Review Article

The Upsurge in Research and Publication on Articular Cartilage Repair in the Last 10 Years

Abstract

This study aims to study the publication trends in articular cartilage repair (ACR) techniques, over the last 10 years. A literature search was performed on the PubMed, Web of Science, and SCOPUS databases. We used suitable keywords and Boolean operators (articular cartilage injury AND "marrow stimulation OR microfracture (MFx)," "osteochondral autograft," "osteochondral allograft" and "autologous chondrocyte implantation (ACI)," "scaffold"), on January 1, 2019. Trends in publication on these topics were analyzed, focusing on publications over the last 10 years, type of research, authors, institution, and country. There was an increasing trend in publications related to ACR. A search on PubMed revealed 698, 225, 293, 857, and 982 documents on searching for "articular cartilage" AND "marrow stimulation OR microfracture," "osteochondral autograft," "osteochondral allograft," "ACI," and "scaffold," respectively. Similar searches revealed 1154, 219, 330, 1727, and 2742 documents on Web of science and 934, 301, 383, 944, and 2026 on SCOPUS, respectively, in the same order of topics. Overall, most papers were published from the United States and European countries, and Cole BJ was the most published author. There was an increasing trend in the number of publications as well as citations, with international collaboration among researchers. It implies that this field is growing rapidly. The authors from globally recognized and leading clinical institutions in the developed world contributed maximally to these publications. Most of these papers were published in high-impact arthroscopy subspecialty journals. Level of evidence: Level IV.

Keywords: *Arthroscopy, articular cartilage repair, cartilage transplantation, microfracture, publication, research*

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Introduction

Regenerative orthopedics is gaining popularity as a new subspecialty in orthopedic surgery. Preservation of a joint by an adequate management in the initial stage of the articular cartilage problem is being increasingly recognized, and emphasis has shifted from "Reconstruction to Regeneration of a joint." The cartilage surgery has benefited from research efforts as traditional methods of articular cartilage repair (ACR), and restoration is undergoing several innovations, leading to the development of novel surgical techniques. Several techniques have been used to repair cartilage lesions. These include abrasion, drilling, microfracture (MFx), osteochondral autologous transplantation, allografts, and autologous chondrocyte implantation (ACI) either as two-stage or as a single-stage procedure, along with several innovative modifications of these techniques. This field is evolving fast, with established and emerging techniques.[1]

Several papers have come up recently in the most influential publications in the field of science,[2] various medical specialties,[3-15] and orthopedics in particular.[16-18] Soon after Lefaivre *et al.*[16] published their article on the top 100 most-cited papers in orthopedics, numerous papers depicting the most-cited articles in different orthopedic subspecialties,[19-35] related to specific disorders[36-39] and publication trends from different countries,[40-44] have appeared. Such reviews provide a useful reference for research quality and evolution of practice, areas of controversy, and future research goals in a particular field. This study was aimed to analyze the recent publication trends (in the last 10 years) in ACR techniques. We hypothesized that there had been an upsurge in research and publications in the field of ACR with accelerating trend in the last decade.

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Methods

A literature search was performed on the PubMed, WoS, and SCOPUS databases. We had used suitable keywords and Boolean operators (articular cartilage injury AND: "marrow stimulation OR microfracture," "osteochondral autograft," "osteochondral allograft," "autologous chondrocyte transplantation," "ACI," and "scaffold"), on January 1, 2019. We also performed a combined search, using search strategy [articular cartilage injury AND (marrow stimulation OR microfracture OR osteochondral autograft OR osteochondral allograft OR ACI OR autologous chondrocyte transplantation OR scaffold)]. These electronic literature databases provided us a systematic and objective means to evaluate the emerging scientific literature in any field critically. Citation data were also provided, by SCOPUS, WoS, and Google Scholar. No language restrictions were used, but these databases mostly covered the English literature. Publication trends and most-cited papers in the field were then analyzed. This trend was compared to the general trend of publications in the field of medicine in the last decade. To derive this trend, SCOPUS advanced search feature was used, using subject-specific search using the key term "SUBJAREA (MEDI)" and the search was then limited to last 10 years. Analysis of results on SCOPUS provided us publication trends.

