Core decompression and bone marrow aspirate concentrate injection for Avascular Necrosis (AVN) of the femoral head: A scoping review

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**Abstract**

**Background:** Various joint preserving treatments are available for use in Avascular Necrosis of the femoral head. Most of these are effective in the pre-collapse stage of the disease. This review aimed to evaluate the effectiveness of core decompression and Bone Marrow Aspirate Concentrate in various stages of AVN, in modifying the progression of the disease and the need for hip replacement.

**Material and methods:** The Preferred Reporting Items for Systematic reviews and Meta-Analysis Extension for Scoping Reviews reporting guidelines were followed. The literature search was conducted from inception till 2nd May 2021, on the PUBMED, SCOPUS, and Google Scholar search engines, using “bone marrow aspirate concentrate osteonecrosis femur” and “bmac osteonecrosis femur” as the keywords. In all these studies, Core Decompression with Bone marrow Aspirate concentrate was performed. The evaluation was done based on the progression of osteonecrosis, improvement in functional outcomes and the conversion to total hip arthroplasty.

**Results:** We have analyzed 612 hips from 11 studies, based on our inclusion and exclusion criteria. The mean age of the patients was 38.27 years. There was a predominance of males. The grade of AVN ranged from grade 1 to 4. The average follow-up period of the cases ranged from 2 to 12 years (average: 4.38 years). The functional scores were improved in the majority of cases. Radiographic progression occurred in 23.5% of hips, and the Total Hip Arthroplasty was performed in 14.9% of hips.

**Conclusions:** Core decompression with Bone Marrow Aspirate Concentrate in pre-collapse stages of the disease is beneficial in improving the functions scores and for reducing the radiological progression of the disease and need for total hip arthroplasty, in the majority of cases.

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1. Introduction

Osteonecrosis (ON) of the femoral head, also known as Avascular Necrosis (AVN), occurs due to the disruption of blood supply to the femoral head. It leads to ischemia, cell death, ultimately causing joint destruction and the development of osteoarthritis (OA). Although the AVN may occur in several other joints, it most commonly involves the hip joint. Multifocal AVN involving more than two anatomic sites is also known to occur.1

Several traumatic and non-traumatic factors are associated with the AVN, however, the exact cause of this pathology remains unclear.2 The disease primarily affects young and middle-aged individuals and negatively impacts their quality of life.3 Various joint preserving treatments like core decompression (CD), bone marrow aspirate concentrate injection (BMAC), bone grafting, muscle pedicle grafting, platelet-rich plasma (PRP), and recombinant Bone Morphogenic Proteins (BMP) are currently being used for its management.4 Most of these treatments play a role only in the pre-collapse stage of the AVN, and once the disease progresses to a stage of collapse, a total hip arthroplasty (THA) is needed. The major drawback of THA is its limited life span, and the patients may require multiple revision surgeries in their lifetime.5 An early diagnosis and treatment in the pre-collapse stage is thus necessary to prevent progression of the disease and to postpone or alleviate the need for THA.

This scoping review aimed to evaluate the role of core decompression and BMAC in various stages of AVN, and to check their effectiveness in modifying the progression of the disease, towards severe OA, and THA.

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2. Materials and methods

The five-stage process as described by Arksey et al. was used to conduct this review.\(^5\) Quality appraisal was not conducted during this review. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis Extension for Scoping Reviews (PRISMA-ScR) reporting guidelines were followed for conducting this review.\(^7\)

2.1. Identification of research question

The following research questions were chosen for this review:

1. What outcomes have been evaluated with the use of CD and BMAC for the treatment of AVN of the femoral head?
2. What research has been conducted on the efficacy of this treatment based on the various stages of AVN?
3. Which studies explored the functional outcome of the cases?

2.2. Identification of eligible studies

The literature search was conducted from inception till 2nd May 2021, on the PUBMED, SCOPUS, and Google Scholar search engines, using “bone marrow aspirate concentrate osteonecrosis femur” and “bmarcosteonecrosisfemur” as the keywords. The references provided in the articles were reviewed to identify the articles which were overlooked or not indexed in the databases. Abstracts of these studies were reviewed for mentions of bone marrow aspiration and ON. The selection criteria included English language studies that reported on the role of BMAC injection in patients with AVN of the head of the femur. Case reports, animal studies, non-English language studies, and those not reporting on outcomes were excluded.

Study selection was conducted based on the Arksey et al. protocol which included the screening of the titles by one reviewer and full-text review by two independent reviewers. A summary of the selection process is described in Fig. 1.

