Does augmented core decompression decrease the rate of collapse and improve survival of femoral head avascular necrosis? Case-control study comparing 184 augmented core decompressions to 79 standard core decompressions with a minimum 2 years' follow-up

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Original article

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Pierre **Martinot** [a,b], Julien **Dartus** [a,b], Arthur **Justo** [c], Hicham **Riouach** [d], Paul **Cremer** [e], Charles-Henri **Flouzat-Lachaniette** [f], Philippe **Hernigou** [f], Luc **Kerboull** [g], Philippe **Chiron** [hi] and the French Society of Orthopaedic Surgery and Traumatology (SoFCOT)[j]

a Univ. Lille, CHU Lille, Hôpital Salengro, Hauts de France, F-59000 Lille, France

b Service d'Orthopédie, Hôpital Salengro, Place de Verdun, CHU Lille, F-59000 Lille, France

c Hôpital Pierre-Paul-Riquet, place du Dr-Baylac, TSA 40 031, 31059 Toulouse cedex 9, France

d Hôpital Gabriel Montpied, CHU de Clermont Ferrand BP 69, 63003 Clermont Ferrand Cedex 01, France

e CHU Pellegrin-Tripode, place Amélie-Raba-Léon, 33076 Bordeaux, France

f Hôpital Henri Mondor, 51 Avenue du Maréchal de Lattre de Tassigny, 94010 Créteil, France
g Codirecteur du symposium de la SOFCOT, Marcel Kerboull Institute, 39 rue Buffon, 75005 Paris, France

h Département de Chirurgie Orthopédique, Traumatologique et Réparatrice, Hôpital Pierre-Paul-Riquet, place du Dr-Baylac, TSA 40 031, 31059 Toulouse cedex 9, France

i Chairman of SOFCOT symposium

j SOFCOT, 56, rue Boissonade, 75014 Paris, France #

*Corresponding author: Pierre Martinot,

Service d'Orthopédie, Hôpital Salengro, Place de Verdun, CHU Lille, F-59000 Lille, France

Email: pierre.martinot@hotmail.fr Phone 06 62 42 76 92 Fax 03 20 44 66 07

The names of the participating SOFCOT members are listed at the end of the article

Abstract

Introduction

Avascular necrosis of the femoral head often progresses to femoral head collapse if not treated. Conservative treatment yields highly variable results and is not standardized, mainly because it is typically evaluated in small patient populations. This led us to conduct a large retrospective comparative study with the goals of 1) analyzing survival and functional outcomes, 2) looking for differences in survival between core decompression techniques (standard versus augmented), and 3) studying the risk factors for femoral head collapse and revision by arthroplasty.

Hypothesis

Core decompression limits the number of patients who suffer femoral head collapse requiring arthroplasty at 2 years' follow-up.

Methods

This multicenter, comparative, retrospective study analyzed 330 patient records (1975-2016) where at least 2 years' follow-up was available. Sixty-two patients were excluded from the analysis: 5 had a stage III with collapse, 5 were lost to follow-up, 2 died within 24 months of the procedure and 50 had incomplete data. The study included 263 patients with a mean age of 42 years (15.7–70). In the Ficat Classification, there were 51 cases of stage I necrosis, 186 cases of stage II and 22 cases of stage II with crescent sign (transition stage). The Kerboull angle on radiographs was between 5° and 20° in 40 patients, between 20° and 40° in 107 patients, between 40° and 60° in 52 patients and more than 60° in 29 patients. A standard core decompression was done in 79 patients and an augmented one in 184 patients. The more severe AVN cases (stage II) were more likely to be treated by augmented CD (160/184 patients, 87%) than by standard CD (48/79 patients, 61%) ($p < 0.001$).

Results

In the 263 patients, the overall survival (no arthroplasty at 2 years) was 73% (196/263). At 2 years, the survival rate (without arthroplasty) was 71% (56/79) in the standard CD group versus 76% (140/184) in the augmented CD group. This difference was significant when adjusted for Ficat stage and Kerboull angle (HR = 0.457, 95% CI [0.247-0.844] ($p = 0.012$)). When the survival data was adjusted to the Ficat stage, augmented CD was better than standard CD with 10-year survival of 58.1% vs 57.9% ($p = 0.0082$). More than 30% necrosis volume increased the risk of failure (HR = 3.291 95%CI [1.494-7.248] ($p = 0.0031$)). Also, a

Kerboull angle above 60° increased the risk of failure (HR = 3.148 95%CI [1.346-7.5] (p = 0.0083)).