Trends in a publication on these topics were analyzed, focusing on some publications over the last 10 years, journals publishing these papers, and type of publication (authors, institution, and country). We studied the citation trends of these articles, in SCOPUS and WoS. SCOPUS was used for studying trends, as it has broader coverage as compared to WoS and PubMed.[45-47] Although we checked these papers in Google Scholar, we did not use it for further analysis because of its inadequate quality control and inaccuracies due to content gaps, incorrect citation counts, duplication, and manipulation of citation numbers.[48,49]

The mapping of citations and keywords for the papers from PubMed using the VOSviewer bibliometric software was also performed.

Results

There was an increasing trend in publications related to ACR (total number of articles' section). The data from SCOPUS were analyzed under several headings (publication and citation trends–most prolific countries' sections) as mentioned below and revealed the following:

Total number of articles

A search on PubMed revealed 698, 225, 293, 857, and 982 documents on searching for "articular cartilage" AND "marrow stimulation OR MFx," "osteochondral autograft," "osteochondral allograft," "ACI," and "scaffold," respectively. Similar searches revealed 1154, 219, 330, 1727, and 2742 documents on Web of science and 934, 301, 383, 944, and 2026 on SCOPUS, respectively, in the same order of topics. The combined search revealed 3655 papers on PubMed (2362 in the last 10 years). Similar combined search on WoS revealed 6202 papers (4554 in the last 10 years) and on SCOPUS revealed 5104 (3489 in the last 10 years). All these data prove that research and publication in this field have accelerated markedly in the last 10 years [Table 1].

Publication and citation trends

There was an increasing trend in the number of publications related to ACR, as well as the number of citations received by these papers in the last 10 years [Figure 1a-c]. We have also studied publication trends in individual areas MFx and marrow stimulation, osteochondral autografting, osteochondral allografting, ACI, and scaffold research on PubMed [Figure 1a] and SCOPUS [Figure 1b] databases. The growth was highest for scaffold research in the recent past, followed by marrow stimulation techniques and ACI, and it was nearly constant for osteochondral grafting techniques. The curve for the entire field of cartilage repair is steeper as compared to the rise of medical literature in general in the last decade [Figure 1d]. Other features related to publication trends have been depicted in

Table 1: Search strategy and number of articles

Articular cartilage repair technique	Search strategy	Papers retrieved in PubMed (last 10 years)	Papers retrieved in SCOPUS (last 10 years)	Papers retrieved in WoS (last 10 years)
Microfracture	Articular cartilage AND "marrow stimulation OR microfracture"	981 (698)	1175 (934)	1399 (1154)
Osteochondral autograft	Articular cartilage AND "osteochondral autograft"	349 (225)	506 (301)	306 (219)
Osteochondral allograft	Articular cartilage AND "osteochondral allograft"	448 (293)	573 (383)	444 (330)
Autologous chondrocyte implantation	Articular cartilage AND ("autologous chondrocyte implantation" OR "autologous chondrocyte transplantation")	1398 (857)	1420 (944)	2287 (1727)
Scaffold research	Articular cartilage AND "scaffold"	1380 (982)	2838 (2026)	3726 (2742)
Combined final search	Articular cartilage AND (marrow stimulation OR microfracture OR osteochondral autograft OR osteochondral allograft OR autologous chondrocyte implantation OR scaffold)	3655 (2362)	5104 (3489)	6202 (4554)

