Observational Study

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Global status of acute pancreatitis research in the last 20 years

A bibliometric study

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Abstract

Acute pancreatitis (AP) is a common digestive disease encountered in Emergency Departments that carries a heavy socioeconomic burden. This study was conducted to determine the global status of AP research. Articles related to AP published in 1999 to 2018 were retrieved from the Web of Science (WOS) database and the 20 highest-output countries or regions were determined based on the total number of publications. Correlation analysis of AP research output and the gross domestic product (GDP) of each country or region was conducted. The quantity and quality of research of these 20 highest-output countries were compared to the total output, outputs per capita, and average impact factor (IF). All annual data were analyzed using time-trend analysis. A keyword co-occurrence analysis was conducted to determine the highlights in AP research. In total, 17,698 publications were retrieved, and 16,461 papers (93.0%) of them were from the 20 highest-output countries. A significantly positive correlation was identified between AP research output and the GDP ($R = 0.973$, $P < .001$). The 5 highest-output countries were the USA (24.9%), China (12.3%), Germany (7.5%), Japan (6.7%), and the UK (6.1%). Finland ranked 1st in the number of publication per capita, the USA had the highest accumulated IF (25,432.758) and total citations (104,592), Switzerland had the highest average IF (6.723), and Netherland had the highest average citations (51.90). Genetic research and AP-related hyperglycemia were research highlights. Analysis of the global output of research of AP research showed signs of growth. Research output was positively correlated with GDP. For the most productive countries, research quality was stable. Although developing countries lagged behind in output per capita and quality, great progress has been made in the past 2 decades.

Abbreviations: AP = acute pancreatitis, GDP = gross domestic product, GERD = gross domestic expenditure on research and development, IF = impact factor, SCIE = science citation index expanded, WOS = web of science.

Keywords: acute pancreatitis, impact factor, journal citation reports, research, science citation index expanded

1. Introduction

Acute pancreatitis (AP) is a devastating type of pancreatic inflammation and one of the most common emergency digestive diseases, thus it needs to be treated quickly and effectively. In addition to pancreatic damage, AP may also cause systematic inflammatory response syndrome which leads to multiple organ failure.[1]

Throughout the world, the incidence of AP ranges from 15 to 42 cases per 100,000 person-years, increasing by 2.7% to 3.4% annually.[2–4] About 20% of cases are severe AP, which has a mortality rate of up to 30%.[5] Patients with persistent organ failure in the early stage of AP have a mortality rate of 36% to 50%.[6] As a result of advances in AP management, the case-fatality rate has decreased over the past 3 decades by more than 60%, from 2.02% to 0.79%. However, the per-million-population-based mortality rate has remained largely unchanged, from 9.28 to 9.9.[7] In the USA, more than 279,000 patients are admitted to hospital because of AP annually, and the aggregate cost is more than 2.7 billion dollars per year.[8] In the UK, there were 29,962 admissions because of AP between March 2018 and March 2019, which is an increase of 4.9% compared to the

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CH, H-YY, Y-WL, and Z-QD contributed equally to this work.

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previous financial year.[9] Given the increasing morbidity, high mortality, and heavy socioeconomic burden of AP, research on AP become even more important.

It has been nearly 400 years since the Dutch anatomist Nicholas Tulp published the first clinical description of AP in 1652.[10] During this time, considerable progress has been made; Claude Bernard initially demonstrated fat necrosis in dogs in 1856; Reginald Fitz first described hemorrhagic, suppurative, and gangrenous changes in AP in 1889; and Hans Chiari unveiled the role of pancreatic enzymes in the pathogenesis of pancreatic necrosis in 1896.[11] In the 21st century, research on the molecular mechanisms of AP (calcium-mediated injury, unfolded protein response, autophagy, and unsaturated fatty acids impact, etc) has brought hope for a novel molecular targeted therapy in AP treatment.[12] Meantime, many large cohort studies have been conducted in the general population, and comprehensive systematic literature reviews on the prognosis and outcomes of AP and optimized treatment strategies for AP have been published.[13]

Although great progress has been made in the study of AP, AP research still lacks in breakthroughs and significant discoveries, especially individualized treatments based on etiological factors and pharmacologic therapies that can improve prognosis.[5] By international cooperation and a multidisciplinary approach, physicians and scientists are attempting to resolve the problems with the prevention and treatment of AP. There are many publications on AP in different fields every year. Hence, this bibliometric analysis was conducted to reveal the distribution and current trends in AP research.

2. Methods

2.1. Data collection

All papers on AP published between January 1999 and December 2018 indexed on the Science Citation Index Expanded (SCIE) database of the Web of Science (WOS)[14] were retrieved and categorized according to document type, source title, year of publication, country, and citations. The total global research paper output for AP was retrieved from the SCIE database using the term "acute pancreatitis" with no language restriction. Gross domestic product (GDP) data and the populations of the publishing countries were retrieved from World Bank Open Data.[15] This study was not required for registration, and ethics approval was not required in this study.

2.2. Data processing

The 20 highest-output countries or were determined based on the total number of publications, and the proportion of publications from each country or region for each document type was calculated. Then, a correlation analysis between AP research output and the economic development of each country or region was performed by evaluating the number of publications and GDP data.

To evaluate the quality and quantity of AP research, the 20 highest-output countries were selected for an analysis of the following 3 aspects:

First, the number of publications per capita was calculated by dividing the total number of publications by the populations of the country in 2018. To determine the time trend of AP research, the number of publications per capita was calculated by dividing the total number of publications by the population the top 20 highest-output countries annually.

Second, the 10 highest-impact factor (IF) journals (*New England Journal of Medicine*, *Lancet*, *Journal of the American Medical Association*, *Cell*, *Lancet Oncology*, *Nature Reviews Disease Primers*, *Nature Medicine*, *Journal of Clinical Oncology*, *British Medical Journal*, *and Nature Genetics*) were identified, and the number of papers published in these journals from the 20 highest-output countries were retrieved.

