Emerging Trends in Intestinal Knowledge Structure Associated With Acute Pancreatitis From 1981 to 2021

A Bibliometric Analysis

Yang Liu, MD, Xiaojiang Zhou, MM, Huifang Xiong, PhD, Conghua Song, PhD, and Yong Xie, PhD

Objectives: Bibliometric analysis has not comprehensively summarized studies of acute pancreatitis (AP)–associated intestinal diseases. This work aimed to evaluate cooperative networks of authors, countries, and institutions and explore the field's developing trends and hot topics.

Methods: Original articles and reviews of AP-associated intestinal diseases were obtained from the Web of Science Core Collection on October 11, 2021. VOSviewer and CiteSpace software were used to perform co-occurrence analyses for authors, countries, and institutions and detect the highest citation burst.

Results: A total of 1634 articles on the intestine associated with AP were identified. The United States, the University of Auckland, and Roland Andersson are the most influential country, research institute, and scholar, respectively. The *World Journal of Gastroenterology* (73 articles) has the highest number of publications, and *Gastroenterology* was the most co-cited journal. The top 5 key words are "acute pancreatitis," "bacterial translocation," "management," "gut," and "inflammatory bowel disease." We find that several emergent key words like "gut microbiota," "pathway," "gut barrier," "risk," and "oxidative stress" experienced a continuous and rapid development as new research directions.

Conclusions: This bibliometric study summarizes current important perspectives and offers comprehensive guidance on the AP-associated intestinal diseases, which may help researchers choose the most appropriate research directions.

Key Words: acute pancreatitis, intestine, visual, bibliometric analysis, CiteSpace

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Acute pancreatitis (AP) is a common inflammatory disorder of the pancreas with serious metabolic disturbances.[1,2] The disease has a variable clinical course because of dynamic changes in the inflammatory response. Most patients with AP are graded as mild according to the revised Atlanta classification, about 20% to 30% develop severe AP (SAP) with local pancreatic inflammation and systemic complications.

Organ failure is one of the most severe complications of AP and is recognized as a key determinant of clinical outcomes in AP patients. Severe AP can often cause intestinal dysfunction, like intestinal barrier injury and intestinal dynamic disorder. It has been reported that 54% to 88% of AP patients have intestinal mucosal barrier dysfunction.[3] Early clinical manifestations include delayed gastric emptying, slow intestinal motility, and paralytic ileus. Gastrointestinal motility weakening leads to the accumulation of bacteria and toxins in the intestine. Excessive bacterial growth in the intestine results in flora dysbiosis and aggravates gastrointestinal barrier dysfunction, causing bacterial translocation, toxin absorption, and bacteremia.[4,5] The bacteremia can aggravate the gastrointestinal motility disorder and lead to systemic inflammatory response syndrome and multiple-organ failure.[6,7] Multiple-organ failure is strongly associated with high morbidity and mortality.[8–10] Hence, intestinal function plays an important role in AP patients. Protecting intestinal function and reducing the occurrence of bacterial translocation are required to reduce the risk of infection and promote patient recovery.

Publications have reported the association between the intestine and AP. However, no studies systematically summarized and analyzed this association through bibliometric analysis. Therefore, this study aims to identify the current status and developing trend on AP-associated intestinal diseases from 1981 to 2021 through comprehensive and systematic bibliometrics. Previous reviews are a personal summary of relevant literature in a specific field that cannot fully demonstrate the collaboration and contribution between authors, countries, institutions, and journals. In addition, the knowledge structures and research priorities are difficult to visualize, and there are few systematic, comprehensive, and visual studies.

Pritchard developed bibliometric analysis in 1969, reflecting the future direction of a specific field.[11,12] Nowadays, there are various research methods to systematically review the current research progress in a field, with bibliometrics being one of the most popular methods.[13] Bibliometrics can qualitatively and quantitatively evaluate the trends in scientific research. It can help scholars identify the research focus and development trend and collaborate between authors, countries, institutions, and journals. Moreover, it can provide a scientific basis for clinical research and guidelines in the medical field.[14,15]

This study aimed to identify the characteristics of literature about the intestine in association with AP; summarize the current knowledge domain of achievements in this field, the associated research hotspots, and potential directions; and provide evidence for future scientific and clinical research.

MATERIALS AND METHODS

Data Sources and Search Strategies

The Web of Science Core Collection database (WoSCC) developed by Thomson Scientific (Boston, Mass) was used to conduct the

From the Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, Nanchang, China.

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Address correspondence to: Yong Xie, PhD, Department of Gastroenterology, The First Affiliated Hospital of Nanchang University, Nanchang, China (e-mail: xieyong_tfahoncu@163.com).

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X.Z. and Y.X. designed this study. Y.L. and C.S. collected the data and performed the analysis. H.X. normalized the pictures. Y.L. wrote the original draft. All authors contributed to the article and approved the submitted version.

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bibliometric analysis. Considering rapid database updates and to avoid deviations, the deadline for the literature retrieval period was October 11, 2021. Article publication dates were set from 1983 to 2021. We chose topic search (TS) to search the literature. Subject searches include title, abstract, author key words, and key words plus. The specific search strategies were TS = (gut OR bowel OR intestine) AND TS = (acute pancreatitis). In addition, the publication type was limited to Articles or Reviews, and the language was restricted to English. In total, 1634 articles were included in the final analysis. The detailed flowchart of the method is displayed in Figure 1. This research did not involve human subjects and extracted data from public databases. Hence, approval by the institutional review board was not required.

