of males with ACP (8), but without quantifying the magnitude of this phenomenon. Other researchers found alcohol to be a predominant etiology of ACP, with hospitalization for acute exacerbation of CP being dose-related (9). The research gap regarding sex stratification and etiology should be filled to develop new strategies best suited to the primary prevention of this disease.

This research was a retrospective multicentric case-control study that aimed to determine if there were any differences between patients with ACP and those with AP regarding congenital anatomical abnormalities within pancreas. The secondary aim was to explore other potential behavioral or medical factors that may contribute to such differences.

Methods

Study Design, Participants, and Sample

This retrospective multicentric case-control study included patients drawn from the BUC-API registry, which registers consecutively admitted cases of AP and ACP from four centers. Details of the extraction of data from electronic health records (EHRs) into the BUC-API registry have been previously described (11). In addition to what was mentioned in the cited paper, we have extended our registry to three new centers with the same data extraction methodology from EHRs and extended the timeframe from April 1, 2022 to December 31, 2023 in regard to all the involved centers.

Inclusion and Exclusion Criteria

The registry inclusion criteria are as follows: 1) positive diagnostic criteria for acute pancreatitis, according to the International Association of Pancreatology (IAP) and American Pancreatology Association (APA) guidelines (12); 2) adult patients with informed consent given

prior to hospitalization; 3) admission to a participating center between January 1, 2015 and December 31, 2023. The exclusion criterion is missing medical documents in the EHRs that prove all the inclusion criteria. For the patients with multiple episodes recorded in the registry, we considered only the latest one, and social IDs were used to account for multiple episodes in the same patient.

The controls were all patients without CP, as defined by the following: 1) a previous diagnosis of CP documented in the EHR; 2) positive diagnostic criteria for CP, in accordance with the 2020 American College of Gastroenterology Guidelines (13).

The etiology was stratified in accordance with Slesienger's and Fordtran's Gastroenterology and Liver Diseases, 10th edition (14). For the statistical analysis, all etiologies with less than 18 patients in the cases group were categorized as other. For the alcoholic and biliary etiologies, we classified the cases according to the IAP/APA guidelines (12), as follows: alcoholic - as described by the attending physician through anamnesis; and biliary-alanine aminotransferase (ALT) > 150 U/L no more than 48 h after the onset of disease together with ultrasonographic signs of gallstones. We considered that intrapancreatic anomalies caused all cases that did not have any other apparent cause after extensive clinical, radiological, and biological investigations and that had any anatomical anomalies except for calcifications, ductal dilation, pseudocysts, or walled-off necrosis. Pancreatic anatomical abnormalities were identified using contrast-enhanced computed tomography and/or magnetic resonance imaging, if necessary. All imaging studies were reviewed by board-certified radiologists at each participating center. Additional details regarding the etiology stratification methodology in the BUC-API registry are available in a previously published paper (11).

This study was not aimed to find any disparities regarding continuous variables, like length of hospitalization.

Setting

We conducted this study in four large tertiary care teaching hospitals in Bucharest, Romania: University Emergency Hospital of Bucharest; Emergency Clinical Hospital of Bucharest; Fundeni Clinical Institute; and Elias University Emergency Hospital. These hospitals have a total of 3600 beds for inpatient care. Apart from the Fundeni Clinical Institute, all focus on acute care. The patients included in the registry were consecutively admitted to these centers between January 1, 2015 and December 31, 2023.

Ethical Considerations

This study was approved by the Research Ethics Committee of the University Emergency Hospital of Bucharest under the umbrella of the Bucharest Acute Pancreatitis Index (BUC-API) registry, currently known as the Romanian Acute Pancreatitis Index (RO-API) registry. Written informed consent of the patients for participation in the study was obtained prior to admission. This study was conducted in accordance with the 1968 Helsinki Declaration version (updated in 2008), and the manuscript has been written according to the principles of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (10) for case-report studies. The cases were handled in the BUC-API registry in compliance with the European Union's (EU) General Data Protection Regulation.

Statistical Analysis

For the descriptive statistics, we deployed frequencies, means, and medians. To quantify the presence of any correlations, we used the Pearson chi-square test. To determine how one categorical variable correlated with another, we used logistic regression. The Shapiro-Wilk test was used to check for normality of distribution of the continuous variables. Mann-Whitney U test was used to compare the differences between two ordinal variables. For statistical significance, we took into account any p-value < 0.05 and/or any 95.0% confidence interval (CI) that excluded 1.0.

