Original Article

Landscape of surgery in Crohn's disease across twenty years: insights from machine learning

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Background: Crohn's disease continues to be a major component of inflammatory bowel disease with increasing incidence and prevalence. Increasing publications of surgery in Crohn's disease have significantly expanded the research scope. The aim of this study is to characterize main topics and a full landscape of surgery in Crohn's disease.

Methods: Studies of surgery in Crohn's disease from 2000 to 2020 were screened and retrieved from the Web of Science Core Collection database. Latent Dirichlet allocation (LDA), one of machine-learning algorithms for natural language processing, was employed for topic modeling. All the studies were processed, analyzed and visualized by R software, CiteSpace and Gephi.

Results: A total of 3,697 original publications were identified from the database. USA was the leading country with the most top institutions such as Cleveland Clin Florida and Mayo Clinic and Mayo Foundation. Increasing impact of institutions from Korea and China was also noticed. Bo Shen was the leading author in publication. A machine learning based topic modeling identified major clusters, including disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence. Three topics attracted continuous high research attention, including expression of intestinal cell, perianal fistula and laparoscopic and open operation.

Conclusions: This study identified key topics relating to the development of surgery in Crohn's disease, and provided bibliometric insights and perspectives for future development in the field of surgery in Crohn's disease.

Keywords: Crohn's disease; bibliometric analysis; surgery; Web of Science (WOS)

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Introduction

Crohn's disease is characterized by chronic transmural granulomatous inflammation across the gut, especially enriched in the ileum and/or colon, and considered to be one of the main components of inflammatory bowel disease (1-3). Both incidence and prevalence of Crohn's disease are rising regardless of ethnics or race, and relevant study intension is rising as well over the years. Countries and regions such as northern Europe, United Kingdom and North America have shown a marked incidence (6–15/100,000) and prevalence (50–200/100,000) over the last fifty years (3,4). By estimation, 23.8 to 29.3 per 100,000 people suffered in Crohn's disease in North America and

Europe with over 40-fold increment in Korea over the last three decades (5,6).

Patients with Crohn's disease frequently complain fever, abdominal pain and clinical manifestations of bowel obstruction or diarrhea (3). Surgery intervention is essential to the course of Crohn's disease for around 70% patients and remains a mainstay of therapy for a considerable long period due to the unchanged general lifetime risk (7-9). Based on population-based studies, a previous meta-analysis reports that 1-, 5- and 10-year of surgery risk for Crohn's disease are 16.3%, 33.3% and 46.6%, respectively (10). Introduction of anti-tumor necrosis factor alpha (anti-TNF-alpha) enables the treatment course of Crohn's disease to be standardized since 1990s (11-13). However, increasingly utilization of anti-TNF-alpha and emerging immunosuppressants may not fully guarantee the overall therapeutic benefit. Whether surgery dependence is alleviated by these drugs remains debatable (11). Lifestyle and daily activities are impacted by the impediments during remissions and flares. The occurrences of progressive strictures or fistulas make surgical therapy necessary. In fact, among pediatric patients with Crohn's disease in progressive condition, early surgery remains unavoidable as most surgery take places within three years since diagnosis (14). A long-term follow-up of Australian patients with Crohn's disease reports that there is no reduction is in emergency surgery rate but an increase in surgical recurrence rate (15). Nonetheless, a nationwide cohort study in Dutch reported that the annual intestinal resection rate decreased from 22.7/100,000 to 2.5/100,000 over decades (16,17).

In fact, Crohn's disease researches have accelerated in the decade as more attention has been drawn to the surgical therapy of Crohn's disease and as minimally invasive surgery achieved prominent techniques support. Numerous groups, such as the Crohn's & Colitis Foundation across the globe and National Association for Colitis & Crohn's Disease, have made efforts to share coalesce consensus and expert opinion to research disputations. Outside of those consensus efforts and mounting publications of surgery of Crohn's disease, a detailed analysis of the publications for identification of prioritized research areas and future research trends has not been undertaken. A whole picture of the entire publication body analysis remains unseen. Such analysis offers insights on developmental clues and identify hotspots in surgery of Crohn's disease and serves as a landscape characterization of the field, highlight where the publications enrich, where specific opportunities exist and where the current researches are intensively increasing. This work can be a baseline to measure future growth and research developmental trajectory. Beyond looking at the publication rising, this study is the first to leverage a machine learning-based topic modeling algorithm, latent Dirichlet allocation (LDA), to provide more descriptive and detailed perspectives for discrete research topics through large amounts of unstructured text input, instead of traditional search patterns.

This study performed a bibliometric analysis using publications retrieved from Web of Science (WOS) and provided a detailed description of countries, authors, journals, studies on the publications in this field. The findings provide insights of research and future perspectives and augment recent consensus efforts and facilitate researchers' inquiries and research needs to alignment. Moreover, these results may also be of benefits to funding agencies as to guide potential greatest research hotspots.

