

Current Status and Future Direction of Albumin-Bilirubin in Hepatocellular Carcinoma: A Bibliometric Analysis

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Keywords

Hepatocellular carcinoma · Albumin-bilirubin · Bibliometric · Frontier · Hotspot · Prognosis

Abstract

Introduction: Hepatocellular carcinoma (HCC) is a common malignant tumor, so we need a convenient and objective way to diagnose and treat HCC. We discuss the current situation, progress, hotspots, and existing problems of Albumin-Bilirubin (ALBI) in HCC, which can provide new ideas for the prevention, diagnosis, and treatment of HCC. **Methods:** We adopt Excel 2019 software and visual analysis tools based on Web of Science database search. This manuscript uses VOSviewer, Co-Occurrence13.3 (COOC13.3) software to conduct overall trend analysis, synonym merging, frequency of countries, journals, institutions, funds, dissimilarity matrices, co-occurrence matrices, bimodal matrices, coupling matrices, cluster analysis of topic evolution time zone graphs. **Results:** A total of 610 papers were included, and the number of papers output showed an overall upward trend. ALBI has been valued by the industry in HCC and plays an important role in diagnosing and treating HCC, even better than the classic Child-Pugh (C-P) grade. At the same time, hot spots in the treatment of HCC

and other applications of ALBI were discovered. **Conclusion:** ALBI score is a convenient and objective liver function evaluation index, which plays an important role in the prediction of patient survival rate and prognosis. Promoting the ALBI score in HCC can help doctors judge the patient's condition and improve the diagnosis and precise treatment effect.

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Introduction

HCC is ranked as the sixth most common tumor and the third leading cause of cancer death [1], it is also the fastest-growing cause of cancer deaths in the USA [2], and an important public safety issue in the Asia-Pacific region [3]. It can be seen that it is very important for the diagnosis and treatment of HCC, and the ALBI score was born. The ALBI score was first proposed in 2015 by Johnson et al. [4] based on 1,313 HCC patients from Japan, and the model was tested on a total of 5,097 HCC patients from other geographic regions ($n = 1,286$ in Japan, $n = 1,356$ in the United Kingdom, $n = 1,112$ in

Youao Zhang and Huiling Yang contributed equally to this work.

China, $n = 834$ in Spain, and $n = 509$ in the USA). The calculation method of ALBI is $ALBI = (\log_{10} \text{bilirubin} \times 0.66) + (\text{albumin} \times -0.085)$, where bilirubin is in $\mu\text{mol/L}$ and albumin is in g/L , and it is proved that ALBI can be used as an indicator of liver reserve function. Since then, more and more studies have shown that ALBI can be used as a new noninvasive evaluation method, which significantly affects liver function evaluation and prognosis in patients with liver cancer [4–7]. Besides, compared with the other scores, such as C-P [8], Model End-stage Liver Disease (MELD) [9], the ALBI score involves only two common continuous parameters that are easily acquired in clinical practice rather than categorical variables and are simply calculated by applying a formula [10, 11]. And, ALBI score is objective and can detect smaller changes in liver dysfunction than the C-P or MELD scores. Thus, the ALBI score increases earlier than the C-P or MELD score and before the development of cirrhosis. Furthermore, bibliometric analysis uses mathematical and statistical methods to study the distribution, structure, quantity, and content evolution of bibliographic information qualitatively or quantitatively. It is of great value to describe the status quo of various research disciplines, publishing trends, and scientific achievements of researchers, institutions, and countries, as well as future research hotspots, academic frontiers, and knowledge maps, which provide researchers and clinicians a comprehensive picture of the current state of development in a particular research area. Thus, in this study, the application of ALBI in HCC was attempted to use bibliometric methods and visual analysis technology to analyze the current status, progress, hotspots, and existing problems in this field and to provide suggestions and references for HCC treatment by ALBI score.

Materials and Methods

Data Retrieval Strategy, Data Extraction, and Cleaning

The research object of this paper is the correlation study of ALBI scores in the diagnosis and treatment of HCC. The Web of Science Core Collection is a comprehensive and authoritative database, containing more than 12,000 high-quality journals. Thus, we select the Web of Science core collection database SCI-EXPANDED database as the search source as the data source of the research object, and select the advanced search, the search formula: $(TS = ALBI \text{ OR } TS = \text{albumin-bilirubin} \text{ OR } TS = ALBI^*) \text{ AND } (TS = HCC \text{ OR } TS = \text{Hepatocellular Carcinoma})$, the time limit was proposed by ALBI score since 2015 to August 1, 2022, and 874 papers were retrieved, excluding duplicate publications, conference abstracts, letters, etc., mainly leaving papers and reviews. And without consulting in advance, we read the title, abstract, and

keywords of the searched literature at the same time, exclude irrelevant literature, and only include what we think can be left. In the end, a total of 610 articles were left.

Scientometric Analysis Methods

COOC13.3 software is an emerging bibliometric analysis software. It can carry out synonym combination, frequency statistics, co-occurrence matrix, dissimilarity matrix, discourse matrix, the second mock examination matrix, coupling matrix, pedigree map, clustering map, research frontier, time zone map, theme evolution path, and other functions. COOC is a software developed by Chinese scholars for bibliometrics and scientific mapping and is constantly iterated [12]. COOC software is also increasingly used in SCI-E articles [12–15]. Besides, VOSviewer usually identifies projects more accurately, and its “overlay visualization” function can be used to highlight the changes in key nodes over time [16]. Thus, we choose COOC13.3 and VOSviewer as the bibliometric tool for our study. The 610 retrieved documents were exported in plain text format, COOC13.3, and VOSviewer; visual map tool was used to perform subject heading cluster analysis and author cooperation degree analysis. In the statistics section, export literature records to Excel for statistical analysis.

Results

Data Distribution

Annual Distribution of Publications

As can be seen from Figure 1, the number of papers on the application of ALBI in HCC is increasing year by year, and the trend line of published papers shows a steady upward trend (as of August 1, 2022). The current peak output of papers is 166 papers in 2021, accounting for 27.2% of the included papers. In 2020, there will be a sharp rise in relevant research, which may be related to the arrival of COVID-19. According to the growth law of scientific literature, the current research in this direction is still on the rise.

Distribution of Published Journals, Countries/Regions, and Institutions

The journal with the most journals is *Cancers* with 36 publications, followed by *Hepatology Research* with 34 publications, of which there are top 10 journals as shown in Table 1. As can be seen in Table 1, this research mainly focuses on East Asia, the USA, and some European countries. Japan has the largest number of publications, publishing 209 related articles; China is the second, publishing 206 related articles, the USA is the third, publishing 81 related articles. The top 10 countries with the most published articles (Table 1).

