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Invited Review

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Management of knee osteoarthritis using bone marrow aspirate concentrate: a systematic review

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Abstract

Introduction: Knee osteoarthritis (OA) is a common degenerative joint condition and a major cause of disability in the general population.
Source of data: Recent published literature identified from PubMed, EMBASE, Google Scholar, and Scopus.
Areas of agreement: Orthobiological therapies try to regenerate articular cartilage and stop the progression of the degenerative lesion. Intra-articular injections of biological derivates have been increasingly used in the last decade.
Areas of controversy: The indications for the use of bone marrow aspirate concentrate (BMAC) are still unclear.
Growing points We systematically reviewed the current literature on BMAC in the management of knee OA, giving an update on the current indications for the selection of the ideal patient and the preparations and efficacy of BMAC compared to other biological alternatives.
Areas timely for developing research: BMAC is a valuable source of mesenchymal stem cells, offering potential benefits in attenuating the inflammatory pathway associated with knee OA. Intra-articular injection of BMAC has shown effectiveness in clinical trials improving functional outcomes of knee OA patients. The superiority of BMAC over other orthobiological treatments cannot be assessed because of conflicting results.

Keywords: knee osteoarthritis; biological derivates; bone marrow aspirate concentrate; BMAC

Introduction

Knee osteoarthritis (OA) is a common degenerative joint condition and a major cause of disability [1–3]. A third of the adult population shows imaging evidence of degenerative joint disease, although only 8.9% were clinically significant with a clear prevalence of knee disease (6%) [4–6]. Factors associated with a higher risk for knee OA include elderly, female sex, overweight or obese, previous knee injury, occupational factors, varus and valgus alignment, and participation in high-impact sports [7–11]. However, the risk is not increased by recreational physical activities [9,12–18]. Hostile biomechanics on a susceptible joint determines the activation of mechanosensitive and biochemical pathways that result in pathological modifications of the knee joint [8,19–22]. Cartilage loss, endochondral ossification with vascular penetration, osteophytes, subchondral bone cysts, and synovial inflammation are the major features of the affected joints [23–27]. Patients report pain, stiffness, reduced joint mobility, and muscle weakness, which lead to long-term consequences such as reduced physical activity, deconditioning, impaired sleep, depression, and disability [14,28,29]. Conventional conservative management modalities [nonsteroidal anti-inflammatory drugs, glucosamine, chondroitin

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sulphate, omega 3 fatty acids, hyaluronic acid (HA), and corticosteroid intra-articular injections (CIS)] are only palliatives and do not prevent the progression of OA to surgical management [5,30,31]. Although knee arthroplasty is advocated in symptomatic patients who experienced failure of conservative management, this widespread procedure is not without complications, with up to 20% of patients reporting persistent pain or loss of function at 12 months from the index operation [32–35]. Orthobiological therapies aim to regenerate the articular cartilage and stop the progression of the degenerative lesion [36–40]. Intra-articular injections of biological derivates have become common in the last decade [41–44]. For example, platelet-rich plasma (PRP) is obtained by centrifugation of autologous blood, with subsequent releases of cytokines and growth factors concentrated in platelet granules [39,45,46]. Mesenchymal stem cell sources (MSCs) include adipose tissue–derived stem cells (ATDSCs), human umbilical cord blood derived mesenchymal stem cells (hUCB-MSCs), and bone marrow aspirate concentrate (BMAC) [47–49]. BMAC contains a heterogeneous mixture of cells with different functions: regenerative repair, immunomodulation, and trophic factor release [50,51]. After density gradient centrifugation to remove red blood cells, granulocytes, immature myeloid precursors, and platelets, progenitor cells constitute a small fraction of the bone marrow (0.001%–0.01%) [52,53]. However, BMAC contains a high concentration of growth factors, including the platelet-derived growth factor, transforming growth factor-β, and bone morphogenetic proteins 2 and 7, which exert anabolic and anti-inflammatory effects [54,55]. MSCs and growth factors in BMAC contribute to tissue regeneration, inflammation reduction, and a favourable healing environment [50,56,57]. The current indications for using BMAC in knee OA are still unclear. The present article systematically reviewed the current literature on BMAC in managing knee OA, giving an update on the current indications to select appropriate patients and the preparations and efficacy of BMAC treatment compared to other biological alternatives.

