Normothermic Regional Perfusion in Organ Transplantation: Trends, Key Topics, and Evolving Research Focus

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Abstract

Objectives: **Normothermic regional perfusion is an emerging technique used to reduce warm ischemic injury during organ recovery in donation after circulatory death. The use of normothermic regional perfusion has become increasingly common as a method to improve the viability and function of organs, particularly for liver, kidney, heart, and lung transplantation. In this study, we performed a bibliometric analysis of normothermic regional perfusion-related research to understand publication trends, key topics, and areas of focus in the field.**

Materials and Methods: **On July 8, 2025, we conducted a comprehensive search using the Web of Science database to identify relevant studies on normothermic regional perfusion. The analysis included 372 studies published between 2014 and 2025. We used VOSviewer and Microsoft Excel to analyze annual trends, countries, institutions, journals, co-occurring key words, and articles. We performed manual screening to refine data on authors and institutions with significant publication and citation frequencies.**

Results: **Analyses of the 372 studies revealed a 22.35% annual growth rate in publication volume and a cumulative citation count of 7552. The United States led in publication output with 146 total documents, and the United Kingdom recorded the highest citation count at 2914 citations. The top 5 key words were "outcomes" (79 occurrences), "donors" (63 occurrences), "preservation" (56 occurrences), "liver transplantation" (55 occurrences), and "experience" (51 occurrences). Recent discussions focused on "outcomes," "experience," and "heart transplantation," and earlier research emphasized "kidney transplantation," "delayed graft function," and "biliary complications."**

Conclusions: **The present bibliometric analysis emphasized the growing interest in normothermic regional perfusion, highlighting its evolving focus from kidney and liver related complications to heart transplantation, offering valuable insights for optimizing future organ transplant practices.**

Key words: *Bibliographic analyses, Donation after circulatory death, Heart transplantation, Kidney transplantation, Liver transplantation*

Introduction

Normothermic regional perfusion (NRP) has emer-ged as a novel technique designed to minimize adverse consequences of warm ischemic injury following circulatory arrest during organ recovery in donation after circulatory death (DCD).[1-3] Normothermic regional perfusion facilitates the restoration of oxygenated blood circulation to the organs through the application of an extracorporeal membrane oxygenation circuit.[1] The technique enables the evaluation of organ function and restores ATP levels, thereby enhancing organ quality for transplant.[4] Normothermic regional perfusion is currently being used widely for the recovery of chest and abdominal solid organs, including the kidneys, liver, heart, and lungs.[3,5] Cases of the pancreas being recovered have also been reported.[2,3,5-8]

In recent years, interest in NRP has increased as preliminary studies have shown its potential to markedly improve outcomes for DCD organs.[4] Compared with the conventional rapid recovery method, which involves the rapid procurement and cold storage of organs after circulatory arrest, NRP works by reducing warm ischemic injury.[2,4] This process has resulted in a substantial rise in the use of

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DCD organs for transplantation, accompanied by enhanced graft survival and thereby diminished complications.[2,6] Increased evidence supporting NRP has encouraged institutions to conduct research focused on enhancing the technique and broadening its application in transplant practice.

In this study, we conducted a bibliometric analysis of the research output associated with NRP, with the aim to improve understanding of the development of this technique and clinical significance. Our analysis aimed to provide valuable insights into future advancements by analyzing publication trends and institutional and international collaborations and by identifying the most productive authors and journals.

Materials and Methods

Data collection and retrieval methods

The Web of Science database was searched on July 8, 2025, to identify research pertaining to NRP. We only included articles or reviews and did not include other document types, such as meeting abstracts, letters, notes, editorials, short surveys, book chapters, and errata. In the query of the Web of Science database query to extract articles published on NRP, we used "normothermic regional perfusion" as a search term restricted to titles. This bibliometric study was exempt from institutional review board approval as the study did not include human subjects.

Data analysis

We used VOSviewer version 1.6.20 and Microsoft Excel to analyze annual trends, countries, institutions, journals, co-occurring key words, and articles and to generate tables and figures.