Relevant research institutions are concentrated in East Asia, with the largest number being Ehime Prefectural Central Hospital with 48 papers and Ogaki Municipal

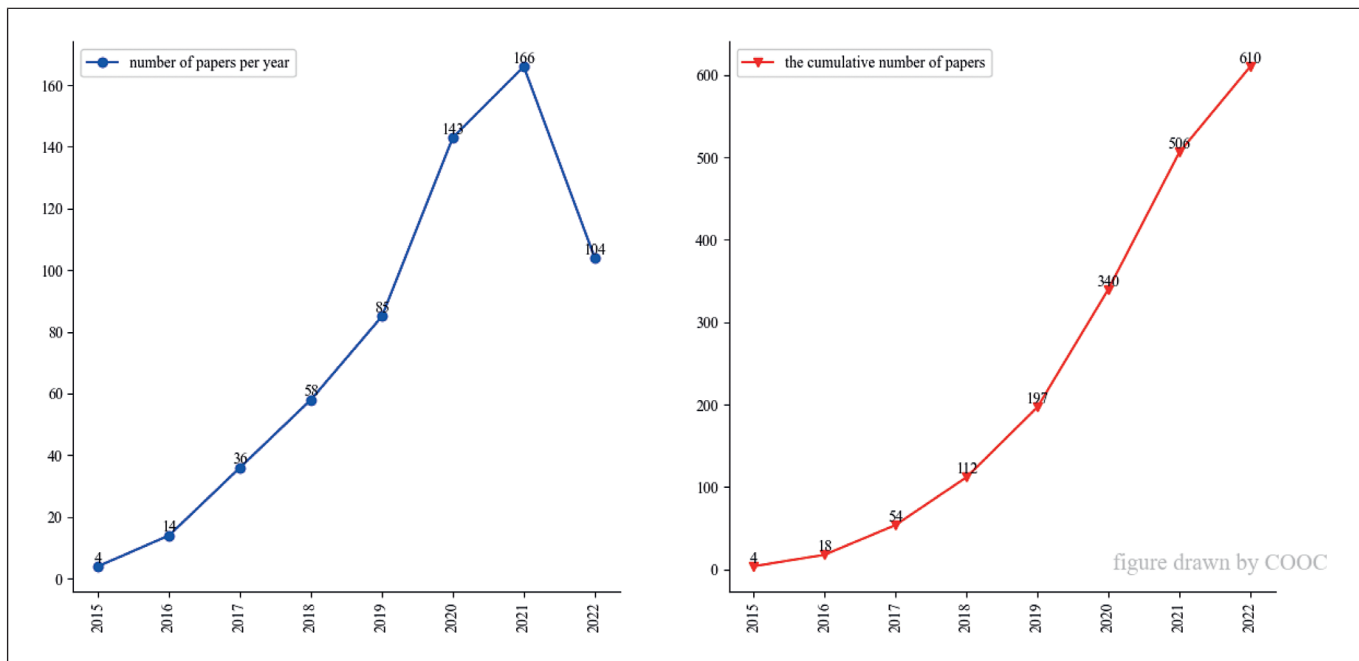


Fig. 1. 2015–2022 Related literature on the application of ALBI in HCC.

Table 1. Distribution of published journals, countries/regions, and institutions of relevant research

Rank	Country/regions	Count	Institution	Count	Author	Count	Journal	Count	2021 impact factor/JCR partition
1	Japan	209	Ehime Prefectural Cent Hosp (Japan)	48	Hiraoka, Atsushi	47	Cancers	36	6.575/Q1
2	China	206	Ogaki Municipal Hosp (Japan)	47	Toyoda, Hidenori	47	Hepatology Research	34	4.942/Q2
3	USA	81	Natl Yang Ming Chia Tung Univ (China)	36	Kumada, Takashi	46	Journal of Gastroenterology and Hepatology	21	4.369/Q2
4	Taiwan	67	Taipei Vet Gen Hosp (China)	33	Tada, Toshifumi	45	Liver Cancer	20	12.430/Q1
5	Italy	42	Kindai Univ (Japan)	30	Huang, Yi-Hsiang	36	Medicine	15	1.817/Q3
6	England	39	Ehime Univ (Japan)	30	Hou, Ming-Chih	35	Annals of Translational Medicine	14	3.616/Q3
7	Germany	35	Okayama City Hosp (Japan)	29	Hirooka, Masashi	32	Cancer Management and Research	13	3.602/Q3
8	South Korea	34	Asahi Gen Hosp (Japan)	28	Tsuji, Kunihiko	31	Scientific Reports	13	4.996/Q2
9	France	19	Toyama Univ Hosp (Japan)	25	Hiasa, Yoichi	31	Frontiers in Oncology	12	5.738/Q2
10	Spain	16	Matsuyama Red Cross Hosp (Japan)	25	Kudo, Masatoshi	31	Journal of Clinical Medicine	11	4.964/Q2