Highlight box

Key findings

- Finding I: this study highlighted the most influential countries, institutions, authors and leading journals associated with the field.
- Finding II: a machine learning based algorithm, latent Dirichlet allocation, was used for topic modeling. Disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence were the main primary clusters from the topic modeling network analysis.

What is known and what is new?

- Increasing publications of surgery for Crohn's disease have significantly expanded the research scope, however with main topics yet to be determined.
- This study provided novel insights on the development of this field using machine learning model.

What is the implication, and what should change now?

- This study highlights several key topics with rising intension, serving to be potential hot spots and research implications. Nonetheless, there are also several directions that may also be less valuable for future, therefore, should be changed now.

Methods

All the studies of surgery in Crohn's disease were searched by the terms: TOPIC (Crohn's disease) AND TOPIC (Surgery) AND Document Type (Article) AND Language (English) AND Year Published (2000–2020) in the WOS Core Collection database ((https://clarivate.

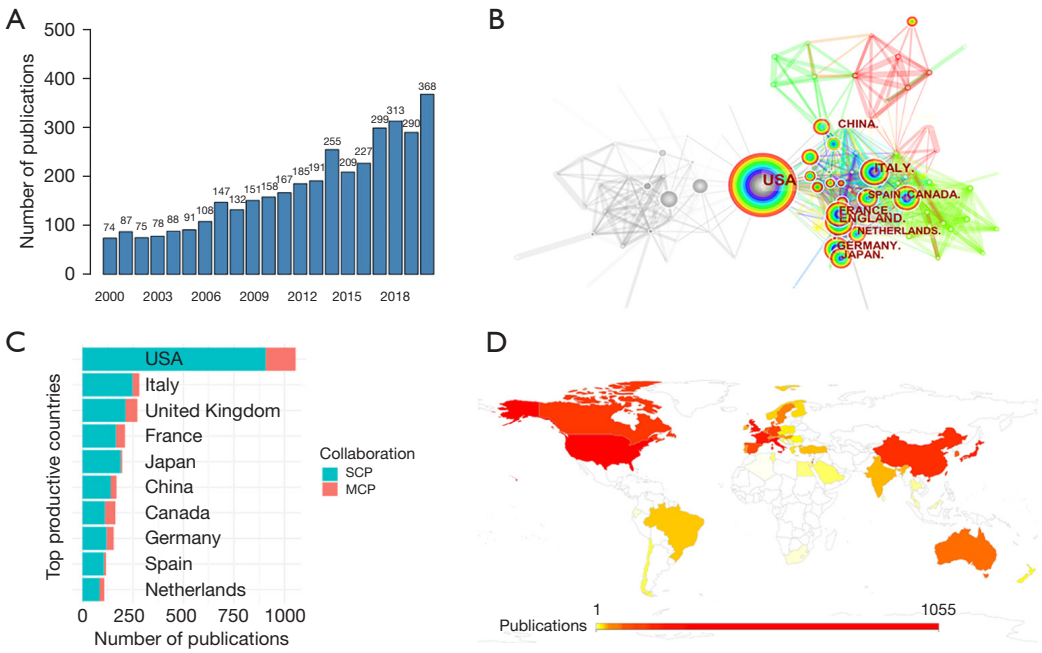

Figure 1 Number of annual publications and most productive ten counties. (A) Number of publications relating to surgery in Crohn's disease (CD) from 2000 to 2020; (B) network demonstration of co-authors' countries, with top ten most-counted countries displayed: USA, Italy, England, France, Canada, China, Japan, Germany, Spain and Netherlands; (C) most ten productive countries with publications categorized as single country publications (SCP) in green and multiple country publications (MCP) in red from 2000 to 2020; (D) countries with contribution in color (red: high publications, yellow: low publications) displayed in world map.

com/webofsciencegroup/solutions/web-of-science-core-collection/) (18,19). The inclusion criteria were as follows: (I) publications with keywords relating to Crohn's disease and surgery; (II) studies with type of "article"; (III) studies published in English; (IV) studies were published between 2000 and 2020. All types of surgery were included in this study. CiteSpace, a scientific literature Java software, was used for visualization and patterns analysis (20). It was designed to facilitate progressive publications visualization and network interpretation as well as citation hotspots. R software (version 4.1.1) was used for data processing and results visualization (bibliometrix package) (https://www.r-project.org/) (21,22). Sankey diagram is also named as three fields plot, to reflect weighted nodes connecting to other items. Sankey diagram is commonly used to assess the association among authors, their keywords and enriched journals. Bradford's law was employed for publication source distribution analysis (23). The core sources illustrated by Bradford's law were defined as the journals with comparably high productivity. In Bradford's law, all journals were arranged in a descending order, with the top one third journals being selected as core sources. Authors keywords are defined by WOS as the keywords written by the authors to be included in articles. Keywords plus are index terms derived from the titles of each article, helping to enrich the characterizations in terms of keywords analysis. LDA, one of the prevailing used text-mining machine learning algorithms were employed in this study. It simplified massive text data into topic modeling, enabling a rapid understanding of the research progress. The network visualization was performed by Gephi software (version 0.9.5).