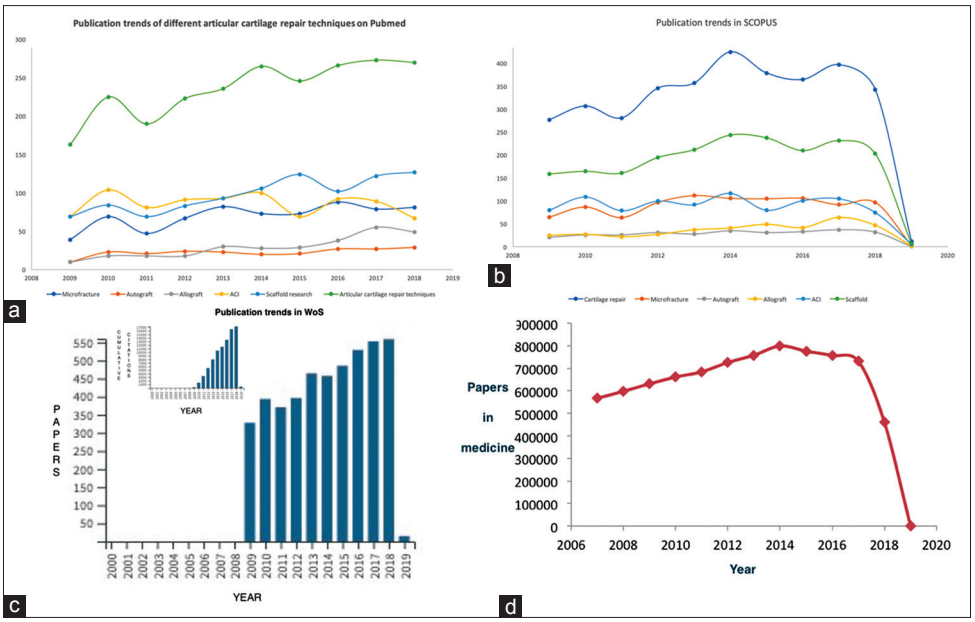

Figure 1: (a) Publication trends in articular cartilage repair on PubMed in the last 10 years. (b) Publication trends in articular cartilage repair in SCOPUS in the last 10 years. (c) Publication and citation trends in articular cartilage repair in WoS in the last 10 years. (d) Publication trend of medical science literature in general in the last decade. (SCOPUS data)

Figures 2 and 3. It shows ACR as one of the most popular topics in orthopedic surgical research, in the last decade.

Top 10 most-cited papers

We extracted the top 10 most-cited papers in the last 10 years, on the SCOPUS and WoS databases. The top ten most-cited papers have been included in Table 2.

Orthopedic Journals publishing most cartilage-related work

Most papers were published in the American Journal of Sports Medicine (AJSM-221), followed by Knee Surgery, Sports Traumatology, Arthroscopy (KSSTA-132); Arthroscopy: The Journal of Arthroscopy and Related Surgery (103), and cartilage (93) [Figure 2a].

Most prolific authors

Overall, Cole BJ from USA (64) was the most published author [Figure 2b], followed closely by Kon E from Italy (54), Marcacci M from Italy (54), Filardo G from Italy (45), and Niemeyer *P* from Germany (45).

Most prolific institutions

Most papers came from the Hospital for Special Surgery, New York (98). It was closely followed by Rizzoli Orthopedic Institute, Bologna (90) and Harvard medical school (86). Most universities or institutes contributing to cartilage-related work were located in the USA, followed by European countries [Figure 2c].

Most prolific countries

The United States accounted for the most work (1, 141), followed by China (449), Germany (359), UK (259), Italy (245), Japan (175), Switzerland (160), South Korea (143), Australia (111), and Canada (110) [Figure 2d].

Keyword, coauthorship, citation, cocitation, and bibliographic coupling maps

These have been depicted in Figures 3a to 3h according to PubMed and SCOPUS data, as analyzed on VOS viewer. To illustrate, in keywords mapping for ACR-related papers [Figure 3a], two terms are said to cooccur if they both occur on the same line. The smaller the distance between the two terms, the more significant the number of cooccurrences of the terms. Timeline color scale is shown in the bottom right of each figure.

Discussion

An increasing trend was observed in the number of publications related to ACR, as well as the number of citations received by these papers in the last 10 years. It shows that ACR was a topic receiving increasing orthopedic research interest in the last decade.