Conclusion

After 2 years, CD for non-collapsed femoral head AVN prevents collapse and revision to arthroplasty in 73% of cases (196/268). Augmented CD improves the 2-year survival and the long-term survival after adjusting for preoperative characteristics (Kerboull angle and Ficat stage). The risk of collapse and need for arthroplasty is greater in patients with 30% necrosis volume on MRI and Kerboull angle above 60°.

Level of evidence: III; Retrospective case-control study

Keywords: osteonecrosis of the femoral head, avascular necrosis, core decompression, stem cells, bone grafting

1. Introduction

Idiopathic avascular necrosis (AVN) of the femoral head progresses with pain towards femoral head collapse that then requires hip arthroplasty in patients who are often still working [1,2]. The risk of progression for non-collapsed stages during a purely medical treatment has led to the development of conservative surgical techniques [2,3]. Better use of imaging modalities such as MRI, radiographs and CT scan provide earlier diagnosis and confirm the absence of subchondral fracture. While the risk factors for AVN have been extensively described [4,5], the indications for conservative treatment have not been.

Simple core decompression (CD) proposed in 1964 by Ficat [6-7] for cases without subchondral fracture are better than osteotomy because it does not deform the proximal femur, thus preserving the mechanical conditions needed to subsequently perform total hip arthroplasty (THA) if needed. Also, standard CD does not require the fibula to be removed, a bone that is typically used as a vascularized bone graft [3,8-11]. Recent studies propose using stem cells to improve the effectiveness of CD and increase the survival rate of AVN [10-13]. They may reduce the number of patients who progress to head collapse when the diagnosis is made early enough. However, no large studies have been done in France comparing standard to augmented CD.

This led us to conduct a large retrospective comparative study with the goals of 1) analyzing survival and functional outcomes, 2) looking for differences in survival between core decompression techniques (standard versus augmented), and 3) studying the risk factors for collapse and revision by arthroplasty. We hypothesized that core decompression limits the number of patients who suffer a collapse requiring arthroplasty at 2 years' follow-up [1].

2. Methods

2.1 Patients

In the context of the 2018 SOFCOT symposium on this topic, 330 patient records from 1975 to 2016 were analyzed. Sixty-two patients were excluded from the analysis: 5 had undergone CD for a stage III in the Arlet and Ficat classification [14], 5 were lost to follow-up before 2 years, 2 died within 24 months of the procedure and 50 had incomplete data for estimating survival. Proximal femoral osteotomy and vascularized fibula grafts were not taken into account since so few cases were done (1 and 4 patients, respectively) (Figure 1).

Excluded were patients with femoral head collapse (stage III in Ficat classification, stage 4 in ARCO classification) [14-15], patients with history of bone radiation, post-traumatic osteonecrosis, inflammatory arthritis, or septic arthritis. Patients in whom we could not analyze the main endpoints (head collapse at 2 years and revision by THA) were excluded.

At a mean follow-up of 31.4 ± 55.2 months (24–505 months), 79 simple CD or 30% (79/263) and 184 augmented CD or 70% (184/263) were analyzed (Table 1). Among the augmented CD procedures, 84 were done with autologous cancellous bone fragments, 65 with bone-marrow derived stem cells, 5 with hematopoietic stem cells including platelet-rich plasma (PRP), 3 with bone marrow-derived stem cells and PRP, and 27 with non-concentrated bone marrow + rhBMP2 injection (Genetics Institute, Boston, MA, USA) [16] (Table 2).

Of the 263 patients included in the analysis, the mean age was 42 ± 13 years (16.5–70 years). The mean weight, height, and body mass index (BMI) were 80 ± 17 kg, 174 ± 8 cm, 26.2 ± 5.3 kg/m^2, respectively. Thirty-three patients (13%) had a BMI above 30 (33/263). There were more men (209) than women (54). The patients were Charnley A in 70 cases, Charnley B in 156 cases and Charnley C in 9 cases [17] (28 cases not specified (10%)). The right side was affected in 141 patients and the left side in 122.