2.3. Data extraction

Data collected followed a predetermined form and included the following: demographic characteristics, stage of avascular necrosis, primary and secondary intervention performed, number of stem cells and colony-forming units, and outcomes in the form of primary and secondary intervention performed, number of stem cells.23

The literature search yielded 8750 references, out of which 12 studies were included in our review (Fig. 1), as per our inclusion and exclusion criteria. Four types of studies were included in this review: Prospective RCT (4), Retrospective Non-RCT (4), and Prospective Non-RCT (3). Out of these studies, 6 were comparative while 5 were non-comparative.

The total number of cases in these studies included 612 hips in 460 cohorts (range: 09–189 hips). The mean age of the patients was 38.27 years. There was a predominance of males with 275 males and 185 females. The grade of AVN ranged from grade 1 to 4 (eight studies have used ARCO classification, while the remaining three have used the FICAT, Steinberg, and JOA classifications). In all these studies CD with BMAC was performed. Eight studies have mentioned the number of stem cells, which ranged from \(2 \times 10^6\) to \(3.46 \pm 0.36 \times 10^6\) cells. The CFU number was measured in eight studies, ranging from \(25 \times 10^3\) cells to \(5 \pm 2 \times 10^6\) cells.

The average follow-up period of the cases ranged from 2 to 12 years (average: 4.38 years) and in no study, the follow-up was less than 2 years.

4. Functional outcomes

Clinical outcome using functional scoring systems was assessed using various scoring methods; HHS (4), WOMAC (3), VAS (2) in 9 out of 12 studies. Radiographic progression occurred in 144/612 hips (23.53%), and THA was performed for 91 hips (14.87%) [Table 3].

Adverse effects of the procedure were reported in 4 studies which included pain (10), fever (2), hematoma (2), pneumonia (1), nausea (1), and secondary alloimmunization (1).

5. Discussion

An overall incidence of AVN of the femoral head is between 1 and 3 per 100000; with higher male preponderance. It is reported that the male to female ratio is 3:1 in the United States.\(^{19}\) Young and middle-aged population is at risk therefore an early diagnosis is of paramount importance as 80% of untreated hips ultimately progress to a stage of collapse and OA.\(^{20}\) AVN is a multi-factorial disease, caused due to disruption of the blood supply of femoral head. Various known factors related to its pathogenesis are listed in Table 4.\(^{21}\)

It is hypothesized that an osteonecrotic femoral head is devoid of progenitor cells which leads to an insufficient creeping substitution. Therefore, the treatment modalities are sought which promote creeping substitution and repair the osteonecrotic head.\(^{22}\) Core decompression (CD) provides a channel for neovascularization to occur and facilitates access to the progenitor cells.\(^{23}\)

Various techniques of CD are reported in the literature. These include the conventional core technique, trapdoor technique, lighbulb technique, percutaneous drilling.\(^{24,25}\) The conventional core technique involves drilling into the femoral head and removal of 8–10 mm of the necrotic lesion, while the lighbulb technique creates a window in the femoral head-neck junction, and debridement is done using a high-speed drill.\(^{26}\) The trapdoor technique involves the dislocation of the hip joint and the creation of a flap over the femoral head for direct visualization of the femoral head. It is an invasive procedure and requires hip dislocation, which itself could lead to damage to the femoral neck vasculature.\(^{27}\) The conventional technique is now modified, and the use of multiple pins is recommended. The percutaneous technique is reported to have excellent results and survivorships.\(^{28}\) Here, multiple channels are created using 3 mm drill bits or Steinmann pins to decompress the femoral head. This procedure is associated with minimum morbidity.\(^{29}\)

Grafts such as vascularized and non-vascularized fibular grafts, as well as tantalum grafts, have been used to aid in bone formation and preventing fractures. These grafts also provide structural support to the void created after the drilling. Non-vascularized cortical strut grafts were previously advocated and are not currently popularly used.\(^{30}\)

The technique of CD supplemented with BMAC injection was first described by Hernigou et al. (2002) in a prospective study with 189 hips which included all stages of AVN. They reported better outcomes in pre-collapse stages of AVN when CD was combined.
with BMAC compared to CD alone. An injection of the BMAC contains the osteogenic precursors which promote healing and regeneration of the osteonecrotic portion of the femoral head. It is also believed to promote healing by increasing vascularity and by releasing various growth factors.

Harvesting of the cells involves aspiration using a 10 ml syringe in small fractions which is shown to contain a greater number of nucleated cell count of 18 × 106 cells. Kawate et al. has described the use of scaffolds along with the use of BMAC to provide mechanical support to the necrotic area. There have been reports of the advantages of using a vascularized fibula after the CD and BMAC, with the instillation of stem cells cultured with beta-tricalcium phosphate (b-TCP) ceramics. Following the procedure, the patient is allowed partial weight-bearing for a few weeks followed by full weight-bearing, as tolerated. Immediate pain relief is reported after the procedure. Serial evaluations are performed, and outcomes are assessed in the form of radiographic progression, functional outcomes, and the need for total hip replacement.