The BUC-API registry data were organized using Microsoft Excel® 2019 (Microsoft Inc., Redmond, Washington, USA) and Google Spreadsheets® (Alphabet Inc., Mountain View, California, USA). SPSS® version 29.0.0.0 (IBM Inc., Armonk, New York, USA) was used to perform all the statistical tests.

Results

Study Sample

In the BUC-API registry, 2303 consecutive cases in 1935 unique patients were recorded. This population included 181 (9.4%) patients with ACP (i.e., the case group) and 1754 (90.6%) patients with AP (i.e., the control group). The AP:ACP ratio was 9.7. In the cases group, the youngest patient was 18 years old and the oldest was 94 years old. The shortest admission was one day while the longest was 79 days. The baseline characteristics of the population are presented in *Table 1*.

Table 1. Baseline characteristics

Characteristic	Cases (n = 181)	Controls (n = 1754)	p-value
Sex, males (%)	77.3%	56.7%	<0.01
Age, median (IQR) (years)	54.0 (45.0–66.0)	58.0 (45.0–70.0)	0.12
Length of hospitalization, median (IQR) (days)	7.0 (5.0–10.5)	7.0 (5.0–11.0)	N/A
Etiology (%)			<0.01
Alcoholic	40.9%	26.9%	
Pancreatic abnormalities	23.8%	0.5%	
Gallstones	12.7%	44.8%	
Other known cause	9.9%	11.0%	
Idiopathic	12.7%	16.8%	
Severity (%)			0.36
Mild	47.5%	51.2%	
Moderately severe	42.0%	36.7%	
Severe	10.5%	12.1%	
Outcome (%)			0.02
Healed/ameliorated	81.8%	82.4%	
Discharge at will	8.3%	5.8%	
Transfer	5.0%	4.2%	
Stationary	2.8%	1.0%	
Deceased	2.2%	6.7%	

IQR: interquartile range.; N/A – Not Available as it was not included in study design or aims

Primary Outcome

A Pearson chi-square test was performed to examine differences between the sexes in the two groups investigated. The result showed a significant difference (χ^2 (1) = 28.9, p < 0.01), suggesting a difference in sex distribution between the cases and the controls.

To observe the relationship between sex and the two groups, a binomial logistic regression was conducted. The results showed that the males had a 2.6 times higher likelihood of developing ACP compared to AP (odds ratio [OR] = 2.6, 95.0% CI 1.8–3.7, p < 0.01). This suggests a significant association between being male and the development of ACP. See the Supplementary Files.

Secondary Outcomes

To determine if there were any significant differences between the etiologies in the cases group, a Pearson chi-square test was conducted (χ^2 (4) = 383.4, p < 0.01). The results suggested a significant difference in the distribution of etiology within the cases group. To describe the relationship between etiology and the development of ACP, a multinomial logistic regression test was run. The test results showed that there was a 51.2 times higher probability of a patient with pancreatic anatomical anomalies developing ACP instead of AP (OR = 51.2, 95.0% CI 21.6–121.8, p < 0.01), but a patient suffering from gallstones was 70% less likely to develop ACP (OR = 0.3, 95.0% CI 0.2–0.6, p < 0.01). See the *Supplementary materials*.

To compare the outcome at discharge between the cases and the controls, a Pearson chi-square test was conducted and showed significant differences (χ^2 (4) = 11.4, p = 0.02). To investigate the differences regarding outcome at discharge, a multinomial logistic regression was conducted, which showed that a patient with ACP had a three times higher probability of surviving than a patient with AP (OR = 3.0, 95.0% CI 1.1–8.2, p = 0.03). See the Supplementary Files.

In regard to severity, no significant differences were observed between the groups (χ^2 (2) = 2.1, p = 0.36). Regarding age, as the Shapiro–Wilk test showed that the data of the entire sample were not normally distributed (p < 0.01), a Mann–Whitney U test was run. This showed no significant differences (p = 0.12) in age between the two groups.

Discussion

ACP is a relatively newly defined condition that shares similarities with both AP and CP. Based on population studies, some authors have suggested a broad spectrum of incidence at around 12%–14% of total admissions for AP (1,15,16). However, these previously made estimations, which suggested a definition for ACP, might be overstated because in our population, we observed a slightly lower percentage. As CP itself is a disease with a great burden on quality of life (QoL) (18), we should develop strategies to prevent any deterioration in patient well-being and any possible complications that can arise from ACP. However, the fact that there are not enough reliable sources

regarding important demographic and clinical factors of ACP, such as sex stratification and etiology, greatly impacts our ability to devise such strategies.

