Four Decades of Clinical Liver Transplantation Research: Results of a Comprehensive Bibliometric Analysis

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Background. Nearly 40 y have passed since the 1983 National Institutes of Health Consensus-Development-Conference, which has turned liver transplantation (LT) from a clinical experiment into a routine therapeutic modality. Since, clinical LT has changed substantially. We aimed to comprehensively analyze the publication trends in the most-cited top-notch literature in LT science over a 4-decade period. **Methods.** A total of 106 523 items were identified between January 1981 and May 2021 from the Web of Science Core Collection. The top 100 articles published were selected using 2 distinct citation-based strategies to minimize bias. Various bibliometric tools were used for data synthesis and visualization. **Results.** The citation count for the final dataset of the top 100 articles ranged from 251 to 4721. Most articles were published by US authors (n = 61). The most prolific institution was the University of Pittsburgh (n = 15). The highest number of articles was published in *Annals of Surgery, Hepatology, and Transplantation*; however, *Hepatology* publications resulted in the highest cumulative citation of 9668. Only 10% of the articles were classified as evidence level 1. Over 90% of first/last authors were male. Our data depict the evolution of research focus over 40 y. In part, a disproportional flow of citations was observed toward already well-cited articles. This might also project a slowed canonical progress, which was described in other fields of science. **Conclusions.** This study highlights key trends based on a large dataset of the most-cited articles over a 4-decade period. The present analysis not only provides an important cross-sectional and forward-looking guidance to clinicians, funding bodies, and researchers but also draws attention to important socio-academic or demographic aspects in LT.

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INTRODUCTION

Since the early efforts of several pioneering groups in the 1960s, liver transplantation (LT) has evolved as the mainstay of treatment for patients with end-stage liver disease.[1] Over the nearly 70-y long history of clinical solid organ transplantation, dozens of groundbreaking studies have been published, contributing to the ultimate goal of improving patient outcomes.[2] According to the Global

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The study was designed by the initiating study team (D.J., T.J., W.L., P.N.M., I.M.A.B., M.S., and Z.C.). Data collection, analysis, and interpretation were performed by D.J., T.J., W.L., J.B., M.S., J.P., G.L., T.C., S.A.L., U.P.N., and Z.C. The article was drafted by D.J., T.J., and Z.C. All authors have substantially contributed to the overall analysis plan, interpreting interim and final results, and critically revising and approving the final version of the article.

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Observatory on Donation and Transplantation, a total of 35 784 LT procedures were carried out in transplant centers around the globe in 2019.[3]

In the present era of academic publishing, with an increasing threat from predatory publishers and the dominance of a "publish or perish" principle, a large number of research data is generated and published in journals every day.[4,5] It is increasingly difficult to discriminate between impactful high-quality science and articles with low scientific merit. As the 2-time Pulitzer Prize–winning author and biologist, the late E.O. Wilson concluded in 1998, "*We are drowning in information, while starving for wisdom.*" (Wilson, 1998, p294). Accordingly, using the keyword "liver transplantation" yields over 160 000 hits in the PubMed database alone. Textbook chapters and review articles are usually suitable to obtain a brief overview of recent advancements on a particular subtopic but cannot cover this large body of accumulated data or depict the successive changes in research focus over the years.

The concept of bibliometrics was first proposed by Alan Pritchard in 1969,[6] being defined as the use of mathematical, statistical methods and visualization tools to analyze trends in the evolution of a certain scientific discipline. Since, bibliometric analysis, including citation analysis, has been widely used in the assessment, synthesis, and mapping of large-scale literature data. Here, we hypothesized that such bibliometric methods might also help to understand the most important trends in LT science.[7,8]

In this study, we aimed to identify the most-cited articles in the field of clinical LT published over the past 40 y and used state-of-the-art bibliometric analysis tools to describe and understand the patterns of research activity and the successive change of scientific interest in the field.

MATERIALS AND METHODS

Literature Screening and Identification of the Dataset

The Clarivate Analytics Web of Science Core Collection (CA-WoSCC) database was systematically searched from January 1981 to May 2021. Two distinct but complementary strategies were used to identify and select the final set of the most-cited articles. The study design and selection approach are depicted in Figure 1.

1. Selection strategy 1 (SS1; main approach): According to the total citation counts (TC) of the article, the data set of the 100 most frequently cited articles was filtered out (Advanced Search: TS = Liver transplantation * or Grafting, Liver or Liver Grafting or Transplantation, Liver or Liver Transplant * or Transplant, Liver or Hepatic Transplantation * or Transplantation, Hepatic). Only original articles and comprehensive/systematic reviews with online full text focusing on clinical research in LT were included. Studies dealing directly with LT patients or LT candidates were included. Non-English language literature was excluded. Literature reviews that summarized published studies only briefly, meeting abstracts, editorials, consensus statements, and guidelines were excluded as well to provide a final selection of articles focusing on articles of high original scientific merit in the field. Because of their largely different design, scientific approach, and citation trends, basic and translational studies and experimental research using animals were excluded and should be analyzed separately.
2. Selection strategy 2 (SS2; validation/supplementary approach): It was described before that a potential selection bias might appear toward older reports, which had a longer period of time to accumulate a large number of overall TC.[9] Therefore, a further SS2 was adopted to assess the validity of our SS1 and to potentially find further articles that were not identified by the main approach. For this, the 40 y period was divided into 2-y intervals (with the exception of the most recent period of January 2019 to May 2021, which was merged into 1 last interval). Five articles with the highest TC within each 2-y period were selected. The other conditions and the search strategy remained the same as for SS1.

The nonoverlapping articles from the 2 selections were divided into 2 subgroups (group 1 and group 2) to explore differences in publication trends, such as year of publication, research topics, citations, number of authors, impact factors (IFs), and journals (Figure 1).

Three reviewers (D.J., T.J., and W.L.) independently screened and identified the top 100 articles and carried out the verification using the above-described 2 strategies. Any disagreement among the 3 reviewers was resolved by consensus involving a fourth reviewer (Z.C.).

Ethics approval was waived because of the specific study design and collection of online available and published bibliometric data without the involvement of any human trials or animal experiments.

