ORIGINAL RESEARCH

Global knowledge map of sentinel lymph node fluorescence mapping in endometrial carcinoma: a visual analysis

Shibo Li[1,†], Mengyao Zeng[1,†], Xiaotong Zhao[1], Weiqin Zheng[1], Xiaowen Lin[1], Sizheng Peng[2], Tao Song[2,*], Yuhui Sun[1,*]

[1]Department of Gynecology, the First Affiliated Hospital of Harbin Medical University, 150001 Harbin, Heilongjiang, China
[2]Department of Cardiology, the First Affiliated Hospital of Harbin Medical University, 150001 Harbin, Heilongjiang, China

*Correspondence
yuhui_sun@vip.163.com
(Yuhui Sun);
shutiao1981@sina.com
(Tao Song)

[†] These authors contributed equally.

Abstract

Endometrial carcinoma (EC) is a prevalent gynecological malignancy in which sentinel lymph node (SLN) fluorescence mapping technique is utilized for staging the diseases and adjuvant treatment guidance. Herein, we aim to assess the research focus on global SLN mapping and determine potential new directions through bibliometric analysis. Articles related to SLN fluorescence mapping of EC from 2000 to October 2022 were searched from the Web of Science database, and research progress in this field was analyzed using bibliometric software HistCite Pro 2.1, VOSviewer 1.6.18 and CiteSpace 5.8.3Rc. A total of 197 related articles published from 2000 to 2022 were identified, and we observed that the number of publications had increased rapidly since 2015. The leading countries in this research area are the United States and Italy. The most influential institutions in this field with close collaboration are located in the United States, Italy and Switzerland. The journal with the highest number of high-quality publications is Gynecologic Oncology. In regards to publication authors, notable contributions have been made by Buda A, Papadia A and Rossi EC in this field. The most recent co-cited cluster label is "#notes", and we found that the current research is focused on optimizing fluorescence mapping technology and improving detection accuracy. With the growing emphasis on lymph node (LN) metastasis, there has been increasing attention on SLN fluorescence mapping. Currently, research in this area primarily focuses on addressing controversial issues, such as investigating factors contributing to mapping failure and investigating ways to enhance the surgical algorithm for improved outcomes.

Keywords

Bibliometric; CiteSpace; Endometrial carcinoma; HistCite; SLN mapping; Vosviewer

1. Introduction

Endometrial cancer (EC) is a prevalent malignancy affecting the female reproductive system. In recent years, its incidence has been rapidly increasing, primarily due to the rise in the geriatric population and obesity rates. According to the American Cancer Society's estimation for 2022, uterine corpus cancer was projected to become the second most common cancer among American women, with approximately 65,950 new cases reported and more than 90% of cases arising in the endometrium [1].

Surgery is the primary treatment for EC. In 1998, the Federation of International Gynecology and Obstetrics (FIGO) changed the staging system for EC from clinical to surgical staging, and since then, lymph node status has played a crucial role in guiding prognosis and determining the use of adjuvant therapies. However, the risk of lymph node metastasis is low in early-stage low-grade EC, and systematic lymphadenectomy,

despite being traditionally performed, is often associated with complications such as vascular nerve injury, lymphedema and lymphatic cysts [2, 3]. In recent years, there has been rapid acceptance of sentinel lymph node (SLN) fluorescence mapping technology in the clinical community. SLNs are the primary sites of lymphatic drainage in the primary tumor region. The aim of SLN detection is to obtain accurate pathological information while reducing surgical morbidity. Indocyanine green (ICG), a tracer recommended by both domestic and international guidelines [4–6], has shown high rates of bilateral detection and sensitivity [7–10]. Consequently, the number of studies focusing on SLN fluorescence mapping has increased rapidly.

To understand the development trends in the field of SLN fluorescence mapping of EC, bibliometrics were employed to systematically evaluate the published literature. Bibliometrics utilizes mathematical and statistical methods to quantitatively analyze a large volume of documents within a specific research

field, enabling the identification of various aspects and research patterns [11]. While related studies using bibliometrics have been conducted in numerous fields [12–15], there is currently no statistical analysis specifically focused on the SLN fluorescence mapping of EC. For this study, we primarily utilized HistCite (Pro 2.1, Eugene Garfield, Philadelphia, PA, USA) [16], VOSviewer (1.6.18, Nees Janvan Eck and Ludo Waltman, Leiden, The Netherlands) [17, 18] and CiteSpace (6.1.3, Chaomei Chen, Philadelphia, PA, USA) [19, 20] for bibliometric analysis to assess research progress in ICG SLN mapping, including countries, institutions, journals, subject areas and authors, with the aim to determine the most influential research outcomes within this field using bibliometric techniques.

