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Original Article

A bibliometric analysis study of blood flow restriction using CiteSpace

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Abstract. [Purpose] To assess the current state-of-the-art and the prevailing trends regarding the global use of blood flow restriction (BFR) in the past 20 years. [Participants and Methods] We retrieved literature relating to BFR from 1999 to 2020 using Web of Science. We conducted a bibliometric analysis of countries/institutions, cited journals, authors/cited authors, cited references, and keywords using CiteSpace. An analysis of counts and centrality was used to examine publication output, countries/institutions, core journals, active authors, foundation references, hot topics, and frontiers. [Results] Seven hundred seventy five references were included and the total number of publications has been continually increasing over the investigated period. Representatives of important academic groups are the Japanese scholars from the University of Tokyo as represented by Takashi Abe. Jeremy Paul Loenneke's article (centrality: 0.15) was the most representative and symbolic reference with the highest centrality. The three topics identified were intervention (intensity resistance exercise, IRE), physiology (ischemia and muscular function) and behavior (adaptation and increase). The four frontier topics were phosphorylation, reduction, low intensity and arterial occlusion. [Conclusion] This study provides an insight into BFR and offers valuable information for BFR researchers to identify new perspectives for potential cooperation with collaborators and their related cooperative institutions.

Key words: Blood flow restriction, Bibliometric analysis, CiteSpace

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INTRODUCTION

Blood flow restricted training (blood flow restricted training, BFRT) is the activity of placing a narrow compressive cuff around an appendicular limb, and inflating the cuff during exercise[1)]. Low intensity resistance exercise (low intensity resistance exercise, LIRE) combined with blood flow restriction (BFR) consistently demonstrates favorable training adaptations, shown by improved muscle strength and an increased cross-sectional area of the quadriceps[2, 3)]. Gains from training combined with BFR in leg extension muscle strength (up to 20–30%) and quadriceps size (up to 6–8%) are comparable to those induced by traditional moderate-to-high-load training, albeit using substantially lighter loads[4)]. Previous studies have reported that muscle hypertrophy and increased strength following BFR is due to its ability to augment the endocrine response as compared to LIRE without BFR[1, 5)]. Fujita and Yasuda reported that muscle protein synthesis and ribosomal S6 kinase 1 (S6K1) phosphorylation were found to be increased after a single bout of BFR+LIRE[6)]. These acute changes in the transcription associated with muscle hypertrophy may be explained by the up-regulation of hypertrophy-associated genes including phosphoinositide 3-kinase (PI3 K), protein kinase B (AKT), and mammalian target of rapamycin complex (mam-

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malian target of rapamycin complex, mTOR)[7]. From a mechanistic standpoint, it has been hypothesized that an ischemic and hypoxic muscular environment is generated during BFR to induce high levels of metabolic stress alongside mechanical tension when BFR is used in tandem with exercise. Both metabolic stress and mechanical tension have been described as 'primary hypertrophy factors'[8] and are theorized to activate other mechanisms for the induction of muscle growth[9]. In all, these proposed mechanisms include: elevated systemic hormone production[10, 11], cell swelling[12], production of reactive oxygen species (ROS)[13, 14], intramuscular anabolic/anti-catabolic signaling[15–17] and increased fast-twitch fiber recruitment[6, 18, 19]. This observation suggests that further exploration into BFR is required.

Bibliometrics is a statistical analysis and quantitative tool to evaluate the scientific literature surrounding a scientific domain. Bibliometric methods have been applied in many research fields to evaluate patterns by country, institution, journal, author, and keywords associated with specific publication types[20]. The CiteSpace software we use was invented in early 2004 by Professor Chaomei Chen, and is characterized by cooccurrence network maps of authors, keywords, institutions, countries, and subject categories and cocitation networks of cited authors, cited references, and cited journals[21, 22].

This study will primarily analyze the research environment and scientific trends that concern the global use of BFR within the past 20 years. CiteSpace was used to perform a bibliometric analysis of related references derived from the Web of Science Core Collection (WOSCC).

PARTICIPANTS AND METHODS

The literature was retrieved from the core collection database of the WOSCC. The data retrieval strategy is as follows: (TS="blood flow-restricted" OR TS="blood flow restriction" OR TS="vascular occlusion" OR TS=kaatsu AND TS="exercise" OR TS="training" OR TS="strength training") AND type of literature is (Article OR Review). Time span was set to be from 1999–2020 (retrieved date September 30, 2020). A total of 1,041 references were obtained; 786 reviews and papers were kept after electronic screening by Citespace excluding 18 letters, 8 collection notices, 22 edited materials and 207 meeting abstracts. Eleven references were excluded due to unknown year of publication and finally, 775 related studies were included for analysis.

The Citespace 5.6 R5 visualization software (Drexel University, Philadelphia, PA, USA) based on the Java platform was used to draw the atlas of scientific knowledge in this paper. The most prominent points of interest can be verified through consultation of the prevailing literature or with experts in the field. Through a series of generated visual knowledge maps, CiteSpace explores the research status, research hotspots, evolution process and discipline structure of a scientific field so as to be able to easily understand the research direction of different institutions and authors. It also allows us to be able to analyse historical literature on the subject and related research based on prior analysis[23]. CiteSpace is widely used in more than sixty fields, including computer science, information science and medicine to identify recent scientific research[24, 25]. This paper uses CiteSpace 5.6, which is relatively stable and new at present, as our data analysis research tool to conduct a scientometric analysis in the field of BFR. Analysis of the changes in research interest in this field by studying the trend of publication volume was performed. Analysis of the academic groups was performed by examining country of origin, regional distributions and high yield authors. Basic knowledge, research history, research hotspots and frontiers by analyzing literature co-citation, related disciplines, key words and burst words were examined.