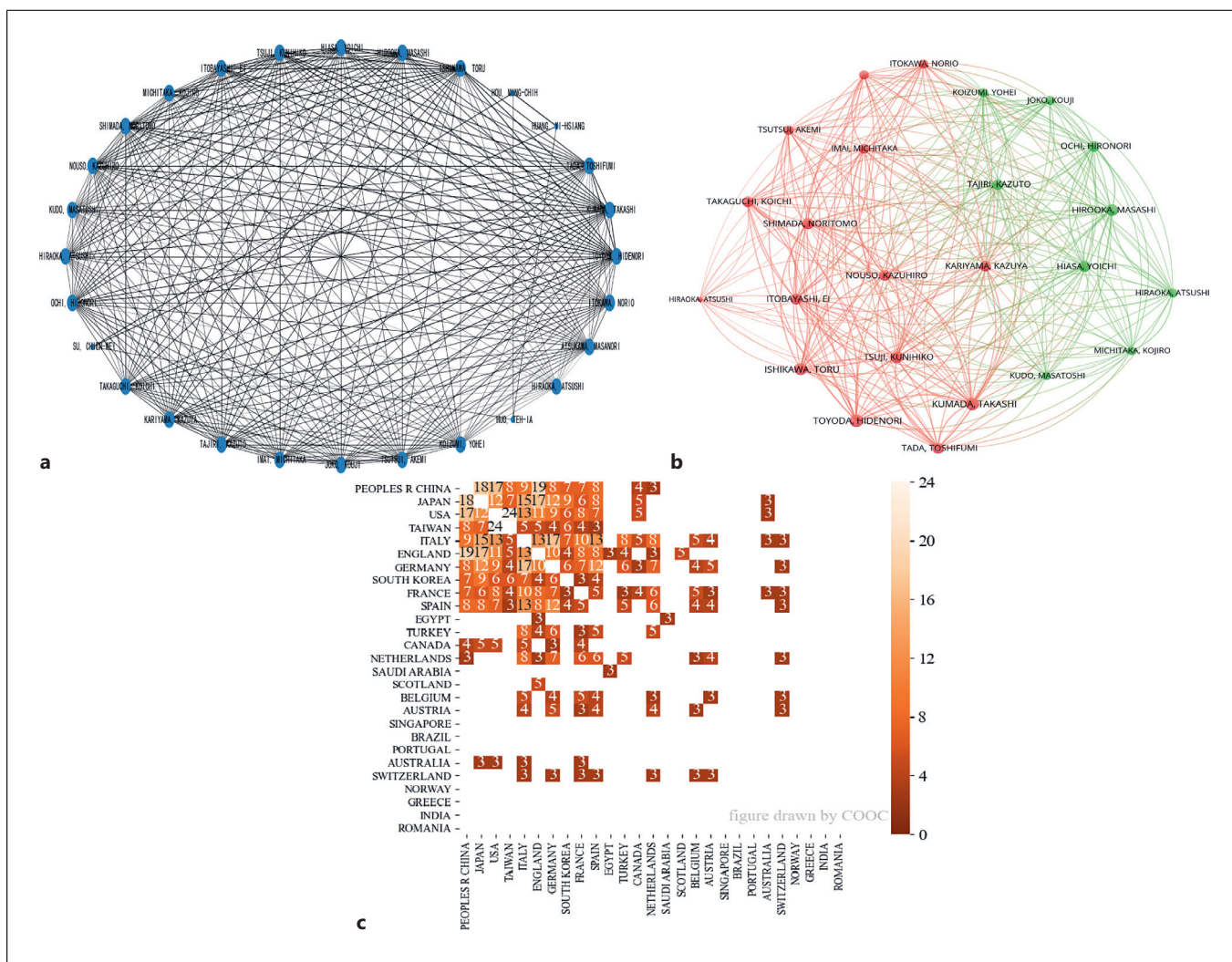


Fig. 2. Cooperation chart of authors and countries/regions. **a** Cooperative network of main authors. **b** Cooperation network of authors with strong relevance. **c** Countries/region co-occurrence matrix.

Hospital with 47 papers. Notably, eight of the ten institutions are from Japan. The top 10 research institutions are shown in Table 1.

Post Author and Countries/Regions Relationship

After the co-occurrence frequency of the COOC software is set to be ≥ 20 , Figure 2a is obtained. The size of the circle in the figure represents the size of the keyword point centrality. The larger the point degree centrality, the larger the circle; contact size. It is mainly oriented to literature data and focuses on the visualization of scientific knowledge. After removing the four authors, the VOSviewer tool is used to analyze

and obtain Figure 2b, and the same color represents the same cluster of authors.

The top ten authors who have published more than 30 papers are shown in Table 1. Eight of them are from Japan and two are from Taiwan. It can be seen that Japan has more research on the application of ALBI in HCC and has more good output. The ten authors with the most papers are distributed in a concentrated area.

The cooperative relationship between countries/regions, it can be obtained through Figure 2c. Among them, the USA and Taiwan have the most cooperation with 24 times, followed by China and England with 19 times, and China and Japan with 18 times.

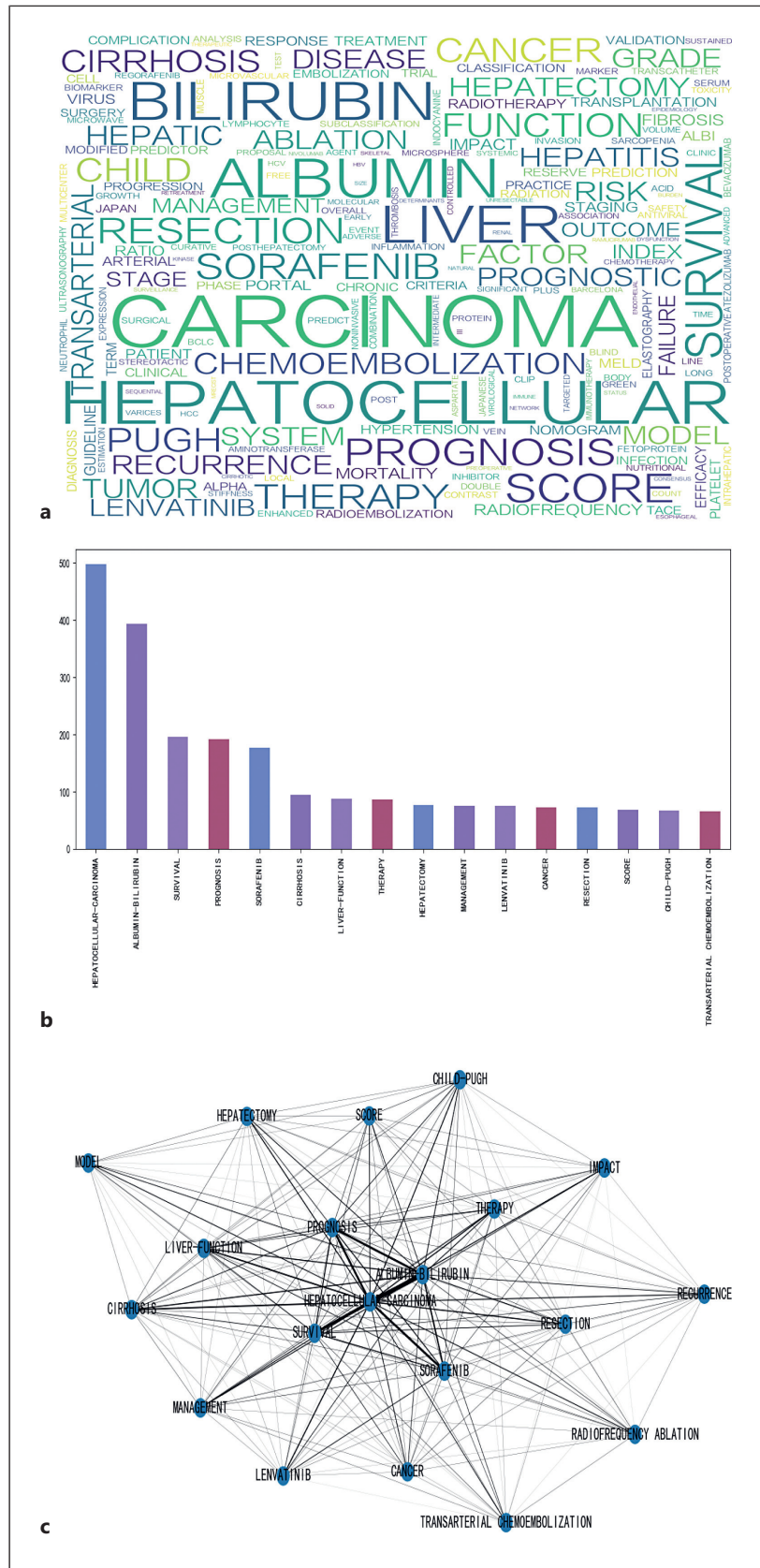


Fig. 3. Keywords analysis. **a** Keyword cloud map. **b** Keyword histogram. **c** Keyword co-occurrence graph.