2. Materials and methods

2.1 Data collection

We searched the Web of Science database from 2000 to October 2022, focusing on studies related to ICG SLN mapping. The search was limited to articles written in English, and the following search terms were used: TS = (Endometrial Neoplasm OR Neoplasm, Endometrial OR Neoplasms, Endometrial OR Endometrial Carcinoma OR Carcinoma, Endometrial OR Carcinomas, Endometrial OR Endometrial Carcinomas OR Endometrial Cancer OR Cancer, Endometrial OR Cancers, Endometrial OR Endometrial Cancers OR Endometrium Cancer OR Cancer, Endometrium OR Cancers, Endometrium OR Cancer of the Endometrium OR Carcinoma of Endometrium OR Endometrium Carcinoma OR Endometrium Carcinomas OR Cancer of Endometrium OR Endometrium Cancers) AND (Sentinel Lymph Node OR Biopsy, Sentinel Lymph Node OR Lymph Node Biopsy, Sentinel OR Sentinel Lymph Node Biopsy OR Sentinel Nodes OR Nodes, Sentinel OR Node, Sentinel OR Sentinel Node OR Sentinel Lymph Nodes OR Lymph Nodes, Sentinel OR Lymph Node, Sentinel) AND (Fluorescence OR Fluorescent Dyes OR Dyes, Fluorescent OR Fluorescent Dye OR Fluorescence Agents OR Agents, Fluorescence OR Fluorochromes OR Fluorescent Agents OR Agents, Fluorescent OR Fluorochrome OR Fluorogenic Substrate OR Substrates, Fluorogenic OR Optical Imaging OR Imaging, Optical OR Fluorescence Imaging OR Imaging, Fluorescence OR Autofluorescence Imaging OR Imaging, Autofluorescence OR Indocyanine Green OR Green, Indocyanine OR ICG).

2.2 Data analysis and visualization

The articles were exported in TXT format. HistCite Pro 2.1 was used to analyze the number of publications, publication date, country, institution, author and citations, VOSviewer 1.6.18 for assessing the cooperative relationships among countries, institutions and authors, as well as creating a visual keyword co-occurrence network, and CiteSpace 5.8.3Rc for performing co-citation analysis and timeline viewing to identify current trends and topics of interest.

3. Results

3.1 Dates of publications and citations

A total of 197 articles on SLN ICG fluorescence mapping in EC were published between 2000 and 2022. The articles had a total local citation score (TLCS) of 1093, with 917 of those being local citation scores excluding self-citations (LCSx). On average, each article had 10.23 cited references, a local citation score (LCS) of 5.55, and an LCSx of 4.65. The research in this field was in an exploratory stage before 2015. In 2014, two articles were published with a TLCS of 66, indicating a breakthrough in understanding. Since 2016, research on SLN ICG fluorescence mapping has developed rapidly, with 27 publications in 2022. The year 2017 had the highest TLCS, suggesting a peak in the field's development. However, the number of LCS has been declining since then, indicating a potential lack of significant advancements. Despite the continued high publication volume, there may be a need for breakthroughs in this field (Fig. 1).

3.2 Contributions of countries and co-authoring relationship

In the field of fluorescence mapping in EC, a total of 197 articles were published by authors from 37 countries, as depicted in the country distribution map (Fig. 2A). The countries are colored from light to dark based on the number of publications. The top 10 countries with the highest number of publications are presented in Fig. 2B. Italy had the most articles published, with 51 articles accounting for 26% of the total. The United States ranked second with 44 articles (22%), and Switzerland ranked third with 21 articles (11%). Regarding LCS (Fig. 2C), the United States ranked first with 512 LCS (47%), followed by Italy with 297 LCS (27%), and Switzerland with 164 LCS (15%). The total LCS of these top three countries accounted for approximately 90% of the overall LCS, highlighting their significant contributions in this field. For co-authorship analysis, VOSviewer was employed to generate a national cooperative network map (Fig. 2D). The criteria set for inclusion were a minimum of five documents from a country. Of the 37 countries, 15 met the criteria, among which 13 countries were found to have collaborative research relationships. The size of the nodes in the country map represents the number of articles published by each country, while the connections between nodes represent the collaborative links between countries. Notably, the United States and Italy, the two major publishing countries, demonstrated close cooperation with other countries.

