

## Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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# Is instillation of bone marrow stem cells at the time of core decompression useful for osteonecrosis of the femoral head?

**Autores:** Jorge Cabroler [1,3 ], Marcelo Molina [2,3 ]

### Affiliation:

[1] Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[2] Departamento de Traumatología y Ortopedia, Facultad de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

[3] Proyecto Epistemonikos, Santiago, Chile

**E-mail:** [mmolinas@med.pu.cl](mailto:mmolinas@med.pu.cl)

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## Abstract

Osteonecrosis of the femoral head leads to degeneration of the head and finally to osteoarthritis of the hip. Decompression is the most widely used treatment, but its effectiveness is limited. It has been proposed instillation of stem cells in addition to decompression would lead to better results. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified two systematic reviews including two randomized trials. We combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. We concluded instillation of bone marrow stem cells at the time of core decompression probably slows progression to osteoarthritis of the hip in patients with osteonecrosis of the femoral head and might reduce the need of subsequent surgeries. It is unclear whether it has any effect on the functionality because the certainty of the evidence is very low.

## Problem

Osteonecrosis of the femoral head mainly affects adults between the third and sixth decade of life. It has multiple causes, but it is generally produced by a severe deficiency of blood flow leading to bone necrosis and subsequent collapse of the femoral head. In the absence of early intervention with intention to preserve the native joint, there is a high risk of developing osteoarthritis of the hip. Decompression is the most widely used treatment for avascular necrosis of the femoral head, but its effectiveness is limited.

Use of mesenchymal stem cells from adult bone marrow, in addition to decompression, would promote bone formation and neovascularization, which could improve prognosis in early stages of osteonecrosis. However, there

is controversy about whether its ability to improve joint function or to increase the time until requirement of total hip arthroplasty.

## Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information, we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

**Key messages**

- Instillation of bone marrow stem cells at the time of core decompression in osteonecrosis of the femoral head probably slows progression to osteoarthritis and may reduce the need for subsequent surgeries.
- It is unclear whether it has any effect on the functionality because the certainty of the evidence is very low.

**About the body of evidence for this question**

What is the evidence. See evidence matrix in Epistemonikos later	We found two systematic reviews [1],[2] which included seven primary studies [3],[4],[5],[6],[7],[8],[9], two of them [3],[4], corresponded to randomized controlled trials. This table and the summary in general are based on the latter.
What types of patients were included	One study [4] included patients between 18 and 55 years of age with osteonecrosis of one or both hips stages IC to IIC according to the ARCO ( Association Research Circulation Osseous) classification with risk factors such as trauma, steroid use, alcohol abuse, Caisson disease or idiopathic aetiology (some patients had more than one cause). The other randomized study [3] included patients without specifying age with osteonecrosis of one or both femoral heads ARCO stage I or II (without subtype specification), of varied aetiologies including traumatic, steroid use, alcohol abuse, Cushing's disease, pregnancy induced and idiopathic.
What types of interventions were included	Both studies included as intervention stem cells derived from bone marrow injected into the necrotic area through a tunnel of decompression. One study [3] used a concentrate of mononuclear cells derived from bone marrow obtained from iliac crest, in doses of 5x10 <sup>8</sup> cells (total mononuclear cell count).The second study [4] used mesenchymal stem cells obtained after two weeks of culture of concentrate mononuclear cells derived from bone marrow obtained from the sub trochanteric region of the affected femur at doses of 2x10 <sup>6</sup> cells (total mesenchymal stem cell count). Both studies compared against core decompression alone
What types of outcomes were measured	Harris Hip Score, progression to a more advanced stage according to ARCO classification, volume of necrotic area assessed by magnetic resonance, progression and need of vascularized bone graft or conversion to total hip arthroplasty.

**Summary of findings**

Information on the effects of instillation of stem cells at the time of core decompression in osteonecrosis of the femoral head is based on two randomized controlled trials [3],[4] including 148 cases in 133 patients. Information about progression, conversion to bone graft and conversion to total hip arthroplasty are based on one study [4]. The functionality is based on a second study [3].

- Instillation of bone marrow stem cells at the time of core decompression probably slows progression in early-stage osteonecrosis of the femoral head. The certainty of the evidence is moderate.
- Instillation of bone marrow stem cells at the time of core decompression in osteonecrosis of the femoral head might decrease conversion to vascularized bone graft. The certainty of the evidence is low.
- Instillation of bone marrow stem cells at the time of core decompression in osteonecrosis of the femoral head might decrease the conversion to total hip arthroplasty. The certainty of the evidence is low.
- It is unclear whether bone marrow stem cells instillation upon core decompression in osteonecrosis of femoral head improves functionality because the certainty of the evidence is very low.