Two evaluators (Xuemei ZHAO and Yue ZHANG) read the literature independently. First, preliminary screening was carried out according to the title and abstract of the article. Further screening was carried out again according to the inclusion and exclusion criteria. After the screening was concluded, in the case of any disputes, a third evaluator (Yi ZHOU) read the whole paper, discussed it together with the other two evaluators and made a decision on whether or not to reject it.

The records were extracted by date, and references were converted into plain text with the name "download_XXX" (XXX being the importing date) and imported into Citespace. The adjustment parameters in CiteSpace were as follows: time slicing (1999–2020), years per slice (1), term source (all selection), node type (choose one at a time), pruning (pathfinder), and visualization (cluster view-static, show merged network), link retaining factor, look back year.

RESULTS

The first study of BFR was published in the *Journal of Applied Physiology* in 1999, and discussed the effect of leg blood flow restriction on heart rate during exercise in patients with spinal cord injuries. As shown in Fig. 1, the volume of published articles in this field was sparse during the period of 1999 to 2009 and increased significantly from 2010 to 2014, and then increased sharply during the period of 2015 to 2019. From January 2020 to September 2020, 88 relevant papers and reviews were published. More than 50 articles in this filed have been published each year since 2015, indicating that more researchers are beginning to pay attention to the impact of BFR.

The size of the node circle indicates the numbers of articles published in the relevant field by country. The number and thickness of the link is proportional to the cooperation between countries, and the color of the connection indicates the time when cooperation was started. A node with a purple-red color indicates that a country has strong centrality, and centrality reflects the importance of the node in the network[21].

By generating a country map using CiteSpace (Fig. 2), we are able to examine the countries important to the field. A total of 28 countries have participated in blood flow restriction studies. The top ten countries that co-published papers accounted for nearly 87.25% of the total published documents (Table 1). The top three countries are United States, Japan, and Brazil. The node centralities of the United States, Britain, Canada and Japan are relatively high. Although cooperative publication volume of Brazil is far ahead of Australia and Canada, its centrality is low, indicating a lack of influence in this field. The node circle in the United States is significantly larger than that of other countries. The fact that 320 references were published in the United States suggests that they are the one of the most active countries in the field.

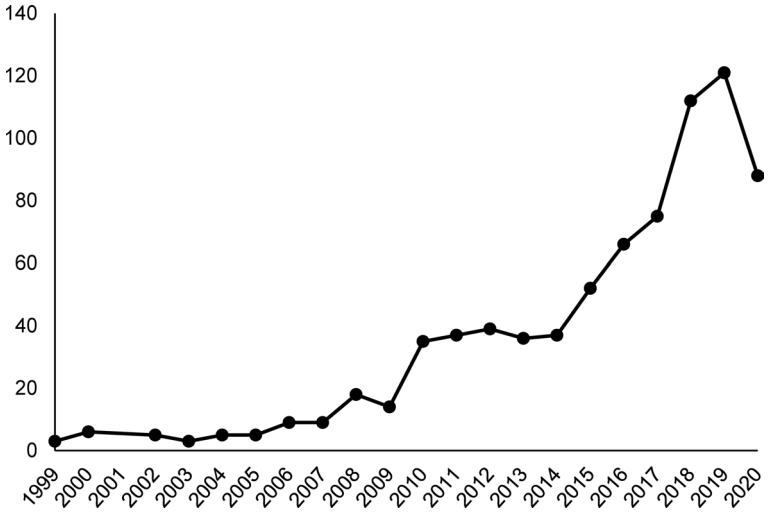

Fig. 1. The number of blood flow restriction (BFR) publications indexed by Web of Science Core Collection (WOSCC) from 1999 to 2016.

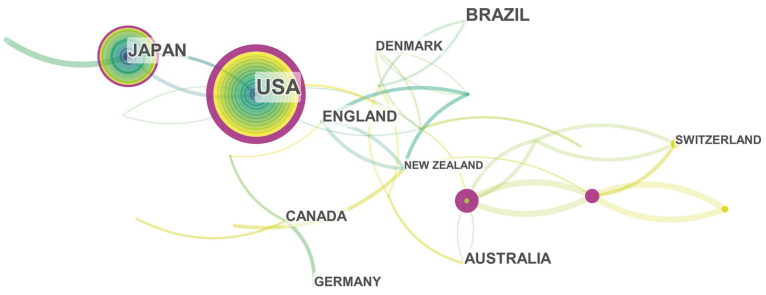

Fig. 2. Map of countries researching blood flow restriction (BFR).

Table 1. Top 10 prolific countries of BFR

Ranking	Country	Publications	Centrality
1	USA	320	0.53
2	Japan	120	0.14
3	Brazil	112	0.02
4	Australia	59	0.11
5	England	54	0.2
6	Canada	39	0.16
7	Denmark	32	0.03
8	Germany	30	0.03
9	Switzerland	20	0.1
10	New Zealand	15	0.04

BFR: blood flow restriction.

Knowledge maps can provide information on the influential research groups, institutions and the content of published articles; this information can help researchers to establish collaborations. We generated an author co-citation map (Fig. 3). Each node represents an author, and the circles of the same color represent the same clusters. The larger the circle corresponds to a larger volume of references. The connection between the nodes indicates the strength of cooperation between scholars. Thicker connections indicate a closer relationship. The color of the line represents the time of the establishment of cooperation. The top five active authors are Takashi, Jeremy, Michael, Scott and J Grant. Table 2 shows the top ten authors who have published articles related to BFR. They are active and professional authors in this field. The most active academic research group are from Japan and America. Representatives of important academic groups included American scholars from the University of Oklahoma represented by Jeremy P Loennek and Michael G Bemben, as well as the University of Mississippi represented by Scott J Dankel and Samuel L Buckner; Japanese scholars from the University of Tokyo are represented by Takashi Abe and Tomohiro Yasuda. The key words identified in the papers from the above-mentioned academic groups primarily included relative pressure, low-restricted exercise, ischemic exercise, and the key words involved in other academic research groups included anterior cruciate ligament, muscle contraction, fibrinolysis, etc.

