SCIENTIFIC ARTICLE

Studies of Articular Cartilage Repair from 2009 to 2018: A Bibliometric Analysis of Articles

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Objective: To perform a bibliometric analysis of research on articular cartilage repair published in Chinese and English over the past decade. Fundamental and clinical research topics of high interest were further comparatively analyzed.

Methods: Relevant studies published from 1 January 2009 to 31 December 2018 (10 years) were retrieved from the Wanfang database (Chinese articles) and six databases, including MEDLINE, WOS, INSPEC, SCIELO, KJD, and RSCI on the website "Web of Science" (English articles), using key words: "articular cartilage" AND "injury" AND "repair". The articles were categorized according to research focuses for a comparative analysis between those published in Chinese *vs* English, and further grouped according to publication date (before and after 2014). A comparative analysis was performed on research focus to characterize the variation in research trends between two 5-year time spans. Moreover, articles were classified as basic and clinical research studies.

Results: Overall, 5762 articles were retrieved, including 2748 in domestic Chinese journals and 3014 in international English journals. A total of 4937 articles focused on the top 10 research topics, with the top 3 being stem cells (32.1%), tissue-engineered scaffold (22.8%), and molecular mechanisms (16.4%). Differences between the numbers of Chinese and English papers were observed for 3 topics: chondrocyte implantation (104 *vs* 316), osteochondral allograft (27 *vs* 86), and microfracture (127 *vs* 293). The following topics gained more research interest in the second 5-year time span compared with the first: microfracture, osteochondral allograft, osteochondral autograft, stem cells, and tissue-engineered scaffold. Articles with a focus on three-dimensional-printing technology have shown the fastest increase in publication numbers. Among 5613 research articles, basic research studies accounted for the majority (4429), with clinical studies described in only 1184 articles. The top 7 research topics of clinical studies were: chondrocyte implantation (28.7%), stem cells (21.9%), microfracture (19.2%), tissue scaffold (10.6%), osteochondral autograft (10.5%), osteochondral allograft (6.3%), and periosteal transplantation (2.8%).

Conclusion: Studies focused on stem cells and tissue-engineered scaffolds led the field of damaged articular cartilage repair. International researchers studied allograft-related implantation approaches more often than Chinese researchers. Traditional surgical techniques, such as microfracture and osteochondral transplantation, gained high research interest over the past decade.

Key words: Cartilage repair; Microfracture; Research trend; Scaffold; Stem cells

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Introduction

Articular cartilage has a cushioning function to relieve external impact and lubricate articulation. As an avascular tissue lacking blood vessels, nerves, and lymphatics, cartilage does not rely on the bloodstream to receive nutrients. Synovial fluid and subchondral bone are the two primary sources for nutrient supply for the cartilage, and, as such, are sensitive to lesions within cartilage. It is well-established that the repair of damaged cartilage is a difficult challenge clinically[1,2]. Rapid advances in tissue regeneration technologies, such as stem cell-based technologies[3,4], tissue-engineered scaffolds[5,6], and three-dimensional (3D) bioprinting[7,8], others, have been made in the past decade, owing to their potential to heal damaged articular cartilage. Traditional treatment methods, including microfracture[9,10,11], osteochondral transplantation[12,13,14], and chondrocyte implantation[15,16,17], can relieve pain and improve joint function. However, these methods are unable to fully prevent cartilage degeneration and restore the desired biomechanical properties of tissues[18,19].

A large number of research studies related to the repair of damaged articular cartilage has been published in past decades due to the huge clinical demand for such treatments. To date, few studies reporting a bibliometric analysis of this field have been published, while research focuses are as varied as the fast-growing biotechnologies. The aim of the present study was to perform bibliometric analysis of research articles published in Chinese and English in this field over the past decade (2009–2018) to better understand the research topics with high interest and their variation tendencies between the Chinese and international research communities.