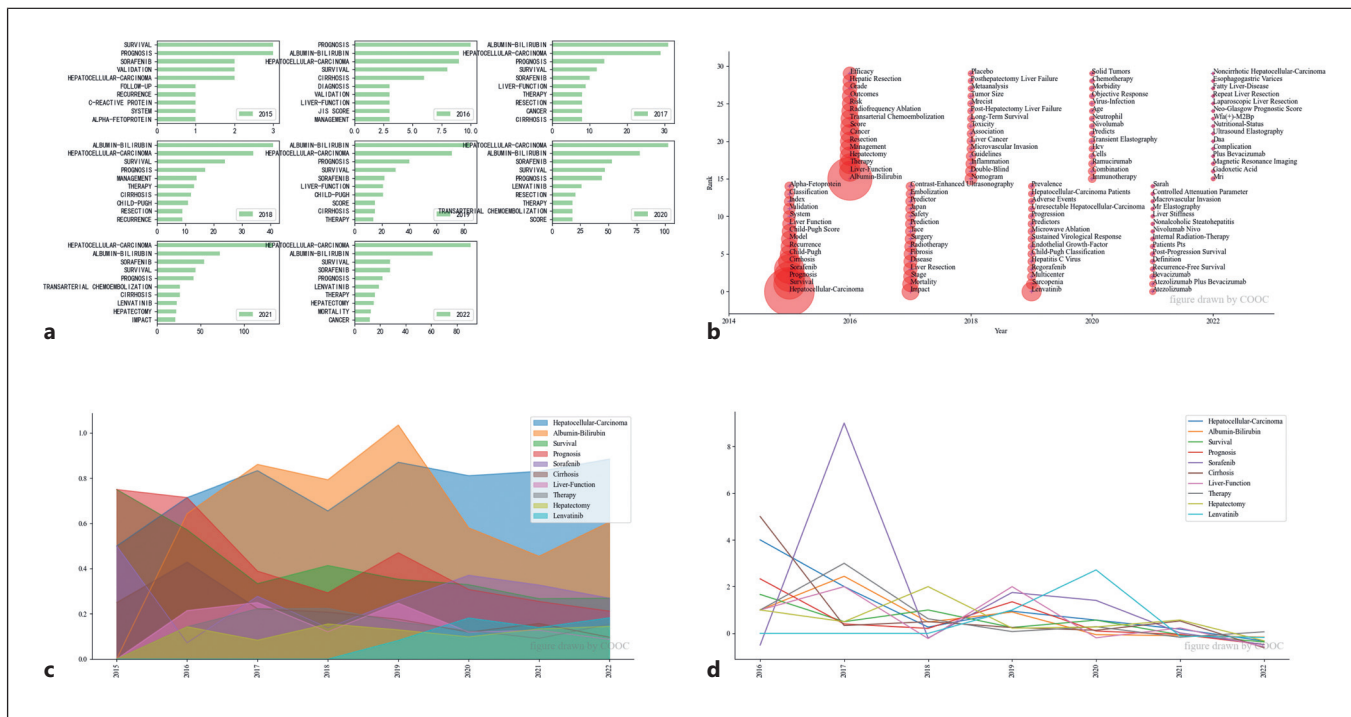


Fig. 4. Keywords and time analysis. **a** Keyword column chart year by year. **b** Time zone diagram of theme evolution path. **c** Keyword attention year by year. **d** Keyword growth rate year by year.

Literature Analysis

Keywords Analysis

Merge similar keyword fields such as Albumin-Bilirubin grade; Albumin-bilirubin score; ALBI; ALBI grade; ALBI score et al. to Albumin-Bilirubin by COOC 13.3. And, Hepatocellular Carcinoma; HCC; Hepatocellular Carcinoma (HCC) keyword fields are merged into Hepatocellular-Carcinoma.

The frequency statistics of keywords can show the research hotspots in the field. From Figure 3a and b, it can be seen that Hepatocellular-Carcinoma appeared 498 times in the top two keywords, and other keywords that appeared in ALBI were Prognosis, Survival, and Sorafenib. It is proved that the ALBI score predicts the prognosis and survival rate of HCC is the hot spot of this research, and Sorafenib treatment of HCC is also one of the hot issues. The size of the circle in the figure represents the size of the point-degree centrality of the keyword. The greater the point degree centrality, the larger the circle; the thickness of the line represents the size of the connection between the keywords. It can be seen from Figure 3c that HCC, ALBI, Prognosis, Survival, and Sorafenib are highly correlated, while Hepatocellular-Carcinoma is the keyword with the highest correlation with other keywords.

Keywords and Time Analysis

As we can see in Figure 4a, since 2016, excluding the subject headings Hepatocellular Carcinoma and Albumin-Bilirubin, the top five keywords have both Prognosis and Survival. It can be seen that the ALBI score is mainly related to the prediction of prognosis and survival rate of HCC. Treatment options have increased from Sorafenib in 2015, to Resection in 2017, to Lenvatinib and Transarterial Chemoembolization (TACE) in 2020.

Each circle represents a keyword. The larger the circle, the higher the frequency of the keyword. The keyword is the year that it first appeared in the analyzed data set. Once a keyword appears, it will be fixed in the year in which it first appeared, although the keyword will still appear in subsequent papers, it will no longer be displayed in the figure, and will only be displayed in the year that just appeared. If the keyword appears again in a later year, the frequency of the keyword will increase by 1 at the position where it first appears, and the frequency will increase after a few times. Figure 4b can reflect the changing trend of research topics in the field over time. It can be found that the themes surrounding ALBI in HCC are mainly prognosis, survival, precision treatment, etc.