Data Acquisition, Analysis, and Visualization

After identification of the final datasets based on the above-described dual approach, we retrieved the records from the CA-WoSCC database, including all available information. Data were extracted using Microsoft Excel spreadsheets (Microsoft Corp, Redmond, WA). The bibliographic information of the selected articles was analyzed and converted automatically using the "bibliometrix" package (version 3.0.4) in R (version 4.0.3). The information was extracted and analyzed, including citations, title, authors, institutions, countries or regions, year of publication, journals, IFs, main topic, subtopic, and level of evidence (according to the current recommendations of the Oxford Center for Evidence-Based Medicine).[10]

To describe author productivity patterns within our dataset, Lotka's approximate inverse-square law was adopted as described before in detail.[11,12] The calculation was based on the following formula:

$$f(x) = \frac{C}{x^{a}},$$

where $f(x)$ is the proportion of the number of authors who published x articles to the total number of authors, C is a subject characteristic constant of the R software, and a is a further constant that almost always equals 2. This bibliometric law assumes that the author-to-article relation is inversely proportional to the square of published articles.[13] Lotka's law follows a hyperbolic distribution, as a large number of authors publish 1 or few articles and only a few contribute to many. This analysis was used to assess the robustness of our data selection and dataset. A

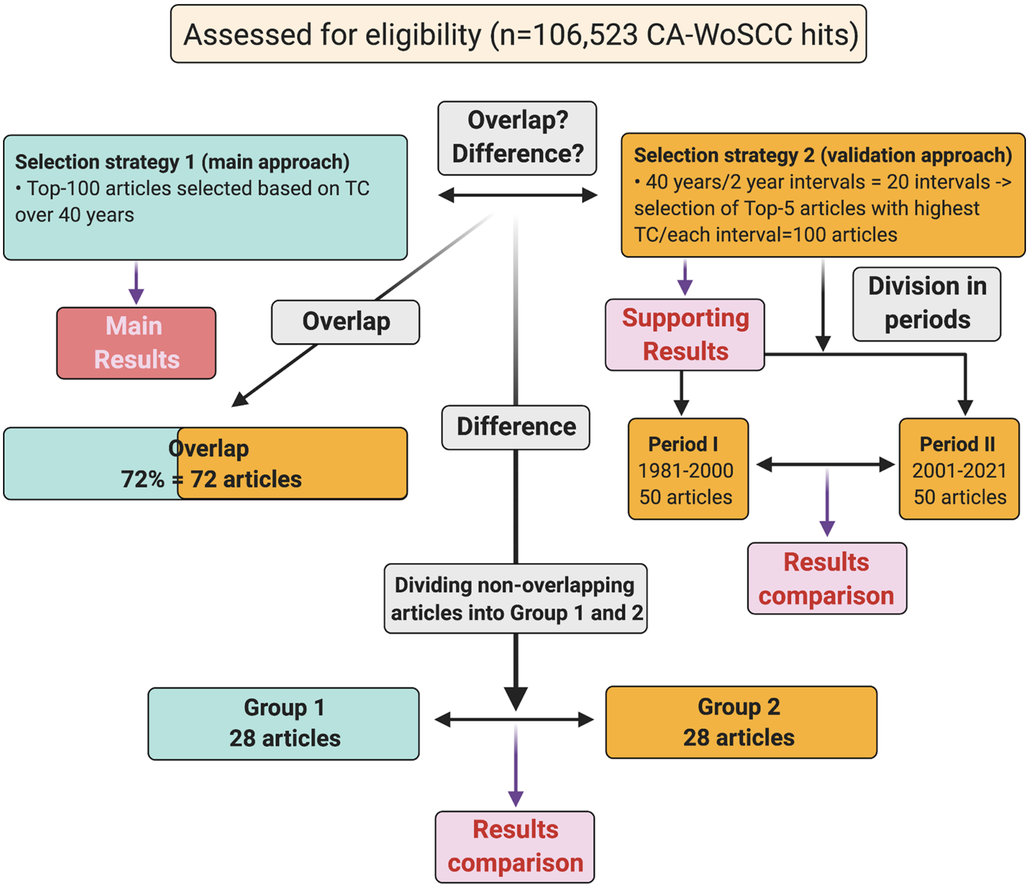

FIGURE 1. Flowchart of the study design and analysis approach used in the present study. This figure was created using BioRender.com (https://biorender.com/). CA-WoSCC, the Clarivate Analytics Web of Science Core Collection; TC, total citation.

$P > 0.05$ comparing the "theoretical" and "observed" data confirms a nonsignificant difference, thus a good compliance with Lotka's law as described before.[13] A nonsignificant result in the goodness of fit testing according to Kolmogorov-Smirnov indicates that the sampled dataset follows the basic rule of Lotka concerning author scientific productivity and that there is a low risk of a nonrepresentative or strongly skewed data selection.

Furthermore, the average annual citation growth-citable item was calculated to investigate the changes in citation accumulation patterns over the years. Comparisons were made using the Mann-Whitney U test while using Fisher's exact test as applicable. Statistical significance was defined as $P < 0.05$. Graphs and figures were created using the R and VOSviewer package (version 1.6.16; https://www.vosviewer.com/). The study flowchart was created using BioRender (https://biorender.com/). The Venn diagram, world map, and sunburst diagram were created using respective online tools (https://www.interactivenn.net/; https://mapchart.net/world-advanced.html/; https://app.rawgraphs.io/).

RESULTS

Citations Counts and Publications Periods

A total of 106 523 search hits focusing on LT were identified from the CA-WoSCC database between January 1981 and May 2021. The complete list of the 100 most-cited articles based on SS1 can be found in **Table S1** (**SDC**, http://links.lww.com/TP/C466). The range of TC of the included articles ranged between 251 and 4721. Chronologically, the first article in the list was published in 1981 with a TC of 440, describing the results of a pilot trial with the use of cyclosporin A in LT.[14] The most recent article related to organ preservation/machine perfusion (MP) was published in 2018 with a TC of 294.[15] As shown in Figure 2A, the top 3 y with the highest number of articles published were 2000 (n = 8), 1991 (n = 7), and 2005 (n = 6). Most articles were published in the time period between 1991 and 2000 (n = 37), followed by 2001 to 2010 (n = 35), 1981 to 1990 (n = 20), and 2011 to 2021 (n = 8). Table 1 shows the top 10 articles based on TC.

When analyzing the patterns of the average annual citation growth/article using the data of all articles published in the digital or "world wide web" era, an overall increasing rate of annual citation accumulation was observed over the years (Figure 3).

