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Original article

Intra-articular injection of autologous bone marrow aspirate concentrate in the treatment of osteoarthritis of the thumb first carpometacarpal joint: A pilot study

Injection de moelle osseuse concentrée totale autologue chez des patients atteints de rhizarthrose: étude pilote

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ABSTRACT

This study aimed to evaluate the effect of bone marrow aspirate concentrate (BMAC) in the treatment of osteoarthritis of the thumb first carpometacarpal joint. Injections were carried out in 27 thumbs. According to the Dell classification, there were 2 stage I, 11 stage II, 13 stage III and 1 stage IV cases. The bone marrow was aspirated from the iliac crest, concentrated by centrifugation, and injected under fluoroscopic control into the pathological thumb. Results were assessed at a mean 16 months' follow-up (range, 8–26). Clinical evaluation comprised QuickDASH and PRWE scores, pain at rest on a numerical analog scale (NAS), and thumb column abduction on goniometry. QuickDASH and PRWE scores were 59 (range, 27–82) and 88 (range, 37–125) preoperatively and 29 (range, 0–64) and 50 (range, 1–99) postoperatively, respectively. Mean pain at rest on NAS improved from 7 (range, 1–10) to 4 (range, 0–9). Thumb abduction improved by a mean 18° over preoperative data. No postoperative complications were found. Two patients had to be operated on for inefficacy of injection. This is the first article presenting the effect of an intra-articular injection of BMAC in the thumb first carpometacarpal joint and the results were encouraging. Many patients showed improved quality of life and pain relief. These injections appear to be an effective means of postponing surgery.

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R É S U M É

Le but de cette étude était d'évaluer l'effet d'une injection de moelle osseuse concentrée totale (MOCT) autologue dans le traitement de la rhizarthrose. Les injections ont été réalisées sur 27 pouces. Selon la classification de Dell, on dénombrait 2 rhizarthroses de stade I, 11 de stade II, 13 de stade III et 1 de stade IV. La moelle osseuse était aspirée au niveau de la crête iliaque, concentrée par centrifugation, puis injectée sous contrôle scopique dans l'articulation. L'évaluation des résultats de l'injection au dernier recul a été faite à 16 mois postopératoires (8–26). L'évaluation comprenait une mesure des scores fonctionnels QuickDASH et PRWE, l'évaluation de la douleur au repos par l'échelle numérique (EN), l'abduction de la colonne du pouce mesurée au goniomètre. Les scores QuickDASH et PRWE étaient respectivement de 59 (27–82) et 88 (37–125) en préopératoire contre 29 (0–64) et 50 (1–99) en postopératoire. La douleur moyenne au repos s'était améliorée en passant de 7 (1–10) à 4 (0–9). L'abduction de la colonne du pouce s'était améliorée de 18° en moyenne. Aucune complication n'a été

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mise en évidence. Deux patients ont dû être opérés du fait de l'inefficacité de l'injection. Il s'agit du premier article dans la littérature étudiant l'effet d'une injection de MOCT dans la rhizarthrose et les résultats rapportés sont encourageants. De nombreux patients semblent ressentir une amélioration de leur qualité de vie et une diminution des douleurs. Celle-ci paraît donc être un moyen efficace pour retarder le traitement chirurgical.

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1. Introduction

Since its discovery by Forestier in 1937 [1], numerous medical and surgical treatments have been proposed to relieve patients suffering from osteoarthritis of the thumb, a relatively common pathology, particularly in women over 50 years of age. To date, first-line treatment is conservative, mainly combining simple level I and II analgesics as well as non-steroid anti-inflammatory drugs (NSAIDs) and orthoses. Other local treatments [2] have also emerged, such as corticosteroid injection, mainly indicated for congestive attacks, but their role has yet to be determined, as shown by a randomized double-blind study in 2004 [3] where no significant difference was found between an intra-articular corticoid injection and a placebo injection. There is no consensus as to the contribution of hyaluronic acid, and the recommendations of the ACR [4] and the EULAR [5] conclude that there is only a weak symptomatic effect of these intra-articular injections. In the absence of curative conservative treatment, surgery is still the only option for patients with symptomatic advanced osteoarthritis of the thumb first carpometacarpal joint.

New therapies are emerging in degenerative joint pathologies and more particularly in osteoarthritis of the knee [6,7]. These cellular therapies involve mesenchymal stem cells, discovered in the 1970s by Friedenstein et al. [8,9], the main characteristics of which are their capacity to generate at least five different types of tissue: bone, cartilage, adipose, fibrous, and stromal, enabling hematopoiesis to be maintained. Finally, these cells are found in many tissues of the body and especially in bone marrow [10] and in the stromal vascular fraction of adipose tissue [11].