Cocited references refer to documents that have the same research content and references. The analysis of cocited references is a correlation analysis of cocited documents. In the document co-citation knowledge graph (Fig. 4), the larger the node is, the more the citation numbers are. The circle on the node indicates a strong burst, and the purple ring outside the node is the key reference. Table 3 shows the result of our analysis by examining main clusters, key words in the cluster and important references[1, 9, 26–30]. Table 4 shows detailed information of classic references with strong burst and that are highly cited[1, 9, 12, 16, 17, 27–29, 31, 32]. It is helpful to understand the formation of hotspots and the evolution of BFR research through the analysis of cocited references in the above documents, and by tracking the research of highly cited and strong burst documents.

Key node 1 is an article published in the *Journal of Strength and Conditioning Research* by Felipe C. Vechin in 2015, titled *Comparisons between low-intensity resistance training with blood flow restriction and high-intensity resistance training on quadriceps muscle mass and strength in elderly*[30]. The burst and centrality of this article are 8.84 and 0.7 respectively and it belongs to cluster 6 with key words including physical function, vascular resistance and surface EMG. The purpose of this article is to compare the effects of high-intensity resistance training (high-intensity resistance training, HRT) and

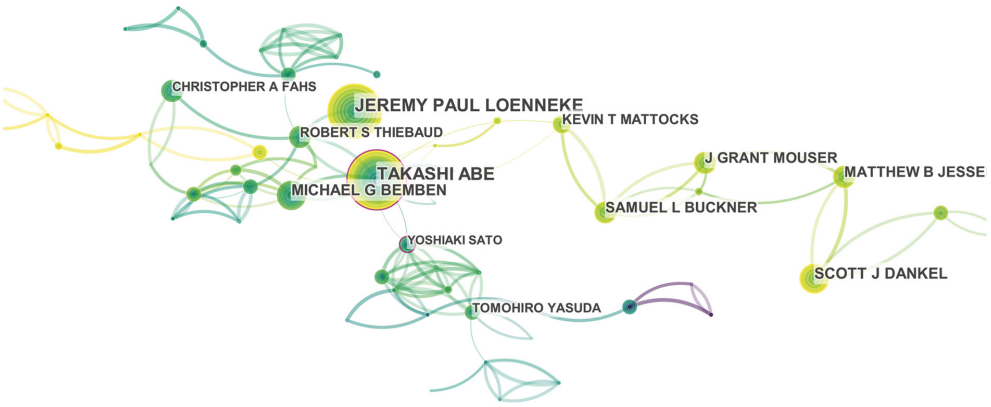

Fig. 3. Authors map related to blood flow restriction (BFR).

Table 2. Top 10 active authors

Authors	Cocitation counts	Institution	Centrality	Country
Takashi Abe	89	The University of Tokyo	0.13	Japan
Jeremy Paul Loenneke	81	The University of Oklahoma	0.15	USA
Michael G Bemben	44	The University of Oklahoma	0.04	USA
Scott J Dankel	43	The University of Mississippi	0	USA
J Grant Mouser	35	The University of Oklahoma	0	USA
Samuel L Buckner	35	The University of Mississippi	0	USA
Matthew B Jessee	34	The University of Mississippi	0	USA
Kevin T Mattocks	31	The University of Mississippi	0	USA
Robert A Thiebaud	28	The University of Oklahoma	0	USA
Tomohiro Yasuda	25	The University of Tokyo	0.04	Japan

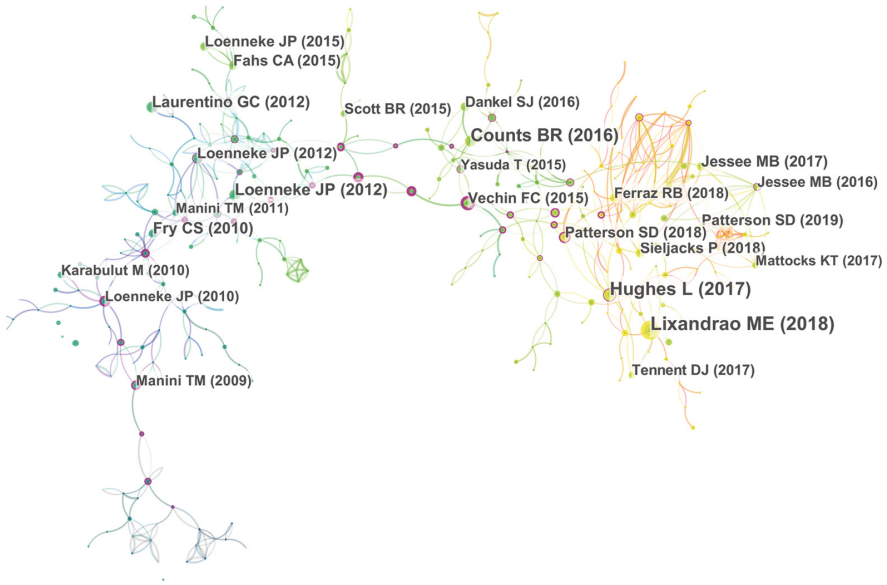

Fig. 4. References cocitation map related to blood flow restriction (BFR).