3.3 Contributions of institutions and co-authoring relationship

Among the top 10 institutions, a total of 116 articles were published, accounting for 59% of all the articles. The University of Bern, Milan Bicocca University and San Gerardo Hospital were the top three institutions regarding the number of publications (Fig. 3A). When considering institutions with the highest LCS, the University of Bern, the University of North Carolina and the Memorial Sloan-Kettering Cancer Center ranked the highest (Fig. 3B). In regard to institution co-authoring relationships, we applied the criterion of a minimum
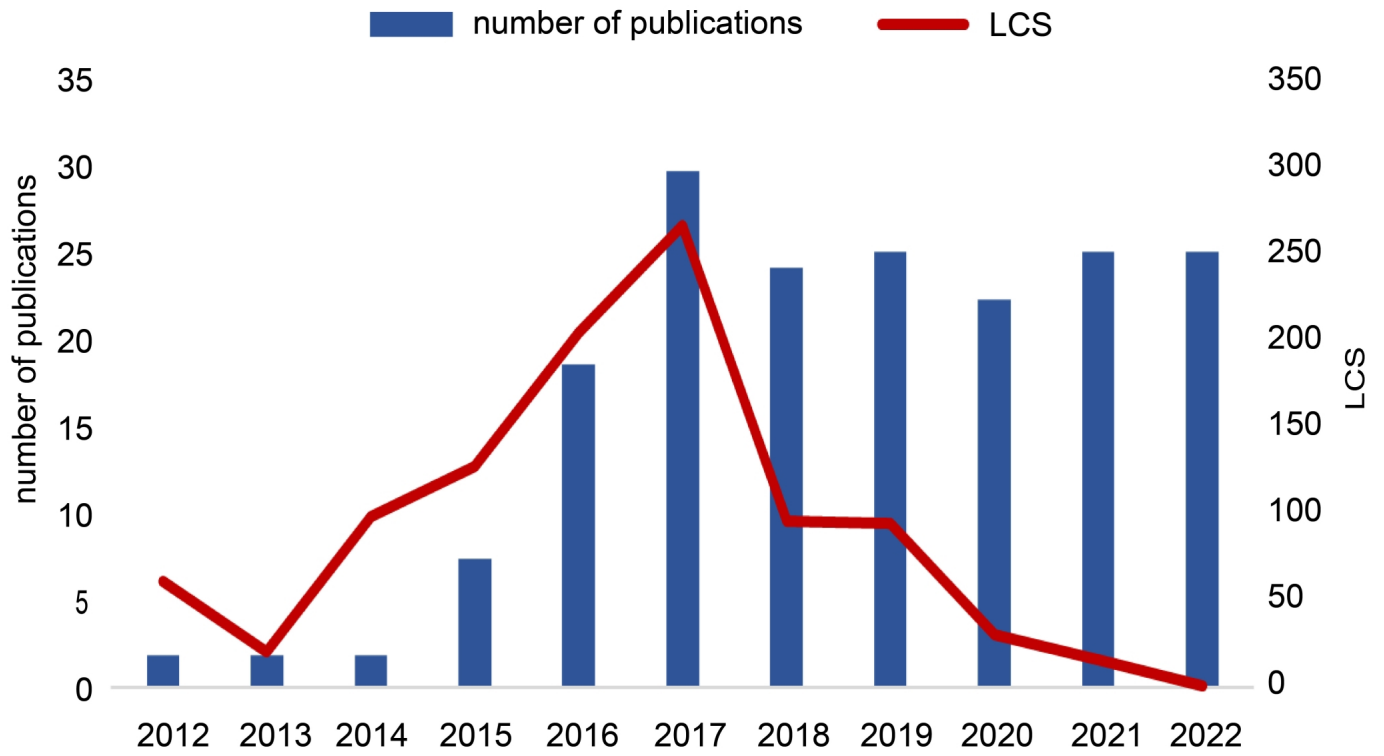
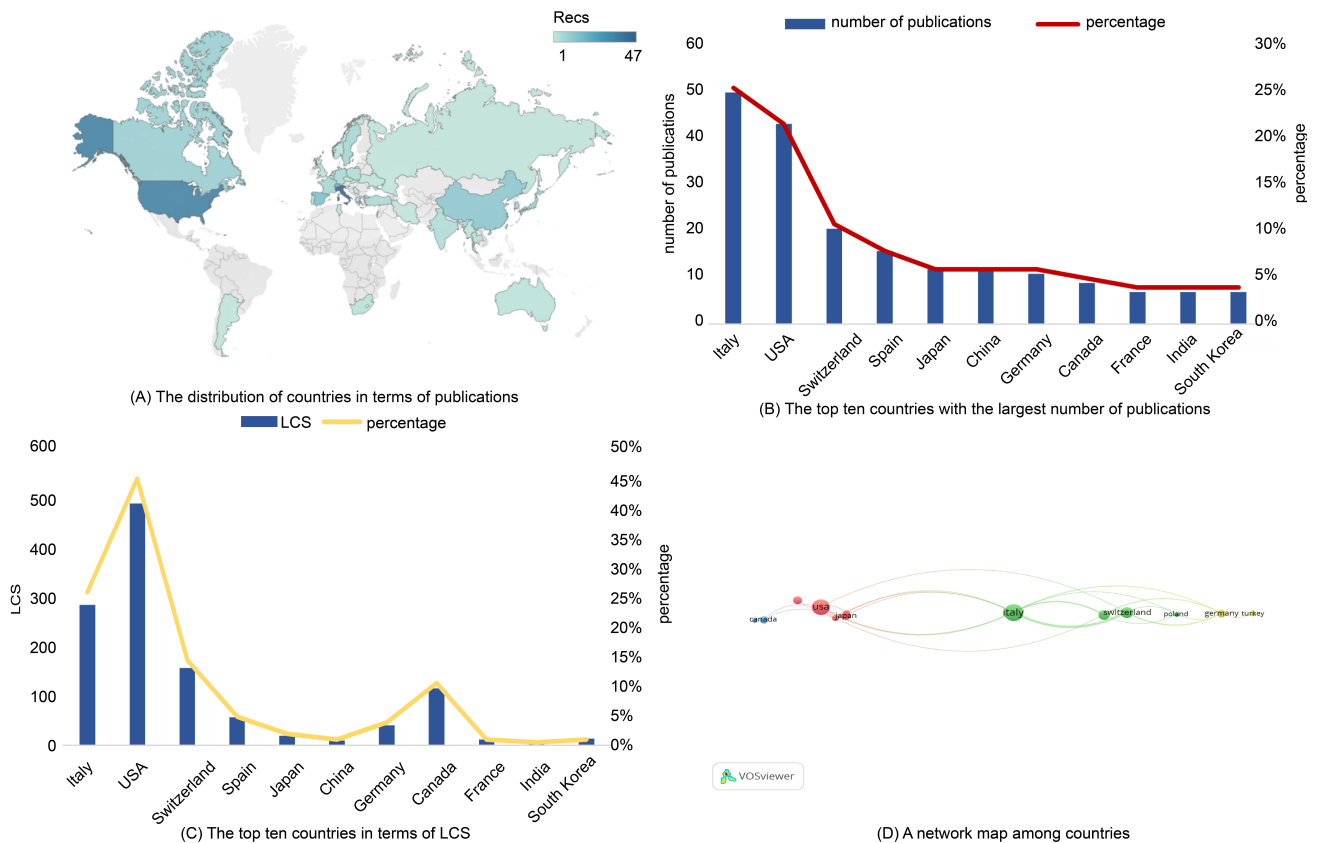**F I G U R E 1. The number of publications and LCS by year.** LCS: local citation score.