Countries, Regions, Institutions, and Authors

When analyzing countries, regions, and institutions, the final set of most-cited articles was from a total of 14 countries or regions. Most articles were published by US institutions (n=61), followed by France (n=9), Japan (n=6), Spain (n=5), and the United Kingdom (n=5) (the geographic distribution is shown in Figure 4A and Table 2). Figure 5

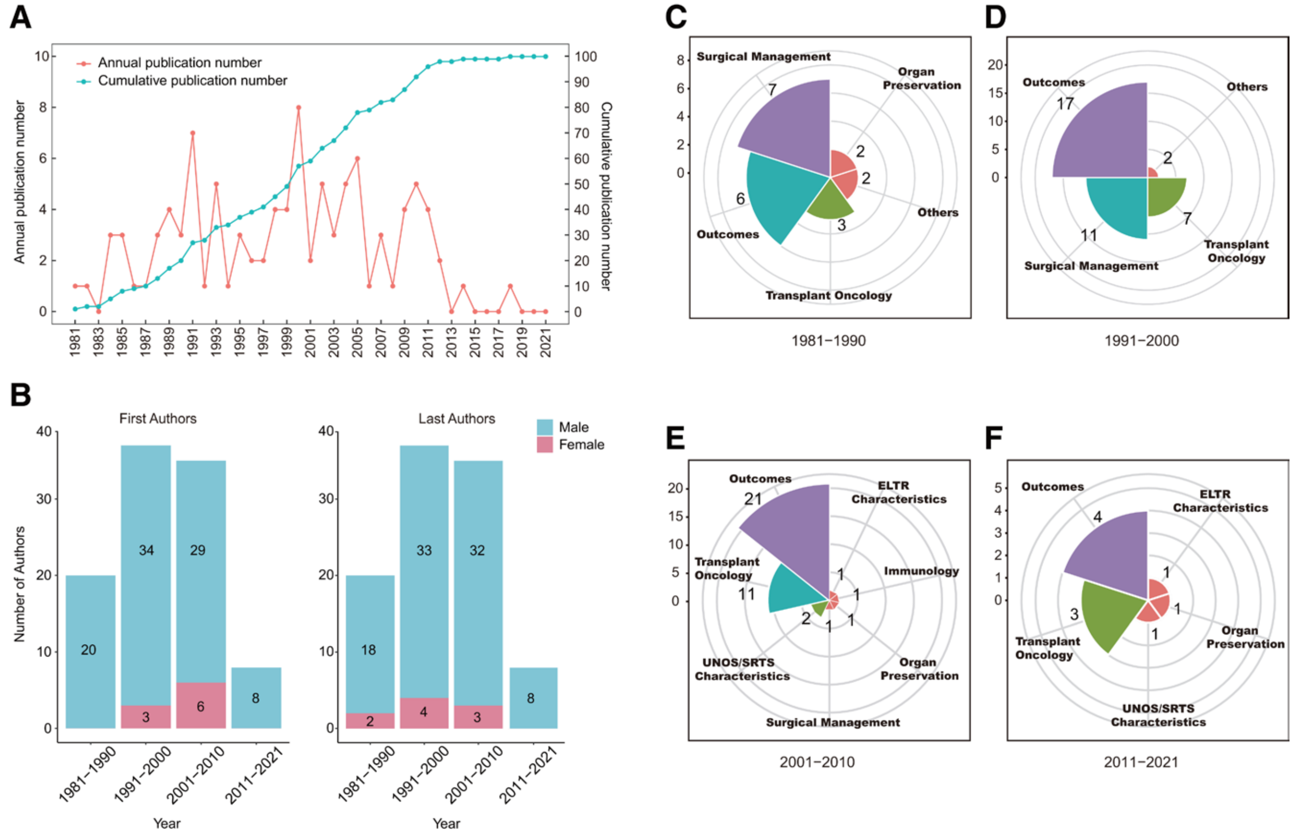

FIGURE 2. Publication trends, gender ratio, and topic trends of the top 100 articles from 1981 to 2021 based on selection strategy 1. A, Annual publication and cumulative publication patterns. B, Gender distribution for first and last authors. C–F, Number of articles classified into different main topics from 1981 to 1990, 1991 to 2000, 2001 to 2010, and 2011 to 2021. ELTR, European Liver Transplant Registry; UNOS/SRTS, United Network for Organ Sharing/Scientific Registry of Transplant Recipients.

illustrates collaborations among countries, showing a complex cooperation network for some countries, such as the United States of America, Italy, France, and the United Kingdom.

As noted in Table 2, the top institutions with the highest number of articles included the University of Pittsburgh (n = 15), Mayo Clinic (n = 7), and the University of California, San Francisco (n = 7) with 7054, 2666, and 4575 citations, respectively. Institutes were classified into 6 clusters. The top 6 organizations with the most cooperation partners were the University of Pittsburgh (n = 15), followed by the Mayo Clinic (n = 8), University of California, San Francisco (n = 8), King's College Hospital (n = 7), Addenbrooke's Hospital (n = 6), and Paul-Brousse Hospital (n = 6) (Figure 4B). Similar patterns were observed in the author cooperation networks with all major collaboration clusters associated with pioneer groups of LT research (Figure 4C).

Some 91% and 91% of the first and last authors were male, respectively (Figure 2B). Despite some slight variations over time, the overwhelming dominance of male authors remained obvious over the whole 4-decade period.

Compliance with Lotka's law was evaluated in relation to the authors and their scientific work in LT. The relationship between the number publications/the number authors within our dataset was in line with the

TABLE 1.

Top 10 articles with the highest number of total citations from 1981 to 2021

Author	Journal	Year	Total citation	Main topic
Mazzaferro V	New Engl J Med	1996	4721	Transplant Oncology
Yao FY	Hepatology	2001	1473	Transplant Oncology
Llovet JM	Hepatology	1999	1253	Transplant Oncology
Feng S	Am J Transplant	2006	1209	Outcomes
Mazzaferro V	Lancet Oncol	2009	1145	Transplant Oncology
Starzl TE	Lancet	1989	900	Outcomes
Starzl TE	Hepatology	1982	846	Others
Forman LM	Gastroenterology	2002	830	Outcomes
Ploeg RJ	Transplantation	1993	814	Outcomes
Samuel D	New Engl J Med	1993	803	Outcomes

