



Characteristics of the top 100 cited original studies on extracorporeal membrane oxygenation: a bibliometric analysis

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Background: Extracorporeal membrane oxygenation (ECMO) has been widely used as a life support for different kinds of acute cardiopulmonary dysfunction. The present study aimed at presenting the global trend of the top 100 cited original studies related to ECMO.

Methods: Bibliometric analysis was the primary methodology for this study. Literature data were collected from Web of Science Core Collection (WoSCC). Indicators were analyzed and visualized by Excel and VOSviewer, the study design, study population, study topic, journal impact factor (IF), Category Rank and Category Quartile, author, country, journal and keywords were included.

Results: The top 100 cited articles were published between 1979 and 2021. With 19 publications, 2020 was the most prolific year. High-income countries or regions, such as the United States of America (USA), France and Canada owned a majority of the articles. Seventeen studies were randomized trials, 52 were finished in single center, and 53 focused on adults. The 100 articles were documented by 31 different journals. The journals were well recognized, with a mean IF₂₀₂₂ of 28.77, a median of 8.8, and a range of 1.6–168.9. The major diseases were viral infection of respiratory system, acute respiratory distress syndrome (ARDS) or respiratory failure, pulmonary hypertension of infants, heart failure/cardiogenic shock, diaphragmatic hernia and cardiac arrest. Specifically, coronavirus disease 2019 (COVID-19) accounted for 72.7% of viral infections. The disease spectrum changed from congenital cardiopulmonary dysfunction to cardiac arrest, ARDS and cardiopulmonary failure, and to severe COVID infection cases. Another fresh hotspot is immune dysfunction.

Conclusions: This bibliometric analysis identified 100 most frequently cited original studies on ECMO and described their characteristics, which may help with further investigations.

Keywords: Extracorporeal membrane oxygenation (ECMO); life support; cardiopulmonary failure; bibliometric analysis

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Introduction

Extracorporeal membrane oxygenation (ECMO) is a vital life support technique by which the functions of lungs and hearts are supported by an extracorporeal device. In the 1960s, the conception of ECMO was induced by the development of silicon (a rubber designed for effective gas exchange) (1). In conjunction with this, the clinicians realized that sustaining anticoagulation was necessary for ECMO, which enables the extended extracorporeal support a reality (2).

Modern ECMO has developed with neonatal intensive care for cardiopulmonary failure, with the publication of randomized trials (3,4). ECMO has also been proved to improve survival rate of severe cardiopulmonary failure, transplantation and cardiac arrest (5-7). The next burst of ECMO was during the H1N1 influenza pandemic, in which acute respiratory distress syndrome (ARDS) caused by viral infection was well treated by ECMO (8,9). Nowadays, ECMO has been increasingly applied to cardiopulmonary failure worldwide. Over 220,000 ECMO cases have been reported to the Extracorporeal Life Support Organization (ELSO) (10). Moreover, the number of ECMO patients in the last 5 years is over 100,000 (10). Accompanied with the popularity of ECMO in clinical practice, scientific reports on ECMO continue to increase.

Bibliometric analysis has been widely used to present

the current status of a certain scientific issue (11,12). Through the analysis of a certain field, not only the influential authors, institutions and countries, but the preferred journals and hot spots, etc., can be easily accessed. Generally, articles with more citations are recognized as high-quality studies. The present study was designed to analyze the 100 most frequently cited original articles on ECMO to provide the characteristics of hot papers and the key points in this area.

Methods

Methodology

The methodology of this study is in accordance with the guidelines for bibliometric analysis (13). Both performance analysis and science mapping were conducted. Performance analysis in this study included publication-related indicators (total publications and number of contributing authors) and citation-related indicators (total citations and average citations). And science mapping included citation analysis and co-occurrence analysis. We also classified the study design (randomized trial, cohort study, case/case series, cross-sectional study, retrospective study, basic and translational science study and other types), study population (infants, children, adults and all age group) and study topic (ARDS/respiratory failure, pulmonary hypertension of infants, diaphragmatic hernia, heart failure/cardiogenic shock cardiac arrest, transplantation, viral infection of respiratory system, cardiac infarction, congenital heart disease and other issues) by reading the title, abstract and methods of the enrolled publications.