ACP involves a complex interplay of mechanisms in its pathophysiology and severity. This disease can develop from a single episode of AP or multiple attacks of recurrent AP, the latter having much more chance of evolving into CP (19). CP modifications of the pancreas result from damage to acinar and/or ductal cells, which promotes their necrosis and/or apoptosis, leading to the transformation of pancreatic stellate cells and the formation of fibrosis and loss of parenchyma (20). In most cases, AP is characterized by a new acute inflammation of the pancreatic tissue with a short duration and sudden onset (21). According to the previously mentioned definition, it seems that ACP has a slightly different pathophysiology, being in fact an amplification of alterations already existing in CP and not a recently surfaced process (22).

Because of the typical changes in the architecture of the organ and the formation of fibrosis, along with increased intrapancreatic fat seen in CP, patients are protected against severe forms of the disease and against developing necrosis when experiencing acute CP flares. These are explained by biochemical and molecular interactions, which result in reduced intercellular lipolytic flux (23). In this study, no difference in severity was observed between the cases and the controls, but there was a lower chance of dying during admission for the ACP patients, which suggests that the classic Revised Atlanta Classification (24) used for stratifying AP severity might not have the same results for ACP.

Alcohol use disorders (AUDs) are a preventable and modifiable risk factor in both AP (25) and CP (26). Although we did not find any statistical associations between alcohol use and ACP, the main cause of ACP in our population was ethanol abuse. Any primary prevention strategies should probably include better counseling of the relevant CP patients, cognitive behavioral therapy, or even oriented drug therapy, such as acamprosate, naltrexone, disulfiram, or baclofen (27,28), under a psychiatrist's guidance. Lessons could also be drawn from the PANDA trial (29) when its results are published. As far as we know, the progression to a chronic form of this disease is probably linked with alcohol consumption after the first AP episode. Alcohol intake may also serve as a primary cause of a sentinel pancreatis attack (30). In addition, alcohol seems to be an important risk factor for recurrent AP (31) and, as such, is probably one of the drivers of the transition to CP.

In regard to AUDs, even if there are more cases in males than in females, it seems there is an increasing trend for females to suffer from AUDs, especially as adolescents (32). The risk of developing AUDs seems to stem not only from psychological or cultural factors, but also from an elaborate hormonal interplay, as it seems that higher levels of testosterone in males and the respectively higher levels of estrogen in females can increase the risk (33). In our study, we found a higher ratio of males suffering from ACP related to alcohol abuse, which might also suggest that testosterone is one of the key hormonal factors in AUDs.

Another interesting result was the higher risk of developing ACP with regard to pancreatic abnormalities. This should not be a striking result, as intrapancreatic tumors are a more frequent finding in males than in females, and women's hormonal profiles may be a protective factor. When discovered, pancreatic tumors are prone to be located in the head of the organ and to appear in obese patients (38). Moreover, ACP is more prevalent in males (39), so our study's results bring up an interesting aspect about the risk of developing ACP due to pancreatic abnormalities.

CP exacerbations lead to alterations in the cellular structure and DNA, and it is known that CP is a risk factor for pancreatic neoplasia (40). An intriguing aspect concerning intraductal papillary mucinous neoplasm, which is more often seen in men, is that AP is considered a risk factor for progression to malignancy; however, further research is needed (41). Mucinous cyst neoplasms and solid pseudopapillary neoplasms are considerably more frequent among women, and benign tumors have been found to be more prevalent than serous cystadenomas (42). Two Norwegian papers that investigated pancreatic cancer in female patients highlighted statistically significant correlations between neoplasia and age at menopause, breastfeeding, and parity after adjusting for breastfeeding (43,44).

Considering everything discussed, we think it important to mention some aspects of demography, clinical evolution, and complications that can occur during an ACP episode. First, males are predominant in ACP incidence, as found by some studies (45,46), and black people have been found to be more prone to developing this disease (46). As such, we emphasize that in our population, most patients were Caucasian. Some factors that seem to be connected with ACP severity include older age, the presence of other underlying pathologies, and weight loss, with alcohol consumption being tied to lower severity in other studies (46).