Data Collection and Cleaning

First, the original data were extracted from the WoSCC database. The recorded information included the number of publications, countries, institutions, authors, journals, references, and key words. Afterward, duplicate records were removed by CiteSpace software (Version 5.8.3c; Drexel University, Philadelphia, Pa). Some inaccurate analyses were unavoidable because of authors with the same initials, synonyms in key words, and different versions of references, but in our study, most of the data were highly reliable.

Bibliometric Analysis

There is no consensus on the best tool for bibliometric analysis.[16] Nowadays, the VOSviewer (Version 1.6.16; Center for Science and Technology Studies, Leiden University, Leiden, Netherlands), CiteSpace, NetDraw, BibExcel, and HistCite are commonly used in bibliometric analysis.[17] Considering different advantages and characteristics of each software, this study used VOSviewer and CiteSpace.[17,18] VOSviewer is a free software tool suitable for constructing network visualization maps based on large-scale bibliographical data.[19,20] CiteSpace, developed by Professor Chaomei Chen, is a bibliometrics visualization tool specializing in discovering and visualizing collaborative relationships, hotspots, knowledge structure, and emerging trends in a specific field.[21]

The number of publications was analyzed by Microsoft Excel 2019 (Microsoft Corporation, Redmond, Wash) and GraphPad Prism 8.0 software (GraphPad Software, San Diego, Calif). CiteSpace and VOSviewer were used to visualize the authors, institutions, countries, and key words by co-occurrence and cooperative relationship analyses. Author co-citation analysis, journal co-citation analysis, highly cited references, and knowledge maps were also performed. Burst key word detection was applied to investigate the emergence of key word popularity effectively. The 50 most cited articles were selected to construct a timeline view using CiteSpace. A timeline view can describe trends in a specific field over time. Moreover, the log likelihood ratio was used to determine the potential clusters. Centrality refers to nodal centrality, which is an indicator to measure the importance of nodes in the network. CiteSpace uses this metric to discover and measure the importance of literature. Among the common functions of the Cluster menu, Cluster Labels is a function that CiteSpace provides to extract cluster names from titles, extract cluster names from index words, and extract cluster names from abstracts. Summarization of Cluster is mainly used to query the list of clusters obtained by different methods, where Cluster ID is the number of the cluster. The larger the cluster size, the smaller the number. Size represents the number of members contained in the cluster, and Silhouette is an index to measure the homogeneity of the entire cluster members. The larger the value, the higher the similarity of the cluster members. The cooperative relationship was determined by the number of articles coauthored by different countries, institutions, and authors, reflecting the collaboration between countries, institutions, and authors.

RESULTS

Annual Growth Trend and Analysis of Publication Outputs

The number of published articles can directly reflect the development trend in a specific field. From 1983 to 2021, the annual publications on the intestine associated with AP included 1634 articles. The distribution map of publications by year is displayed in Figure 2A. In 1991, 2009, and 2020, publications rapidly increased. In 2020, the number of publications exceeded 100. The number of publications declined in some years, but the number of articles published increases each year. From the cumulative number of articles published each year, a significant upward trend is shown in Figure 2B.

According to the article's title, abstract, and key words, 2 experienced personnel (Y.L. and S.C.) screened and marked each record, finally summarized the article types and the number of research subjects each year, and plotted Figures 3A and B.

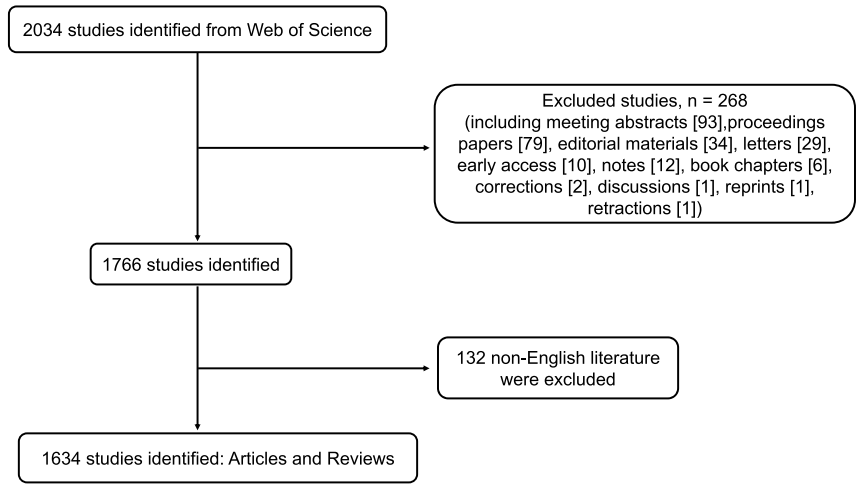


FIGURE 1. Flowchart for including and excluding literature studies.