Data acquisition

The inclusion and exclusion criteria were determined before literature retrieval. Studies were eligible if they reported ECMO in the abstract, either as the primary or secondary objective. Studies were excluded if they were not original research, such as reviews, study protocols, commentaries, letters, proceeding papers and editorials, or were not written in English.

The strategy of literature retrieval for a bibliometric analysis should not only ensure the high volume of articles, but be closely related to the research target (13). Synonyms for ECMO were applied to search in Web of Science Core Collection (WoSCC) on 18 March 2024. As the target of this study is original study, the document was restricted

Highlight box

Key findings

- The top 100 original studies on extracorporeal membrane oxygenation (ECMO) have high journal impact factor (IF) and a large number of citations. Authors in North America and Europe published most of the articles.

What is known and what is new?

- ECMO has been widely used as a life support for different kinds of acute cardiopulmonary dysfunction.
- Between 1979 and 2021, 1,320 authors from 33 countries or regions created articles and published them in 31 journals. The journals had a mean IF₂₀₂₂ of 28.77, a median of 8.8, and a range of 1.6–168.9. *JAMA*, *Lancet* and *New England Journal of Medicine* are the core journals. Cardiopulmonary failure caused by reasons were the hot spots. Coronavirus disease 2019 (COVID-19) has attracted broad attention in recent years.

What is the implication, and what should change now?

- Studies with high-level evidence, such as randomized controlled trials, are needed to catalyze guidelines, and further, save more lives.

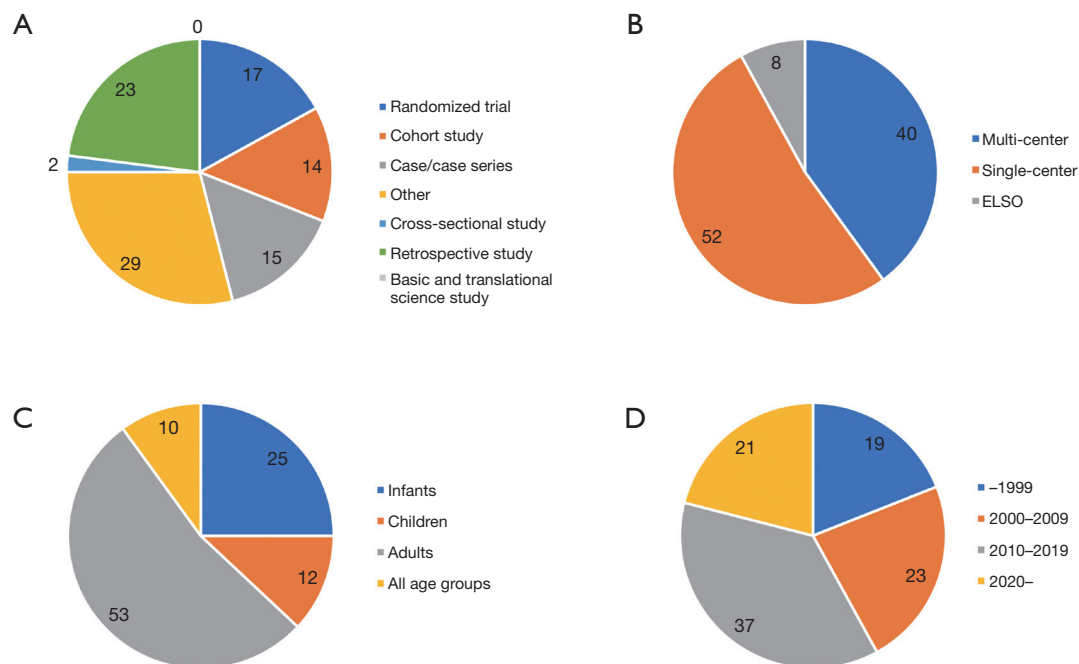


Figure 1 Characteristics of the 100 most frequently articles. (A) Study type; (B) setting; (C) study population; (D) publication year. ELSO, Extracorporeal Life Support Organization.

to “Article” and artificial screening was performed by two investigators separately. All the records were ranked according to the citations and the top 100 cited articles were selected. Conflicts on opinions of the two authors were discussed by the study group.

The selected 100 studies were exported as a plain text file and a sheet for analysis. All the 29 bibliometric indicators in WoSCC were extracted, including “Author, Title, Source”, “Abstract, Keyword, Addresses”, “Cited References and Use” and “Funding and Other”. Journal impact factor (IF) (version 2022 and 5-year mean) in line with the Journal Citation Reports (JCR), Category Rank and Category Quartile of Web of Science system were manually collected. In addition, for journals involved in more than one category, the highest Category Rank and Category Quartile were displayed in this study.