A trend in scientific research can be visually depicted by the number of citations received per annum. A paper gaining increasing citation counts reflects an increasing trend in a specific topic and indicates the importance given by the author of an article to others' work on related topics.[17] Cocitation is the frequency with which any two documents are cited together by other documents. Bibliographic coupling occurs when two works refer a third common work in their bibliographies. Both cocitation and bibliographic coupling are similarity measure that uses citation analysis for establishing a similarity relationship between documents. Citation numbers

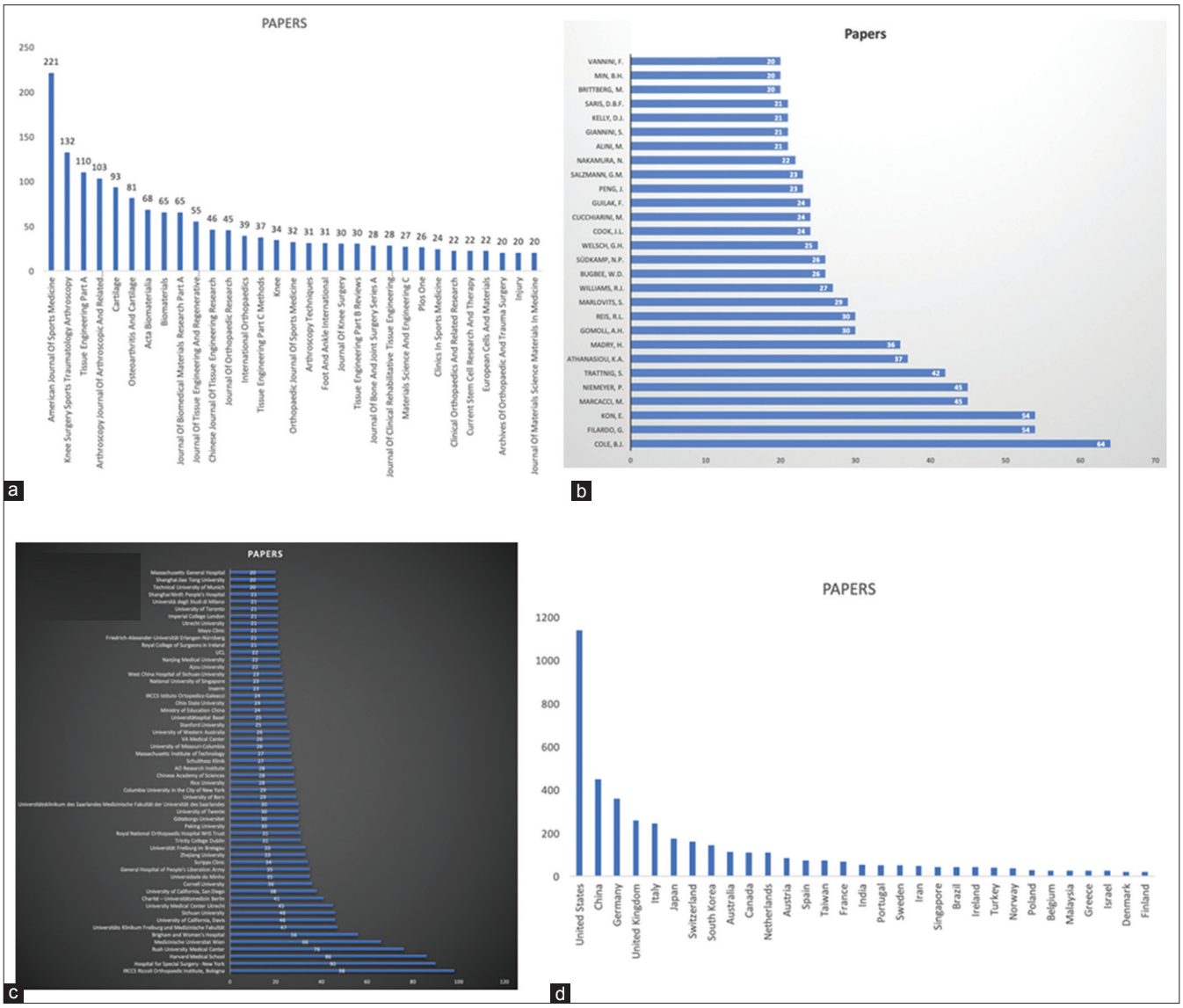

Figure 2: (a) A bar chart showing journals publishing most cartilage-related work (SCOPUS data). (b) Bar chart showing most prolific authors in articular cartilage repair (SCOPUS data). (c) A bar chart showing most prolific institutions in publishing articular cartilage repair work (SCOPUS data). (d) A bar chart showing most prolific countries in publishing articular cartilage repair work (SCOPUS data)

vary markedly in different databases.[45-49] The problems related to citations are self-citation, preferential citation of papers from the target journal, preferential citation of articles published in the English language, and missing citations from textbooks.[16,50,51] Recent papers are always at a disadvantage, as citations rise with time. Several authors are prone to snowball effect (citing an already well-cited paper due to its previous citations, rather than its quality).[16] "Obliteration by incorporation" occurs when truly classic and original papers are infrequently cited as they gradually merge into the body of current knowledge. Sometimes, their only existence is in the bibliography of so-called top-cited articles. "Incomplete citing" refers to wrong citations, which are made to persuade readers, in place of giving credit to real workers. Omission bias (not citing competitors), powerful person bias, national, state, or institutional bias, in-house bias, and language bias also contribute to confounding the overall picture.[13,17]

The bibliometric study is particularly relevant to newly established subspecialties, like cartilage repair surgery, where the gradual transition from basic science articles to clinical observational and experimental studies is required and is in process.

The United States accounted for the most work in cartilage repair, followed by European countries, China, Japan, South Korea, Australia, and Canada. Overall, we found a strong and widespread international presence in cartilage-related research. As of now, institutions in the first world have contributed most to cartilage repair work. Developing countries like India and Taiwan also did have some contribution. It reflects the influence of well-known