Results

A total of 3,697 original publications were identified from WOS database, with steady increment for the past twenty years (*Figure 1A-1D*). Network and global map of all countries were demonstrated (*Figure 1B,1D*). USA was the leading country with not only most single country publications (SCP) but also multiple country publications (MCP) in surgery research of Crohn's disease, followed by Italy, United Kingdom, France, Japan, China, Canada, Germany, Spain and Netherlands (*Figure 1C*).

Next, to further characterize those institutions with most

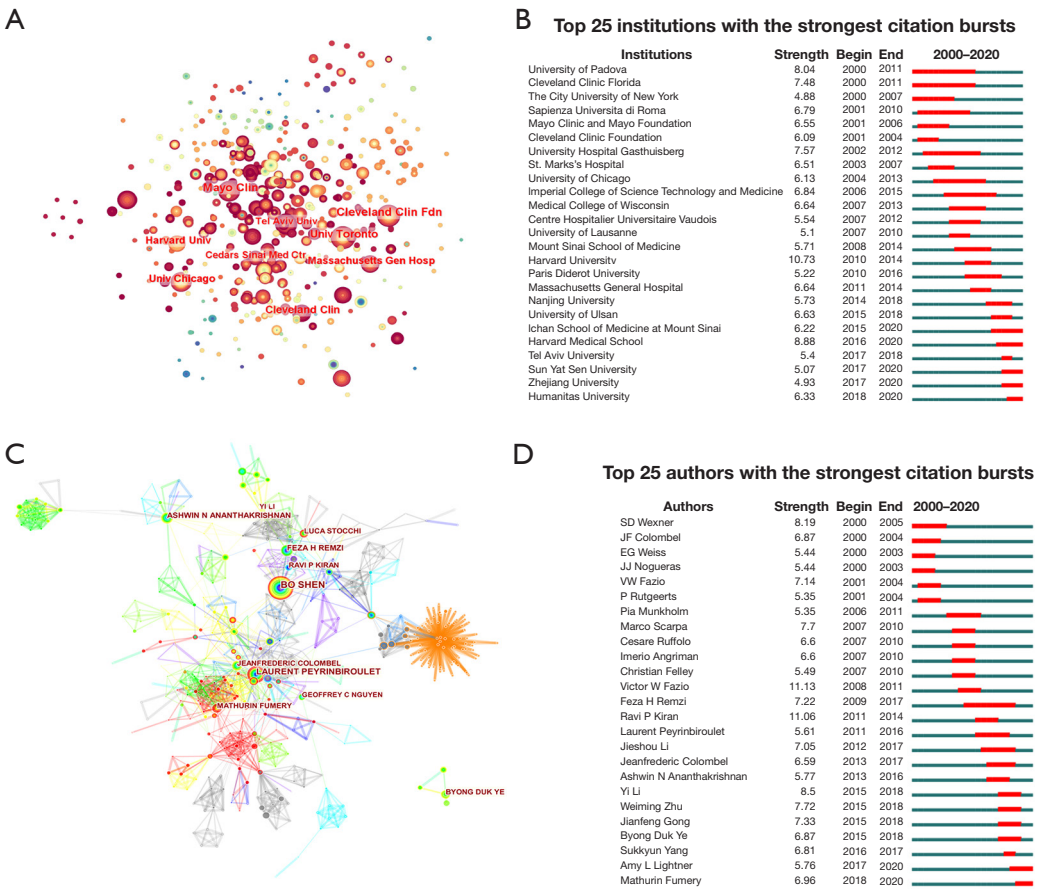

Figure 2 Contributing global institutions and contributing authors in network with citation burst analysis. (A) Network demonstration of co-authors' institutions, with top most-counted displayed: Cleveland Clinic Foundation, Mayo Clinic and Mayo Foundation, Cleveland Clinic Florida, University of Chicago, Massachusetts General Hospital, Harvard University and others; (B) top twenty-five institutions with the strongest citation bursts; (C) network demonstration of co-authors, with top ten most-counted displayed: Bo Shen, Laurent Peyrinbiroulet, Feza H Remzi, Ashwin N Ananthakrishnan, Byong Duk Ye, Ravi P Kiran, Mathurin Fumery, Luca Stocchi, Jeanfrederic Colombel, Yi Li and Geoffrey C Nguyen (equal count to Yi Li); (D) top twenty-five authors with the strongest citation bursts red bar indicated frequent occurrence of citation and green bar indicated common citation; red bar indicated frequent occurrence of citation and green bar indicated common citation.