(A) The distribution of countries in terms of publications

(B) The top ten countries with the largest number of publications

(C) The top ten countries in terms of LCS

(D) A network map among countries

Figure 2 Analysis of countries

F I G U R E 2. Analysis of countries. (A) The distribution of countries in terms of publications. (B) The top ten countries with the largest number of publications. (C) The top ten countries in terms of LCS. (D) A network map of the cooperation of countries. LCS: local citation score.

of five co-authors. Of the 14 institutions that met this criterion, 11 had cooperative relationships (Fig. 3C). Notably, the red cluster and green cluster exhibited close interrelations.

3.4 Contributions of authors and co-authoring relationship

A total of 1018 authors contributed to the study of ICG SLN mapping in EC. Among the top 10 authors based on the number of publications (Fig. 4A), seven are from Italy, while three are from Switzerland. The author with the highest LCS is from Italy, and the second and third authors with the highest LCS are from the United States (Fig. 4B). Regarding co-authoring relationships, with a minimum requirement of five co-authors for inclusion, 31 of the 1018 authors met the criteria. Among them, 22 authors exhibited were found to have mutual research collaboration, particularly among the top 10 authors in terms of publication (Fig. 4C). Additionally, a co-citation analysis of scholars was conducted, with a minimum citation threshold set to 20. Of the 1018 authors, 46 authors reached this threshold. The size of the nodes in the graph represents the frequency of citations for each author, while the clustering of nodes with the same color indicates that the scholars share similar research directions. Notably, Rossi EC was the author with the highest number of citations. Considering the number of publications, co-creation relationships and co-citation analysis, Papadia A and Buda A have made significant contributions, suggesting their success in this field (Fig. 4D).

3.5 Contributions of published journals

Seventy journals have published articles on SLN ICG fluorescence mapping in EC, with the top 10 journals contributing 115 publications, accounting for 58% of the total. The three journals with the highest number of publications in this field were Gynecologic Oncology, International Journal of Gyneco-

logical Cancer, and Journal of Minimally Invasive Gynecology (Fig. 5A). The three journals with the largest number of LCS were Gynecologic Oncology, Annals of Surgical Oncology and Lancet Oncology (Fig. 5B).

3.6 Research status and topics of interest

We used VOSviewer to analyze keywords that appeared at least 15 times per article in all included publications. After merging synonyms, 127 terms in this field reached this threshold, and 45 keywords were obtained by self-screening. These keywords were then divided into three clusters of different colors (Fig. 6A), with the blue cluster representing the effect of different tracers on the detection rate and treatment of SLN mapping, the red cluster representing the study of factors influencing fluorescence mapping, and the green cluster representing the sensitivity, specificity and negative predictive value of ICG fluorescence technique in different stages and grades of EC. The time trend map (Fig. 6B) showcases the evolution of research in this field. The color gradient from blue to yellow indicates changes in research focus, particularly emphasizing the differences between ICG and other imaging techniques. The yellow nodes represent the current research frontiers, primarily focused on technological advancements and improvements.

3.7 Clusters and bursts of co-cited references

The collected 197 articles were inputted into CiteSpace software to generate a visual timeline of co-cited references (Fig. 7A). Table 1 presents the top 10 references with the highest number of co-citations. After clustering analysis, eleven clusters were generated, with the modular Q (0.5982) and weighted mean silhouette S (0.8073), with both exceeding 0.5. The clusters were labeled based on the Log-likelihood
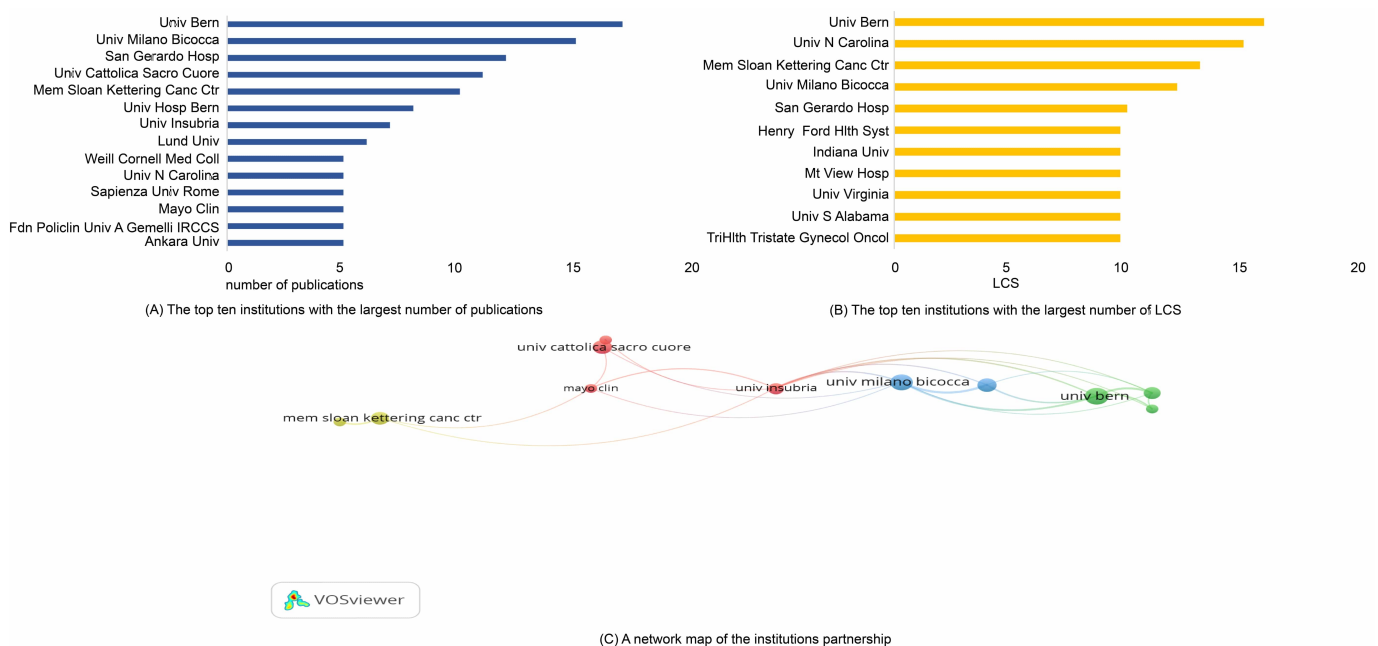