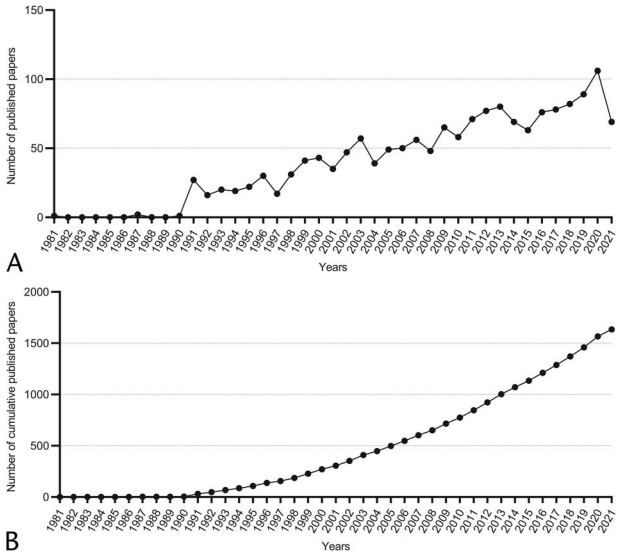


FIGURE 2. Trends in the number of publications from 1981 to 2021. A, Annual number of publications. B, Cumulative number of publications.

Scientific Collaboration Network

Sixty-seven countries contributed to the publications on the intestine associated with AP. The top 10 productive and influential countries are shown in Table 1. The top 5 countries by the number of articles were the United States, China, Germany, Japan, and the United Kingdom. The top 5 countries by centrality were the United States, Italy, Germany, the United Kingdom, and France. The point where centrality exceeds 0.1 was considered a key node. Our analyses showed that the United States (publications, 368; centrality, 0.89), Italy (publications, 71; centrality, 0.14), and Germany (publications, 105; centrality, 0.13) were the most predominant in the field. The network collaboration map between countries is shown in Figure 4A. Each node represents a country, and the node sizes indicate the number of publications. Links between the nodes represent collaborations, and greater link widths mean closer collaborations between countries.

A total of 1787 institutions published from 1981 to 2021. Table 1 displays the top 10 institutions in terms of publications and centrality. The top 5 institutions with the most prominent influence on this field were the University of Auckland (33 articles), Shanghai Jiao Tong University (32 articles), Sichuan University (23 articles), Jagiellonian University (22 articles), and the University of Pittsburgh (18 articles). The top 5 institutions according to the centrality were Karolinska Institute, Beaujon University Hospital, Hadassah Hebrew University, Kyushu University, and University Medical Center (Netherlands). The institution collaboration research network on the intestine associated with AP is presented in Figure 4B.

A knowledge domain map for the coauthorship network on the field is shown in Figure 4C. The generated coauthorship network map included 75 items, 25 clusters, and 106 link lines. Each node represents an author, and the node sizes indicate the number of coauthored publications. Links between the nodes represent collaborations, with greater link widths meaning closer collaborations between authors. Different clusters are represented by different colors. Through this view, each individual cluster can be viewed, and a research clique can be found through author cooperation (authors of the same color are considered as a research clique). The author's centrality is not described here because of their very low centrality (<0.01).

Analysis of Journals and Co-cited Journals

Articles of the intestine associated with AP have been published in 575 journals. The top 10 journals and co-cited journals in the field are shown in Table 2. The *World Journal of Gastroenterology* published the most (73 articles), followed by *Pancreas* (63 articles), *Pancreatology* (36 articles), *Digestive Diseases and Sciences* (33 articles), and the *American Journal of Gastroenterology* (27 articles). Among the top 10 journals, 4 were at the Q1 and Q2 Journal Citation Reports (JCR) division, 8 had an impact factor (IF) of more than 3, and the highest IF was 23.059.

Among 6553 co-cited journals, the citations of each journal exceed 1000. Table 2 shows that *Gastroenterology* had the most co-citations (3108 times), followed by *Gut* (2138 times), the *American Journal of Gastroenterology* (1652 times), *Pancreas* (1613 times), and the *Annals of Surgery* (1583 times). Clarivate Analytics publishes JCR annually. The JCR divides the journals into 176 different subject categories. Each subject category is divided into 4 areas according to the IF of the journal: journals with an IF of the top 25% (including 25%) are in the Q1 area, journals with an IF of the top 25% to 50% (including 50%) are the Q2 area, journals with an IF of the top 50% to 75% (including 75%) are in the Q3 area, and journals with an IF less than 75% are in the Q4 area. Division in JCR is a very important reference index for researchers to choose journals for submission, and it also reflects the quality level of journals. Among the top 10 co-cited journals, 7 were at the Q1and Q2 JCR division with an IF exceeding 5, and the journal of highest IF was *Lancet* (79.321).

Analysis of Authors and Co-cited Authors

A total of 8006 authors contributed to the research on the intestine associated with AP. Eight authors published more than 10 articles. Roland Andersson published the most articles (n = 18), followed by Maxim S. Petrov (n = 15), John A. Windsor (n = 13), Zygmunt Warzecha (n = 13), and Piotr Ceranowicz (n = 12; Table 3).