Methods

The resources for literature retrieval included the Wanfang database for Chinese articles and Web of Science for English articles. To find research papers related to damaged cartilage repair, we used the following topic words to search the Chinese and English literature: "articular cartilage" AND "injury" AND "repair". Relevant English articles were collected from six databases: MEDLINE, WOS, INSPEC, SCIELO, KJD, and RSCI on the website "Web of Science." We set the publication date range from 1 January 2009 to 31 December 2018 (10-year time span). Article types included: research papers, reviews, and published conference papers. Only abstracted literature, newspaper articles, and patents were excluded.

Comparative Analysis of Articles Published by Chinese and International Investigators

The publication metrics for papers published by Chinese researchers and investigators from all other countries included the total number of published articles and the annual numbers of published articles.

Comparative Analysis of Research Focuses of Chinese and International Investigators

We summarized the research focuses on damaged cartilage repair by counting the number of relevant publications in Chinese and English journals. Published articles on each research focus were further separated according to publication date (i.e. before and after 2014). Comparative analyses of the numbers of published articles between two 5-year time spans were performed to shed light on the variation tendencies of research interests.

Bibliometric Analysis of Basic and Clinical Studies

To understand the status of the transformation from basic research to clinical application of cartilage injury repair, all published papers were classified as basic or clinical research studies. The bibliometric analysis included the total numbers and annual numbers of both types of published articles. A comparative analysis between Chinese and English articles focused on basic and clinical aspects was further conducted.

Results

Analysis of the Total and Annual Publication Amounts

A total of 5762 articles were selected from the databases. English articles accounted for 59% (3397/5762), and the remaining 41% of articles were published in Chinese (2365/5762). The peak number of related publications was 649 in 2015, and the total article number increased from 467 in 2009 to 581 in 2018 (Fig. 1A, Table 1). The number of Chinese papers increased from 197 in 2009 to 299 in 2015 and then declined to 165 by the end of 2018 (Fig. 1A, Table 1). The English article numbers started at 270 in 2009 and reached 417 in 2017 and 416 in 2018 (Fig. 1A, Table 1).

English articles for which the first author's affiliation was a Chinese institute accounted for 11.4% (383) over the past decade. The number of these articles increased from 13 in 2009 to 81 in 2018 (Fig. 1A, Table 1). We recalculated the Chinese publication number to include these English articles. From the new calculation, the total number of Chinese publications was 2748 (47.7%), while the number of English publications from researchers in other countries was 3014 (52.3%) (Fig. 1B). Roughly equal numbers of Chinese and foreign articles were published from 2012 to 2016. The amount of foreign publications was higher during the last 2 years, with 364 in 2017 and 335 in 2018, whereas the number of Chinese publications showed a downward trend during the same period, with 259 in 2017 and 246 in 2018 (Fig. 1B).

Research Topic-Based Bibliometric Analysis

We summarized the top 10 research topics studied in 4937 articles as follows: pathogenesis, gene therapy, 3D printing, tissue scaffold, stem cells, chondrocyte implantation, osteochondral allograft, osteochondral autograft, periosteal transplantation, and microfracture. The top 3 research topics based on publication number over the past decade were:

