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Bibliometric visualization of hepatocellular carcinoma and metabolic syndrome research: trends and emerging areas

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Abstract
A growing body of research has highlighted the increasing relevance of hepatocellular carcinoma (HCC) and metabolic syndrome (MetS). However, a comprehensive bibliometric visualization analysis on this topic remains lacking. In this study, we retrieved 310 related articles from the Web of Science Core Collection, spanning from January 1, 2014, to December 31, 2023. Using VOS viewer and Cite Space software, we analyzed the relationships among authors, journals, institutions, countries, keywords, and citations. Between 2014 and 2023, there has been a steady increase in publications on HCC and MetS, with the United States and China being the leading contributors in terms of publication volume. The visualization analysis revealed that obesity, insulin resistance, MAFLD, and liver cirrhosis are emerging areas in the intersection of HCC and MetS. Additionally, the international community is increasingly adopting the disease diagnosis term MAFLD, which, compared to NAFLD, shows improved diagnostic performance for predicting both hepatic and extra-hepatic outcomes. Furthermore, hypertension and cardiovascular diseases are emerging as promising new research fields.

Keywords Bibliometrics · Hepatocellular carcinoma · Metabolic syndrome · Visualization

1 Introduction

Hepatocellular carcinoma (HCC) is the predominant hepatic malignancy, characterized by its subtle onset, rapid progression, and poor prognosis [1, 2]. Metabolic syndrome (MetS) is a clinical condition marked by the clustering of abdominal obesity, dysregulated blood glucose levels, dyslipidemia, and hypertension, all of which significantly compromise overall health. The pathophysiological features of MetS, including insulin resistance (IR) and systemic inflammation, are both linked to carcinogenesis [3]. Epidemiological researches have established that MetS increases the risk of developing various cancers [4, 5], including HCC [6, 7]. Additionally, these conditions may emerge as adverse events during systemic treatment for advanced HCC [8]. Despite this, the relationship between MetS and HCC has not been comprehensively explored through bibliometric and visual analysis. Therefore, a thorough bibliometric analysis of publications, countries, institutions, journals, authors, and keywords is essential.

Bibliometric analysis employs mathematical and statistical methods to quantitatively assess a large body of literature within a particular field [9]. This approach helps identify key areas of focus and emerging topics in the evolution of a

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particular domain. In this study, we conducted a comprehensive review of 310 global articles related to HCC and MetS published between 2014 and 2023. Utilizing VOS viewer and Cite Space as bibliometric tools, we analyzed and visualizedknowledge maps. The goal of this analysis is to trace the development trajectory and highlight the current hotspots in HCC and MetS research, thereby offering valuable insights to guide both clinical and basic research.

2 Method

2.1 Data source

The literature was sourced from the Web of Science Core Collection (WOSCC), with the search period limited to January 1, 2014, to December 31, 2023. Only articles classified as "papers" were included. The search strategy is detailed in Supplementary Information 1, Table S1 and S2. The data was then exported as plain text, including all relevant information and references.

2.2 Data analysis

The bibliometric tools used in this study include R studio (version 4.4.1), Microsoft Office Excel 2019, VOS viewer (version 1.6.18), and Cite Space (version 6.3. R1). R studio (version 4.4.1) was employed for statistical analysis of publication trends and journal distribution by country. Microsoft Office Excel 2019 was used for data organization and the preparation of related tabulations. VOS viewer (version 1.6.18) was used to analyze collaborative networks among countries, authors, and institutions, as well as for co-occurrence and density analyses of keywords. Cite Space (version 6.3. R1) was applied for co-citation analysis and citation burst analysis.

3 Results

3.1 Analysis of publishing trend

This study included 310 articles related to HCC and MetS, with the detailed process illustrated in Fig. 1A. Although the number of articles fluctuated from 2014 to 2023, there was a discernible upward trend, with the cumulative publications steadily increasing (Fig. 1B). By evaluating this trend using an exponential growth function, we found that the growth in cumulative publications closely aligned with the publication years ($R^2 = 0.999$). This indicates that over the past decade, research on HCC and MetS has garnered increasing attention from the academic community.

3.2 Analysis of research output and cooperative networks

3.2.1 Publications and nations/areas

A total of 48 countries have contributed to research on HCC and MetS. In terms of publication volume, the USA leads with 88 articles, followed by China with 81, Japan with 37, Italy with 34, and South Korea with 27 (Fig. 2A**,** Table 1). These 5 countries are the leading contributors in HCC and MetS research. Figure 2B illustrates the collaboration network between countries, showing extensive collaboration among nations with high publication output, particularly between the USA and China.

3.2.2 Publications and institutions

Table 2 lists the top ten institutions by publication volume, showing no significant discrepancies among them. Figure 2C illustrates the institutional collaboration network, with Seoul National University, The Chinese University of Hong Kong, and Stanford University being particularly prominent. Additionally, institutions with higher publications numbers

