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Bibliometric Analysis of Lymph Node Changes Following Neoadjuvant Therapy for Colorectal Cancer

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ABSTRACT

Background: As neoadjuvant therapy (NAT) use in colorectal cancer (CRC) increases, changes in lymph nodes post-treatment are crucial for prognosis and treatment decisions. However, a comprehensive quantitative analysis of research in this area is needed to identify trends and future research directions.

Methods: This study analyzed 904 pertinent publications sourced from the Web of Science Core Collection (2000-2025) using bibliometric tools such as CiteSpace, HistCite Pro, and alluvial flow visualization. The analyses encompassed publication trends, co-citation networks, collaborative patterns among countries, institutions, and authors, as well as burst detection of keywords, subject categories, references, and the temporal evolution of clusters.

Results: Post-2019, publication volume surged, peaking in 2022, with EJSO and Annals of Surgical Oncology as key journals. The co-citation network showed a shift from foundational literature to specialized clusters. Major collaborative hubs included China, the U.S., Sun Yat-sen University, and APHP. Burst analysis highlighted a focus shift from staging and sentinel lymph nodes to lateral lymph node dissection, neoadjuvant immunotherapy, MRI-guided assessment, and organ preservation. Timeline and alluvial Visualizations illustrated the transition from traditional pathology to imaging-based and molecular markers.

Conclusion:this bibliometric analysis elucidates the intellectual framework and dynamic progression of research concerning lymph node alterations following neoadjuvant therapy for colorectal cancer. The domain is marked by an escalating trend of interdisciplinary collaboration and a discernible shift towards non-invasive evaluation and personalized therapeutic approaches. Future investigations are expected to increasingly incorporate imaging biomarkers, enhance nodal staging criteria, and examine immune-mediated pathological responses.

1 Introduction

Neoadjuvant therapy (NAT), which includes chemoradiotherapy and the recently emerging immunotherapy, has become a cornerstone of multimodal management for locally advanced colorectal cancer (CRC)[1, 2]. Therapy-induced lymph node changes, encompassing alterations in number, size, morphology, and metastatic involvement, bear important prognostic value and directly inform subsequent surgical planning and adjuvant treatment decisions[3, 4]. Over the past two decades, the research paradigm for NAT in CRC has undergone a profound shift. Investigators are increasingly recognizing that the lymph node response to treatment constitutes a dynamic biological process whose clinical significance extends beyond conventional static histopathological staging.

Current research focuses on several key issues in NAT, including standardizing post-treatment lymph node assessment, clarifying the prognostic value of changes in lymph node detection, and evaluating the predictive power of advanced imaging—particularly high-resolution MRI—for pathological response[5-8]. Meanwhile, AI applications in medical imaging and pathology are providing new insights into this domain.Deep learning–driven MRI analysis shows potential for preoperative nodal staging and treatment-response assessment[9-11], while digital and computational pathology enable quantitative feature extraction from tissue sections that surpass traditional microscopy, enhancing prognostic accuracy[12]. These advances and clinical studies reinforce each other, driving more precise and quantitative lymph node evaluation after NAT in CRC and supporting more personalized treatment strategies.

As research in this field deepens and the literature expands rapidly, topics become increasingly diverse and specialized. This growth gives rise to a complex, interconnected body of knowledge, yet it also challenges clinicians and researchers to fully grasp the overall development trajectory, core evolutionary trends, and future directions. Traditional narrative reviews struggle to quantify the dynamic evolution of this knowledge structure systematically. Bibliometric analysis offers a powerful solution: through mathematical and statistical methods, it quantifies vast literature to objectively reveal development trajectories, collaboration networks, research hotspots, and emerging frontiers within specific domains[13, 14]. Visualization tools such as CiteSpace and HistCite further translate complex citation relationships and collaboration patterns into intuitive maps, aiding the identification of key publications, disciplinary inflection points, and latent knowledge structures[15, 16]. Although bibliometric methods have been successfully applied across multiple

oncology domains, systematic bibliometric research specifically addressing the critical topic of lymph node changes following NAT for CRC remains lacking.

Using systematic bibliometric and visualization techniques, our study analyzes literature from 2000 to 2025, quantifying publication trends, identifying core academic strengths, and delineating knowledge structures and collaboration patterns via co-citation and co-authorship networks. It also tracks evolving research hotspots through keyword salience and temporal evolution analyses. We aims to map the field's knowledge landscape and offered evidence-based guidance to clinicians and researchers for understanding dynamics and informing future directions.

2 Methods

2.1 Data Collection and Statistical Analysis

Data for this study were collected from the Web of Science Core Collection (WoSCC). A comprehensive search strategy covering the core concepts of "colorectal cancer," "neoadjuvant therapy," and "lymph nodes" was systematically constructed, and publications from 2000 to 2025 were retrieved using the following terms:
"((((((((((((((((((((((((((TS=("Colorectal Neoplasms")) OR TS=("Colorectal Neoplasm")) OR TS=("Neoplasm, Colorectal")) OR TS=("Neoplasms, Colorectal")) OR TS=("Colorectal Tumors")) OR TS=("Colorectal Tumor")) OR TS=("Tumor, Colorectal")) OR TS=("Tumors, Colorectal")) OR TS=("Colorectal Cancer")) OR TS=("Cancer, Colorectal")) OR TS=("Cancers, Colorectal")) OR TS=("Colorectal Cancers")) OR TS=("Colorectal Carcinoma")) OR TS=("Carcinoma, Colorectal")) OR TS=("Carcinomas, Colorectal")) OR TS=("Colorectal Carcinomas")) OR TS=(CRC)) OR TS=("Colonic Neoplasm*")) OR TS=("Colon Cancer*")) OR TS=("Colonic Cancer*")) OR TS=("Colon Adenocarcinoma*")) OR TS=("Cancer of the Colon")) OR TS=("Rectal Neoplasm*")) OR TS=("Rectal Tumor*")) OR TS=("Rectum Cancer*")) OR TS=("Cancer of the Rectum")) OR TS=("Rectum Cancer*") AND ((((((((((TS=("Neoadjuvant treatment")) OR TS=("Neoadjuvant therapy")) OR TS=("Neo-adjuvant treatment")) OR TS=("Neo-adjuvant therapy"))))) OR TS=("Neoadjuvant*")) OR TS=("Neoadjuvant Immunotherapy")) OR TS=("neoadjuvant chemotherapy")) OR TS=("Preoperative chemotherapy")) OR TS=("Preoperative Immunotherapy") AND(TS=("Lymph Node*")) OR TS=("Node, Lymph")". A total of 904 records were ultimately included. Full records and cited references were exported in plain-text format and merged into a DATA dataset. Subsequently, essential information including country/region, institution, journal, author, and document type was extracted from the dataset. Preliminary data organization and statistical analysis were then performed using Excel (WPS 2019) software.

2.2 Bibliometric Analysis Tools

2.2.1 CiteSpace

Collaboration Network Research collaboration is typically manifested as the co-authorship of academic publications by multiple authors, institutions, or countries. Analyzing these collaboration patterns helps reveal the research landscape and developmental trajectory of a discipline at the author, institutional, and national levels[17]. For this purpose, the relevant literature data were imported into CiteSpace software to generate visualization maps depicting collaboration networks. In this network, the colors of nodes and links were used to identify collaboration clusters formed in different periods, and link colors corresponded to the year when the collaboration first occurred. Nodes consist of multiple "tree rings", where the thickness of each ring represents the collaborative activity of that node in a given year. Specifically, red rings indicate citation bursts for that node in a specific year, while purple rings denote betweenness centrality. Nodes with high

betweenness centrality play a pivotal role in the co-occurrence network, serving as hubs that connect different modules and facilitate interdisciplinary knowledge flow.

Burst Detection As proposed by Jon Kleinberg, in text streams such as emails or academic literature, a topic often emerges intensively during a specific period and then gradually wanes. Specialized text-mining algorithms can detect these temporal dynamics and characterize them as "bursts of activity"[18]. Building on this, Chen and colleagues further introduced the concept of "citation burst" as a pivotal indicator of topic activity[19]. This approach identifies abrupt, pronounced rises in citations over multiple years or within a specific year. Using CiteSpace, citation burst detection can be performed for subject categories, keywords, and references. The presence of citation bursts indicates that the corresponding content exhibits a strong correlation with sharp increases in citation frequency during a specific period, reflecting concentrated scholarly attention.

Cluster Analysis CiteSpace employs clustering algorithms based on titles, abstracts, and keywords to group publications into concept clusters with distinct characteristics[20, 21]. These clusters can be visualized to trace their evolution across designated time periods. Meanwhile, the timeline view clearly show the emergence and decline phases of each cluster, and the nodes associated with other clusters. We imported the literature dataset into CiteSpace (version 6.2.R4) to investigate the progress of NAT and lymph nodes in CRC. The parameters were set as follows: time span 2000–2025 with a 1-year intervals; term sources were extracted from "Title," "Abstract," "Author Keywords," and "Keywords extension"; node types were selected per analytical objective, with other parameters remaining at default. First, we generated collaboration networks for countries/regions, institutions, or authors. These network maps were then manually adjusted to improve visual clarity. Keyword cluster maps were drawn in a similar procedure, except that the node type was set to "Keyword" and the time was divided into four phases: 2000–2007, 2008–2015, 2016–2020, and 2021–2025. Additionally, when constructing the reference co-citation network, we chose 'Timeline View' from the 'Layout' menu in the control panel to create a timeline plot of citation evolution. Finally, using the "Burst Detection" function, burst-intensity maps can be obtained for keywords, subject categories, or cited references, respectively.