publications, network and strongest citation bursts were analyzed (*Figure 2A*,*2B*). Top most-counted institutions were Cleveland Clinic Foundation, Mayo Clinic and Mayo Foundation, University of Chicago, Massachusetts General Hospital, Harvard University and others. In citation bursts analysis, Harvard University (strength =10.73) was the top institution among the ranking list (*Figure 2B*). University Padua, Cleveland Clinic Florida and University Hospital Gasthuisberg were the top institutions with ten years of citation bursts. Increasing impact of institutions from East Asia was also noticed during the last few years, including Nanjing University, University Ulsan, Sun Yat Sen University and Zhejiang University (*Figure 2B*).

Specific authors contributing to surgery in Crohn's disease were also identified. Top ten most-counted in the network were Bo Shen, Laurent Peyrinbiroulet, Feza H Remzi, Ashwin N Ananthakrishnan, Byong Duk Ye, Ravi P Kiran, Mathurin Fumery, Luca Stocchi, Jeanfrederic Colombel, Yi Li and Geoffrey C Nguyen (*Figure 2C*). Victor W Fazio was the top author with the strongest citation bursts, while Feza H Remzi showed the longest citation bursts. Of note, during the last ten years, more authors with strong citation bursts were from East Asia, including Jieshou Li, Yi Li and others (*Figure 2D*).