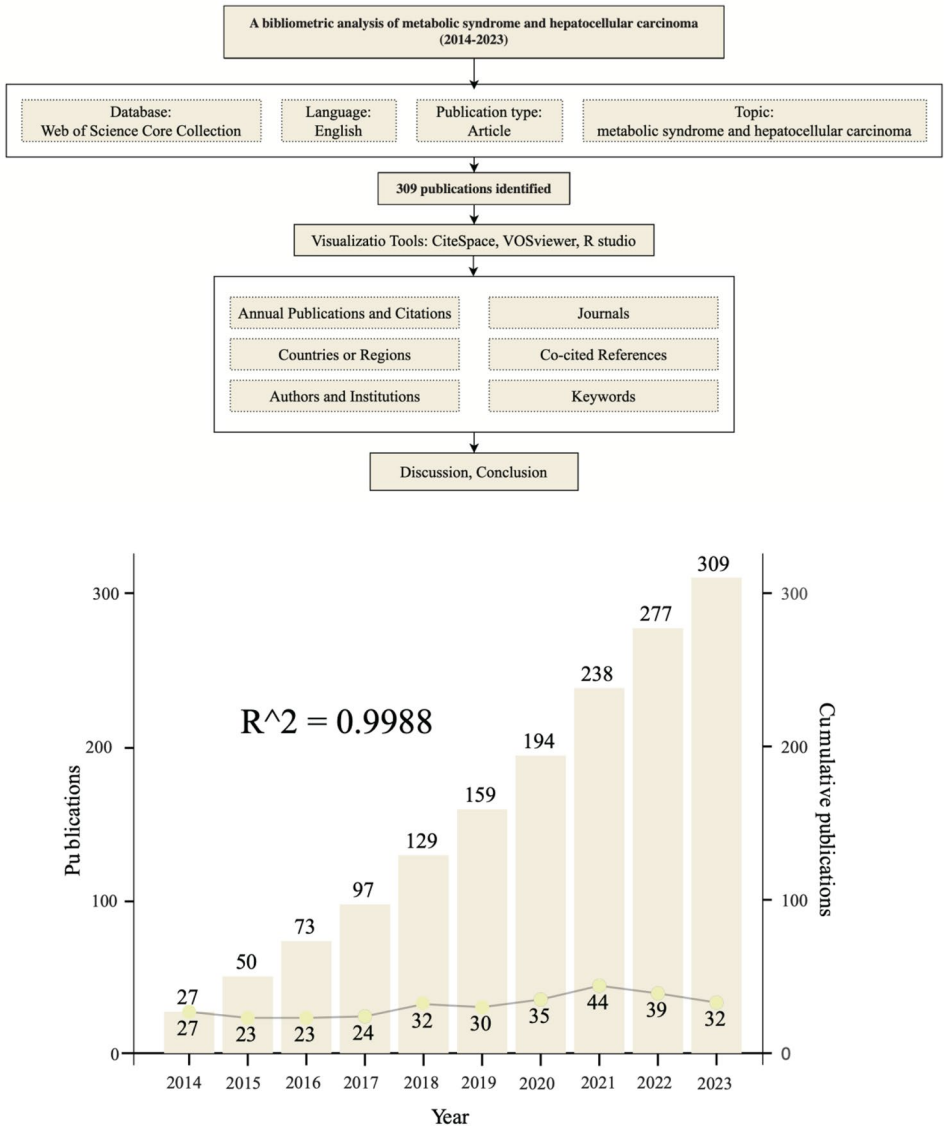

Fig. 1 Research flow chart (**A**) and article publication trend chart (**B**)

generally have extensive collaborative relationships, with minimal differences between domestic and international collaborations.

3.2.3 Publications and authors

Although 2,370 researchers have participated in studies on HCC and MetS, the publication volumes of the top ten authors are relatively low and show little disparity (Table 3). The co-authorship analysis indicates that while there are collaborative relationships among multiple researchers, the cohesiveness of these collaborations is not strong. The cooperation among these researchers may be related to overlapping research interests, career paths, or funding support (Fig. 3).

3.2.4 Publications and journals

From 2014 to 2023, 186 SCI journals published articles on HCC and MetS. Table 4 lists the journals that published more than five articles. HEPATOLOGY is the most-cited journal, with 781 citations, followed by JOURNAL OF HEPATOLOGY with 627 citations. Both journals are highly regarded in the field of HCC research.

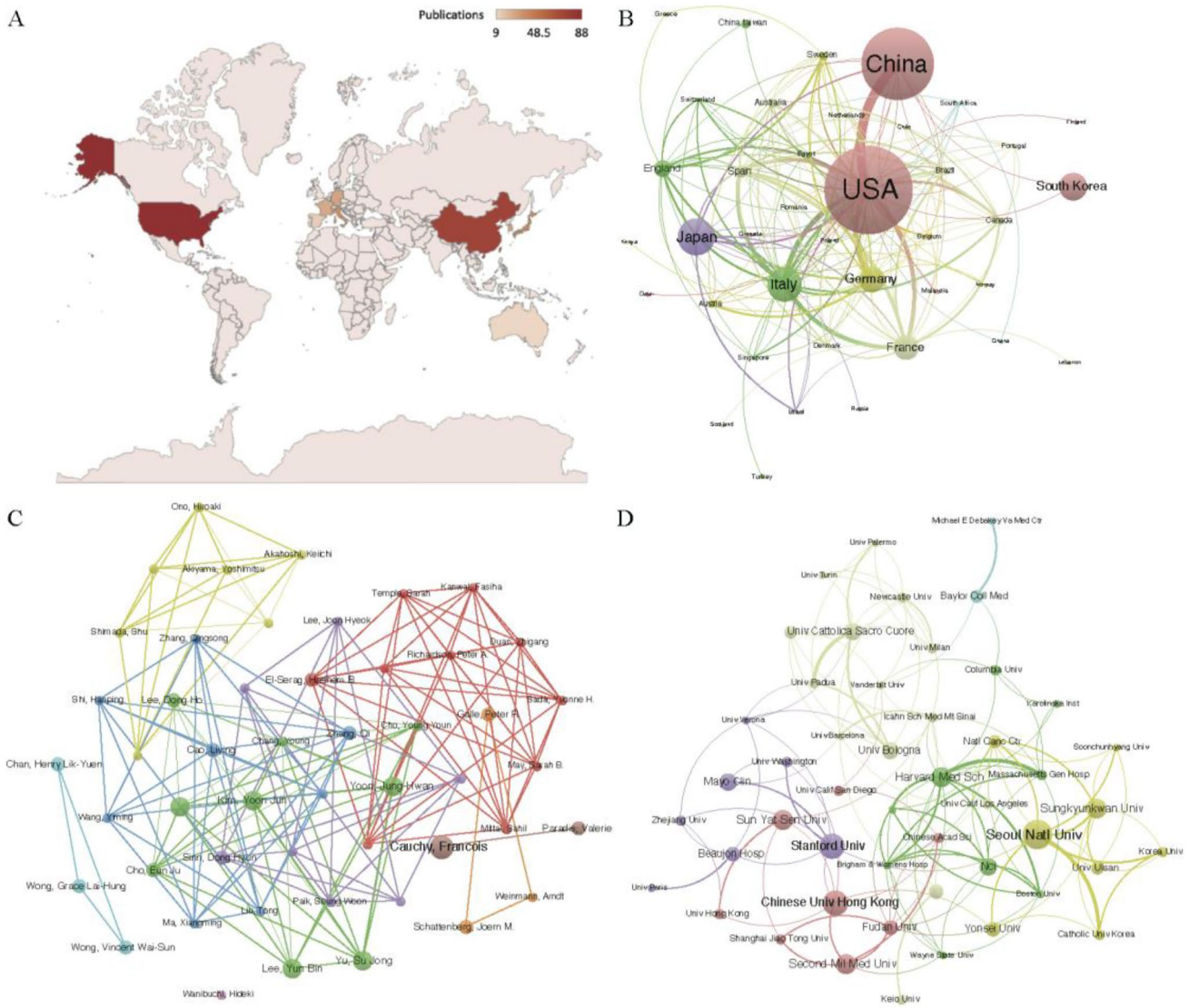

Fig. 2 Graphs of the number of national published journals (**A**, **B**), authors' cooperation (**C**), institutions' cooperation (**D**)