2.2.2. HistCite

HistCite generates citation-mapping diagrams and highlights the most influential publications, thereby intuitively presenting the most frequently cited studies in the field. Articles were evaluated using the Local Citation Score (LCS) and Global Citation Score (GCS): LCS represents the number of citations within the current dataset, whereas GCS denotes total citations in the WoSCC.

Our dataset comprised 904 publications on NAT and lymph node changes in CRC. After importing them into HistCite, we set the "Limit" parameter to 30, kept other settings at default, and selected "Make Graphs". The resulting historiography of research on NAT–related lymph node changes in CRC helped clarify the main developmental trajectory of the field and rapidly identified pivotal publications.

2.2.3. The Alluvial Generator

Alluvial diagrams can effectively illustrate how dynamic networks evolve over time[22]. For alluvial visualization, we constructed keyword co-occurrence networks for each time slice using the CiteSpace. These networks were individually exported and then imported into the Alluvial Generator tool to create the figure(http://www.mapequation.org/apps/AlluvialGenerator.html) . In the generated diagram, each keyword was treated as a node and assigned to a corresponding cluster according to its membership across time slices, with each cluster representing a module. As time

goes by, nodes underwent splitting and merging between slices to form new modules. Thus, the modular structure within the current time slice was determined by the interaction and reorganization of nodes from the preceding phase.

2.2.4. R

The donut chart in Figure 9 was produced in R (version 4.2.2) using the geom_bar function from the ggplot2 package (version 3.4.4).

3 Results

3.1 The historical features of the literature

3.1.1 Distribution of publications

We performed a bibliometric analysis to quantify the knowledge evolution and landscape of research landscape on NAT and lymph node-related research in CRC. Of the 904 publications retrieved, 784 were original articles, and 120 were reviews. These works involved 5,738 authors and 1,432 institutions, spanning 281 journals across 37 subject categories (Table 1).

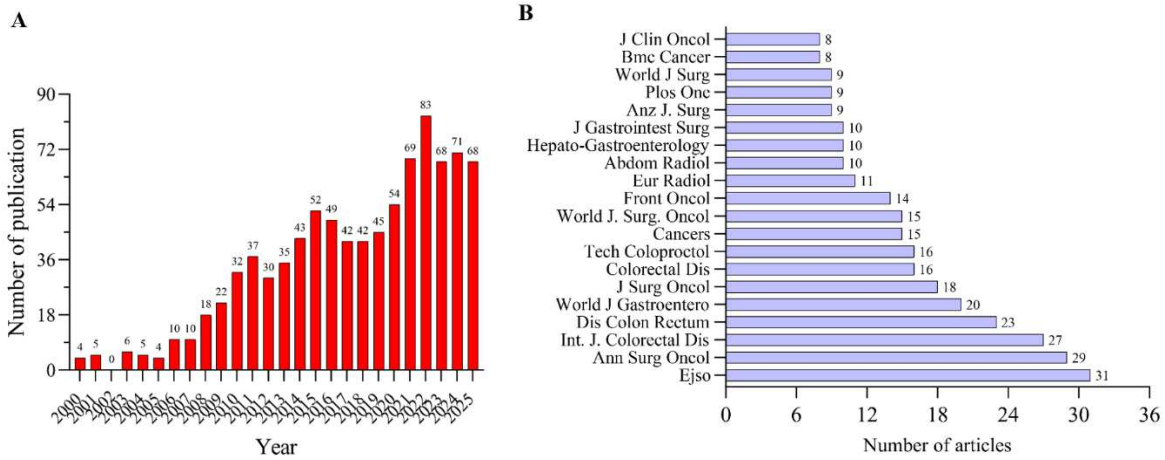
The annual publication trend, illustrated in Figure 1A, showed minimal output in 2000 (n=4) and 2001 (n=5), remained low during 2000-2005, increased steadily from 2006 to 2019, accelerated after 2019, and peaked in 2022.

Among the journals, EJSO published the most papers (n=30), followed by Annals of Surgical Oncology (n=22) and the International Journal of Colorectal Disease (n=17). Figure 1B lists the top 20 journals by publication volume, providing empirical reference for authors selecting where to submit their work.

Table 1 Basic Information on Publication Distribution

Categories	Publication	Articles	Review	Authors	Institutions	Journals	Subject categories
Amount	904	784	120	5738	1432	281	37

Fig.1.



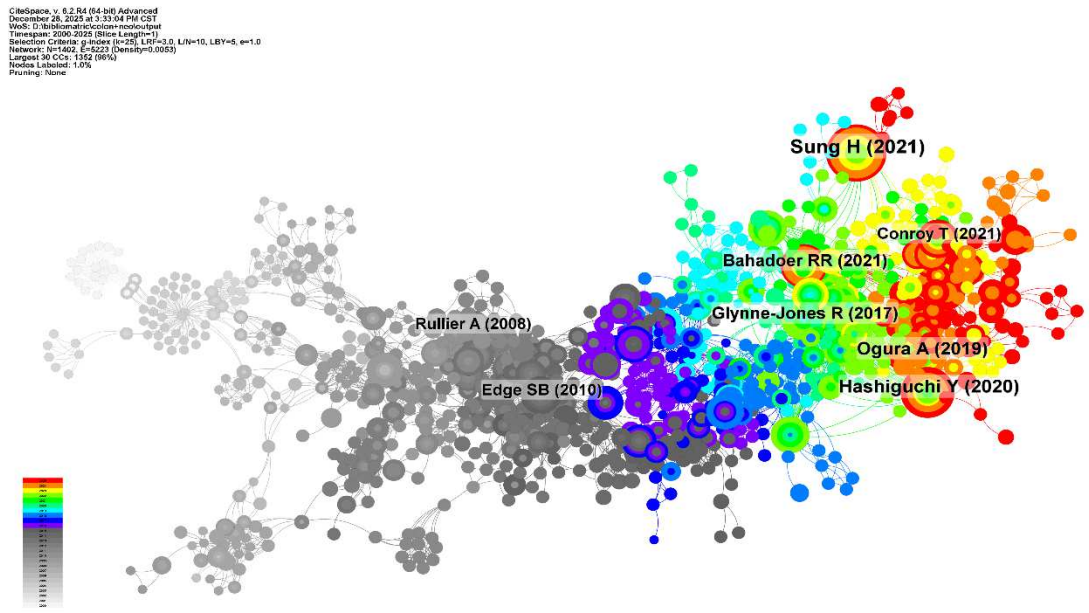
A: Annual number of publications (publications per year).. B: Journal publication output (publications in the top 20 journals).

3.1.2 Research Trajectory of NAT on Lymph Nodes in CRC

We used a reference co-citation network (Figure 2) to delineate the knowledge structure and

intellectual evolution of research on NAT and lymph node–related issues in CRC over two decades. The network, comprising 936 nodes and 2,759 links, revealed dense citation relationships among publications in this field. In the early stage (2000–2015; gray nodes), the publications showed high node density and extensive connectivity, thereby establishing the foundational knowledge base of the field. Mid-period publications (2016–2020; blue nodes) gradually expanded and gave rise to the major research branches. Recent work (2021–2025; multicolored nodes) further converged into compact clusters, reflecting both thematic consolidation and diversification.

Fig.2.



Reference co-citation network (the color bar from left [white] to right [red] indicates the years 2000–2025).

In terms of co-citation frequency, 10 publications demonstrated substantial academic influence, with co-citation counts ranging from 19 to 45 (e.g., Sung H [2021], Hashiguchi Y [2020], Ogura A [2019]). Additionally, we utilized HisCite Pro 2.1 to construct a citation historiography graph for the research articles (Table S1). The key landmark publications are prominently featured in Table 2, the top three GCS papers are “Lymph nodes after Preoperative chemoradiotherapy for rectal carcinoma: Number, status, and impact on survival” 、”Lymph node evaluation in colorectal cancer patients: A population-based study”and”Challenging the Feasibility and Clinical Significance of Current Guidelines on Lymph Node Examination in Rectal Cancer in the Era of Neoadjuvant Therapy”. In the co-citation network, node size correlates with importance, and link number is associated with betweenness centrality.Collectively,these analyses clarified the field’s citation backbone and facilitated the identification of pivotal references. The subsequent timeline visualization will more intuitively illustrate the clustering patterns of these key themes.

Table 2.

The information of the top 30 literature sorted by LCS score.