Among the risk factors studied, 129 patients were smokers, 92 had undergone corticosteroid therapy, 61 were alcoholics, 42 had a chronic disease (Crohn's disease, cancer, etc.), 39 had high blood pressure, 31 had high blood lipids, 19 were asthmatic, 13 had arteritis, 13 were diabetic, 9 had systemic lupus, 8 had a received a kidney transplant, 3 had sickle cell disease, 3 were taking anticoagulants and 1 was undergoing dialysis. The two groups were not comparable in terms of medical history, with more asthmatic patients in the augmented CD group and more patients who had a kidney transplant and who were alcoholics in the standard CD group (Table 1).

In the Ficat classification of AVN of the femoral head [14], 51 patients were stage 1, 186 were stage 2, 22 were transition stage (stage 2 with crescent sign) (4 not specified (1.5%)). The Kerboull angle [18] on radiographs was between 5° and 20° in 40 patients, between 20° and 40° in 107 patients, between 40° and 60° in 52 patients and more than 60° in 29 patients (35 not specified (13%)). The necrosis volume on MRI was less than 15% in 45 patients, 15% to 30% in 121 patients and more than 30% in 60 patients (37 not specified (14%)).

The mean preoperative clinical outcome scores were 5.5 (1-10) for the UCLA activity score [19], 12.8 (7-18) for the Merle d'Aubigné Postel (MDP) [20], 63.6 (11-100) for the Harris Hip score [21], and 3.2 (1-5) for the Devane activity score [22]. In terms of occupation before the surgery, 8 patients were unemployed, 69 were on medical leave, 33 worked seated, 62

alternated between sitting and standing, 36 worked while standing, 37 carried heavy loads and 10 were retired (Table 1).

The augmented CD group had significantly younger patients in it (41.2 ± 14 years versus 45.2 ± 11 years ($p = 0.015$)), had more severe disease (Stage 2 = 43/79 (54%) versus 143/263 (78%), Stage 2 with crescent sign = 5/79 (6%) versus 17/263 (9%) ($p < 0.001$)), had a larger Kerboull angle [18] ((40° to 60° = 11/79 (14%) versus 41/263 (22%); more than 60° = 1/79 (1%) versus 28/263 (15%) ($p = 0.002$)). Thus, the patients in the augmented CD group had more advanced disease than those in the standard CD group.

2.2 Methods

The study included all patients with primary AVN of the hip who underwent conservative non-arthroplasty surgical treatment and who agreed to their data being used in the context of this study. Conservative surgery was divided into two groups: standard CD and augmented CD. The CD technique was left up to the surgeon given the multicenter nature of this study. Generally, multiple holes were made manually using a small-caliber trephine. This was the only intervention done in the standard CD group. In the augmented CD group, an adjunctive treatment was added (autograft, bone marrow or hematopoietic stem cells, with or without PRP) (Table 2).

2.3 Assessment methods

Current demographic, surgical and radiological data were collected either during an office visit, over the telephone or by consulting the medical records. Data on the treatment done, complications and other adverse events were collected throughout the hospital stay and during the follow-up period. The clinical outcomes consisted of the Devane score [22], the UCLA score [19], the Harris Hip score [21], the MDP score [20] and the occupation before surgery. The change in these parameters was calculated from preoperative to follow-up. The radiographic analysis consisted of measuring the Kerboull angle [18] on radiographs and the necrosis volume on MRI.

The main endpoint was the absence of THA for head collapse within 2 years of CD for AVN. The secondary endpoints were the clinical scores, radiographic data, and complication rates. The patient records were reviewed retrospectively irrespective of the surgery date as long as the follow-up was at least 24 months.

2.4 Data processing and statistical analysis

The quantitative variables were summarized by their mean and standard deviation or median and interquartile interval. The normality of the data distribution was verified graphically and using the Shapiro-Wilk test. Qualitative variables were described by their counts and percentage. If the sample size was large enough, qualitative variables were compared between groups using the Chi-square test. If this test could not be used (expected count < 8), the Fisher exact test was used. When the sample size was large enough, quantitative variables were compared between groups using Student's *t* test. If the data were not normally distributed, the Wilcoxon test was used instead.