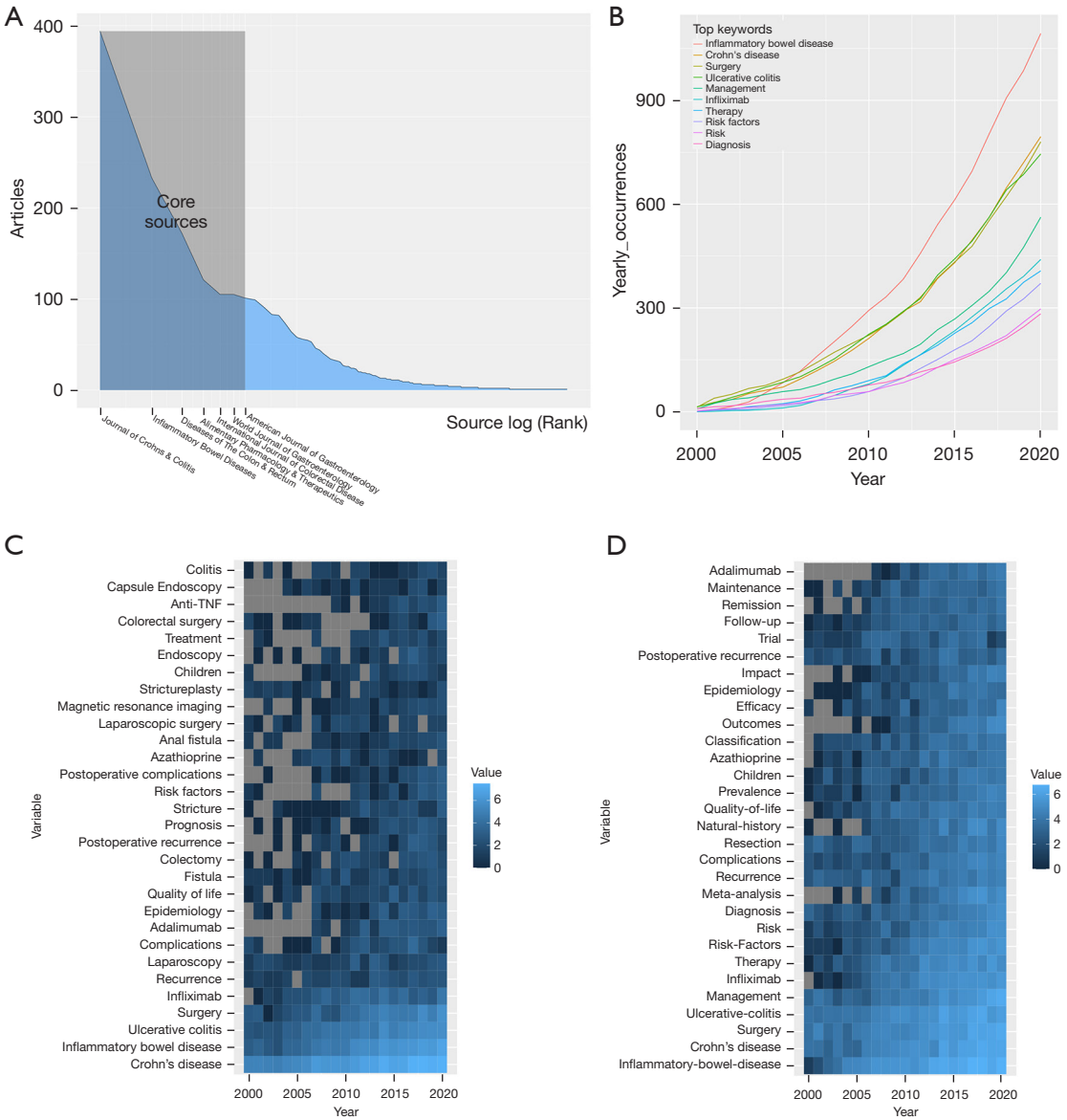

Figure 3 Publication distribution and yearly occurrence of keywords. (A) The Bradford's law source distribution of publications and journals in surgery research relating to Crohn's disease; the core sources were marked in grey area, with seven journals identified, including *Inflammatory Bowel Diseases*, *Journal of Crohns & Colitis*, *Diseases of The Colon & Rectum*, *Alimentary Pharmacology & Therapeutics*, *International Journal of Colorectal Disease*, *World Journal of Gastroenterology*, *American Journal of Gastroenterology*; (B) top ten keywords were counted annually, including inflammatory bowel disease, Crohn's disease, surgery, ulcerative colitis, management, infliximab, therapy, risk factors, risk and diagnosis; (C) yearly occurrence of top thirty author keywords; (D) yearly occurrence of top thirty keywords plus associated with Web of Science (WOS) database; light blue indicated high occurrence, dark blue indicated low occurrence, grey indicated zero occurrence; the value was log2 transformed for visualization.

To further characterize the contributing journals in surgery of Crohn's disease, a total of top fifty cited journals were demonstrated (Figure S1). Notably, *Journal of Crohns & Colitis* (strength =96.6), *American Journal of Surgery* (strength =36.12) and *Surg Endosc-Ultras* (strength =30.22) were the top three journals with strongest citation bursts. In addition, based on Bradford's law, a source distribution of journals' publications was displayed (*Figure 3A*).

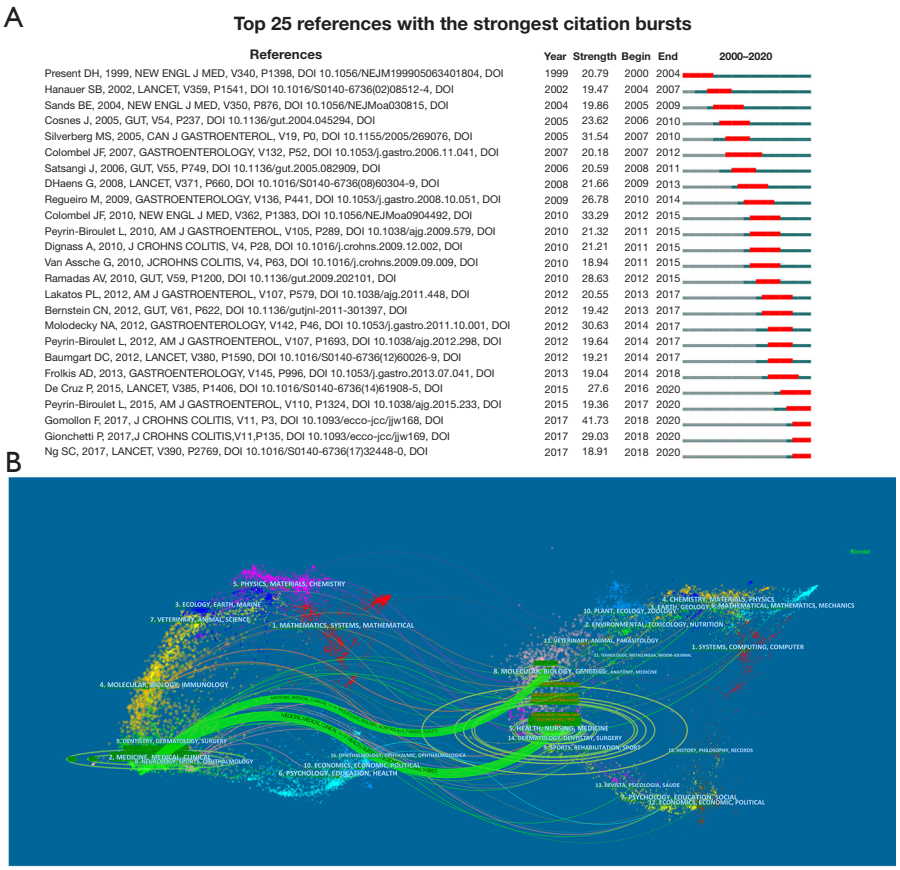

Figure 4 Top cited references and publication analysis. (A) Top twenty-five references with the strongest citation bursts from 2000 to 2020. Red bar indicated frequent citation occurrence; (B) publication portfolios analysis by a dual-map thematic overlays in the field of surgery in Crohn's disease.