NO.	Article information	Journal	LCS	GCS
48	Lymph nodes after Preoperative chemoradiotherapy for rectal carcinoma:Number, status, and. impact on survival	AM J SURG PATHOL	57	156
22	Lymph node evaluation in colorectal cancer patients: A population-based study	J NATL CANCER I	44	433
153	Challenging the Feasibility and Clinical Significance of Current Guidelines on Lymph Node Examination in Rectal Cancer in the Era of Neoadjuvant Therapy	J CLIN ONCOL	29	81
90	Lymph node yield in rectal cancer surgery: Effect of preoperative chemoradiotherapy	EJSO-EUR J SURG ONC	28	76
171	The Effects of Preoperative Chemoradiotherapy on Lymph Node Sampling in Rectal Cancer	DIS COLON RECTUM	27	73
369	Lymph node yield after rectal resection in patients treated with neoadjuvant radiation for rectal cancer: A systematic review and meta-analysis	EUR J CANCER	26	86
55	Prognostic implications of the distribution of lymph node metastases in rectal cancer after neoadjuvant chemoradiotherapy	J CLIN ONCOL	26	72
66	Reduced Lymph Node Yield in Rectal Carcinoma Specimen After Neoadjuvant Radiochemotherapy Has No Prognostic Relevance	WORLD J SURG	26	78
222	Prognostic implications of the lymph node count after neoadjuvant treatment for rectal cancer	BRIT J SURG	25	50
98	Fewer Than 12 Lymph Nodes Can be Expected in a Surgical Specimen After High-Dose Chemoradiation Therapy for Rectal Cancer	DIS COLON RECTUM	24	68
100	Open versus laparoscopic surgery for mid or low rectal cancer after neoadjuvant chemoradiotherapy (COREAN trial): short-term outcomes of an open-label randomised controlled trial	LANCET ONCOL	23	816
81	Lymph Node Retrieval in Rectal Cancer is Dependent on Many Factors-the Role of the Tumor, the Patient, the Surgeon, the Radiotherapist, and the Pathologist	AM J SURG PATHOL	20	102
83	Lymph Node Status After Neoadjuvant Radiotherapy for Rectal Cancer Is a Biologic Predictor of Outcome	CANCER	19	61
52	The impact of surgeon and pathologist on lymph node retrieval in colorectal cancer and its impact on survival for patients with Dukes' stage B disease	COLORECTAL DIS	17	101
75	The Prognostic Impact of the Number of Lymph Nodes Retrieved After Neoadjuvant Chemoradiotherapy With Mesorectal Excision for Rectal Cancer	J SURG ONCOL	17	34
86	Preoperative Chemoradiotherapy Does Not Necessarily Reduce Lymph Node Retrieval in Rectal Cancer	J GASTROINTES	15	34

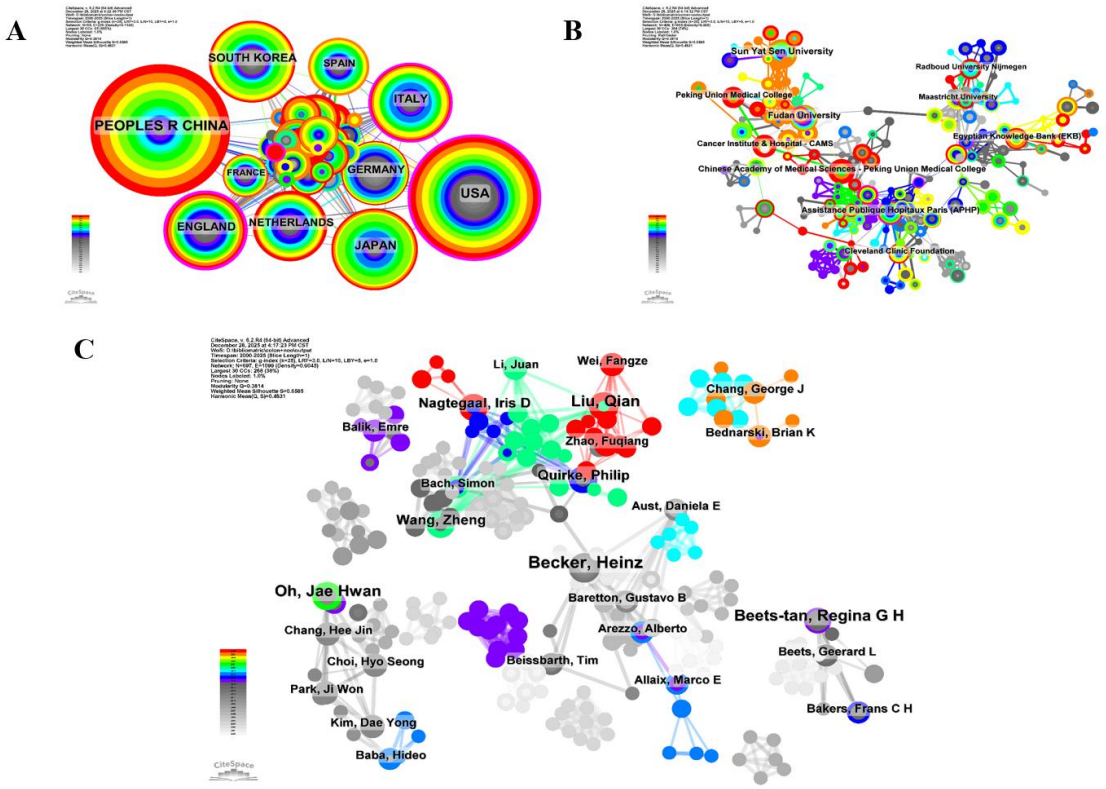
	Specimens-Results from a Prospective Evaluation with Extensive Pathological Work-up	T SURG		
196	Prognostic significance of lymph node yield after long-course preoperative radiotherapy in patients with rectal cancer: a systematic review	COLORECTAL DIS	13	127
41	Colorectal tumour deposits in the mesorectum and pericolon; a critical review	HISTOPATHOLOGY	13	22
377	Tumor Deposits in Colorectal Cancer: Improving the Value of Modern Staging-A Systematic Review and Meta-Analysis	J CLIN ONCOL	12	325
79	Randomized clinical trial comparing laparoscopic and open surgery in patients with rectal cancer	BRIT J SURG	12	220
227	Prognostic significance of tumor budding in rectal cancer biopsies before neoadjuvant therapy	MODERN PATHOL	11	120
308	Impact of Total Lymph Node Count on Staging and Survival After Neoadjuvant Chemoradiation Therapy for Rectal Cancer	ANN SURG ONCOL	10	34
385	Lymph node yield is an independent predictor of survival in rectal cancer regardless of receipt of neoadjuvant therapy	J CLIN PATHOL	10	33
239	Metastatic lymph node ratio in stage III rectal carcinoma is a valuable prognostic factor even with less than 12 lymph nodes retrieved: a prospective study	AM J SURG	9	66
206	Lymph Node Metastases in Rectal Cancer After Preoperative Radiochemotherapy Impact of Intramesorectal Distribution and Residual Micrometastatic Involvement	AM J SURG PATHOL	9	24
290	MRI of Rectal Cancer: An Overview and Update on Recent Advances	AM J ROENTGENOL	9	28
31	Lymph node status and TS gene expression are prognostic markers in stage II/III rectal cancer after neoadjuvant fluorouracil-based chemoradiotherapy	J CLIN ONCOL	9	116
285	Implications of lymph node retrieval in locoregional rectal cancer treated with chemoradiotherapy: A California Cancer Registry Study	EJSO-EUR J SURG ONC	8	99
205	Gadofosveset-enhanced MRI for the assessment of rectal cancer lymph nodes: predictive criteria	ABDOM IMAGING	8	20
120	The Prognostic Value of Lymph Node Ratio After Neoadjuvant Chemoradiation and Rectal Cancer Surgery	DIS COLON RECTUM	8	22

LCS: The total local citation score.GCS: The total global citation score. NO: The number of the literature in the database import into HistCite Pro 2.1.

3.1.3 Scientific cooperation

The co-occurrence network revealed extensive research partnerships across countries, institutions, and authors, as indicated by the high density of nodes and links (Figure 3) . The country collaboration network (Figure 3A) comprises 65 nodes and 239 links, with China, the United States, Japan, and South Korea showing the largest node sizes. The institutional network (Figure 3B, 409 nodes, 665 links) highlighted several key nodes, including Sun Yat-sen University, Fudan University, and the Chinese Academy of Medical Sciences & Peking Union Medical College in China, as well as Assistance Publique–Hôpitaux de Paris (AP-HP). Furthermore, the author collaboration network (Figure 3C) identified active individual contributors, such as Heinz Becker, Qian Liu, Jae Hwan Oh, and Regina G. H. Beets-Tan. The tight links among these author nodes signified close cooperative relationships.

Fig.3.



The scientific collaboration network.A:Country collaboration network,B:Institutional collaboration network (institutions show strong collaboration both internationally and within individual countries),C. Author collaboration network.