Materials and Methods

Eligibility criteria

All the clinical studies that investigated the use of BMAC in the management of knee OA were accessed. According to the author's language capabilities, articles in English, German, Italian, French, and Spanish were eligible. Only studies with levels I–III of evidence, according to the Oxford Centre of Evidence-Based Medicine [58], were considered. Reviews, opinions, letters, and editorials were not considered, as were animals, *in vitro*, biomechanics, computational, and cadaveric investigations. Only trials that reported clinical outcomes of BMAC therapy in the management of knee OA or compared BMAC with one or more alternative orthobiological procedures for knee OA or with a control group were eligible. Missing quantitative data under the outcomes of interests warranted the exclusion of the study.

Search strategy

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses: the 2020 PRISMA statement [59]. The following algorithm was established for the database search:

- Problem: degenerative knee OA
- Intervention: BMAC
- Outcomes: cartilage regeneration, pain, and function

In August 2024, PubMed, Web of Science, Google Scholar, and Embase were accessed without constraints. The medical subject headings used in each database to accomplish the search were: (cartilage diseases OR chondral lesions OR knee osteoarthrosis) OR (knee joint surgery OR arthroplasty, subchondral OR regenerative medicine OR cartilage repair OR injections, intra-articular) AND (bone marrow aspirate concentrate OR BMAC) AND (biological derivates OR osteoarthritis, knee/drug therapy OR mesenchymal stem cell sources OR hyaluronic acid OR fat-derived mesenchymal stem cells OR autologous conditioned serum).

Selection and data collection

Two authors (J.A. and M.P.) independently performed the database search. All the resulting titles were screened by hand, and the abstract of the articles that matched the topic was read. The full texts of the abstracts of interest were accessed. The bibliographies of the full-text articles were also screened by hand. Any disagreements were discussed and settled by a third senior author (N.M.).

Data items

Two authors (J.A. and M.P.) independently performed data extraction. The following data at baseline were extracted: author and year of publication, name of the journal, study design, level of evidence, length of the follow-up (month), number of included patients with related mean age, mean body mass index (BMI) and number of women, type of orthobiological treatment, and main findings. Data concerning the orthobiological treatments using BMAC were considered. Data

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were extracted in Microsoft Office Excel version 16.72 (Microsoft Corporation, Redmond, USA).

Assessment of the risk of bias

The risk of bias was evaluated following the guidelines in the Cochrane Handbook for Systematic Reviews of Interventions [60]. Two reviewers (J.A. and M.P.) evaluated the risk of bias in the extracted studies independently. Randomized controlled trials (RCTs) were evaluated using the revised Risk of Bias assessment tool (RoB2) [61,62] of the Cochrane tool for assessing Risk of Bias in randomized trials (RoB) [63]. The following endpoints were evaluated: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in the measurement of the outcome, and bias in the selection of the reported result. Nonrandomized controlled trials (non-RCTs) were evaluated using the Risk of Bias in Nonrandomised Studies of Interventions (ROBINS-I) tool [64]. Seven domains of potential bias in non-RCTs were assessed. Possible confounding and the nature of patient selection before the start of the comparative intervention are assessed by two domains. A further domain is used to assess bias in the classification during the intervention. The final four domains assess the methodological quality after the intervention comparison has been implemented and relate to deviations from previously intended interventions, missing data, erroneous measurement of outcomes, and bias in the selection of reported outcomes. The figure of the ROBINS-I was elaborated using the Robvis Software (Risk-of-bias VISualization, Riskofbias.info, Bristol, UK) [65].

Synthesis methods

For descriptive statistics, the IBM software version 25 was used. The arithmetic mean and standard deviation were used for continuous variables.

