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Research Article

The Most Cited Articles on ECMO: A Life-Saving Bibliometric Analysis

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Abstract

Objectives: Extracorporeal Membrane Oxygenation or ECMO, currently is a life-saving intervention in patients with severe respiratory and cardiac failures. The aim of the present bibliometric study was to evaluate the characteristics of the most influential articles on ECMO.

Methods: In the retrospective clinical study, the search term "ECMO" was queried into Thomson Reuter's Web of Science database between years 1975-2019 to list all the articles on this term. The top 100 cited articles were analyzed by topic, journal, author, year, institution, level of evidence, Adjusted Citation Index.

Results: Out of screened 46.606 articles on ECMO, an analysis of the most cited articles among these results was performed. The analyzed articles had a median (IQR) 109 (82-1273) citation. Out of Top 100 cited articles, 58 of them had more than 100 citations. There was an increasing trend in number of publications on ECMO between years 2009-2014. In the Top 100cited articles list, 94 were clinical research studies, 5 were reviews and 1 article was an expert commitee report. The majority of the clinical research articles were retrospective comparative clinical studies (n=37). The majority of the articles were published in the Intensive Care Medicine (n=15) and was followed by Annals of Thoracic Surgery (n=11) and Circulation (n=7).

Conclusion: Although ECMO currently is defined as an effective life supporting tool for patients with reversible cardiac and pulmonary failure; there has been tremendous differences since the first use of ECMO in means of technology and indicated diseases as well as patient groups over time.

Keywords: Bibliometric analysis, extracorporeal membrane oxygenation

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ECMO is a cardiopulmonary bypass circuit providing temporary life support in patients with reversible cardiac and pulmonary failure.[1] The prior form of ECMO was developed as a membrane oxygenator for prolonged cardiopulmonary bypass operations.[2] The first large randomized controlled studies, defined ECMO as an inconvenient intervention in adults regarding no significant effect on survival as well as high mortality rates and adverse effects.[3, 4] Thus, in the following 30 years, use of ECMO was substantially restricted to neonatal and pediatric patients. Bartlett et al.[5] reported the first successful use of ECMO in neonates with severe respiratory distress. The Conventional Ventilatory Support versus Extracorporeal Membrane Oxygenation for Severe Adult Respiratory Failure (CESAR) trial was the first

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and the largest study demonstrating favourable outcomes of ECMO in adults.[6] Consequently, during the H1N1 outbreak, ECMO was frequently used in the treatment of patients with ARDS.[7] Advances in technology and improved protocols initated the widely use of ECMO in patients with severe cardiac and pulmonary dysfunction refractory to conventional management. The increasing data registered to Extracorporeal Life Support Organization (ELSO) also demonstrates the important role of ECMO in the management of variety of diseases in neonatals, infants and adults.[8] Additionally, growing evidence supports the use of ECMO in extended indications such as acute hypoxemic respiratory failure, cardiac arrest and cardiogenic shock.[1]

Bibliometric studies define the quantitative analysis of written publications on a specific field and are important for determining and evaluating the influential literature as well as the trends of research over time.[9, 10] Web of Science (WoS) and PubMed are frequently used tools providing data identifying the quality of an article. Number of citations of the article and the impact factor of the journal the article has been published are the main factors used for defining the quality of an article. Furthermore, data regarding the list of authors and journals with the most number of publications on a topic as well as change in trends through time intervals can be accessed.[11] Thus, bibliometric studies guide the researchers for further investigating certain topics in a field.

Despite currently ECMO is defined as an effective life supporting tool for patients with reversible cardiac and pulmonary failure; there has been tremendous differences since the first use of ECMO in means of technology and indicated diseases as well as patient groups over time. In the present study, we aimed to review the characteristics of the top 100 most cited articles (T100) in ECMO in the literature so far. The findings of the study are expected to provide new insights on the research trends in ECMO.

Methods

Study Design

Study type: Retrospective clinical research.