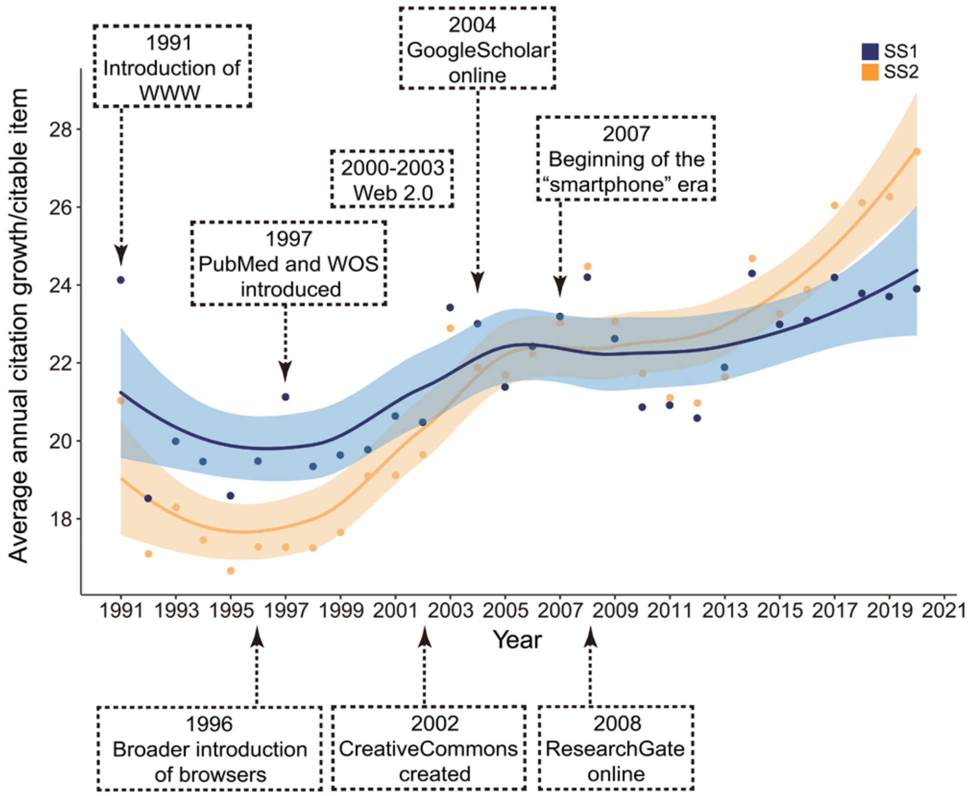

FIGURE 3. Changes in the trends of the average annual citation growth/citable item for selection strategies 1 and 2. SS1, selection strategy 1; SS2, selection strategy 2; WWW, World Wide Web.

assumption of Lotka's law (*P* = 0.627 "observed" versus "theoretical") (**Figure S1a and b, SDC,** http://links.lww.com/TP/C466). Briefly, based on Lotka's formula in SS1, *a* was calculated in R as *a* = 2.4862, and *C* was 0.6084, suggesting that an expected 60.84% of 710 authors would sign 1 article within the 100 included articles, whereas the observed number was 78.87% or 560. Some 149 (20.99%) authors were listed in 2 to 9 publications, and 1 author signed 16 publications (**Figure S1b, SDC,** http://links.lww.com/TP/C466). Similar patterns were recorded for SS2 (**Figure S1c and d, SDC,** http://links.lww.com/TP/C466).

Journals, Topics, and Article Types

The top 100 articles were published in a total of 21 different journals. The top 10 journals are shown in Table 2. Although *Annals of Surgery* published the highest number of articles with 22 articles, *Hepatology* publications resulted in the highest TC with 9668 citations. In total, there were 5 journals with a ratio of TC to publications exceeding 500: *New England Journal of Medicine* (1053), *Gastroenterology* (570), *Hepatology* (537), *Journal of Hepatology* (540), and the *Lancet* (509).

The ten most highly cited articles were predominantly focusing on LT outcomes (n = 5) and transplant oncology (n = 4) (Table 1). To better describe patterns in topics and evidence, the main topic, subtopic, and level of evidence were determined for each article, and the relationship network was visualized in form of a Sankey diagram (Figure 6). The most frequent main topic was transplantation outcomes (n = 48), followed by transplant oncology (n = 24) and surgical management (n = 19) (**Table S2, SDC,** http://links.lww.com/TP/C466). Hepatocellular carcinoma (HCC) (n = 20) was the most frequent subtopic, followed by living donor LT (LDLT) (n = 10), risk factors (n = 10), and viral hepatitis (n = 10). Ten percent of articles (n = 10) were classified as evidence level 1; 72% of articles (n = 72) were classified as level 2; 4% (n = 4) and 14% (n = 14) of articles were defined as level 3 and level 4, respectively (**Table S2, SDC,** http://links.lww.com/TP/C466). In the early years of the analyzed period (1981–1990), surgical management obviously had a large impact on the LT community generating multiple top-cited articles that later gradually shifted toward outcome research and transplant oncology (Figure 2C–F).

Characteristic Differences Between the 2 Selection Strategies

Based on SS2, we found a 72% overlap with the initial selection (SS1). For this secondary dataset, the relevant analyses were repeated and fully included as online supplementary material (Figure 3; **Figures S1–S3 and Tables S3 and S4, SDC,** http://links.lww.com/TP/C466). Out of the 28 articles that were newly identified in SS2, 9 were from the first period (1981–2000), and 19 articles were from the second period (2001–2021) (Figure 7A). The characteristic differences between group 1 (28 articles of SS1 not overlapping with those of SS2) and group 2 (28 articles of SS2 not overlapping with those of SS1) are shown in **Table S5** (**SDC,** http://links.lww.com/TP/C466). Two charts (Figure 7B and C) were used to describe the major differences in research topics of articles belonging to groups 1 and 2, respectively.