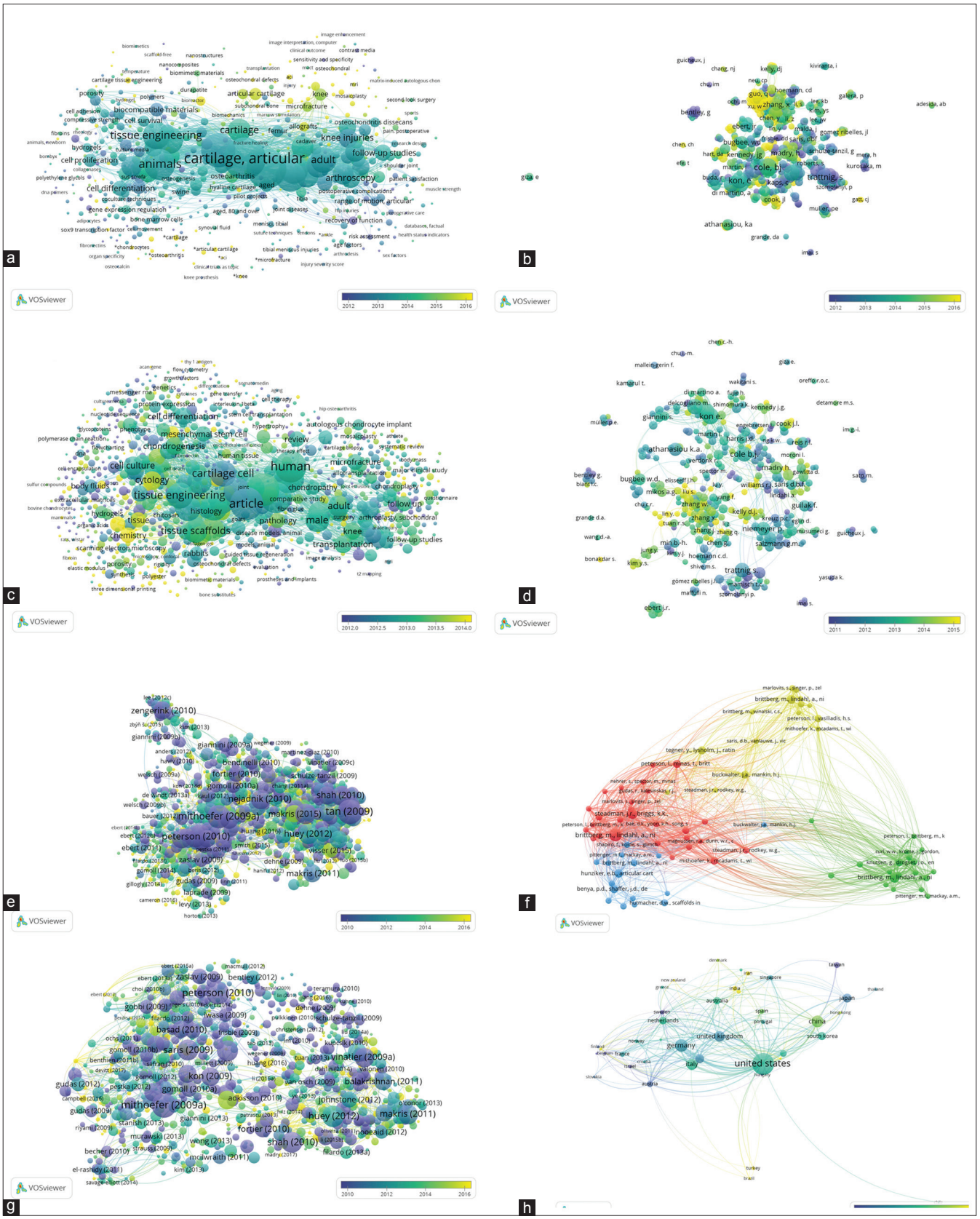

Figure 3: (a) Keywords are mapping for articular cartilage repair-related papers (PubMed). (b) Coauthorship mapping for articular cartilage-related papers (PubMed). (c) Keywords are mapping for articular cartilage repair-related papers (SCOPUS data). (d) Coauthorship mapping for articular cartilage-related papers (SCOPUS data). (e) Citation mapping for articular cartilage-related papers (SCOPUS data). (f) Cocitation mapping for articular cartilage-related papers (SCOPUS data). (g) Bibliographic coupling for articular cartilage-related papers (SCOPUS data). (h) Coauthorship among different countries for articular cartilage-related papers (SCOPUS data)

Table 2: Top ten most-cited articles in articular cartilage repair surgery in the last 10 years