Results

Study selection

The systematic literature search resulted in 127 investigations concerning the topic of interest. Of them, 33 were excluded because they were duplicates. After screening the abstracts of the remaining 94 articles, a further 51 studies were excluded because they did not fulfil the eligibility criteria. The reasons that led to exclusion were in detail: inappropriate study design ($N = 23$), improper level of evidence ($N = 6$), not investigating BMAC in knee OA management ($N = 10$), not matching the topic of interest ($N = 5$), and language limitations ($N = 7$). An additional 17 articles were excluded because they did not offer quantitative data on the outcomes of interest. In conclusion, 26 investigations were included in the present review. Of them, 10 were RCTs, 9 had a prospective study design, and 7 had a retrospective study design. The results of the literature search are shown in Fig. 1.

Risk of bias assessment

In 38.5% (10 of 26) of the investigations included in the present systematic review, the Cochrane risk of bias assessment tool (RoB2) for RCTs was performed. Most of the included studies established a good intervention group comparability at baseline, resulting in a low bias arising from the randomization process. Risk of bias based on the deviations from the intended intervention, missing outcome data, and the selection of the reported outcome were occasionally noted with some concerns, leading to a low-to-moderate overall risk of bias in these domains. Missed assessor blinding resulted in a high risk of bias in measuring the outcome in one of the articles; in all other studies, a low-to-moderate risk was raised for this domain. In conclusion, the risk of bias graph evidenced a predominantly good quality of the methodological assessment of RCTs (Fig. 2).

The risk of bias of non-RCTs was assessed using the ROBINS-I risk of bias tool. Sixty-one point five percent (16 of 26) of the included trials were non-RCTs. Of them 9.5% (2 of 21) were rated as having a serious or critical risk of bias in at least one domain but no critical risk of bias in each domain. Most authors reported high-quality allocation concealments, resulting in comparable study groups at baseline leading to a low-to-moderate risk of bias based on confounding and the participant selection process. The risk of bias in the classification of intervention resulted mostly low, as neither nondifferential misclassification nor differential misclassification was identified. In domains assessed for risk of bias after the intervention, some concerns were identified in the measurement of outcomes. No concerns were raised about the selection of the reported results. The overall risk of bias was low to moderate in 53.8% (14 of 26) and serious to critical in 7.7% (2 of 26) of the studies, indicating a broadly acceptable methodological quality (Fig. 3).

Study characteristics and results of individual studies

Data from 2207 patients were retrieved. The mean length of follow-up was 17.6 ± 13.3 months. Fifty-six percent (1239 of 2207) were women. The mean age was 56.7 ± 7.5 years, and the mean BMI was 26.9 ± 1.7 kg/m^2. The generalities of the included studies are shown in Table 1.

In comparison with the placebo, BMCA showed a statistically significant improvement in the visual