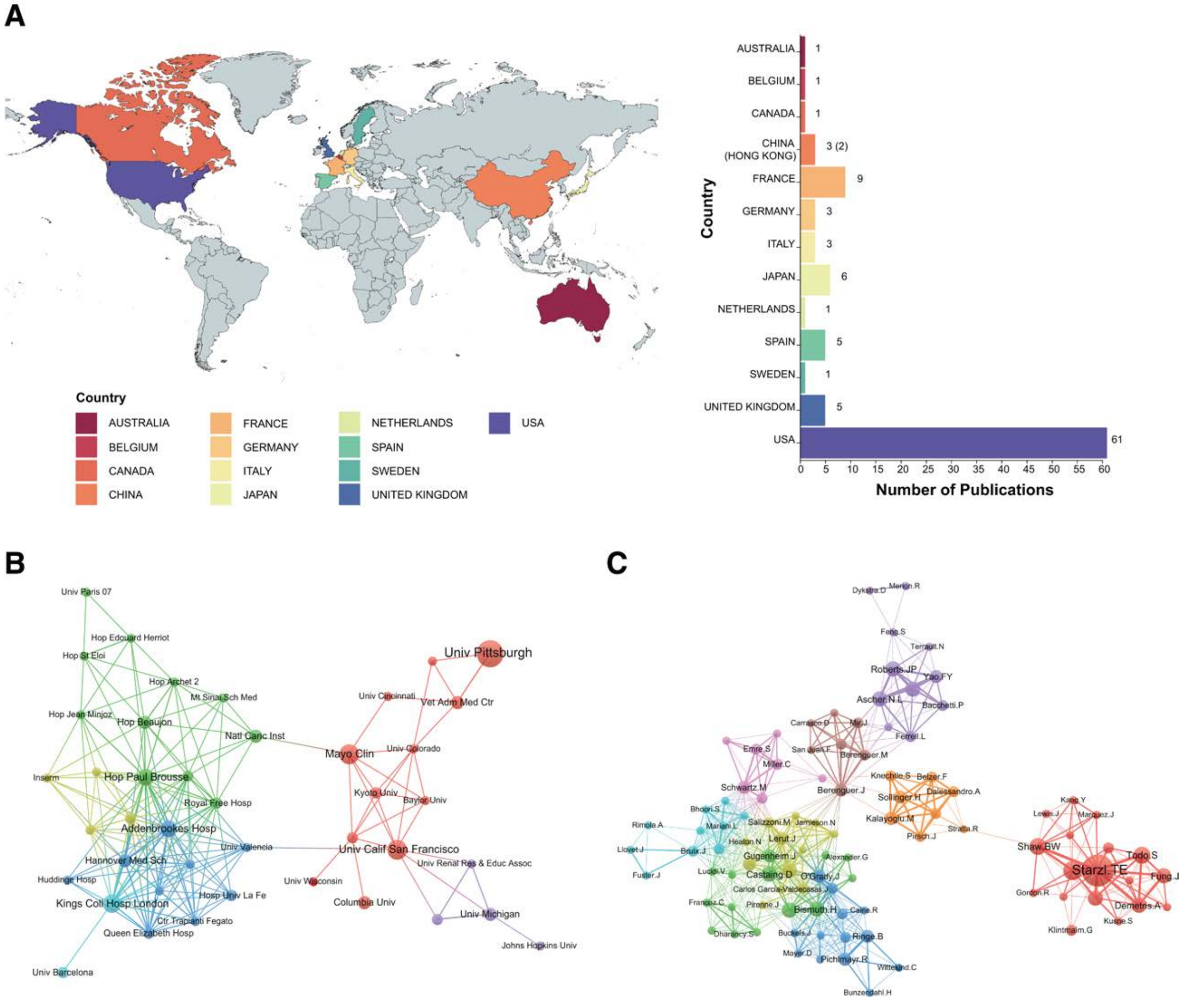

FIGURE 4. Geographical distributions, institutional and author clusters, and collaboration network analysis based on selection strategy 1. A, Country of origin for the top 100 most-cited articles in LT over 40 y. The country of origin was defined by the primary affiliation of the corresponding author. B, The co-operation relationships of institutions that published the top 100 most-cited articles from 1981 to 2021. Co-operation with >1 collaborative work was depicted. C, The cooperation relationships of authors that published the top 100 articles from 1981 to 2021. Cooperation with >1 collaborative work was depicted.

As shown in Figure 7D, distribution was different in the 2 groups, with most of the articles of group 1 published between 1989 and 2011, whereas articles of group 2 were mainly published from 1981 to 1985 and after 2012. A significant difference was identified in the TC of the 2 groups with a median TC of 306 (interquartile range 328–285) for group 1 and 167 (interquartile range 217–111) for group 2 ($P < 0.001$) (Figure 7E). No significant difference was found in terms of the number of authors/articles or in IF in the year of publication (Figure 7F and G). Interestingly, the analysis of gender ratios for the first author has shown significantly more female first authors in group 2 than group 1 (28:1 (male to female) and 21:7, respectively; Fischer's exact test: $P < 0.05$). Although the gender ratio of the senior or last authors in the 2 groups remained largely unchanged (**Table S5, SDC**, http://links.lww.com/TP/C466). In terms of journals, the largest number of articles were published in *Annals of Surgery* and *Liver Transplantation* with 6 articles in group 1, respectively. *American Journal of Transplantation* was the leading journal in group 2 with 7 articles.

Altogether, the major overlap of 72% between SS1 and SS2 shows the overall robustness of our approach in identifying relevant articles; however, the characteristic differences between groups 1 and 2 also demonstrate a certain selection bias in SS1 toward earlier articles.

DISCUSSION

In this study, we comprehensively analyzed a large dataset of the most-cited scientific publications in clinical LT literature from the past 40 y. For the first time in this context, state-of-the-art bibliometric methods were adopted for descriptive data analysis and visualization of various trends and the successive evolution of topics. Our data show that the influence of surgical advancements on the community was accentuated in the early pioneering era with surgical techniques being refined and adopted promptly. Meanwhile, the increasing relevance of LT using marginal organs and the optimization of organ preservation, such as by MP, became prominent research topics in the recent years.[16,17]

TABLE 2.

Distribution of top 10 countries, institutions, and journals from 1981 to 2021

No.	Country	Number of publications	TC	TC/publication	IF
1	USA	61	26571	435.59	
2	France	9	4177	464.11	
3	Japan	6	2831	471.83	
4	Spain	5	2736	547.20	
5	United Kingdom	5	1987	397.40	
6	China (Hong Kong)	3 (2)	1317	439.00	
7	Germany	3	1539	513.00	
8	Italy	3	6176	2058.67	
9	Australia	1	551	551.00	
10	Belgium	1	783	783.00	
No.	**Institute**	**Number of publications**	**TC**	**TC/publication**	**IF**
1	University of Pittsburgh	15	7054	470.27	
2	Mayo Clinic	7	2666	380.86	
3	University of California, San Francisco	7	4575	653.57	
4	The Paul-Brousse Hospital	6	2891	481.83	
5	The University of Wisconsin	4	1806	451.50	
6	National Cancer Institute, Milan	3	6176	2058.67	
7	King's College Hospital	3	1657	552.33	
8	Kyoto University Columbia University	3	1470	490.00	
9	Columbia University	3	937	312.33	
10	Hannover Medical School	2	815	407.55	
No.	**Journal**	**Number of publications**	**TC**	**TC/publication**	**IF**
1	Annals of Surgery	22	8871	403.23	12.962
2	Hepatology	18	9668	537.11	17.420
3	Transplantation	10	4137	413.70	4.932
4	Liver Transplantation	9	2974	330.44	5.792
5	American Journal of Transplantation	8	3598	449.75	8.083
6	New England Journal of Medicine	8	8424	1053.00	91.242
7	The Lancet	5	2543	508.60	79.322
8	Gastroenterology	4	2281	570.25	22.684
9	Journal of Hepatology	2	1079	539.50	25.082
10	Journal of The American College of Surgeons	2	736	368	6.113

IF, impact factor; TC, total citation.

It represents a particular challenge to comprehensively analyze publication trends and identify articles, topics, and subtopics with the strongest impact on the community over the span of 40 y. Bibliometric citation analysis and its visualization tools are increasingly used to meet such challenges of data presentation and synthesis.[7] Although there is no clear consensus on how to measure and compare the real impact of scientific publications on the scientific community, most recognized quality indicators are citation based.[9] The frequency of citations and IFs may largely differ between various disciplines; however, it is certain that, despite its limitations, the number of times a particular scientific article is referenced indicates the scientific interest, visibility, and its sustained canonical impact on the scientific community.[18,19]

The online availability of scientific contents and the rapid introduction of new journals, as well as the recent era of open science facilitated publication activity and citations.[20] This was also manifested in an overall increase in the annual citation growth/citable item over the years in our study. The use of TC as a single indicator to select the most impactful articles, like in previous studies,[7] is not suitable to depict these changes in publication and citation activity that are described above momentarily, therefore, carries a high risk of selection bias.[21] A recent study by Chu et al demonstrated that, as the number of articles published per year in a scientific field grows large, citations flow disproportionately to already well-cited articles; this may lead to an entrapment in an existing canon rather than the advancement of new ideas.[9] To normalize for this potential bias, we introduced a novel supplementary selection approach by dividing the 40-y period into 2-y intervals and selecting the top 5 articles with the highest citations in each interval.