<b>Instillation of bone marrow stem cells in addition to core decompression in osteonecrosis of femoral head</b>				
<b>Patients</b>	Osteonecrosis of the femoral head			
<b>Intervention</b>	Core decompression and stem cell instillation			
<b>Comparison</b>	Core decompression			
Outcomes	Absolute effect*		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITHOUT stem cells	WITH stem cells		
	Difference: patients per 1000			
Progression to ARCO stages III or IV	227 per 1000	39 per 1000	RR 0.17 (0.04 to 0.72)	⊕⊕⊕○ Moderate <sup>1</sup>
	Difference: 188 patients less per 1000 (Margin of error: 64 to 218 less)			
Conversion to vascularized bone graft	114 per 1000	38 per 1000	RR 0.33 (0.07 to 1.63)	⊕⊕○○ <sup>1 2</sup> Low
	Difference: 76 patients less per 1000 (Margin of error: 106 less to 72 more)			
Conversion to total hip arthroplasty	114 per 1000	9 per 1000	RR 0.08 (0.00 to 1.33)	⊕⊕○○ <sup>1 2</sup> Low
	Difference: 105 patients less per 1000 (Margin of error: 114 less to 38 more)			
Harris Hip Score (HHS) 12 months follow-up	76.7 points on average	83.7 points on average	MD 6.97 (0.72 to 13.22)	⊕○○○ <sup>3 4</sup> Very low
	Difference: 7 points better with stem cells (Margin of error: (9.95 to 16.30 points better))			

RR: Risk ratio.  
MD: Mean difference  
Margin of error = 95% confidence interval (CI).  
GRADE: evidence grades of the GRADE Working Group (see later in this article)

\* The risk **WITHOUT stem cells** is based on the risk of the control group of the trials. The risk **WITH stem cells** (and its margin of error) is calculated from relative effect (and its margin of error)

1. The certainty of the evidence was downgraded in one level for publication bias because the information comes from a single study, and the only review identified might have missed relevant studies.
2. The certainty of the evidence was downgraded in one level for imprecision.
3. The certainty of the evidence was downgraded in two levels for imprecision.
4. The certainty of the evidence was downgraded in one level for risk of bias.

## About the certainty of the evidence (GRADE)\*

⊕⊕⊕⊕

**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

**Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

\*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

## Other considerations for decision-making

### To whom this evidence does and does not apply

- This evidence applies to adult patients with diagnosis of osteonecrosis of femoral head of traumatic or atraumatic aetiology, in ARCO stages I or II.

### About the outcomes included in this summary

- This summary considers functionality, progression to more advanced ARCO stages (III or IV ), and subsequent need of vascularized bone graft or need of total hip arthroplasty, outcomes considered critical for decision making by the authors of this summary.

### Balance between benefits and risks, and certainty of the evidence

- Since there is uncertainty about the benefits of stem cell therapy for osteonecrosis of femoral head, it is not possible to make an adequate risk/benefit balance .
- If the observed benefit were real, it would be an intervention with a very favorable risk/benefit ratio.

### Resource considerations

- Stem cells therapy currently represents a high cost and limited access intervention, so it is likely that patients and physicians would not be inclined to use it, even more considering the existent uncertainty about its effects.
- It is not possible to determine whether it is a cost effective intervention that would generate long-term savings, because the certainty of the evidence regarding their benefits is poor.

### Differences between this summary and other sources

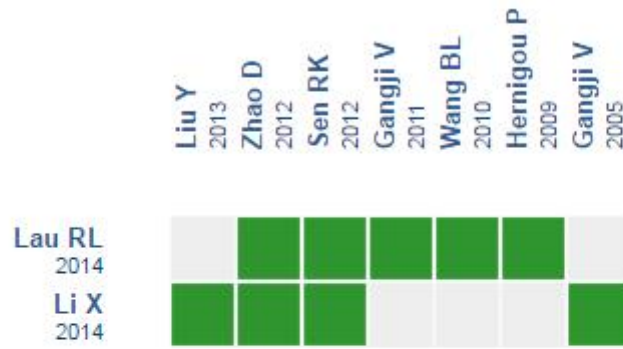
- The key messages of our summary are partially consistent with the conclusions of the individual systematic reviews identified, which give a more optimistic conclusion, because of the weight given to observational studies included. They also highlight the proven benefits of stem cell therapy in preclinical studies.
- Our summary is consistent with the main clinical guidelines [10],[11] concerning the treatment of osteonecrosis of femoral head, where the need for prospective studies with documentation of the initial stage of disease, progression and time to total hip arthroplasty is suggested.