Data analysis

Descriptive statistics were applied to do the performance analysis and describe the study design, study population, study topic, IF, Category Rank and Category Quartile. The analysis tools were VOSviewer and Excel. Science

mapping was created by VOSviewer to present the citation relationship (an analysis that is based on the times that articles cited each other) and co-occurrence analysis of keywords (an analysis that is based on the times that keywords co-exist in an article).

Statistical analysis

Correlation analysis was conducted by SPSS 26.0 software to present the relationship between citations and usage count.

Results

Characteristics of the top 100 cited studies

A total of 28,070 records were initially identified in WoSCC, of which 17,153 publications were tagged “Article”. The 100 articles that met the inclusion and exclusion criteria and had the most citations were enrolled into the final analysis (online table available at <https://cdn.amegroups.com/static/public/jtd-24-597-1.pdf>). *Figure 1* shows the characteristics of the 100 most frequently cited articles. There were 17 randomized trials, 14 cohort studies, 15 case/case series, 23

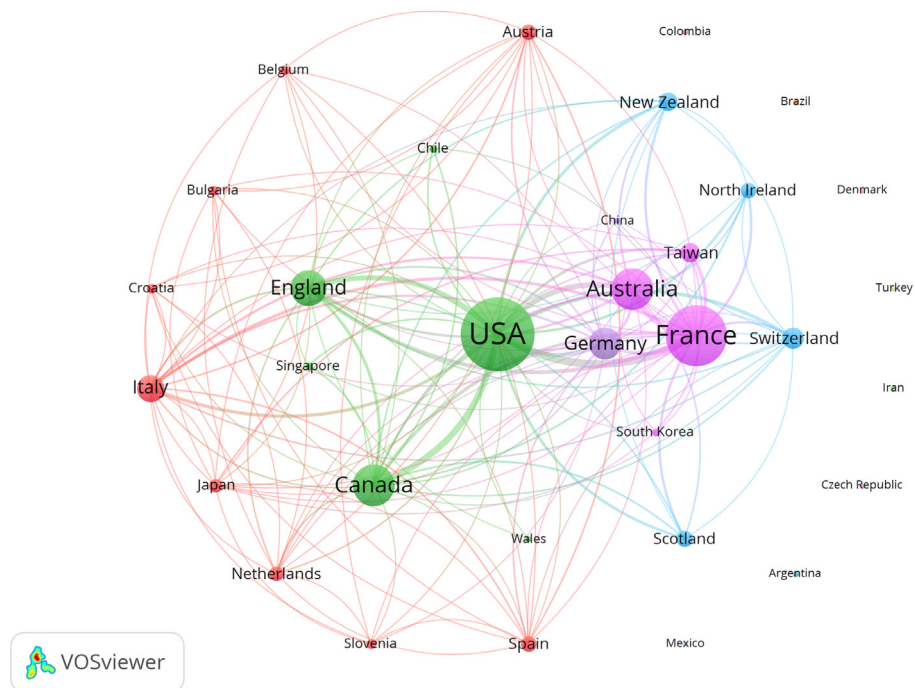


Figure 2 Citation analysis of the countries or regions. The size of nodes is based on total citations. The thickness of lines is based on the times they cited each other. USA, United States of America.

retrospective studies, 2 cross-sectional studies and 29 other types, while no basic and translational science study ranked in the top-100 (*Figure 1A*). Forty out of the 100 studies were conducted in multiple centers, 52 in a single center, and 8 were based on data from ELSO (*Figure 1B*). Over half of the articles ($n=53$) focused on adults, 25 on infants, 12 on children, and 10 involved all age groups (*Figure 1C*). As for publication year, 19 highly cited articles were published in the last century, 23 in the 2000s, 37 in the 2010s, and 21 in the early 2020s (*Figure 1D*).