Co-cited authors are 2 or more authors cited by 1 or more articles. The number of articles published by these authors refers to

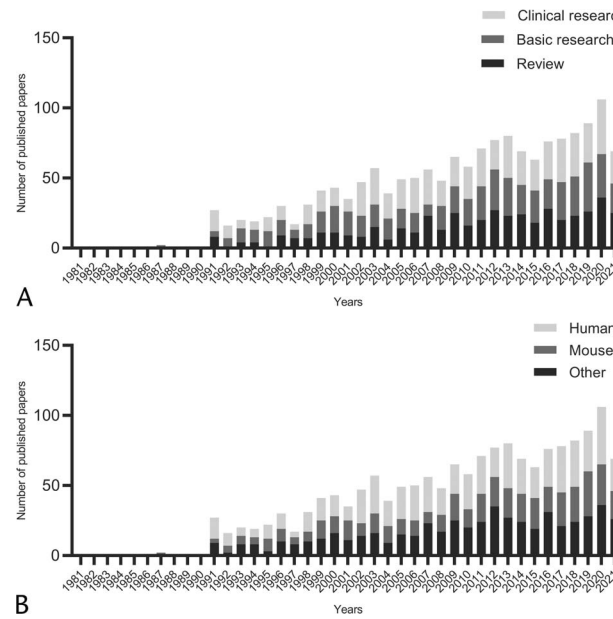


FIGURE 3. Number of publications from 1981 to 2021. A, Number of publications in terms of article types. B, Number of publications in terms of research subjects. Other include pigs, cats, dogs, monkeys, and others.

TABLE 1. Top 10 Countries and Institutions in Terms of Publications and Centrality

	Publication			Centrality		
	Rank	Name	No.	Rank	Name	No.
Country	1	United States	368	1	United States	0.89
	2	China	365	2	Italy	0.14
	3	Germany	105	3	Germany	0.13
	4	Japan	105	4	United Kingdom	0.10
	5	United Kingdom	80	5	France	0.10
	6	Italy	71	6	Spain	0.07
	7	Netherlands	64	7	Australia	0.05
	8	France	54	8	Canada	0.03
	9	Canada	39	9	Sweden	0.03
	10	Sweden	43	10	Denmark	0.03
Institution	1	University of Auckland, Auckland, New Zealand	33	1	Karolinska Institute, Stockholm, Sweden	0.09
	2	Shanghai Jiao Tong University, Shanghai, China	32	2	Beaujon University, Hospital Clichy, France	0.08
	3	Sichuan University, Chengdu, China	23	3	Hadassah Hebrew University, Jerusalem, Israel	0.07
	4	Jagiellonian University, Kraków, Poland	22	4	Kyushu University, Fukuoka, Japan	0.06
	5	University of Pittsburgh, Pittsburgh, Pa	18	5	University Medical Center, Leiden, the Netherlands	0.06
	6	Nanjing University, Nanjing, China	17	6	Tongji University, Shanghai, China	0.05
	7	Tongji University, Shanghai, China	16	7	University of Toronto, Toronto, Canada	0.05
	8	University of Sao Paulo, Sao Paulo, Brazil	16	8	Tel Aviv University, Tel Aviv, Israel	0.05
	9	University Medical Center, Leiden, the Netherlands	15	9	Maastricht University, Maastricht, the Netherlands	0.05
	10	Zhejiang University, Hangzhou, China	15	10	NIDDK, Bethesda, Md	0.05

NIDDK indicates National Institute of Diabetes and Digestive and Kidney Diseases.

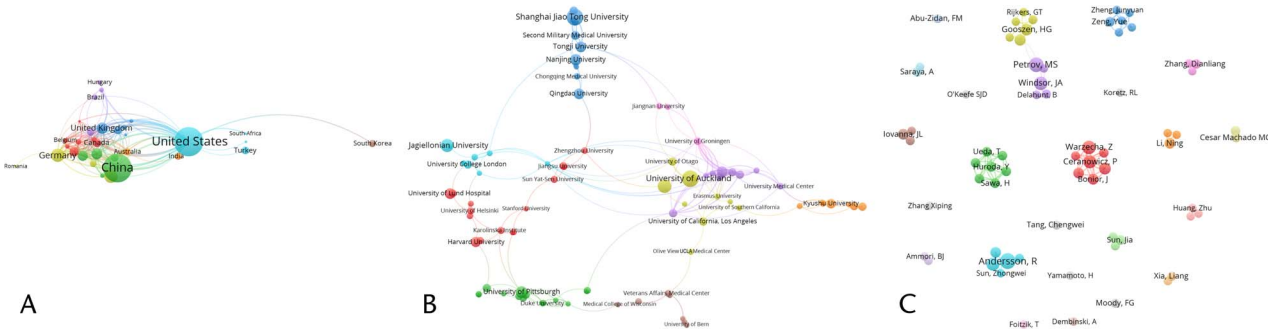
the number of articles published by independent first authors or co-first authors. Coauthored articles are not counted in the multiple-person article count. Among 37,902 co-cited authors, 16 authors had a co-cited frequency of more than 100. Maxim S. Petrov (n = 247) ranked first, followed by Edwin A. Deitch (n = 227), Hans G. Beger (n = 224), Peter A. Banks (n = 200), and Basil J. Ammori (n = 199). The remaining 5 top authors were co-cited frequency from 127 to 182 (Table 3).