To address inconsistencies arising from variations in author and institutional nomenclature, we also performed a manual screening protocol in which efforts were made to consolidate data concerning authors and institutions demonstrating substantial publication and citation frequency. The most frequently occurring key words were studied by limiting them to a minimum of five occurrences. Moreover, we manually excluded key words relevant to the study's design and subject such as "NRP," "normothermic regional perfusion," "donation," and so forth. Unnecessary words such as "male," "female," and "human," were also removed.

We used VOSviewer 1.6.20, a software tool developed by 2 software researchers at Leiden University (Ludo Waltman and Ness Jan Van Eck, revolu-tionaries in the scientometrics field), to generate figures and network illustrations. The tool produced bibliometric networks by organizing interlinked items into clusters; each color in the network repre-sented a cluster, and the lines between clusters anditems represented the links identified between them.

Results

Included studies

The analyses included 372 studies published between 2014 and 2025 (260 primary studies and 112 review articles). Of these, 365 were published in English, 3 in French, 3 in Spanish, and 1 in Russian. The yearly growth rate of publications was 22.35%. In total, the documents included an average of 20.3 citations per document and were an average age of 2.83 years. Furthermore, 21.51% of the documents had international co-authorships. The articles garnered a total of 7552 citations, with 4496 citations excluding self-citations (Table 1).

Annual trends

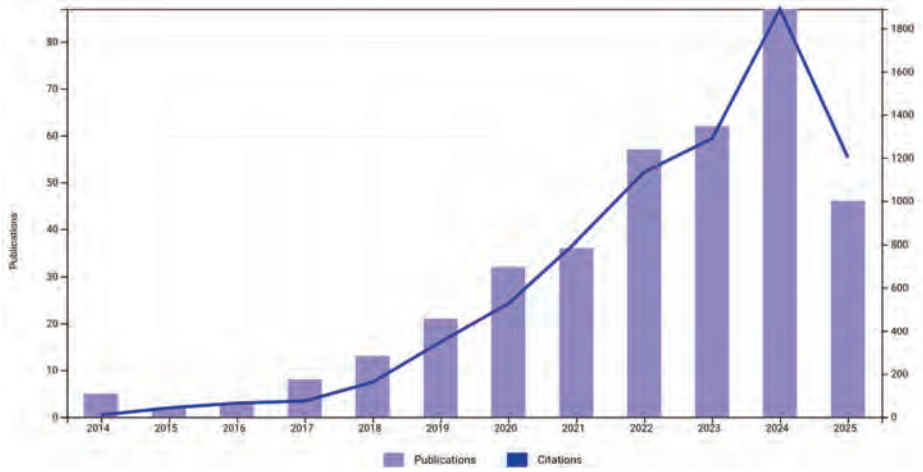
The number of publications and citations related to NRP generally demonstrated an upward trajectory between 2014 and 2025, with some fluctuations. The output remained relatively consistent from 2014 to 2017, with an average of 3 articles per year. In 2018, 13 papers were published, marking an initial notable peak. In 2020, the number of publications doubled to 32, resulting in another substantial peak. In 2023, there was a third surge, with 62 papers discussing NRP. The year 2024 was the most notable, with 87 documents and nearly 1890 citations at the time of data extraction (Figure 1).

Table 1. Main Information About Documents Related to Normothermic Regional Perfusion

Description	Result
Time span	2014-2025
No. of sources (journals, books, etc)	120
No. of documents	372
Annual growth rate, %	22.35%
Document average age, years	2.83
Average No. of citations per document	20.32
International co-authorships , %	21.51

International collaboration was assessed using the multiple country publication (MCP) metric as implemented in the bibliometrix package using R language. A publication was classified as internationally collaborative if it included author affiliations from ≥2 different countries. International collaboration rate (%) was calculated as the proportion of MCPs relative to the total number of publications.