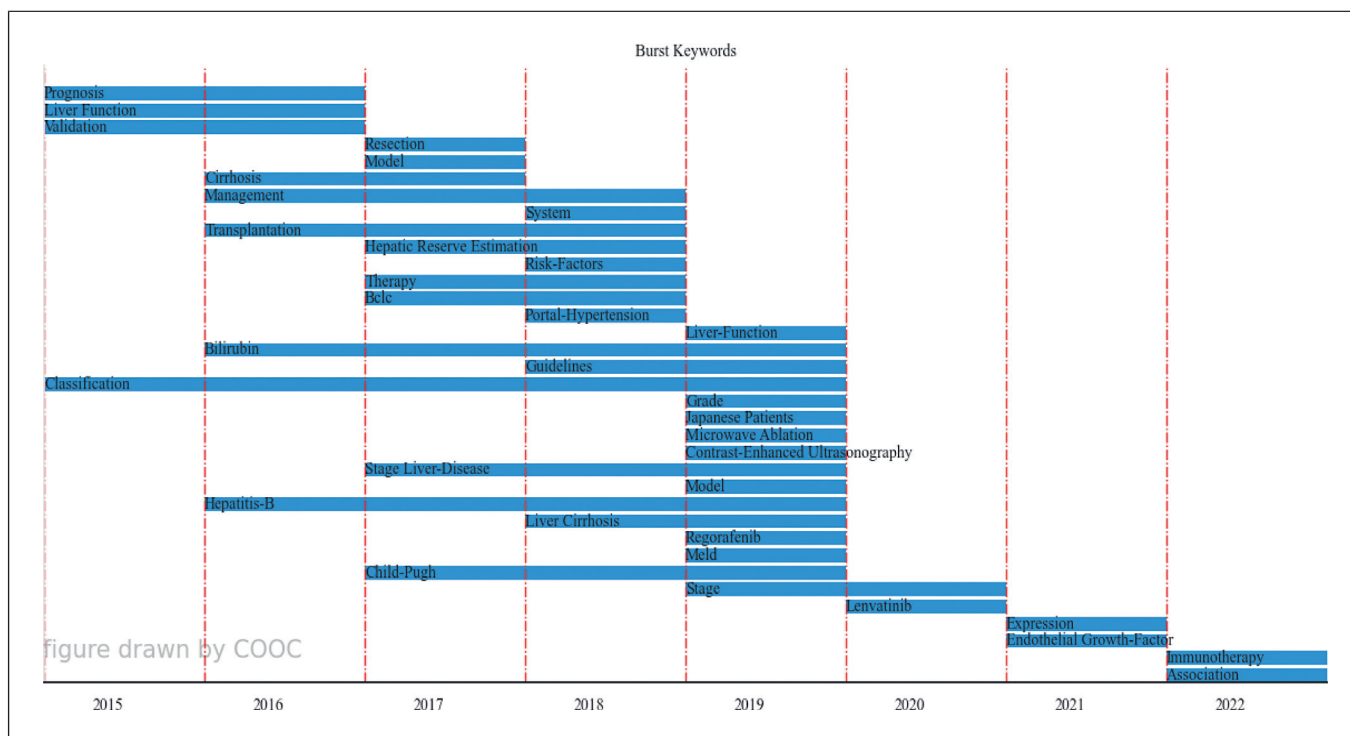


Fig. 5. Time distribution for burst word.

According to Figure 4c, it can be seen that the attention of lenvatinib increased from 2018, while the attention of ALBI increased rapidly with the proposal of ALBI in 2015. Although it decreased in 2020, it was still in a high state, but it recovered in 2022. Sorafenib showed a rapid decline in 2016, but there was a significant recovery in 2017, and the follow-up attention was basically flat. In Figure 4d, the most obvious is the recovery of sorafenib growth rate in 2017 as also mentioned in Figure 4c. The growth rate of lenvatinib also increased significantly from 2018, and the research growth rate of lenvatinib also increased significantly in 2020.

We identified 35 burst keywords in Figure 5. In 2019, for Microwave Ablation (MWA), Contrast-Enhanced Ultrasonography, and Regorafenib became an emergent term. We can see that the research on HCC therapy in 2019 is more diversified, proving that the research on HCC is more in-depth. Similarly, the emergence of Japanese Patients proves that Japan has increased its investment in the research topic of this paper. In 2020, Lenvatinib appeared in both Figure 4c, d. The Endothelial Growth-Factor in 2021 and Immunotherapy in 2022 also provide references for the improvement of ALBI score and the new treatment of HCC.

Discussion

The Application of ALBI in HCC Has Received Attention

From the research status and practice of the application of ALBI in HCC, 610 articles have been cited 8,421 times, with an average of 13.8 citations per article. The related literature on the application of ALBI in HCC (Fig. 1) shows an overall upward trend, which proves that the research on the application of ALBI in HCC has received a high degree of attention and has received extensive attention from the industry. From the table of countries/regions and authors (Table 1). Japan is the top country in the number of publications, and Japan accounts for eight of the top 10 institutions and authors, demonstrating that research on the subject is more concentrated in Japan, to some extent. It also reflects the application of ALBI in HCC to a certain extent in East Asia. It would be good if future issues could be investigated to confirm whether there are any differences between various racial groups.

ALBI Score Has a High Application Value in HCC

From the keyword histogram (Fig. 3b), the keyword co-occurrence diagram (Fig. 3c), and the year-by-year keyword histogram (Fig. 4a), we can find that, after

removing the core keywords of Hepatocellular Carcinoma and Albumin-Bilirubin, there are always three words Survival, Prognosis and Liver-Function after ranking, proving that ALBI in the prognosis of HCC and the accuracy of the estimation of survival rate and liver function has always been the focus of this research. The prognosis, liver function, and survival rate are very important in the treatment of HCC. Child-Turcotte classification [17] proposed in 1964 to the C-P score modified in 1973 [8], the C-P score has been regarded as an important indicator for the prognosis and liver function evaluation of HCC for a period of time and was included in HCC management guidelines [18]. From Figures 3–5, it can also be found that the C-P score as a keyword field also appears in ALBI in related research on HCC, which reflects that in recent years, there have been many studies comparing the application of the C-P score and ALBI score in HCC. Many of these articles have concluded that ALBI has similar or even better effects than C-P scores, and ALBI scores are simpler, more convenient, and more objective indicators than C-P scores [19–22]. Furthermore, the age-male-ALBI-platelets (aMAP) is a new HCC risk score with excellent discrimination and calibration in terms of HCC risk that also incorporates ALBI as a component [23]. In the Barcelona Clinic Liver Cancer (BCLC) strategy for prognosis prediction and treatment recommendation published in 2022, compensatory liver function can be further stratified by using the ALBI score [7]. And, the ALBI grade provides objective hepatic reserve estimation across each BCLC stage of HCC [20]. It can be seen that ALBI has a high application value in HCC.