Our study has revealed important trends in the distribution of contributing authors, countries/regions, and collaboration networks. These data are not accessible elsewhere without our bibliometric analysis and data synthesis.

To characterize what kind of scientific articles obtained the highest citations over time, we classified all articles based on their main topic, subtopic, and evidence level. One of the most important observations in this context was the relatively low number of top articles (10%) being level 1 evidence, which is in general considered

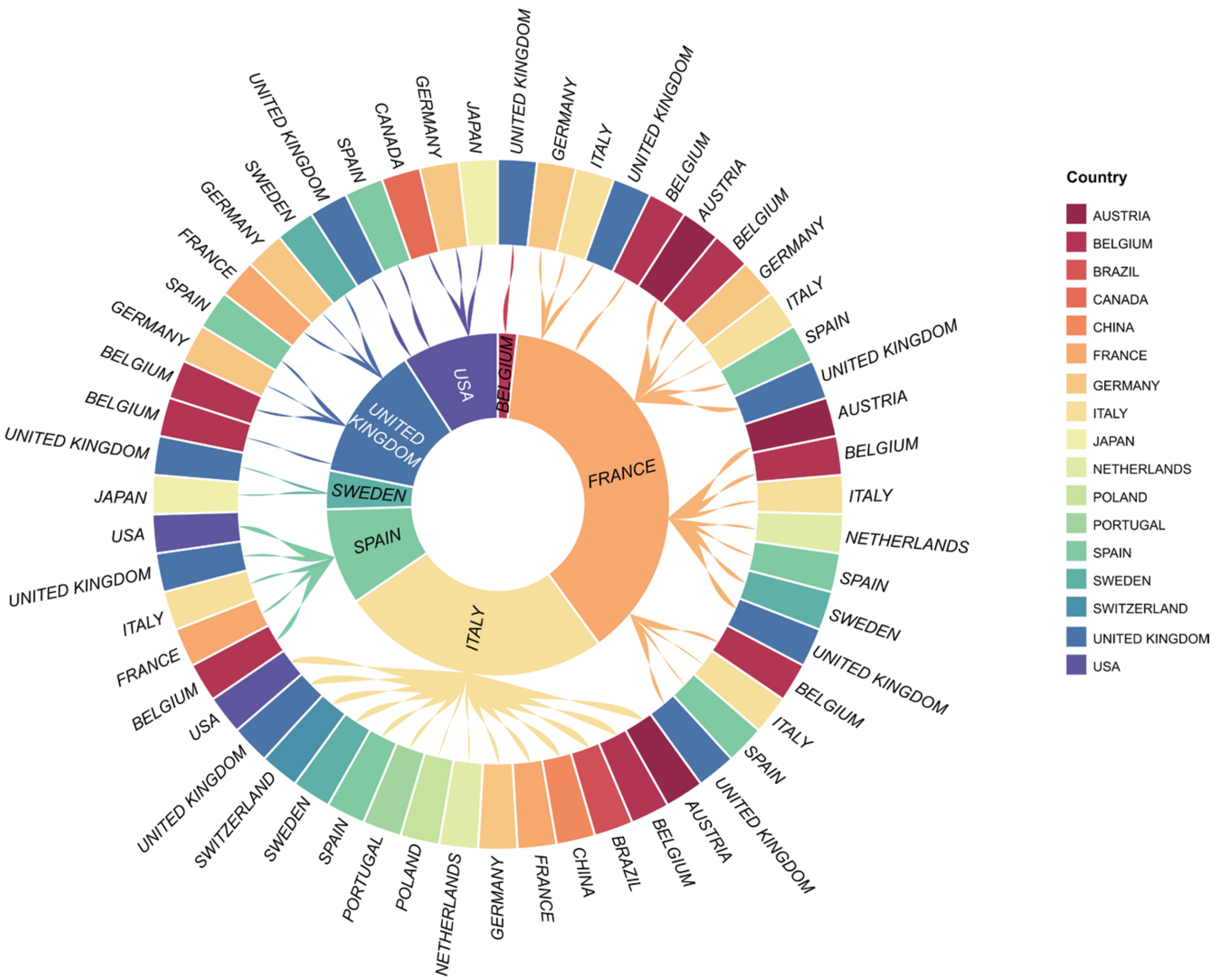

FIGURE 5. The co-operation relationships of countries/regions that published the top 100 articles from 1981 to 2021 based on selection strategy 1. Country of origin was defined based on the author affiliations listed in the Web of Science Core Collection. The inner circle represents the primary affiliation of the corresponding author. External circle shows the collaborating countries, based on the coauthor's primary affiliations.

as high-level evidence (eg, randomized controlled trials [RCTs] or meta-analyses).[10] These patterns might be associated with known limitations and difficulties in performing quality RCTs in highly complex settings, such as LT with multiple confounding factors and often heterogeneous patient groups.[22] Ultimately, these may have resulted in a more "generous" acceptance of studies with less scientific rigor by to the community than that which is observed in other disciplines.[23,24]

In general, there was a surprisingly low representation of immunological research among the highly cited articles. Although the exact reason for this observation cannot be explored properly using our data, one possible explanation would be that most groundbreaking clinical research on novel immunosuppression was performed first in other organs, most often in kidney transplantation, and was later translated to the liver transplant setting.[2]

Analyzing the subtopics, LT in the context of hepatic malignancies, studies on clinical risk factors, and viral hepatitis have accounted for a large proportion of the highly impactful research. Most studies on LT for hepatic malignancies were published in the 1990s and 2000s. Over this period, clinicians and researchers had a further understanding of tumor biology, end-stage liver diseases, and techniques of effective and safe liver surgery in cirrhosis.[25-29] Coupled with the development of an increasing number of LT programs worldwide, many large-scale studies appeared comparing the outcomes of LT with surgical resection. Well-known criteria and therapy algorithms were developed for HCC patients, such as the Milan criteria and the Barcelona Clinic Liver Cancer staging system.[27,30]

The number of articles on LT for NASH increased after 2010. At that time, NASH was already reported as the third-most common indication for LT in the United States of America by Charlton et al[31] while currently being the fastest growing indication for LT worldwide and already the leading cause for LT waitlist registrations among females in the United States.[32,33]