The radiographic progression does not always correlate with the need for THA, as some of the cases with worse functional scores have been found to have a less severe radiographic progression. For early AVN stages, BMAC implantation is safe and effective in delaying femoral head collapse. BMAC may be useful in early stage AVN. BMAC is an effective joint preserving treatment, especially for early AVN disease stage.

Table 1
Characteristics of the included studies.

<table>
<thead>
<tr>
<th>No.</th>
<th>Author, Year of publication</th>
<th>Reference Number</th>
<th>Type of Study</th>
<th>Comparative or Non-Comparative</th>
<th>Number of Patients</th>
<th>Disease Stage</th>
<th>Primary Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hauzeur et al. (2017)</td>
<td>7</td>
<td>Prospective RCT</td>
<td>Comparative</td>
<td>19 (23 Hips)</td>
<td>3 ARCO</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>2</td>
<td>Hernigou et al. (2002)</td>
<td>8</td>
<td>Prospective Non RCT</td>
<td>Non-Comparative</td>
<td>116 (189 Hips)</td>
<td>STEINBERG 1-4</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>3</td>
<td>Zhao et al. (2012)</td>
<td>9</td>
<td>Prospective RCT</td>
<td>Comparative</td>
<td>100 (104 Hips)</td>
<td>1c to 2c ARCO</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>4</td>
<td>Tabatabaei et al. (2015)</td>
<td>10</td>
<td>Prospective RCT</td>
<td>Comparative</td>
<td>18 (28 Hips)</td>
<td>1 to 3 ARCO</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>5</td>
<td>Gangji et al. (2004)</td>
<td>11</td>
<td>Prospective RCT</td>
<td>Comparative</td>
<td>13 (18 Hips)</td>
<td>1 and 2 ARCO</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>6</td>
<td>Gangji et al. (2011)</td>
<td>12</td>
<td>Prospective RCT</td>
<td>Comparative</td>
<td>19 (24 Hips)</td>
<td>1 and 2 ARCO</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>7</td>
<td>Tomaru et al. (2019)</td>
<td>13</td>
<td>Retrospective Non RCT</td>
<td>Non-Comparative</td>
<td>44 (80 Hips)</td>
<td>1 to 4 ARCO</td>
<td>CD + BMAC</td>
</tr>
<tr>
<td>8</td>
<td>Wang et al. (2013)</td>
<td>14</td>
<td>Prospective Non RCT</td>
<td>Non-Comparative</td>
<td>15 (20 Hips)</td>
<td>2 and 3 ARCO</td>
<td>CD + BMAC</td>
</tr>
<tr>
<td>9</td>
<td>Yoshio et al. (2011)</td>
<td>15</td>
<td>Retrospective Non RCT</td>
<td>Non-Comparative</td>
<td>6 (9 Hips)</td>
<td>JOA C1−C2 (1 −3B)</td>
<td>CD + BMAC</td>
</tr>
<tr>
<td>10</td>
<td>Kang et al. (2018)</td>
<td>16</td>
<td>Retrospective Non RCT</td>
<td>Comparative</td>
<td>100 (106 Hips)</td>
<td>1 to 4 ARCO</td>
<td>CD ± BMAC</td>
</tr>
<tr>
<td>11</td>
<td>Chotivitchit et al. (2012)</td>
<td>17</td>
<td>Retrospective Non RCT</td>
<td>Non-Comparative</td>
<td>10 (11 Hips)</td>
<td>FICAT 1-3</td>
<td>CD + BMAC</td>
</tr>
</tbody>
</table>

(Abbreviations: CD - Core Decompression; BMAC — Bone Marrow Aspirate Concentrate; ARCO - Association Research Circulation Osseous; RCT — Randomized Control Trial).

Table 2
Clinical and Radiological parameters of the included studies.