Third, according to Journal Citation Reports 2018,[16] the accumulated IFs were calculated as the sum of the IFs of all the publications, and the average IF was obtained by dividing accumulated IF by the total number of publications. These 20 countries were compared to identify differences in AP research output. Similarly, the average citations from these countries were calculated by dividing the total number of citations by the total number of publications.

In addition, the 10 highest-output journals for each country were retrieved from the SCIE database and the proportion of publications in AP to total papers of each journal was calculated.

2.3. Data visualization

In scientific publications, keywords are the words or phrases that convey the thematic concepts of an article, and can be analyzed as important indicators in bibliometrics. Keyword co-occurrence analysis can be used to analyze the strength of the association among co-occurrent keywords by evaluating their relationship. Determining the internal structure and connections within a particular discipline can reveal the research highlight, including the combination of cutting-edge research issues and basic concepts, as well as emerging or unexpected research trends or theoretical topics.

In the present study, keyword co-occurrence analysis was chosen to determine the research highlights in AP research. The titles and abstracts of all the retrieved publications were compiled and used to construct a co-occurrence map using VOSviewer software (Leiden University, Leiden, the Netherlands). Keywords occurring more than 50 times were defined as the key terms and the most relevant key terms (top 60%) were used to create this map.

2.4. Data analysis

Statistical Package for Social Sciences software (version 22.0, Statistical Package for Social Sciences, Chicago, IL) was applied for the analysis. Regression analysis was used to determine whether the change in AP research in each country was significant or not. Pearson correlation coefficient test was used to analyze the correlations between AP research publication productivity and GDP. Tests for significance were 2-tailed, and P value <.05 were considered significant.

3. Results

3.1. Numbers of total articles, original articles, and reviews

Based on the SCIE database, the total number of papers on AP published between January 1999 and December 2018 was 17,698, with an average annual productivity of 884.9 papers. The global research output included 11,133 original articles (62.9%), 3375 meeting abstracts (19.1%), 1604 reviews (9.1%), 883 letters (5.0%), and 703 other types of papers (4.0%). Most of these publications were written in English (n = 16,818, 95.0%), followed by French (n = 284, 1.6%) and German (n = 278, 1.6%).

The 20 highest-ranking countries were determined based on the total number of publications. The research outputs from these 20 countries accounted for 93.0% of publications (16,462/17,698, shown in Fig. 1 and Table 1). The correlation between research output and the GDP of each country or region was significantly positive (R = 0.973, P < .05, shown in Fig. 2).

The USA had the largest number of publications, with 4398 papers, accounting for 24.9% of the global research output, China, Germany, Japan, and the UK ranked second, third,

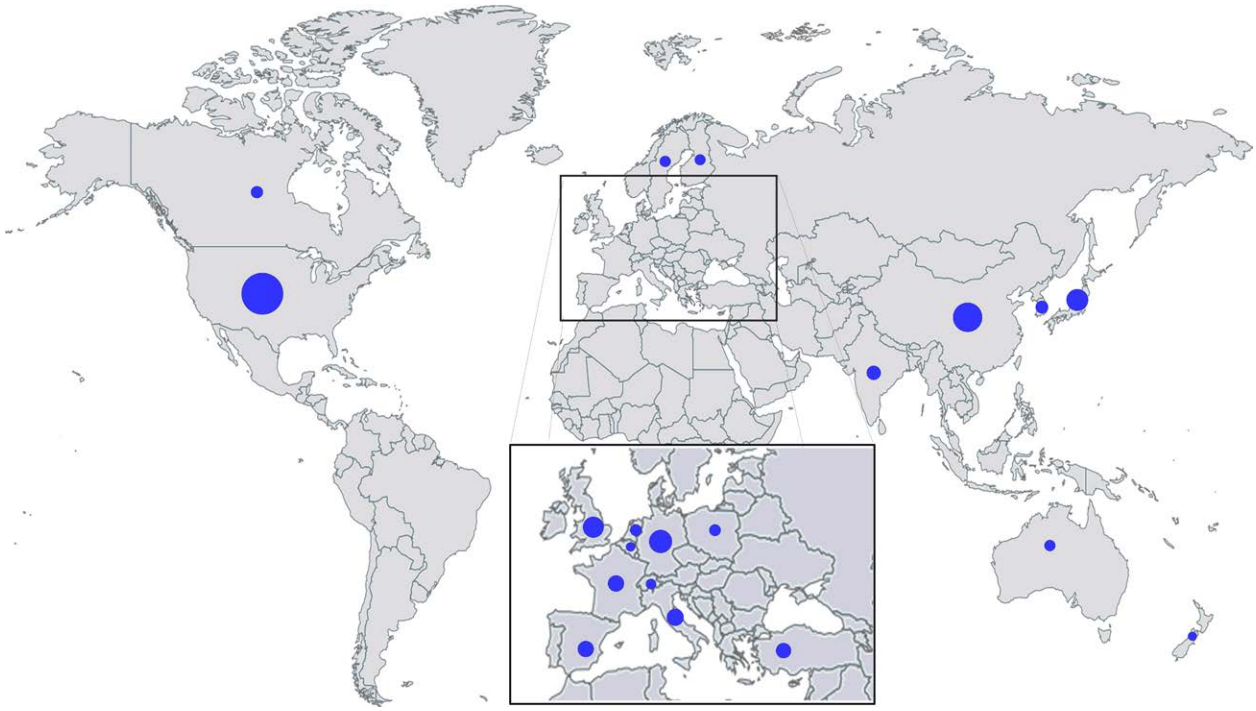

Figure 1. The geographic distributions of AP research output. The locations of the 20 highest-output countries were indicated as blue dots. The size of the blue spot is proportional to the research output of these countries, the larger the blue dot area, the higher the research output. AP = acute pancreatitis.