Table 1 The top 10 productive countries/regions

Institution	Publications	Citations	Per citations
USA	88	8549	97.15
China	81	1975	24.38
Japan	37	3525	95.27
Italy	34	4957	145.79
South korea	27	592	21.93
Germany	26	1289	49.58
France	25	2860	114.40
England	16	553	34.56
Spain	12	3905	325.42
Australia	9	424	47.11
Sweden	9	409	45.44

Table 2 The top 10 productive institutions

Institution	Publications	Citations
Seoul Natl Univ	12	241
Chinese Univ Hong Kong	10	372
Stanford Univ	10	392
Harvard Med Sch	8	341
Second Mil Med Univ	8	283
Sun Yat Sen Univ	8	220
Sungkyunkwan Univ	8	45
Mayo Clin	7	1275
Nci	7	1064
Univ Bologna	7	282

Table 3 The top 10 productive authors

Name	Publication years	Publications	Total citations	Per citations
Cauchy, Francois	2020	5	72	14.40
Lee, Yun Bin	2019	4	115	28.75
Kim, Yoon Jun	2019	4	40	10.00
Yoon, Jung-Hwan	2019	4	40	10.00
Yu, Su Jong	2020	4	40	10.00
Lee, Jeong-Hoon	2019	4	39	9.75
El-Serag, Hashem B	2016	3	643	214.33
Galle, Peter R	2021	3	94	31.33
Schattenberg, Joern M	2021	3	94	31.33
Chan, Henry Lik-Yuen	2022	3	60	20.00

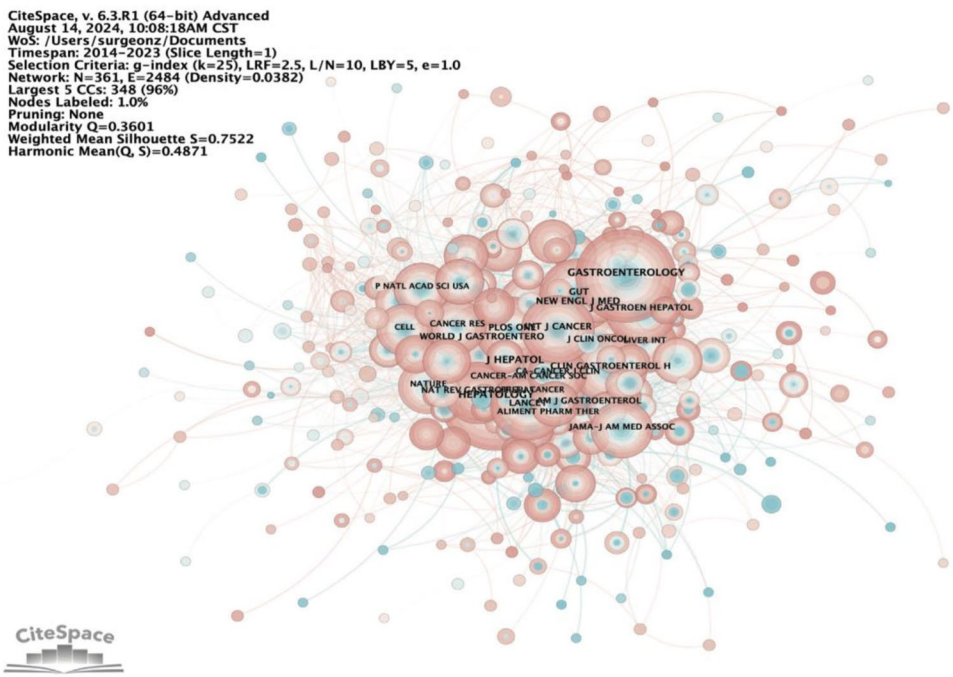

Fig. 3 Graph of the number of papers published by journals

Table 4 The journals that published more than five articles

Journal	Category	Impact factor (2023)	Total publications	Total citations
Cancers	ONCOLOGY	4.5	9	91
Liver International	GASTROENTEROLOGY & HEPATOLOGY	6	8	148
Hepatology	GASTROENTEROLOGY & HEPATOLOGY	12.9	7	781
Journal of Hepatology	GASTROENTEROLOGY & HEPATOLOGY	26.8	6	627
Frontiers in oncology	ONCOLOGY	3.5	6	18
Journal of clinical gastroenterology	GASTROENTEROLOGY & HEPATOLOGY	2.8	5	182
BMC Cancer	ONCOLOGY	3.4	5	144
Annals of surgical oncology	ONCOLOGY; SURGERY	3.4	5	120

3.3 Analysis of co-cited references

Figures 4A–D present the co-citation analysis of research on HCC and MetS, aiming at exploring the background and knowledge foundation of this field. Figure 4A shows the co-citation network distribution from 2014 to 2023, with references cited more than ten times highlighted on the map. Additionally, the color of the nodes indicates the citation period: the bluer the node, the earlier it was cited, and the redder the node, the more recent the citation.

Table 5 lists the top 10 co-cited references. The article titled "*Metabolic syndrome increases the risk of primary liver cancer in the United States: a study in the SEER-Medicare database*" ranks first, with 50 co-citations [10]. The articles titled "*Hepatocellular carcinomas in patients with metabolic syndrome often develop without significant liver fibrosis: a pathological analysis* [11]," "*Nonalcoholic fatty liver disease and hepatocellular carcinoma: a weighty connection* [12]," "*Metabolic syndrome and hepatocellular carcinoma: two growing epidemics with a potential link* [13]," and "*Management of hepatocellular carcinoma: an update*[13]" are tied for second place, each with 42 co-citations. Among these five references, four were published in HEPATOLOGY, and one was published in CANCER. The top ten articles are primarily concentrated in the period from 2009 to 2011.