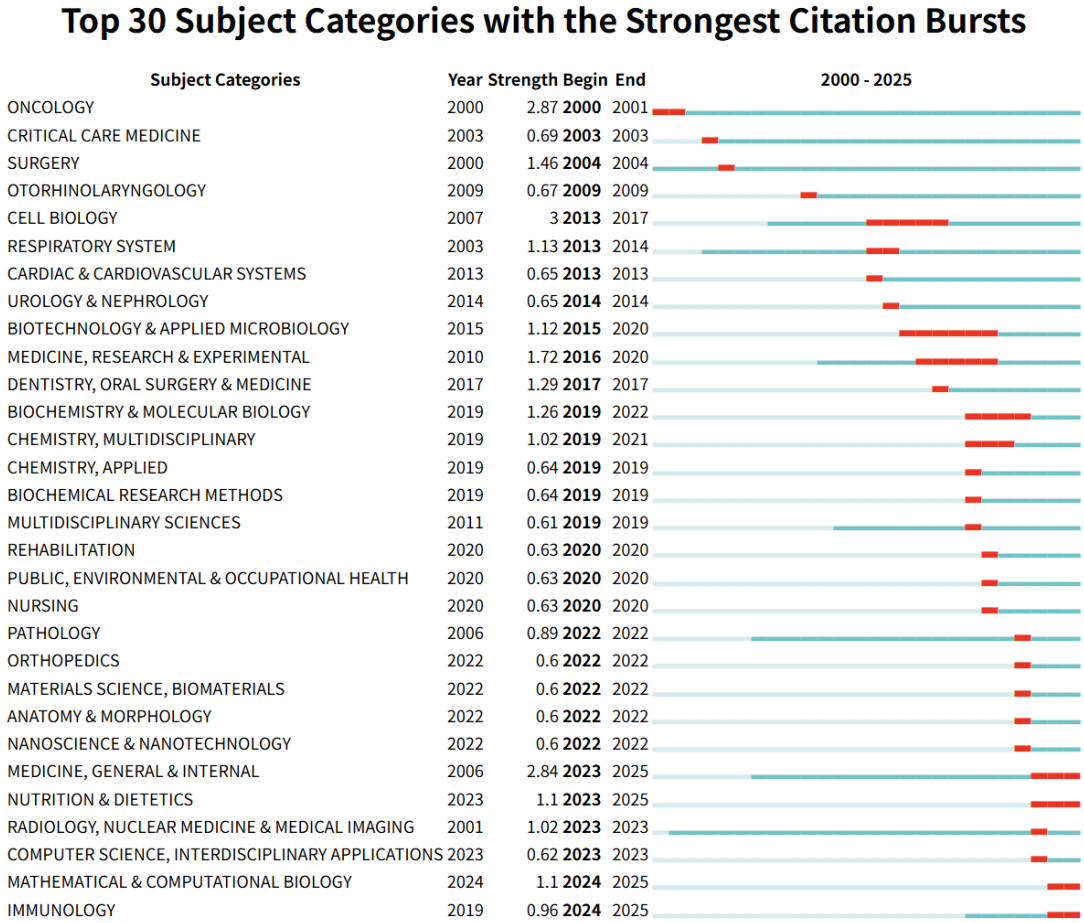
3.2 Variation of the most active topics

3.2.1 Subject category citation bursts

Our analysis detected citation bursts in 34 of the 37 subject categories between 2000 and 2023 (Figure 4). In this figure, the overall timeline is represented by blue bars, with active burst periods for each category highlighted in red. Among the top 50 categories ranked by burst strength, ONCOLOGY showed the earliest and strongest burst (2.87) during 2000–2001. Over time, burst activity diversified across disciplines, with notable surges in CRITICAL CARE MEDICINE (2003),

CELL BIOLOGY (2013–2017), MEDICINE, RESEARCH & EXPERIMENTAL (2016–2020), and MEDICINE, GENERAL & INTERNAL (2023–2025). This pattern reflects the field's strong interdisciplinary character. Notably, 20 subject categories showed persistent bursts through 2025 (Table S2). The three strongest ongoing bursts were in MEDICINE, GENERAL & INTERNAL, NUTRITION & DIETETICS, and MATHEMATICAL & COMPUTATIONAL BIOLOGY.

Fig.4.

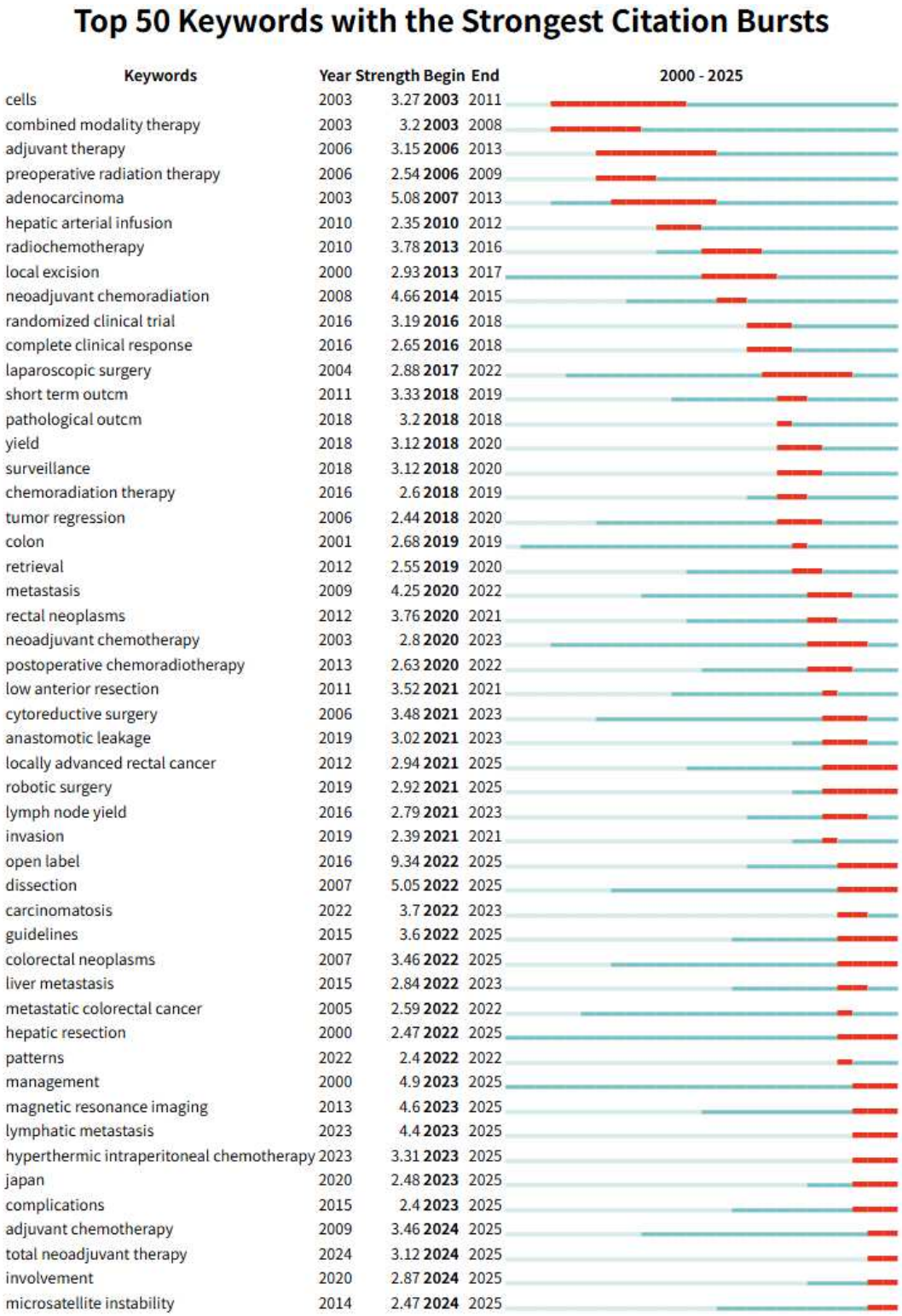


Top 30 most-cited subject categories. Year: First occurrence year; Strength: Burst strength; Begin: Burst start year; End: Burst end year.

3.2.2 Keywords burst

By analyzing keyword burst patterns, we further elucidated the evolutionary trends of research hotspots in NAT and lymph node-related fields of CRC from 2000 to 2025. A total of 500 keywords exhibited citation bursts, with the top 50 shown in Figure 5. Specifically, "open label" demonstrated the strongest burst (9.34) during 2022–2025. "adenocarcinoma" showed a notable burst (5.08) from 2007 to 2013, while "dissection" emerged with a burst strength of 5.05 (2022–2025). Notably,20 keywords maintained active bursts through 2025 (Table S2), potentially indicating future research directions in this field. For example, "MRI" showed a burst strength of 4.6 in 2023–2025, "lymphatic metastasis" 4.4 in 2023–2025, "guidelines" 3.6 in 2022–2025, and "adjuvant chemotherapy" 3.46 in 2024–2025. Overall, these persistently active keywords, to some extent, reflect the field's current research priorities and trajectory.

Fig.5.



Top 50 keywords with the strongest citation bursts.

3.2.3 Reference burst

A total of 1,361 references with citation bursts were identified. Table 3 presents the top 30 most frequently cited references from 2000 to 2025. The reference with the strongest citation burst was “Neoadjuvant (Chemo)radiotherapy With Total Mesorectal Excision Only Is Not Sufficient to Prevent Lateral Local Recurrence in Enlarged Nodes: Results of the Multicenter Lateral Node Study of Patients With Low cT3/4 Rectal Cancer” (2020–2025). The study included 1,216 patients with low cT3/T4 rectal cancer to investigate the clinical significance of lateral lymph nodes (LLNs) in rectal cancer treatment and the value of LLND. Key findings demonstrated that a preoperative MRI‐measured LLN short-axis diameter ≥7 mm was an independent risk factor for lateral local recurrence (LLR). Critically, for these high-risk patients, adding LLND to chemoradiotherapy and total mesorectal excision (TME) significantly reduced the 5-year LLR rate from 19.5% to 5.7%, indicating that LLND substantially decreased the risk of lateral recurrence.