The aim of this study was to evaluate the results of the injection of autologous bone marrow aspirate concentrate in the treatment of osteoarthritis of the thumb first carpometacarpal joint.

2. Patients and method

2.1. Patients

A single-center retrospective descriptive pilot study was carried out over a 27-month period (September 2018 to November 2020). The inclusion criteria were the presence of osteoarthritis of the thumb first carpometacarpal joint, at all stages, according to the Dell classification [12] on X-ray, but

Table 1
Characteristics of the study population.

Total number of thumbs	27
Men	4 (17%)
Women	20 (83%)
Age (years)	55 (37–77)
Dominant hand	12 (44%)
Dell stage I	2 (7%)
Dell stage II	11 (41%)
Dell stage III	13 (48%)
Dell stage IV	1 (4%)
Follow-up (months)	16 (8–26)

without scapho-trapezio-trapezoid damage, after failure of 6 months' to 1 year's well-conducted conservative treatment combining level I and II analgesics, NSAIDs, orthoses and sometimes intra-articular injections of hyaluronic acid. Twenty-seven thumbs were included, in 20 women and 4 men, followed for a period of more than 8 months, with a mean age of 55 years (range, 37–77) (Table 1). The dominant side was involved 12 times. According to the Dell classification, there were 2 stage I, 11 stage II, 13 stage III and 1 stage IV cases. The main complaint was pain on mobilization of the thumb column and decreased opening of the first web space. All patients were reviewed at 1 month to check tolerance, and then at a mean 16 months (range, 8–26) to evaluate efficacy.

2.2. Surgical technique

The operation was performed in theater under general anesthesia, with the patient in supine position, the upper limb installed on a hand table. Bone marrow aspiration was performed at the anterior part of the iliac crest using a trocar (Fig. 1). Twenty cubic centimeters (cc) of bone marrow were aspirated from the cancellous bone and placed in a Heragen Max¹ centrifuge (DSM Biomedical, Exton, Pennsylvania, USA) for 60 s to isolate the nucleated elements from the harvested bone marrow (Fig. 2). We then injected 2 cc BMAC into the trapeziometacarpal joint under fluoroscopic control (Fig. 3) with an injection site at the posterior lateral edge of the joint to avoid damaging the tendon and nerve structures of the thumb. Once the procedure was completed, the patients returned home without postoperative immobilization and without prescription of NSAIDs.

2.3. Follow-up

Last follow-up was on average 16 months after injection (8–26). The main endpoint was improvement in QuickDASH functional score. Secondary end points were improvements in PRWE functional score; pain at rest on numerical analog scale (NAS), active complete abduction of the thumb column, measured by the angle between the first and second metacarpal, hand flat on a table, using a goniometer; pre- and post-operative pinch strength (kg) won pinch gauge (B and L EngineeringTM, North Coast Medical Inc., USA); radiological evaluation with posterior-anterior, lateral and Kapandji views; and the absence of intra- and post-operative adverse effects.

2.4. Total nucleated cell count

We estimated the number of nucleated cells present in the bone marrow of 4 iliac crests and 3 radii before and after centrifugation, using a Nucleocounter NC-200TM (ChemoMetec[®], Lillerød, Denmark).

¹ BD Stemflow hMSC Analysis Kit. For reproducible multicolor phenotyping of MSC expansions.

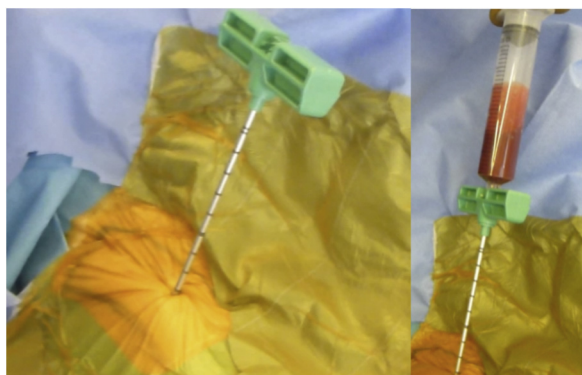


Fig. 1. Bone marrow collection from the anterior part of the iliac crest.

Table 2
Synthesis of pre- and post-operative results.