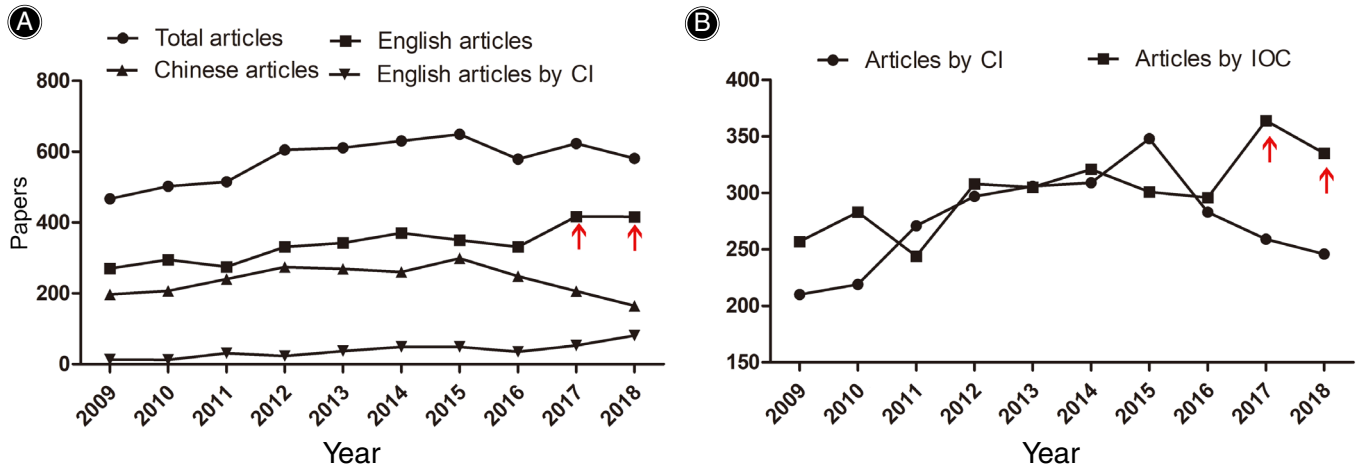

Fig 1 Annual numbers of Chinese and English research articles. (A) Annual number of related research articles, Chinese articles, English articles, and English articles published by researchers at Chinese institutions. English research articles published in 2017 and 2018 are denoted by red arrows. (B) The annual numbers of research articles published by researchers in China and other countries. Research articles published by researchers in countries other than China in 2017 and 2018 are denoted by red arrows. CI, Chinese institutions; IOC, institutions outside China.

TABLE 1 Annual numbers of published research articles in the field of cartilage repair

Items	Year										Total
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	
Annual total number	467	502	515	605	611	630	649	579	623	581	5762
Chinese articles	197	207	240	274	269	260	299	248	206	165	2365
English articles	270	295	275	331	342	370	350	331	417	416	3397
English articles authored by researchers in China	13	12	31	23	37	49	49	35	53	81	383

stem cells, with 1586 (32.1%); tissue scaffold, with 1129 (22.8%); and molecular mechanisms, with 810 (16.4%). Overall, studies on these 3 topics accounted for 71.3% of articles related to damaged cartilage repair (Fig. 2A, Table 2). The publication number related to the 3D printing was the smallest among the 10 topics, with only 48 (1.0%) articles.

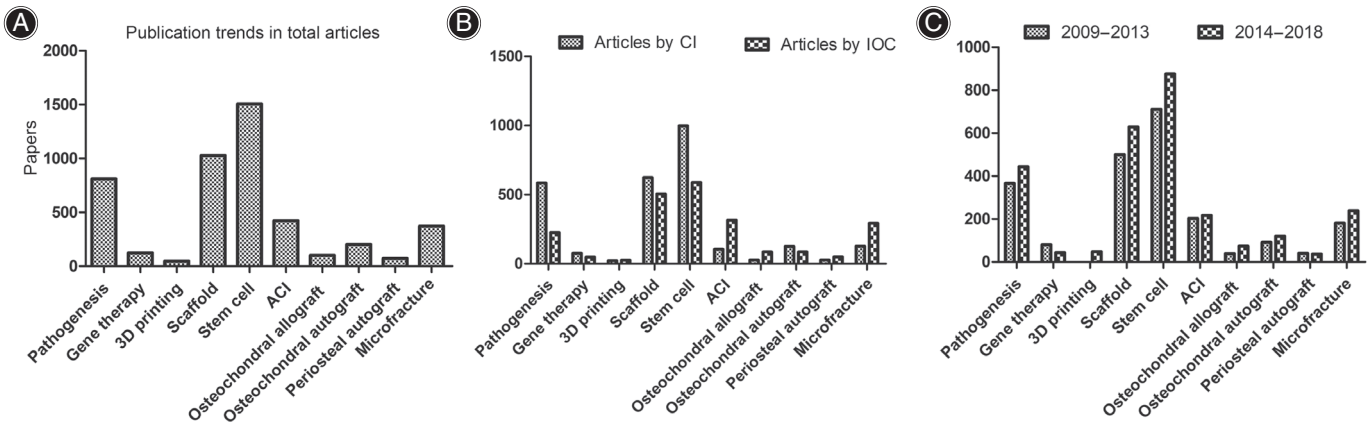

Fig 2 Numbers of articles in each topic cluster over the past decade. (A) Bar chart showing publication numbers for each research topic. (B) Numbers of articles on each topic published by researchers in China and elsewhere. (C) Numbers of articles published on each topic during the two 5-year time spans. CI, Chinese institutions; IOC, institutions outside China.