Article	Authors	Journal	Citations (WoC) (citation density)	Citations (SCOPUS) (citation density)
Injectable *in situ* forming biodegradable chitosan-hyaluronic acid-based hydrogels for cartilage tissue engineering	Tan H, Chu CR, Payne KA, Marra KG.	Biomaterials 2009;30:2499-506	459 (51)	498 (55.33)
Clinical efficacy of the microfracture technique for articular cartilage repair in the knee an evidence-based systematic analysis	Mithoefer K, McAdams T, Williams RJ, Kreuz PC, Mandelbaum BR.	Am J Sports Med 2009;37:2053-63	393 (43.67)	443 (49.22)
Autologous chondrocyte implantation a long term followup	Peterson L, Vasiliadis HS, Brittberg M, Lindahl A.	Am J Sports Med 2010;38:1117-24	333 (41.62)	384 (48)
Regeneration of the articular surface of the rabbit synovial joint by cell homing: A proof of concept study	Lee CH, Cook JL, Mendelson A, Moioli EK, Yao H, Mao JJ.	Lancet 2010;376:440-8	323 (40.38)	356 (44.5)
Unlike bone, cartilage regeneration remains elusive	Huey DJ, Hu JC, Athanasiou KA	Science 2012;338:917-21	315 (52.5)	326 (54.33)
Supramolecular design of self-assembling nanofibers for cartilage regeneration	Shah RN, Shah NA, Lim MM, Hsieh C, Nuber G, Stupp SI.	Proceedings of the National Academy of Sciences; 2010	304 (38)	323 (40.38)
Treatment of symptomatic cartilage defects of the knee: Characterized chondrocyte implantation results in better clinical outcome at 36 months in a randomized trial compared to microfracture	Saris DB, Vanlauwe J, Victor J, Almqvist KF, Verdonk R, Bellemans J, Luyten FP.	Am J Sports Med 2009;37 1 Suppl: 10-9	251 (27.89)	323 (35.89)
Autologous bone marrow-derived mesenchymal stem cells versus autologous chondrocyte implantation: An observational cohort study	Nejadnik H, Hui JH, Feng Choong EP, Tai BC, Lee EH.	Am J Sports Med 2010;38:1110-6	278 (34.75)	313 (39.125)
Cartilage engineering: A crucial combination of cells, biomaterials, and biofactors	Vinatier C, Mrugala D, Jorgensen C, Guicheux J, Noël D.	Trends Biotechnol 2009;27:307-14	250 (27.78)	281 (31.22)
Treatment of osteochondral lesions of the talus: A systematic review	Zengerink M, Struijs PA, Tol JL, Van Dijk CN.	Knee Surg Sports Traumatol Arthrosc 2010;18:238-46	222 (27.75)	276 (34.5)

Top 10 papers

international researchers and clinicians who have been monumental in the evolution of cartilage surgery. It is also confirmed from several Bibliometric studies about the importance of international discovery and collaboration.[39-44]

We noticed that most papers in cartilage repair have come from the Hospital for Special Surgery (New York), closely followed by Rizzoli Orthopedic Institute (Bologna) and Harvard medical school (USA). Most universities or institutes contributing to cartilage-related work were located in the USA, followed by European countries. Again, it reflects relatively lesser quantum of research work related to cartilage repair being carried out in institutions located in other resource-poor settings.

The AJSM published most papers in cartilage repair, followed by KSSTA, Osteoarthritis and Cartilage, and Arthroscopy: The Journal of Arthroscopy and Related Surgery. All of these are relatively well-established and high-impact journals. We also see that most cartilage repair-related work gets published in subspecialty journals focusing on arthroscopy and sports medicine or cartilage itself, though a quite significant quantum of clinical research on cartilage repair gets published in general orthopedic journals such as Journal of Bone and Joint Surgery, Clinical Orthopedics and Related Research, and Injury. Basic science work in cartilage frequently gets published in basic science and bioengineering journals such as Tissue Engineering, Biomaterials, Journal of Orthopaedic Research, and Acta Biomaterialia.

It can be seen from basic science data that the overall majority of the work undertaken by the science community at present was to (a) investigate the outcome of enhanced tissue scaffolding to regenerate articular cartilage and (b) investigate the usage of mesenchymal stem cells to help regenerate articular cartilage.[38]

We observed that Cole BJ was the most published author, followed closely by Kon E (Italy), Marcacci M (Italy), Filardo G (Italy), and Niemeyer P (Germany). Key words, coauthorship, cocitation, and bibliographic coupling maps generated in VOSviewer [Figure 3a to 3h] revealed that a strong coauthor network of research scholars focusing on

cartilage repair existed. It, in turn, reflects robust research collaboration and knowledge sharing in different countries and institutions.

