

REVIEW ARTICLE

Bibliometric Analysis of Published Articles on Acute Pancreatitis and Acute Lung Injury from 2004 to 2024

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SUMMARY

Background: Recent evidence suggests a significant connection between acute pancreatitis and acute lung injury. This study employs bibliometric methods to visually analyze research papers on these topics from the last two decades, establishing a scientific basis for future research directions and key issues in the field.

Methods: The paper on acute pancreatitis and acute lung injury from 2004 to 2024 was sourced from the SCI-Expanded of Web of Science. Only English articles were analyzed, using VOSviewer and CiteSpace for data visualization.

Results: A total of 257 publications underwent analysis. Dalian Medical University was recognized as the top institution based on the number of publications, citation counts, and H-index scores. The most productive author identified was Chen HL, while the journal featuring the highest volume of publications was the World Journal of Gastroenterology. Key terms that appeared most frequently included "acute lung injury," "acute pancreatitis," "severe acute pancreatitis," and "inflammation".

Conclusions: The research highlights ARDS, mortality rates, mechanisms, Atlanta classification, organ failure, and protective measures as central themes in ongoing studies. These insights are crucial for upcoming research. Nonetheless, investigating the causes of lung injury due to acute pancreatitis remains in its preliminary stages and necessitates further exploration.

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KEYWORDS

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INTRODUCTION

Acute pancreatitis (AP) refers to a sudden inflammatory disorder of the pancreas, marked by the untimely activation of digestive enzymes within the organ, leading to the self-digestion of pancreatic tissue [1]. The updated Atlanta Classification categorizes the clinical severity of AP into three levels: mild (MAP), moderately severe (MSAP), and severe (SAP) [2]. It is estimated that around 15% - 20% of patients with AP may develop SAP, which is linked to a high mortality rate [3]. In the initial phases of SAP, there is a substantial release of in-

flammatory cytokines that may give rise to systemic inflammatory response syndrome (SIRS) and multiple organ dysfunction syndrome (MODS), which could result in the death of the patient if not addressed promptly [4, 5]. In Europe and America, the primary cause of AP is alcohol consumption. In China, biliary factors are predominant, with the global incidence of AP rising annually [6]. Despite ongoing optimization of treatment strategies, the mortality rate for SAP remains between 10% and 30% [7].

Acute lung injury (ALI) is the most common and earliest complication of SAP, increasing the mortality rate to 60% - 70% [8-10]. Unlike primary lung diseases, ALI resulting from SAP is an indirect lung injury, typically characterized by decreased surfactant substances, increased oxygen free radicals and alveolar epithelial cell permeability, accumulation of inflammatory proteins, and damage to pulmonary microvascular endothelial cells [11-13]. The cascade release of inflammatory mediators due to SAP can impair intestinal barrier function, thereby exacerbating bacterial translocation and endotoxemia, significantly affecting the course of SAP-ALI [14,15]. Moreover, the immune dysregulation caused by SAP intensifies the systemic inflammatory response, attracting immune cells to the lungs, where they contribute to alveolar epithelial cell death and impaired lung barrier function [16,17]. Presently, the pathogenesis of SAP-ALI involves multiple mechanisms, including pancreatic necrosis, bacteremia, and intestinal barrier dysfunction, with interactions among these factors; however, it remains incompletely understood [18, 19].

With the advancement of bibliometrics, it has become increasingly easier to perform both quantitative and qualitative literature analyses, which facilitates a more thorough evaluation of the quantity, quality, distribution, and influence of research papers within a specific domain [20]. Common bibliometric visualization tools, such as VOSviewer and CiteSpace, are widely utilized for data analysis and visualization [21]. These tools allow for the examination of literature in a research area from various angles, including authors, countries/regions, affiliated institutions, keyword analysis, and collaboration patterns, thereby helping readers to gain a clearer understanding of the prominent research themes and the current state of development in a particular field [22-24].

So far, there has been a lack of bibliometric studies specifically focused on the domains of AP and ALI. This research aims to address that void and is rooted in the Web of Science Core Collection (WoSCC). Data encompassing annual publications, nations/regions, authors, institutions, fields of study, journals, references, and keywords were gathered, with descriptive statistics computed. This paper investigates the research landscape, key topics, and emerging trends in AP and ALI, utilizing CiteSpace and VOSviewer for knowledge mapping, thereby providing a foundation for future investigations in this area.

MATERIALS AND METHODS

Data source and retrieval

Within this framework, the Web of Science Core Collection (WoSCC) was meticulously searched for relevant articles [25]. The search, spanning January 1, 2004 to January 1, 2024, had no language or document type limits and concluded on January 20, 2024. It yielded 506 articles, with the selection process wrapping up by January 25, 2024. The search criteria were designed to be precise; it involved a combination of keywords related to acute pancreatitis, such as "acute pancreatitis", "sudden pancreatic inflammation", "rapid pancreatic gland inflammation", "acute pancreatic disease", and "sudden inflammation of the pancreas" in combination with terms pertaining to acute lung injury and its variants, including "acute lung injury", "ALI", "acute respiratory distress syndrome", "ARDS", or "pulmonary edema". As a result, a diverse collection of 506 records was compiled, encompassing ten distinct types of documents. To ensure the integrity and relevance of the data, two independent reviewers actively evaluated and discussed any potential inconsistencies in the findings during the data searching process. After filtering out non-English articles and those whose titles and abstracts did not align with the research objectives and were not articles, the analysis was narrowed down to a total of 257 articles that met the established criteria. The collected records were subsequently exported as full-text records, including cited references, and were saved in plain text format and analysis. The flow of screening was presented in Figure 1.

Data analysis

To facilitate a thorough bibliometric analysis, we subsequently imported this data into two analytical tools: VOSviewer (version 1.6.19) and CiteSpace (version 6.2.R3). CiteSpace provides various analytical tools, including clustering analysis and keyword co-occurrence analysis, which assist researchers in pinpointing significant research themes, emerging hotspots, and key publications in their respective academic domains [26]. VOSviewer provides a means to quickly gain insights into large volumes of literature data, which helps in pinpointing emerging trends, field hotspots, and relevant literature resources tied to specific research queries [27]. This research adhered to the guidelines of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) for cross-sectional studies.

RESULTS

The annual trend of paper publication quantity

Figure 2 illustrates the patterns in the yearly volume of publications and the frequency of citations. Starting in 2004, there has been a consistent emergence of publications focusing on acute pancreatitis and acute lung injury, reflecting an increasing interest in these topics.

Table 1. Contribution of the top 10 authors in acute pancreatitis and acute lung injury.

Rank	Author	Institution	Country	Publications	Citations	Average per item	H-index
1	Chen HL	Dalian Medical University	China	15	234	16.93	41
2	Xia Q	Sichuan University	China	10	152	15.8	29
3	Xu CM	Dalian Medical University	China	9	186	21.56	17
4	Andersson R	Lund University and Skane University Hospital	Sweden	8	282	35.5	39
5	Tang WF	Sichuan University	China	8	139	18	21
6	Zhang GX	Dalian Medical University	China	8	104	14.25	20
7	Chen BC	Wenzhou Medical University	China	7	246	36	36
8	Li J	Sichuan University	China	7	141	20.43	14
9	Li WQ	Nanjing University	China	7	132	18.86	28
10	Luo YL	Dalian Medical University	China	7	58	9	7

Table 2. Contribution of the top 10 institutions in acute pancreatitis and acute lung injury.