Therapeutic Hotspots in HCC

Through the images related to the keywords (Fig. 3–5), it can be found that the hotspots for the treatment of HCC from 2015 to the present are roughly divided into three categories: drug treatment, surgical treatment, and chemotherapy.

Drug treatment: From sorafenib proposed in 2008 [24] to lenvatinib officially approved globally in 2015, the effect is no less than sorafenib [25, 26]. Furthermore, several molecularly targeted agents are currently used for unresectable HCC, such as regorafenib, cabozantinib, and ramucirumab [27]. The application of immune checkpoint inhibitors has also enriched the treatment options for advanced HCC [10]. Surgical treatment: hepatectomy, resection from a very early but still used surgical treatment [28, 29]. Chemotherapy: for surgical treatment where resection is impossible, TACE plays an important role [30, 31]. Other means: through other images (Fig. 4, 5), it can also be found that radio-frequency ablation (RFA) applied to early HCC has also been studied in HCC [32]. Furthermore, RFA and TACE are also the hot spots of many researchers [33–35].

ALBI Is Not Just an Independent Score in HCC

More and more articles have proved that ALBI can be used not only in HCC but also in liver cirrhosis, hepatectomy, viral hepatitis, liver transplantation, acute liver failure, and a series of general measurements of liver function [36–43]. ALBI can be modified or assembled as part of a new evaluation indicator. One of ALBI weaknesses is that the range of grade 2 is very wide, thus, the ALBI was modified to produce the modified ALBI (mALBI) [44]. mALBI combined with TNM staging (TNM) to produce mALBI-TNM (mALBI-T) yielded more detailed prognostic stratification [44]. Additionally, albumin simplified is a simplified fraction of mALBI that forgoes the complex logarithmic calculation required for the ALBI score, and it was also proved to be helpful in predicting the prognosis of patients with HCC treated with lenvatinib [45]. Moreover, ALBI, as an independent score or combined with other scores, can also provide help for prognosis prediction and precise treatment of other cancers. ALBI grade associated with myosteatosis or APRI (AST/platelet ratio index), showed wonderful value in identifying survival in patients with colorectal cancer and metastatic colorectal cancer [46–49]. And, it is a clinically useful predictor of prognosis in patients with pancreatic cancer [50–52]. Besides, ALBI is also an effective independent prognostic factor for patients undergoing surgical resection, anti-PD-1-based therapy, and immune checkpoint inhibitors treatment [53–55]. Furthermore, its assessment of liver function helps stratify the prognosis of patients with intrahepatic cholangiocarcinoma and can effectively predict the outcome of patients with intrahepatic cholangiocarcinoma after undergoing percutaneous MWA [56–61]. Thus, ALBI is a very potential marker that can play a role in many fields.

Statement of Ethics

All authors read and approved the publication.

Conflict of Interest Statement

The authors have no relevant financial or nonfinancial interests to disclose. The data are all from the public database Web of Science, which does not involve ethical issues. Ethical approval was not required as this study was based on publicly available data. The authors declare no competing interests

Funding Sources

This work was supported by Special Fund Project for Science and Technology Innovation Strategy of Guangdong Province (Grant No. pdjh2023b0107), National College Students Innovation and Entrepreneurship Training Program (Grant No. 202212121008), Project of

Guangdong Medical Science and Technology Research Fund (Grant No. A2022362), Shenzhen Fundamental Research Project (Grant No. JCYJ20220530165014033), and Scientific Research Projects of Medical and Health Institutions of Longhua District, Shenzhen (Grant No. 2021017), Medical Key Discipline of Longhua, Shenzhen (No. MKD202007090201).

Qi Zhou: conceptualization, methodology, and reviewing and editing. Ke Chen: reviewing and editing. Jieyan Wang and Hui Liang: conceptualization, methodology, investigation, and reviewing.

Author Contributions

Youao Zhang: conceptualization, methodology, investigation, data analysis, and writing, reviewing and editing. Huiling Yang: conceptualization, methodology, investigation, and writing and reviewing.

Data Availability Statement

The datasets generated during the current study are available in the Web of Science (<http://www.webofknowledge.com>), and further inquiries can be directed to the corresponding author.