The most-cited paper on articular cartilage [Table 2], in the last 10 years, is by Tan *et al*.[52] It discusses injectable, biodegradable scaffolds for cartilage tissue engineering. Hydrogels derived from natural polysaccharides are considered ideal scaffolding as they resemble the extracellular matrix of tissues comprised of various glycosaminoglycans. Authors have reported a new class of biodegradable and biocompatible composite hydrogels made from water-soluble chitosan and oxidized hyaluronic acid on mixing, without adding any chemical crosslinking agent. The gelation occurs due to the Schiff base reaction between the amino and aldehyde groups of polysaccharide derivatives. N-succinyl-chitosan and aldehyde hyaluronic acid were synthesized for making composite hydrogels. The polysaccharide derivatives and composite hydrogels were characterized by Fourier-transform infrared spectroscopy. The effect of the ratio of N-succinyl-chitosan and aldehyde hyaluronic acid on the gelation time, surface morphology, microstructure, compressive modulus, equilibrium swelling, and *in vitro* degradation of composite hydrogels was examined. The potential of the composite hydrogel as an injectable scaffold was demonstrated by the encapsulation of bovine articular chondrocytes within the composite hydrogel matrix *in vitro*. Composite hydrogel supported cell survival and retention of chondrocytic morphology. Authors conclude that there is a potential opportunity to use the injectable, composite hydrogels in tissue engineering applications.

The second most-cited paper[53] is a systematic review of MFx for the treatment of knee articular cartilage injuries [Table 2]. Twenty eight studies involving 3,122 patients were included. Mean followup was 41 months, and five studies reported a followup of 5 years or more. The MFx improved functioning in all studies in the first 24 months, but these functional gains were not durable in longer term. Defect filling on magnetic resonance imaging varied a lot and correlated with functional outcomes. Gross cartilage quality predicted long term failure rate, but the value of histologic cartilage quality remained inconclusive. Thus, MFx provided useful short term functional improvement, but insufficient data were there on its long term results. The review is called for further better quality studies.

The third most-cited paper is a survey on ACI cases with long followup.[54] Lysholm, Tegner-Wallgren, Brittberg-Peterson, modified Cincinnati (Noyes), and KOOS score questionnaires were sent to 341 patients and 224 replied. Preoperative Lysholm, Tegner-Wallgren, and Brittberg-Peterson scores were retrieved from patients' files. Patients graded their status during the last 10 years as better, worse, or unchanged. They were also asked about the need for repeat surgery; 74% were better or the same as the previous years and 92% were satisfied and liked to have the ACI again. Average cartilage defect size was 5.3 cm^2. All scores had improved significantly. Bipolar lesions led to worse final outcome than multiple unipolar lesions. Meniscal injuries or prior bone marrow procedures did not affect the outcomes. Similarly, age at surgery or lesion size did not affect outcome. Authors conclude that clinical and functional outcomes of ACI remain high at 10–20 years.

Although there has been a significant and sustained increase in the research published on the ACR, we believe that there is still a sea of opportunity for further research and collaboration in ACR surgery. Highly specialized societies (e.g., International Cartilage Regeneration and Joint Preservation Society and Indian Cartilage society) dedicated to cartilage repair have come up in the last two decades.[55] Single-stage arthroscopic techniques of cartilage repair, tissue engineering techniques, including stem cells and biomimetic tissues, are likely to become the basis for the next generation of cartilage regeneration.[55,56]

Conclusion

There has been a marked and accelerated increase and a healthy trend in the research and publications in ACR in the recent past, with most publications coming from the USA and European countries. Not only there is an increasing trend in the number of publications but also the number of citations has seen a significant increase. ACR was seen as a hot topic in orthopedic surgical research in the last decade in our study, as indicated in earlier literature also.[57] The authors from globally recognized and leading clinical institutions in the developed world contributed maximally to these research and publications. Most of these papers were published in arthroscopy subspecialty journals, with high-impact factors. Citation and keyword maps were found to be useful tools in identifying the coauthor network of research scholars focusing on cartilage repair. It reflected robust research collaboration and knowledge sharing in different countries and institutions. Although there has been a significant and sustained increase in the research published on the ACR, we believe that there is still a sea of opportunity for further research and collaboration in ACR surgery. Tissue engineering techniques, three-dimensional printed artificial scaffoldings, stem cells, and biomimetic tissues are likely to become the basis for the next generation of cartilage regeneration.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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