Rank	Institution	Publications	Citations	Average per item	H-index
1	Dalian Medical University	22	460	22.41	14
2	Sichuan University	20	309	16.1	12
3	Shanghai Jiao Tong University	11	289	26.45	9
4	Wenzhou Medical University	10	349	35.6	8
5	Lund University	9	500	55.89	9
6	Nanjing University	8	153	19.13	6
7	Skane University Hospital	8	282	35.5	8
8	Wuhan University	8	187	24.13	8
9	Dalian University	6	110	18.5	5
10	Flinders University South Australia	6	89	16.83	5

Table 3. Contribution of the top 10 journals in acute pancreatitis and acute lung injury.

Rank	Journal	Publications	Citations	Average Per Item	JCR	IF
1	World Journal of Gastroenterology	18	493	27.50	Q1	4.30
2	Pancreatology	10	226	22.90	Q2	2.80
3	Pancreas	7	151	21.57	Q3	1.70
4	Digestive Diseases and Sciences	5	65	13.00	Q2	2.50
5	Evidence Based Complementary and Alternative Medicine	5	43	8.80	Q3	2.65
6	Hepato-Gastroenterology	5	84	17.00		/
7	International Immunopharmacology	5	102	20.60	Q1	4.8
8	Biomedicine Pharmacotherapy	4	67	16.75	Q1	6.9
9	European Review for Medical and Pharmacological Sciences	4	75	18.75	Q3	3.02
10	Experimental and Therapeutic Medicine	4	86	21.75	Q3	2.40

Table 4. The number of citations, time of publication, year of publication, impact factor, etc., were combined to recommend 20 papers.

	Title	Journal	Date	IF
1	Emodin attenuates severe acute pancreatitis-associated acute lung injury by suppressing pancreatic exosome-mediated alveolar macrophage activation [11]	Acta Pharmaceutica Sinica B	2022/10/1	14.5
2	Acute pancreatitis [28]	The Lancet	2021/1/1	168.9
3	Intestinal barrier damage, systemic inflammatory response syndrome, and acute lung injury: A troublesome trio for acute pancreatitis [19]	Biomedicine & Pharmacotherapy	2020/12/1	7.5
4	Gamma-enolase predicts lung damage in severe acute pancreatitis-induced acute lung injury [12]	Journal of Molecular Histology	2018/5/4	3.2
5	Extracellular Vesicle ITGAM and ITGB2 Mediate Severe Acute Pancreatitis-Related Acute Lung Injury [29]	ACS Nano	2023/4/6	17.1
6	Acadesine alleviates acute pancreatitis-related lung injury by mediating the barrier protective function of pulmonary microvascular endothelial cells [13]	International	2022/10/1	5.6
7	14 - Pancreatic and Hematopoietic Calcineurin Independently Mediate Pancreatic Local Injury and Distant Organ Damage During Acute Pancreatitis [30]	Gastroenterology	2019/5/1	29.4
8	XGBoost model predicts acute lung injury after acute pancreatitis [31]	Signa Vitae	2023/1/1	1.1
9	JMJD3 Is Required for Acute Pancreatitis and Pancreatitis-Associated Lung Injury [32]	Journal of Immunology	2023/1/15	4.4
10	Intestinal Microbiota - An Unmissable Bridge to Severe Acute Pancreatitis-Associated Acute Lung Injury [33]	Frontiers in Immunology	2022/6/14	7.3
11	Alleviation of acute pancreatitis-associated lung injury by inhibiting the p38 mitogen-activated protein kinase pathway in pulmonary microvascular endothelial cells [34]	World Journal of Gastroenterology	2021/5/14	4.3
12	Pancreatic involvement in murine antibody-mediated transfusion-related acute lung injury? [35]	Transfusion	2021/3/1	2.9
13	Emodin Ameliorates Severe Acute Pancreatitis-Associated Acute Lung Injury in Rats by Modulating Exosome-Specific miRNA Expression Profiles [36]	International Journal of Nanomedicine	2023/11/1	8
14	Mo1438 Study of Lung Function Tests to Predict Development of Acute Lung Injury in Patients With Acute Pancreatitis [37]	Gastroenterology	2016/4/1	29.4
15	Neutrophil-specific ORAI1 Calcium Channel Inhibition Reduces Pancreatitis-associated Acute Lung Injury [38]	Function	2023/10/23	6.2
16	Effects of Daphnetin on Experimental Acute Pancreatitis-Associated Acute Lung Injury in Mice [39]	Journal of Clinical Pharmacy and Therapeutics	2023/9/4	2
17	Peripancreatic fat necrosis worsens acute pancreatitis independent of pancreatic necrosis via unsaturated fatty acids increased in human pancreatic necrosis collections [40]	Gut	2014/12/10	24.5
18	Fighting Fire with Fire: Exosomes and Acute Pancreatitis-Associated Acute Lung Injury [41]	Bioengineering	2022/10/26	/
19	Fighting Fire with Fire: Exosomes and Acute Pancreatitis-Associated Acute Lung Injury [41] Prediction of acute lung injury in severe acute pancreatitis by routine clinical data [42]	European Journal of Gastroenterology & Hepatology	2022/11/7	2.1
20	Ultrastructural changes in the pulmonary mechanical barriers in a rat model of severe acute pancreatitis-associated acute lung injury [43]	Ultrastructural Pathology	2015/10/29	1

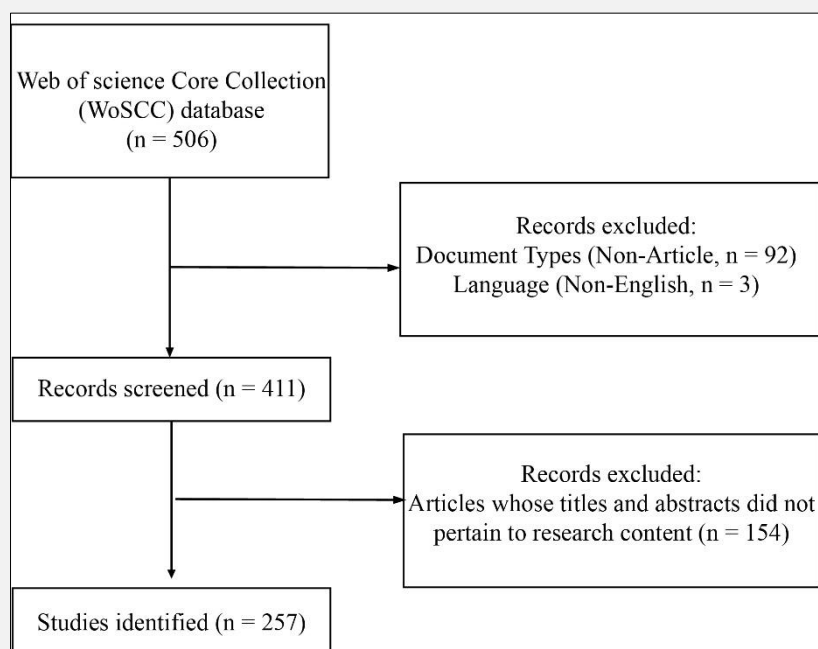


Figure 1. The flowchart illustrating the search strategy and selection process in acute pancreatitis and acute lung injury.