A number of highly cited articles in our dataset were focusing on novel surgical-technical techniques, especially in the earlier period.[34,35] Since the 1990s, LDLT was another significant research focus, including pediatric LDLT and split/reduced-size transplants. Accordingly, several groundbreaking reports on LDLT, donor safety, the use of right lobe grafts, and pioneering techniques in

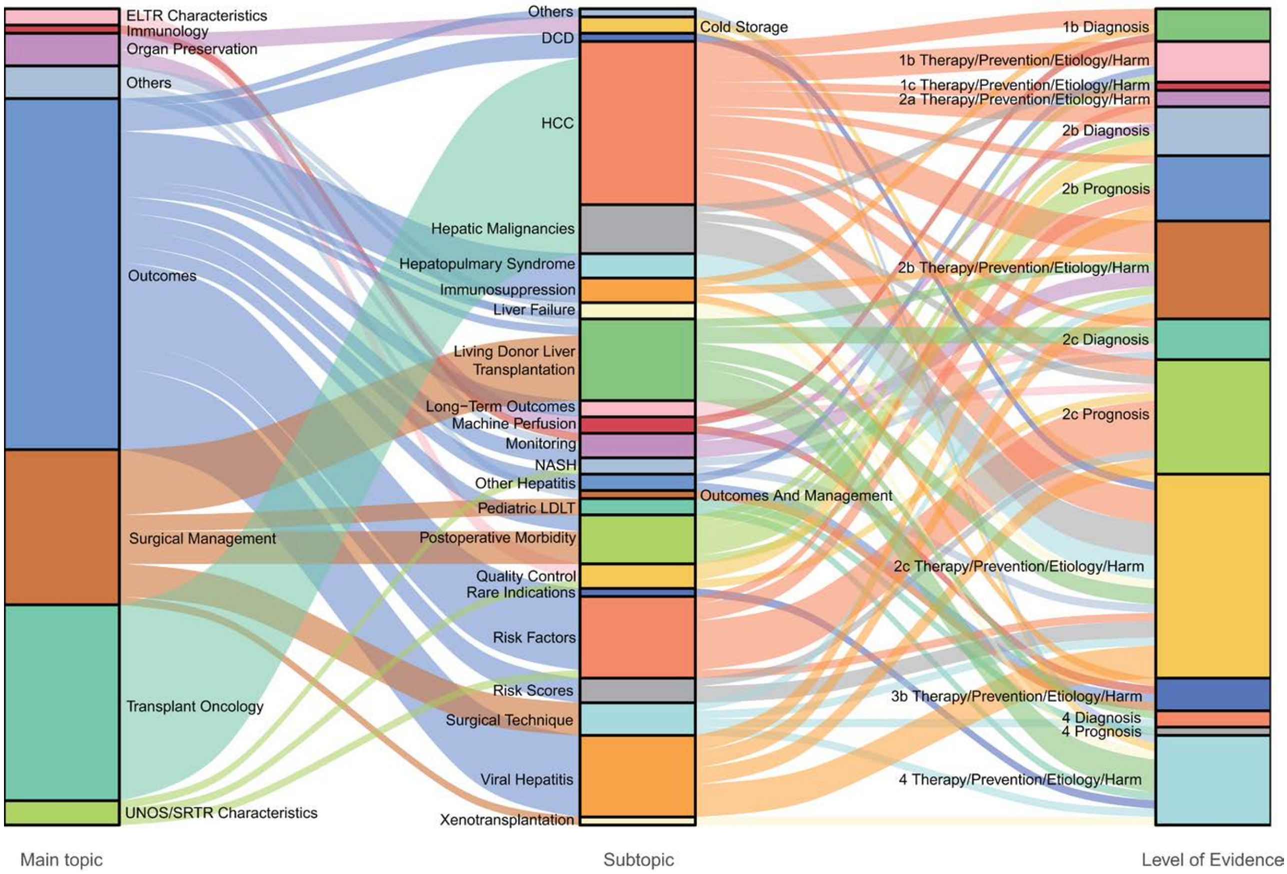

FIGURE 6. Article topics, subtopics, and level of evidence for the 100 most-cited publications from 1981 to 2021 based on selection strategy 1. DCD, donation after circulatory death; ELTR, European Liver Transplant Registry; HCC, hepatocellular carcinoma; LDLT, living donor liver transplantation; NASH, nonalcoholic steatohepatitis; UNOS/SRTR, the United Network for Organ Sharing/the Scientific Registry of Transplant Recipients.

pediatric LT were included in to our final dataset of most-cited articles.[36-41]

In addition to the aforementioned topics, multiple groundbreaking studies were included on perioperative morbidity,[42-45] post-LT infectious diseases,[46] and biliary complications.[47] Furthermore, the identification of risk factors and risk scores also attracted the attention of the transplant community with numerous highly cited publications being in our final selection.[48-51] Several studies investigated and innovatively proposed the role of pretransplant renal function (hepato-renal syndrome,[52] renal failure[53]), low serum sodium,[54] and sarcopenia[55,56] as risk factors to predict survival after LT. The neutrophil–lymphocyte ratio was reported as an independent predictor of inferior outcomes after LT for HCC.[57]

As a subsequent step, we examined the second set of 100 articles based on SS2. Although there was a major overlap of 72% between the 2 datasets confirming the robustness of our initial selection for the majority of the impactful studies, our SS2 has newly identified 28 nonoverlapping but important articles, which warranted further investigation and comparison. To this end, nonoverlapping articles were divided into group 1 (n = 28) and group 2 (n = 28). As we expected, most of the articles of group 2 were landmark publications of the past few years, which were presumably not mature enough to obtain a competitively high TC to be included in our primary selection. This assumption was further supported by a significantly lower median TC between the 28 articles belonging to group 2 compared with group 1.

In fact, concerning the topics of these studies, almost one third of the articles of group 2 were related to dynamic organ preservation and MP. Interestingly, the latest study in our initial SS1 was the first RCT on clinical MP by the Oxford group, which might be considered as one of the most impactful RCTs on LT in the recent years. In this multicenter trial, Nasralla et al demonstrated the safety and feasibility of normothermic-MP in a large cohort of 220 LTs.[15] Other landmark articles on MP were only included in group 2, such as the early "first in man" clinical pilot studies on normothermic-MP by Op den Dries et al[58] and Ravikumar et al,[59] the first reports on the clinical use of hypothermic oxygenated MP by Dutkowski et al,[60,61] and normothermic regional perfusion studies by the Cambridge and Barcelona groups.[62,63]

In line with previous studies focusing on gender inequality and inequity in the field of LT,[64-66] we also noticed a major dominance of male scientists as first and last authors. Nonetheless, in group 2 based on SS2, we could show a positive tendency with 1 out of 4 first authors being female (7 of 28). It should be noted, however, that these observations were quite predictable and were