Level of evidence: 3 or Group B (Scottish Intercollegiate Guidelines Network-SIGN 100, 2019).[12]

Data Collection and Inclusion Rules

In the present bibliometric citation analysis, data were obtained from Thomson Reuters' WoS Core Collection database (Philadelphia, Pennsylvania, USA) and PubMed (US National Library of Medicine-National Institutes of Health). A search through WoS database was performed on March 15, 2019. The search term "ECMO" was used for accessing data between years 1975-2019. The selected T100 articles were analyzed based on the number of citations, authorship, journal, country of origin, institution, impact factor, main topics, study design and levels of evidences. Adjusted citation index was used in order to overcome a potential time-related bias and was determined by dividing the number of citations by the number of years since publication. Relevance of the selected publications were evaluated by two independent reviewers(X and Y) with a consensus and articles irrelevant to the study topic were excluded. Original research articles, editorials, correspondences and reviews in English language were included. Additional data were accessed through PubMed. The quantitative values in the tables were limited as "2 or more" and "3 or more". SIGN 100 was used as the source of information regarding level of evidence (from 1 to 4).[12, 13]

Statistical Analysis

Mainly, descriptive statistical methods were used in the present study. Data were expressed as median (interquartile range [IQR]), percentage, number or bar chart in the tables. All statistical analysis were performed using SPSS package software for Windows® (Version: 21.0).

Results

Out of screened 46.606 articles on ECMO, an analysis of the T100 among these results was performed. The analyzed articles had a median (IQR) 109 (82-1273) citation. T100 and Adjusted Citation Index are listed in Appendix 1 and ranked by the number of citations in a decreasing manner. The most cited article (times cited: 1273) on ECMO was a randomized trial conducted by Peek GJ et al. with the title "Efficacy and economic assessment of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR): a multicentre randomised controlled trial" published in Lancet 2009;374(9698): 1351-63. The most cited article also had the highest ACI among T100 list. Out of T100 articles, 58 of them had more than 100 citations. Also according to the Appendix 1, 7 of the articles were included in both the highest ACI and the top 10 cited article list. T100 articles were published between year 1985-2016. There was an increasing trend in number of publications on ECMO between years 2009-2014, with the highest number of publications on 2014. Thus, number of citations also demonstrated an increasing trend starting with 2009 and highest number of citations was recorded in 2017 (Figs. 1, 2). The oldest study that is among the T100 list was conducted by the Towne BH et al. and it was published on "Journal of Pediatric Surgery". On the other hand, the most recent study in the T100 list was conducted by Combes A et al. and it was published on

"the New England Journal of Medicine-the NEJM". Seventy-three of the T100 articles were published after year 2000 and 45 of them were published after 2010 (Appendix 1). In the T100 list, 94 were clinical research studies, 5 were reviews and 1 article was an expert commitee report (Table 1). The majority of the clinical research articles were retrospective comparative clinical studies (n=37), followed by retrospective cohort studies (n=15), prospective comparative studies (n=12) and randomized controlled trials (n=12) (Table 1). The level of evidences of the analyzed articles are demonstrated in Table 1. Among the main topics of T100 articles, ARDS was the most frequently used topic as it was examined in 16 studies. Subsequently, the other main topics included complications (n=14), mortality (n=11), H1N1 (n=8), CPR (n=7) and congenital diaphragmatic hernia (n=7). The distrubution of all of the main topics in T100 articles are listed in Table 2. In the present study, 18 journals having published at least two T100 articles were identified and included 82 articles in total. The journals had a median IF 7.95 (range=1.49-53.25). The majority of the articles were published in the Intensive Care Medicine (n=15) and was followed by Annals of Thoracic Suregery (n=11) and Circulation (n=7). Three articles were published in Lancet, which was the journal with the highest IF. Lowest IF belonged to Journal of Pediatric Surgery, in which 4 articles were published (Table 3). According to the geographic origin of the T100 list, publications from 19 countries were observed and the USA had the highest number of publication (n=56). Following USA, France (n=14) and Australia (n=12) had the highest number of contributions (Table 4). The highest number of publications among T100 articles were reported from University of Michigan (n=18) and Univer-

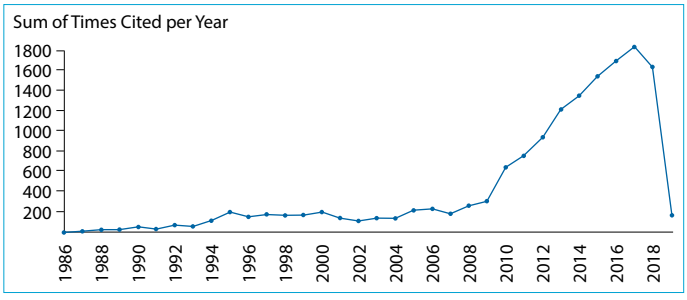

Figure 1. Times cited per years.