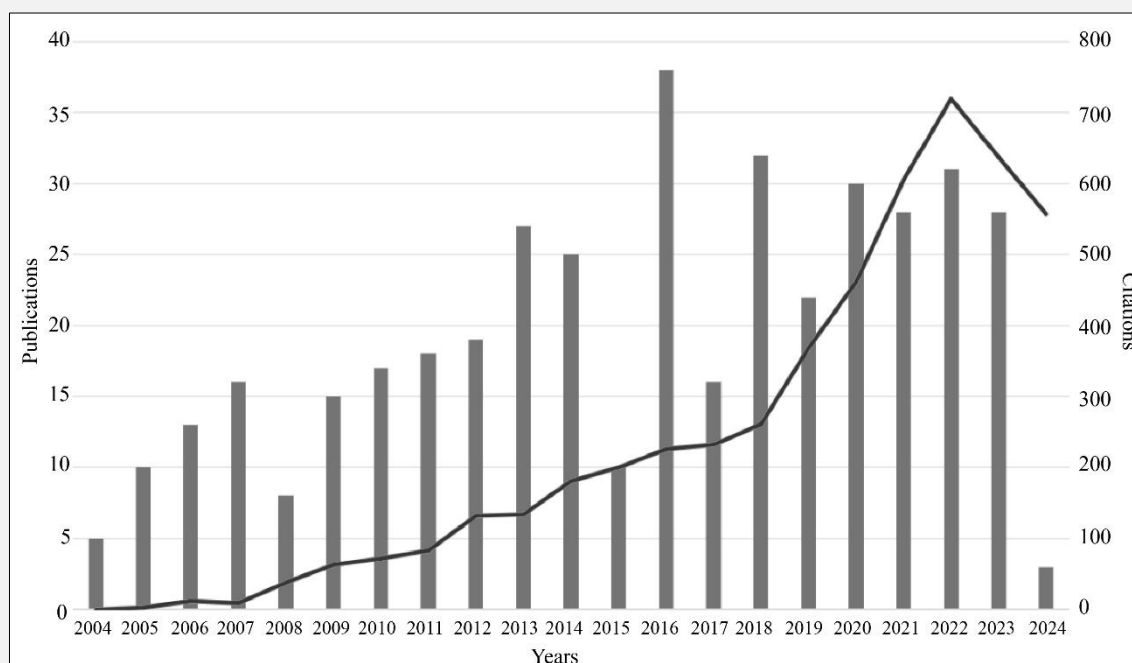


Figure 2. Trends in the growth of publications and the number of citations.

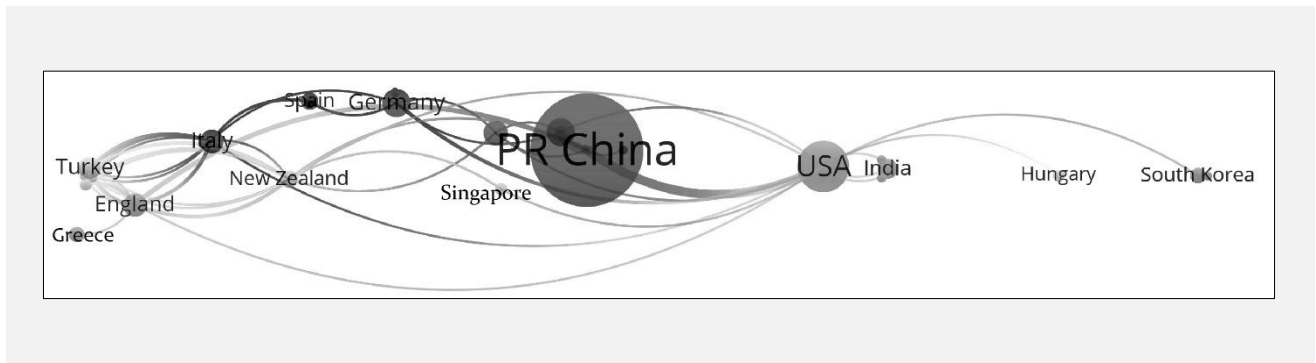


Figure 3. Cooperation map of countries/regions in acute pancreatitis and acute lung injury.

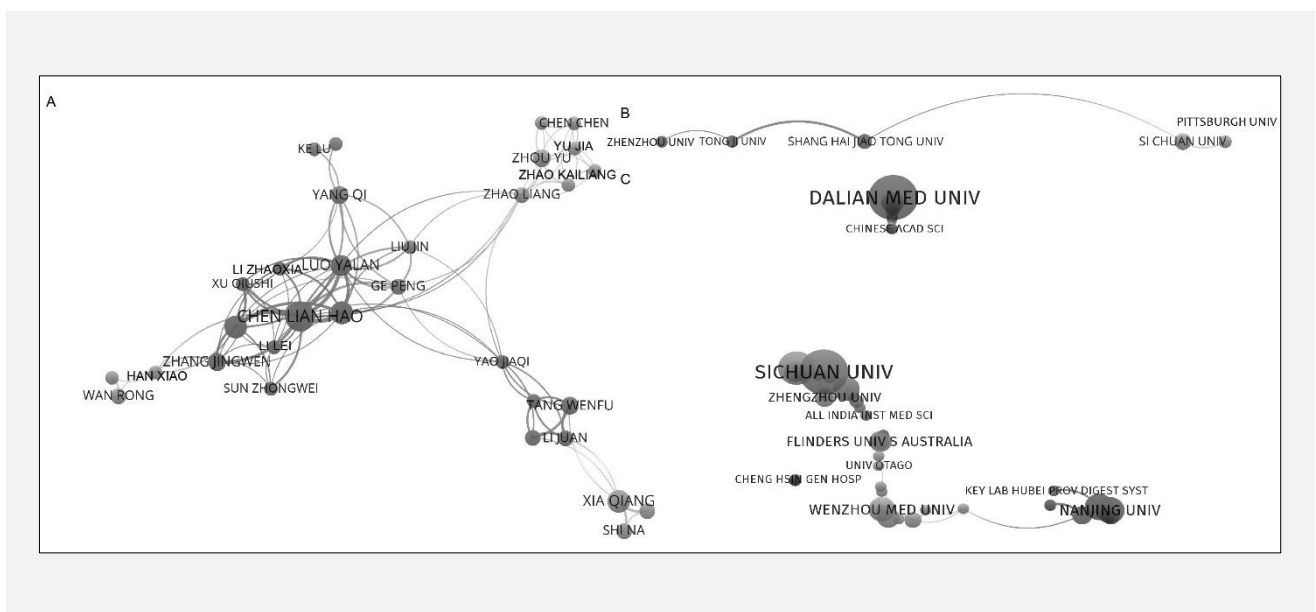


Figure 4. A A visual map for VOSviewer network among authors. B A visual map for VOSviewer network among institutions. C Networks among authors and among institutions in acute pancreatitis and acute lung injury.

From 2004 to 2016, the count of publications experienced an annual increase, which eventually stabilized at approximately 25 articles each year. In the recent five-year span, from 2019 to 2024, a total of 170 papers were published, suggesting a relatively steady level of research activity in this area. The number of citations rose dramatically from fewer than five in the early years to nearly 600 annually.

Distribution of countries/regions

In this study, the parameters applied within VOSviewer included the Method, specifically Linlog/modularity, alongside a requirement for each country to have a minimum of two documents. The dataset was compiled from a total of 40 different countries, of which 17 met

the specified criteria for inclusion. Through a detailed co-authorship analysis, VOSviewer effectively categorizes the participating countries into distinct clusters. Notably, the size of each node in the visualization is indicative of the number of documents associated with that country, while the thickness of the lines connecting the nodes serves to illustrate the intensity of collaboration and interactions between them. The collaboration map depicted in Figure 3 sheds light on the partnerships among countries and regions within the field of acute pancreatitis and acute lung injury research. As shown in the figure, China emerges as a prominent collaborator with several countries, including the USA, Japan, Sweden, New Zealand, and the UK. The USA also demonstrates significant collaborative ties, not only with Chi-

na but also with countries such as Japan, Sweden, New Zealand, the UK, Germany, Italy, Singapore, India, South Korea, and Hungary. Additionally, Sweden is frequently identified as a partner of the USA, China, Japan, and Germany, showcasing a robust network of cooperation in this area of research.