The occurrence of head collapse and revision by THA was estimated using the Kaplan-Meier method. To look for risk factors for THA at 2 years postoperative, a proportional Cox risk model was used. The significance threshold was set at 0.05. The statistical analysis was performed with SAS software (version 9.4, SAS Institute, Cary NC, USA).

3. Results

Seven patients died more than 2 years after the CD procedure, an average of 80 months later (35–119 months). At 2 years' follow-up, 74% of all patients (196/263) had not undergone THA (Figure 2). When broken down by procedure, 71% (56/79) of patients who had undergone standard CD and 76% (140/184) of those who had undergone augmented CD did not require THA (Figs. 3 and 4). The survival at 2 years and the maximum follow-up was not statistically different based on the standard statistical analysis (at 2 years, HR = 0.816 95%CI [0.493-1.35] (p = 0.429) / and at maximum follow-up, HR = 0.936 95%CI [0.619-1.41] (p = 0.756)) (Figs. 3 and 4). After adjusting the data to account for initial differences in Kerboull angle and Ficat stage, the augmented CD procedure had significantly better survival than standard CD at 2 years: 70.9% versus 76.1% [HR = 0.457 95%CI [0.247-0.844] (p = 0.012)] and at the maximum follow-up 57.9% versus 58.1% [HR = 0.504, 95%CI [0.304-0.83] (p = 0.0082)].

At the review, the mean clinical scores were 5.7 (1-10) for the UCLA, 15 (7-18) for the MDP, 81.6 (30-100) for the Harris, and 3.2 (1-5) for the Devane. In terms of occupation at the final assessment, 14 patients were unemployed, 65 were on medical leave, 23 did seated work, 70 alternated between sitting and standing, 40 worked while standing, 24 carried heavy loads and 18 were retired.

Calculating the change (delta) between the preoperative measure and the final follow-up identified significantly better functional improvement after augmented CD than standard CD with 0.51 ± 2.1 versus −0.21 ± 1.95 for the UCLA score (p = 0.009), 11.56 ± 21.42 versus

18.69 ± 20.89 for the Harris Hip score (p = 0.019) and 1.18 ± 3.69 versus 2.49 ± 3.14 for the MDP (p = 0.020) (Table 3).

In terms of postoperative complications, there were two superficial infections, one pulmonary embolism and one pertrochanteric fracture. There were too few complications to look for a difference between groups (Table 4).

When the success of the procedure was analyzed relative to Ficat stage, the success rate was 84% for stage I (41/49), 66% for stage II (121/184) and 73% (16/22) for stage transition (stage II with crescent sign) (Table 5). When the success of the procedure was analyzed relative to the necrosis volume, the success rate was 74% for less than 15% volume (35/47), 84% for 15% to 30% volume (96/114) and 48% for volume greater than 30% (26/56) (Table 5). The subset of patients with more than 30% necrosis volume had a significantly higher risk of failure than the other patients [HR = 3.291, 95%CI [1.494-7.248] (p = 0.0031)] (Table 6).

When the success rate of the procedure was analyzed relative to the necrosis size (Kerboull angle on radiographs), the success rate was 76% for angles below 20° (29/38), 82% for angles between 20° and 40° (85/104), 55% for angles between 40° and 60° (27/100), 41% for angle greater than 60° (12/29) (Table 5). The subset of patients with necrosis size greater than 60° had a significantly higher risk of failure than the other patients [HR = 3.148, 95%CI [1.346-7.5] (p = 0.0083)] (Table 6). Thus the risk factors for failure of conservative treatment were necrosis volume above 30% [HR = 3.291 95%CI [1.494-7.248] (p = 0.0031)] and necrosis angle greater than 60° [HR = 3.148 95%CI [1.346-7.5] (p = 0.0083)].