### Could this evidence change in the future?

- The probability that future evidence change the key findings of this summary is high due to the limitations of the existing evidence .
- There are multiple ongoing studies that could provide relevant information for this question.

## How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.

The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.

The *rows* represent systematic reviews that share at least one primary study, and *columns* display the studies.

The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Core decompression and stem cell instillation versus core decompression alone for early stage osteonecrosis of the femoral head](#)

## Notes

The upper portion of the matrix of evidence will display a warning of “new evidence” if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here

<http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

## Conflicts of interest

The authors do not have relevant interests to declare.

## References

1. Lau RL, Perruccio AV, Evans HM, Mahomed SR, Mahomed NN, Gandhi R. Stem cell therapy for the treatment of early stage avascular necrosis of the femoral head: a systematic review. *BMC Musculoskelet Disord.* 2014 May 16;15:156. | [CrossRef](#) | [PubMed](#) |
2. Li X, Xu X, Wu W. Comparison of bone marrow mesenchymal stem cells and core decompression in treatment of osteonecrosis of the femoral head: a meta-analysis. *Int J Clin Exp Pathol.* 2014 Jul 15;7(8):5024-30. | [PubMed](#) |
3. Sen RK, Tripathy SK, Aggarwal S, Marwaha N, Sharma RR, Khandelwal N. Early results of core decompression and autologous bone marrow mononuclear cells instillation in femoral head osteonecrosis: a randomized control study. *J Arthroplasty.* 2012 May;27(5):679-86. | [CrossRef](#) | [PubMed](#) |

4. Zhao D, Cui D, Wang B, Tian F, Guo L, Yang L, Liu B, Yu X. Treatment of early stage osteonecrosis of the femoral head with autologous implantation of bone marrow-derived and cultured mesenchymal stem cells. *Bone*. 2012 Jan;50(1):325-30. | [CrossRef](#) | [PubMed](#) |
5. Hernigou P, Poignard A, Zilber S, Rouard H. Cell therapy of hip osteonecrosis with autologous bone marrow grafting. *Indian J Orthop*. 2009 Jan;43(1):40-5. | [CrossRef](#) | [PubMed](#) |
6. Liu Y, Liu S, Su X. Core decompression and implantation of bone marrow mononuclear cells with porous hydroxylapatite composite filler for the treatment of osteonecrosis of the femoral head. *Arch Orthop Trauma Surg*. 2013 Jan;133(1):125-33. | [CrossRef](#) | [PubMed](#) |
7. Wang BL, Sun W, Shi ZC, Zhang NF, Yue DB, Guo WS, et al. Treatment of nontraumatic osteonecrosis of the femoral head with the implantation of core decompression and concentrated autologous bone marrow containing mononuclear cells. *Arch Orthop Trauma Surg*. 2010 Jul;130(7):859-65. | [CrossRef](#) | [PubMed](#) |
8. Gangji V, De Maertelaer V, Hauzeur JP. Autologous bone marrow cell implantation in the treatment of non-traumatic osteonecrosis of the femoral head: Five year follow-up of a prospective controlled study. *Bone*. 2011 Nov;49(5):1005-9. | [CrossRef](#) | [PubMed](#) |
9. Gangji V, Hauzeur JP. Treatment of osteonecrosis of the femoral head with implantation of autologous bone-marrow cells. Surgical technique. *J Bone Joint Surg Am*. 2005 Mar;87 Suppl 1(Pt 1):106-12. | [PubMed](#) |
10. Carli A, Albers A, Séguin C, Harvey EJ. The Medical and Surgical Treatment of ARCO Stage-I and II Osteonecrosis of the Femoral Head. *JBJS Rev*. 2014;2(2):e2. | [CrossRef](#) |
11. Zalavras CG, Lieberman JR. Osteonecrosis of the Femoral Head: Evaluation and Treatment. *J Am Acad Orthop Surg*. 2014;22 (7 ):455-464. | [CrossRef](#) |

**Author address:**

[1] Facultad de Medicina  
Pontificia Universidad Católica de Chile  
Lira 63  
Santiago Centro  
Chile



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