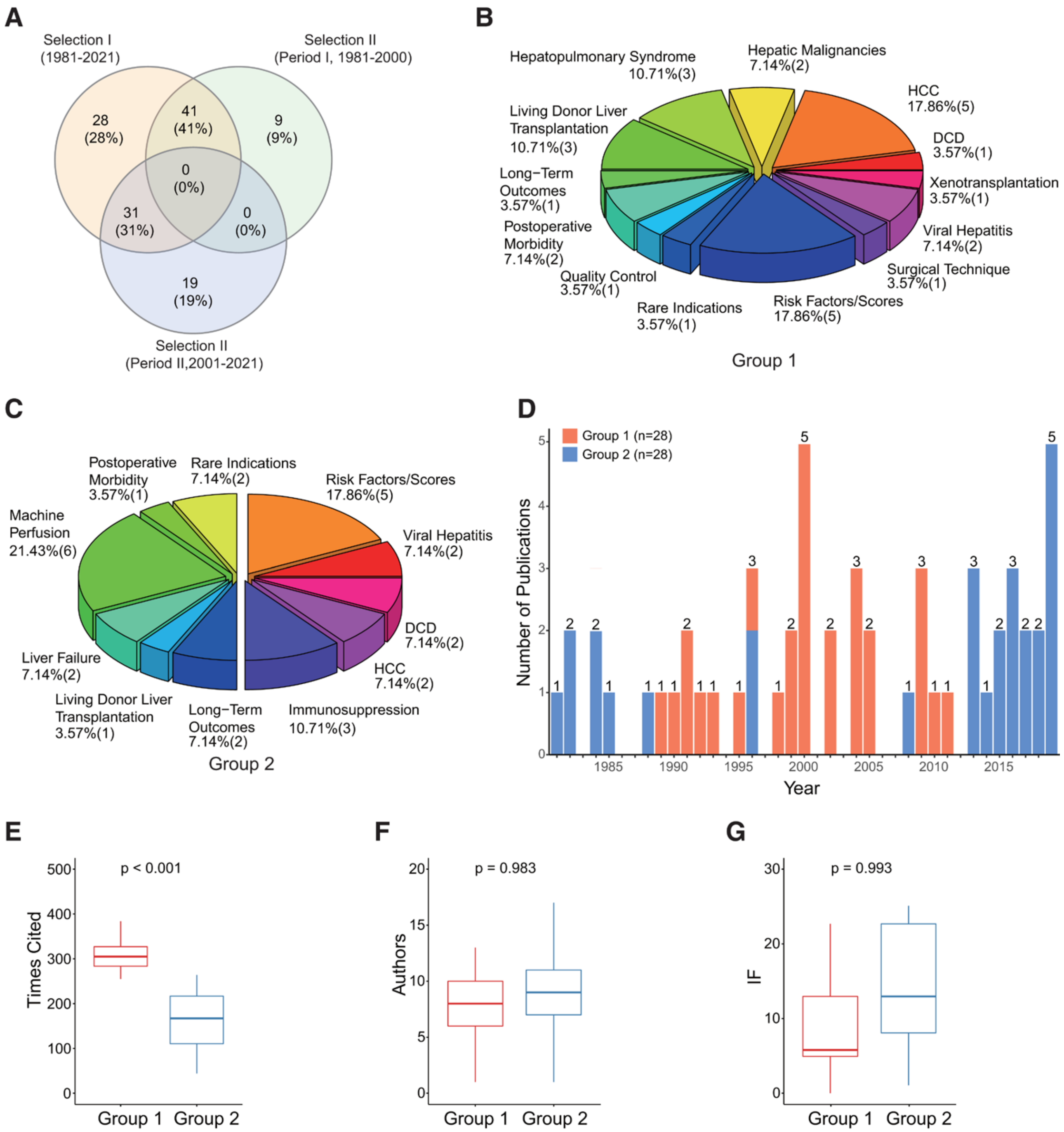

FIGURE 7. Comparative analysis of the datasets of selection strategies 1 and 2 including groups 1 and 2. A, Venn diagram showing overlaps and differences in the number of articles between selection strategies 1 and 2. B and C, The 3-dimensional pie chart shows the distribution of different research topics in group 1 and group 2. D, Differences in the annual publication characteristics between groups 1 and 2. E–G, Boxplots comparing total citations/article, number of authors, and impact factors between group 1 and group 2, respectively. Between-group comparisons were made using the Mann-Whitney U-test. DCD, donation after circulatory death; HCC, hepatocellular carcinoma.

not specific to LT science but rather pertinent to clinical medicine in general during the 4-decade period under evaluation here. Therefore, even though these data are important to report and raise awareness, it should not lead to overinterpretation and implicate a negative bias toward female authors in terms of publications practices but rather just mirror a generally lower representation of female clinicians in most transplant units during the earlier decades of LT history.

CONCLUSIONS AND FUTURE PERSPECTIVES

The findings of this study should be interpreted in the light of potential limitations. First, it should be acknowledged that the use of 100 articles as the cutoff and definition of "most-cited" is arbitrary even though this approach was frequently adopted by various authors in the past.[7,67-70] Second, the use of citations as the sole indicator for quantitatively measuring scientific "influence" and "impact" might be limited. Third, this study was focusing on the top 100 most-cited articles published over the past 4 decades; we did not aim to include all available articles in the literature with practice-changing significance, which would have represented a dataset of several hundred articles. Based on this, some studies with practice-changing impact were not considered or analyzed here. This fact and the differences in the rate of citations between various fields might have resulted in the under-representation of certain subtopics (eg, immunology, quality of life). Fourth, because of comparability issues with various bibliometric tools, we used the CA-WoSCC as the only source of data for this study. Therefore, despite our thorough review, it is still possible that certain studies were overlooked and not included in our final datasets.

Notwithstanding the aforementioned limitations, this is the first study describing global trends of top-notch research in the field of clinical LT over a long 4-decade period using modern bibliometric tools. With the help of innovative data presentation, thorough article selection, and analysis, we were able to reveal and visualize some unique trends in groundbreaking LT science. Most of the included articles represent landmark studies with direct paradigm-shifting significance. The findings of this work do not only outline the scientific trends of the past but also have several forward-looking elements. Recent citation and publication trends in high-impact LT research are in line with the increasing interest and renaissance of organ preservation research, including the use of marginal organs, and preservation by MP, which is expected to have major significance in clinical LT research during the upcoming years.[1,71] It is also expected that NASH as the most rapidly growing LT indication worldwide will further increase its significance, whereas viral hepatitis will be losing more ground because of its relatively declining relevance as an LT indication.[32] Furthermore, because of an increasing awareness and the continuously increasing number of talented female clinician-scientists working in leading LT units around the globe, a major shift in gender inequality and inequity is expected that should also manifest in further positive changes on the level of the number of female authorships on top-cited research articles.[65]

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