Analysis of Highly Co-cited References

Highly co-cited references showed that publications are highly co-cited and considerably influence the field. Co-cited references are defined as if 2 articles (or more articles) are cited by 1 or more later articles at the same time, it is said that the 2 articles constitute a co-citation relationship. There were 53,514 co-cited references, and 17 articles were co-cited more than 50 times. The detail of the highly co-cited articles is displayed in Table 4.[22–31] The article by Beger et al published in *Gastroenterology* in 1986 is the most co-cited article (106 times). In this article, the authors demonstrated that bacterial infection could occur in early pancreatic necrosis, which is closely associated with high morbidity and mortality, especially in the early stages of the disease. The second and fourth publications introduce the classification system for AP. The third and fifth pieces of the literature clarify the intestine's role in developing AP, and that bacterial cultures in part organs and body fluids of mice were positive in the AP model.

Analysis of Co-occurring Key Words and Burst Term

Co-occurring key word analyses were used to revealed important terms and research hotspots. The co-occurring key word map of this field is shown in Figure 5. According to the link strength



A B C

FIGURE 4. Co-occurrence map of countries (A), institutions (B), and authors (C) in the field ($T \geq 5$). Note that the size of node reflects the co-occurrence frequencies, the link indicates the co-occurrence relationship, and the same color of node represents the same cluster. **Editor's note**: A color image accompanies the online version of this article.

TABLE 2. Top 10 Journals and Co-cited Journals in the Field

Items	Rank	Name	Counts	IF (2020)	JCR Division
Journal	1	*World Journal of Gastroenterology*	73	5.742	Q2
	2	*Pancreas*	63	3.327	Q3
	3	*Pancreatology*	36	3.996	Q2
	4	*Digestive Diseases and Sciences*	33	3.199	Q3
	5	*American Journal of Gastroenterology*	27	10.864	Q1
	6	*Journal of Clinical Gastroenterology*	21	3.062	Q3
	7	*Journal of Surgical Research*	20	2.192	Q3
	8	*Gut*	19	23.059	Q1
	9	*Scandinavian Journal of Gastroenterology*	18	2.423	Q4
	10	*Gut and Liver*	16	4.519	Q3
Co-cited journal	1	*Gastroenterology*	3108	22.682	Q1
	2	*Gut*	2138	23.059	Q1
	3	*American Journal of Gastroenterology*	1652	10.864	Q1
	4	*Pancreas*	1613	3.327	Q3
	5	*Annals of Surgery*	1583	12.969	Q1
	6	*British Journal of Surgery*	1407	6.939	Q1
	7	*World Journal of Gastroenterology*	1145	5.742	Q2
	8	*Digestive Diseases and Sciences*	1142	3.199	Q3
	9	*Lancet*	1024	79.321	Q1
	10	*American Journal of Surgery*	1005	2.565	Q3

of term co-occurrence, the network was mainly divided into 7 clusters. Cluster 1 (red) is the largest cluster focused on the mechanisms of pancreatitis with 130 co-occurrence terms: expression, injury, model, apoptosis, intestine, rat, severity, and barrier. Cluster 2 (green) is mainly related to a complication of pancreatitis, which includes 84 terms: acute pancreatitis, complication, management, diagnosis, system, risk factors, and small bowel. Cluster 3 (blue) focuses on other causes of pancreatitis and contains 72 terms: inflammatory bowel disease, autoimmune pancreatitis, drug-induced pancreatitis, infectious, nutrition, and therapy. Cluster 4 (yellow) is mainly related to the intestine with 55 terms: gut barrier dysfunction, gut permeability, necrosis, and translocation. Cluster 5 (purple) is related to clinical research of pancreatitis, including 55 terms: double-blind, enteral nutrition, mild acute pancreatitis, randomized clinical trial, meta-analysis, and parenteral nutrition. Cluster 6 (cyan) is related to the invasive treatment of pancreatitis, containing 33 terms: drainage, guidelines, necrosectomy, surgical management trial, and cholecystectomy. Cluster 7 (orange) focuses on the medical treatment of pancreatitis, which contains 20 terms: octreotide, enzyme secretion, total parenteral nutrition, energy expenditure, amino acids, and supplementation, and growth.

A total of 4032 key words were found in this study—the top 30 key words are displayed in Table 5 according to the frequency of co-occurrence. The analysis of co-occurrence key words shows that "acute-pancreatitis" ranks first, "bacterial translocation" ranks second, "management" is third, "gut" ranks fourth, and the fifth place is "inflammatory bowel disease."

According to the key word timeline (Supplemental Fig. 1, http://links.lww.com/MPA/A976), the evolution and development trend on the intestine associated with AP can be identified. The key word timeline presents the research progress for each cluster over time and can be used to evaluate the research themes. In Supplemental Figure 1 (http://links.lww.com/MPA/A976), the *y* axis is key word clusters, the *x* axis is the publication year, and the connecting line represents the co-occurrence relationship between key words. Key words are classified into 20 categories, and each category contains several key words. The largest 8 clusters are summarized in Table 6. Several clusters and research themes were derived from the co-occurring key words analysis by CiteSpace. The cluster with the silhouette value >0.7 was considered highly credible; the cluster with the silhouette value >0.5 was considered reasonable. All clusters in our analysis had a silhouette value >0.7. The 8 clusters include "acute pancreatitis," "abdominal compartment syndrome," "arginine-induced acute pancreatitis," "Crohn's disease," "bacterial translocation," "intestinal permeability," "double balloon endoscopy," and "multiple organs." Based on the aforementioned analysis, bacterial translocation, permeability, management, and gut are all hot research topics.