	Preoperative			Last follow-up		
	Mean	Median	(Range)	Mean	Median	(Range)
QuickDASH	59	59	(27–82)	29	27	(0–64)
PRWE	88	87	(37–125)	50	52	(1–99)
Pain on DPS	7	7	(1–10)	4	3	(0–9)
Abduction (M1–M2 angle)	56	55	(30–80)	74	80	(30–110)
Pinch (kg)	4.8	4.5	(1–8)	5	4.9	(2.5–8)

QuickDASH: quick version of the Disabilities of the Arm, Shoulder and Hand questionnaire; PRWE: patient-rated wrist evaluation; DPS: digital pain scale.

3. Results

3.1. Clinical results

Twenty-seven patients were reviewed (Table 2). We found clear improvement in functional scores, with QuickDASH and PRWE of respectively 29 and 50 at last follow-up compared to 59 and 88 before injection. Pain score was 4 after injection, compared to 7 before. Goniometric abduction of the thumb first carpometacarpal joint was 74° compared to 56° previously. Finally, key-pinch strength increased from 4.8 kg to 5 kg on average.

3.2. Postoperative X-rays

Eleven patients who had an X-ray between 6 months and 1 year postoperatively were still classified at the same Dell stage and

therefore did not show any obvious worsening. In 1 patient with stage III osteoarthritis of the thumb first carpometacarpal joint, a large medial osteophyte appeared on postoperative X-ray and the patient required surgical management.

3.3. Complications

After 1 month, no adverse effects or complications were noted at either the puncture or the injection site. Nevertheless, two patients requested operative surgery at 5 and 6 months due to the ineffectiveness of the treatment.

3.4. Total nucleated cell count

The average concentration of nucleated elements was 1.3×10^7 per ml and 6.4×10^7 per ml before and after centrifugation, respectively, in the anterior part of the iliac crest. After centrifugation, the concentration of nucleated elements was therefore 4.9 times higher after this procedure.

4. Discussion

In spite of the small number of patients in this study, the results seem encouraging in terms of pain and recovery of thumb mobility and function; Patient recruitment should be continued to in order to obtain a larger and thus more representative sample.

It would be interesting to be able to make an exact estimate of the number of mesenchymal stem cells that we inject into each thumb first carpometacarpal joint after centrifugation. Unfortunately, at present there is no technology that allows this number to be measured accurately without first carrying out an amplification procedure in culture and then phenotyping by flow cytometry [13]. In order to have an idea of the number of stem cells present in the bone marrow, we therefore relied on Pittenger’s study [14], which concluded that the rate of nucleated cells in adult human bone marrow is low, ranging from 0.01% to 0.001%. We therefore began by estimating the number of nucleated cells present in the bone marrow of four of our patients; the average concentration of nucleated elements was 1.3×10^7 per ml and 6.4×10^7 per ml before and after centrifugation, respectively: i.e., 4.9 times higher after centrifugation. According to Pittenger, this gives a stem cell concentration ranging from 13 to 1300 MSC/cc of bone marrow before centrifugation and 64 to 6400 MSC/cc of bone marrow after centrifugation. These results are consistent with the concentrations of mesenchymal stem cells found by Hernigou et al. [15] in the iliac crest bone marrow of 16 patients with non-union of the tibia.

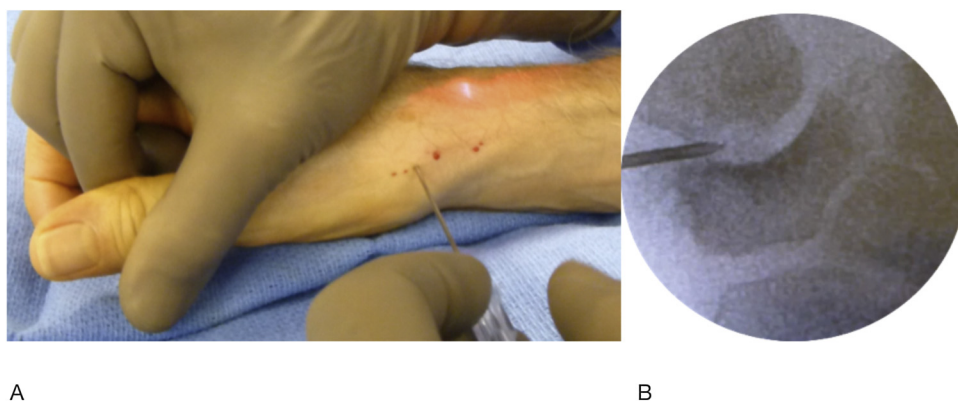


Fig. 3. Injection of BMAC into the thumb first carpometacarpal joint (A) under fluoroscopic control (B).