In addition to these aspects, in one study, interstitial pancreatitis was the most common form during ACP attacks (developed in 51% of cases) (45), similar to AP cases (47), and another team of researchers found that pseudocysts appeared as the morphological type in

41.8% of the cases (15). In a study comparing developments in both AP and CP, the most affected by both diseases were men, and the most prevalent etiology was alcohol-related, although AP has other etiologies that are found in a fairly significant proportion (48). Outlining pancreatic cancer and the risk of developing such a pathology, it has been established that both AP and CP increase the chance of pancreatic neoplasia and pancreatic abnormalities, but a fairly recent study demonstrated a greater likelihood of an extended and increased risk of malignant transformation of the pancreas (49). In the same paper, women who had CP with AP were at a higher risk of pancreatic cancer. Further research is essential for advancing studies on biomarkers and risk factors that could predict the probability of ACP. Moreover, a thorough investigation of the pathophysiological mechanism of the disease is required.

Conclusion

As far as we know, this is probably one of the first studies to be conducted after a clear definition of ACP was made to measure the direction and magnitude of the risk factor associations. Our results were expected in regard to our clinical practice and the previous literature published on ACP, CP, and AP. Males with pancreatic abnormalities are at risk of developing ACP, and strategies to prevent this might improve the QoL of CP patients.

Acknowledgements

The authors would like to acknowledge the contribution the following people have made to data curation in the RO-API registry: Andrada Georgiana Badea, Miruna Alexandra Untea, Ioana Vaipan, Teodor Baciu, Maria Alexandra Almăşan, Andreea Treteanu, Ioana Gîia, Elena Ghizilă, Cosmin Andrian, Arina Gheorghe, Elena Alupei, and Ana Băiceanu.

Author's Contributions

A.F.P. and M.R.P had contributed to: analysis and interpretation of data; drafting the article and had approved the final version of the manuscript. All other authors had a substantial contribution in: conception and design; review for important intellectual content had approved the final version of the manuscript.

Conflicts of Interest

None to disclose.

Funding

All the funds required for this study were supported by the personal funds of the first and corresponding authors (A.F.P. and M.R.P.).

Supplementary Materials

Supplementary material associated with this article can be found, in the online version.

References

1. Bouça-Machado T, Bouwense SAW, Brand M, Demir IE, Frøkjșr JB, Garg P, et al. Position statement on the definition, incidence, diagnosis and outcome of acute on chronic pancreatitis. Pancreatology. 2023;23(2):143–50.
2. Duca NS, Feterik K, Ho J. Pancreatitis: The great masquerader? Cleve Clin J Med. 2018;85(10):752–3.
3. Agarwal M, Giri S, Gandhi V, Sharma A, Gupta R, Sharma V. Gastrointestinal: A cutaneous clue to painless acute on chronic pancreatitis. J Gastroenterol Hepatol. 2012;27(4):842–842.
4. Liao YT, Chiu NC, Chen CK, Su KC. Acute-on-chronic pancreatitis complicated with mediastinal pseudocysts and cardiac tamponade: A case report and literature review. Respirol Case Rep. 2022;10(4):e0929.
5. Dar S, Dar KH, Hussain U, Rafiq I, Zuhair HMU. A Case of Multi-Organ Failure Secondary to Malabsorption Occurring in the Presence of Acute-on-Chronic Pancreatitis. CUREUS J Med Sci. 2023;15(11):e48274.
6. Olesen SS, Kuhlmann L, Novovic S, Nøjgaard C, Kalaitzakis E, Jensen NM, et al. Association of multiple patient and disease characteristics with the presence and type of pain in chronic pancreatitis. J Gastroenterol Hepatol. 2020;35(2):326–33.
7. Bouça-Machado T, Andrea-Ferreira P, Pedersen JB, Mortensen MB, Novovic S, Windsor JA, et al. Confusion with the definition and diagnostic criteria for acute on chronic pancreatitis: review and recommendations. Scand J Gastroenterol. 2022;57(6):719-725.
8. Sharma D, Mallick B, Samanta J, Gupta V, Sinha SK, Kochhar R, et al. Acute-on-Chronic Pancreatitis: Analysis of Clinical Profile and Outcome. Cureus. 2021;13(4):e14242.
9. Szücs Á, Marjai T, Szentesi A, Farkas N, Párniczky A, Nagy G, et al. Chronic pancreatitis: Multicentre prospective data collection and analysis by the Hungarian Pancreatic Study Group. PLOS ONE. 2017;12(2):e0171420.
10. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. Int J Surg Lond Engl. 2014; 12(12):1495–9.
11. Pahomeanu MR, Constantinescu DI, Diaconu IS, Corbu DG, Negreanu L. Acute Pancreatitis - Drivers of Hospitalisation Cost - A Seven-Year Retrospective Study from a Large Tertiary Center. Healthcare. 2023;11(18):2482.
12. Besselink M, van Santvoort H, Freeman M, Gardner T, Mayerle J, Vege SS, et al. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13(4, suppl 2):E1–15.
13. Gardner TB, Adler DG, Forsmark CE, Sauer BG, Taylor JR, Whitcomb DC. ACG Clinical Guideline: Chronic Pancreatitis. Off J Am Coll Gastroenterol ACG. 2020;115(3):322.
14. Feldman M, Friedman LS, Brandt LJ, editors. Front Matter. In: Sleisenger and Fordtran's Gastrointestinal and Liver Disease (Ninth Edition). Philadelphia: W.B. Saunders; 2010. p. i–iii.
15. Kim KO, Kim TN. Acute Pancreatic Pseudocyst Incidence, Risk Factors, and Clinical Outcomes. Pancreas. 2012;41(4):577*81.
16. Garg SK, Sarvepalli S, Campbell JP, Obaitan I, Singh D, Bazerbachi F, et al. Incidence, Admission Rates, and Predictors, and Economic Burden of Adult Emergency Visits for Acute Pancreatitis: Data From the National Emergency Department Sample, 2006 to 2012. J Clin Gastroenterol. 2019 Mar;53(3):220–5.
17. Li C li, Jiang M, Pan C qiu, Li J, Xu L gang. The global, regional, and national burden of acute pancreatitis in 204 countries and territories, 1990–2019. BMC Gastroenterol. 2021;21:332.
18. Mokrowiecka A, Pinkowski D, Malecka-Panas E. Assessment of quality of life in patients with chronic pancreatitis. Med Sci Monit. 2011;17(10):CR583–8.
19. Sankaran SJ, Xiao AY, Wu LM, Windsor JA, Forsmark CE, Petrov MS. Frequency of Progression From Acute to Chronic Pancreatitis and Risk Factors: A Meta-analysis.