Since the beginning of 2004, 1,463 researchers have engaged in studies related to acute pancreatitis and acute lung injury. Table 1 illustrates the leading 10 core contributors, including their associated institutions, nations, number of published works, total citation counts, and H-index scores. These top 10 authors have produced a cumulative total of 86 articles, which have received an aggregate of 1,674 citations. In terms of the number of publications, Chen HL is in the lead with 15 articles, followed by Xia Q with 10. For total citations, Andersson R holds the top position with 282 citations, while

The partnership between writers in this domain was examined utilizing VOSviewer software. For our statistical analysis, we set a criterion that required authors to have published at least three articles (Figure 4A); consequently, only 62 authors met this threshold. After removing isolated nodes, 32 authors were left who fulfilled the requirement. In the visualization of the network, the dimensions of each node indicate the number of contributions from the authors. A larger node signifies a greater number of published articles by that author.

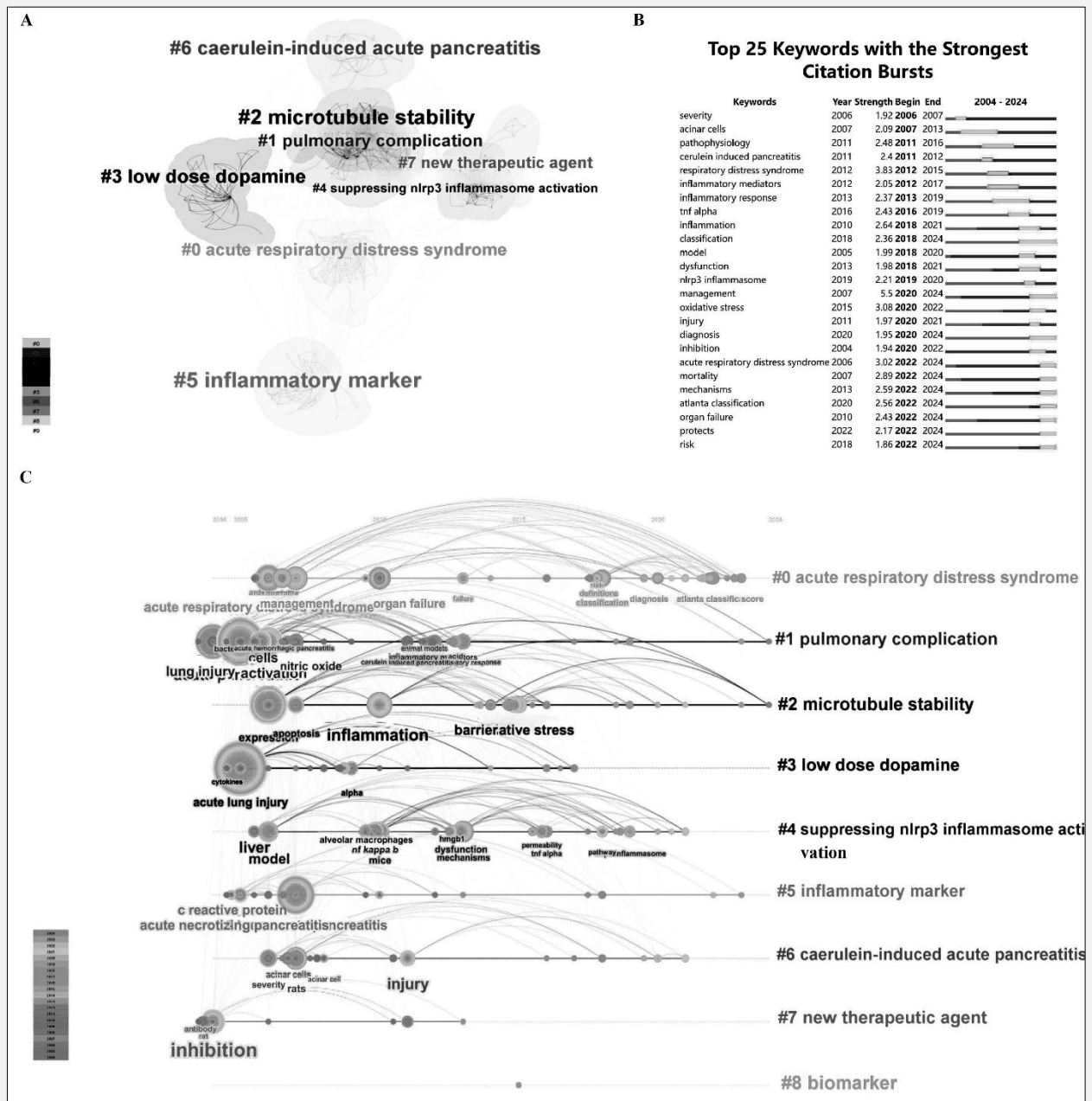


Figure 6. A The cluster of keywords in the studies of acute pancreatitis and acute lung injury. **B** Top 25 keywords with the strongest citation bursts. **C** Timeline viewer related to acute pancreatitis and acute lung injury.

Analysis of institutions

A comprehensive analysis reveals that a total of 339 academic institutions have actively contributed to the body of research literature on the topics of acute pancreatitis and acute lung injury. Notably, when considering the institutions with the highest publication counts, it is evident that the majority, specifically seven out of the

top ten, are situated in China. The remaining three institutions are Lund University, Skåne University Hospital, and Flinders University, all of which are located in Australia. This highlights a significant concentration of research activity in China in this particular field. Dalian Medical University stands out as the leading institution in China, not only in terms of the number of published

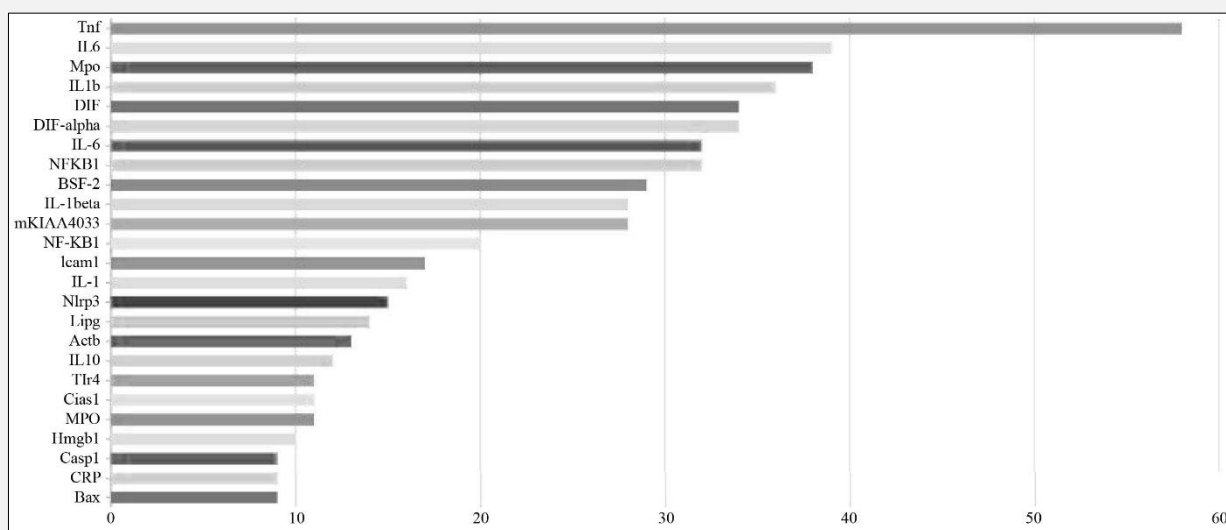


Figure 7. Analysis of genes associated with acute pancreatitis and acute lung injury.

papers but also with regards to total citation counts and h-index metrics. It has achieved an impressive record with 22 publications that collectively garnered 460 citations, resulting in an h-index of 14, which indicates a substantial impact on the academic community. Following closely behind is Sichuan University, which ranks second with 20 publications, 309 citations, and an h-index of 12, showcasing its considerable contributions to the research area. In third place, Shanghai Jiao Tong University has published 11 papers that have received 289 citations, leading to an h-index of 9. These statistics are illustrated in Table 2, underscoring the competitive landscape of research in acute pancreatitis and acute lung injury among these top institutions.