(A) The top ten institutions with the largest number of publications

(B) The top ten institutions with the largest number of LCS

(C) A network map of the institutions partnership

F I G U R E 3. The contribution of institutions. (A) The top ten institutions with the largest number of publications. (B) The top ten institutions with the largest number of LCS. (C) A network map of the institution partnerships. LCS: local citation score.
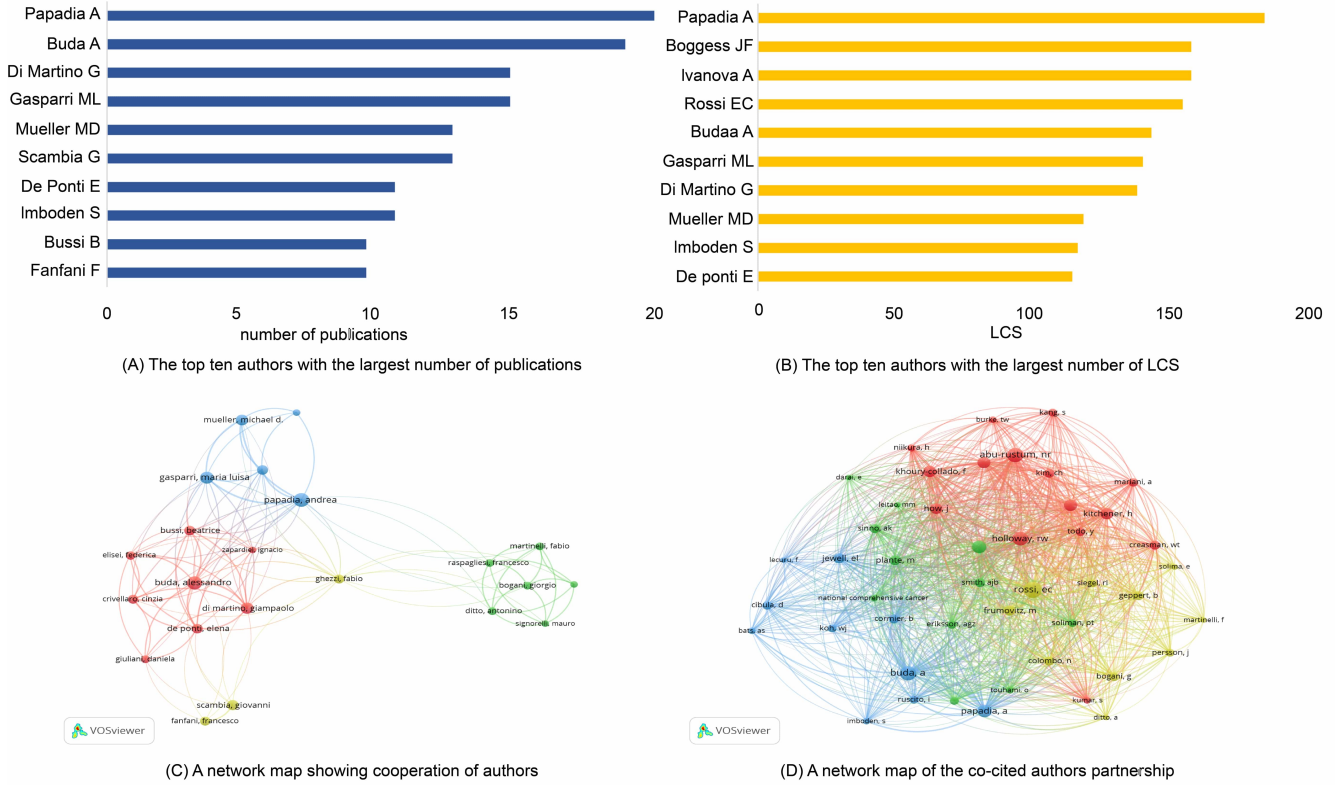
(A) The top ten authors with the largest number of publications