Table 1

Share of articles regarding acute pancreatitis for 20 highest-output countries.

	Total articles (n = 17,698)			Original articles (n = 11,133)			Reviews (n = 1604)		
Rank	**Country/Region**	**Number**	**Percentage (%)**	**Country/Region**	**Number**	**Percentage (%)**	**Country/Region**	**Number**	**Percentage (%)**
1	USA	4398	24.9%	USA	2516	22.6%	USA	513	32.0%
2	China	2170	12.3%	China	1786	16.0%	UK	175	10.9%
3	Germany	1328	7.5%	Germany	977	8.8%	Germany	158	9.9%
4	Japan	1191	6.7%	Japan	913	8.2%	China	131	8.2%
5	UK	1085	6.1%	UK	565	5.1%	Italy	92	5.7%
6	Italy	726	4.1%	France	473	4.2%	Canada	62	3.9%
7	France	665	3.8%	Italy	470	4.2%	France	59	3.7%
8	Spain	628	3.5%	Turkey	467	4.2%	Japan	57	3.6%
9	Turkey	563	3.2%	Spain	420	3.8%	Australia	49	3.1%
10	India	504	2.8%	South Korea	309	2.8%	Spain	48	3.0%
11	South Korea	416	2.4%	India	306	2.7%	Netherlands	47	2.9%
12	Canada	373	2.1%	Poland	268	2.4%	New Zealand	41	2.6%
13	Poland	345	1.9%	Sweden	260	2.3%	Switzerland	36	2.2%
14	Netherland	340	1.9%	Canada	252	2.3%	India	33	2.1%
15	Australia	320	1.8%	Netherlands	219	2.0%	Turkey	27	1.7%
16	Sweden	306	1.7%	Finland	215	1.9%	Poland	25	1.6%
17	Finland	298	1.7%	Australia	200	1.8%	South Korea	24	1.5%
18	Switzerland	272	1.5%	Switzerland	196	1.8%	Belgium	24	1.5%
19	Belgium	207	1.2%	Belgium	149	1.3%	Finland	22	1.4%
20	New Zealand	203	1.1%	New Zealand	122	1.1%	Sweden	21	1.3%

fourth, and fifth, with 2170 (12.3%), 1328 (7.5%), 1191 (6.7%), and 1085 (6.1%) papers, respectively. It is worth mentioning that the number of publications from China increased by more than 250 times over the past 20 years ($P < .001$). The number of publications from most countries has steadily risen ($P < .05$), while the number of papers from Japan, Finland and Belgium changed very little during this time period ($P = .977$, .187, and .059, respectively). In contrast, Germany, France and Switzerland showed a significant downward trend over the past 2 decades ($P < .05$, shown in Fig. 3). Regarding original articles, the ranking of the top 5 countries remained unchanged, with 2516 (22.6%) papers from the USA, 1786 (16.0%) papers from China, 977 (8.8%) papers from Germany, 913 (8.2%) papers from Japan, and 565 (5.1%) papers from the UK. When it comes to reviews, the USA ranked first, with 513 papers (32.0%), while the UK, Germany, China, and Italy ranked second, third, fourth, and fifth, with 175 (10.9%), 158 (9.9%), 131 (8.2%), and 92 (5.7%) papers, respectively.

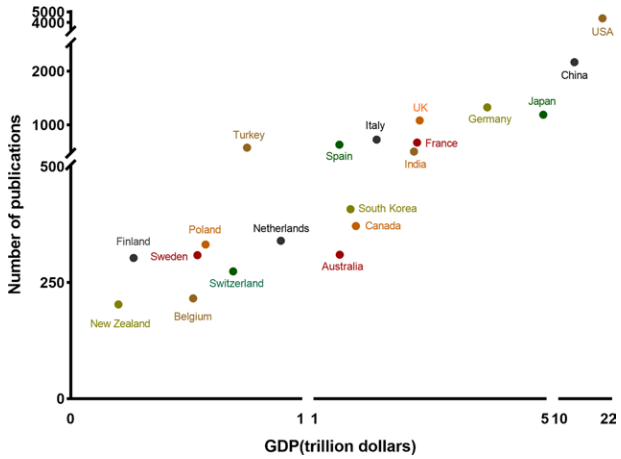

Figure 2. The correlation between the number of publications and GDP from 20 highest-output countries. GDP = gross domestic product.

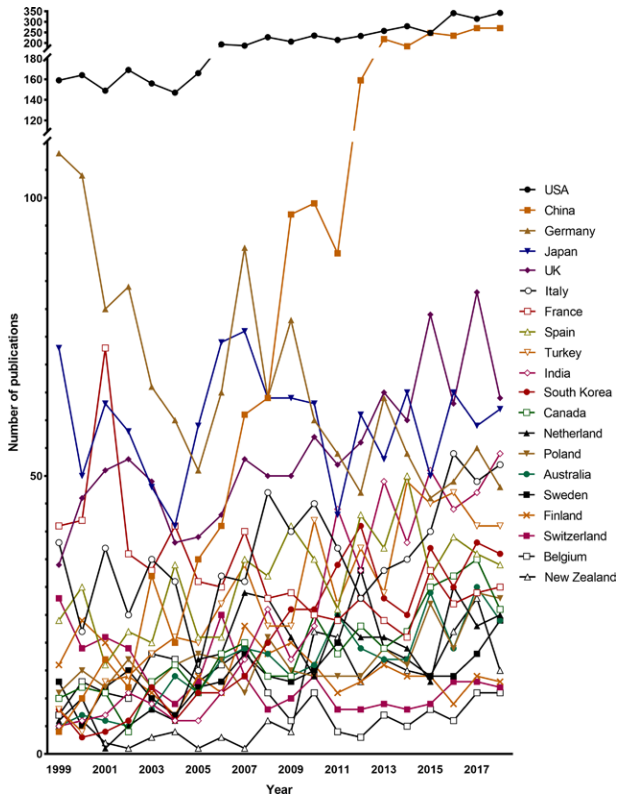

Figure 3. The trends of research output on AP of the top 20 countries over the past 2 decades. The number of publications from most countries has risen steadily ($P < .05$), while the number of papers from Japan, Finland and Belgium changed very little during this time period ($P = .977$, .187, and .059, respectively). In contrast, Germany, France and Switzerland showed a significant downward trend over the past 2 decades ($P < .05$). AP = acute pancreatitis.