The analysis of institutional collaboration was performed utilizing VOSviewer software, and maps depicting institutional visualization and collaboration networks were created (Figures 4B and 4C). A minimum publication threshold of 3 was established, resulting in 26 institutions meeting this criterion. Following the removal of unconnected nodes, 8 institutions remained that satisfied the requirements. As illustrated in Figures 5A and 5B, these institutions exhibit strong collaborative ties.

Analysis of journals

A total of 257 studies focused on acute pancreatitis and acute lung injury appeared in 142 different journals, as detailed in Table 3. The publication that has the highest count of articles and overall citations is the World Journal of Gastroenterology, featuring 18 articles and accumulating 493 citations. Following this is Pancreatology, which includes 10 articles and has received a total of

226 citations. Next in line is Pancreas, with 7 publications and 151 citations. Other notable journals consist of Digestive Diseases and Sciences (5 published articles), Evidence Based Complementary and Alternative Medicine (5 articles), Hepato Gastroenterology (5 articles), International Immunopharmacology (5 articles), Bio-medicine & Pharmacotherapy (4 articles), European Review for Medical and Pharmacological Sciences (4 articles), and Experimental and Therapeutic Medicine (4 articles).

Research hot-spots and Frontier analysis

The VOSviewer software was configured with specific parameters to facilitate the analysis of keyword co-occurrence. The method employed was Linlog/modularity, and the minimum occurrence threshold for keywords was established at five. Through this process, a total of 1,211 keywords were identified, of which 91 exceeded the predetermined cutoff of five occurrences. For each of these keywords, a comprehensive analysis of the strength of co-occurrence links with other keywords was carried out. The keywords exhibiting the highest total link strength were selected for further examination. The resulting keyword co-occurrence network diagram, as illustrated in Figure 5, provides a visual representation of these relationships. In the diagram, thicker lines connecting the nodes signify a more substantial frequency of co-occurrence between the respective keywords. This visualization allows for an easier understanding of the interconnections among the keywords. Furthermore, the keywords were categorized into four distinct clusters, each represented by a different color.

These clusters correspond to the four main research areas associated with acute pancreatitis and acute lung injury, highlighting the diverse yet interconnected nature of the research landscape in these domains.

The analysis conducted using CiteSpace software resulted in the classification of keywords into eight distinct clusters, as illustrated in Figure 6A. This organization process allows for the automatic grouping of keywords that share a close relationship, culminating in the formation of cohesive clusters. Each cluster is named according to the keyword that has the highest log-likelihood ratio (LLR), which serves as a statistical indicator of that keyword's relevance to the cluster. It is important to note that a higher LLR suggests that the keyword more effectively represents its associated cluster. The eight clusters identified within this particular field encompass various medical and therapeutic themes, such as #0 acute respiratory distress syndrome, #1 pulmonary complication, #2 microtubule stability, #3 low dose dopamine, #4 suppression of NLRP3 inflammasome activation, #5 inflammatory marker, #6 caerulein-induced acute pancreatitis, and #7 new therapeutic agent, with cluster #0 standing out as the most significant among them.

Utilizing the keyword co-citation network, we performed an analysis of keyword emergence detection. The 25 most frequently cited keywords that exhibited the strongest bursts within the domains of acute pancreatitis and acute lung injury are presented. In Figure 6B, the blue line represents the time axis, while the red segment on this axis indicates the burst detection period, illustrating the onset year, conclusion year, and duration of the burst. Notably, management (5.5) exhibited the highest citation bursts, trailed by respiratory distress syndrome (3.83), oxidative stress (3.08), acute respiratory distress syndrome (3.02), mortality (2.89), inflammation (2.64), mechanisms (2.59), Atlanta classification (2.56), pathophysiology (2.48), TNF- α (2.43), organ failure (2.43), inflammatory response (2.37), classification (2.36), NLRP3 inflammasome (2.21), and protective strategies (2.17). From the emergence start times, it is evident that severity, acinar cells, pathophysiology, caerulein-induced pancreatitis, respiratory distress syndrome, inflammatory mediators, and inflammatory response gained early recognition and focus. Currently, acute respiratory distress syndrome, mortality, mechanisms, Atlanta classification, organ failure, protective strategies, and risk represent cutting-edge research areas in the context of acute pancreatitis and acute lung injury which are already experiencing considerable growth. The timeline viewer has the capability to illustrate the evolving trajectory of research hotspots indicated by keywords and to investigate the temporal patterns inherent in research areas as represented by clusters, alongside the fluctuations in the focus of hotspot keyword research. Documents contained within the same cluster are aligned horizontally, with time moving from left to right, progressing from earlier to more recent. The quantity of documents within each cluster emphasizes

the depth and significance of the research contributions within that particular area. Utilizing CiteSpace parameters, a network was generated comprising 261 nodes, 1,224 connections, and exhibiting a density of 0.0361 (refer to Figure 6C). This figure effectively illustrates, from a temporal perspective, the key hotspots and developmental trajectories associated with research into acute pancreatitis and acute lung injury. Each cluster is identified by a numerical label following the clustering process, designated as #0, #1, #2, etc. Clusters with a greater size indicate a higher number of constituent members. In Figure 7C, eight clusters are displayed: #0 acute respiratory distress syndrome, #1 pulmonary complication, #2 microtubule stability, #3 low-dose dopamine, #4 inhibition of NLRP3 inflammasome activation, #5 inflammatory marker, #6 caerulein-induced acute pancreatitis, and #7 new therapeutic agent. Observations from Figure 7C reveal that the primary keywords from 2004 and 2005 included ARDS, mortality, lung injury, C-reactive protein, cytokines, antibody, and inhibition. Conversely, the keywords predominantly associated with 2015-2024 included diagnosis, Atlanta classification, pathway, NLRP3 inflammasome, TNF- α , permeability, oxidative stress, and barrier.

Associated gene analysis

The entity word mining and statistical analysis of genes in article abstracts were conducted using the BioBERT biomedical language representation model. Figure 7 illustrates that TNF leads with the most publications at 58, followed by IL-6 with 39 publications in the second position, and MPO in third place with 38 publications.

Artificial intelligence recommended literature

Among the literature retrieved by the search terms, 20 pieces of literature were recommended by combining the number of citations, publication time, year, impact factor, and other conditions, as shown in Table 4 [11-13,19,28-43].