Gastroenterology. 2015;149(6):1490-1500.e1.
20. Ashraf H, Colombo JP, Marcucci V, Rhoton J, Olowoyo O. A Clinical Overview of Acute and Chronic Pancreatitis: The Medical and Surgical Management. Cureus. 2021;13(11):e19764.
21. Banks PA, Conwell DL, Toskes PP. The Management of Acute and Chronic Pancreatitis. Gastroenterol Hepatol. 2010;6(2 Suppl 5):1–16.
22. Bouça-Machado T, Bouwense SAW, Brand M, Demir IE, Frøkjșr JB, Garg P, et al. Position statement on the definition, incidence, diagnosis and outcome of acute on chronic pancreatitis. Pancreatology. 2023;23(2):143–50.
23. Acharya C, Cline RA, Jaligama D, Noel P, Delany JP, Bae K, et al. Fibrosis Reduces Severity of Acute-on-Chronic Pancreatitis in Humans. Gastroenterology. 2013; 145(2):466–75.
24. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis - 2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-11.
25. Sorrento C, Shah I, Yakah W, Ahmed A, Tintara S, Kandasamy C, et al. Inpatient Alcohol Cessation Counseling Is Associated With a Lower 30-Day Hospital Readmission in Acute Alcoholic Pancreatitis. J Clin Gastroenterol. 2022;56(9):e313.
26. Göltl P, Murillo K, Simsek O, Wekerle M, Ebert MP, Schneider A, et al. Impact of alcohol and smoking cessation on the course of chronic pancreatitis. Alcohol. 2024; 119:29–35.
27. Agabio R, Saulle R, Rosner S, Minozzi S. Baclofen for alcohol use disorder. COCHRANE DATABASE Syst Rev. 2023;(1):CD012557.
28. Attilia F, Perciballi R, Rotondo C, Capriglione I, Iannuzzi S, Attilia ML, et al. Pharmacological treatment of alcohol use disorder. Scientific evidence. Riv Psichiatr. 2018;53(3):123–7.
29. Sissingh NJ, Nagelhout A, Besselink MG, Boermeester MA, Bouwense SAW, Bruno MJ, et al. Structured alcohol cessation support program versus current practice in acute alcoholic pancreatitis (PANDA): Study protocol for a multicentre cluster randomised controlled trial. Pancreatology. 2023;23(8):942–8.
30. Weiss FU, Laemmerhirt F, Lerch MM. Etiology and Risk Factors of Acute and Chronic Pancreatitis. Visc Med. 2019;35(2):73–81.
31. Seppanen H, Puolakkainen P. Classification, Severity Assessment, and Prevention of Recurrences in Acute Pancreatitis. Scand J Surg. 2020;109(1):53–8.
32. Agabio R, Pisanu C, Gessa GL, Franconi F. Sex Differences in Alcohol Use Disorder. Curr Med Chem. 2017;24(24):2661–70.
33. Erol A, Ho AMC, Winham SJ, Karpyak VM. Sex hormones in alcohol consumption: a systematic review of evidence. Addict Biol. 2019;24(2):157–69.
34. Granell S, Pereda J, Gómez-Cambronero L, Cassinello N, Sabater L, Closa D, et al. Circulating TNF-α and its soluble receptors during experimental acute pancreatitis. Cytokine. 2004;25(4):187-91.
35. Milanesi E, Dobre M, Manuc TE, Becheanu G, Tieranu CG, Ionescu EM, et al. Mucosal gene expression changes induced by anti-TNF treatment in inflammatory bowel disease patients. Drug Dev Res. 2019;80(6):831-836.