3.2. Number of publications per capita

Finland topped the list with 541.8 papers per 10 million population, followed by New Zealand (419.33), Switzerland (320.0 papers), and Sweden (300.0 papers). However, the number of publications from China and India were only 15.6 papers and 3.7 papers per 10 million population, which was far less than that of Finland. In terms of the trend in the number of publications per capita of these 20 countries, most countries had significantly increasing trends ($P < .05$), while Japan and Finland remained nearly unchanged ($P = .988$ and .108, respectively) and 3 countries (Germany, France and Switzerland) dropped significantly ($P < .05$, shown in Fig. 4).

3.3. Papers published in top journals

The top 20 countries published 175 papers in journals with the 10 highest IFs (shown in Table 2). There were only 6 countries published more than 10 papers in theses influential journals. The USA was at the top of the list, with 52 papers published in these influential journals, followed by the UK (28 papers), Canada (13 papers), Germany (12 papers), Italy (12 papers) and Netherland (11 papers). In addition, the USA ranked first in 9 of the 10 highest IF journals, except for *British Medical Journal*, which had published 10 papers from the UK. Regarding the proportion of papers published in these 10 journals to total papers from these top 20 countries, Canada ranked first (3.49%, 13/373), followed by Netherland (3.24%, 11/340), UK (2.58%, 28/1085), Belgium (1.93%, 4/207), and Australia (1.88%, 6/320), while China (0.18%, 4/2170) and South Korea (0.00%, 0/416) were at the bottom of the list.

3.4. Accumulated IF, average IF, total citations and average citations

The USA had the highest accumulated IF (25,432.758) and total citations (104,592), followed by the UK (6598.371, 29,517) and Germany (6580.753, 34,222), which was nearly one fourth of the value for the USA. However, Switzerland had the highest average IF (6.723), followed by Netherland (6.620), Canada (6.242), and the UK (6.081). Meanwhile, Netherland had the highest average citations (51.90), followed by Canada (51.82), Belgium (45.68), and Switzerland (40.10, Table 3). In terms of the trend in the average IFs for these 20 countries, France had an increasing trend ($P < .05$), Spain and South Korea had decreasing trends ($P < .05$), while other countries remained unchanged ($P > .05$, shown in Fig. 5).

3.5. Most popular journals

In the past 2 decades, the most popular journal was *Pancreas* (1.049 papers), which was followed by *American Journal of Gastroenterology* (628 papers) and *World Journal of Gastroenterology* (311 papers). In terms of the proportion of publication in AP research to total publications in these top 10 journals, *Pancreatology* topped the list with 16.4%, followed by *Pancreas* (12.5%) and *World Journal of Gastroenterology* (1.7%, Table 4). American authors preferred to submit to *American Journal of Gastroenterology*, which ranked the first in the USA with 580 papers, followed by *Pancreas* (450 papers) and *Gastroenterology* (138 papers). *World Journal of Gastroenterology* was the favorite journal for Chinese authors, with 202 papers, followed by *Pancreas* (192 papers) and *Journal of Gastroenterology and Hepatology* (94 papers). *Pancreas* was the most popular journal in both Germany (115 papers) and Japan (179 papers). As for the UK, *British Journal of Surgery* topped the list of journals in which the British authors published, with 147 papers, while *Pancreas* ranked second, with 113 papers. From a worldwide perspective, *Pancreas* was the most popular journal in the past 2 decades, with 1393 papers, accounting for 7.9% of the global outputs (shown in Table 5).

3.6. Keywords in AP research

VOSviewer software was used to create the bibliometric co-occurrence map. The minimum number of occurrences was set at 50, and 1742 out of 148,025 terms met this criterion.

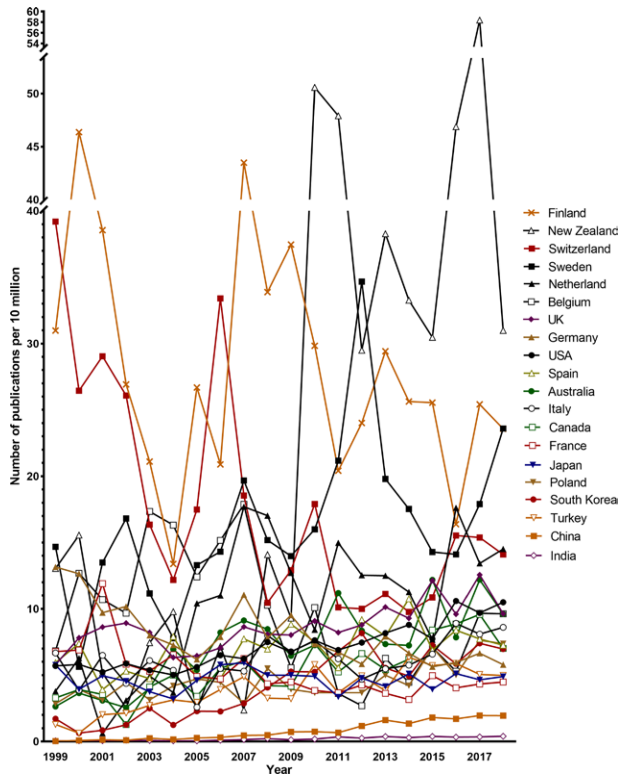

Figure 4. The trends of numbers of publications per 20 million on AP in the top 20 countries over the past 2 decades. Most countries had significantly increasing trends ($P < .05$), while Japan and Finland remained nearly unchanged ($P = .988$ and .108, respectively) and 3 countries (Germany, France and Switzerland) dropped significantly ($P < .05$). AP = acute pancreatitis.