DISCUSSION

In this research, we examined existing literature regarding Acute Pancreatitis (AP) and Acute Lung Injury (ALI) and evaluated research outcomes and advancements utilizing quantitative analysis tools such as CiteSpace and VOSviewer. We performed a quantitative assessment of fundamental data, including yearly publication numbers, contributing countries, authors, institutions, academic disciplines, and journals. The data indicates a consistent increase in publications related to AP and ALI since 2004, culminating in a total of 257 articles. A paper's citation frequency correlates with its influence within the field and serves as an indicator of its quality. As illustrated in Figure 2, there has been a yearly rise in citations associated with this domain. By statistically analyzing publication output from various countries or regions and institutions, we can pinpoint

key contributors with substantial publication rates and impact, as well as ascertain their collaborative networks. China stands out as a leading nation in AP and ALI research. Meanwhile, the United States demonstrates a more established presence in this area of study. Among the ten leading institutions, seven are located in China, two in Sweden, and one in Australia, with Dalian Medical University recognized as the institution that has published the most papers and holds the highest h-index. Furthermore, there is a notable closeness in cooperation among different countries and institutions. Among the leading 10 researchers, Chen HL has authored 15 papers, making him the most prolific contributor, followed by Xia Q with 10 papers and Xu CM with 9 papers. This highlights the remarkable contributions made by these three scholars in the domains of acute pancreatitis (AP) and acute lung injury (ALI). The h-index serves as a multifaceted quantitative measure for assessing both the volume and the impact of a researcher's scholarly contributions. Professor Chen HL, affiliated with Dalian Medical University, boasts the highest h-index at 41. His investigations reveal that severe acute pancreatitis (SAP) can induce ALI through various molecular pathways and treatment approaches. Traditional Chinese medicines, such as Qingyi Decoction (QYD) and Qingyi Granules (QYKL), exhibit promise for mitigating lung damage associated with SAP by modulating crucial signaling pathways and influencing the gut microbiota [44,45]. Moreover, compounds like emodin (EMO) have shown beneficial effects by altering miRNA expression in exosomes and impacting apoptotic processes [36]. These discoveries offer novel avenues and possible therapeutic targets for the clinical management of SAP-ALI. Additionally, researchers Andersson R from Lund University and Skåne University Hospital, along with Chen BC from Wenzhou Medical University, are also noted. Andersson R's investigations delve into the possible therapeutic properties and underlying mechanisms of various pharmaceuticals and compounds regarding ALI triggered by AP. The research indicated that Schisandra sphenanthera extract (SSBE) noticeably reduced ALI related to SAP by suppressing the PI3K/Akt signaling cascade and NF-kappa B activity [46]. Furthermore, transforming growth factor-beta (TGF-beta) could emerge as a promising therapeutic target for early lung injury stemming from acute pancreatitis [47]. Lipoxins (LXs) and their synthetic variants have demonstrated robust anti-inflammatory properties, offering protection against acute lung injury (ALI) by obstructing inflammatory mechanisms and increasing levels of the cellular protective enzyme HO-1 [48]. The study also highlights the crucial involvement of macrophages in the extent of lung injury in both ALI and acute respiratory distress syndrome (ARDS), while underscoring the important function of the protein kinase C (PKC) signaling pathway in lung injury related to pancreatitis [49]. Moreover, antioxidants and signaling inhibitors, such as N-acetylcysteine (NAC), have displayed promising thera-

peutic benefits in modulating inflammatory responses and diminishing organ damage. These findings contribute significant insights towards the creation of innovative therapies aimed at addressing acute pancreatitis (AP) and ALI [50]. Chen BC investigated the therapeutic potential of various compounds on ALI induced by SAP. The research revealed that acadesine mitigated inflammation and tissue injury in ALI linked to SAP through the activation of AMPK and Nrf2-dependent antioxidant pathways [13]. Additionally, sildenafil was found to lessen inflammation and lung injury in ALI rats associated with SAP by facilitating cell proliferation and preventing apoptosis [51]. Furthermore, Lipoxin A4 (LXA4) reduced inflammation and ALI resulting from AP by inhibiting inflammatory factor production and preventing reactive oxygen species (ROS) generation, while activating the Nrf2 signaling pathway and its corresponding downstream gene HO-1 [52]. These findings furnish novel concepts and potential treatment approaches for managing SAP-related lung injury. Notably, none of the authors exhibit a centrality of 0.10 or higher, indicating a lack of highly influential authors within this research domain.

Based on the distribution of journals presented in Table 3, the publication featuring the largest number of articles on AP and ALI is the World Journal of Gastroenterology, which has 18 articles. This is followed by Pancreatology with 10 articles and Pancreas with 7 articles. The World Journal of Gastroenterology also boasts the highest citation frequency. The JCR (Journal Citation Reports) ranking serves as a specific metric related to impact factor, ranking, and category for journals. Among the 20 journals with the most citations, three are classified within the JCR Q1 category, with Biomedicine & Pharmacotherapy leading in impact factor at 6.9. Studies focusing on AP and ALI have consistently attracted the attention of researchers globally. Through the examination of highly cited references, co-occurrences of keywords, clustering techniques, and analysis of emerging trends, the primary directions and key areas of interest in AP and ALI have been discerned, highlighting the evolution and variations in their thematic frameworks.

Utilizing keyword clustering analysis alongside an evaluation of the most cited keywords, key research areas and frontiers within AP and ALI have been established. Diverse cell populations, including parenchymal and immune cells, interact to modulate pulmonary inflammation [53]. In acute pancreatitis, neutrophils are activated and release substances that can kill bacteria but also cause tissue injury and prolong inflammation [54]. Macrophages are also key in regulating inflammation, with Resolvin D1 promoting their apoptosis and reducing inflammatory cytokines. Interferon-gamma (IFN- γ) increases inflammation by promoting hyperreactivity in macrophages and monocytes, potentially leading to pulmonary damage [55]. PI3K/Akt/eNOS signaling pathway activation stabilizes the endothelial barrier and reduces inflammation, while FoxM1 enhances BMSCs'

protection of endothelial cells via Wnt/ β -catenin signaling [56]. Microtubule stability is linked to inflammation regulation, with miR-92a inhibition improving endothelial cell migration and structure through PI3K/Akt pathway activation [57]. miR-150 targets AKT3 to inhibit NF- κ B signaling, reducing inflammatory factors and protecting against acute lung injury, indicating the complex relationship between microtubule dynamics and endothelial inflammation [58]. Increased permeability of the alveolar-capillary barrier can lead to pulmonary edema and worsen respiratory function. Oxidative stress triggers signaling pathways that amplify inflammation, activating transcription factors like NF- κ B and AP-1, which in turn upregulate inflammatory cytokines and chemokines [59]. This attracts more inflammatory cells, perpetuating lung injury. Oxidative stress also disrupts cellular metabolism and signaling by depleting antioxidants and altering protein and lipid functions, impairing cell membrane and receptor functionality [60].

This research employed bibliometric techniques to perform a visual examination of the connection between AP and ALI, assisting researchers in gaining a clearer insight into the key areas and emerging trends in this domain. Nevertheless, our research has certain limitations. We focused solely on English-language publications within a designated period available on WoSCC, which may lead to the exclusion of findings from other databases. Nevertheless, applying visualization techniques to grasp the existing landscape, important focal points, and trends within a field continues to be beneficial.

CONCLUSION

In summary, this study provides a comprehensive analysis of the current research status, hotspots, and frontiers of AP and ALI through bibliometric methods. We found that ARDS, mortality, mechanisms, Atlanta classification, organ failure, and protection are current research hotspots and frontier areas. These findings offer references and insights for future related research.

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Data Availability:

The original contributions presented in the study are included in the article. Further inquiries can be directed to the corresponding authors.

Declaration of Interest:

All the authors declare that they have no conflicts of interest.