Table 3. Main clusters, key words and important reference in the cluster

Clusters number	Counts	Key words	Important reference	Author	Publication year
0	42	Vascular occlusion; mitochondria; arterial stiffness; pulse wave analysis	Body position influences arterial occlusion pressure: implications for the standardization of pressure during blood flow restricted exercise[26]	Peter Sieljacks	2018
1	34	Kaatsu; muscle soreness; maximal voluntary contraction	Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise[27]	Jeremy P. Loenneke	2012
2	33	Altitude; high-intensity exercise; blood flow occlusion; blood volume	Influence of relative blood flow restriction pressure on muscle activation and muscle adaptation[28]	Brittany R. Counts	2016
3	32	Ischemia; protein metabolism; muscle oxygenation; somatotropin; plasma noradrenaline	Cross-transfer effects of resistance training with blood flow restriction[29]	Haruhiko Madarame	2008
4	28	Vascular conductance; muscle oxygen kinetics; arterial compliance	Blood flow restricted exercise and skeletal muscle health[1]	Todd M. Manini	2009
5	28	Rehabilitation; blood flow restriction exercise; handgrip strength; mobility	Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis[9]	Luke Hughes	2017
6	22	Aging-water exercise; physical function; vascular resistance; surface EMG	Comparisons between low-intensity resistance training with blood flow restriction and high-intensity resistance training on quadriceps muscle mass and strength in elderly[30]	Felipe C Vechin	2015

low-intensity resistance training combined with BFR (low-intensity resistance training combined with BFR, LRT-BFR) on the quadriceps muscles strength and mass in elderly. Twenty three elderly individuals including 14 males and 9 females were subject to 12 weeks of training. It was the first study that provides data that suggests that LRT-BFR constitutes an important surrogate approach to HRT as an effective training method to induce gains in muscle strength and muscle mass in the elderly.

Key node 2 is an article published in the *Journal of Strength and Conditioning Research* by Paul E. Luebbers in 2014, titled *The effects of a 7-week practical blood flow restriction program on well-trained collegiate athletes*[33]. The burst and centrality of this article are 4.45 and 0.6 respectively and it belongs to the same cluster as key node 1. The purpose of this

study was to examine the effects of a 7-week practical BFR protocol used in conjunction with a strength training program on measures of muscular strength and size in collegiate American football players. The results suggest that a practical BFR program used in addition to a traditional strength training program can be effective at increasing 1 repetition maximum (repetition maximum, RM) squat performance.

Related disciplines analysis refers to a comprehensive analysis of the disciplines in the field. As shown as Fig. 5 and Table 5, analysis of centrality show that the top five disciplines were "RESEARCH & EXPERIMENTAL MEDICINE",

Table 4. Top 10 cocited references in BFR in terms of burst

Author	Burst	Centrality	Cited frequency	Important reference	Journal	Publication year	Country
Luke Hughes[9]	18.7	0.15	43	Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic reviewand meta-analysis	Br J Sports Med	2017	UK
Manoel E. Lixandrao[31]	17.33	0.09	54	Magnitude of muscle strength and mass adaptations between high-load resistance training versus low-load resistance training associated with blood-flow restriction: a systematic review and meta-analysis	Sports Med	2018	Brazil
Brittany R. Counts[28]	15.73	0.09	39	Influence of relative blood flow restriction pressure on muscle activation and muscle adaptation	Muscle & Nerve	2016	USA
Jeremy P. Loenneke[27]	13.2	0.04	27	Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise	Eur J Appl Physiol	2012	USA
Christopher S. Fry[16]	12.23	0.02	22	Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men	J Appl Physiol	2010	USA
Gilberto Candido Laurentino[17]	10.95	0	23	Strength training with blood flow restriction diminishes myostatin gene expression	Med Sci Sports Exerc	2012	Brazil
Todd M. Manini[1]	9.65	0.31	16	Blood flow restricted exercise and skeletal muscle health	Exerc Sport Sci Rev	2009	USA
Jeremy P. Loenneke[12]	9.51	0.15	20	The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling	Med Hypotheses	2012	USA
Matthew B Jessee[32]	9.01	0.05	21	The cardiovascular and perceptual response to very low load blood flow restricted exercise	Int J Sports Med	2017	USA
Haruhiko Madarame[29]	8.97	0.04	14	Cross-transfer effects of resistance training with blood flow restriction	Med Sci Sports Exerc	2008	Japan

BFR: blood flow restriction.

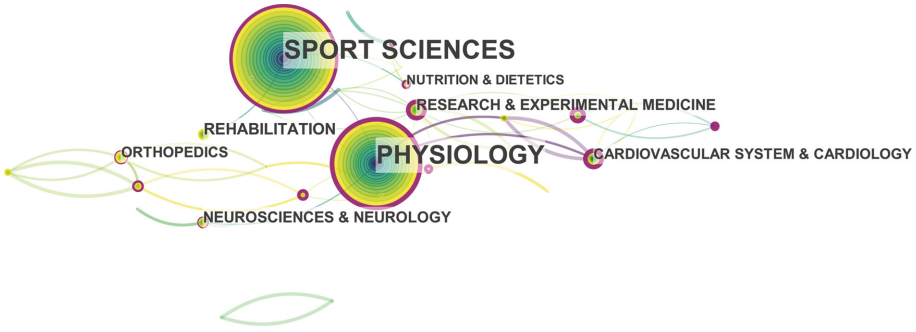

Fig. 5. Disciplines map related to blood flow restriction (BFR).

Table 5. Top 10 discipline in BFR in terms of centrality

Centrality	Discipline	Year
0.77	RESEARCH & EXPERIMENTAL MEDICINE	2010
0.72	PHYSIOLOGY	1999
0.71	CARDIOVASCULAR SYSTEM & CARDIOLOGY	2000
0.69	RESPIRATORY SYSTEM	2011
0.68	GENERAL & INTERNAL MEDICINE	2011
0.55	PUBLIC, ENVIRONMENTAL & OCCUPATIONAL HEALTH	2019
0.5	SPORT SCIENCES	2000
0.42	BIOPHYSICS	2018
0.35	NUTRITION & DIETETICS	2012
0.35	ENGINEERING	2017

Table 6. Disciplines integrated into BFR field in the past 5 years

Centrality	Discipline	Year
0	UROLOGY & NEPHROLOGY	2020
0	EMERGENCY MEDICINE	2020
0	ENVIRONMENTAL SCIENCES & ECOLOGY	2020
0.55	PUBLIC, ENVIRONMENTAL & OCCUPATIONAL HEALTH	2019
0.42	BIOPHYSICS	2018
0.1	SURGERY	2018
0	BIOCHEMISTRY & MOLECULAR BIOLOGY	2018
0	RHEUMATOLOGY	2018
0.35	ENGINEERING	2017
0	ENGINEERING, BIOMEDICAL	2017
0.19	ORTHOPEDICS	2016
0.1	CELL BIOLOGY	2016
0	PSYCHOLOGY	2016
0	BEHAVIORAL SCIENCES	2016
0	PSYCHOLOGY, BIOLOGICAL	2016
0	SCIENCE & TECHNOLOGY-OTHER TOPICS	2015
0	MULTIDISCIPLINARY SCIENCES	2015
0	CLINICAL NEUROLOGY	2015
0	PHARMACOLOGY & PHARMACY	2015

BFR: blood flow restriction.