(B) The top ten authors with the largest number of LCS

(C) A network map showing cooperation of authors

(D) A network map of the co-cited authors partnership

F I G U R E 4. The analysis of the authors. (A) The top ten authors in terms of the number of publications. (B) The top ten authors with the largest number of LCS. (C) A network map showing the cooperation of authors. (D) A network map of the co-cited author partnerships. LCS: local citation score.
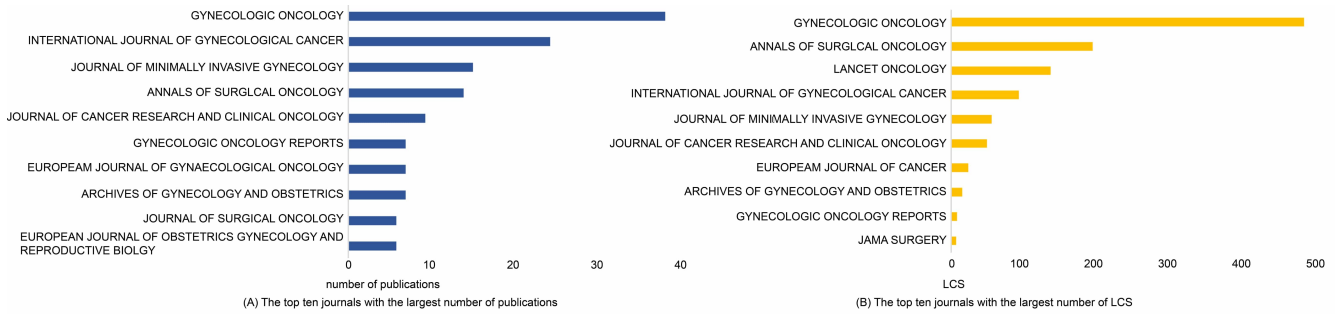

(A) The top ten journals with the largest number of publications

(B) The top ten journals with the largest number of LCS

F I G U R E 5. The contributions of the journals. (A) The top ten journals with the largest number of publications. (B) The top ten journals with the largest number of LCS. LCS: local citation score.
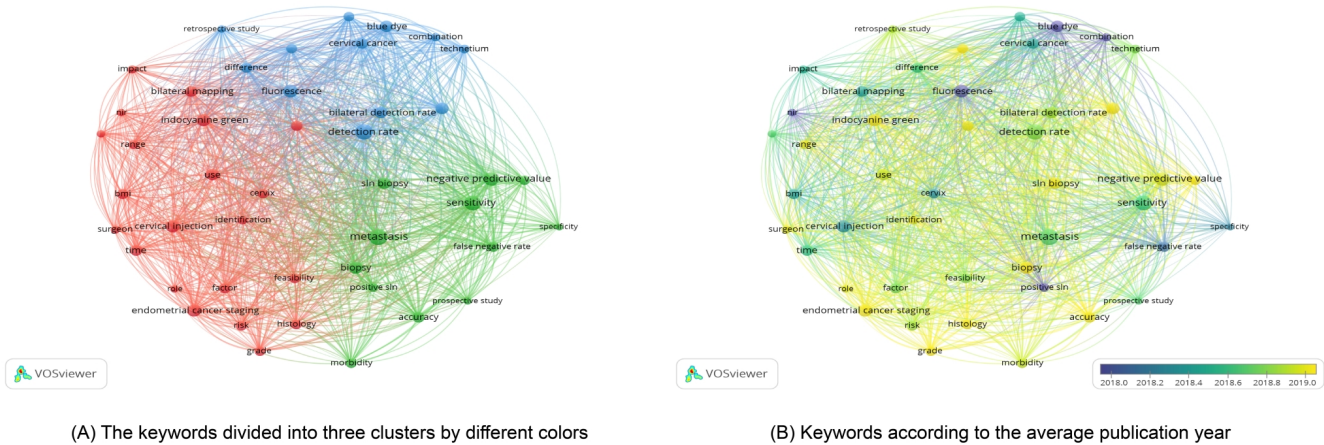

(A) The keywords divided into three clusters by different colors

(B) Keywords according to the average publication year

F I G U R E 6. The analysis of the key words. (A) The keywords were divided into three clusters by different colors. (B) Visualization of keywords according to the average publication year.

T A B L E 1. The top ten co-cited references involved in research on SLN ICG fluorescence mapping.