We further analyzed the specific distribution of the articles in term of publication year, annual citations and usage count since 2013. The usage count in WoS system is determined by the times that users access to the full text. The earliest top-100 article in this field was published in 1979, and the latest one was in 2021 (*Table S1*). Nineteen articles were published in 2020, far ahead of the other years (*Table S1*), 16 of which were related to coronavirus disease 2019 (COVID-19). Interestingly, the most frequently cited article, published in 2020, was also corelated to COVID-19 (online table available at <https://cdn.amegroups.com/static/public/jtd-24-597-1.pdf>). The citation count ranged from 211 to 5,248 in WoS, with a total citation of 50,758 and

a median of 307.5 (online table available at <https://cdn.amegroups.com/static/public/jtd-24-597-1.pdf>). In terms of usage count, the usage count since 2013 ranged from 4 to 234 times (online table available at <https://cdn.amegroups.com/static/public/jtd-24-597-1.pdf>). Spearman Rho correlation analysis showed that there was a positive correlation between citations and usage count (since 2013) ($r=0.663$, $P<0.001$).

Assessment of global contribution to the 100 studies

A total of 33 countries participated in publishing the top-100 original studies on ECMO. There were 8 countries (24.2%) published at least 5 articles, and 19 (57.6%) published more than 1 article. The United States of America (USA) was the most productive and influential country, with 59 publications and 22,732 citations. France was in the second tier, with 21 publications and 11,358 citations. Citation analysis indicated that USA had the broadest interaction with other countries or areas, and the link strength between USA and France, Australia, Canada or England, or between France and Australia was obviously stronger (*Figure 2*). North America had 81 publications

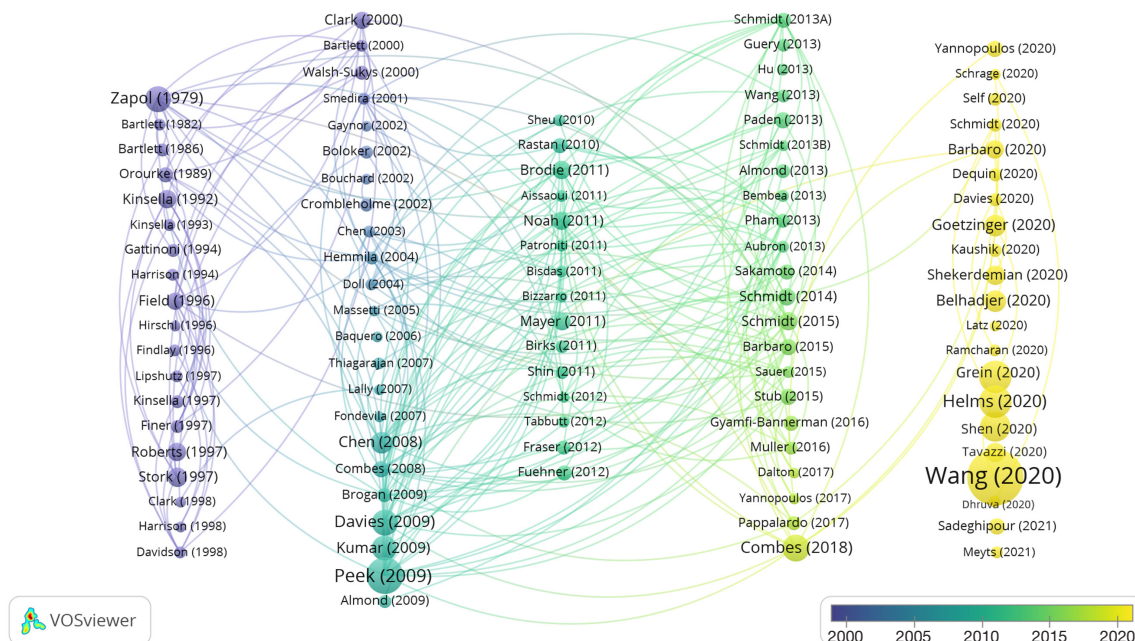


Figure 3 The first author and publication year of the 100 articles. The size of nodes is based on total citations. The thickness of lines is based on the times they cited each other.

that came from 3 countries, Europe had 79 publications from 17 countries or regions, Asia owned 13 articles from 7 countries or regions, Oceania owned 8 articles from 2 countries, and 4 countries of South America contributed 5 papers (Figure S1).

Four hundred and ninety-one institutions were involved in the 100 influential studies. Eight of them published at least 5 articles, and 102 published more than 1 article. With 11 publications, University of Michigan was the most prolific institution, followed by Emory University ($n=9$). As for individuals, 1,320 authors participated in the publications. The first authors of these articles are displayed in Figure 3 where they are arranged by publication year and the node size represents the number of citations. The article published by Dawei Wang in 2020 was cited most (Figure 3).