Figure 1. Annual Publication Trends From 2014 Through 2025 in the Field of Normothermic Regional Perfusion, Showing an Increase in Research Output Over the Years



Top countries

The United Kingdom had the highest citation count, totaling 2914 across 66 documents, whereas the United States followed with 2245 citations from 146 documents. Spain, the United Kingdom, and France were early contributors to research activity, whereas the United States experienced a significant increase in research output beginning in 2022, becoming more engaged in NRP-related studies (Figure 2 and Table 2).

Table 2. Top Contributing Countries in Research on Normothermic Regional Perfusion According to Total Citations, Document Numbers, and Total Link Strength

Country	No. of Citations	No. of Documents	Total Link Strength[a]
United Kingdom	2914	66	1956
United States	2245	146	2124
Spain	2039	72	2105
Italy	1034	63	1304
Scotland	981	23	1024
France	727	29	816
Netherlands	689	24	778
Canada	636	21	617
Belgium	608	18	641
Switzerland	467	16	475
Austria	342	6	207
Australia	274	14	362
Sweden	216	6	238
Germany	120	6	94
Denmark	83	7	143

[a] Total link strength, as obtained from VOSviewer, indicates the cumulative strength of collaborative relationships between different countries.

Top cited authors

The top 5 cited authors contributing to literature were Simon Messer with 719 citations, Christopher J. E. Watson with 716 citations, Beatriz Dominguez-Gill with 651 citations, and Gabriel C. Oniscu and Andrew J. Butler, each with 595 citations (Table 3).

Table 3. Top Contributing Authors on Normothermic Regional Perfusion According to Citations and Number of Publications

Author	No. of Citations	Total Link Strength[a]
Messer, Simon	719	505
Watson, Christopher J.E	716	710
Dominguez-Gil, Beatriz	651	895
Oniscu, Gabriel C.	595	695
Butler, Andrew J.	595	545
Large, Stephen	488	435
Minambres, Eduardo	477	805
Coll, Elisabeth	451	647
Gardiner, Dale	429	420
Catarino, Pedro	304	162

[a] Total link strength corresponds to the sum of an author's links to other authors, highlighting their level of integration within the research network.