Key word burst was detected based on literature published between 1981 and 2021. The light gray line indicates the time interval, and the dark gray line indicates the duration of the burst, showing the evolution of hot topics. Figure 6 shows the top 50 key words with the strongest citation bursts. Inflammation had the highest burst strength (12.93), followed by multiple-organ failure (10.52), infection (8.97), pathogenesis (8.27), sepsis (7.91), and gut microbiota (7.28). Key words that last until 2021 include the following: gut microbiota, pathway, gut barrier, risk, and oxidative stress, which reflect the latest research trends. The result shows

TABLE 3. Top 10 Authors and Co-cited Authors in the Field

Rank	Author	Count	Co-cited Author	Co-citation
1	Andersson R.	18	Petrov M.S.	247
2	Petrov M.S.	15	Deitch E.A.	227
3	Windsor J.A.	13	Beger H.G.	224
4	Warzecha Z.	13	Banks P.A.	200
5	Ceranowicz P.	12	Ammori B.J.	199
6	Wang X.D.	12	Bradley E.L.	182
7	Dembinski A.	10	Oláh A.	175
8	Gooszen H.G.	10	McClave S.A.	151
9	van Santvoort H.C.	9	Lankisch P.G.	146
10	Bonior J.	8	Balthazar E.J.	127

TABLE 4. Top 10 Highly Co-cited References in the Field

Rank	Co-cited by	Study	Title	Year
1	106	Beger et al[22]	Bacterial contamination of pancreatic necrosis. A prospective clinical study	1986
2	104	Banks et al[23]	Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus	2013
3	98	Ammori et al[24]	Early increase in intestinal permeability in patients with severe acute pancreatitis: correlation with endotoxemia, organ failure, and mortality	1999
4	94	Bradley[25]	A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992	1993
5	92	Runkel et al[26]	The role of the gut in the development of sepsis in acute pancreatitis	1991
6	89	Besselink et al[27]	Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial	2008
7	85	Schmidt et al[28]	A better model of pancreatitis for evaluating therapy	1992
8	77	Oláh et al[29]	Randomized clinical trial of specific lactobacillus and fibre supplement to early enteral nutrition in patients with acute pancreatitis	2002
9	71	Kalfarentzos et al[30]	Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial	1997
10	65	Medich et al[31]	Pathogenesis of pancreatic sepsis	1993

that studies have increasingly focused on the gut microbiota and oxidative stress in the field of AP in recent years.

DISCUSSION

Acute pancreatitis is a common acute abdominal condition that can lead to a mortality rate of 36% to 50% when it develops into SAP with early organ failure.[23,32,33] Notably, the intestine plays an important role in developing multiple-organ dysfunction syndromes (MODS) in severe diseases. The intestine has been regarded as a "promoter" of MODS.[34–36] Intestinal barrier dysfunction and flora dysbiosis are related to SAP. Severe AP can destroy normal intestinal mucosal function, leading to systemic bacterial and endotoxin translocation and ultimately to MODS.[37,38] It is essential to summarize the development of this field. Therefore, our study shows a more comprehensive overview of AP development by summarizing publications on the intestine associated with AP. This study is the first bibliometric analysis of research on the intestine associated with AP involving 1634 research articles retrieved from WoSCC.

Our analysis showed an increasing trend in the number of publications since 1991. The United States, the University of Auckland, and Roland Andersson are the most influential country, institute, and author. The *World Journal of Gastroenterology* was the most productive journal, and *Gastroenterology* was the most influential co-cited journal. Among the articles, the number of clinical and basic research is comparable; similar studies were conducted on mice and humans.