Extraction of the most relevant 60% of terms yielded 1045 terms to analyze. These terms were classified into 4 main clusters shown in 4 colors. According to the terms of the 4 clusters, they were named "clinical research," "animal experiment," "gene research," and "AP-related hyperglycemia study," which contained 580, 429, 18, and 18 terms, and shown in red, green, yellow, and blue, respectively (shown in Fig. 6). In the "clinical research" cluster, the top 5 keywords were: complication (5163 times), year (3407 times), diagnosis (3293 times), risk (2790 times), and management (2391 times). The top 5 keywords in the "animal experiment" cluster were: effect (5022 times), rat (4253 times), pancreas (3989 times), expression (3033 times), and mouse (2683 times). As for the "gene research" cluster, the term gene occurred 1181 times and ranked first, followed by mutation (944 times), polymorphism (530 times), variant (301 times), and family (182 times). In "AP-related hyperglycemia study" cluster, the term diabetes ranked first (862 times), followed by peptide (521 times), GLP (328 times), glucagon (198 times), and exenatide (196 times).

4. Discussion

Bibliometric research is considered as a useful tool for policy-making in public health and scientific research. Research status and highlights will be helpful for reasonable and efficient investments on scientific research. A large amount of funding has been invested into the clinical and basic research of AP, but the current status and social effects of these studies are still unclear. Using bibliometric data from SCIE database in WOS, the trends of global status of AP research of major countries over the past 20 years could be evaluated in quantity and quality, which would be beneficial to promote AP research.

The study results indicated that the USA had an absolute advantage in scientific research on AP, which may be explained by 3 things. First, the USA had the highest gross domestic expenditure on research and development (GERD) at 483.676 billion dollars.[17] This huge amount of funds provides powerful financial support for research on AP. Second, the USA had a larger pool of practitioners in the medical industry than average. In 2015, the number of physicians per 1000 in the USA was 2.586, which was far more than the global average of 1.502.[18] According to the State Physician Workforce Data Report, there were 27.5 students per 100,000 population enrolled in doctor of medicine-granting schools in the 2018 to 2019 academic year, with a 24.7% increase in Doctor of Medicine enrollment compared with that in the 2008 to 2009 academic year.[19] Third, AP-related admissions in the USA showed a significant increasing trend. There were 1070,792 AP-related hospitalizations in 2009 to 2012, which is an 13.2% increase compared with the number in 2002 to 2005.[20] This grim situation prompted the USA government and scientists to expand AP research.

The present study also demonstrated the extraordinary advances in AP research made in China. Over the past 2 decades, the annual number of AP-related publications from China increased by more than 65 times, and the total IF increased by more than 80 times. One possible explanation is the increase in China's GERD. In 2017, the GERD was over 444.755 billion dollars, which was almost 3 times that in 2008 (148.821 billion dollars).[17] The dominate funder was the National Natural Science Foundation of China. The Medical Science Department of the National Natural Science Foundation of China was established in 2010. Over the past 10 years, funding for medical science has increased more than 2.5 times, from 994.96 million Ren Min Bi in 2010 to 2.52 billion Ren Min Bi in 2018, and keep increasing steadily.[21] Additionally, China's physicians and scientists can recruit more participants for their research because of the large Chinese population and the increasing prevalence of AP.[22] Despite this remarkable progress, the average IF and the number of publications per 10 million population still lagged far behind the values for developed countries. This result was consistent with other studies of medical disciplines.[23–25] This imbalance between the quantity and quality of publications can probably be attributed to the current academic evaluation system, which puts too much emphasis on the number of papers, forcing scientists and physicians to blindly pursue quantity and ignore the quality of publications.[26] To improve this situation, the Ministry of Science and Technology of China has recently introduced relevant measures to encourage high-quality scientific publications.[27]

According to our study, AP research in Europe is relatively complicated. As the major European countries, France had an increasing trend in AP research both quantity and quality, the UK and Italy had increasing trends only in quantity but kept stable in quality, while Germany had a decreasing trend in quantity but remained unchanged in quality. In general, AP research in Europe is still at the top-level which may be the result of high-level investigation and development in medical education.[28,29] Since the Association for Medical Education in Europe was established in 1972, there were many programs initiated by Association for Medical Education in Europe, such as the ASPIRE-to-Excellence Initiative which was established to provide a unique system to encourage excellence in medical education and the healthcare professions by identifying, recognizing and rewarding excellence in key aspects of education delivery. In addition to this kind of multi-national medical training research program, each European country has its own medical education program according to its own actual situation. For instance, medical education in France is made up of 3 cycle with a minimum of 9 years, and there were less than 20% students pass the exam at the end of the first year. This kind of strict training of medical students may contribute to the high-level development

Table 2

The number of publications regarding acute pancreatitis in 10 highest impact factors (IF) journals.