Assessment of the journals

The 100 articles were documented by 31 different journals (online table available at <https://cdn.amegroups.com/static/public/jtd-24-597-1.pdf>). *Journal of the American Medical Association (JAMA)* published the largest proportion of articles (14%), followed by *Lancet* (8%) and *New England Journal of Medicine* (8%). There were 8 journals (25.8%) where at least 5 of the included studies were published, and

19 journals (61.3%) where more than 1 of enrolled studies was recorded. Only 4 journals (12.9%) just published 1 study. The density visualization of these journals was depicted in Figure 4. An IF_{2020} was available for 30 (96.8%) of the journals. The mean IF_{2022} for the 100 studies was 28.77, and the median was 8.8, with an IF_{2022} range of 1.6–168.9. These journals were of high-quality and well recognized by the peers, with 11 journals (35.5%) ranking top 3 in the categories and 26 journals (83.9%) located in the first quartile (Q1). The papers published in *JAMA* were the most frequently cited, with a total citation of 12,796, an average citation of 914. Table 1 shows the top 12 journals in terms of publication number.

Assessments of keywords and study topic

The keywords provided by authors and added by WoS were analyzed by VOSviewer with co-occurrence analysis. The keywords that appeared at least twice are exhibited in Figure 5 where they were arranged according to mean publication year. In these highly cited articles, primary focus of the ECMO-related disease spectrum changed from congenital cardiopulmonary dysfunction to cardiac arrest, ARDS and cardiopulmonary failure, and to severe COVID infection cases. Another fresh hotspot is immune

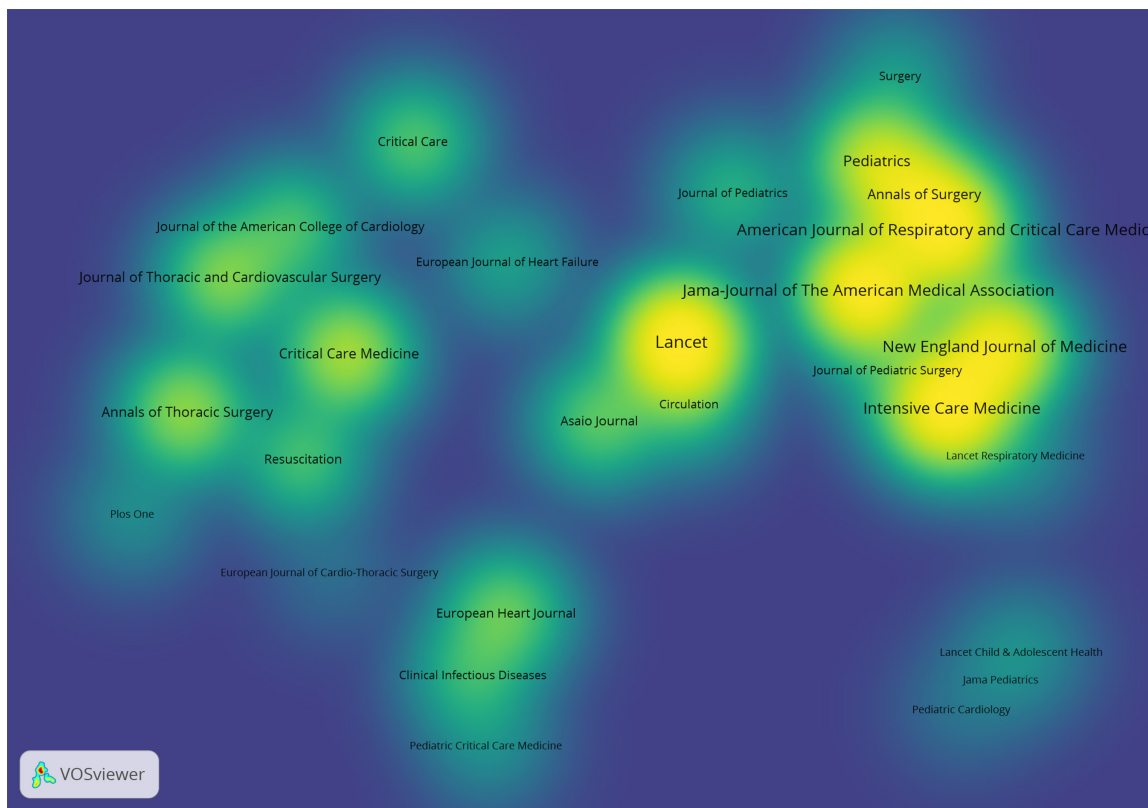


Figure 4 Heatmap of the journals that record the 100 articles.