Table 3

The references with citation bursts at different period.

References	Year	Strength	Begin	End	2000 - 2025
Sauer R, 2004, NEW ENGL J MED, V351, P1731, DOI 10.1056/NEJMoa040694, DOI	2004	9.98	**2006**	2009	
Baxter NN, 2005, INT J RADIAT ONCOL, V61, P426, DOI 10.1016/j.ijrobp.2004.06.259, DOI	2005	6.08	**2008**	2010	
Rullier A, 2008, AM J SURG PATHOL, V32, P45, DOI 10.1097/PAS.0b013e3180dc92ab, DOI	2008	9.95	**2009**	2013	
Habr-Gama A, 2008, DIS COLON RECTUM, V51, P277, DOI 10.1007/s10350-007-9148-5, DOI	2008	7.45	**2009**	2013	
Frédérique P, 2008, ANN SURG, V248, P1067, DOI 10.1097/SLA.0b013e31818842ec, DOI	2008	6.29	**2010**	2013	
Edge SB, 2010, AJCC CANCER STAGING MANUAL, V649, P0	2010	9.75	**2011**	2015	
Doll D, 2009, WORLD J SURG, V33, P340, DOI 10.1007/s00268-008-9838-8, DOI	2009	6.32	**2011**	2014	
van Gijn W, 2011, LANCET ONCOL, V12, P575, DOI 10.1016/S1470-2045(11)70097-3, DOI	2011	7.07	**2013**	2016	
Al-Sukhni E, 2012, ANN SURG ONCOL, V19, P2212, DOI 10.1245/s10434-011-2210-5, DOI	2012	6.63	**2013**	2017	
Edge SB, 2010, ANN SURG ONCOL, V17, P1471, DOI 10.1245/s10434-010-0985-4, DOI	2010	6.07	**2013**	2015	
Miller ED, 2012, DIS COLON RECTUM, V55, P1002, DOI 10.1097/DCR.0b013e3182536d70, DOI	2012	9.31	**2014**	2017	
van der Pas MHGM, 2013, LANCET ONCOL, V14, P210, DOI 10.1016/S1470-2045(13)70016-0, DOI	2013	9.15	**2015**	2018	
Sauer R, 2012, J CLIN ONCOL, V30, P1926, DOI 10.1200/JCO.2011.40.1836, DOI	2012	6.79	**2015**	2017	
Govindarajan A, 2011, J CLIN ONCOL, V29, P4568, DOI 10.1200/JCO.2011.37.2235, DOI	2011	6.44	**2015**	2016	
Kim HJ, 2015, ANN SURG ONCOL, V22, P2075, DOI 10.1245/s10434-014-4235-z, DOI	2015	5.97	**2017**	2020	
Mechera R, 2017, EUR J CANCER, V72, P84, DOI 10.1016/j.ejca.2016.10.031, DOI	2017	8.66	**2018**	2022	
Glynne-Jones R, 2017, ANN ONCOL, V28, P22, DOI 10.1093/annonc/mdx224, DOI	2017	13.12	**2019**	2022	
Beets-Tan RGH, 2018, EUR RADIOL, V28, P1465, DOI 10.1007/s00330-017-5026-2, DOI	2018	7.21	**2019**	2023	
Ogura A, 2019, J CLIN ONCOL, V37, P33, DOI 10.1200/JCO.18.00032, DOI	2019	13.47	**2020**	2025	
Benson A III, 2018, J NATL COMPR CANC NE, V16, P874, DOI 10.6004/jnccn.2018.0061, DOI	2018	8.24	**2020**	2023	
Fujita S, 2017, ANN SURG, V266, P201, DOI 10.1097/SLA.0000000000002212, DOI	2017	8.11	**2020**	2022	
Sung H, 2021, CA-CANCER J CLIN, V71, P209, DOI 10.3322/caac.21660, DOI	2021	18.23	**2021**	2025	
Hashiguchi Y, 2020, INT J CLIN ONCOL, V25, P1, DOI 10.1007/s10147-019-01485-z, DOI	2020	12.72	**2021**	2025	
Bahadoer RR, 2021, LANCET ONCOL, V22, P29, DOI 10.1016/S1470-2045(20)30555-6, DOI	2021	10.86	**2021**	2025	
Conroy T, 2021, LANCET ONCOL, V22, P702, DOI 10.1016/S1470-2045(21)00079-6, DOI	2021	9.39	**2022**	2025	
Chalabi M, 2020, NAT MED, V26, P566, DOI 10.1038/s41591-020-0805-8, DOI	2020	6.69	**2022**	2025	
Morton D, 2023, J CLIN ONCOL, V41, P1541, DOI 10.1200/JCO.22.00046, DOI	2023	7.29	**2023**	2025	
Cercek A, 2022, NEW ENGL J MED, V386, P2363, DOI 10.1056/NEJMoa2201445, DOI	2022	6.24	**2023**	2025	
Benson AB III, 2022, J NATL COMPR CANC NE, V20, P1139, DOI 10.6004/jnccn.2022.0051, DOI	2022	9.16	**2024**	2025	
Benson A, 2021, J NATL COMPR CANC NE, V19, P329, DOI 10.6004/jnccn.2021.0012, DOI	2021	6.86	**2024**	2025	

The second-ranked reference was “Japanese Society for Cancer of the Colon and Rectum (JSCCR) guidelines 2019 for the treatment of colorectal cancer” (2021–2025). As colorectal cancer mortality in Japan continues to rise (exceeding 50,000 in 2016), the guideline aimed to narrow inter-institutional practice gaps, prevent over- and undertreatment, and foster shared understanding between clinicians and patients. Formulated by an expert committee, they integrated the latest evidence with Japan’s clinical practice. Notably, the guidelines adopted a question-oriented format, grading each recommendation by level of evidence and strength. This structured approach provided a critical tool for guiding clinical practice and facilitating individualized treatment decisions.

The reference with the third-highest citation burst was “Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial.” The trial evaluated the efficacy of short-course radiotherapy followed by chemotherapy with delayed surgery (experimental arm) versus conventional long-course preoperative chemoradiotherapy (standard treatment arm) in patients with high-risk locally advanced rectal cancer. As a result, the experimental regimen significantly reduced disease-related treatment failure (3-year cumulative incidence 23.7% vs 30.4%;HR 0.75; p=0.019), primarily by lowering the rate of distant metastasis. Although the experimental group had a higher incidence of severe (grade ⩾3) diarrhea during NAT, overall serious adverse event rates were comparable between groups. Thus, the RAPIDO trial established this NAT approach as a viable new standard of care for this high-risk patient population.

Since 2025, citation bursts have been detected in 78 references. Table 4 presents the top 20 references ranked by impact index, including five reviews and 15 original studies. Notably, the citation burst for each of these publications began either in its year of publication or the year immediately following. Review articles provided a crucial theoretical framework and future direction for research on lymph node changes after neoadjuvant treatment for CRC. In contrast, the original studies offered direct reference value for clinical practice and further research. This finding suggests that researchers should pay more attention to these high-impact publications better grasp the field’s leading edge and central advances.

Table 4
The references with citation bursts from beginning to 2025.

be’gin	end	Strebgth	Year	Type	Title
2020	2025	13.47	2019	Article	Neoadjuvant (Chemo)radiotherapy With Total Mesorectal Excision Only Is Not Sufficient to Prevent Lateral Local Recurrence in Enlarged Nodes: Results of the Multicenter Lateral Node Study of Patients With Low cT3/4 Rectal Cancer
2021	2025	10.86	2021	Article	Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial
2022	2025	9.39	2021	Article	Neoadjuvant chemotherapy with FOLFIRINOX

					and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial
2024	2025	9.16	2022	Article	Rectal Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology
2023	2025	7.29	2023	Article	Preoperative Chemotherapy for Operable Colon Cancer: Mature Results of an International Randomized Controlled Trial
2024	2025	6.86	2021	Review	Colon Cancer, Version 2.2021, NCCN Clinical Practice Guidelines in Oncology
2022	2025	6.69	2020	Article	Neoadjuvant immunotherapy leads to pathological responses in MMR-proficient and MMR-deficient early-stage colon cancers
2023	2025	6.24	2022	Article	PD-1 Blockade in Mismatch Repair-Deficient, Locally Advanced Rectal Cancer
2023	2025	5.72	2020	Review	Localised colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up
2023	2025	5.37	2020	Article	Pembrolizumab in Microsatellite-Instability-High Advanced Colorectal Cancer
2023	2025	4.68	2022	Article	Organ Preservation in Patients With Rectal Adenocarcinoma Treated With Total Neoadjuvant Therapy
2024	2025	4.57	2023	Article	Preoperative Treatment of Locally Advanced Rectal Cancer
2024	2025	4.57	2023	Review	Metastatic colorectal cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up
2023	2025	3.63	2022	Article	Pembrolizumab versus chemotherapy for microsatellite instability-high or mismatch repair-deficient metastatic colorectal cancer (KEYNOTE-177): final analysis of a randomised, open-label, phase 3 study
2024	2025	3.42	2022	Article	Magnetic Resonance Imaging Directed Surgical Decision Making for Lateral Pelvic Lymph Node Dissection in Rectal Cancer After Total Neoadjuvant Therapy (TNT)
2024	2025	3.18	2020	Review	The multidisciplinary management of rectal cancer
2024	2025	3.14	2020	Article	Oncological Impact of Lateral Lymph Node Dissection After Preoperative Chemoradiotherapy in Patients with Rectal Cancer