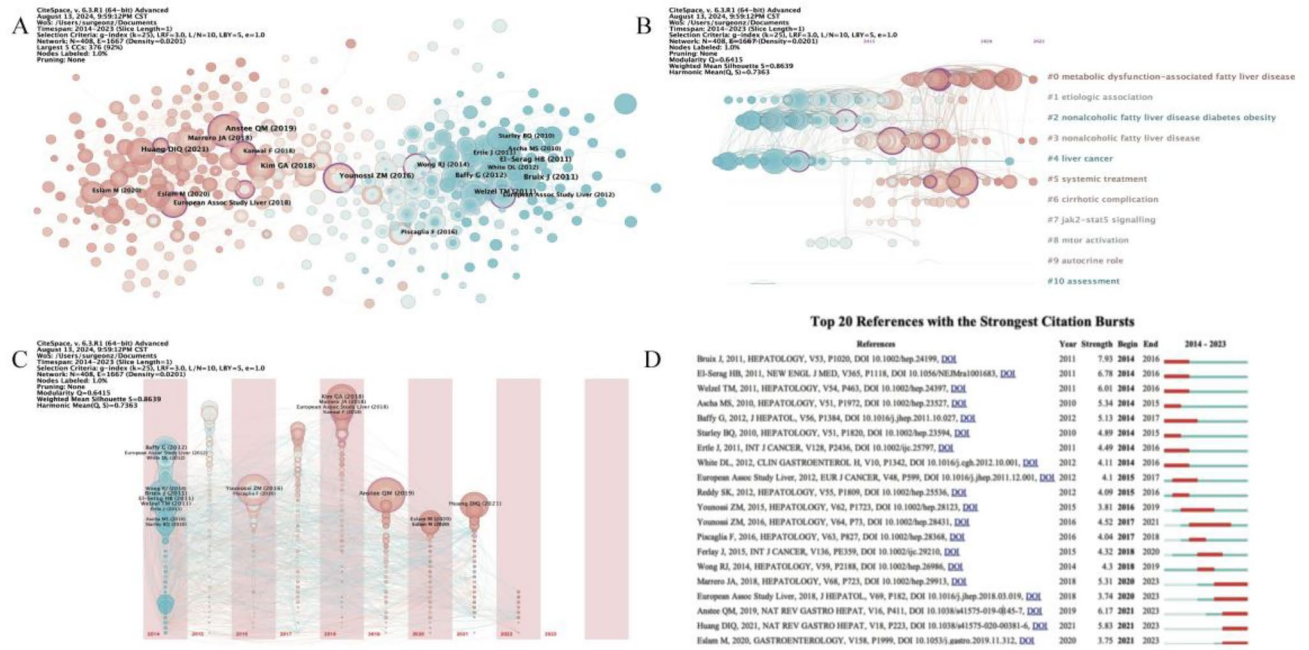

Fig. 4 The co-citation analysis of research related to HCC and MetS (**A**-**D**)

Table 5 The top 10 co-cited references

First author	Year	Journal	Title	Co-citations
Tania M Welzel, et al	2011	Hepatology	Metabolic syndrome increases the risk of primary liver cancer in the United States: a study in the SEER-Medicare database	50
Jordi Bruix, et al	2011	Hepatology	Management of hepatocellular carcinoma: an update	42
Valérie Paradis, et al	2009	Hepatology	Hepatocellular carcinomas in patients with metabolic syndrome often develop without significant liver fibrosis: a pathological analysis	42
Brad Q Starley, et al	2010	Hepatology	Nonalcoholic fatty liver disease and hepatocellular carcinoma: a weighty connection	42
Abby B Siegel, et al	2009	Cancer	Metabolic syndrome and hepatocellular carcinoma: two growing epidemics with a potential link	42
Mustafa S Ascha, et al	2010	Hepatology	The incidence and risk factors of hepatocellular carcinoma in patients with nonalcoholic steatohepatitis	35
Eugenia E Calle, et al	2003	The New England of Medicine	Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults	34
György Baffy, et al	2012	Journal of Hepatology	Hepatocellular carcinoma in non-alcoholic fatty liver disease: an emerging menace	28
Judith Ertle, et al	2011	International Journal of Cancer	Non-alcoholic fatty liver disease progresses to hepatocellular carcinoma in the absence of apparent cirrhosis	23
Kohichiroh Yasui, et al	2011	Clinical Gastroenterology and hepatology	Characteristics of patients with nonalcoholic steatohepatitis who develop hepatocellular carcinoma	21

Using Cite Space, we identified 12 clusters. With the top ten clusters shown in Fig. 4B. The cluster labels are displayed on the right side. Nodes of different colors represent citations from different years, with those closer to the right indicating more recent citations. The modularity Q value (0.6415) > 0.3, and the average silhouette value (0.8639) > 0.7, suggesting that the clusters are both persuasive and structurally meaningful. The top ten cluster labels are as follows: cluster #0: metabolic dysfunction-associated fatty liver disease; cluster #1: etiologic association; cluster #2: nonalcoholic fatty liver disease diabetes obesity; cluster #3: nonalcoholic fatty liver disease; cluster #4: liver cancer; cluster #5: systemic treatment; cluster #6: cirrhotic complication; cluster #7: jak2-stat5 signaling; cluster #8: mTOR activation; cluster #9: autocrine role; cluster #10: assessment. Cluster #0 is the largest and most recent cluster.

Figure 4C presents the timeline view of co-cited references, showing that new key references emerge almost every year, indicating that research related to HCC and MetS is highly active and continuously evolving. Citation bursts occur when a reference is cited far more frequently during a specific period than its usual citation rate. By analyzing these bursts, we can track how research hotspots in HCC and MetS have evolved over time. Figure 4D highlights the top 20 references with the most significant citation bursts. References with high citation bursts are marked in red, while those with lower citation bursts are marked in blue. The reference with the highest burst intensity (intensity = 7.93, burst period = 2014–2016) is "*Management of hepatocellular carcinoma: An update*" by Bruix J et al.[13], which ranks second among the co-cited references (Table 5).