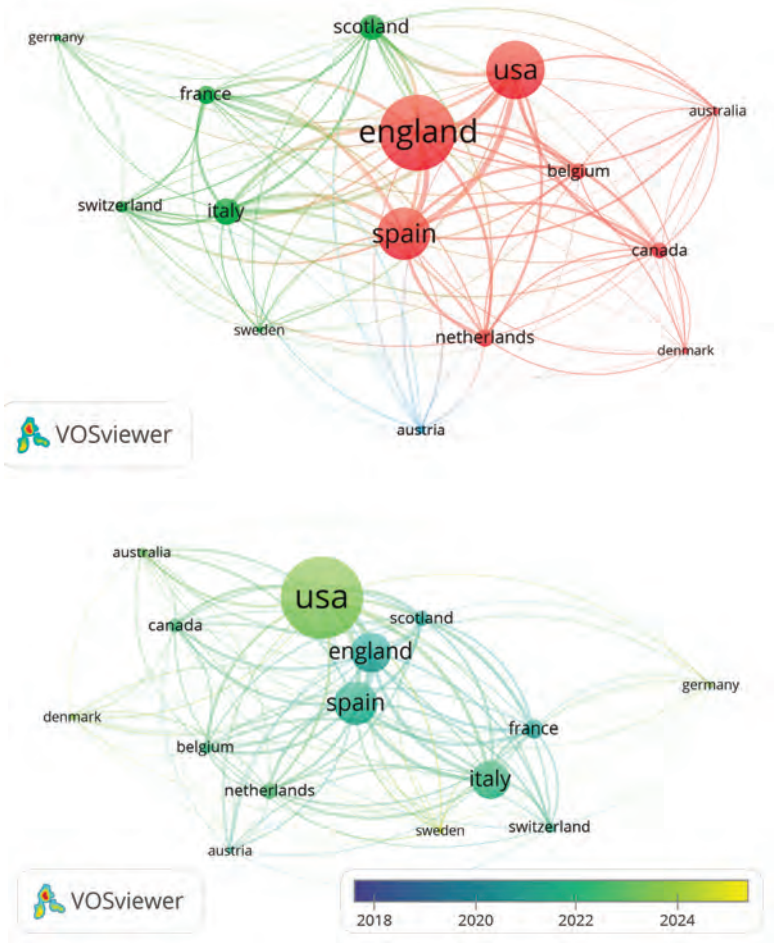
Institutions

The top 5 organizations were University of Cambridge (United Kingdom) with 1239 citations, Royal Infirmary of Edinburgh NHS Trust (United Kingdom) with 858 citations, University of Cantabria (Spain) with 627 citations, University of Edinburgh (United Kingdom) with 524 citations, and University of Barcelona (Spain) with 519 citations (Table 4).

Top journals

The top 5 contributing journals were American Journal of Transplantation with 1494 citations and 34 documents, followed by Journal of Heart and Lung Transplantation with 1175 citations and 20 documents, Transplantation with 871 citations and 36 documents, Transplant International with 537 citations and 17 documents, and Liver Transplantation with 458 citations and 14 documents (Table 5).

Figure 2. Network Visualization Map of Top Contributing Countries in the Field of Normothermic Regional Perfusion According to Citation Count and Publication Count



Top, Network visualization map of top contributing countries according to citations count. Each country is represented with a circle; circle size reflects the number of citations of publications from that country. The connecting links between circles represent the total link strength of international collaboration. **Bottom,** Network overlay visualization of top countries according to publications count through the years, showing temporal progression of countries expanding their research in normothermic regional perfusion. Countries are colored according to the timeline gradient scale; earlier contributors are shown as blue clustering and recent contributors are shown as green clustering.

Table 4. Top 15 Leading Institutions on Normothermic Regional Perfusion Based on Number of Citations, Documents Count, Total Link Strength, and Their Corresponding Countries

Country	No. of Citations	Total Link Strength[a]	Country
University of Cambridge	1239	1353	United Kingdom
Royal Infirmary of Edinburgh NHS Trust	858	1128	United Kingdom
University of Cantabria	627	1304	Spain
University of Edinburgh	524	682	United Kingdom
University of Barcelona	519	640	Spain
Newcastle University	352	394	United Kingdom
Vanderbilt University	303	662	United States
Stanford University	303	433	United States
Leuven University Hospital	285	531	Belgium
University of Toronto	274	331	Canada

[a] Total link strength represents the sum of the strengths of all links between different institutions, reflecting the intensity and extent of their collaborations and citation connections within the field of normothermic regional perfusion.

Table 5. Top 10 Journals Publishing on Normothermic Regional Perfusion-Related Research, According to Citation Count, Documents Count, and Total Link Strength

Country	No. of Citations	No. of Documents	Total Link Strength[a]
American Journal of Transplantation	1494	34	578
Journal of Heart and Lung Transplantation	1175	20	264
Transplantation	871	36	447
Transplant International	537	17	237
Liver Transplantation	458	14	190
Current Opinion in Organ Transplantation	314	25	220
Clinical Transplantation	187	16	167
Transplantation Direct	126	8	107
Artificial Organs	84	9	83
Journal of Clinical Medicine	82	7	56

[a] Total link strength, as calculated by VOSviewer, denotes the cumulative strength of all citation-base links between a journal and other journals, revealing the interconnectedness degree and the influence within the field of normothermic regional perfusion.

Top frequent key words

In the analysis of the most frequently discussed key words in NRP research, "outcomes" was the most frequent key word, mentioned 79 times, followed by "donors" at 63 times, "preservation" at 56 times, "liver transplantation" at 55 times, and "experience" at 51 times. The terms "ischemic cholangiopathy" and "early allograft dysfunction" were referenced 24 and 15 times, respectively (Figure 3 and Table 6). Figure 4 shows the chronological sequence of these prominent key words, indicating that recent discus-sions focused on "outcomes," "experience," and "heart transplantation," whereas prior investigations highlighted "kidney transp-lantation," "delayed graft function," and "biliary complications."