Table 1. Study design and levels of evidence by SIGN100 of the top 100 cited articles

Study type and sub-type	Level of evidence	Group	Number
Clinical research			
Meta-analysis of RCT	1	A	3
Systematic review	1	A	5
Randomized controlled trial	1	A	12
Prospective cohort study	1	A	3
Prospective comparative study (clinical)	2	B	12
Retrospective comparative study (clinical)	3	B	37
Retrospective cohort study	3	B	15
Case–control study	3	B	3
Observational–descriptive study	3	B	3
Cross-sectional–correlation study	3	B	1
Review	4	C	5
Expert committee report	4	C	1

SIGN100: Scottish Intercollegiate Guidelines Network 2019; RCT: Randomized control trial.

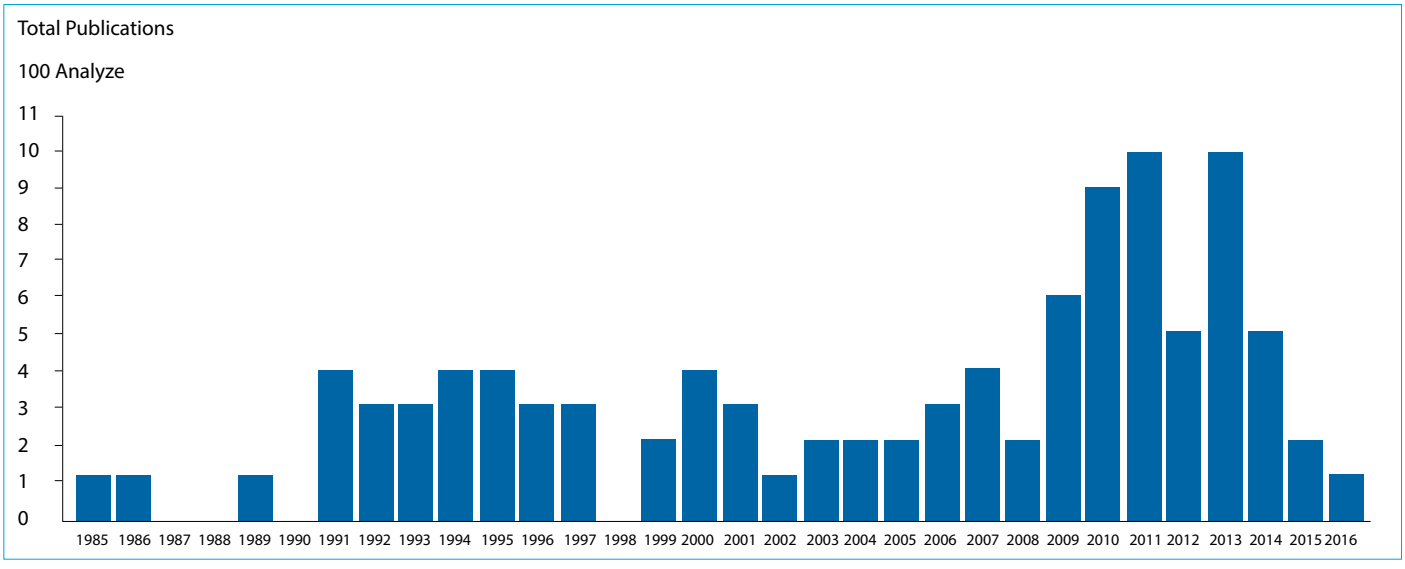

Figure 2. Total publication per years.

Table 2. Main topics of highly cited articles on ECMO

Subject	Number
ARDS	16
H1N1(ARDS)	8
CPR	7
Complications	14
Transportion (referral)	2
Technicial Specifications	2
Mortality	11
Cardiogenic Shock	4
Lung Transplantation	6
Cardiac Diseases	5
Survival analysis	2
Cost-Analysis	2
Study analysis (meta-analysis)	1
Heart Transplatation	3
Congenital Diaphragmatic Hernia	7
Trauma- bleeding shock	1
Others (NO, Surfactans, Pharmacokinetic, and etc.)	6
Septic Shock	1
Heart Valvuler Surgery	1

sity of Michigan System UMHS (n=18). Additionaly, 9 out of 25 institutions with highest number of publications were reported from USA (Table 5). Among the authors of T100 articles, 11 authors were the first author of at least 2 articles (Appendix 1). Bartlett RH was the author with the highest number of articles and contributed to 12 articles. Subconsequently, Combes A contributed to 11 articles and was the first author of 4 of them (Table 6). Two group studies were conducted by the UK Collaborative ECMO Trial study group and 1 study was conducted by Pediatric Critical Care Study Group (Appendix 1).