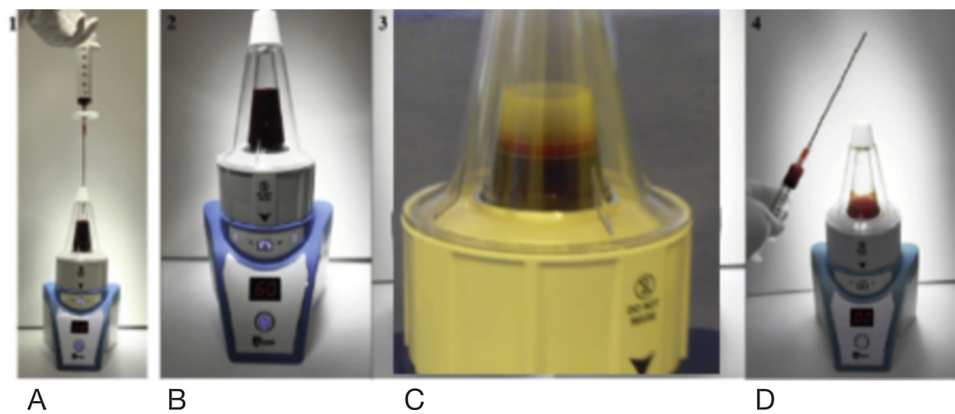


Fig. 2. Centrifugation and bone marrow concentration method. Injection of the bone marrow sample into the centrifuge (A). Centrifugation for 60 s (B). Individualization in 3 distinct phases (C). Sampling of the BMAC (buffy-coat) between the 2 horizontal markers (D).

In order to simplify the surgical procedure, we also measured the concentration of nucleated elements in the bone marrow of the distal end of the radius in three patients, without injecting it into the thumb first carpometacarpal joint afterwards, so that we could carry out this procedure under locoregional anesthesia and not under general anesthesia as we do at present. However, as the quantity of nucleated elements is about 8 times less ($8 \times 10^6/\text{ml}$ on average after centrifugation) than in the iliac crest, we abandoned this idea in order to maximize the effectiveness of our injections. Nevertheless, with a little experience, bone marrow harvesting from the anterior iliac crest could subsequently be performed under local anesthesia and thus reduce the intraoperative risk associated with general anesthesia. Note that it is also possible or even preferable to collect bone marrow from the posterior part of the iliac crest because it contains a greater number of mesenchymal stem cells [16].

In the scientific literature, few articles [17–25] studied the effect of BMAC injection for osteoarthritis in humans, and only that of Murphy et al. [26] concerned open surgery for osteoarthritis of the thumb after debridement and microfractures. The majority of these studies reported improvement in functional scores. However, Shapiro et al.'s study at the Mayo Clinic [27], which was the only placebo-controlled study to date, found no significant difference between injection of 5cc of BMAC and injection of saline in patients with bilateral osteoarthritis of the knee, with equivalent improvement in functional scores in both groups. All these studies therefore reach the same conclusions as ours and suggest an effect of BMAC injection on symptoms linked to osteoarthritis. The aim, of course, is to determine a treatment that is less cumbersome than arthroplasty, enabling same-day discharge, at lower cost, and avoiding the risk of surgical complications.

In a second step, it would be interesting to continue this study in a larger sample of patients, with a placebo group. Although it is ethically difficult to create a hyaluronic acid or corticosteroid injection control group, results recently published concerning PRP injection in knee osteoarthritis [28] and osteoarthritis of the first carpometacarpal joint [29] make it an ideal candidate for the creation of a control group because of the significant clinical improvement obtained.

Finally, we will have to determine the place of bone-marrow stem-cell injections in the therapeutic armamentarium of patients with osteoarthritis of the thumb first carpometacarpal joint. Should it be reserved for the early or moderate stages awaiting surgery? Or can it compete with prosthetic replacement surgery, given the excellent results obtained with certain prostheses and implants?

5. Conclusion

Cellular therapies based on mesenchymal stem cells could prove to be an innovative curative therapeutic alternative, but there is still a long way to go before developing a treatment that would allow real cartilage regeneration. This study has the merit of being a first approach to the as yet unexplored therapeutic possibilities of these famous stem cells whose pluripotency and self-renewal capacities make them a first-choice therapeutic target. They open the doors to a new type of treatment for osteoarthritis of the thumb first carpometacarpal joint and the present results should encourage hand surgeons to become more involved in these cellular therapies, which could, perhaps one day, profoundly change our surgical practices.

Conflicts of interest

The authors declare they have no competing interests.

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Ethics

No declaration.

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