Top cited articles

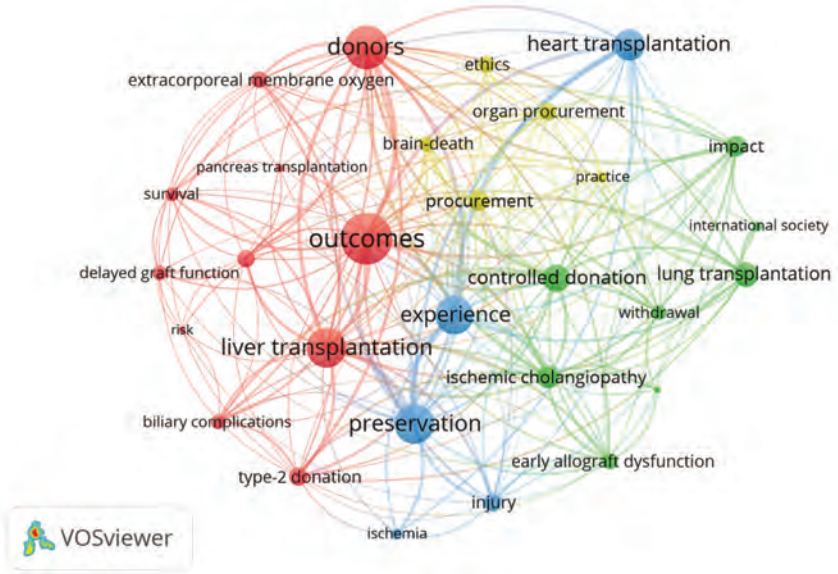
The top 3 cited articles were the article titled "In situ normothermic regional perfusion for controlled donation after circulatory death: the United Kingdom experience" by Gabriel Oniscu, published in *American Journal of Transplantation* in 2014 with 237 citations (Table 7). Next was the article "Outcome after heart transplantation from donation after circulatory-determined death donors" by Simon Messer, published by *Journal of Heart and Lung Transplantation* in 2017 with 231 citations. The third article was "In situ normothermic perfusion of livers in controlled circulatory death donation may prevent ischemic cholangiopathy and improve graft survival" by Christopher J. Watson published in *American Journal of Transplantation* in 2019 with 206 citations.

Table 6. Top Frequent Key Words in Normothermic Regional Perfusion-Related Literature

Author	No. of Citations	Total Link Strength[a]
Outcomes	79	557
Donors	63	440
Preservation	56	463
Liver transplantation	55	428
Experience	51	364
Heart transplantation	40	235
Controlled donation	32	248
Lung transplantation	27	182
Ischemic cholangiopathy	24	213
Procurement	21	152
Impact	21	131
Type 2 donation	19	186
Kidney transplantation	18	143
Injury	18	137
Organ procurement	17	138
Extracorporeal membrane oxygenation	16	117
Ethics	16	101
Brain death	15	125
Early allograft dysfunction	15	109
Biliary complications	14	99

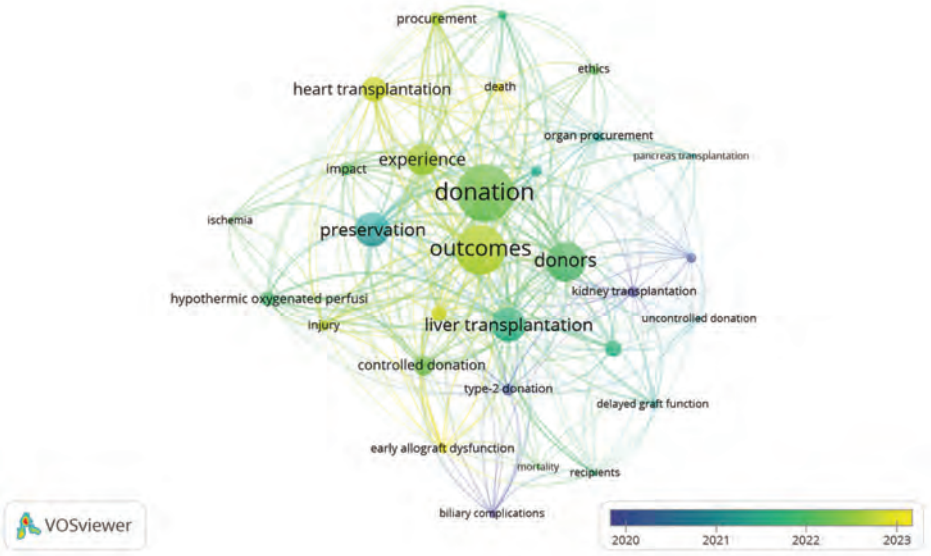
[a] Total link strength reflects how frequently a keyword appears with other keywords in the bibliometric network, indicating connectivity within normothermic regional perfusion-related research.