<table>
<thead>
<tr>
<th>No.</th>
<th>Author, year of publication</th>
<th>Reference Number</th>
<th>Follow-Up Period (Years)</th>
<th>Radiographic Progression (Control)</th>
<th>Radiographic Progression (Cases)</th>
<th>Conversion to Arthroplasty (Control)</th>
<th>Conversion to Arthroplasty (No. of Cases)</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hauzeur et al. (2017)</td>
<td>7</td>
<td>2</td>
<td>9</td>
<td>10</td>
<td>15</td>
<td>15</td>
<td>No advantage of BMAC implantation with CD in Stage 3</td>
</tr>
<tr>
<td>2</td>
<td>Hernigou et al. (2002)</td>
<td>8</td>
<td>7</td>
<td>NA</td>
<td>71</td>
<td>NA</td>
<td>25</td>
<td>CD + BMAC may be useful in advanced stages</td>
</tr>
<tr>
<td>3</td>
<td>Zhao et al. (2012)</td>
<td>9</td>
<td>5</td>
<td>10</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>CD + BMAC is effective in delaying femoral head collapse</td>
</tr>
<tr>
<td>4</td>
<td>Tabatabaei et al. (2015)</td>
<td>10</td>
<td>10</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>CD + BMAC could be effective in early stages of AVN</td>
</tr>
<tr>
<td>5</td>
<td>Gangji et al. (2004)</td>
<td>11</td>
<td>2</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>CD + BMAC implantation is safe and effective in early stages of AVN</td>
</tr>
<tr>
<td>6</td>
<td>Gangji et al. (2011)</td>
<td>12</td>
<td>5</td>
<td>8</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>CD + BMAC is an effective procedure in early stages of AVN</td>
</tr>
<tr>
<td>7</td>
<td>Tomaru et al. (2019)</td>
<td>13</td>
<td>12</td>
<td>NA</td>
<td>21</td>
<td>NA</td>
<td>27</td>
<td>CD + BMAC is an effective joint preserving treatment, especially for early AVN</td>
</tr>
<tr>
<td>8</td>
<td>Wang et al. (2013)</td>
<td>14</td>
<td>2</td>
<td>NA</td>
<td>4</td>
<td>NA</td>
<td>0</td>
<td>Most effective in small lesions in early stages; further evaluation necessary for post-collapse stages</td>
</tr>
<tr>
<td>9</td>
<td>Yoshio (2011)</td>
<td>15</td>
<td>3.41</td>
<td>NA</td>
<td>4</td>
<td>NA</td>
<td>1</td>
<td>Effective and safe procedure</td>
</tr>
<tr>
<td>10</td>
<td>Kang et al. (2018)</td>
<td>16</td>
<td>4.28</td>
<td>20</td>
<td>19</td>
<td>26</td>
<td>15</td>
<td>Lowers rate of THA but does not lower progression of the ARCO Stage</td>
</tr>
<tr>
<td>11</td>
<td>Chotivitchit et al. (2012)</td>
<td>17,18</td>
<td>3.55</td>
<td>NA</td>
<td>8</td>
<td>NA</td>
<td>1</td>
<td>CD + BMAC may be useful in early stage</td>
</tr>
</tbody>
</table>

(Abbreviations: CD - Core Decompression; BMAC — Bone Marrow Aspirate Concentrate; AVN — Avascular Necrosis; NA - Not Applicable).
serious adverse effect was reported. In this review of 11 studies, better clinical outcomes were observed in the improvement of functional scores and lesser radiological progression (average: 23.5%). There was also a decreased need for THA when CD was combined with BMAC (average: 14.9%) [Table 3]. There was a general improvement in the functional hip scores as demonstrated in nine studies. The efficacy of this treatment has been linked to the higher number of stem cells implanted and the use of ex-vivo culture is recommended to ensure the delivery of a sufficient number of stem cells at the necrotic site.42,43 Another study, conducted by Sen et al. reported significant improvement in cases with poor preoperative functional score, presence of radiographic changes and edema seen on MRI, although, the cases with post traumatic osteonecrosis were also included.44

Another crucial factor is that the potency of the stem cells may vary with age as regards their differentiation potential.45

5.1. Limitations of this study and future research directions

We acknowledge some limitations in this study. There was heterogeneity in the data for stages of AVN, number of stem cells, number of colony-forming units, and the functional scoring system used to evaluate the outcome. Two studies did not evaluate the functional scores. Only six of the studies were comparative, leading to a lower level of evidence for the comparison. Information such as the etiology, post-operative protocol, and complications was missing in some studies. Not all studies reported the adverse effects of this procedure. The review also revealed a lack of standard terminology regarding the classification of AVN which poses challenges in comparative analysis. Since we limited our search to randomized controlled trials, we may have excluded some longitudinal studies which include relevant data.

The findings of this review highlight the need for more rigorous research on evaluating the outcome of BMAC and CD in various
stages of AVN. A broader perspective on the dose of BMAC, the number of CFU’s and the role in the late stages of AVN would be beneficial. Addressing these knowledge gaps could provide evidence-based protocols on the use of CD and BMAC.

6. Conclusions

Avascular necrosis of the femoral head is a multi-factorial condition, with many identifiable risk factors. Core decompression with Bone Marrow Aspirate Concentrate in the pre-collapse stages of the disease is beneficial in improving the functions scores and for reducing the radiological progression of the disease and the need for total hip arthroplasty in the majority of cases.

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Declaration of competing interest

None.

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References