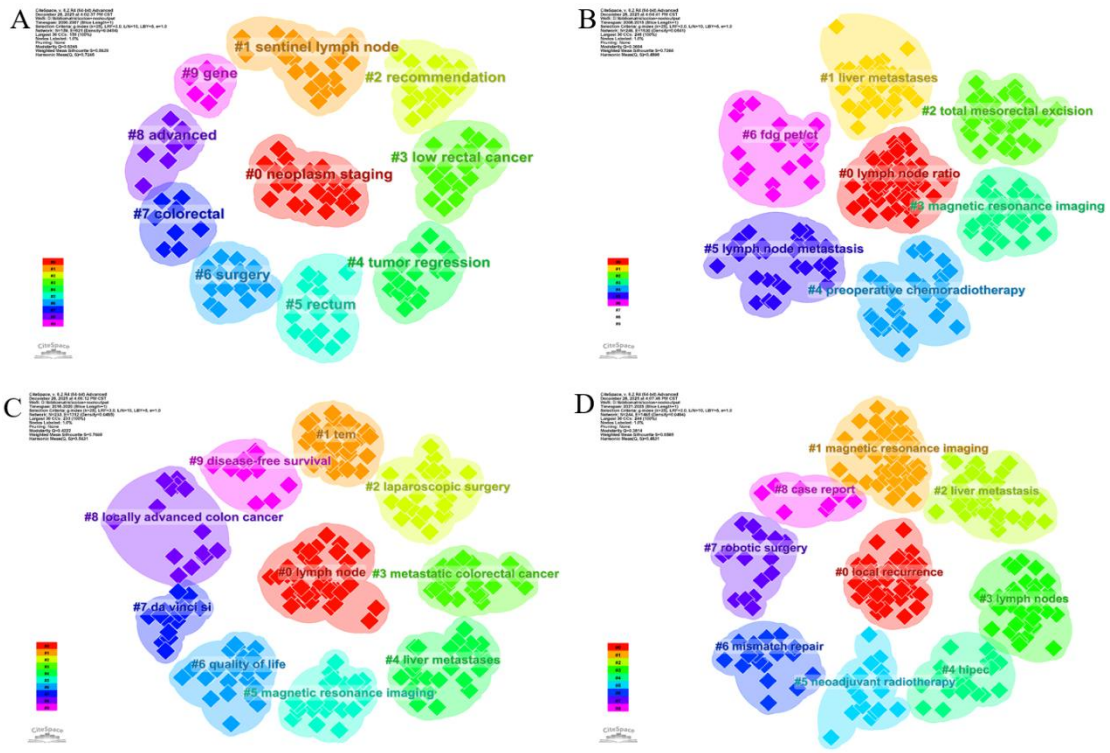
2023	2025	3.11	2021	Review	Neoadjuvant chemotherapy in locally advanced colon cancer: a systematic review and meta-analysis
2024	2025	2.85	2023	Article	Locoregional Failure During and After Short-course Radiotherapy Followed by Chemotherapy and Surgery Compared With Long-course Chemoradiotherapy and Surgery: A 5-Year Follow-up of the RAPIDO Trial
2024	2025	2.6	2021	Article	Optimal Size Criteria for Lateral Lymph Node Dissection After Neoadjuvant Chemoradiotherapy for Rectal Cancer

3.3 Emerging trends and new developments

3.3.1 Temporal evolution of keyword clusters

Keyword clustering analysis identified hotspot themes and evolutionary trends in lymph node–related research on NAT for CRC. Figure 6 depicts the cluster distributions across four time periods from 2000 to 2025. In 2000–2010, 52 publications formed 10 clusters, centered on tumor staging, sentinel lymph nodes, and therapeutic guidelines. From 2011 to 2015, 50 publications were clustered into 7 groups involving lymph node ratio, liver metastasis, and total mesorectal excision (TME). In 2016–2020, 88 publications were assigned to 10 clusters, including lymph node assessment, TME, and laparoscopic surgery. In 2021–2025, 354 publications formed nine clusters, with emphasis on local recurrence, MRI, and liver metastasis.

Fig.6.



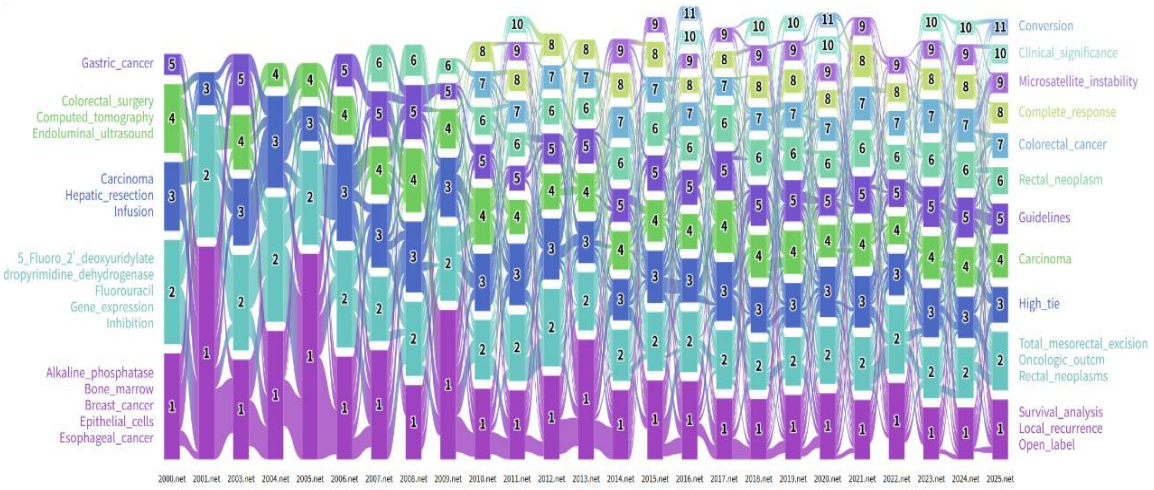
A:Keyword clustering for 2000–2007 (different colors indicate different clusters),B: Keyword clustering for 2008–2015, C:Keyword clustering for 2016–2020,D: Keyword clustering for 2021-

2025.

We noticed that classic topics (e.g., sentinel lymph nodes, low rectal cancer) remained actively studied, while emerging clusters (e.g., local recurrence, robotic surgery, mismatch repair) have become increasingly prominent in recent years, indicating a dynamic shift in research hotspots. Publications within these emerging clusters primarily address current key issues regarding lymph node changes in CRC in the context of NAT. Specifically, the "local recurrence" cluster (#0) included 49 publications on this topic. The "liver metastasis" cluster (#2) encompassed 38 related studies, the "mismatch repair" cluster (#6) contained 17 publications, and the "robotic surgery" cluster (#7) covered 16 studies. Detailed data for phase IV clusters in 2021–2025 were provided in Table S3. Notably, the representative keywords within clusters help pinpoint the core research directions of NAT in the field of lymph node changes in CRC in this recent period.