Figure 3. Network Visualization of Most Occurring Key Words After Excluding Search Related Key Words and Key Words That Occurred <5 Times



Each node represents a key word; the size of the node indicates the frequency of occurrence. Four thematic clusters were identified according to color. Red clusters indicate clinical outcomes and complications of normothermic regional perfusion (NRP), green clusters indicate procedural context of NRP in different organs, yellow clusters indicate ethical and legal consequences of NRP, and blue clusters indicate preservation and procurement strategies.

Figure 4. Overlay Visualization of Top Occurring Key Words From 2014 Through 2025



Color of each circle corresponds to the average year of appearance in the literature (see key).

Table 7. Top-Cited Articles in the Field of Normothermic Regional Perfusion

Author	Title	Year	Journal and Publication Details	No. of Citations
Oniscu GC, et al	In situ normothermic regional perfusion for controlled donation after circulatory death: the United Kingdom Experience	2014	*Am J Transplant*. 2014;14(12):2846-2854	237
Messer S, et al	Outcome after heart transplantation from donation after circulatory-determined death donors	2017	*J Heart Lung Transplant*. 2017;36(12):1311-1318	231
Watson CJ, et al	In situ normothermic perfusion of livers in controlled circulatory death donation may prevent ischemic cholangiopathy and improve graft survival	2019	*Am J Transplant*. 2019;19(6):1745-1758	206
Lomero M, et al	Donation after circulatory death today: an updated overview of the European landscape	2020	*Transpl Int*. 2020;33(1):76-88	204
Messer S, et al	A 5-year single-center early experience of heart transplantation from donation after circulatory-determined death donors	2020	*J Heart Lung Transplant*. 2020;39(12):1463-1475	198
Hessheimer AJ, et al	Normothermic regional perfusion vs super-rapid recovery in controlled donation after circulatory death liver transplantation	2019	*J Hepatol*. 2019;70(4):658-665	195
Morrissey PE, et al	Donation after circulatory death: current practices, ongoing challenges, and potential improvements	2014	*Transplantation*. 2014;97(3):258-264	194
Messer SJ, et al	Functional assessment and transplantation of the donor heart after circulatory death	2016	*J Heart Lung Transplant*. 2016;35(12):1443-1452	187
Miñambres E, et al	Improving the outcomes of organs obtained from controlled donation after circulatory death donors using abdominal normothermic regional perfusion	2017	*Am J Transplant*. 2017;17(8):2165-2172	169
Hoffman JR, et al	Early US experience with cardiac donation after circulatory death (DCD) using normothermic regional perfusion	2021	*J Heart Lung Transplant*. 2021;40(11):1408-1418	141

Discussion

This study offers an in-depth review of recent scientific literature on NRP, highlighting its growing adoption within the transplant community. The increasing implementation of NRP is driven by the necessity to optimize outcomes and enhance the use of solid organs from DCD donors. Multiple factors have influenced this trend, such as the widening disparity between organ availability and transplant demand, a rising number of DCD cases, the necessity for enhanced graft monitoring and usability as-

sessment (especially for extended criteria donors), and efforts to optimize organ reconditioning before transplantation.[9-12] The surge in research output over the past decade reflects the growing interest in NRP, with a notable increase in studies addressing outcomes and the ongoing debates surrounding this technique. The increased interest has been reflected in the research output, where studies addressing outcomes and the ongoing debates surrounding NRP have been increasing in number over the past 10 years.