	Journal (2018 IF)										
Country	*NEJM* (70.670)	*Lancet*(59.102)	*JAMA*(51.373)	*Cell*(36.216)	*LO*(35.386)	*NRDP*(32.274)	*NM*(30.641)	*JCO* (28.245)	*BMJ*(27.604)	*NG*(24.455)	Total
USA	19	7	5	1	5	1	1	7	5	1	52
UK	4	7	0	0	4	1	1	0	10	1	28
Canada	4	3	0	0	1	0	1	1	3	0	13
Germany	2	6	0	0	2	1	0	0	0	1	12
Italy	4	4	0	0	2	1	0	0	1	0	12
Netherland	3	3	1	0	2	1	0	0	1	0	11
France	3	1	0	0	1	0	1	0	1	0	7
Australia	2	1	1	0	1	0	0	0	1	0	6
Switzerland	0	5	0	0	0	0	0	0	0	0	5
China	2	0	0	1	0	0	0	0	1	0	4
Spain	1	2	0	0	0	0	0	1	0	0	4
Belgium	1	0	1	0	2	0	0	0	0	0	4
Japan	1	0	0	0	2	0	0	0	0	0	3
India	2	0	1	0	0	0	0	0	0	0	3
Poland	1	0	0	0	1	0	0	0	1	0	3
Sweden	1	0	1	0	0	0	0	0	1	0	3
Finland	0	2	0	0	1	0	0	0	0	0	3
Turkey	0	1	0	0	0	0	0	0	0	0	1
New Zealand	0	1	0	0	0	0	0	0	0	0	1
South Korea	0	0	0	0	0	0	0	0	0	0	0
Total	50	43	10	2	24	5	4	9	25	3	175

BMJ = British medical journal, IF = impact factor, JAMA = journal of the American medical association, JCO = journal of clinical oncology, LO = lancet oncology, NEJM = New England journal of medicine, NG = nature genetics, NM = nature medicine, NRDP = nature reviews disease primers.

Table 3

The accumulated IF and average IF of 20 top-ranking countries.

Country	Average IF	Accumulated IF	Total articles	Total citation	Average citation
Switzerland	6.723	1828.660	272	10,909	40.11
Netherland	6.620	2250.929	340	17,647	51.90
Canada	6.242	2328.359	373	19,330	51.82
UK	6.081	6598.371	1085	37,636	34.69
Belgium	5.937	1228.910	207	9456	45.68
USA	5.783	25,432.758	4398	121,853	27.71
Finland	4.973	1481.970	298	6145	20.62
Germany	4.955	6580.753	1328	39,209	29.52
Italy	4.805	3488.499	726	24,231	33.38
Australia	4.614	1476.587	320	10,558	32.99
Sweden	4.512	1380.570	306	9787	31.98
New Zealand	4.260	864.752	203	6839	33.69
Spain	3.951	2480.992	628	13,809	21.99
India	3.816	1923.047	504	9199	18.25
Japan	3.726	4437.476	1191	22,081	18.54
France	3.627	2411.680	665	19,314	29.04
South Korea	3.337	1388.263	416	6932	16.66
Poland	3.100	1069.524	345	8427	24.43
China	2.899	6291.686	2170	28,393	13.08
Turkey	2.109	1187.466	563	5700	10.12

IF: impact factor.

of medical education and research in France. Besides, according to guidance published by the Medical School Council and General Medical Council in 2016, a doctor in the UK must have not only a high standard of knowledge, skills, and performance, but also an academic character, which may benefit the quality of academic research.[30] In addition, the UK medical education database includes data on the performance of UK medical students and trainee doctors across their undergraduate and postgraduate education and professional career, which could present unique opportunities for multicenter longitudinal studies on medical education and provide timely feedback on the UK medical policy implementation.[31,32]

Interestingly, Netherland ranked 14th in the total number of publications, 6th in the number of papers published in the 10 highest IF journals, 2nd in the average IF, and 1st in average citation. With a population only a quarter the size of the UK and France, Netherland made significant achievement in AP research in the past 2 decades. This may be attributed to the key role played by the Dutch Pancreatitis Study Group in AP clinical research. Up to now, there are many research programs established by Dutch Pancreatitis Study Group, such as POEMA trial in AP, POLAR trial in pancreatic duct disconnection, PONCHO trial in biliary pancreatitis, PWN-CORE trial in genetic research in AP, and FLUYT trial in post-ERCP pancreatitis, etc.[33] Among these, PONCHO

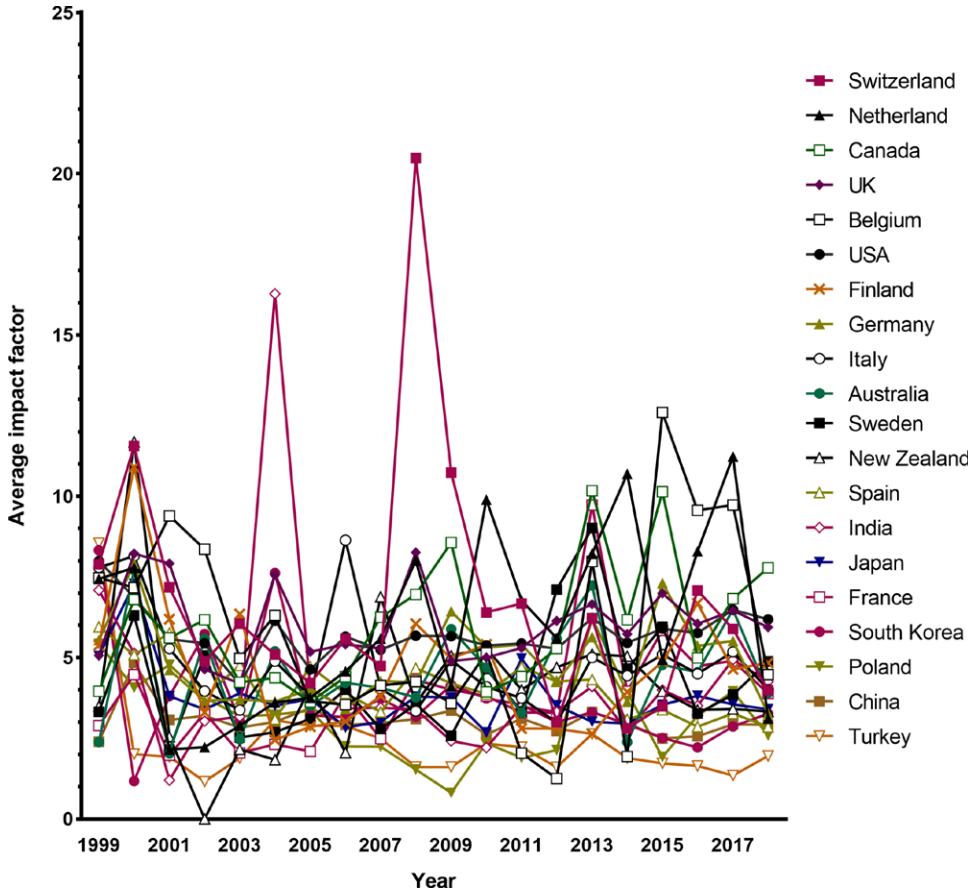

Figure 5. The trends of average impact factor of top 20 countries over the past 2 decades. France had an increasing trend ($P < .05$), Spain and South Korea had decreasing trends ($P < .05$), while other countries remained unchanged ($P > .05$).