TABLE 2 Numbers of published articles according to the most published topics

Items	SCT	Scaffold	Pathogenesis	ACI	MR	Auto-OC	GT	Allo-OC	Auto-P	3D-P
Publications from CI	998	623	584	104	127	125	76	27	27	22
Publications from IOC	588	506	226	316	293	86	48	86	49	26
Total	1586	1129	810	420	420	211	124	113	76	48

ACI, autologous chondrocyte implantation; Allo-OC, osteochondral allograft; Auto-OC, osteochondral autograft; Auto-P, periosteal autograft; CI, Chinese institutions; GT, gene therapy; IOC, institutions outside China; MR, micro-fracture; SCT, stem cell therapy; 3D-P, 3D printing.

We separately performed bibliometric analysis of Chinese and English papers. The top three research topics among Chinese articles were the same as those described above, including stem cells, scaffolds, and molecular mechanisms. Research articles related to the three topics accounted for 81.4% of all collected Chinese papers (Fig. 2B, Table 2). The top five research topics based on publication number among the published English articles were: stem cells, with 588 (26.4%); tissue scaffold, with 506 (22.8%); chondrocyte implantation, with 316 (14.2%); microfracture, with 293 (13.0%); and molecular mechanisms, with 226 (10.2%) (Fig. 2B, Table 2). As shown in Fig. 2B, the following research topics showed considerable discrepancy in terms of publication between the Chinese and English articles: chondrocyte implantation (104 *vs* 316), osteochondral allograft (27 *vs* 86), and microfracture (127 *vs* 293).

We divided all articles into two groups in terms of the publication date: before and after 2014. As shown in Fig. 2C, 2211 of 4937 papers were published in the first period, 2009–2013, and the remaining 2726 papers were published in the second period, 2014–2018. Two research topics, chondrocyte implantation and periosteal transplantation, accounted for roughly the same publication numbers in the two periods, 200 and 40 for each topic. Published articles covering five research topics, microfracture, osteochondral allograft, osteochondral autograft, stem cells, and tissue scaffold, showed a sharp rise in the second period compared with the first period. 3D printing was a major new research topic, with 48 papers published in the second period.

Comparative Statistical Analysis of Basic and Clinical Studies

A total of 5613 research articles were divided into two groups: basic and clinical research studies. Articles presenting basic research accounted for 78.9% (4429/5613), and clinical research studies accounted for the other 21.1% (1184/5613; Fig. 3B). An approximately equal number of basic research articles were published in Chinese (2257) and