Seven journals were among the core sources, including *Inflammatory Bowel Disease*, *Journal of Crohns & Colitis*, *Diseases of the Colon & Rectum*, *Alimentary Pharmacology & Therapeutics*, *International Journal of Colorectal Disease*, *World Journal of Gastroenterology* and *American Journal of Gastroenterology*.

To further characterize annual alteration of keywords, yearly occurrence of top ten keywords (keywords plus) was displayed, including "inflammatory bowel disease", "Crohn's disease", "surgery", "ulcerative colitis", "management", "infliximab", "therapy", "risk factors", "risk" and "diagnosis" (*Figure 3B*). Given two types of keywords, including author keywords and keywords plus, were essential for characterization, dynamic alterations of keywords were visualized in heatmap (*Figure 3C,3D*). In author keywords, Infliximab, recurrence, laparoscopy, complications, adalimumab, epidemiology, quality of life, fistula, colectomy and postoperative recurrence were top ten frequently occurred keywords besides Crohn's disease, inflammatory bowel disease and surgery (*Figure 3C*). In keywords plus, management, infliximab, therapy, risk factors, risk, diagnosis, meta-analysis, recurrence, complications, resections were the top ten frequently occurred keywords besides Crohn's disease, inflammatory bowel disease and surgery (*Figure 3D*). Meanwhile, associations between top twenty authors, keywords and journals were also illustrated by Sankey diagram (Figure S2).

Top twenty-five references with the strongest citation bursts were identified (*Figure 4A*). Gomollon F, 2017 published in *Journal of Crohns & Colitis* was the top reference (strength =41.73). Most of the references showed a strong citation bursts less than five years. *Lancet* contributed five out of twenty-five references whereas *Journal of Crohns & Colitis*, *Gastroenterology*, *Gut* and *American Journal of*

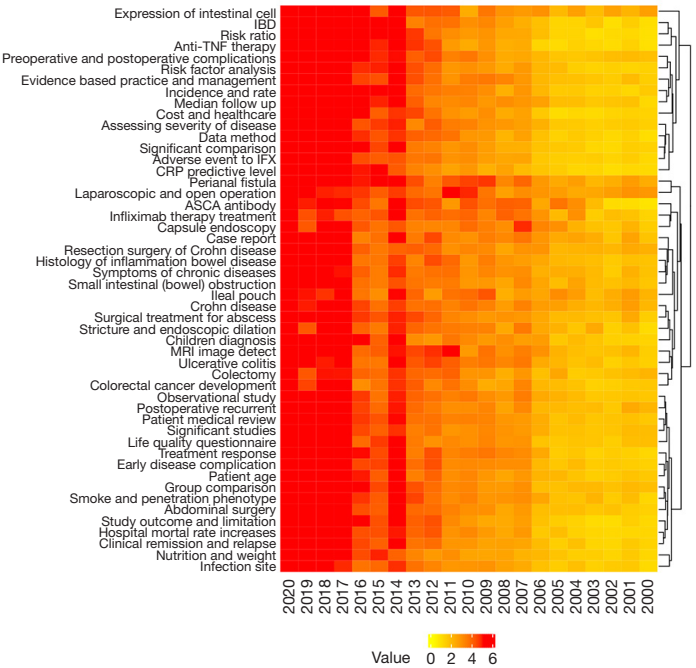

Figure 5 Increased publications relevant to fifty topics identified by latent Dirichlet allocation (LDA) associated with surgery in Crohn's disease were demonstrated.

Gastroenterology contributed four references, respectively (*Figure 4A*).

A dual-map thematic overlays was to address the feature of publication portfolios relating to surgery in Crohn's disease. The two main connections were found between subject of medicine, medical, clinical and subject of health, nursing, medicine areas, and between subject of medicine, medical, clinical and subject of molecular, biology, genetics (*Figure 4B*).

A total of fifty most significant topics associated with surgery in Crohn's disease were identified by LDA. In fact, most of the topics showed remarkable attention over the years (*Figure 5*). Specifically, three topics attracted continuous high research attention, including expression of intestinal cell, perianal fistula and laparoscopic and open operation. Three stages of developments were also identified, 2000–2006, 2007–2016, 2017–2020. Comparing to 2000–2006, most of research topics were rising since 2007. Nonetheless, the most significant increment was found since 2017 (*Figure 5*). Topics network was also established, with five primary clusters identified, including disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence (*Figure 6*).