References

- 1 Forner A, Reig M, Bruix J. Hepatocellular carcinoma. *Lancet*. 2018;391(10127):1301–14.
- 2 Kanwal F, Singal AG. Surveillance for hepatocellular carcinoma: current best practice and future direction. *Gastroenterology*. 2019;157(1):54–64.
- 3 Omata M, Cheng AL, Kokudo N, Kudo M, Lee JM, Jia J, et al. Asia-Pacific clinical practice guidelines on the management of hepatocellular carcinoma: a 2017 update. *Hepatol Int*. 2017;11(4):317–70.
- 4 Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, et al. Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach—the ALBI grade. *J Clin Oncol*. 2015;33(6):550–8.
- 5 Hiraoka A, Kumada T, Michitaka K, Kudo M. Newly proposed ALBI grade and ALBI-T score as tools for assessment of hepatic function and prognosis in hepatocellular carcinoma patients. *Liver Cancer*. 2019;8(5):312–25.
- 6 Kariyama K, Nouse K, Hiraoka A, Wakuta A, Oonishi A, Kuzuya T, et al. EZ-ALBI score for predicting hepatocellular carcinoma prognosis. *Liver Cancer*. 2020;9(6):734–43.
- 7 Reig M, Forner A, Rimola J, Ferrer-Fàbrega J, Burrel M, Garcia-Criado Á, et al. BCLC strategy for prognosis prediction and treatment recommendation: the 2022 update. *J Hepatol*. 2022;76(3):681–93.
- 8 Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973;60(8):646–9.
- 9 Kamath PS, Kim WR. The model for end-stage liver disease (MELD). *Hepatology*. 2007;45(3):797–805.
- 10 Demirtas CO, D'Alessio A, Rimassa L, Sharma R, Pinato DJ. ALBI grade: evidence for an improved model for liver functional estimation in patients with hepatocellular carcinoma. *JHEP Rep*. 2021;3(5):100347.
- 11 Wan SZ, Nie Y, Zhang Y, Liu C, Zhu X. Assessing the prognostic performance of the child-pugh, model for end-stage liver disease, and albumin-bilirubin scores in patients with decompensated cirrhosis: a large asian cohort from gastroenterology department. *Dis Markers*. 2020;2020:5193028.
- 12 Zhou T, Qu J, Sun H, Xue M, Shen Y, Liu Y. Research trends and hotspots on montessori intervention in patients with dementia from 2000 to 2021: a bibliometric analysis. *Front Psychiatry*. 2021;12:737270.
- 13 Qin F, Li J, Zhang C, Zeng G, Huang D, Tan X, et al. Biochar in the 21st century: a data-driven visualization of collaboration, frontier identification, and future trend. *Sci Total Environ*. 2022;818:151774.
- 14 Tan H, Li J, He M, Li J, Zhi D, Qin F, et al. Global evolution of research on green energy and environmental technologies: a bibliometric study. *J Environ Manage*. 2021;297:113382.
- 15 Fu Q, Ge J, Xu Y, Liang X, Yu Y, Shen S, et al. The evolution of research on depression during COVID-19: a visual analysis using Co-Occurrence and VOSviewer. *Front Public Health*. 2022;10:1061486.
- 16 Wu H, Tong L, Wang Y, Yan H, Sun Z. Bibliometric analysis of global research trends on ultrasound microbubble: a quickly developing field. *Front Pharmacol*. 2021;12:646626.
- 17 Child CG, Turcotte JG. Surgery and portal hypertension. *Major Probl Clin Surg*. 1964;1:1–85.
- 18 Song P, Cai Y, Tang H, Li C, Huang J. The clinical management of hepatocellular carcinoma worldwide: a concise review and comparison of current guidelines from 2001 to 2017. *Biosci Trends*. 2017;11(4):389–98.
- 19 Johnson PJ, Pinato DJ, Kalyuzhnyy A, Toyoda H. Breaking the child-pugh dogma in hepatocellular carcinoma. *J Clin Oncol*. 2022;40(19):2078–82.
- 20 Pinato DJ, Sharma R, Allara E, Yen C, Arizumi T, Kubota K, et al. The ALBI grade provides objective hepatic reserve estimation across each BCLC stage of hepatocellular carcinoma. *J Hepatol*. 2017;66(2):338–46.
- 21 Hiraoka A, Kumada T, Kudo M, Hirooka M, Tsuji K, Itobayashi E, et al. Albumin-bilirubin (ALBI) grade as part of the evidence-based clinical practice guideline for HCC of the Japan society of Hepatology: a comparison with the liver damage and child-pugh classifications. *Liver Cancer*. 2017;6(3):204–15.
- 22 Kumada T, Toyoda H, Tada T, Yasuda S, Tanaka J. Changes in background liver function in patients with hepatocellular carcinoma over 30 years: comparison of child-pugh classification and albumin bilirubin grade. *Liver Cancer*. 2020;9(5):518–28.
- 23 Fan R, Papatheodoridis G, Sun J, Innes H, Toyoda H, Xie Q, et al. aMAP risk score predicts hepatocellular carcinoma development in patients with chronic hepatitis. *J Hepatol*. 2020;73(6):1368–78.
- 24 Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, Blanc JF, et al. Sorafenib in advanced hepatocellular carcinoma. *N Engl J Med*. 2008;359(4):378–90.
- 25 Kudo M, Finn RS, Qin S, Han KH, Ikeda K, Piscaglia F, et al. Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: a randomized phase 3 non-inferiority trial. *Lancet*. 2018;391(10126):1163–73.
- 26 Scott LJ. Lenvatinib: first global approval. *Drugs*. 2015;75(5):553–60.
- 27 Fulgenzi C, Talbot T, Murray SM, Silletta M, Vincenzi B, Cortellini A, et al. Immunotherapy in hepatocellular carcinoma. *Curr Treat Option Oncol*. 2021;22(10):87.
- 28 Llovet JM, Bruix J, Gores GJ. Surgical resection versus transplantation for early hepatocellular carcinoma: clues for the best strategy. *Hepatology*. 2000;31(4):1019–21.
- 29 Song TJ, Ip EW, Fong Y. Hepatocellular carcinoma: current surgical management. *Gastroenterology*. 2004;127(5 Suppl 1):S248–60.
- 30 Burrel M, Reig M, Forner A, Barrufet M, de Lope CR, Tremosini S, et al. Survival of patients with hepatocellular carcinoma treated by transarterial chemoembolisation (TACE) using Drug Eluting Beads. Implications for clinical practice and trial design. *J Hepatol*. 2012;56(6):1330–5.