3.4 Analysis of keywords

High-frequency keywords represent research hotspots and trends. Among the 1,381 keywords extracted from 310 papers, the top 100 most frequent keywords (each appearing at least five times) were analyzed (Fig. 5A). The keywords formed three clusters, with different colors representing different clusters. These clusters contain 37, 34, and 29 keywords respectively, and are roughly distributed between 2017 and 2020 on average. Cluster 1 (red) focuses on metabolic syndrome, with keywords such as "NAFLD," "liver disease," "IR," and "obesity." Cluster 2 (green) pertains to research strategies related

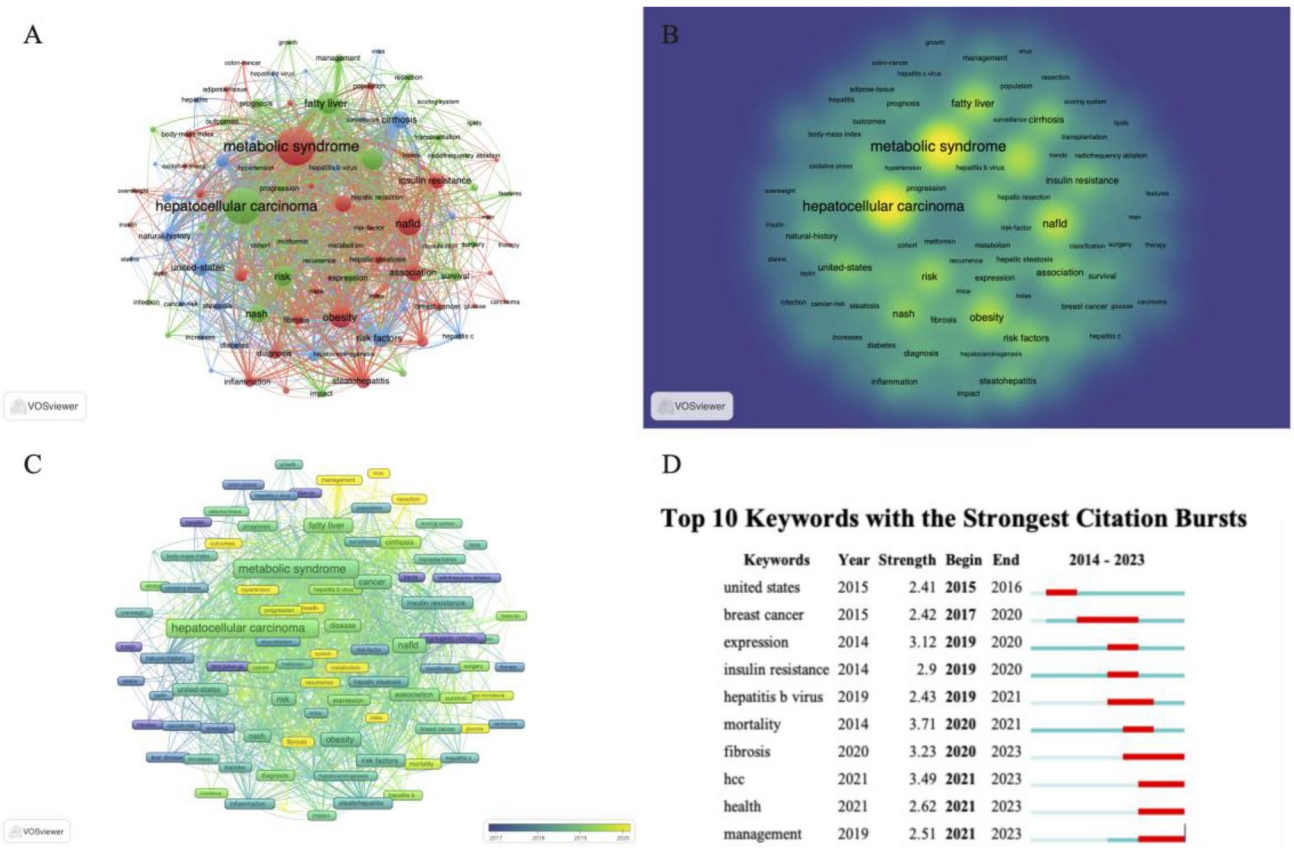

Fig. 5 Keyword clustering (**A**), keyword density (**B**), keyword time (**C**), keyword burning (**D**)

to hepatocellular carcinoma, including keywords like "survival," "risk," "prognosis," and "recurrence." Cluster 3 (blue) primarily addresses "cirrhosis," "hepatitis B virus," and "hepatitis C virus." Fig. 5B highlights the potential focal points of research related to HCC and MetS, including "hepatocellular carcinoma," "metabolic syndrome," "NAFLD," "obesity," "fatty liver," "cirrhosis," and "IR."

Topredict emerging hotspots, we conducted a temporal analysis and burst detection of keywords. In Fig. 5C, keywords that appeared earlier are shown in purple, while those that appeared later are shown in yellow. Recent keywords include "recurrence," "metabolism," "fibrosis," "resection," and "outcomes." Several keywords in the HCC and MetS research field that are currently in a burst state, as shown in Fig. 5D, including "fibrosis," "HCC," "health," and "management," indicating potential future research hotspots.

4 Discussion

4.1 Trends in publishing

We conducted a systematic literature search on research related to HCC and MetS from 2014 to 2023 in the WOSCC database, followed by a bibliometric analysis. NAFLD is one of the fastest-growing MetS globally, potentially leading to cirrhosis and HCC [14]. Metabolic comorbidities associated with NAFLD include obesity, type 2 diabetes, hyperlipidemia, and hypertension [15]. As a result, research on HCC and MetS has been steadily increasing. Moreover, significant changes in global lifestyles have contributed to a substantial disease burden [16]. Developed nations (Europe/North America) exhibit predominant consumption of high-fat, high-sugar diets, with the United States demonstrating a mean daily caloric intake of 3800 kcal [17] and EU populations consuming over 50 kg of red meat per capita annually [18]. In contrast, developing regions (Asia/Africa) maintain traditional dietary patterns centered on cereals and tuber crops. Urbanized areas globally show accelerating adoption of Westernized diets, evidenced by an 8% annual growth in ultra-processed food consumption. Notably, sub-Saharan Africa maintains relatively high dietary fiber intake (~ 20 g/day, exceeding Western averages of 15 g/day), though faces significant aflatoxin contamination in staple grains [19]. China exhibits marked urban–rural disparities in obesity prevalence (35% in urban vs. 18% in rural populations) [20]. Metabolic implications are evident: high-fat/sugar diets directly correlate with visceral adiposity and IR progression, while traditional diets confer metabolic protection offset by hepatocarcinogenic risks from synergistic aflatoxin-HBV exposure (accounting for > 60% of Africa's hepatocellular carcinoma burden) [21]. Sedentary behavior dominates developed societies, with daily sitting durations reaching 8–10 h and only 30% of adults meeting WHO-recommended 150 min of moderate-intensity exercise weekly [19]. Developing nations retain higher baseline activity levels through agricultural labor and non-mechanized transport. However, urbanization drives rapid sedentarization, with 45% of Asian urbanites now classified as physically inactive by WHO criteria. In developed nations, MetS demonstrates a prevalence rate of 30%-35% [22], predominantly manifesting as central obesity and hypertriglyceridemia. In developing countries, accelerated urbanization has precipitated a dual disease burden characterized by the coexistence of traditional undernutrition with emerging MetS. Epidemiological data from India reveal a striking urban–rural disparity, with MetS prevalence rates of 22% in urban populations versus 9% in rural communities [23]. These factors have contributed to the growing burden of non-viral HCC. Therefore, early prevention and treatment are particularly important for patients with MetS. Additionally, economic growth has led to increased funding for research institutions, facilitating rapid advancements in this field.