Discussion

This study showed notable escalation of publications in surgery of Crohn's disease. A whole picture of field development in this area is characterized. With the publications and extracted unconstructed text and machine learning algorithms, this study not only reported the top countries, authors, journals and institutions, but also rising research topics and future areas, including disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence, therefore enabling researchers to better align their directions.

Among all the studies, USA published 1,184 original studies, covering both SCP and MCP, and that is almost equal to publication sums of next five countries, Italy, England, France, Canada and China. Top eight out of ten institutions in this field are from USA. Given the fact that increasing incidence and prevalence of Crohn's disease are rising in China, the publications are markedly increasing (24-27). Recently, institutions from China and Chinese authors are gaining strongest citation bursts in the field of surgery in Crohn's disease (28,29).

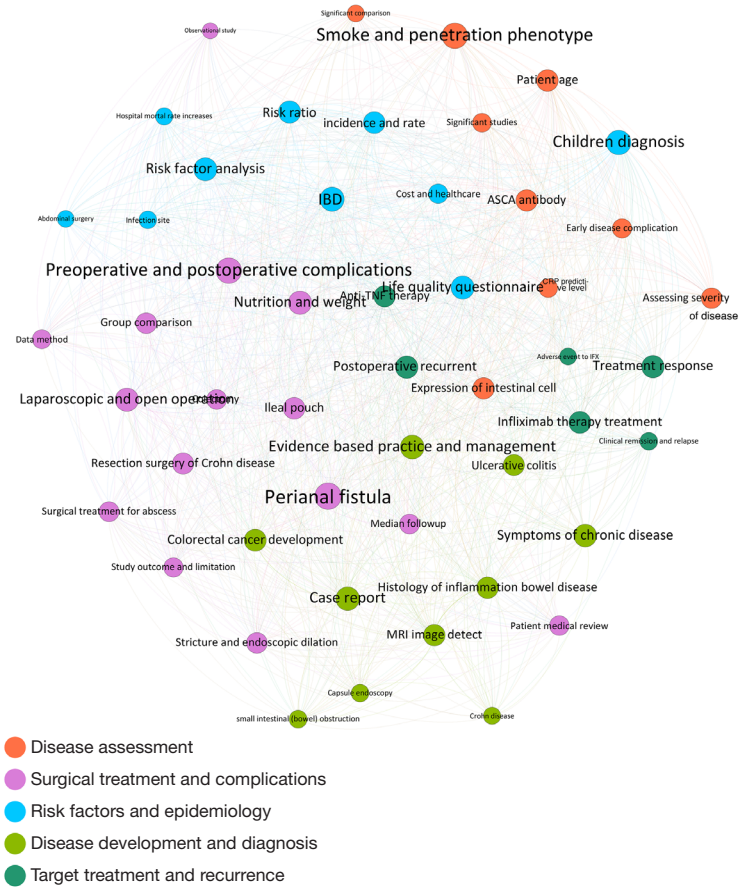

Figure 6 Network analysis of the fifty topics. Five primary clusters were identified among the fifty topics, including disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence.

LDA remains one of the prevailing text mining algorithms with advanced modeling performance. In this study, fifty topics were determined by LDA with high level of consistency to the trajectory of keywords. There are five primary clusters identified, including disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence. In fact, surgical treatment and complications serves as the leading cluster, covering surgical types, surgery limitations, surgery for abscess, stricture and endoscopic dilation, study follow-up and nutrition. Machine learning based modeling analysis in deed provides an advanced method for mining hidden connections among the development of such field. Another primary cluster, target treatment and recurrence, was also listed as well. It covered several aspects, such as anti-TNF therapy, infliximab therapy treatment, clinical remission and relapse. Reasonably to presume, the role of surgery in this field is closely associated with the targeted drugs, as combinational study could be more attractive in clinical practice.

Noticeably, *Journal of Crohns & Coltis* is not only the top one in strongest citation bursts, but also among the core source distribution based on Bradford's law. Meanwhile, it also contributes to four out of twenty-five strongest cited references, including Gionchetti P. 2017 (30), Gomollon F. 2017 (31), Van Assche G. 2010 (32) and Dignass A. 2010 (33). In fact, twenty-one out of twenty-five references relating to surgery in Crohn's disease were published by the five journals, including *Lancet* (34-37), *Journal of Crohns & Colitis* (12,13,32,33), *Gut* (38-41), *American Journal of Gastroenterology* (42-45) and *Gastroenterology* (46-49).

Development of keywords of surgery studies in Crohn's disease is of essence. Two types of keywords have been analyzed, including author keywords and keywords plus. Keywords plus and author words have been included in database since 1991 with considerable marker functions.

Keywords plus are determined by the words or phrases frequently occurred in the titles of references but absent in the title of the study itself (50). It enhances the cited-reference searching process and identifies the overlapped references. Author keywords are defined by author to fully reflect the study itself. In some cases, articles without author keywords may still have keywords plus presented. Keywords plus terms maybe more broadly descriptive with equal effectiveness, but less comprehensive in reflecting article's content.