Table 1 The 12 journals with most highly cited publications

Rank	Journals	Documents	Citations	Mean citations	IF ₂₀₂₂	IF _{5-year}	Category rank	Category quartile
1	<i>Journal of the American Medical Association (JAMA)</i>	14	12,796	914	120.7	81.4	3	Q1
2	<i>Lancet</i>	8	5,738	717	168.9	118.1	1	Q1
3	<i>New England Journal of Medicine</i>	8	5,981	748	158.5	115.7	2	Q1
4	<i>Intensive Care Medicine</i>	7	3,484	498	38.9	27	2	Q1
5	<i>Pediatrics</i>	7	1,902	272	8	8.2	5	Q1
6	<i>Circulation</i>	6	2,137	356	37.8	33.2	1	Q1
7	<i>Journal of Pediatric Surgery</i>	6	1,474	246	2.4	2.6	58	Q2
8	<i>American Journal of Respiratory and Critical Care Medicine</i>	5	1,947	389	24.7	21.9	3	Q1
9	<i>Journal of Thoracic and Cardiovascular Surgery</i>	4	1,384	346	6	5.9	13	Q1
10	<i>Critical Care Medicine</i>	3	1,019	340	8.8	8.4	6	Q1
11	<i>Annals of Thoracic Surgery</i>	3	670	223	4.6	4.5	24	Q1
12	<i>Journal of Pediatrics</i>	3	847	282	5.1	5.2	12	Q1

The highest ranking of the journals that belong to more than one category and homologous category quartile in the WoS system were shown. IF_{5-year}, the average impact factor for the last 5 editions.