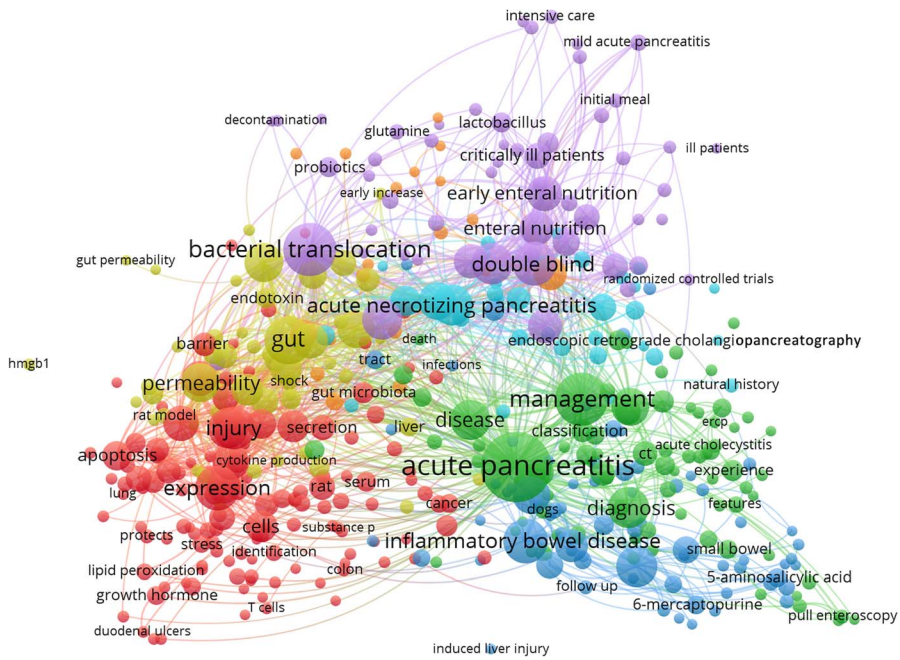


FIGURE 5. Co-occurrence map of key words in the field ($T \geq 5$, contains 449 items, 7 clusters and 10,527 links). Note that the size of node and word reflects the co-occurrence frequencies, the link indicates the co-occurrence relationship, and the same color of node represents the same cluster. **Editor's note**: A color image accompanies the online version of this article.

TABLE 5. Top 30 Key Words in Terms of Frequency

Rank	Key Word	Frequency	Rank	Key Word	Frequency
1	Acute pancreatitis	266	16	Permeability	74
2	Bacterial translocation	144	17	Mortality	71
3	Management	142	18	Complications	71
4	Gut	122	19	Therapy	70
5	Inflammatory bowel disease	102	20	Organ failure	69
6	Expression	99	21	Activation	66
7	Double-blind	96	22	Model	64
8	Injury	93	23	Early enter nutrition	62
9	Acute necrotizing pancreatitis	87	24	Necrosis	62
10	Crohn's disease	86	25	Inflammation	60
11	Severe acute pancreatitis	83	26	Parenteral nutrition	59
12	Diagnosis	83	27	Oxidative stress	59
13	Infection	80	28	Meta-analysis	58
14	Rats	78	29	Enteral nutrition	58
15	Sepsis	75	30	Ulcerative colitis	54

The largest theme cluster is "acute pancreatitis," reflecting a solid foundation for this research field. Since 2017, the hot research topic has been "gut microbiota." In addition, "pathway," "gut barrier," "risk," and "oxidative stress" reflect research hotspots of the field in recent years. Our results include valuable information and thus provide important insights for research on the intestine associated with AP. These findings may be helpful for future researchers to choose an appropriate direction, topic and provide good guidance for clinical and scientific research through our visual and comprehensive bibliometrics analysis over time.

Collaboration network analysis can provide useful information about research collaborations and potential cooperators. The United States has a clear advantage over all countries, probably because of its greater availability of research ideas and better financial support in scientific research. Because research on the intestine's role in sepsis development in AP was launched in 1991,[26] the number of publications increased rapidly, partly owing to the important hotspot, "bacterial translocation," ranked the second-highest frequency key word in 1991. However, China ranks second in the number of published articles, slightly inferior to the United States in this field, possibly because of the lack of international communication and cooperation. The University of Auckland played a key role in all institutions, possibly owing to the more influential researchers of this field at this institute (including Maxim S. Petrov and John A. Windsor). Overall, close international scientific cooperation was found in this field. Nevertheless, some high-influential scholars did not cooperate enough, which may be related to comparatively mature research or less collaboration between institutions. For example, Roland Andersson had the most publications in this field. His article about bacterial infection in AP was published in 1995[39]; however, he has few contacts with other scholars according to the collaboration network.

Journal analysis and co-cited journal analysis can be used to identify important journals and for the latest literature information tracking or manuscript submission. Our analysis shows only 2 journals with Q1 (JCR) and few publications among the top 10 most active journals. In addition, the consistency between the top 10 most active journals and co-cited journals is only 40%, suggesting that the research quality in this field needs to be improved, and the close collaboration and communication among scholars should be enhanced to produce more high-quality studies.[31] Almost all the top 10 highly co-cited references were published before 2010 and discussed infection, one of the complications of AP.[22,26,27,31] These findings suggest that early attention to infectious pancreatitis is quite important. It is currently believed that most of the bacteria in infection pancreatitis are derived from intestinal flora translocation caused by the destruction of the intestinal barrier.[3,40] Hence, the intestine plays a key role in AP development.

The co-occurring key word analysis was used to identify the key topics in this field over the past 4 decades, including acute pancreatitis, bacterial translocation, management, gut, inflammatory bowel disease, and expression, indicating that the study mainly focused on the intestinal progression of AP.[41–43] Most key words are in the center of the network map, reflecting the research interest in this field. Several strong burst key words associated with hot topics of intestine-related research have emerged recently, including gut microbiota, gut barrier, barrier, and risk. Currently, "gut microbiota" showed the highest strength with ongoing bursts. The gut microbiota is emerging as a critical determinant of human body homeostasis and balance health and disease. An imbalance in the gut microbiota is termed "dysbiosis" and is associated with gastrointestinal diseases.[44,45] Several studies support a gut microbiota–pancreas axis.[46] On the one hand, pancreatic secretions can alter the gut microenvironment, which plays a key role in the gut microbiota, and on the other hand, the gut microbiota may influence pancreatic diseases. The relationship between pancreatic disease and the gut microbiota is determined by the interplay of the immune system,

TABLE 6. Key Words Cluster Analysis*

Cluster ID	Size	Silhouette	Label (LLR)
0	37	0.819	Acute pancreatitis
1	34	0.801	Abdominal compartment syndrome
2	32	0.877	Arginine-induced acute pancreatitis
3	25	0.966	Crohn's disease
4	25	0.978	Bacterial translocation
5	24	0.945	Intestinal permeability
6	23	0.938	Double balloon endoscopy
7	23	0.928	Multiple organs

*The silhouette value is greater than 0.5.
LLR indicates log likelihood ratio.