4.2 Trends in countries/regions publishing

A total of 48 countries have contributed to research in this area, with the USA, China, Japan, Italy, and South Korea leading in number of publications. Among these, the United States, Italy, and China have particularly close international collaborations. These findingshighlight the significant influence and leading roles of the United States, China, and Italy in HCC and MetS research. As a major economic power with a unique dietary structure and a large number of dedicated researchers, along with its distinctive research funding mechanisms and talent cultivation system, the United States maintains a leading position in research output. China and Italy also show substantial research activity, likely due to lifestyle and dietary changes driven by economic growth, which have influenced HCC incidence rates. The traditional Chinese diet, historically centered on rice and noodle consumption, has been progressively supplanted by Western-style dietary patterns characterized by high-sugar and high-fat content, notably exemplified by fast food and carbonated beverages. In contrast, Italy maintains stronger adherence to traditional dietary practices, particularly the Mediterranean

diet. However, globalization trends have driven increased consumption of Western fast food and processed foods among younger populations. Both Chinese and Italian populations are adopting increasingly sedentary lifestyles accompanied by insufficient physical activity. This behavioral shift correlates with rising prevalence rates of obesity and type 2 diabetes mellitus—core metabolic disturbances associated with MetS. These metabolic derangements constitute primary risk factors for MAFLD, which itself emerges as a significant prognostic determinant for HCC development. Strengthening close international collaboration will significantly enhance the overall quality of research in this field.

4.3 Trends in institutional publishing

Of the top 10 institutions by publication count, four are based in the United States, three in China, two in South Korea, and one in Italy. The top three institutions with the highest publication counts are from South Korea, China, and the United States, which aligns closely with the national publication volumes. The relatively small differences in the number of papers published by these top institutions suggest that they are all major contributors to HCC and MetS research. Moreover, it is evident that these prolific institutions maintain close collaborations with others, highlighting the importance of institutional cooperation. Especially in contexts with limited resources and platforms, such collaborations can significantly enhance research capabilities.

4.4 Journal publication output and influence

Analyzing published literature can help researchers identify suitable publication outlets for their work. *HEPATOLOGY* has published the most articles in this area, with 7 articles and an impact factor of 12.9. Research on HCC and MetS is primarily concentrated in Q1-Q2 journals, which researchers should consider for their submissions. Research fundamentals and hotspots.

4.5 Co-cited literature analysis tracking research basis

Co-cited references are those that are cited together by researchers. Conducting a co-citation analysis of studies related to HCC and MetS helps identify their common research foundations. Using Cite Space, we analyzed, clustered, and visualized the highly co-cited references over time. Among the top ten co-cited references, the following studies were conducted:

1. 2009, Valérie Paradis et al. [11]: This study investigated the pathological features of HCC and non-tumorous hepatic disease in patients where MetS was the sole risk factor. It compared these features with those ofother chronic liver diseases to better understand the pathophysiology of MetS-related HCC. The results showed that HCC with MetS as the sole risk factor had distinct morphological features and primarily occurred in livers without significant fibrosis. This study provided pathological evidence of the critical role of MetS in HCC development, laying the groundwork for future basic research.
2. 2009, Abby B Siegel et al. [13]: This paper explored the relationship between MetS and HCC. It highlighted that, while many HCC risk factors have been clearly defined—such as HBV, HCV, and alcohol—a significant portion of HCC cases (5% to 30%) lack identifiable cancer risk factors. In the U.S., most "cryptogenic" HCC cases are attributed to NAFLD, a hepatic expression of MetS. The study focused on the increased HCC risk in patients with MetS, the potential worsening of carcinoma outcomes in this population, the pathogenic mechanisms explaining these relationships, and treatment strategies for NAFLD and non-alcoholic steatohepatitis (NASH) patients. This study provided foundational thoughts and evidence for subsequent research.
3. 2010, Brad Q Starley et al. [12]: This highly co-cited review summarized the relationship between NAFLD and HCC. It highlighted that the rise in diabetes and obesity has contributed to the increasing prevalence of NAFLD and NASH. NAFLD, particularlyits progressive form NASH, is closely linked to HCC development. NASH can progress to cirrhosis and its complications. Importantly, NASH accounts for a significant portion of cryptogenic cirrhosis, which shares typical NASH risk factors. Although HCC is a rare complication of NAFLD, diabetes and obesity are recognized as independent HCC risk factors. Additionally, liver iron deposition increases HCC risk in NASH-derived cirrhosis. Existing evidence, including case reports and reviews, supports the association between diabetes, obesity, age, advanced fibrosis, and elevated HCC risk in NASH patients. This suggests that IR and the inflammatory cascade in NASH play crucial roles in HCC carcinogenesis. The study recommended close monitoring of disease progression in NAFLD patients and emphasized the importance of early prevention and treatment.

4. 2011, Tania M Welzel et al. [10]: This study explored the association between MetS and HCC risk in the USA using data from the SEER-Medicare database. The inclusion criteria for HCC patients required participation in Medicare Parts A and B for at least three years prior to HCC or ICC diagnosis, ensuring adequate time for recording previous diagnoses. The results suggest that MetS significantly increases the risk of HCC and ICC in the general U.S. population. This study laid the foundation for further research on the link between HCC and MetS.
5. 2011, Jordi Bruix et al. [24]: This paper interpreted the practice guidelines for the management of HCC issued by the American Association for the Study of Liver Diseases (AASLD), presenting new or revised recommendations. It covered surveillance, diagnosis, staging, and treatment of HCC. The updated guidelines marked a significant shift in HCC management, from an almost universally fatal outcomes to one that can be prevented, detected early, and treated effectively. The guidelines emphasized high-quality screening and appropriate management of lesions, particularly in cases of HCC not caused by viral hepatitis.