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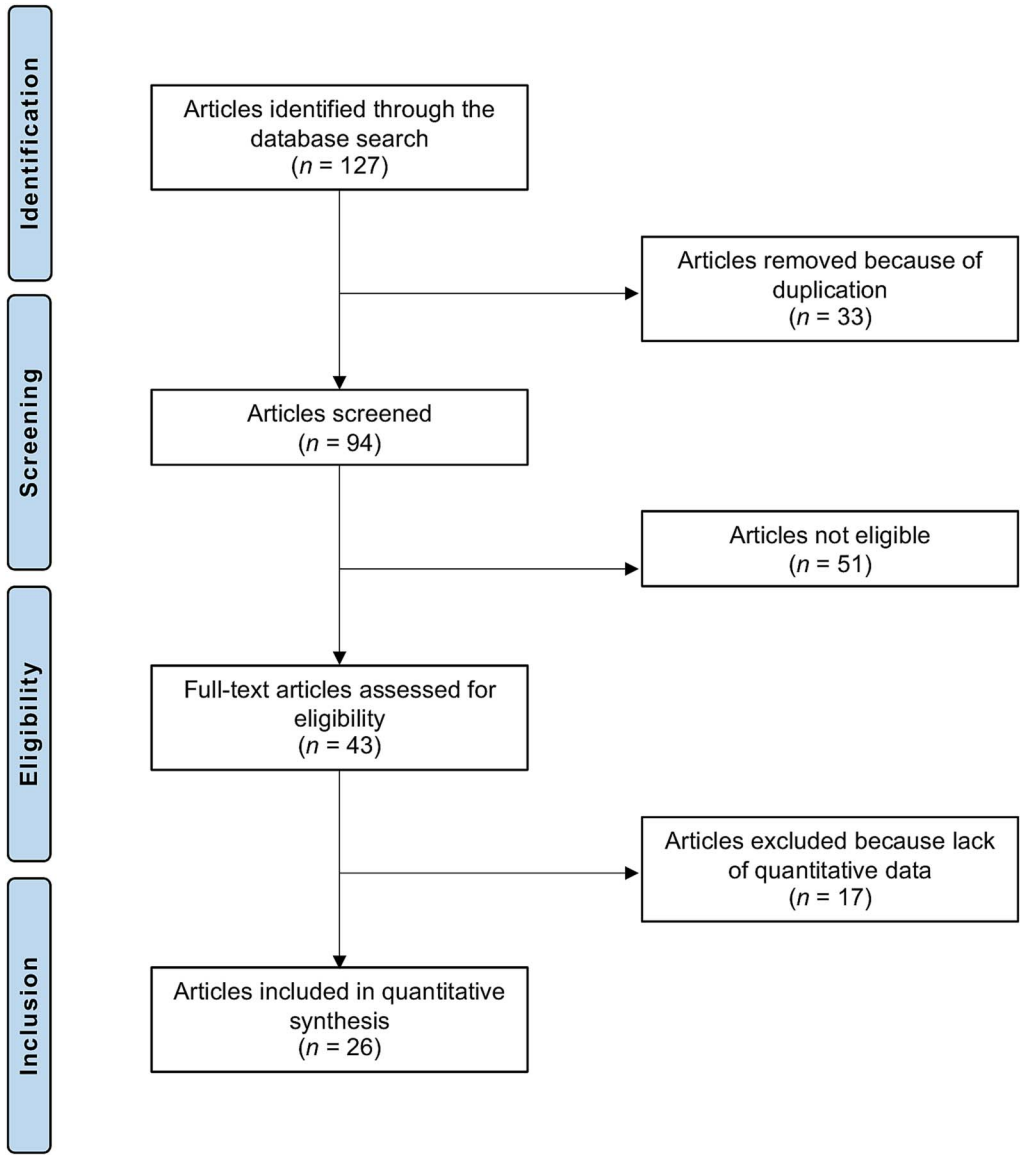


Figure 1. PRISMA flow chart of the literature search.

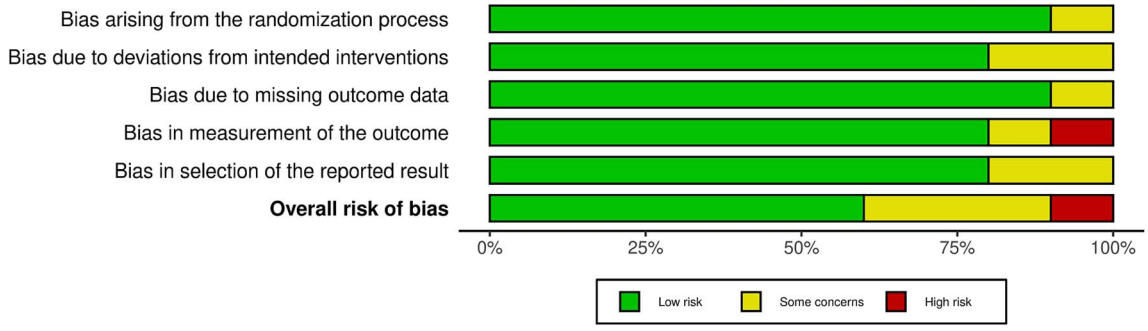


Figure 2. Cochrane RoB2 tool.