Rank	Co-cited reference	Count	Type
1	Rossi EC, 2017, LANCET ONCOL, V18, P384	99	Clinical Trial
2	SmithAJB, 2017, AM J OBSTET GYNECOL, 216, 459	50	Meta-Analysis
3	Holloway RW, 2017, GYNECOL ONCOL, 146, 405	47	Review
4	Jewell EL, 2014, GYNECOL ONCOL, 133, 274	47	Clinical Trial
5	How J, 2015, GYNECOL ONCOL, 137, 436	44	Clinical Trial
6	Ruscito I, 2016, ANN SURG ONCOL, 23, 3749	36	Meta-Analysis
7	Buda A, 2016, ANN SURG ONCOL, 23, 2183	33	Clinical Trial
8	Frumovitz M, 2018, LANCET ONCOL, 19, 1394	33	Clinical Trial
9	Sinno AK, 2014, GYNECOL ONCOL, 134, 281	33	Clinical Trial
10	Plante M, 2015, GYNECOL ONCOL, 137, 443	31	Review
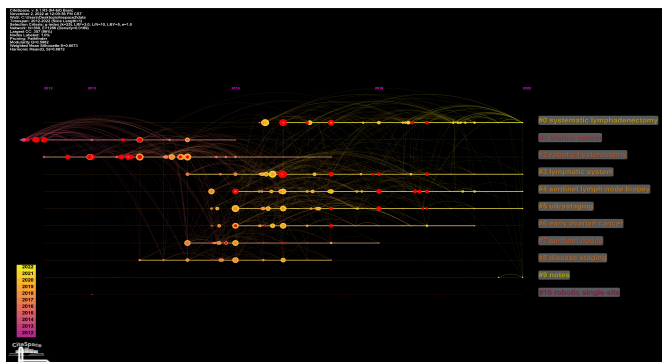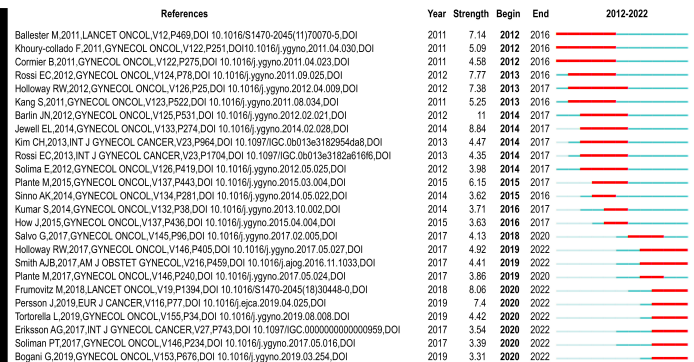
(A) The timeline view of the references of SLN fluorescence mapping (B) Top 25 with strongest citation burst

Figure 7 The analysis of the reference

F I G U R E 7. The analysis of the references. (A) The timeline view of the references of SLN fluorescence mapping. (B) Top 25 references with the strongest citation burst.

rate, and the largest cluster was labeled "#0 systematic lymphadenectomy". In the timeline visualization, nodes of different colors on the same row represent different years, with nodes on the left indicating older references and nodes on the right representing newer references. The nearest clusters on the timeline include "#9 notes", "#0 systematic lymphadenectomy", and "#4 sentinel lymph node biopsy". Furthermore, we explored cited references with strong citation outbreaks using CiteSpace software. References with citation bursts are defined as references that are frequently cited over a period of time. The top 25 references with the strongest citations are ranked in ascending order based on the starting year of the citation outbreak (Fig. 7B). The most intense citation burst was associated with an article published by Barlin JN in Gynecologic Oncology in 2012 (strength 11). This article emphasizes the significance of surgical algorithms in SLN detection of EC. The most recent references with citation bursts are "Persson J, 2019, EURJCANCER, V116, P77, DOI10.1016/j.ejca.2019.04.025" (strength 7.4), "Tortorella L, 2019, GYNECOLONCOL, V155, P34, DOI10.1016/j.ygyno.2019.08.008" (strength 4.4), and "Bogani G, 2019, GYNECOLONCOL, V153, P676, DOI10.1016/j.ygyno.2019.03.254" (strength 3.3).

4. Discussion

SLN ICG fluorescence mapping has emerged as a novel technique for predicting lymph node metastasis in EC. In recent years, it has gained significant attention, leading to a gradual increase in the publication of related studies [21, 22]. Literature visualization analysis plays a crucial role in assisting researchers to gain a better understanding of the current research landscape, identify research hotspots, identify key research centers, and explore collaboration patterns in this field. Bibliometrics is an important method promoting the advancement and development of this field through quantitative analysis of publications and citations.

4.1 General information

A total of 197 articles were included in the analysis, and the local citation scores (LCS) were examined using HistCite. LCS reflects the citation rate and peer recognition of research, with a higher LCS indicating higher recognition. Before 2014, relatively few studies were published in this field, which then increased in 2015. This may be attributed to the inclusion of SLN mapping in the National Comprehensive Cancer Network (NCCN) guidelines in 2014. In addition, the research conducted by Jewell El *et al.* [23] in 2014 gained significant attention and obtained the second-highest LCS of 66. This

study comprised 227 patients and reported a high detection rate (95%) and bilateral detection rate (79%) using ICG imaging. It also found that combining ICG and blue dye reduced the detection rate compared to using ICG alone (95% *vs.* 93%) [23]. This research served as a breakthrough in the field. The United States, being the first country to perform research in this field, had the second-largest number of published articles and the highest LCS, indicating its pioneering and leading role in this field. Regarding co-creation, the United States and Italy demonstrated close cooperation with other countries. The distribution of influential institutions roughly corresponds to that of the countries involved, with the top 10 institutions primarily located in the United States, Italy and Switzerland. However, the collaboration among institutions is more closely intertwined. Gynecologic Oncology had the highest publication volume and LCS, suggesting a significant focus on the study of SLN mapping in this journal. Among the scholars in this field, Buda A and Papadia A have published the most literature and share a certain level of collaboration. Additionally, Rossi EC published four articles in this field, obtaining the second-highest total local citation score (132) and the largest number of citations in the co-cited network, indicating the significant impact of their research in the field.