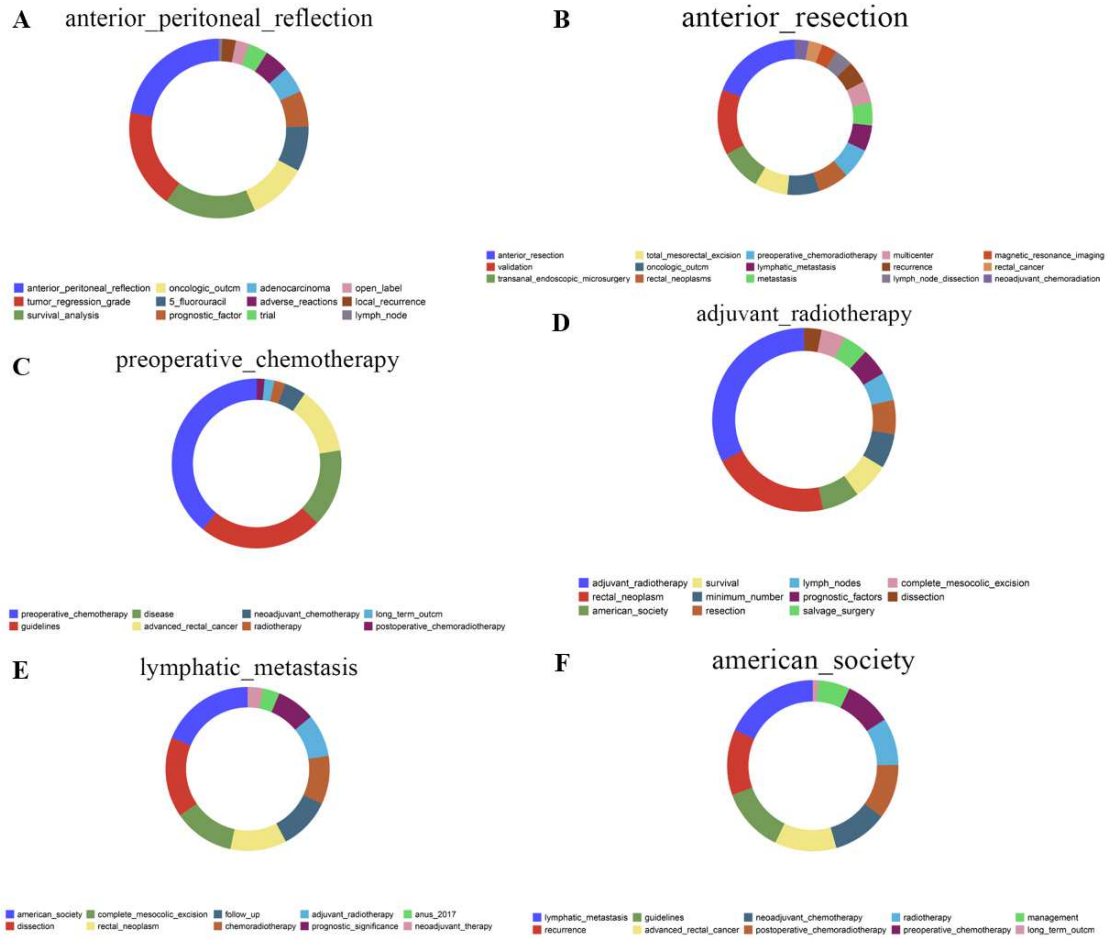
3.3.2 Keyword alluvial flow visualization

Figure 7 showed the alluvial flow diagram illustrating how keywords reorganize over time into dynamically evolving research modules. Over the two-decade analysis period (2000–2025), some keywords sustained persistent activity, others emerged as new trends, while some gradually faded. Table S4 (supplementary materials) presents the most frequently used keyword annually for each of the top five modules.The keywords comprising Module 1 demonstrated remarkable continuity through divergence and convergence, establishing it as the largest and most enduring research tributary (purple-marked section). We further mapped the keywords from the top six modules in 2025 (Figure 8). Specifically, Module 1, named "anterior_peritoneal_reflection," comprises 12 keywords, including tumor_regression_grade, survival_analysis, and oncologic_outcome (Figure 8A). Module 2, named "anterior_resection," comprises 15 keywords, including validation and transanal_endoscopic_microsurgery (Figure 8B). Module 3, named "preoperative_chemotherapy," comprises 8 keywords, including guidelines and disease (Figure 8C). Module 4, named "adjuvant_radiotherapy," comprises 11 keywords, including rectal_neoplasm and american_society (Figure 8D). Module 5, termed "lymphatic_metastasis," collected 10 keywords, including recurrence and guidelines (Figure 8E). Module 6, termed "american_society," contained 10 keywords, including dissection and complete_mesocolic_excision (Figure 8F). Collectively, these modules may represent emerging trends in studies of lymph node changes following NAT for CRC in forthcoming years.
Fig.7.



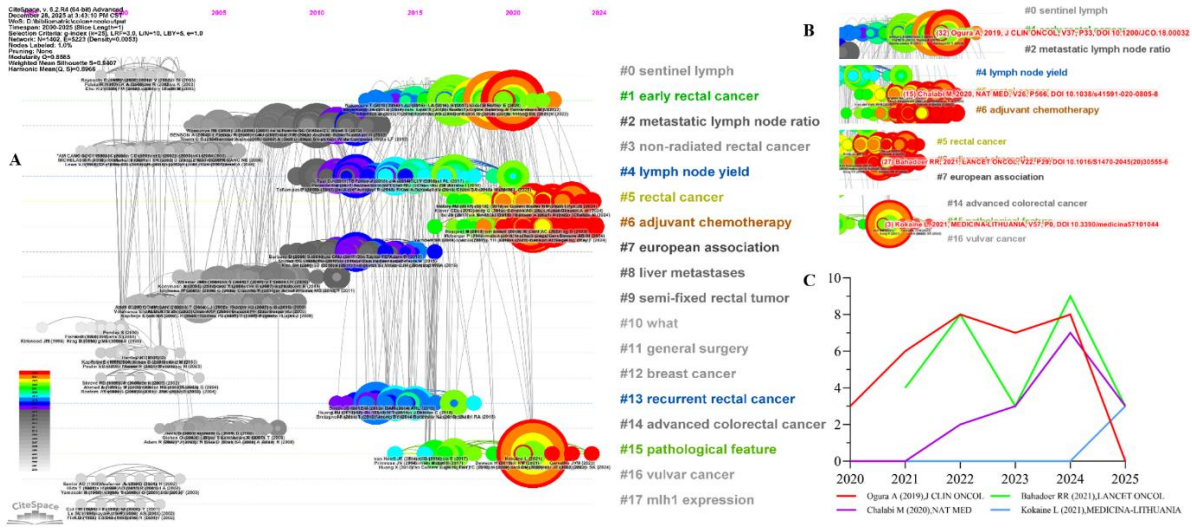
Alluvial diagram of keywords for 2000-2025; the x-axis represents time and the y-axis represents modules. Number: Modules per time slice sorted by node count.

Fig.8.



The keywords of top 6 modules in 2025. A: Module 1. B: Module 2. C: Module 3. D: Module 4. E: Module 5. F: Module 6.

Fig.9.



The reference clusters map. A: Timeline view of co-cited references,B:Burst references in clusters #1, #5, #6, and #15, C:Burst citation frequency distribution.

3.3.3. Timeline visualization of references

Timeline visualization clearly depicted the dynamic evolution of research themes, delineating emerging foci, classic topics, and areas of declining interest. The timeline mapping of research on NAT and lymph nodes in colorectal cancer (Figure 9A) identified 18 clusters. However, classic topics such as lymph node ratio (#2), lymph node yield (#4), European society association (#7), and rectal cancer recurrence (#13) were no longer current hotspots, they maintained broad connections across the network and continued to underpin the field's knowledge structure. In contrast,emerging trends such as early rectal cancer (#1), rectal cancer (#5), adjuvant chemotherapy (#6), and pathological features (#15) have remained persistent activity.The sustained prominence suggests they are likely priority directions for future research(see Supplementary Table S5).

As shown in Figure 9B, several high-impact publications (indicated by large, red-circled nodes) played a pivotal role in driving the development of key subdomains. Through bibliometric analysis, we identified four major categories of pivotal publications in this field of lymph node changes following NAT for CRC, each defining a distinct research trajectory.

Studies on the clinical value of LLND. In Neoadjuvant Chemoradiotherapy With Total Mesorectal Excision Only Is Not Sufficient to Prevent Lateral Local Recurrence in Enlarged Nodes: Results of the Multicenter Lateral Node Study of Patients With Low cT3/4 Rectal Cancer (cited 32 times), Ogura et al. (2019) investigated the role of LLNs in local recurrence of rectal cancer based on multicenter data. The authors reported that patients with an LLN short-axis diameter ≥7 mm on MRI, adding LLND to TME significantly reduced the 5-year lateral local recurrence rate from 19.5% to 5.7% (P=0.042). This finding provided evidence for LLND to support improved local control in these high-risk patients.

Studies on pathological responses to neoadjuvant immunotherapy. Neoadjuvant immunotherapy leads to pathological responses in MMR-proficient and MMR-deficient early-stage colon cancers (co-occurring 15 times) evaluated the application of neoadjuvant immunotherapy in early-stage colon cancer. The results showed a 100% pathological response rate in dMMR tumors

(with 60% achieving complete response). In contrast, responses were observed in only 27% of pMMR tumors. The study found that intratumoral infiltration of $CD^{8+}PD\text{-}1^{+}$ T cells could predict efficacy in pMMR patients. This key insight highlights the translational potential of this strategy for biomarker-selected populations.

Efficacy validation of intensified neoadjuvant strategies. The landmark RAPIDO phase 3 trial(Short-course radiotherapy followed by chemotherapy before TME versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial) established a new treatment paradigm for high-risk locally advanced rectal cancer. It demonstrated that a strategy of short-course radiotherapy followed by chemotherapy and delayed surgery significantly reduced the risk of disease-related treatment failure compared to conventional long-course chemoradiotherapy (3-year incidence: 23.7% vs. 30.4%; HR 0.75; p=0.019).

Assessment of complete response and individualized treatment. Evaluation and Predictive Factors of Complete Response in Rectal Cancer after Neoadjuvant Chemoradiation Therapy systematically reviewed methods for assessing complete response and predictive factors after NAT. The authors emphasized that reliably identifying patients with complete response depends on multidisciplinary collaboration. This approach is crucial for selecting candidates for non-operative management and for developing individualized strategies.