Table 4. The most common listed countries with two and more in the most cited articles on ECMO

Country	Number
The United States of America	56
France	14
Australia	12
Germany	10
England	9
Canada	6
Italy	6
Taiwan	4
Sweden	3
Belgium	2
Scotland	2
Singapore	2

Discussion

Extracorporeal Membrane Oxygenation as a life saving intervention in patients with severe respiratory and cardiac failure has been a topical issue for researchers over decades. Investigators trying to determine ECMO indica-

Table 3. List of journals in which two and more published articles

Rank	Journal	Number of articles	Impact Factor*
1	Intensive Care Medicine	15	15.008
2	Annals of Thoracic Surgery	11	3.849
3	Circulation	7	18.880
4	Journal of Pediatrics	6	3.667
5	American Journal of Resp. and Crit. Care Med.	5	15.239
6	Critical Care Medicine	5	6.630
7	Pediatric Critical Care Medicine	5	3.092
8	Annals of Surgery	4	9.203
9	Journal of Pediatric Surgery	4	1.494
10	Lancet	3	53.254
11	Pediatrics	3	5.515
12	Chest	2	7.652
13	Critical Care	2	3.590
14	European Heart Journal	2	23.425
15	Jama Journal of The American Medical Association	2	8.530
16	Journal of Heart and Lung Transplantation	2	7.955
17	Journal of The American College of Cardiology	2	16.834
18	Journal of Thoracic and Cardiovascular Surgery	2	3.504

*Clarivate Analytics, 2018.

Table 5. Institutions of origin with four or more in the top 100 cited articles on ECMO

Rank	Institution	Number
1	University of Michigan (USA)	18
2	University of Michigan System UMHS (USA)	18
3	Assistance of Publique Hopitaux Paris APHP (France)	12
4	Hopital Universitaire Pitie Salpetriere APHP (France)	12
5	Sorbonne Universite (France)	12
6	Extracorporeal Life Support Org (The UK)	9
7	Harvard Univerty (USA)	9
8	Columbıa Universty (USA)	8
9	Unıversty of Leıcester (The UK)	8
10	Pennsylvanıa Commonwealth System of Hıgher Educatıon Pcshe (USA)	7
11	Unıversty of Pıttsburg (USA)	7
12	Florey Institute of Neuroscıence Mental Health(Australia)	6
13	Monash Universty (Australia)	6
14	Universty of London (The UK)	6
15	Universty og Utah (USA)	6
16	Utah System of Higher Education (USA)	6
17	Glenfield Hospital (The UK)	5
18	London School of Hygiene Tropical Medicine (The UK)	5
19	Universty Hospital of Leıcester NHS Trust (The UK)	5
20	Universty of Milano Bicocca (Italian)	5
21	Universty of Toronto (Canada)	5
22	Institut National De La Sante Et De La Recherce Medicale Inserm (France)	4
23	IRCCS Ca Granda Ospedale Maggiore Policlinico (Italian)	4
24	Newyork Presbyterian Hospital (USA)	4
25	Royal Childrens Hospital Melbourne (Australia)	4

Table 6. The most common authors with three and more in the top 100 cited articles

Author	Affliation	Number
Bartlett RH		12
Combes A		11
Brodie E		8
Rycus PT		7
Thiagarajan RR		7
Pellegrino V		6
Elbourne D		5
Leprince P		5
Pesentia A		5
Bratton SI		4
Chastre J		4
Firmin RK		4
Gattinoni L		4
Laussen PC		4
Luyt CE		4
Peek GJ		4
Schmıdt M		4
Thompson AE		4
Trouillet JL		4
Zangrillo A		4
Bacchetta M		3
Bailey M		3
Chen YS		3
Cooper DJ		3
Ehren H		3

tions, the patient population and the effects on survival vs complications have been reporting increasingly supportive results since last decade along with the developing technology. The present bibliometric study, being the first study evaluating the most influential citations regarding ECMO, evaluated the dynamics in the research trends of ECMO through time.