The functional outcome scores were also predictive of progression to head collapse at 2 years (stage III). Indeed, patients who had low preoperative clinical scores (Devane, UCLA, Harris Hip and MDP) had a significantly higher risk of progression to head collapse with respectively, HR = 0.797 (95%CI [0.637-0.997] (p = 0.0468)), HR = 0.873 95%CI ([0.775-0.983] (p = 0.0253)), HR = 0.973 (95%CI [0.959-0.988] (p = 0.003)) and HR = 0.895 (95%CI [0.809-0.997] (p = 0.0453)) (Table 6).

4. Discussion

In France, no large recent studies on the outcome of hips after conservative treatment for AVN have been conducted as far as we know. Our study found a high survival rate (74%) 2 years after CD. The overall survival rate of all techniques pooled, all necrosis volumes in stage I and II of the Ficat classification with THA due to head collapse as the endpoint was

74%, which appears to be clearly better than isolated medical treatment reported in the literature [6,16,23,24].

By factoring in the preoperative differences between groups (Kerboull angle and Ficat stage), the patients who underwent augmented CD had significantly better survival at 2 years ($p = 0.012$) and at the maximum follow-up ($p = 0.0082$). Given the introduction of cell therapy, several authors endorse doing CD in combination with stem cells to improve the hip survival (augmented CD) [24-30]. Our statistical analysis took into account the dissimilarities in the two CD groups since there was a large share of severe necrosis cases in the augmented CD group (Ficat stage and Kerboull angle). We could not compare the augmented CD techniques among each other given the large differences between them (5 different techniques). Different techniques were used because the choice was left up to the surgeons who participated in our study. The magnitude of improvement in the functional scores that we assessed (UCLA, Harris, MDP) was better in the augmented CD group than in the standard CD group.

A large volume of necrosis on MRI and high Kerboull angle were risk factors for revision by THA, which is consistent with other published studies on this topic [31,32]. Thus, it is crucial to carefully analyze these two parameters before considering doing CD [33]. While there was a statistical trend in stage II with crescent sign cases, we did not find an impact of the Ficat stage on the occurrence of head collapse, despite what is said in the literature [34]. This may explain the uneven distribution of patients (Table 1 difference based on Ficat stage ($p < 0.001$)) in each group and the heterogeneous nature of the groups studied. The fact that patients with less than 15% necrosis volume (A in ARCO) had the same probability of needing THA than those with 15% to 30% necrosis volume (B in ARCO) is inconsistent and does not correspond to published data [32]. This may be explained by the position of the necrosis [35,36], which was not evaluated in our study. Moreover, drilling 8 mm holes could weaken the subchondral bone; small size necrosis or volume < 10% was not always an indication for CD, since the natural history is more favorable [1]. Conversely, drilling 4 mm holes and injecting stem cells may not have these effects, although this needs to be confirmed.

Determining the clinical outcome scores in the entire study cohort was important because the patients with the worst preoperative scores (Devane, UCLA, Harris and MDP) were more likely to need THA. The direct relationship between the necrosis stage and the clinical symptoms explains this finding well in our opinion [37]. Thus, it seems preferable to do conservative treatment in these patients since it primarily consists of patients with low grade necrosis on the Ficat classification, with smaller necrosis volume and size [16,38].

Our study has several limitations.

1) This was a retrospective study, which implies missing data (1% to 14% of main parameters) and exclusion of patients who did not have 2 years of follow-up available.

2) The population in our study was diverse and the study was not randomized. However, the large number of patients analyzed limits the impact of this factor.

3) We used recourse to THA for head collapse as the primary endpoint. This is certainly a bias because certain patients could have benefited from THA before they experienced head collapse or certain patients may have undergone CD later after pain symptoms appeared.

4) The augmented CD technique differed between participating sites. Thus, it is undeniable that the various CD done did not have the same impact on the clinical outcomes, which may contribute to bias. The fact that we could not do a sub-group analysis because these sub-groups were too small limits our interpretation of how using these augmented CD techniques impacted the outcome. The difference in effectiveness between multiple CD versus standard CD has not been studied, although the first appears more effective [39,40].

5) We did not look at the effect of the necrosis location on the risk of head collapse, although this appears to be linked to the collapse risk [36]. It would be interesting to do a larger study to compare the effectiveness of various types of augmented CD techniques to each other.