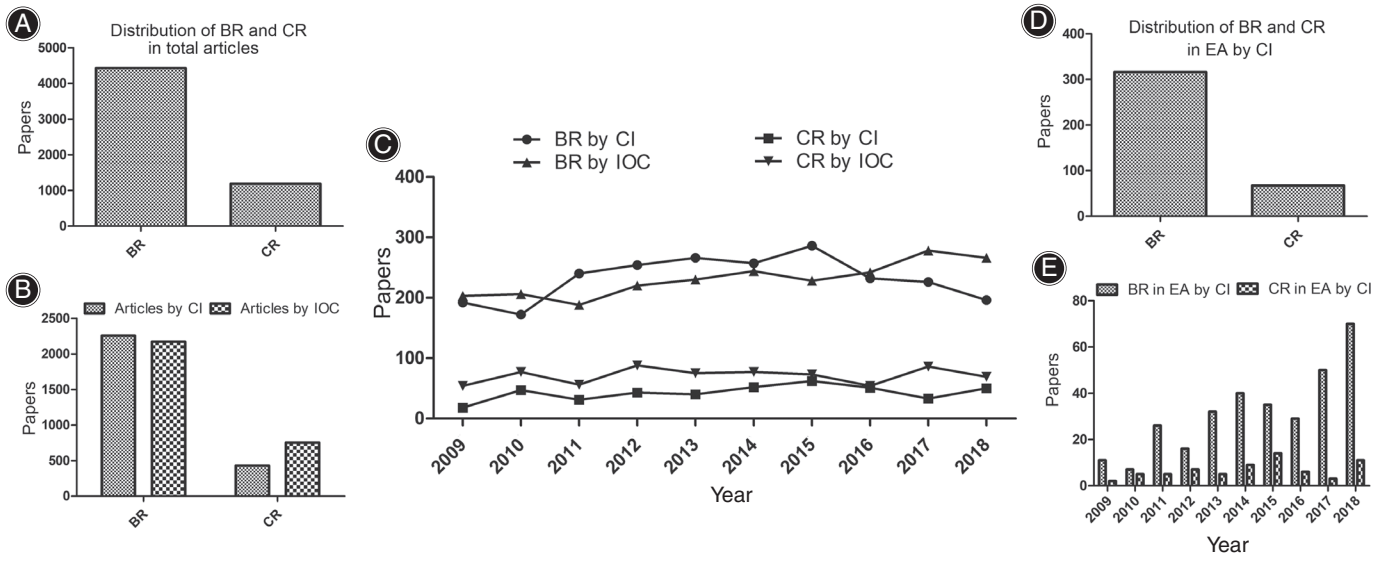

Fig 3 Distribution of basic and clinical research articles. (A) Published article numbers on basic and clinical research over the past decade. (B) Article numbers published by researchers in China and elsewhere in fundamental and clinical areas. (C) Annual article numbers published by researchers in China and elsewhere in fundamental and clinical areas. (D) The total number of English articles describing basic and clinical research studies published by authors from Chinese institutions. (E) Annual numbers of English articles published by researchers in China in fundamental and clinical areas. BR, basic research; CI, Chinese institutions; CR, clinical research; IOC, institutions outside China; EA, English articles.

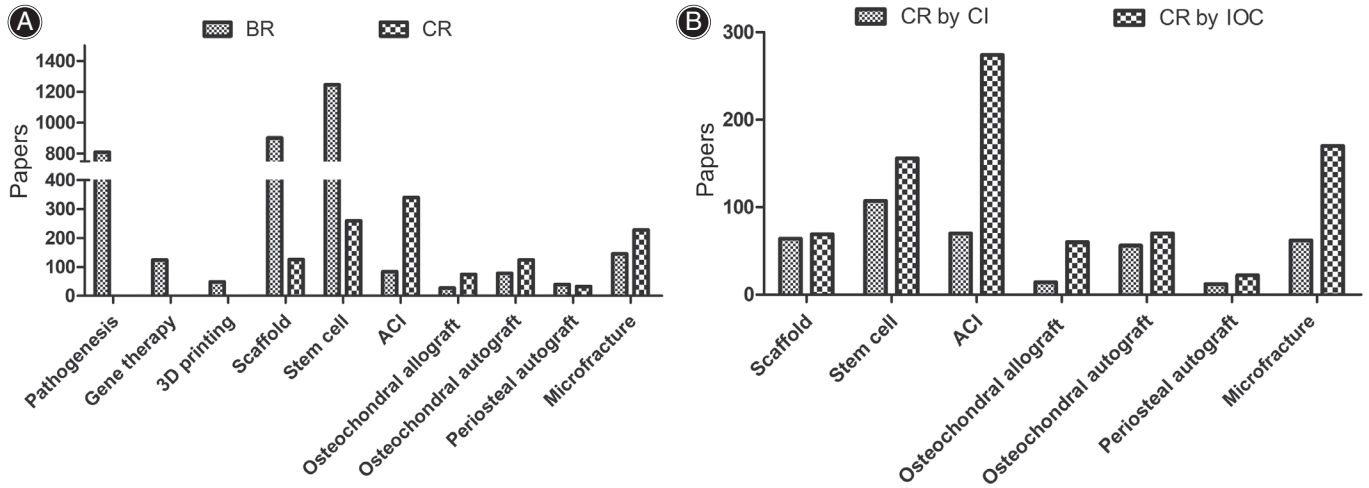

Fig 4 Analysis of basic and clinical research studies on each topic. (A) The total numbers of published articles presenting basic and clinical research in each topic. (B) The numbers of published articles on clinical research in each topic published by researchers in China and elsewhere. BR, basic research; CI, Chinese institutions; CR, clinical research; IOC, institutions outside China.