These highly co-cited references demonstrate the foundational research and significant contributions to the understanding and management of HCC and MetS. Although numerous studies have established a link between MetS and an increased risk of HCC, this association may vary across different populations, age groups, or regions. Therefore, future research should further investigate the impact of these factors to gain a more comprehensive understanding.

4.6 Identifying research hotspots from highly cited literature

Among the top 10 cited articles (Table 6), six are related to NAFLD, three to MetS, two to liver cirrhosis, and one to NASH. These results indicate that the common research focuses in the HCC and MetS fields are associated with NAFLD, MetS, liver cirrhosis, and NASH. These aspects have already become significant research directions.

In 2014, a meta-analysis investigated the relationship between MetS and HCC, revealingthat individuals with MetS face a substantially elevated risk of developing HCC [7]. In 2015, a cohort analysis in the United States foundthat the percentage of HCC cases related to NAFLD (NAFLD-HCC) remained fairly constant from 2005 to 2010. However, patients with NAFLD-HCC received less monitoring and treatment for HCC [25]. Therefore, early prevention and surveillance of NAFLD are crucial for NAFLD patients. Nevertheless, clinical information regarding HCC within the context of NAFLD remains limited. In 2016, a multicenter prospective study evaluated the clinical characteristics of NAFLD-HCC patients and compared them with those of HCV-related HCC [26]. NAFLD-HCC was more often detected at an advanced tumor stage and could occur even in the absence of cirrhosis, with a significantly shorter survival time compared to HCV-related HCC [26]. In the same year, another study confirmed that NAFLD-HCC was frequently diagnosed at a more advanced tumor stage and could develop without cirrhosis, with patients experiencing significantly shorter survival times compared to those with HCV-related HCC [27]. In 2017, a retrospective cohort study indicated that type II diabetes and hypertension are independent risk factors for HCC in the absence of cirrhosis [28]. These results clinically confirmed the significant association between MetS and HCC.Subsequent research discovered that NAFLD is associated with the occurrence of HCC, male colorectal cancer, and female breast cancer. High NAFLD fibrosis scores and high fibrosis-4 scores were closely related to the occurrence of all cancers and HCC [29].

In summary, cutting-edge research focuses on the association between MetS and its various components (especially NAFLD) and HCC. The main limitation of the term NAFLD is its reliance on exclusive confounding factors and the use of potentially stigmatizing language [30]. Therefore, in a multisociety Delphi consensus statement, the term "metabolic dysfunction-associated steatotic liver disease" (MASLD) has been proposed to replace NAFLD [31]. Whether the previous research results on NAFLD can be applied to MASLD is still under investigation [32–34]. Consequently, research on the relationship between MASLD and HCC remains a key focus in the field of MetS and HCC.

MASLD, as an emerging diagnostic term, has a significant impact, not only influencing clinical diagnosis and treatment but also potentially altering the direction of future research in this field. Regarding the redesign of research frameworks, the introduction of MASLD highlights the need to further clarify the relationship between metabolic factors and fatty liver. Future studies may need to place greater emphasis on the interaction between metabolic diseases and liver diseases. Consequently, research designs might need to focus on metabolic indicators (such as blood glucose, IR, blood lipids, etc.) and the degree of hepatic fat accumulation as core factors, rather than solely relying on traditional definitions of alcoholic liver disease or NAFLD.

Furthermore, establishing a unified research framework is critical, as the standards and definitions for MASLD are still evolving, and there may be varying diagnostic criteria and methods globally. To ensure consistency and comparability of data, a standardized diagnostic framework, disease staging system, and treatment outcome evaluation should be

Table 6 The top 10 cited literatures

First author	Year	Journal	Title	Co-citations
Josep M. Llovet, et al	2021	Nature reviews disease primers	Hepatocellular carcinoma	2512
Monika Julia Wolf, et al	2014	Cancer cell	Metabolic Activation of Intrahepatic CD8+T Cells and NKT Cells Causes Nonalcoholic Steatohepatitis and Liver Cancer via Cross-Talk with Hepatocytes	490
Sahil Mittal, et al	2016	Clinical gastroenterology and hepatology	Hepatocellular Carcinoma in the Absence of Cirrhosis in United States Veterans Is Associated with Nonalcoholic Fatty Liver Disease	434
Piscaglia, Fabio, et al	2016	Hepatology	Clinical patterns of hepatocellular carcinoma in nonalcoholic fatty liver disease: A multicenter prospective study	415
Gi-Ae Kim, et al	2018	Journal of hepatology	Association between non-alcoholic fatty liver disease and cancer incidence rate	211
Sahil Mittal, et al	2015	Clinical gastroenterology and hepatogy	Temporal Trends of Nonalcoholic Fatty Liver Disease–Related Hepatocellular Carcinoma in the Veteran Affairs Population	190
Jinjuvadia, Raxitkumar, et al	2014	Journal of clinical gastroenterology	The Association Between Metabolic Syndrome and Hepatocellular Carcinoma Systemic Review and Meta-analysis	91
Luca Viganò, et al	2015	Journal of hepatology	Liver resection for hepatocellular carcinoma in patients with metabolic syndrome: A multicenter matched analysis with HCV-related HCC	86
Allison J. Kasmari, et al	2017	The American journal of medicine	Independent of Cirrhosis, Hepatocellular Carcinoma Risk Is Increased with Diabetes and Metabolic Syndrome	79
Carrie R Wong, et al	2016	World journal of gastroenterology	Hepatocellular carcinoma in patients with non-alcoholic fatty liver disease	71

established worldwide. This is crucial for the design of future clinical trials, drug development, and international research collaborations.

Lastly, the challenge of globally promoting the new diagnostic standard is a very practical issue. Differences in culture, lifestyle, dietary habits, and resource distribution across regions may present obstacles to the widespread acceptance and implementation of MASLD. To address these challenges, researchers and policymakers will likely need to strengthen education and training on a global scale, ensuring that healthcare systems in different countries understand and properly apply MASLD diagnostic criteria. Moreover, considering the resource limitations in low- and middle-income countries, adaptive diagnostic schemes may need to be developed for these regions to ensure fairness in global healthcare access.