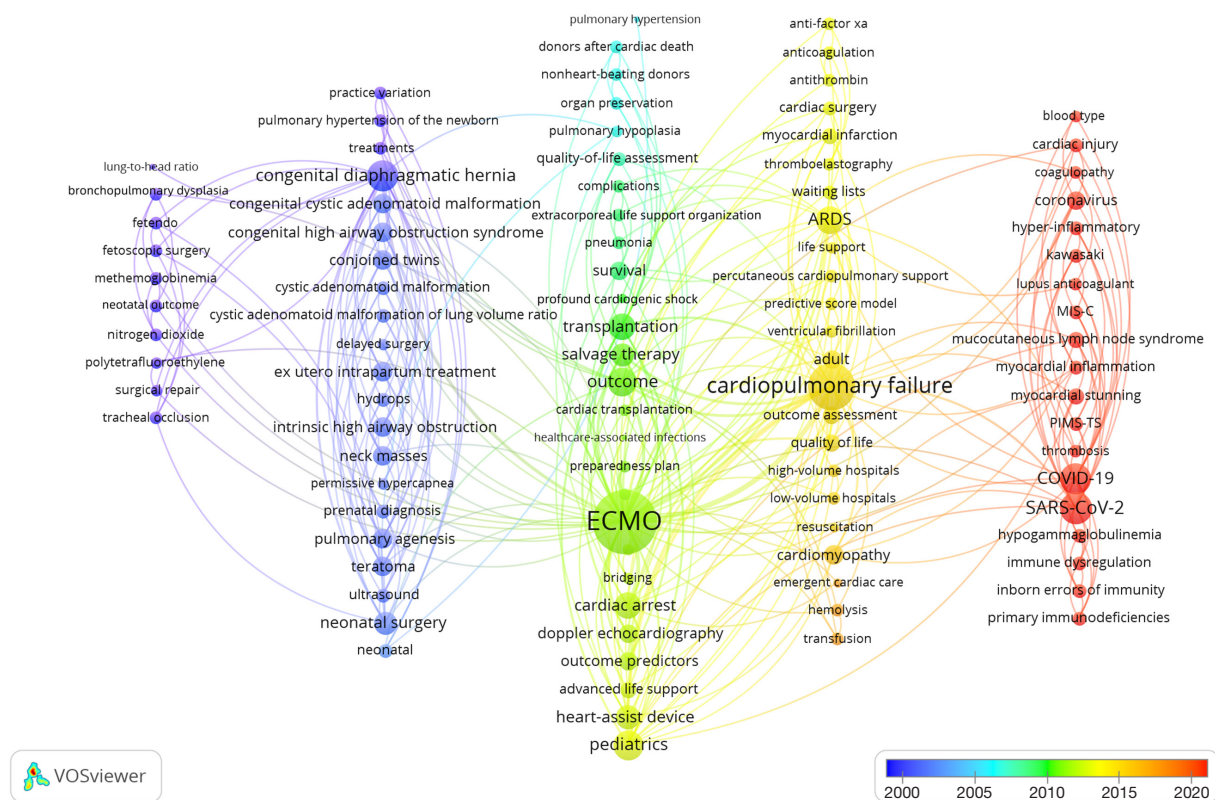


Figure 5 Co-occurrence analysis of keywords. Keywords in the map have at least two occurrences. The size of nodes is based on total occurrences. The thickness of lines is based on the times they occurred together. ECMO, extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; MIS-C, Multisystem Inflammatory Syndrome in Children; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; PIMS-TS, pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2.

dysfunction. The 100 articles investigated many kinds of diseases or research points. There were 22% for the viral infection of respiratory system (A H1N1, A H7N9, Middle East Respiratory Syndrome coronavirus and COVID-19), 18% for ARDS/respiratory failure, 10% for pulmonary hypertension of infants, 10% for heart failure/cardiogenic shock, 7% for diaphragmatic hernia, 7% for cardiac arrest, 4% for transplantation, 3% for acute cardiac infarction, 2% for congenital heart disease, and 17% for other issues (Figure 6). Specifically, COVID-19 accounted for 72.7% of viral infections (Figure 6).

Discussion

The present study is the first bibliometric analysis of the 100 most cited original studies on ECMO. Bibliometric analysis has been used to explore the gross features of

published articles in a certain area via quantitative methods (11-13). The highly cited articles are generally those with higher visibility in a particular field, and bibliometric analysis of these articles is able to quantitatively identify major research focuses and provide clues on research dynamics (14,15).

Most of the top articles distribute in North American and Europe, a few of them are present in Asia, South Africa and Oceania. The distribution is in the high consistence of the ECMO Ability Center Map (<https://www.elseo.org/membership/leafletcentermap.aspx>). The high-income countries are the pivot area of ECMO centers, especially excellent centers. Since the cost of ECMO is extremely high, it is reported that the median of total medical costs for 1 year accumulates to 46,308 United States dollars in South Korea (16). In Canada, the number reaches 130,157 Canadian dollars and 70% are spent in hospital (17). The

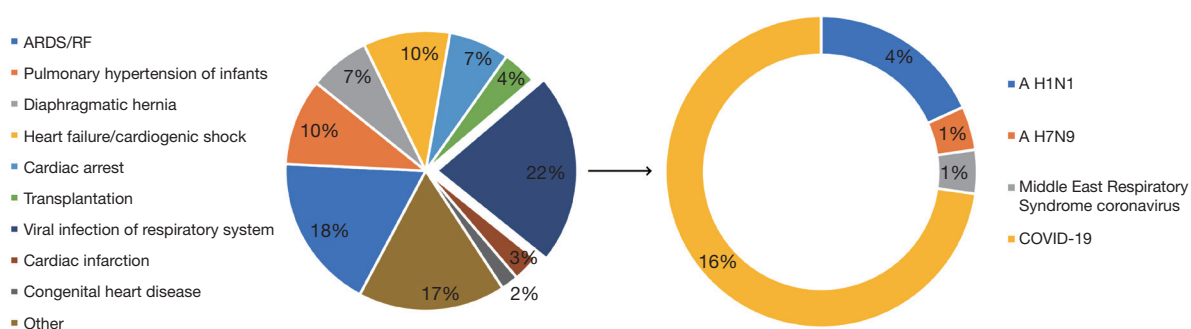


Figure 6 Disease profiles that ECMO-related studies focused on. ARDS/RF, acute respiratory distress syndrome/respiratory failure; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation.

heavy economic burden would impede, at least partly, the application of ECMO in low-income countries.