English (2172), whereas English articles presenting clinical studies far outnumbered Chinese articles (754 *vs* 430). The annual numbers of English articles presenting clinical studies over the past decade varied from 54 to 88 (19.4% to 28.4% of all English articles), and the corresponding metrics for Chinese articles were 18 to 62 and 19.4% to 28.4% (Fig. 3C). A total of 383 English articles had first authors whose affiliations were Chinese institutes. Basic research studies accounted for 82.5% (316) in these articles, and clinical studies accounted for 17.5% (67; Fig. 3D). The annual numbers of clinical papers authored by Chinese researchers over the past decade ranged from 2 to 14 (5.7% to 30.4%; Fig. 3E).

No clinical research articles focused on the topics of molecular mechanisms, gene therapy, and 3D printing technology. Basic research studies concerning the topics of tissue scaffold and stem cells accounted for 87.7% and 82.8% of the total amounts of articles on each topic (Fig. 4A, Table 3). The top seven most common topics of clinical articles and their percentages among the total number of clinical articles over the past decade were: chondrocyte implantation (340, 28.7%); stem cells (259, 21.9%); microfracture (228, 19.2%); tissue scaffold (126, 10.6%); osteochondral autograft (124, 10.5%); osteochondral allograft (74, 6.3%) and; periosteum transplantation (33, 2.8%) (Fig. 4A, Table 3). The topics of chondrocyte implantation, microfracture, osteochondral autograft, and osteochondral allograft were covered by many more clinical studies than basic research studies (Table 1). Chinese authors published 198 clinical research studies on those topics, while authors in all other countries published 568 studies (Table 3).

Researchers in countries other than China published 24 clinical research articles on chondrocyte implantation in 2009. The annual number of corresponding articles showed slight increases in the subsequent 3 years, reaching 39 in 2012 before dropping to 18 by 2018. The annual average number of fundamental research articles on the theme published by authors outside of China was 10 over the past decade, while the average number was 5 for both corresponding clinical and basic research studies published by Chinese authors (Fig. 5A). Figure 5B illustrates

TABLE 3 Basic and clinical research studies regarding articular cartilage repair

Study type		ACI	SCT	MR	Scaffold	Auto-OC	Allo-OC	Auto-P
Basic	CI	41	814	51	462	65	10	12
	IOC	42	432	94	440	13	17	27
	Total	83	1246	145	902	78	27	39
Clinical	CI	70	103	60	60	54	14	11
	IOC	270	156	168	66	70	60	22
	Total	340	259	228	126	124	74	33

ACI, autologous chondrocyte implantation; Allo-OC, osteochondral allograft; Auto-OC, osteochondral autograft; Auto-P, periosteal autograft; CI, Chinese institutions; IOC, institutions outside China; SC, stem cell therapy; MR, micro-fracture.