"PHYSIOLOGY", "CARDIOVASCULAR SYSTEM & CARDIOLOGY", "RESPIRATORY SYSTEM", "GENERAL & INTERNAL MEDICINE". In the BFR research process, new disciplines are constantly being integrated. As of October 2020, a total of nearly 35 disciplines are paying attention to BFR. The new disciplines are "PUBLIC, ENVIRONMENTAL & OCCUPATIONAL HEALTH", "BIOPHYSICS", "ENGINEERING", "ORTHOPEDICS" in the most recent 5 years (Table 6).

A knowledge map of keyword cooccurrence reflect the hot topics in the field, and burst keywords (keywords that are cited frequently over a period) indicate the frontier topics. An analysis of strong bursts revealed that the hot keywords are muscular function, ischemia, growth hormone, rehabilitation, hormonal response, vascular occlusion (Fig. 6). In recent years, keywords that have gradually entered people's field of vision included gender difference, power, muscular adaptation, ultrasound, muscle protein synthesis, occlusion training.

Keywords were classified into participant, intervention, method and content according to different topics. An analysis of keywords was shown in terms of its frequency, burst and centrality (Table 7). The three topics in BFR were intervention (intensity resistance exercise, IRE), physiology (ischemia and muscular function) and behavior (adaptation and increase). The detailed information of the topics are as follows:

1. Participant: human beings were the most common research participant used to study the efficacy of BFR[30, 33]. Recently, animals have been gradually included by researchers in this field to explore the deeper mechanisms of BFR, such as laboratory rats.

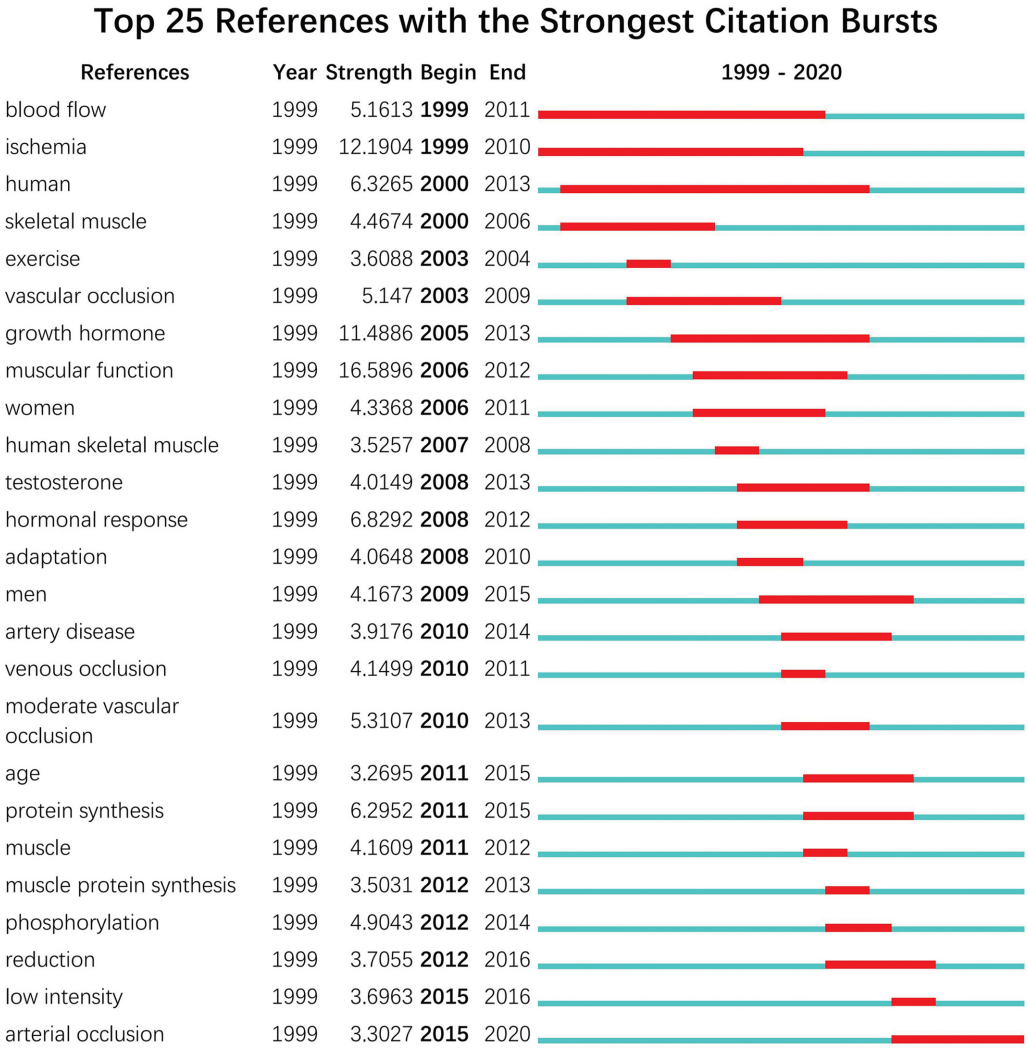

Fig. 6. Top 25 keywords in terms of frequency and centrality in blood flow restriction (BFR) research.