4.7 Identifying key research areas via keyword co-occurrence and burst analysis

To identify all research hotspots, we performed co-occurrence analysis of keywords. The key research areas related to HCC and MetS mainly focus on NAFLD, NASH, liver cirrhosis, obesity, IR, and risk (Fig. 5A-B). We found that precursors of HCC, along with obesity and IR, occupy prominent research positions. Obesity and IR are both potential risk factors for fatty liver disease. Therefore, early prevention of these conditions (such as obesity and IR) and timely intervention in diseases such as MASLD, MASH, and liver cirrhosis are important steps for future clinical decision-making. Regarding temporal distribution, we found that recent keywords mainly consist of recurrence, metabolism, fibrosis, resection, and outcomes (Fig. 5C). These results suggest that recent research has peaked on recurrence after liver cancer resection and patient outcomes, which could be due to the fact that surgical treatment for liver cancer, particularly curative resection, has reached a therapeutic plateau. Modifying surgical techniques to improve postoperative survival and quality of life has shown limited success. Therefore, early intervention in precancerous liver diseases remains crucial to reducing the incidence of liver cancer.

To further identify potential research trends in the past 5 years, we conducted a burst analysis of keywords. The keywords from the past five years primarily include expression, IR, hepatitis B virus, mortality, fibrosis, HCC, health, and management. IR, hepatitis B virus, liver cirrhosis, and their impact on survival and health continue to be major long-term research hotspots. This indicates that breakthroughs in the progression from hepatitis B to HCC and the management of IR in HCC patients still face significant obstacles.

IR is a common risk factor for MASLD and is closely associated with the development and progression of HCC [35]. Impaired intestinal insulin signaling increases the risk of HCC, and this can be mitigated by restoring insulin function in diabetes [36]. First, under IR conditions, the ability of insulin to regulate hepatic glucose metabolism is impaired, but its ability to regulate hepatic fatty acid synthesis remains relatively intact [37, 38]. The deletion of key molecules in the hepatic insulin signaling pathway (such as insulin receptor (INSR) [39, 40], IRS [39], AKT [41], etc.) can suppress the ability of insulin to promote hepatic fatty acid synthesis. Recently, new molecules (such as CREBZF [42, 43], WDR6 [44]) have been identified that mediate insulin regulation of liver lipid metabolism under insulin-resistant conditions. Second, similar to insulin's regulation of hepatic glucose metabolism, the driving ability of insulin for hepatic lipid synthesis decreases under IR. However, due to increased hepatic glucose output, glucose can serve as a substrate to drive hepatic lipid synthesis, ultimately resulting in increased liver fat content [37]. Third, in the insulin-resistant state, external factors affecting the liver play an important role in liver lipid accumulation [37]. These include increased lipolysis in adipose tissue, decreased glucose uptake in skeletal muscle, and elevated levels of glucose, free fatty acids, and glycerol, which in turn promote hepatic gluconeogenesis and hepatic lipid synthesis.

Based on these insights, future research should focus on the following areas: 1. Elucidating the mechanisms of cross-talk between hepatic glucose and lipid metabolism pathways; 2. Exploring potential new pathways for insulin signaling and regulation of hepatic fatty acid synthesis under IR; 3. Defining the interaction mechanisms between the liver and other metabolic organs in the insulin-resistant state. Based on the direct and/or indirect pathways through which insulin regulates hepatic lipid metabolism, these studies may provide theoretical evidence and potential therapeutic targets for improving hepatic lipid deposition in clinical settings.

In an era of rapid advancements in omics technologies, metabolomics and gut microbiomics offer new perspectives for the future development of this field. Metabolomics, by providing a comprehensive analysis of metabolites in the body, can reveal how metabolic disturbances affect liver function and provide important clues for the early diagnosis and disease classification of fatty liver diseases. For instance, metabolomics studies have found that certain metabolites (such as short-chain fatty acids, amino acids, etc.) are significantly altered in patients with MASLD or HCC, and these changes may be closely related to the development of MetS. Future research could improve the accuracy of early diagnosis by screening metabolomic biomarkers while also providing potential targets for novel drug development [45].

Additionally, research on the gut microbiome is increasingly becoming a key bridge linking metabolic diseases with liver diseases. The gut microbiota plays an essential role not only in digestion and immunity but also in the development of metabolic disorders such as fatty liver and IR. Growing evidence suggests that gut dysbiosis may promote liver inflammation and fibrosis, exacerbating the progression of fatty liver disease and even contributing to the transformation into hepatocellular carcinoma. The analysis of the gut microbiome provides a novel perspective for understanding the development and progression of MASLD. For example, certain gut microbiota may directly influence liver lipid metabolism and inflammation through metabolic products like short-chain fatty acids. Therefore, studying the role of the gut microbiome in MASLD and HCC may help identify new biomarkers and intervention strategies. Combining metabolomics and gut microbiomics holds great promise for providing new tools for the early screening, personalized treatment, and precision medicine of MASLD. For instance, personalized dietary or pharmacological interventions could improve the clinical manifestations of fatty liver and metabolic syndrome by modulating the gut microbiota and metabolic pathways, thereby delaying the progression of liver fibrosis and liver cancer. Integrating multiple omics data (such as genomics, metabolomics, microbiomics, etc.) offers novel approaches for a multi-dimensional understanding of the disease and comprehensive interventions.

5 Limitations of the research

This study has several limitations. First,we selected the WOSCC database and limited the papers to English articles, which might result in missing some relevant data. Secondly, inconsistencies in name formatting for certain authors or institutions within the WOSCC database may cause a discrepancy in the attribution of research. Lastly, this research cannot ensure that all publications perfectly align with the search criteria for topic relevance. Nevertheless, the analysis offers ample insights to accurately represent the current state of the field.

6 Conclusion and perspective

Using bibliometric methods, we analyzed the study related to HCC and MetS. The USA, China, and Japan continue to lead in publication volume. Key areas of focus in HCC and MetS researchinclude: 1. IR: IR is not only associated with MetS and HCC but also with other cancers. Therefore, targeting IR could be a promising strategy for treating HCC patients with MetS. 2. Interactions among MAFLD, MASH, and liver cirrhosis: These conditions interplay with HCC and MetS, highlighting the importance of understanding their relationships. 3. Potential mechanisms of interaction between HCC and MetS: These mechanisms are closely linked to obesity, hypertension, and metabolism, highlighting the need for future research in this area. Emerging trends suggest that studying MAFLD-related HCC patients might lead to new therapeutic approaches. This study of trends and hotspots associated with HCC and MetS could drive further developments in the field and lay the groundwork for future research.

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Declarations

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