Bibliometric studies serve a vital role in the medical field as they analyze trends, impact, and dissemination of research across different fields.[13-15] These studies have facilitated the identification of key papers, prominent authors, and leading institutions, offering insights into the development of scientific knowledge.[16,17] Bibliometric studies have facilitated the identification of publication trends and research scope, thereby directing future research trajectories.[17-19] Within the framework of NRP, bibliometric analysis could facilitate tracking of the increasing interest and research output associated with this technique, highlighting areas of ongoing debate and progress.

Normothermic regional perfusion was initially developed in Spain as a strategy to alleviate the detrimental consequences of warm ischemic injury subsequent to circulatory death. Initially, NRP experienced extensive use in Europe, subsequently attracting growing interest in the United States. In 2020, Vanderbilt University and New York University were the first US institutions to implement NRP for DCD heart donors.[20] Normothermic regional perfusion is uniformly applied at a rate of 100% in France, Italy, and Switzerland, in contrast to its selective implementation in other nations, where rates vary from below 10% to 50%.[21]

The use of NRP yields more transplanted organs per donor compared with super-rapid recovery method. Oniscu and colleagues showed an increased number of organs transplanted from donors when NRP was used during the procurement of a controlled DCD in the UK, with a mean of 3.3 organs with NRP versus 2.6 organs without NRP.[22] Similar data were also noted in the United States, with usage of NRP in DCD donors being associated with increased rates of liver use of 70.6% versus 39.0%.[23]

Numerous studies have been conducted to assess the outcomes of NRP across different organs. In kidney transplantation, NRP has been shown to reduce the incidence of delayed graft function and ischemic-reperfusion injury.[24] For liver transplantation, the technique has proven crucial in increasing the use of DCD organs, significantly improving graft viability, and reducing complications such as ischemic cholangiopathy.[22,24] In heart transplantation, NRP has demonstrated success in reconditioning DCD hearts by reducing myocardial injury, leading to similar 1-year outcomes compared with non-NRP DCD cases.[25-27] Although lung transplantation has been the subject of fewer studies, preliminary findings have indicated that the implementation of strategies to prevent pulmonary edema can lead to satisfactory outcomes after lung transplantation, making it an attractive field for future research.[6,28] Similarly, although use of NPR in pancreas transplantation is so far limited, NRP has been shown to enhance the use and outcomes of DCD pancreas transplants, with several studies suggesting that the results are comparable to more conventional methods.[23,29] Together, these studies affirm NRP's transformative effect on organ transplantation across multiple organ systems.

Our study indicated that the United States dominated in research output, generating the largest number of publications with 146 papers. The United Kingdom, however, excelled in research impact, recording the highest citation count at 2914. This further emphasizes the United Kingdom's fundamental role and continuous impact in the development and implementation of NRP.

In our analysis of the most frequently discussed key words in NRP research, "outcomes" was the dominant topic, highlighting the principal aim of NRP studies: to assess posttransplant success and long-term graft survival. Researchers aimed to demonstrate how NRP improved the viability of organs from DCD donors, leading to enhanced transplantation outcomes across various organs, including liver, heart, and kidney. The focus on outcomes signifies the growing interest in assessing the clinical benefits of NRP in minimizing complications, enhancing graft function, and improving patient survival rates.

The occurrence of "ischemic cholangiopathy" and "delayed graft function" among the most common key words emphasized the considerable focus of these posttransplant complications in NRP research.

Ischemic cholangiopathy, especially in DCD liver transplants, is a major issue due to warm ischemic injury, with NRP being investigated as an approach for restoring blood flow and mitigating the risk of biliary complications. Similarly, delayed graft function, especially in DCD kidney transplants, is frequently investigated as researchers work to minimize ischemic-reperfusion injury. These findings highlighted the ongoing focus in NRP research to address these specific challenges.