In this present bibliometric study, 25 journals were screened for evaluating T100 articles in field of ECMO using the ISI Web of Science, published between years 1985-2016. The majority of the articles were retrospective clinical studies mainly with level evidences group A and B. Among the T100 published in 18 journals, the highest number of articles were published in Intensive Care Medicine (n=15) and was followed by Annals of Thoracic Surgery (n=11), Circulation (n=7) and Journal of Pediatrics (n=6). The diversity of the topics and the target patient groups evaluated by these journals summarize the efforts in the use of ECMO for a variety of different indications in critically ill patients since 1950's. Despite having relatively lower impact factors compared to remaining journals, pediatric-specific journals in T100 list play an important role for having published a substantial number of preliminary articles on ECMO, particularly on subjects with congenital diaphragmatic hernia.

Eventually, Bartlett RH, being the main author of the first study reporting the first successful use of ECMO in neonates with severe respiratory distress[5] was also the author with the highest number of T100 articles.[14] Morever, Bartlett RH is well recognized for studies on both pediatric and adult patients with a wide spectrum of diseases. On the other hand, the second author with highest number of articles in T100 list, Combes A; has conducted studies in the last decade solely in adults particularly having ARDS.[15, 16] Consequently, the institutions and countries (USA and France) with highest number of T100 articles are also related with the authors with the highest number of T100 articles.

The relatively lower number of ECMO studies on adults compared to pediatric patients in early years is remarkable in T100 list. First randomized studies conducted in adults on ECMO with unfavourable outcomes in means of survival account for this situation.[3, 4] The CESAR trial conducted by Peek et al.,[6] can be defined as a milestone in ECMO literature for being the first study suggesting ECMO as a reliable tool for adults having severe respiratory failure. Additionally, it is the study with the highest number of citations-creating a big gap with the citations of following studies-on the topic.

Although occasionally, number of citations tend to be directly related to the time past since publication; we could not detect a linear relationship over time in our study. On the contrary, there was a rapid increase in the number of citations between years 2009-2017. The significantly increase in the number of publications and citations starting with 2009 can be primarily attributed to the publication of CESAR trial.[6] The common use of ECMO during the 2009 Influenza outbreak also has a great impact in this increase. Furthermore, H1N1 was reported as the second main topic among evaluated articles following ARDS.

Two different configurations of ECMO circuit; veno-venous (VV) and veno-arterial (VA) are seperately used for respiratory and cardiac support, respectively. Acute respiratory distress syndrome, lung transplantation, congenital diaphragmatic hernia and cardiogenic shock are among important indications of ECMO support.[17] However, among the main topics of T100 articles, technical procedures, mortality, cost and complications are also listed. Since ECMO is applied on patients with severe respiratory and cardiac failures, deciding on whether the mortality origin from the patient or the procedure can also be challenging. Moreover, despite all the advances, ECMO is also known for high complications resulting in mortality.[18] Thus, identification of the accurate indications and the management of ECMO with the safest techniques play important roles. Technical advances in the field of ECMO have also been allowing for expanded indications and improving safety.[19]

Strengths and Limitations

The strength of the current study is the provision of a quick and direct reach to determine topic trends and up-to-date information regarding ECMO with no requirements of any advanced analysis or statistical methods.

The lack of article-based self-citation analyses can be count as a limitation of the study. Only the total number of citations (excluding self-citations) and the total number of self-citations were presented in the present study. Furthermore, performing the bibliometric analyses based on citations may not be invariably an objective, reliable and accurate approach for determining the most influential articles on a certain topic.

Conclusion

In the present study, the most influential articles on ECMO has been assessed through the most related authors, institutions, countries, topics and change in trends througout years. Despite some flaws, the study has identified the most important publications on ECMO. The results of the current study are expected to guide researcher for further studies investigating the extensive use of ECMO for managing life threatening situations resulting in cardiac and respiratory failures in subjects with different ages.

Disclosures

Ethics Committee Approval: All authors (S.K.,C.G.,M.D.,and E.P.) declared that this research was conducted according to the principles of the World Medical Association' Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects". This research article did not need an ethics committee approval since only a bibliometric analysis or citation analysis of existing published classical studies were performed within the scope of this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship Contributions: Concept – S.K., M.D.; Design – S.K., M.D., C.G.; Supervision – S.K., C.G., E.P.; Materials – S.K., M.D., C.G.; Data collection &/or processing – M.D., E.P.; Analysis and/or interpretation – S.K., C.G.; Literature search – C.G., E.P.; Writing – C.G., M.D.; Critical review – S.K., C.G., M.D., E.P.

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