5. Conclusion

Doing CD for femoral head AVN reduces the need for THA in a large portion of patients at 2 years (74%). A large necrosis volume (> 30%) and large necrosis size (>60°) were risk factors for revision by THA. Augmented CD improves 2-year survival and long-term survival after adjusting for preoperative characteristics (Kerboull angle and Ficat stage). Augmented CD yields better clinical outcomes. While the literature suggests adding stem cells in these patients' hip, the large range of techniques employed in this study precludes us from drawing any conclusions about this method.

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Outside this study, Philippe Hernigou declares being a consultant for Ceraver, Philippe Chiron declares having received royalties from Adler, Luc Kerboull declares being a consultant for Medacta and Zimmer-Biomet, Charles Henri Flouzat Lachaniette declares being a consultant for Ceraver and Lépine. The other authors have no conflict of interest outside this study.

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Author contributions:

P. Martinot: acquisition, analysis and interpretation of data, writing of article
J. Dartus: analysis of data and critical review of the article for intellectual content
A. Justo: acquisition of data
H. Riouach: acquisition, analysis and interpretation of data
P. Cremer: acquisition, analysis and interpretation of data
CH. Flouzat Lachaniette: acquisition, analysis and interpretation of data; surgical procedures
P. Hernigou: surgical procedures; critical review of article for intellectual content
L. Kerboull: acquisition, analysis and interpretation of data; surgical procedures
P. Chiron: acquisition, analysis and interpretation of data; surgical procedures; critical review of article for intellectual content; final approval of version being submitted.

References

[1] Mont MA, Zywiel MG, Marker DR, Mcgrath MS, Delanois RE. The natural history of untreated asymptomatic osteonecrosis of the femoral head: a systematic literature review. J Bone Joint Surg Am 2010;92:2165-70.

[2] Fukushima W, Fujioka M, Kubo T, Tamakoshi A, Nagai M, Hirota Y. Nationwide epidemiologic survey of idiopathic osteonecrosis of the femoral head. Clin Orthop Relat Res 2010;468:2715-24.

[3] Marciniak D, Furey C, Shaffer JW. Osteonecrosis of the femoral head. A study of 101 hips treated with vascularized fibular grafting. J Bone Joint Surg Am 2005;87:742–747.

[4] Cui L, Zhuang Q, Lin J, Jin J, Zhang K, Cao L, et al. Multicentric epidemiologic study on six thousand three hundred and ninety-five cases of femoral head osteonecrosis in china. Int Orthop 2016;40:267-76.

[5] Yoon BCH, Lee YK, Kim KC, Ha YC, Koo KH. No differences in the efficacy among various core decompression modalities and non-operative treatment: a network meta-analysis. Int Orthop 2018;42:2737-2743.

[6] Ficat P, Arlet J, Vidal R, Ricci A, Fournial JC. Therapeutic results of drill biopsy in primary osteonecrosis of the femoral head (100 cases). Rev Rhum Mal 1971;38:269-76.

[7] Ficat P, Grijalvo P. Long-term results of the forage-biopsy in grade I and II osteonecrosis of the femoral head. Apropos of 133 cases re-examined after an average time of 9 years 6 months. Rev Chir Orthop 1984;70:253-5.

[8] Calori G, Mazza E, Colombo A, Mazzola S, Colombo M. Core decompression and biotechnologies in the treatment of avascular necrosis of the femoral head. EFORT Open Rev 2017;2:41-50.

[9] Mont MA, Cherian JJ, Sierra RJ, Jones LC, Lieberman JRr. Nontraumatic osteonecrosis

of the femoral head: where do we stand today? a ten-year update. J Bone Joint Surg Am 2015;97:1604-27.

[10] Hernigou P, Trousselier M, Roubineau F, Bouthors C, Chevallier N, Rouard H, Flouzat-lachaniette CH. Stem cell therapy for the treatment of hip osteonecrosis: a 30-year review of progress.Clin Orthop Surg 2016;8:1-8.

[11] Hernigou P, Flouzat-Lachaniette CH, Delambre J, Pignard A, Allain J, Chevallier N, Rouard H. Osteonecrosis repair with bone marrow cell therapies: state of the clinical art. Bone 2015;70:102-9.