In this study, the most frequently occurred keywords plus terms were associated with "management", "infliximab", "therapy", "risk", "diagnosis", "complications", "recurrence" and "resections", whereas in author keywords, the most frequently occurred terms were associated with "infliximab", "recurrence", "laparoscopy", "complications", "adalimumab", "epidemiology", "quality of life", "fistula", "colectomy" and "postoperative recurrence". Based on the availability of data, keywords plus indeed was superior. However, author keywords indeed offered a well-descripted developmental trajectory in the field. In fact, surgical complications and recurrence, surgery and infliximab are growing to be hotspots.

Interestingly, 50 research topics from 2000 to 2020 clearly delineate a developmental trajectory, as most of topics begin to increase since 2007, and dramatically increase after 2017. By cluster, we found that there were nineteen topics in comparably high research attention, including: perianal fistula, laparoscopic and open operation, anti-Saccharomyces cerevisiae antibodies (ASCA), infliximab therapy treatment, capsule endoscopy, case report, resection surgery of Crohn's disease, histology of inflammation bowel disease, symptoms of chronic disease, small intestinal obstruction, ileal pouch, Crohn's disease, surgical treatment for abscess, stricture and endoscopic dilation, children diagnosis, MRI image detect, ulcerative colitis, colectomy and colorectal cancer development.

Laparoscopy and open surgery for Crohn's disease is one of the prioritized future researches. Like traditional open surgery, the role of minimally invasive surgery is increasingly applied to patients with Crohn's disease (51,52). Laparoscopic surgery for Crohn's disease appears to be a feasible and safe approach in repeated ileocolic resection as postoperative morbidity and the conversion rates are relatively low (51). A retrospective study of 5,158 patients with Crohn's disease in National Surgical Quality Improvement Program (NSQIP) database reports that the rates of anastomotic leaks, reoperation and wound infection are lower in laparoscopic and robotic-assisted ileocecal resection comparing to open surgery, highlighting certain advantages of minimally invasive patterns (52). To further standardize the surgical treatment of Crohn's disease, the European Crohn's and Colitis Organization (ECCO) and European Society of Colo-Proctology (ESCP) are gathered for European consensus guidelines of standard operating procedures (30,31,53). Meanwhile, global consensus of classification, diagnosis and multidisciplinary treatment on specific type of Crohn's diseases, such as perianal fistulizing ones, is also produced (54).

Ileocecal resection is one of the most commonly surgeries performed in paediatric Crohn's disease. However, either open or laparoscopic assisted surgery approach is still under disputation. Based on a sixty-two cases retrospective analysis, laparoscopic approach showed no significant difference to open surgery, but with a less hospital stay. Therefore it was recommended for preferred surgical approach for primary ileocecal resection (55). To further compare the benefits between laparoscopy and robotic-assisted approach, a meta-analysis of eleven non-randomized studies with 5,566 cases was conducted (56). In results, safety and feasibility of robotic platforms was comparable to that of traditional laparoscopic techniques. Moreover, for penetrating type of Crohn's disease, laparoscopic surgery is also feasible and safe in selected group of patients (57). However, for complex fistulizing or recurrent Crohn's disease patients, laparoscopic or robotic assisted approaches may not be preferred as technical and theoretical challenges increasing. Only skilled colorectal surgeons may achieve a better outcome than open surgery (58).

Similar bibliometrics studies have been performed for inflammatory bowel disease (59,60). Bibliometric analysis of stem cell therapy identified 674 articles and highlighted strongest citation bursts on animal experiments, immunocytes and intestinal epithelial cells (59). Another study characterized the association of intestinal microbiome and inflammatory bowel disease, showing that the metabolites, signaling pathways of the gut microbiome are highly related to inflammatory bowel disease (60). Topics network was also established, with five primary clusters identified, including disease assessment, surgical treatment and complications, risk factors and epidemiology, disease development and diagnosis, target treatment and recurrence (*Figure 6*).

Limitation in this study remains as numerous databases and search tools are available for bibliometric analysis, including WOS, Scopus, Google Scholar and PubMed.

Of note, the Scopus database is in rapid growth, aiming at one of the major resources for publication analysis in near future. Meanwhile, novel surgical techniques or procedures may likely to be initially published in meeting abstract or proceeding reports. A full-range exploration of studies may be complementary to the findings.

Conclusions

This study identified key topics relating to the development of surgery in Crohn's disease, and provided bibliometric insights and perspectives for future development in the field of surgery in Crohn's disease.

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Footnote

Peer Review File: Available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-113/prf

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tgh.amegroups.com/article/view/10.21037/tgh-23-113/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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