2. Intervention: IRF was the most effective research intervention to explore the effects of BFR. In addition, eccentric exercise has gradually become an important intervention by exercise.

3. Method: The evaluation of the efficacy of BFR includes procedures such as electromyography[34], near infrared spectroscopy[35], hemodynamic response[29], ultrasound[36] and magnetic resonance imaging[29]. Ultrasound was the most widely used to measure the cross-sectional area and thickness of muscle after BFR training[36]. Neuromuscular function was assessed by electromyography by examining the ischemia efficacy[34].

4. Content: Researchers primarily focus on the influence of BFR on four different aspects, including the molecular mechanism, physiology, behavior and blood flow restricted training (blood flow restricted training, BRFT) parameters. Early studies showed that the changes following BFR were significant increased in activation related gene expression, induction of muscle RNA transcription and production of growth factors. Fry reported that LIRE in combination with BFR enhanced mTORC1 signaling and muscle protein synthesis (muscle protein synthesis, MPS) in older males[16]. In addition, a large number of studies have shown that BFR accelerated adaptations in human neuromuscular function and increase muscular function under ischemic conditions at a behavioral level[30, 31, 33, 34].

So-called "burst words" are words that are cited frequently over a specific period. CiteSpace was used to detect burst keywords, which are considered to be indicators of research frontier topics over time. As shown in Fig. 6 the four frontiers in BFR are as follows:

1. Arterial occlusion: unresolved questions in resistance training combined with BFR include what percentage of estimated arterial occlusion pressure provides the most robust acute muscular response[37].

2. Low intensity: researchers are gradually exploring the deeper impact of LIRE combined with BFR, with a focus on muscular function and physiology, adaptation and changes in behavior.

Table 7. Key words in terms of frequency, burst and centrality in BFR research

Topic	Key words (frequency, burst and centrality)
Participant	Human (50, 6.32,0.03); Young (35, 3.26, 0.02); Men (30, 4.16, 0.03); Adult (16, 0, 0.05); Older adult (14, 0, 0.04); Aging (14, 0, 0.03); Artery disease (9, 3.92, 0.04); Sarcopenia (8, 0, 0.07); Age (8, 3.27, 0.02); Women (8, 4.34, 0.01)
Intervention	Resistance exercise (257, 0, 0.05); Blood flow restriction (221, 0, 0); Exercise (195, 3.61, 0.09); Kaatsu training (140, 0, 0.06); Intensity resistance exercise (121, 0, 0.17); Eccentric exercise (12, 4.59, 0.06); High intensity (7, 3.49, 0.01); Low intensity (7, 3.7, 0.05)
Method	Electromyography (32, 0, 0.02); Near infrared spectroscopy (23, 3.31, 0.09); Hemodynamic response (15, 0, 0); Ultrasound (13, 0, 0.13); Magnetic resonance imaging (4, 0, 0)
Content	
Molecular mechanism	Response (104, 0, 0.05); Activation (60, 0, 0.21); Gene expression (26, 0, 0.07); Expression (18, 0, 0.01); Mechanism (16, 0, 0); Muscle RNA (13, 0, 0); Endothelial growth factor (2, 0, 0); Factor messenger RNA (2, 0, 0); Growth factor response (2, 0, 0); IGF-1 (2, 0, 0)
Physiology	Strength, (272, 0, 0.05); Vascular occlusion (308, 5.15, 0.05); Skeletal muscle (172, 4.47, 0.09); Hypertrophy (124, 0, 0.01); Occlusion, (91, 0, 0.14); Human skeletal muscle, (85, 3.53, 0.06); Growth hormone (80, 11.48, 0.1); Ischemia (67, 12.19, 0.45); Muscular function (54, 16.58, 0.34)
Behavior	Adaptation, (96, 4.07, 0.17); Increase (52, 0, 0.24); Performance (50, 0, 0.04); Rehabilitation (32, 7.85, 0); Risk (14, 0, 0.09); Perceptual response (10, 0, 0); Reduction (10, 3.7, 0.06); Recovery (8, 0, 0.05); Injury (7, 3.49, 0)
BRFT parameter	Intensity (74, 0, 0.02); Pressure (47, 0, 0.19); Cuff width (21, 6.34, 0); Program (5, 0, 0.08); Validity (3, 0, 0.08)

BFR: blood flow restriction; BFRT: blood flow restricted training; Muscle RNA: muscle ribonucleic acid; factor messenger RNA: factor messenger ribonucleic acid; IGF-1: insulin-like growth factor-1.

3. Reduction: low-load BFR training to volitional failure exhibits lower levels of muscle activation than high-load exercise[38]. High-intensity resistance training is also contraindicated for hypertensive individuals and future research may examine potential reductions in blood pressure for hypertensive individuals with consistent application of BFR during resistance training[14].

4. Phosphorylation: BFR resistance exercise resulted in increased ribosomal S6K1 phosphorylation concurrent with decreased phosphorylation of eukaryotic translation elongation factor 2 resulting in a 46% increase in muscle protein synthesis[15]. A study found an increase in mTOR1 and S6K1 phosphorylation, as well as ribosomal protein S6, resulting in a 56% increase in muscle protein synthesis following BRFT in older males of approximately 70 years old[16]. Phosphorylation is a key factor in cellular and molecular signaling to analyse the molecular mechanism of BFR.

DISCUSSION

BFR research originated from the late 1990s, and high-yield countries are included—the United States, Japan, the United Kingdom and Canada. The article published by Jeremy Paul Loennek was widely cited because of its rigorous research methods and comprehensive research content, and is titled *Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise*[27]. High-yield authors have been condensed into high-yield academic groups and institutions with characteristics of regional gathering. Research institutions in the United States and Japan radiate their influence on institutions in various countries. Even though most of the other countries had extensive exchanges and cooperation within their individual countries, and it was difficult to extend this cooperative relationship to the international arena. The 35 pivotal disciplines included “RESEARCH & EXPERIMENTAL MEDICINE”, “PHYSIOLOGY”, “CARDIOVASCULAR SYSTEM & CARDIOLOGY”, “RESPIRATORY SYSTEM” and “PUBLIC-ENVIRONMENTAL & OCCUPATIONAL HEALTH”. In recent years, more disciplines have also begun to pay attention to BFR.