The top 100 studies were published between 1979 and 2021. Stepping into the 21st century, more than 20 of these articles were published in each 10-year interval. There are two distribution characteristics. For one thing, articles (15/19, 78.9%) mainly focused on newborns in the last century. This may give the credit to one of the 100 articles (published in 1982 by RH Bartlett), in which 45 infants with respiratory failure were supported by ECMO and 25 of them survived (18). The authors improved the survival rate up to 63% 4 years later (19). Professor RH Bartlett then turned to adults and published several important studies in top journals, such as *JAMA* (20,21). For another, COVID is absolutely the protagonist since 2020, with 18 out of 21 (85.7%) highly cited papers. Moreover, most of them were published in top journals, such as *Lancet*, *New England Journal of Medicine* and *JAMA* (22-24). For patients with severe respiratory failure induced by COVID-19, ECMO is believed to significantly reduce in-hospital mortality in specialist centers and mortality at 90 days after ECMO (22,25).

Total citations of the time intervals were stably increased, and citations of each study remained high level. The article with the most citations was published in 2020, in which the clinical features of inpatients with COVID-19 in Wuhan, China were demonstrated (24). Generally, citations of articles accumulate over time, so recent articles usually have less citations (26). In the present study, the recent articles published between 2020 and 2021 had comparable citations with the old ones. This can be attributed to the great importance related to COVID.

The study design was also analyzed. Approximately a half of the articles were conducted at a single center, 40% of them were multicenter studies and 8% were based

on data from ELSO. Considering the relatively fewer patients who need ECMO, it is advised to cooperate with other institutions. Otherwise, it would take a long time to recruit enough sample size, which may cause more bias. Another vital indication is that well designed single-center studies can also be widely recognized and cited. Unlike some other medical issues, such as hematopoietic stem cell transplantation (27), lupus nephritis (28) and diabetes mellitus in COVID-19 (29), only 17% of the 100 ECMO-related studies were randomized trials, a large amount of them were retrospective and descriptive studies. The limited sample size for a specific group of ECMO patients makes randomization more difficult.

Our keywords analysis via VOSviewer and research topic analysis via artificial classification indicate that the hotspots are congenital cardiopulmonary diseases, acute heart failure and ARDS caused by different kinds of reasons. As a life-support device, ECMO can win valuable time for the rescue of critical patients (30). O'Rourke PP *et al.* (31) observed that ECMO increased the survival rate to 97% in infants with persistent pulmonary hypertension. Schrage *et al.* (32) suggested that ECMO with left ventricular unloading was associated with a lower short-term mortality. Although ECMO is widely recommended, there can be severe complications, such as major bleeding and hemorrhagic stroke (33). Thus, the perioperative care is crucial. In 2013, Bembea *et al.* (34) published a survey where anticoagulation management for ECMO was investigated. They pointed out the lack of unified strategy and called for optimal guidelines. Several years later, another top 100 study, published by *JAMA* in 2021, indicated that 1 mg/kg daily use of enoxaparin failed to improve thrombosis-related events and overall outcomes of critical patients who underwent ECMO (35). At the same year, guidelines for venovenous

ECMO came out (36). Together with the support of ELSO, ECMO is capable to save more lives.

Strengths and limitations

In the present study, we focused on the top 100 original studies of ECMO. By artificial screening, we ensure eligibility of the enrolled studies. We also extracted some uncommon characteristics for bibliometric analysis, such as study design, study population and research topic, which provides more references. In addition, we conducted this bibliometric analysis in line with the guidelines (13).

Nevertheless, there are some limitations. Firstly, although the literature was searched in the WoSCC, the most commonly used and recognized database, some publications were inevitably missed. This would lead to underestimation of the contribution analysis. Secondly, the classification of study design may be different from study groups. As it is hard to determine the unique category according to the description of some articles, some studies were called “other types”. Lastly, the complications and causes of death in patients with ECMO support are not specifically assessed in our study. Because it is difficult for the authors to distinguish the specific causes of death, since patients who need ECMO support are critically ill and more likely to suffer death.

Conclusions

The present study analyzed the characteristics and global trend of the top 100 cited original studies on ECMO. Between 1979 and 2021, 1,320 authors from 33 countries or regions created the articles and published them in 31 journals. Cardiopulmonary failure caused by different kinds of reasons were the hot spots. COVID-19 has attracted broad attention in recent years. However, studies with high-level evidence, such as randomized controlled trials, are needed to catalyze guidelines, and further, save more lives.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-24-597/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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