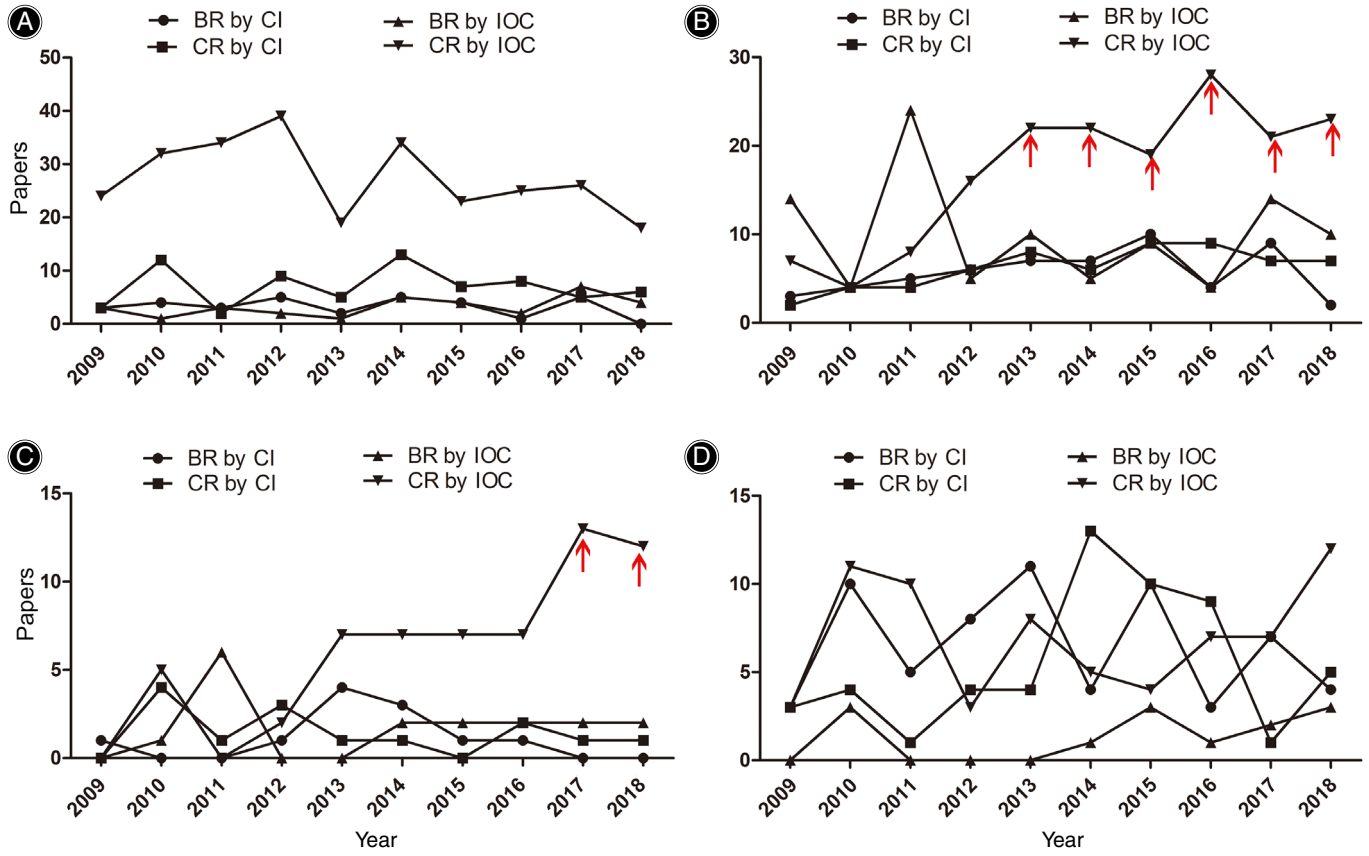

Fig 5 Annual numbers of published articles on basic and clinical research related to the following topics: (A) Chondrocyte implantation; (B) microfracture; (C) osteochondral allografting; and (D) osteochondral autografting. Significant increases in the number of clinical articles published by researchers outside of China are denoted by red arrows. BR, basic research; CI, Chinese institutions; CR, clinical research; IOC, institutions outside China.

the increased tendency of microfracture-related clinical studies performed outside of China. Over 20 papers per year were published since 2013 (peak number 26 in 2016). By contrast, the annual numbers of corresponding articles published by Chinese researchers remained fewer than 10 in the past decade (Table 4). The annual numbers of English clinical articles related to osteochondral allografting published by researchers in countries other

TABLE 4 Annual numbers of clinical research articles addressing cartilage repair

Study topics		Year										Total
		2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	
ACI	CI	3	12	2	9	5	13	7	8	5	6	70
	IOC	24.	32	34	39	19	34	23	25	26	18	274
MR	CI	2.	4	4	6	8	6	9	9	7	7	62
	IOC	7	4	8	16	22	22	19	28	21	23	170
Allo-OC	CI	0	4	1	3	1	1	0	2	1	1	14
	IOC	0	5	0	2	7	7	7	7	13	12	60
Auto-OC	CI	3	4	1	4	4	13	10	9	1	5	56
	IOC	3	11	10	3	8	5	4	7	7	12	70

ACI, autologous chondrocyte implantation; Allo-OC, osteochondral allograft; Auto-OC, osteochondral autograft; CI, Chinese institutions; IOC, institutions outside China; MR, micro-fracture.

than China increased from single digits to double digits in the past decade, with 13 in 2017 and 12 in 2018, while no more than 2 papers per year were published by Chinese researchers since 2013 (Fig. 5C, Table 4). However, the same numbers of basic and clinical research articles on osteochondral autografting were published by researchers in China and elsewhere during the past decade (Fig. 5D, Table 4).