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Table 1. Generalities and patient baseline of the included studies (LoE, level of evidence; BMI, body mass index; RCT, randomized controlled trial; ACS, autologous conditioned serum; BMAC, bone marrow aspirate concentrated; HA, hyaluronic acid; MFAT, fat-derived mesenchymal stem cell; MSC, mesenchymal stem cell; PRP, platelet-rich plasma; hUCB-MSC, human umbilical cord blood–derived mesenchymal stem cell; CSI, corticosteroid injection; SVF, autologous stromal vascular fraction; AMIC, autologous matrix-induced chondrogenesis; ATDSC, adipose tissue–derived stem cells; MFx, microfracture; OA, osteoarthritis; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster universities osteoarthritis; IKDC, The International Knee Documentation Committee; KOOS: Knee Injury and Osteoarthritis Outcome Score).

Author, year	Journal	Protocol	LoE	Method	Patients (*n*)	Female (*n*)	BMI (kg/m^2)	Age (y)	Follow up (m)	Main findings
Anz *et al*., 2022 [66]	*Am J Sports Med*	RCT	II	BMAC/PRP	84	35	28	54	12	BMAC was not superior to PRP.
Baek *et al*., 2024 [67]	*Medicina (Kaunas)*	Prospective	III	BMAC	231	172	25	64	7	Reliable and effective outcomes over 6 months
Boffa *et al*., 2022 [68]	*Knee Surg Sports Traumatol Arthrosc*	RCT	I	BMAC/HA	56	21	28	57	24	BMAC was not significantly superior to HA. BMAC had more stable results over time.
De Girolamo *et al*., 2019 [69]	*J Clin Med*	RCT	II	AMIC/AMIC +BMAC	24	9		30	24	AMIC and AMIC+ are effective with durable results over time. AMIC+ had better short-term clinical outcomes.
Dulic *et al*., 2021 [70]	*Medicina (Kaunas)*	RCT	II	HA/B-MAC/PRP	175	80	29	57	12	BMAC was superior than PRP and HA. PRP had better outcomes than HA (not statistically significant).
El-Kadiry *et al*., 2022 [71]	*BMC Muscoloskelet Disord*	Retrospec-tive	III	BMAC/PRP	30	18		56	12	BMAC reduced pain and improved functionality to a greater extent than PRP.
Estrada *et al*., 2020 [72]	*Clin Med Insights Arthritis Musculoskelet Disord*	Prospective	III	BMAC/ATD-SC/PRP	89	51		61	12	BMAC, ATDSC, and PRP improved statistically significant improvements in pain and function for knee OA in a comparable way. Results remained at 1 year.
Jin *et al*., 2021 [73]	*Knee Surg Sports Traumatol Arthrosc*	Retrospec-tive	III	MFx/BMAC	91	67	25	56	34	MFx with BMAC did not provide significantly improved clinical outcomes but had a synergistic effect for cartilage regeneration.
Kim *et al*., 2014 [74]	*Eur J Orthop Surg Traumatol*	Prospective	III	BMAC	41	24		61	12	Significantly improved pain and functions in patients with knee OA.
Kon *et al*., 2021 [75]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	III	BMAC	30	11	25	56	12	Combined intra-articular and subchondral treatment provided a significant clinical improvement.
Kon *et al*., 2023 [76]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	III	BMAC	30	11	25	56	24	Combined intra-articular and subchondral BMAC treatment provided clinical and imaging benefits.
Kuebler *et al*., 2022 [77]	*Stem Cells Int*	Retrospec-tive	III	BMAC	160	83		63	6	VAS and WOMAC scores exceeded the levels reported in previous knee OA studies.

(*Continued*)