4.2 Knowledge Base

Co-citation relationships refer to the joint citation of two publications by a third publication [24]. Therefore, the most frequently cited publications or highly influential studies can be regarded as the knowledge base and main focus of researchers in a particular field. The top 10 most frequently cited studies are shown in Table 1, which were predominantly published in high-impact journals and comprised six clinical trials, two meta-analyses, and two reviews. Among the six clinical trials, two studies highlighted the high detection rate of SLN mapping. Notably, the article published by Rossi EC in 2017 received the highest number of citations. This multicenter prospective trial demonstrated the diagnostic accuracy of ICG fluorescence mapping technique, reporting a sensitivity of 97.2% (95% confidence interval (CI) 85.0–100) and a negative predictive value of 97.6% (95% CI 97–100) [25], emphasizing the feasibility and advantages of ICG fluorescence mapping compared to lymph node dissection. The remaining four articles compared the advantages of fluorescent dyes over other tracers. The remaining four articles compared the benefits of fluorescent dyes over other tracers. In 2018, Frumovitz M *et al.* [26] conducted a randomized, prospective clinical trial revealing that the use of ICG significantly increased the detection rate of metastatic diseases, particularly in obese patients, compared to blue dye. These top 10 articles primarily confirm the role of SLN mapping in EC staging and emphasize the advantages of fluorescent dyes over other tracers.

4.3 Research topics of interest

Using VOSviewer, we conducted keyword co-occurrence analysis, and the most recent keywords identified were primarily related to "accuracy", "negative predictive value", "grade" and "endometrial cancer staging". The current research focus is primarily on improving the accuracy of SLN

diagnosis, particularly in patients with high-risk EC (HREC). The application and feasibility of SLN mapping in HREC remain controversial, and researchers are dedicated to finding the optimal surgical algorithm [27, 28]. In the analysis of recent articles with strong citation bursts using CiteSpace, the most significant outbreak was associated with the article published by Persson J *et al.* [29] in 2019. Persson J *et al.* [29] proposed a pelvic SLN algorithm for HREC, enabling bilateral development of the upper paracervical and lower paracervical pathways. A prospective study demonstrated a high bilateral labeling rate (95%) and complete sensitivity for detecting pelvic lymph node metastases [29]. Then, in 2020, Bollino M *et al.* [30] further simplified the algorithm to enhance its feasibility, suggesting the potential to replace lymphatic dissection in HREC without the need for para-aortic lymph node dissection. In the co-citation literature analysis, the closest cluster on the timeline is "#9 notes", and the median year of all references is 2022. The development of minimally invasive gynecological surgery has progressed from traditional laparoscopy to laparoscopic single-site surgery and transvaginal natural orifice endoscopic surgery (vNOTES). The tail-to-head view in vNOTES facilitates easier access to the internal iliac lymph nodes, making SLN biopsies more feasible [31–33]. This procedure can be achieved with low carbon dioxide (CO_2) blowing pressure, rendering SLN biopsies more feasible, particularly for elderly and obese patients with compromised cardiopulmonary function [34–36]. Wang Y *et al.* [37] found that vNOTES had a higher detection rate (92.2% *vs.* 95.7%) than laparoscopy. However, larger prospective studies with a larger sample size are required to confirm these findings. Overall, the current research direction of SLN ICG fluorescence mapping primarily revolves around optimizing the technology, identifying the most suitable SLN algorithm, and improving the accuracy of SLN detection.

In 2020, the European Society of Gynaecological Oncology (ESGO)-European Society for Radiotherapy and Oncology (ESTRO)-European Society of Pathology (ESP) management guidelines for EC incorporated molecular typing and molecular markers [6] to evaluate patients' prognoses [6]. The biggest addition was the inclusion of DNA polymerase Epsilon (POLE) mutation in FIGO stage I–II cancer, which was classified as low risk regardless of tumor grade, pathological type, or lymphovascular involvement. EC with p53 mutation and myometrial invasion, similar to non-endometrioid carcinoma, was categorized as high risk, whereas p53-mutated carcinoma without myometrial invasion was classified as low risk. Raffone A *et al.* [38] conducted a meta-analysis and reported that the rate of lymph node metastasis was 0% in cases with a POLE mutation, suggesting that lymphadenectomy may not be necessary. In patients with p53 wild type, the lymph node metastasis rate was 4.3%, indicating the feasibility of SLN biopsy. However, patients with mismatch repair deficiency and p53 mutations had a high lymph node metastasis rate, highlighting the need for SLN resection [38]. Nonetheless, prospective studies are required to validate these conclusions, which may have implications for the comprehensiveness of SLN staging and provide a basis for stratification in SLN ICG fluorescence mapping. Future research may focus on determining the indications for SLN detection in EC based on

molecular typing.

5. Conclusions

Bibliometric analysis has demonstrated that SLN ICG fluorescence mapping technology has reached a mature stage and holds significant promise. Indocyanine green (ICG) has been recommended as a tracer in the NCCN guidelines. Cervical injection is widely employed due to its simplicity and high detection rate. Notably, Buda A, Papadia A and Rossi EC have contributed extensively to the research in this field. The United States and Italy have made noteworthy contributions, while Gynecologic Oncology has emerged as the leading journal in publishing studies on this topic. Despite the progress made, there are still areas of controversy that need to be addressed. Current research efforts are focused on the development of standardized SLN mapping techniques. In the future, it will be crucial to investigate the indications for SLN mapping in EC under the framework of molecular typing.

AVAILABILITY OF DATA AND MATERIALS

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

AUTHOR CONTRIBUTIONS

YHS and TS—designed the research study. SBL and MQZ—performed the research. XTZ, WYZ, XWL and SZP—analyzed the data. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

No applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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