Discussion

Research related to damaged articular cartilage repair has gained increased interest over the past decade[20,21,22]. The statistical analysis presented in the present study demonstrated an increasing trend in published articles in this field over the past 10 years. The percentage of Chinese articles among all published articles approached 50%, suggesting significant attention to this research. An increasing number of English research papers, accounting for over 10% of all retrieved articles, were published by researchers in China. The annual number of those papers in 2018 was 6-fold greater than that in 2009.

Tissue engineering technology has been one of the top research focuses in the field of articular cartilage repair[23]. Stem cells and tissue scaffold were two subtopics occupying the primary portion of the overall publication numbers in the field of cartilage repair[24,25]. The research topic of stem cells topped all topics, accounting for nearly one-third of all published articles. The topic was also dominant among both Chinese and English papers. Significant progress has been achieved in studies of mesenchymal stem cells[26,27,28], adipose-derived stem cells[29], and other stem cell types for articular cartilage repair. A tissue-engineered scaffold serves as an extracellular matrix for the formation of new tissues[30,31]. The research articles related to tissue-engineered scaffolds were second only to stem cell-based articles. Over one-fifth of Chinese and English research articles published over the past decade have addressed the tissue scaffold topic. Importantly, more research articles regarding the topics of stem cells and tissue scaffolds were published in the second period (2014–2018) than in the first period (2009–2013), suggesting increasing trends for those research topics. A 3D printed tissue scaffold was an emerging research topic that appeared in 2014 and quickly became one of the most popular research focuses, as per its rapid increase in terms of publication number[32,33].

Although there are many published studies on tissue engineering cartilage, the cartilage lesions remain a challenging clinical practice due to the limited intrinsic healing capacity of the cartilage tissue. Moreover, microfracture is still considered the first-line treatment for the chondral defects, and it shows good short-term results[34,35]. Similarly, in the past decade, a growing interest in microfracture-related studies has been observed[36–38], and clinical studies have accounted for the major portion.

Osteochondral transplantation is required for chondral defects greater than 2 cm[239,40]. The results of a meta-analysis showed that osteochondral autograft transplantation had significantly more excellent or good results compared to microfracture. Osteochondral autograft transplantation provided higher quality repair of tissue and had lower failure and higher return-to-activity rates. Microfracture had significantly more poor results than autologous chondrocyte implantation[41]. Studies on these implantation techniques were always present in the list of top research topics, such as autologous chondrocyte implantation (ACI), and periosteum and osteochondral transplantation. Clinical studies exceeded the basic research counterparts among those investigating osteochondral transplantation. There were approximately equal numbers of articles published on osteochondral autografting from within and outside China.

Due to the surgical complications and paucity of donor sites for autografts, researchers in countries other than China have been focused more on the topic of osteochondral allografting and have contributed triple the number of published studies compared with researchers in China[42-44]. Fresh osteochondral allograft transplantation is a treatment option for large posttraumatic osteochondral defects in young high-demand patients[45]. A systematic review of clinical outcomes and failure rates after osteochondral allograft transplantation of the patellofemoral joint revealed 5-year and 10-year survival rates of 87.9% and 77.2%, respectively, and improved patient-reported outcome measures with high patient satisfaction rates[46].

In conclusion, research focused on stem cells and tissue-engineered scaffolds led the field of damaged articular cartilage repair. We observed a significant increase in the number of English publications from investigators in China over the 10-year study period. Two traditional surgical techniques, microfracture and osteochondral transplantation, continued to receive considerable attention from researchers. Researchers outside China were more keen to study allograft-related implantation strategies than were researchers in China.

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