[12] Xu S, Zhang L, Jin H, Shan L, Zhou L, Xiao L, Tong P. Autologous stem cells combined core decompression for treatment of avascular necrosis of the femoral head: a systematic meta-analysis. Biomed Res Int 2017;2017:6136205. doi: 10.1155/2017/6136205.

[13] Zhou W, Qu M, Lv Y, Zhu J. New advances in stem cell therapy for osteonecrosis of the femoral head. Curr Stem Cell Res Ther 2019;14:226-229.

[14] Ficat RP. Idiopathic bone necrosis of the femoral head. Early diagnosis and treatment. J Bone Joint Surg Br 1985;67:3-9.

[15] Gardeniers JWM. ARCO (Association Research Circulation Osseous): Committee on terminology and classification. ARCO News 1992;4:41–46

[16] Lieberman JR, Conduah A, Urist MR. Treatment of osteonecrosis of the femoral head with core decompression and human bone morphogenetic protein. Clin Orthop Relat Res 2004;429:139-45.

[17] Charnley J, Halley DK. Rate of wear in total hip replacement. Clin Orthop Relat Res 1975;112:170-9

[18] Kerboull M, Thomine J, Postel M, Merle d'Aubigné R. The conservative surgical treatment of idiopathic aseptic necrosis of the femoral head. J Bone Joint Surg Br 1974;56:291-6.

[19] Zahiri CA, Schmalzried TP, Szuszczewicz ES, Amstutz HC. Assessing activity in joint replacement patients. J Arthroplasty 1998;13:890-5.

[20] Merle d'Aubigné R. Numerical classification of the function of the hip. 1970. Rev Chir Orthop 1990;76:371-4

[21] Harris WH. Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. J Bone Joint Surg Am 1969;51:737–755.

[22] Devane PA, Horne JG, Martin K, Coldham G, Krause B. Three-dimensional polyethylene wear of a press-fit titanium prosthesis. Factors influencing generation of polyethylene debris. J Arthroplasty 1997;12:256-66.

[23] Mont MA, Marulanda GA, Seyler TM, Plate JF, Delanois RE. Core decompression and nonvascularized bone grafting for the treatment of early stage osteonecrosis of the femoral head. Instr Course Lect 2007;56:213-20.

[24] Andriolo L, Merli G, Tobar C, Altamura SA, Kon E, Filardo G. Regenerative therapies increase survivorship of avascular necrosis of the femoral head: a systematic review and meta-analysis. Int Orthop 2018;42:1689-1704.

[25] Papakostidis C, Tosounidis TH, Jones E, Giannoudis PC. The role of "cell therapy" in osteonecrosis of the femoral head. a systematic review of the literature and meta-analysis of 7 studies. Acta Orthop 2016;87:72-8.

[26] 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;87 suppl 1:106-12.

[27] 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;7:5024-30.

[28] Piuzzi NS, Chahla J, Jiandong H, Chughtai M, Laprade RF, Mont MA, Muschler GF,

Pascual-Garrido C. Analysis of cell therapies used in clinical trials for the treatment of osteonecrosis of the femoral head: a systematic review of the literature. J Arthroplasty 2017;32:2612-2618.

[29] Wang Z, Sun QM, Zhang FQ, Zhang QL, Wang LG, Wang WJ. Core decompression combined with autologous bone marrow stem cells versus core decompression alone for patients with osteonecrosis of the femoral head: A meta-analysis. Int J Surg 2019;69:23-31.

[30] Hua KC, Yang XG, Feng JT, Wang F, Yang L, Zhang H, et al. The efficacy and safety of core decompression for the treatment of femoral head necrosis: a systematic review and meta-analysis. J Orthop Surg Res 2019;14:306.

[31] Rajagopal M, Balch Samora J, Ellis TJ. Efficacy of core decompression as treatment for osteonecrosis of the hip: a systematic review. Hip Int 2012;22:489-93.

[32] Mazières B, Marin F, Chiron P, Moulinier L, Amigues JM, Laroche M, Cantagrel A. Influence of the volume of osteonecrosis on the outcome of core decompression of the femoral head. Ann Rheum Dis 1997;56:747-50.

[33] Steinberg DR, Steinberg ME, Garino JP, Dalinka M, Udupa JK. Determining lesion size in osteonecrosis of the femoral head. J Bone Joint Surg Am 2006;88 suppl 3:27-34.