References:

- Shah AU, Sarwar A, Orabi AI, et al. Protease activation during *in vivo* pancreatitis is dependent on calcineurin activation. *Am J Physiol Gastrointest Liver Physiol* 2009;297(5):G967-73. (PMID:20501444)
- Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. *Gut* 2013;62(1):102-11. (PMID: 23100216)
- Portelli M, Jones CD. Severe acute pancreatitis: pathogenesis, diagnosis and surgical management. *Hepatobiliary Pancreat Dis Int* 2017;16(2):155-9. (PMID: 28381378)
- Trikudanathan G, Wolbrink D, van Santvoort HC, Mallory S, Freeman M, Besselink MG. Current Concepts in Severe Acute and Necrotizing Pancreatitis: An Evidence-Based Approach. *Gastroenterology* 2019;156(7):1994-2007.e3. (PMID: 30776347)
- Schietroma M, Pessia B, Carlei F, Mariani P, Sista F, Amicucci G. Intestinal permeability and systemic endotoxemia in patients with acute pancreatitis. *Ann Ital Chir* 2016;87:138-44. (PMID: 27179282)
- Mederos MA, Reber HA, Girgis MD. Acute Pancreatitis: A Review. *JAMA* 2021;325(4):382-90. (PMID: 33496779)
- Heckler M, Hackert T, Hu K, Halloran CM, Büchler MW, Neoptolemos JP. Severe acute pancreatitis: surgical indications and treatment. *Langenbecks Arch Surg* 2021;406(3):521-35. (PMID: 32910276)
- Wu J, Zhang J, Zhao J, Chen S, Zhou T, Xu J. Treatment of Severe Acute Pancreatitis and Related Lung Injury by Targeting Gasdermin D-Mediated Pyroptosis. *Front Cell Dev Biol* 2021; 9:780142. (PMID: 34858995)
- Zhou J, Zhou P, Zhang Y, Wang G, Fan Z. Signal Pathways and Markers Involved in Acute Lung Injury Induced by Acute Pancreatitis. *Dis Markers* 2021;2021:9947047. (PMID: 34497676)
- Xu C, Zhang J, Liu J, et al. Proteomic analysis reveals the protective effects of emodin on severe acute pancreatitis induced lung injury by inhibiting neutrophil proteases activity. *J Proteomics* 2020;220:103760. (PMID: 32244009)
- Hu Q, Yao J, Wu X, et al. Emodin attenuates severe acute pancreatitis-associated acute lung injury by suppressing pancreatic exosome-mediated alveolar macrophage activation. *Acta Pharm Sin B* 2022;12(10):3986-4003. (PMID: 36213542)
- Owusu L, Xu C, Chen H, et al. Gamma-enolase predicts lung damage in severe acute pancreatitis-induced acute lung injury. *J Mol Histol* 2018;49(4):347-56. (PMID: 29728894)
- Zhu X, Duan F, Zhang Y, et al. Acadesine alleviates acute pancreatitis-related lung injury by mediating the barrier protective function of pulmonary microvascular endothelial cells. *Int Immunopharmacol* 2022;111:109165. (PMID: 35987144)
- Teodoro T, Odisho T, Sidorova E, Volchuk A. Pancreatic β -cells depend on basal expression of active ATF6 α -p50 for cell survival even under nonstress conditions. *Am J Physiol Cell Physiol* 2012; 302(7):C992-1003. (PMID: 22189555)

15. Gunjaca I, Zunic J, Gunjaca M, Kovac Z. Circulating cytokine levels in acute pancreatitis-model of SIRS/CARS can help in the clinical assessment of disease severity. *Inflammation* 2012;35(2): 758-63. (PMID: 21826480)
16. Manohar M, Verma AK, Venkateshaiah SU, Sanders NL, Mishra A. Chronic Pancreatitis Associated Acute Respiratory Failure. *MOJ Immunol* 2017;5(2):00149. (PMID: 29399623)
17. De Campos T, Deree J, Coimbra R. From acute pancreatitis to end-organ injury: mechanisms of acute lung injury. *Surg Infect (Larchmt)* 2007. 8(1): 107-20. (PMID: 17381402)
18. Liang XY, Jia TX, Zhang M. Intestinal bacterial overgrowth in the early stage of severe acute pancreatitis is associated with acute respiratory distress syndrome. *World J Gastroenterol* 2021; 27(15):1643-54. (PMID: 33958849)
19. Ge P, Luo Y, Okoye CS, et al. Intestinal barrier damage, systemic inflammatory response syndrome, and acute lung injury: A troublesome trio for acute pancreatitis. *Biomed Pharmacother* 2020; 132:110770. (PMID: 33011613)
20. Jiang S, Liu Y, Zheng H, et al. Evolutionary patterns and research frontiers in neoadjuvant immunotherapy: a bibliometric analysis. *Int J Surg* 2023;109(9):2774-83. (PMID: 37216225)
21. Liu S, Sun YP, Gao XL, Sui Y. Knowledge domain and emerging trends in Alzheimer's disease: a scientometric review based on CiteSpace analysis. *Neural Regen Res* 2019;14(9):1643-50. (PMID: 31089065)
22. Smith DR. Bibliometrics, dermatology and contact dermatitis. *Contact Dermatitis* 2008;59(3):133-6. (PMID: 18759892)
23. Chandra SP, Singh A, Goyal N, et al. Analysis of changing paradigms of management in 179 patients with spinal tuberculosis over a 12-year period and proposal of a new management algorithm. *World Neurosurg* 2013;80(1-2):190-203. (PMID: 23348057)
24. da Silva TF, Casarotti SN, de Oliveira G, Penna A. The impact of probiotics, prebiotics, and synbiotics on the biochemical, clinical, and immunological markers, as well as on the gut microbiota of obese hosts. *Crit Rev Food Sci Nutr* 2021;61(2):337-55. (PMID: 32156153)
25. Liu X, Zhao S, Tan L, et al. Frontier and hot topics in electrochemiluminescence sensing technology based on CiteSpace bibliometric analysis. *Biosens Bioelectron* 2022;201:113932. (PMID: 35065388)
26. Synnestvedt MB, Chen C, Holmes JH. CiteSpace II: visualization and knowledge discovery in bibliographic databases. *AMIA Annu Symp Proc* 2005;2005:724-8. (PMID: 16779135)
27. van Eck NJ, Waltman L. Software survey: VOSviewer, a computer program for bibliometric mapping. *Scientometrics* 2010; 84(2):523-38. (PMID: 20585380)
28. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. *Lancet* 2015;386(9988):85-96. (PMID: 25616312)
29. Hu Q, Zhang S, Yang Y, et al. Extracellular Vesicle ITGAM and ITGB2 Mediate Severe Acute Pancreatitis-Related Acute Lung Injury. *ACS Nano* 2023;17(8):7562-75. (PMID: 37022097)
30. Wen LJ, Tanveer Dobbs A. 14 - Pancreatic and Hematopoietic Calcineurin Independently Mediate Pancreatic Local Injury and Distant Organ Damage During Acute Pancreatitis. *Gastroenterology* 2019;156:S-6. DOI:10.1016/S0016-5085(19)36786-1
31. Lu W, Chen X, Liu W, et al. XGBoost model predicts acute lung injury after acute pancreatitis. *Signa Vitae* 2023;19(5):206-12. DOI:10.22514/sv.2023.087
32. Chen L, Zhang X, Liu Y, et al. JMJD3 Is Required for Acute Pancreatitis and Pancreatitis-Associated Lung Injury. *J Immunol* 2023;210(2):180-90. (PMID: 36458991)
33. Wang Z, Li F, Liu J, et al. Intestinal Microbiota - An Unmissable Bridge to Severe Acute Pancreatitis-Associated Acute Lung Injury. *Front Immunol* 2022;13:913178. (PMID: 35774796)
34. Zhang XX, Wang HY, Yang XF, et al. Alleviation of acute pancreatitis-associated lung injury by inhibiting the p38 mitogen-activated protein kinase pathway in pulmonary microvascular endothelial cells. *World J Gastroenterol* 2021;27(18):2141-59. (PMID: 34025070)
35. Kapur R, Rebetz J, van der Velden S, Semple JW. Pancreatic involvement in murine antibody-mediated transfusion-related acute lung injury. *Transfusion* 2021;61(3):987-9. (PMID: 33719042)
36. Yang Q, Luo Y, Ge P, et al. Emodin Ameliorates Severe Acute Pancreatitis-Associated Acute Lung Injury in Rats by Modulating Exosome-Specific miRNA Expression Profiles. *Int J Nanomedicine* 2023;18:6743-61. (PMID: 38026528)
37. Samanta J, Ashat M, Prasad R, et al. Mo1438 Study of Lung Function Tests to Predict Development of Acute Lung Injury in Patients With Acute Pancreatitis. *Gastroenterology* 2016;150(4): S712-S713. <https://eurekamag.com/research/064/880/064880507.php>
38. Niu M, Zhang X, Wu Z, et al. Neutrophil-specific ORAI1 Calcium Channel Inhibition Reduces Pancreatitis-associated Acute Lung Injury. *Function (Oxf)* 2024;5(1):zqad061. (PMID: 38020066)
39. Chen T. Effects of Daphnetin on Experimental Acute Pancreatitis-Associated Acute Lung Injury in Mice. *J Clin Pharm Ther* 2023(1):1-8. DOI:10.1155/2023/9822900
40. Noel P, Patel K, Durgampudi C, et al. Peripancreatic fat necrosis worsens acute pancreatitis independent of pancreatic necrosis via unsaturated fatty acids increased in human pancreatic necrosis collections. *Gut* 2016;65(1):100-11. (PMID: 25500204)
41. Yang Q, Luo Y, Lan B, et al. Fighting Fire with Fire: Exosomes and Acute Pancreatitis-Associated Acute Lung Injury. *Bioengineering (Basel)* 2022;9(11):615. (PMID: 36354526)
42. Jia M, Xu X, Zhou S, et al. Prediction of acute lung injury in severe acute pancreatitis by routine clinical data. *Eur J Gastroenterol Hepatol* 2023;35(1):36-44. (PMID: 36468567)
43. Wang F, Lu F, Huang H, Huang M, Luo T. Ultrastructural changes in the pulmonary mechanical barriers in a rat model of severe acute pancreatitis-associated acute lung injury. *Ultrastruct Pathol* 2016;40(1):33-42. (PMID: 26512751)
44. Cao Y, Li F, Sun Z, et al. Regulation of Microtubule Stability in Pulmonary Microvascular Endothelial Cells in Rats with Severe Acute Pancreatitis: Qingyi Decoction is a Potential CDK5 Inhibitor. *J Inflamm Res* 2024;17:2513-30. (PMID: 38699595)
45. Ge P, Luo Y, Zhang J, et al. Mechanism Investigation and Clinical Retrospective Evaluation of Qingyi Granules: Pancreas Cleaner About Ameliorating Severe Acute Pancreatitis with Acute Respiratory Distress Syndrome. *Drug Des Devel Ther* 2024;18:2043-61. (PMID: 38863767)