36. Alcalá S, Sancho P, Martinelli P, Navarro D, Pedrero C, Martín-Hijano L, et al. ISG15 and ISGylation is required for pancreatic cancer stem cell mitophagy and metabolic plasticity. Nat Commun. 2020;11(1):2682.
37. Tieranu CG, Dobre M, Manuc TE, Milanesi E, Plesea IE, Popa C, et al. Gene expression profile of endoscopically active and inactive ulcerative colitis: preliminary data. Rom J Morphol Embryol [Internet]. 2017;58(4):1301–7. Available from: https://www.webofscience.com/wos/woscc/full-record/WOS:000428660300020
38. Masoudi S, Sanat ZM, Saleh AM, Nozari N, Ghamarzad N, Pourshams A. Menstrual and Reproductive Factors and Risk of Pancreatic Cancer in Women. Middle East J Dig Dis. 2017 Jul;9(3):146.
39. Lankisch PG, Assmus C, Maisonneuve P, Lowenfels AB. Epidemiology of Pancreatic Diseases in Lüneburg County: A Study in a Defined German Population. Pancreatology. 2002 Oct 10;2(5):469–77.
40. McGuigan A, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS. Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes. World J Gastroenterol. 2018 Nov 21;24(43):4846–61.
41. Xu JH, Ni CY, Zhuang YY, Li L, Lin Y, Xia ZS, et al. Acute pancreatitis in intraductal papillary mucinous neoplasm: a single-center retrospective cohort study with systematic review and meta-analysis. BMC Gastroenterol. 2023;23(1):424.
42. Farrell JJ. Prevalence, Diagnosis and Management of Pancreatic Cystic Neoplasms: Current Status and Future Directions. Gut Liver. 2015;9(5):571–89.
43. Alvarez A, Borch KB, Rylander C. Reproductive Factors, Use of Exogenous Hormones, and Pancreatic Cancer Incidence: The Norwegian Women and Cancer Study. Clin Epidemiol. 2021;13:67-80.
44. Heuch I, Jacobsen BK, Albrektsen G, Kvțle G. Reproductive factors and pancreatic cancer risk: a Norwegian cohort study. Br J Cancer. 2008;98(1):189-93.
45. Sharma D, Mallick B, Samanta J, Gupta V, Sinha SK, Kochhar R. Acute-on-Chronic Pancreatitis: Analysis of Clinical Profile and Outcome. Cureus. 2021;13(4):e14242.
46. Akshintala VS, Hutfless SM, Yadav D, Khashab MA, Lennon AM, Makary MA, et al. A Population-Based Study of Severity in Patients With Acute on Chronic Pancreatitis. Pancreas. 2013;42(8):1245.
47. Ortiz Morales CM, Girela Baena EL, Olalla Muñoz JR, Parlorio de Andrés E, López Corbalán JA. Radiology of acute pancreatitis today: The Atlanta classification and the current role of imaging in its diagnosis and treatment. Radiol Engl Ed. 2019;61(6): 453–66.
48. Drake M, Dodwad SJM, Davis J, Kao LS, Cao Y, Ko TC. Sex-Related Differences of Acute and Chronic Pancreatitis in Adults. J Clin Med. 2021 Jan 15;10(2):300.
49. Park SM, Kim KB, Han JH, Kim N, Kang TU, Swan H, et al. Incidence and risk of pancreatic cancer in patients with acute or chronic pancreatitis: a population-based cohort study. Sci Rep. 2023 Nov 2;13(1):18930.