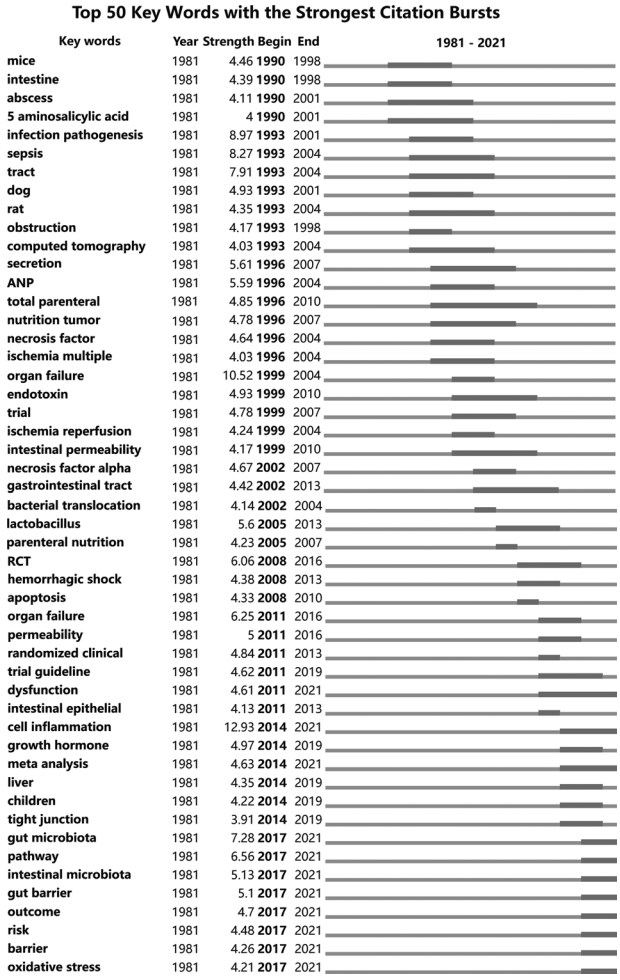


FIGURE 6. Top 50 key words with strongest citation bursts. ANP, acute necrotizing pancreatitis; RCT, randomized controlled trial.

proinflammatory status, and dysbiosis.[47] The alteration in gut microbiota balance may occur early in AP patients and participate in the deterioration of disease.[40] Thus, modifying the gut microbiota in AP patients may become a future research direction.

Other research hotspots in the field, such as "oxidative stress" and "pathway," have currently continuous bursts. The concept of oxidative stress was introduced for research in redox biology and medicine in 1985.[48] New insights emerge on the link between oxidative stress and inflammation response. Current reports indicate that the pathogenesis and prognosis of AP might be associated with oxidative stress–related acinar cell necrosis, and antioxidation could reduce pancreatic necrosis.[49,50] Recent studies have shown that AP is associated with oxidative stress, and levels of oxidative stress markers are significantly related to the severity and prognosis of disease.[51] Some molecules could be used as early biomarkers of this disease in the future. Thus, future clinical studies could pay attention to the therapeutic effect of antioxidants in SAP patients, who may recover better by reducing oxidative stress biomarkers such as 8-hydroxy-2 deoxyguanosine and thioredoxin.[52,53] All the studies mentioned previously discussed oxidative stress from different signaling pathways. Therefore, future research can also focus on oxidative stress–related pathways in this field.

There are some disadvantages to our research. First, data were only extracted from the WoSCC database, which may not represent all studies in the field. Second, we only included articles and reviews in English; therefore, a language bias may exist. Third, bibliometric analysis is mainly based on the abstract, title, key words, and references, without examining the main text, leading to inaccurate results. We hope that the function of the database will be more comprehensive, and future research will also pay attention to these problems and solve them as much as possible. We believe that our data are very reliable because of the comprehensiveness of the data we extract, the long-time span, and the careful and careful screening process.

CONCLUSIONS

In conclusion, the key hotspots and trends of research on the intestine associated with AP from 1981 to 2021 are visually displayed through bibliometric analysis. In terms of scientific productivity, the top country was the United States. Frequent and effective cooperation between countries, institutions, and authors is necessary for the academic community. The top 3 journals are the *World Journal of Gastroenterology*, *Pancreas*, and *Pancreatology*. Recently, oxidative stress–related pathways and gut microbiota have become hotspots of AP research. Using 2 practical bibliometric tools, VOSviewer and CiteSpace, the results of this study summarized the research status of this field from various perspectives and predicted the future research trends in this field.

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