Table 4

Top 10 journals related to acute pancreatitis at global level during 1999 to 2018.

Rank	Journal	2018 IF	Number of publications in AP (%)	Total number of publications
1st	*Pancreas*	2.675	1049 (12.5)	8413
2nd	*American Journal of Gastroenterology*	10.241	628 (1.6)	39,892
3rd	*World Journal of Gastroenterology*	3.411	311 (1.7)	18,344
4th	*Pancreatology*	3.241	291 (16.4)	1777
5th	*Gastroenterology*	19.233	264 (0.3)	98,546
6th	*Gastrointestinal Endoscopy*	7.229	176 (0.6)	28,556
7th	*British Journal of Surgery*	5.586	170 (0.8)	21,562
8th	*Journal of Gastroenterology and Hepatology*	3.632	163 (0.7)	24,254
9th	*Gut*	17.943	146 (0.7)	20,740
10th	*Digestive Diseases and Sciences*	2.937	127 (1.4)	9374

IF: impact factor.

trial showed that early laparoscopic cholecystectomy could reduce the combined endpoint of mortality and re-admissions for biliary events.[34] The clinical data from these high-quality multi-center clinical trials provided sufficient scientific evidence to further research and kept the Netherland at the top-ranking in AP research.

With keywords co-occurrence map, we discovered the directions and popular topics in AP research over the past 2 decades. Regarding clinical research, global physicians concentrated on hospitalization management, complications, and patient characteristics. Through animal experiments, researchers studied aspects of the etiology and pathogenesis of AP, such as oxidative stress and cytokines. In the term "gene research," "gene" topped the list, followed by "mutation," along with several other major related terms, such as "family," "arp," "child," and "polymorphism." This result demonstrated that scientists were aware that gene mutations may play a key role in acute recurrent pancreatitis and pediatric AP.[35] In a recent study, researchers found that the progression from AP to chronic pancreatitis was faster in patients with certain variants of the cystic fibrosis transmembrane conductance regulator gene, serine protease inhibitor Kazal type 1 gene, or the p.R122H mutation in the cationic trypsinogen gene. Meanwhile, serine protease inhibitor Kazal type 1 mutation was shown to be significantly associated with faster progression to acute recurrent pancreatitis.[36] As for "AP-related hyperglycemia study," "diabetes" was the most common term, and the other major related terms were "risk," "trial," "effect," "inhibitor," and "glp," which indicate that hyperglycemia maybe not only an essential adaptive response to

Table 5

The most popular journals of 5 highest-output countries.

USA		China		Germany		Japan		the UK	
Journal	**Number**	**Journal**	**Number**	**Journal**	**Number**	**Journal**	**Number**	**Journal**	**Number**
AJG	580	*WJG*	202	*Pancreas*	115	*Pancreas*	179	*BJS*	147
Pancreas	450	*Pancreas*	192	*Pancreatology*	68	*JG*	68	*Pancreas*	113
Gastroenterology	138	*JGH*	94	*Gastroenterology*	67	*HG*	43	*Gut*	56
GIE	137	*Pancreatology*	51	*ZFG*	47	*JGH*	41	*Pancreatology*	36
Pancreatology	107	*Plos One*	49	*Gut*	36	*IM*	33	*ARCSE*	32
AJPGLP	69	*CMJ*	46	*DMW*	26	*Gastroenterology*	32	*Gastroenterology*	22
JGS	65	*MMR*	44	*LAS*	24	*JHBPS*	32	*WJG*	16
CGH	62	*IJCEM*	39	*Internist*	23	*Pancreatology*	29	*CDSR*	15
COG	59	*HBPDI*	38	*Chirurg*	22	*WJG*	28	*ICM*	13
DDS	58	*Medicine*	37	*CG*	21	*DE*	24	*CC*	10

AJG = American Journal of Gastroenterology, IF = 10.241; Pancreas, IF = 2.675; Gastroenterology, IF = 19.233; GIE = gastrointestinal endoscopy, IF = 7.229; Pancreatology, IF = 3.241; AJPGLP = American Journal of Physiology Gastrointestinal and Liver Physiology, IF = 3.729; JGS = Journal of Gastrointestinal Surgery, IF = 2.686; CGH = Clinical Gastroenterology and Hepatology, IF = 7.958; COG = Current Opinion in Gastroenterology, IF = 2.741; DDS = Digestive Diseases and Sciences, IF = 2.937; WJG = World Journal of Gastroenterology, IF = 3.411; JGH = Journal of Gastroenterology and Hepatology, IF = 3.632; Plos One, IF = 2.776; CMJ = Chinese Medical Journal, IF = 1.555; MMR = Molecular Medicine Reports, IF = 1.851; IJCEM = International Journal of Clinical and Experimental Medicine, IF = 0.181; HBPD = Hepato-Biliary Pancreatic Diseases International, IF = 1.576; Medicine: IF = 1.87; ZFG = Zeitschirift Fur Gastroenterologie, IF = 1.236; Gut, IF = 17.943; DMW = Deutsche Medidizinische Wochenschrift, IF = 0.635; LAS = Langenbecks Archives of Surgery, IF = 2.039; Internist, IF = 0.427; Chirurg, IF = 0.669; CG = Chirurgische Gastroenterologie, IF = 0.048 (JCR report 2010); JG = Journal of Gastroenterology, IF = 5.13; HG = Hepato Gastroenterology, IF = 0.792 (JCR report 2015); IM = Internal Medicine, IF = 0.956; JHPS = Journal of Hepato-Biliary-Pancreatic Sciences, IF = 2.353; DE = Digestive Endoscopy, IF = 3.64; BJS = British Journal of Surgery, IF = 5.586; ARCSE = Annals of the Royal College of Surgeons of England, IF = 1.259; CDSR = Cochrane Database Systematic Reviews, IF = 7.755; ICM = Intensive Care Medicine, IF = 18.967; CC = Critical Care, IF = 6.959.