Our analysis revealed a chronological pattern in the discourse surrounding key topics. Earlier studies, particularly between 2018 and 2019, concentrated on kidney transplantation, with repeated discussions on delayed graft function and ischemia-reperfusion injury. Moving forward, around 2021, preservation, perfusion, liver transplantation, and the use of normothermic and hypothermic perfusion machines became more prevalent in research output. From 2022 onward, focus was on outcomes and experiences, indicating a transition toward assessing clinical outco-mes and procedural expertise in NRP. One of the consistent topics of discussion during this period was the effect of NRP on the graft biliary system and its complications. Figure 4 illustrates that biliary complications were a prominent key word in earlier publications, whereas ischemic cholangiopathy emerged as a particularly significant topic of discourse from 2022 onward, underscoring persistent concerns on graft health and long-term outcomes.

Among the most frequently discussed organs in NRP research, the liver received the most attention, with 55 publications. This was followed by the heart, which was the focus of 40 documents, and kidney transplantation, which was the topic of 18 articles. Research on the lung was with 27 documents, whereas pancreas transplantation was the least addressed, featuring only 6 articles. This distribution underscores the crucial function of NRP in enhancing liver transplantation outcomes, especially regarding the use of DCD organs, where NRP has demonstrated a substantial improvement in graft survival and posttransplant outcome.

Finally, our study revealed that ethical considerations have become a central focus in discussions surrounding NRP, with a noticeable peak in attention around 2021. The ethical debate is particularly prominent in thoracoabdominal-NRP, where concerns have been raised, especially by the American College of Physicians, regarding the potential reversal of circulatory death through extracorporeal membrane oxygenation and the induction of brain death via limited cerebral perfusion. Controversy has emerged concerning NRP, particularly regarding the unintentional perfusion of the brain via collateral circulation. Nonetheless, the data did not support this. However, neurophysiological studies of both abdominal and thoracoabdominal-NRP donors showed no evidence of cerebral perfusion.[30-33] Several studies, including those by Wall and colleagues, revealed that thoracoabdominal-NRP does not resuscitate the donor, as death is determined based on circulatory criteria before initiation of NRP.[30] Both NRP and non-NRP DCD donors entail the reinitiation of cardiac activity for organ evaluation, yet neither reinstates autonomous circulatory function.[30,33] Legal issues pertaining to brain perfusion are mitigated by clamping arch vessels to eliminate ambiguity concerning brain death.[33] The American Society of Transplant Surgeons subsequently endorsed NRP, asserting that it is ethically justifiable because of improved organ use and recipient outcomes and is consistent with US legal death definitions.[31]

A key limitation of our study was the reliance on bibliometric analysis, which primarily focused on quantifying research output rather than evaluating the quality or clinical relevance of the studies. Although key word frequency and publication trends offer valuable insights into research priorities, they do not fully capture the depth or outcomes of individual studies. In addition, only a single database was used for analysis, which, although well-known for its extensive range of papers, may have resulted in the exclusion of relevant studies from other databases. This limitation could have led to the omission of important research, particularly from institutions or regions that predominantly publish on different platforms. Moreover, our analysis may be limited by the inclusion of only published and indexed literature, potentially overlooking unpublished data or ongoing trials that could further shape the understanding of NRP. Variations in terminology across different regi-ons and institutions may also have influenced our key word analysis, leading to potential underrepre-sentation of certain topics. Finally, the relatively recent adoption of NRP means that longer-term outcomes and trends may not yet be fully represented in the current body of research.

Conclusions

This bibliometric analysis provided a comprehensive overview of the scientific literature on NRP. The results illustrated a substantial growth in research output, highlighting the increasing interest in optimizing organ utilization and improving outcomes in DCD transplants. The United Kingdom and the United States emerged as key contributors in terms of citations, whereas the United States led in publication count. The analysis identified 5 predominant topics—outcome, preservation, liver transplantation, experience, and perfusion—illustrating the evolving priorities within the NRP field. These insights reflect the progression and expanding influence of NRP on transplant practices globally.

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