BFR has gone through four development stages, from safety research to efficacy research, to system mechanism research and finally to understanding the molecular mechanisms of blood flow restriction. In the first stage, researchers focused on the risks of pulmonary embolism, venous thrombosis, hemorrhage and increased blood pressure owing to BFR[39]. In the second stage, attention was paid on the exploration of the efficacy of BFR on muscle function, muscle strength, cardiopulmonary exercise tolerance[6, 33]. In the third stage, systemic mechanisms were studied, such as the promotion of growth hormone secretion, thickening of muscle cells and increasing vascular compliance[8, 40]. In recent years, the research focus has shifted into research on the molecular mechanisms of BFR, such as the increase of ribosomal S6K1 phosphorylation concurrent with decreases in phosphorylation of eukaryotic translation elongation factor 2[15, 16]. However, the number of publications on molecular biological mechanism are still relatively low and with low influence.

BFR is becoming increasingly popular in physical therapy[41] and evidence suggests that both aerobic and resistance exercise have been performed with BFR by practitioners such as strength and conditioning coaches, sport scientists and physical therapists[42]. Most of the keywords were focused on theoretical words with high generality and were selected alone in the current studies. Analogously, clinical researchers were primarily focused on the research of aging and musculoskeletal

system diseases. The development of trends in the applications of BFR, as revealed by the hot topics and research frontiers discussed in this study, may help researchers to identify new directions with renewed focus. In all, we suggest that there is still room for improvement in the field.

Our article is not free of limitations. First, our study was performed based on a limited number of articles, and our conclusions should hence be interpreted with caution. More studies will be needed to confirm our present findings. Second, only published articles and reviews in English language were analyzed, suggesting that this article may suffer from a language bias in study selection.

In conclusion, this study provides an insight into BFR and also offers valuable information for BFR researchers to identify new perspectives for potential cooperation with collaborators and their related institutions, together with identification of hot topics and the current research frontiers.

Funding and Conflict of interest

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REFERENCES

1) Manini TM, Clark BC: Blood flow restricted exercise and skeletal muscle health. Exerc Sport Sci Rev, 2009, 37: 78–85. [Medline] [CrossRef]
2) Ellefsen S, Hammarström D, Strand TA, et al.: Blood flow-restricted strength training displays high functional and biological efficacy in women: a within-subject comparison with high-load strength training. Am J Physiol Regul Integr Comp Physiol, 2015, 309: R767–R779. [Medline] [CrossRef]
3) Martín-Hernández J, Marín PJ, Menéndez H, et al.: Muscular adaptations after two different volumes of blood flow-restricted training. Scand J Med Sci Sports, 2013, 23: e114–e120. [Medline] [CrossRef]
4) Cook SB, Scott BR, Hayes KL, et al.: Neuromuscular adaptations to low-load blood flow restricted resistance training. J Sports Sci Med, 2018, 17: 66–73. [Medline]
5) Abe T, Sakamaki M, Fujita S, et al.: Effects of low-intensity walk training with restricted leg blood flow on muscle strength and aerobic capacity in older adults. J Geriatr Phys Ther, 2010, 33: 34–40. [Medline]
6) Yasuda T, Brechue WF, Fujita T, et al.: Muscle activation during low-intensity muscle contractions with restricted blood flow. J Sports Sci, 2009, 27: 479–489. [Medline] [CrossRef]
7) Park SY, Kwak YS, Harveson A, et al.: Low intensity resistance exercise training with blood flow restriction: insight into cardiovascular function, and skeletal muscle hypertrophy in humans. Korean J Physiol Pharmacol, 2015, 19: 191–196. [Medline] [CrossRef]
8) Pearson SJ, Hussain SR: A review on the mechanisms of blood-flow restriction resistance training-induced muscle hypertrophy. Sports Med, 2015, 45: 187–200. [Medline] [CrossRef]
9) Hughes L, Paton B, Rosenblatt B, et al.: Blood flow restriction training in clinical musculoskeletal rehabilitation: a systematic review and meta-analysis. Br J Sports Med, 2017, 51: 1003–1011. [Medline] [CrossRef]
10) Takarada Y, Nakamura Y, Aruga S, et al.: Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J Appl Physiol, 2000, 88: 61–65. [Medline] [CrossRef]
11) Reeves GV, Kraemer RR, Hollander DB, et al.: Comparison of hormone responses following light resistance exercise with partial vascular occlusion and moderately difficult resistance exercise without occlusion. J Appl Physiol, 2006, 101: 1616–1622. [Medline] [CrossRef]
12) Loenneke JP, Fahs CA, Rossow LM, et al.: The anabolic benefits of venous blood flow restriction training may be induced by muscle cell swelling. Med Hypotheses, 2012, 78: 151–154. [Medline] [CrossRef]
13) Kawada S, Ishii N: Skeletal muscle hypertrophy after chronic restriction of venous blood flow in rats. Med Sci Sports Exerc, 2005, 37: 1144–1150. [Medline] [CrossRef]
14) Pope ZK, Willardson JM, Schoenfeld BJ: Exercise and blood flow restriction. J Strength Cond Res, 2013, 27: 2914–2926. [Medline] [CrossRef]
15) Fujita S, Abe T, Drummond MJ, et al.: Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. J Appl Physiol, 2007, 103: 903–910. [Medline] [CrossRef]
16) Fry CS, Glynn EL, Drummond MJ, et al.: Blood flow restriction exercise stimulates mTORC1 signaling and muscle protein synthesis in older men. J Appl Physiol, 2010, 108: 1199–1209. [Medline] [CrossRef]
17) Laurentino GC, Ugrinowitsch C, Roschel H, et al.: Strength training with blood flow restriction diminishes myostatin gene expression. Med Sci Sports Exerc, 2012, 44: 406–412. [Medline] [CrossRef]
18) Takarada Y, Sato Y, Ishii N: Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. Eur J Appl Physiol, 2002, 86: 308–314. [Medline] [CrossRef]
19) Yasuda T, Loenneke JP, Ogasawara R, et al.: Influence of continuous or intermittent blood flow restriction on muscle activation during low-intensity multiple sets of resistance exercise. Acta Physiol Hung, 2013, 100: 419–426. [Medline] [CrossRef]
20) Chen D, Liu Z, Luo Z, et al.: Bibliometric and visualized analysis of emergy research. Ecol Eng, 2016, 90: 285–293. [CrossRef]