Overall, these four categories of publications defined the field's core priorities across four dimensions: optimizing local control, advancing systemic therapy, refining treatment sequencing, and improving treatment-response assessment. We further analyzed the citation distributions of these four articles in recent years (Figure 9C), suggesting that they may be cited again in the coming years.

4 Discussion

4.1 Evolutionary Trajectory and Cutting-Edge Directions in the Field

Using bibliometric analysis, we systematically reviewed the structural and temporal dynamics of research on lymph node changes following NAT for CRC from 2000 to 2025. Our analysis reveals that the field is in a highly active and pivotal phase of development, characterized by a rapid increase in publications(Figure 1), extensive interdisciplinary collaboration, and densely interconnected citation networks(Figure 2). Although hotspots have shifted over time, our integrated analysis revealed a significant convergence on several key frontiers. This convergence is evident across multiple metrics: emerging keywords (Figure 5), references with citation bursts (Table 2), and recent keyword (Figure 6D) and co-citation clusters (Figures 9A).

The identified frontier directions are: (1) Refinement of LLN management: the emergent term "dissection" appears in 2022–2025 in Figure 5, with highly emergent LLN publications such as Ogura et al., listed in Table 4). (2) Standardization of imaging and pathological assessment for response evaluation after NAT: the rising term "MRI" in 2023–2025 in Figure 5, and keyword cluster #0 "local recurrence" in 2021–2025 in Figure 6D. (3) Exploration of neoadjuvant immunotherapy regimens and their pathological response characteristics: keyword cluster #6 "mismatch repair" in 2021–2025 in Figure 6D, with related high-frequency literature in Table 4. (4) Individualized treatment strategies and organ preservation based on deep remission: emergent term "deep remission" in 2023–2025 in Figure 5, with relevant high-frequency literature in Table 4. These findings reveals a coherent research trajectory that underpins the current core network and guides

future exploration.

The evolving research landscape and its clinical implications. Our analysis revealed a notable acceleration in annual publication output after 2019, peaking in 2022. This surge in research activity directly parallels the clinical shift towards intensified neoadjuvant strategies, such as total NAT, and the adoption of immunotherapy for mismatch repair–deficient (dMMR) tumors. Essentially,the growing literature reflects an urgent clinical need to better understand and standardize the assessment of treatment-induced lymph node changes—a factor critical for prognosis and subsequent therapy[23]. Furthermore,the field's strong foundation in surgical and oncological research is evidenced by its primary publication venues (e.g.,EJSO,Annals of Surgical Oncology).At the same time,its broad span across 37 subject categories underscores its fundamentally interdisciplinary character.

The co-citation network (Figures 3 and 10) showed a tightly interwoven knowledge system. In the early 21st century, foundational research on the prognostic impact of lymph node detection rates and nodal status following chemoradiotherapy gradually emerged as a major direction in oncology[24-27]. Subsequently, research branches diverged into specialized clusters addressing specific challenges: the clinical significance of lymph node ratios amid declining detection rates, the role of MRI in restaging, the controversy surrounding LLND, and the recent focus on pathological responses to neoadjuvant immunotherapy[28-34]. This evolution—from "foundation building" to "topic deepening"—signifies a field transitioning from an exploratory phase toward maturity and refinement.

Cooperative Models and Evolving Geographic Patterns in Scientific Research. The extensive collaboration networks at national, institutional, and author levels reflect a concerted global effort to address this complex clinical challenge. Research leadership is concentrated in countries such as China, the United States, and Japan, and in major institutions like Sun Yat-sen University and Assistance Publique–Hôpitaux de Paris (AP-HP), which serve as hubs for large-scale clinical trials and multi-institutional studies. These hubs are pivotal, as they generate high-level evidence and drive the standardization of clinical practice[35, 36]. Moreover, the tight interconnections within these networks facilitate the rapid cross-border dissemination of knowledge and methodologies. This, in turn, accelerates consensus on debated issues, such as establishing the optimal lymph node yield threshold after neoadjuvant therapy.

The trajectory of research focus from anatomy to biology and imaging.

Analysis of keyword emergence and clustering across four time periods clearly maps the evolution of this field's academic priorities. The early phase (2000–2007) was dominated by anatomical and pathological themes—such as "staging," "sentinel lymph nodes," and "number of detected lymph nodes"—focusing on standardizing the assessment of static, postoperative specimens. Substantial shifts emerged thereafter. The emergence of terms such as "LLND" and "MRI" in the recent phase (2021–2025), together with a sharp rise in citation intensity for core literature on "neoadjuvant immunotherapy" (Tables 3 and 4). Collectively, these signals signify a transformation toward spatial precision (targeting specific lymph node regions like the lateral zone), functional and biological assessment (MRI-based prediction of treatment response and preoperative lymph node status), and novel systemic response patterns driven by immune checkpoint inhibitors.

Moreover, a surge in recent high-impact studies (e.g., trials on organ preservation following full-course neoadjuvant therapy) has emerged (Table 4). Though not forming an independent trunk in early keyword clusters, this trend clearly foreshadows a clinical goals: enabling treatment de-

escalation or avoiding radical surgery for select responders through precise response assessment, including nodal status[37, 38]. In summary,this trajectory demonstrates a paradigm shift—from static, post-treatment pathological description toward dynamic, multidimensional precision assessment and treatment optimization. The core objective is to transition from “group-based” to personalized therapy

4.2 Exploring Emerging Topics

Innovation, Limitations, and Future Directions. This study was the first bibliometric analysis to systematically map the evolution of lymph node research following neoadjuvant therapy for

CRC. Using complementary tools (CiteSpace, HistCite, alluvial plots, etc.), it provided a more comprehensive, quantitative overview of trends and latent connections within the literature than traditional narrative reviews.

Nevertheless, several limitations should be acknowledged. First,our analysis relied solely on the WoSCC, which may exclude relevant studies published in regional journals or non-English languages. Second,despite extending the search to 2025, the rapid pace of immunotherapy research may leave some recent breakthroughs underrepresented. Finally,bibliometrics assess impact and connectivity rather than direct research quality or clinical efficacy. Therefore, “hot” topics identified require careful appraisal through conventional critical reading [39, 40].

Notwithstanding these limitations, our findings highlight several promising avenues for future research.

Refining imaging-based lymph node staging. The prominent emergence of MRI as a restaging modality underscores a major research drive to enhance its accuracy. Future work should focus on integrating radiomics, AI-based image analysis, and novel contrast agents to reliably distinguish fibrotic lymph nodes from residual tumor deposits[41-44].

Defining novel lymph node response classifications. The prognostic value of traditional lymph node yield assessment has diminished in the context of neoadjuvant therapy. Consequently, there is a pressing need to develop and validate novel composite endpoints. These should integrate pathological tumor regression grade (TRG), residual nodal disease burden (including micro-metastases), and patterns of immune cell infiltration[45, 46].

Exploring new paradigms of lymph node response in the era of immunotherapy. The rapid rise in citations for recent literature underscores an urgent priority: to understand the distinct pathological alterations in lymph nodes following neoadjuvant immunotherapy. These include phenomena such as pathological complete response and the formation of tertiary lymphoid structures. Addressing this knowledge gap necessitates systematic translational research embedded within prospective clinical trials [47-50].

Optimizing surgical scope based on lymph node response. In the TNT era, the role of LLND requires further refinement. Future work should focus on identifying patient subgroups with LLN disease who may benefit from dissection despite a good systemic response, potentially integrating baseline MRI features and molecular biomarkers [51].

Integrating Artificial Intelligence into Pathology. Digital pathology and computational morphometrics offer objective, quantitative assessments of lymph node atrophy that outperform traditional microscopy. This approach promises to deliver more reproducible and prognostically powerful tools[52-54].

In summary, research advances are directly addressing pressing clinical challenges in diagnosis and treatment, sustaining a dynamic and collaborative global research ecosystem. The field’s focus

has evolved from fundamental pathological assessment toward image-guided, biology-integrated approaches for evaluating lymph node response. Translating insights on post-NAT nodal changes is thus critical for developing precise, individualized strategies that promise improved oncologic outcomes with reduced treatment-related morbidity. Future progress will hinge on integrating advances across imaging, molecular pathology, and immunotherapy.

Author contributions

Chun-Feng Xie: Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation. Pei-Dan Yang: Writing –review & editing ,original draft, Visualization. Wei-wei Qian: Investigation and data curation. Yun-xiang Xu: Investigation and data curation. Xu-shan Pan: Validation. Ren-chan Liao: Investigation. Dong-ming Luo: Supervision, Resources. Wen-ying Shang: data curation. Hai-hui Chen: Writing – review & editing, Supervision, Conceptualization. Jie Zheng: Supervision, Funding acquisition, Conceptualization.

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Declarations

Data availability statement:

This bibliometric analysis was conducted using publicly available published literature retrieved from Web of Science Core Collection. All data extracted and analyzed in this study are available within the article and its supplementary materials. The bibliometric analysis was performed using (CiteSpace/ HistCite Pro / R). No original patient data, clinical registries, or laboratory datasets were used in this study.

Conflict of interest statement

The authors have no conflict of interest.

Ethics statement

Not Applicable.

Clinical trial number

not applicable.

Consent to Publish declaration

not applicable.

Consent to Participate declaration:
not applicable.

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