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Table 1. Continued

Author, year	Journal	Protocol	LoE	Method	Patients (*n*)	Female (*n*)	BMI (kg/m^2)	Age (y)	Follow up (m)	Main findings
Mariani *et al.*, 2023 [78]	*J Clin Orthop Trauma*	Retrospective	III	BMAC	55	17		45	57	A single BMAC injection has a lasting effect on knee OA.
Mautner *et al.*, 2019 [79]	*Stem Cells Transl Med*	Retrospective	III	BMAC/MFAT	76	40		63	12	BMAC and MFAT significantly improved pain and function without a significant difference between the two groups.
Mautner *et al.*, 2023 [80]	*Nature Medicine*	RCT	I	BMAC/SVF/ hUCB-MSCs/CSI	480	261	30	58	12	No superiority of any therapy over CSI at 1 year
Pabinger *et al.*, 2024 [81]	*Sci Rep*	Prospective	III	BMAC	37	12	25	58	48	Long-term significant improvement
Pintore *et al.*, 2023 [82]	*Journal Orthop Surg Res*	RCT	I	BMAC/MSC	102	56	28	60	6	Both significantly improved pain and functional outcomes with no statistical difference.
Ruane *et al.*, 2021 [83]	*J Stem Cells Regen Med*	RCT	II	BMAC+PRP/HA	32	13	29	58	12	BMAC+PRP experienced a more consistent reduction in pain compared to HA.
Ryu *et al.*, 2020 [84]	*Cell Transpl*	Retrospective	III	BMAC/hUCB-MSCs	52	28	26	47	24	MSCs are safe and effective
Shapiro *et al.*, 2017 [85]	*Am J of Sports Med*	RCT	II	BMAC/Placebo	25	18	27	60	6	Similar pain relief in BMAC and placebo.
Shapiro *et al.*, 2019 [86]	*Cartilage*	RCT	I	BMAC/Placebo	25	18	27	60	12	BMAC is not superior to placebo. Absence of clear evidence for cartilage regeneration.
Themistocleus *et al.*, 2018 [87]	*Heliyon*	Retrospective	III	BMAC	121	85		70	11	BMAC appears to provide long-term benefits.
Varady *et al.*, 2020 [88]	*Knee*	Prospective	III	BMAC	17	10			3	Positive pain and function outcomes with a fenestrated trocar system.
Viganò *et al.*, 2022 [89]	*Int Orthop*	Prospective	III	BMAC	10	6		52	24	Significantly improved IKDC score, KOOS subscales and VAS at 24 months.
Vitali *et al.*, 2022 [90]	*Acta Biomed*	RCT	II	BMAC/ACS	24	13		59	6	Both are effective therapies for early-stage knee OA; better outcomes with BMAC.
Yang *et al.*, 2022 [91]	*Knee Surg Sports Traumatol Arthrosc*	Prospective	III	BMAC/hUCB-MSCs	110	80	27	56	33	Both had similar clinical outcomes. hUCB-MSC had superior articular cartilage regeneration.

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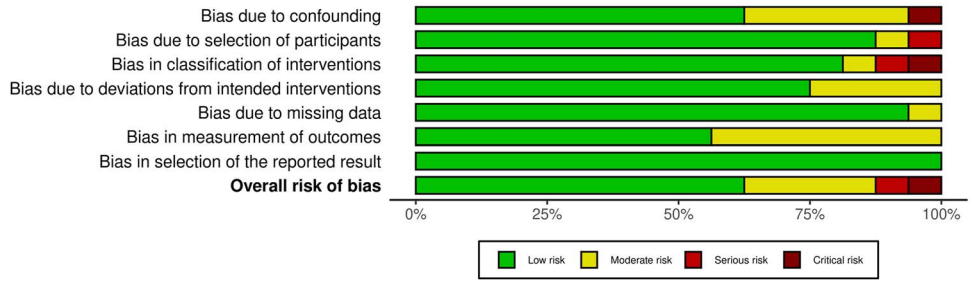


Figure 3. The ROBINS-I of non-RCTs.

analogue scale (VAS) and functional parameters [Tegner and Western Ontario and McMaster Universities Osteoarthritis (WOMAC) score] after a follow-up period of 11 months. After 12 months, however, no statistically significant difference was found between BMCA and placebo. When compared with MFAT and BMCA, both procedures showed a statistically significant improvement in clinical and functional scores, but no difference was found between the two groups. Compared with HA, BMCA had higher Knee Injury and Osteoarthritis Outcome Score (KOOS) and International Knee Documentation Committee (IKCD) and WOMAC scores in the first 12 months. PRP showed lower KOOS, IKCD, and WOMAC scores in the first 6 months compared to the BMAC group. However, this difference was no longer evident in the following six months and after a follow-up period of 2 years. Investigations of the injection site showed higher clinical and MRI improvements in the subchondral injection group compared to the intra-articular injection group after a follow-up period of 2 years.