46. Jin Y, Liu L, Chen B, et al. Involvement of the PI3K/Akt/NF- κ B Signaling Pathway in the Attenuation of Severe Acute Pancreatitis-Associated Acute Lung Injury by *Sedum sarmentosum* Bunge Extract. *Biomed Res Int* 2017;2017:9698410. (PMID: 29359164)
47. Akbarshahi H, Sam A, Chen C, Rosendahl AH, Andersson R. Early activation of pulmonary TGF- β 1/Smad2 signaling in mice with acute pancreatitis-associated acute lung injury. *Mediators Inflamm* 2014;2014:148029. (PMID: 24688224)
48. Lv W, Lv C, Yu S, et al. Lipoxin A4 attenuation of endothelial inflammation response mimicking pancreatitis-induced lung injury. *Exp Biol Med (Maywood)* 2013;238(12):1388-95. (PMID: 24000382)
49. Akbarshahi H, Menzel M, Posaric Bauden M, Rosendahl A, Andersson R. Enrichment of murine CD68⁺ CCR2⁺ and CD68⁺ CD206⁺ lung macrophages in acute pancreatitis-associated acute lung injury. *PLoS One* 2012;7(10):e42654. (PMID: 23110041)
50. Zhou MT, Chen CS, Chen BC, Zhang QY, Andersson R. Acute lung injury and ARDS in acute pancreatitis: mechanisms and potential intervention. *World J Gastroenterol* 2010;16(17):2094-9. (PMID: 20440849)
51. Fang D, Lin Q, Wang C, et al. Effects of sildenafil on inflammatory injury of the lung in sodium taurocholate-induced severe acute pancreatitis rats. *Int Immunopharmacol* 2020;80:106151. (PMID: 31931368)
52. Ye W, Zheng C, Yu D, et al. Lipoxin A4 Ameliorates Acute Pancreatitis-Associated Acute Lung Injury through the Antioxidative and Anti-Inflammatory Effects of the Nrf2 Pathway. *Oxid Med Cell Longev* 2019;2019:2197017. (PMID: 31781326)
53. Zhou H, Fan EK, Fan J. Cell-Cell Interaction Mechanisms in Acute Lung Injury. *Shock* 2021;55(2):167-76. (PMID: 32694389)
54. Potey PM, Rossi AG, Lucas CD, Dorward DA. Neutrophils in the initiation and resolution of acute pulmonary inflammation: understanding biological function and therapeutic potential. *J Pathol* 2019;247(5):672-85. (PMID: 30570146)
55. Verma AK, McKelvey M, Uddin MB, et al. IFN- γ transforms the transcriptomic landscape and triggers myeloid cell hyperresponsiveness to cause lethal lung injury. *Front Immunol* 2022;13:1011132. (PMID: 36203588)
56. Luo Y, Ge S, Chen Q, Lin S, He W, Zeng M. Overexpression of FoxM1 optimizes the therapeutic effect of bone marrow mesenchymal stem cells on acute respiratory distress syndrome. *Stem Cell Res Ther* 2023;14(1):27. (PMID: 36788588)
57. Xu F, Zhou F. Inhibition of microRNA-92a ameliorates lipopolysaccharide-induced endothelial barrier dysfunction by targeting ITGA5 through the PI3K/Akt signaling pathway in human pulmonary microvascular endothelial cells. *Int Immunopharmacol* 2020;78:106060. (PMID: 31841757)
58. Li P, Yao Y, Ma Y, Chen Y. MiR-150 attenuates LPS-induced acute lung injury via targeting AKT3. *Int Immunopharmacol* 2019;75:105794. (PMID: 31398659)
59. Yang S, Zhang T, Ge Y, et al. Ferritinophagy Mediated by Oxidative Stress-Driven Mitochondrial Damage Is Involved in the Polystyrene Nanoparticles-Induced Ferroptosis of Lung Injury. *ACS Nano* 2023;17(24):24988-5004. (PMID: 38086097)
60. Yang H, Lv H, Li H, Ci X, Peng L. Oridonin protects LPS-induced acute lung injury by modulating Nrf2-mediated oxidative stress and Nrf2-independent NLRP3 and NF- κ B pathways. *Cell Commun Signal* 2019;17(1):62. (PMID: 31186013)