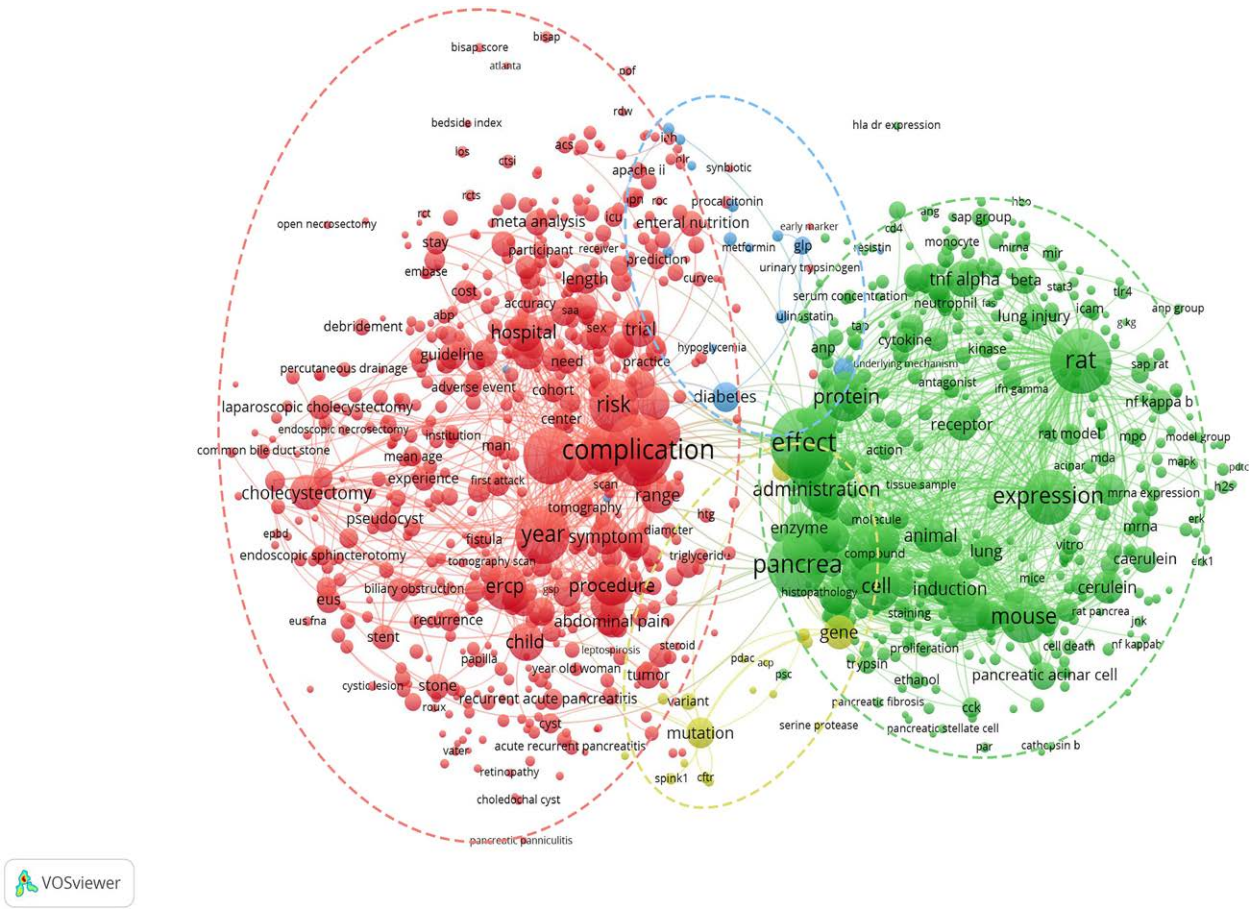

Figure 6. The co-occurrence map about keywords of AP research between 1999 and 2018. AP = acute pancreatitis.

acute illness but also a complication of AP.[37,38] A recent study of glucose counter-regulatory hormones demonstrated that glucagon and cortisol may be related to the mechanisms underlying hyperglycemia after AP.[39]

There are some limitations to our study. First, China's output was retrieved using the "People's Republic of China" in "Countries/Regions" category of WOS and output from Taiwan were not included. Second, because of the classification rule of the WOS database, a single paper from an international collaboration would be attributed to more than 1 country, thus some papers were counted repeatedly. Third, publications from non-WOS journals were not retrieved, which may have caused bias in this study.

In conclusion, our analysis of the global output of AP research showed signs of growth. Research output was positively correlated with the GDP of each country. For the most productive countries, research quality was stable. Although developing countries lagged behind in output per capita and quality, great progress was made over the past 2 decades.

Author contributions

Chao Han, Huai-Yu Yang, and Zhi-Qi Dong participated in the acquisition, analysis, and interpretation of data, as well as in the manuscript drafting; Yu Liu and Yan-Wei Lv participated in data acquisition and manuscript drafting; Dan Wang, Liang-Hao Hu and Zhao-Shen Li contributed to the conception, design, and data interpretation.

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All data included in this study can be accessed publicly. All authors have no conflicts of interest to disclose.

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