Discussion

BMAC has been recognized as a reservoir of MSCs and growth factors, facilitating the attenuation of the inflammatory pathway underlying OA [50,82]. Chondrogenic differentiation of MSCs is based on different cofactors, including insulin, selenium, and transferrin, but the most important is TGF-β [92,93], which plays a crucial role in type II collagen production, T-lymphocyte differentiation, and metalloprotease activity level [94,95]. BMAC can be collected through multiple sessions or in a single step without any variation in the number of MSCs harvested [96,97]. The amount of MSCs harvested does not depend on the patient's demographic such as sex, age, and BMI when using a single processing system [98]. Schafer *et al*. [99] showed a statistically significant difference in BMAC composition using different extraction tools. These results were confirmed by Dragoo *et al*. [100], who compared Harvest SmartPrep3, Biomet BioCUE, and Arthrex Angel. The consistency was similar, but the composition differed across the systems [100]. Marx *et al*. [101] examined the optimal yield of bone harvesting, comparing anterior iliac crest, posterior iliac crest, and tibial plateau. No difference was found between the anterior and posterior iliac crest in MSC concentration [101]. The quantity of MSCs obtained from the tibial plateau was approximately half of the MSCs gathered from the iliac crest [101].

Intra-articular injections of BMAC reduce the inflammatory response of synovium and articular cartilage through the inhibition of the nuclear factor kappa B (NFkB) pathway and decrease pain through the interaction with the cannabinoid receptors [102]. Mariani *et al*. [78] analysed 55 patients who received BMAC in a 5-year follow-up study. A statistically significant improvement was shown in the VAS, Tegner, and WOMAC scores [78]. These results were supported by a study on 121 patients [87]. A statistically significant improvement was shown in functional parameters after 11 months of follow-up [87]. Shapiro *et al*. [86] analysed 25 patients with bilateral knee OA. Knees were randomized to receive BMAC or saline placebo. An increment in functional parameters was shown both in the BMAC and saline placebo groups. No statistically significant difference was shown between the two groups after 12 months of follow-up [86]. This result could partially be explained because MSCs and growth factors travel from the injection site into the general circulation, leading to systemic spikes demonstrated in human trials and animal models [103,104]. These findings imply a potential therapeutic influence of circulating systemic elements from BMAC on both knees [86].

Other sources of MSCs and growth factors have been recently used to manage knee OA [70,71]. Mautner *et al*. [79] compared BMAC with MFAT harvested from the abdomen and subsequently processed. Forty-one patients received BMAC and 35 received MFAT [79]. Both groups showed a statistically significant

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improvement in clinical and functional scores, with no difference between the two groups [79]. This result was supported by Pintore *et al.* [82] No difference in clinical and functional outcomes was observed between 51 patients who received BMAC and 51 patients who received MFAT [82]. The best improvement in clinical and functional scores was shown in patients with mild knee OA (Kellgren and Lawrence II) [82].

There is ongoing debate comparing the effectiveness of BMAC versus PRP [70,71]. Dulic *et al.* [70] analysed 175 patients, randomly divided into three groups: BMAC group, PRP group, and HA group. The BMAC group showed higher values of KOOS, IKCD, and WOMAC scores than the HA group in the first 12 months [70]. In the initial 6 months, the BMAC group demonstrated elevated values for KOOS, IKCD, and WOMAC scores compared to the PRP group [70]. However, this distinction was not evident in the subsequent 6 months [70]. The BMAC group exhibited significantly higher levels of IL-1Ra compared to LR-PRP and LP-PRP in a comprehensive analysis of growth factors [105]. This suggests that the elevated IL-1Ra concentration in BMAC may potentially explain its superior clinical outcomes [105]. The superiority of BMAC was confirmed by El-Kadiry *et al.* [71], who compared functional outcomes in 20 patients who received BMAC and 10 who received PRP. Anz *et al.* [66] found different results in an RCT on 84 patients who received BMAC or PRP. After 2 years of follow-up, no difference was found in functional parameters between the two groups [66]. Indeed, the improvement plateau was reached in 3 months in both groups [66]. Given the higher morbidity and cost associated with BMAC, it is not worthwhile to prefer it to other conservative treatments [66].