- 31 Cammà C, Schepis F, Orlando A, Albanese M, Shahied L, Trevisani F, et al. Transarterial chemoembolization for unresectable hepatocellular carcinoma: meta-analysis of randomized controlled trials. *Radiology*. 2002; 224(1):47–54.
- 32 Callstrom MR, Charboneau JW. Technologies for ablation of hepatocellular carcinoma. *Gastroenterology*. 2008;134(7):1831–5.
- 33 Zhu AX, Salem R. Combining transarterial chemoembolization with radiofrequency ablation for hepatocellular carcinoma: one step forward? *J Clin Oncol*. 2013;31(4):406–8.
- 34 Zhu AX, Abou-Alfa GK. Expanding the treatment options for hepatocellular carcinoma: combining transarterial chemoembolization with radiofrequency ablation. *JAMA*. 2008;299(14):1716–8.
- 35 English K, Brodin NP, Shankar V, Zhu S, Ohri N, Golowa YS, et al. Association of addition of ablative therapy following transarterial chemoembolization with survival rates in patients with hepatocellular carcinoma. *JAMA Netw Open*. 2020;3(11): e2023942.
- 36 Ko CC, Ho SY, Liu PH, Hsu CY, Hsia CY, Huang YH, et al. Dual hepatitis B and C-associated hepatocellular carcinoma: clinical characteristics, outcome, and prognostic role of albumin-bilirubin grade. *Int J Clin Oncol*. 2022;27(4):739–48.
- 37 Rimini M, Kudo M, Tada T, Shigeo S, Kang W, Suda G, et al. Nonalcoholic steatohepatitis in hepatocarcinoma: new insights about its prognostic role in patients treated with lenvatinib. *ESMO Open*. 2021;6(6):100330.
- 38 Liao R, Du CY, Gong JP, Luo F. HBV-DNA load-related peritumoral inflammation and ALBI scores predict HBV associated hepatocellular carcinoma prognosis after curative resection. *J Oncol*. 2018;2018:9289421.
- 39 Bernardi N, Chedid MF, Grezzana-Filho T, Chedid AD, Pinto MA, Leipnitz I, et al. Pre-transplant ALBI grade 3 is associated with increased mortality after liver transplantation. *Dig Dis Sci*. 2019;64(6):1695–704.
- 40 Chedid MF, Picon RV, Chedid AD. ALBI and PALBI: novel scores for outcome prediction of cirrhotic outpatients awaiting liver transplantation. *Ann Hepatol*. 2018;17(6):906–7.
- 41 Peng Y, Qi X, Tang S, Deng H, Li J, Ning Z, et al. Child-Pugh, MELD, and ALBI scores for predicting the in-hospital mortality in cirrhotic patients with acute-on-chronic liver failure. *Expert Rev Gastroenterol Hepatol*. 2016;10(8):971–80.
- 42 Mohammed M, Khalaf MH, Liang T, Wang DS, Lungren MP, Rosenberg J, et al. Albumin-bilirubin score: an accurate predictor of hepatic decompensation in high-risk patients undergoing transarterial chemoembolization for hepatocellular carcinoma. *J Vasc Interv Radiol*. 2018;29(11):1527–34.e1.
- 43 Toyoda H, Johnson PJ. The ALBI score: from liver function in patients with HCC to a general measure of liver function. *JHEP Rep*. 2022;4(10):100557.
- 44 Hiraoka A, Michitaka K, Kumada T, Izumi N, Kadoya M, Kokudo N, et al. Validation and potential of albumin-bilirubin grade and prognostication in a nationwide survey of 46,681 hepatocellular carcinoma patients in Japan: the need for a more detailed evaluation of hepatic function. *Liver Cancer*. 2017;6(4): 325–36.
- 45 Kariyama K, Hiraoka A, Kumada T, Yasuda S, Toyoda H, Tsuji K, et al. Chronological change in serum albumin as a prognostic factor in patients with hepatocellular carcinoma treated with lenvatinib: proposal of albumin simplified grading based on the modified albumin-bilirubin score (ALBS grade). *J Gastroenterol*. 2022;57(8):581–6.
- 46 Koh HH, Cho ES, Lee JH, Shin SJ, Lee HS, Park EJ, et al. Association of albumin-bilirubin grade and myosteatosis with its prognostic significance for patients with colorectal cancer. *Ann Surg Oncol*. 2022;29(6): 3868–76.
- 47 Watanabe D, Fujii H, Yamada Y, Matsuhashi N, Makiyama A, Iihara H, et al. Association of albumin-bilirubin score in patients with colorectal cancer receiving later-line chemotherapy with regorafenib. *Int J Clin Oncol*. 2021;26(7):1257–63.
- 48 Abdel-Rahman O. Prognostic value of baseline ALBI score among patients with colorectal liver metastases: a pooled analysis of two randomized trials. *Clin Colorectal Cancer*. 2019;18(1):e61–8.
- 49 Pereyra D, Starlinger P. ASO author reflections: APRI + ALBI: a novel tool for estimating chemotherapy-associated liver injury in patients with colorectal cancer liver metastasis undergoing liver resection. *Ann Surg Oncol*. 2019;26(Suppl 3):598–9.
- 50 Imamura T, Okamura Y, Sugiura T, Ito T, Yamamoto Y, Ashida R, et al. Clinical significance of preoperative albumin-bilirubin grade in pancreatic cancer. *Ann Surg Oncol*. 2021;28(11):6223–35.
- 51 Zhang TN, Yin RH, Wang LW. The prognostic and predictive value of the albumin-bilirubin score in advanced pancreatic cancer. *Medicine*. 2020;99(28):e20654.
- 52 Yagyu T, Saito H, Sakamoto T, Uchinaka EI, Morimoto M, Amisaki M, et al. Preoperative albumin-bilirubin grade as a useful prognostic indicator in patients with pancreatic cancer. *Anticancer Res*. 2019;39(3):1441–6.
- 53 Matsukane R, Watanabe H, Hata K, Suetsugu K, Tsuji T, Egashira N, et al. Prognostic significance of pre-treatment ALBI grade in advanced non-small cell lung cancer receiving immune checkpoint therapy. *Sci Rep*. 2021;11(1):15057.
- 54 Kinoshita F, Yamashita T, Oku Y, Kosai K, Ono Y, Wakasu S, et al. Prognostic impact of albumin-bilirubin (ALBI) grade on non-small lung cell carcinoma: a propensity-score matched analysis. *Anticancer Res*. 2021;41(3):1621–8.
- 55 Takada K, Takamori S, Shimokawa M, Toyokawa G, Shimamatsu S, Hirai F, et al. Assessment of the albumin-bilirubin grade as a prognostic factor in patients with non-small-cell lung cancer receiving anti-PD-1-based therapy. *ESMO Open*. 2022;7(1): 100348.
- 56 Li Q, Chen C, Zhang J, Wu H, Qiu Y, Song T, et al. Prediction efficacy of prognostic nutritional index and albumin-bilirubin grade in patients with intrahepatic cholangiocarcinoma after radical resection: a multi-institutional analysis of 535 patients. *Front Oncol*. 2021;11:769696.
- 57 Yang H, Cheng Z, Han Z, Liu F, Yu X, Yu J, et al. Assessment of the outcomes of intrahepatic cholangiocarcinoma after ultrasound-guided percutaneous microwave ablation based on albumin-bilirubin grade. *Cardiovasc Intervent Radiol*. 2021;44(2):261–70.
- 58 Kaneko S, Kurosaki M, Tsuchiya K, Yasui Y, Inada K, Kirino S, et al. Prognosis of intrahepatic cholangiocarcinoma stratified by albumin-bilirubin grade. *Hepatol Res*. 2021; 51(8):902–8.
- 59 Tsilimigras DI, Hyer JM, Moris D, Sahara K, Bagante F, Guglielmi A, et al. Prognostic utility of albumin-bilirubin grade for short- and long-term outcomes following hepatic resection for intrahepatic cholangiocarcinoma: a multi-institutional analysis of 706 patients. *J Surg Oncol*. 2019;120(2): 206–13.
- 60 Li H, Li J, Wang J, Liu H, Cai B, Wang G, et al. Assessment of liver function for evaluation of long-term outcomes of intrahepatic cholangiocarcinoma: a multi-institutional analysis of 620 patients. *Front Oncol*. 2020;10:525.
- 61 Ni JY, An C, Zhang TQ, Huang ZM, Jiang XY, Huang JH. Predictive value of the albumin-bilirubin grade on long-term outcomes of CT-guided percutaneous microwave ablation in intrahepatic cholangiocarcinoma. *Int J Hyperther*. 2019;36(1): 328–36.