21) Chen C: CiteSpace II: detecting and visualizing emerging trends and transient patterns in scientific literature. J Am Soc Inf Sci Technol, 2006. [CrossRef]
22) Liu Z, Yin Y, Liu W, et al.: Visualizing the intellectual structure and evolution of innovation systems research: a bibliometric analysis. Entometrics, 2015, 103.
23) Gao J, Wu X, Luo X, et al.: Scientometric analysis of safety sign research: 1990–2019. Int J Environ Res Public Health, 2021, 18: 18. [Medline]
24) Xue X, Yang X, Deng Z, et al.: Global trends and hotspots in research on rehabilitation robots: a bibliometric analysis from 2010 to 2020. Front Public Health, 2022, 9: 806723. [Medline] [CrossRef]
25) Huang X, Bai J, Liu X, et al.: Scientometric analysis of dental implant research over the past 10 years and future research trends. BioMed Res Int, 2021, 2021: 6634055. [Medline] [CrossRef]
26) Sieljacks P, Knudsen L, Wernbom M, et al.: Body position influences arterial occlusion pressure: implications for the standardization of pressure during blood flow restricted exercise. Eur J Appl Physiol, 2018, 118: 303–312. [Medline] [CrossRef]
27) Loenneke JP, Fahs CA, Rossow LM, et al.: Effects of cuff width on arterial occlusion: implications for blood flow restricted exercise. Eur J Appl Physiol, 2012, 112: 2903–2912. [Medline] [CrossRef]
28) Counts BR, Dankel SJ, Barnett BE, et al.: Influence of relative blood flow restriction pressure on muscle activation and muscle adaptation. Muscle Nerve, 2016, 53: 438–445. [Medline] [CrossRef]
29) Madarame H, Neya M, Ochi E, et al.: Cross-transfer effects of resistance training with blood flow restriction. Med Sci Sports Exerc, 2008, 40: 258–263. [Medline] [CrossRef]
30) Vechin FC, Libardi CA, Conceição MS, et al.: Comparisons between low-intensity resistance training with blood flow restriction and high-intensity resistance training on quadriceps muscle mass and strength in elderly. J Strength Cond Res, 2015, 29: 1071–1076. [Medline] [CrossRef]
31) Lixandrão ME, Ugrinowitsch C, Berton R, et al.: Magnitude of muscle strength and mass adaptations between high-load resistance training versus low-load resistance training associated with blood-flow restriction: a systematic review and meta-analysis. Sports Med, 2018, 48: 361–378. [Medline] [CrossRef]
32) Jessee MB, Dankel SJ, Buckner SL, et al.: The cardiovascular and perceptual response to very low load blood flow restricted exercise. Int J Sports Med, 2017, 38: 597–603. [Medline] [CrossRef]
33) Luebbers PE, Fry AC, Kriley LM, et al.: The effects of a 7-week practical blood flow restriction program on well-trained collegiate athletes. J Strength Cond Res, 2014, 28: 2270–2280. [Medline] [CrossRef]
34) Clark BC, Fernhall B, Ploutz-Snyder LL: Adaptations in human neuromuscular function following prolonged unweighting: I. Skeletal muscle contractile properties and applied ischemia efficacy. J Appl Physiol, 2006, 101: 256–263. [Medline] [CrossRef]
35) Millet GY, Muthalib M, Jubeau M, et al.: Severe hypoxia affects exercise performance independently of afferent feedback and peripheral fatigue. J Appl Physiol, 2012, 112: 1335–1344. [Medline] [CrossRef]
36) Thiebaud RS, Loenneke JP, Fahs CA, et al.: The effects of elastic band resistance training combined with blood flow restriction on strength, total bone-free lean body mass and muscle thickness in postmenopausal women. Clin Physiol Funct Imaging, 2013, 33: 344–352. [Medline] [CrossRef]
37) Loenneke JP, Kim D, Fahs CA, et al.: Effects of exercise with and without different degrees of blood flow restriction on torque and muscle activation. Muscle Nerve, 2015, 51: 713–721. [Medline] [CrossRef]
38) Cook SB, Murphy BG, Labarbera KE: Neuromuscular function after a bout of low-load blood flow-restricted exercise. Med Sci Sports Exerc, 2013, 45: 67–74. [Medline] [CrossRef]
39) Nakajima T, Kurano M, Iida H, et al.: Use and safety of KAATSU training: results of a national survey. Int J KAATSU Train Res, 2006, 2: 5–13. [CrossRef]
40) Loenneke JP, Wilson GJ, Wilson JM: A mechanistic approach to blood flow occlusion. Int J Sports Med, 2010, 31: 1–4. [Medline] [CrossRef]
41) Patterson SD, Brandner CR: The role of blood flow restriction training for applied practitioners: a questionnaire-based survey. J Sports Sci, 2018, 36: 123–130. [Medline] [CrossRef]
42) Lambert B, Hedt C, Daum J, et al.: Blood flow restriction training for the shoulder: a case for proximal benefit. Am J Sports Med, 2021, 49: 2716–2728. [Medline] [CrossRef]