Boffa *et al.* [68] conducted an RCT comparing the efficacy of BMAC versus HA injections for knee OA over 2 years. Sixty patients with bilateral knee OA were randomized to receive BMAC in one knee and HA in the other [68]. There were no severe adverse events or significant differences in mild adverse events and treatment failures between BMAC and HA groups [68]. A statistically significant improvement in VAS was demonstrated by BMAC compared to HA at both 12 and 24 months [68].

The role of subchondral bone in OA is being reconsidered, with a main role in the onset of OA [106,107]. A deficiency of MSCs in the subchondral region has been noted during the ageing process [108,109]. Hernigou *et al.* [110] performed an RCT on a cohort of 60 patients with bilateral knee OA. One knee received intra-articular BMAC, and the other received subchondral BMAC [110]. After 2 years of follow-up, the clinical and MRI improvements were higher in the subchondral BMAX group [110]. After 15 years, 70% of the intra-articular group's knees underwent total knee arthroplasty (TKA), and 20% of the subchondral group's knees underwent TKA [110]. Kon *et al.* [75] conducted a pilot study on 30 patients treated with a combination of intra-articular and two subchondral BMAC injections. After 1 year of follow-up, functional parameters were improved, and bone oedema was reduced [75], with a reduction of synovitis after subchondral BMAC injection [87,102]. There is a bidirectional communication between bone marrow and synovium in OA, and MSCs in subchondral bone may modulate this communication leading to a decrease in synovitis [111,112].

The clinical efficacy of BMAC in knee OA may arise from both its anti-inflammatory and regenerative effects. This systematic review, based on the most updated study on BMAC available in the present literature, explores diverse treatment comparisons, conducts simultaneous assessments, addresses conflicting results, critically evaluates clinical superiority, and contributes to ongoing debates surrounding BMAC's effectiveness.

This study incorporated different study designs, including clinical trials and observational studies. We are aware that this heterogeneity in study methodologies may introduce variability in the quality of evidence and the reliability of outcomes. Indeed, a meta-analysis was not performed because of the heterogeneity of data, the diversity of functional scores used across the studies, and the lack of a consistent number of match-controlled studies of BMAC versus another conservative treatment. Differences in the preparation protocols for BMAC across studies may contribute to variations in treatment outcomes. Standardization of BMAC preparation is crucial to ensure consistency in therapeutic effects. The included studies analysed patients with different grades of OA, and the functional results were not parameterized to the level of the disease. Further studies should be conducted to define the appropriate timing to treat the patient. Given the lack of data in the current literature, it was not possible to compare the results of BMAC to nonsteroidal anti-inflammatory drugs (NSAIDs). Very few studies exist on the role of subchondral BMAC injection in limiting OA progression. Given its initial promising results, it would be desirable to conduct adequately powered RCTs with long-term follow-up and robust objective and subjective outcome measures.

Conclusion

BMAC shows promise for managing knee OA, given its anti-inflammatory and regenerative effects. Intra-articular injections of BMAC have shown effectiveness in clinical trials, improving the functional outcomes of patients with knee OA. Given the conflicting results, the superiority of BMAC over other orthobiological treatments remains to be assessed.

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Author contributions

Filippo Migliorini (Conceptualization, Data curation), Formal analysis), Marco Pilone (Methodology, Visualization), Jacopo Ascani (Conceptualization, Formal analysis), Luise Schäfer (Data curation, Validation), Madhan Jeyaraman (Data curation, Investigation), Nicola Maffulli (Data curation, Validation).

Conflict of interest statement

None declared.

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Ethical approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent

For this type of study, informed consent is not required.

Data availability

The data underlying this article are available in the article and its online supplementary material.

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