[34] Castro FP JR, Barrack RL. Core decompression and conservative treatment for avascular necrosis of the femoral head: a meta-analysis. Am J Orthop (Belle Mead NJ) 2000;29:187-94.

[35] Sugano N, Atsumi T, Ohzono K, Kubo T, Hotokebuchi T, Takaoka K. The 2001 revised criteria for diagnosis, classification, and staging of idiopathic osteonecrosis of the femoral head. J Orthop Sci. 2002;7(5):601-5.

[36] Escudier JC, Ollivier M, Donnez M, Parratte S, Lafforgue P, Argenson JN. Superimposition of maximal stress and necrosis areas at the top of the femoral head in hip aseptic osteonecrosis. Orthop Traumatol Surg Res 2018;104:353-358.

[37] Hernigou P, Poignard A, Nogier A, Manicom O. Fate of very small asymptomatic stage-I osteonecrotic lesions of the hip. J Bone Joint Surg Am 2004;86:2589-93.

[38] Tripathy SK, Goyal T, Sen RK. Management of femoral head osteonecrosis: current concepts. Indian J Orthop 2015;49:28-45.

[39] Al omran A. Multiple drilling compared with standard core decompression for avascular necrosis of the femoral head in sickle cell disease patients. Arch Orthop Trauma Surg 2013;133:609-13.

[40] Mohanty SP, Singh KA, Kundangar R, Shankar V. Management of non-traumatic avascular necrosis of the femoral head-a comparative analysis of the outcome of multiple small diameter drilling and core decompression with fibular grafting. Musculoskelet Surg 2017;101:59-66.

Figure legends

Figure 1: Study flow chart for inclusions

Figure 2: Survival analysis at 2 years after conservative surgical treatment (endpoint was revision by THA)

Figure 3: Survival analysis at 2 years follow-up: standard CD versus augmented CD (endpoint was revision by THA)

Figure 4: Survival analysis at maximum follow-up: standard CD versus augmented CD (endpoint was revision by THA)

Table 1: Preoperative characteristics of the patients

Technique		Standard CD N=79 (%)	Augmented CD N=184 (%)	*p* value
Sex	Male	58 (73)	151 (82)	0.10
	Female	21 (27)	33(18)	
Occupation	Unemployed	5 (6.3)	2 (1.1)	ND
	Medical leave	20 (25.3)	48 (26)	
	Seated work	7 (8.9)	26 (14)	
	Seated/Standing work	17 (21.5)	42 (22.8)	
	Standing work	4 (5)	32 (17.4)	
	Carry heavy loads	14 (17.7)	23 (12.5)	
	Retired	8 (10)	2 (1.1)	
	Stage 1	31 (39)	20 (10.9)	
Ficat & Arlet stage [14]	Stage 2	43 (54.4)	143 (77.7)	**<0.001**
	Stage 2 with crescent sign	5 (6.3)	17 (9.2)	
4 not specified (1.5%)				
MRI volume	Less than 15%	12 (15)	33 (17.9)	
	15-30%	31 (39)	90 (48.9)	0.29
	More than 30%	22 (28)	38 (20.7)	
37 not specified (14%)				
Kerboull angle	5-20°	14 (17.7)	26 (14.1)	
[18]	20-40°	28 (35.4)	79 (42.9)	**0.002**
	40-60°	11 (13.9)	41 (22.3)	
	> 60°	1 (1.3)	28 (15.2)	
35 not specified (13.3%)				
Predisposition	Chronic disease	13 (16.5)	28 (15.2)	0.93
	Corticosteroid therapy	28 (35.5)	62 (33.7)	0.76
	Alcoholism	29 (36.6)	31 (16.9)	**0.002**
	Smoker	40 (50.6)	88 (47.8)	0.70
	High blood lipids	9 (11.4)	22 (11.9)	0.68
	Asthma	2 (2.5)	17 (9.3)	**0.034**
	High blood pressure	8 (10.1)	29 (15.8)	0.13
	Lupus	1 (1.3)	8 (4.3)	0.28
	Sickle cell disease	1 (1.3)	2 (1.1)	ND
	Arteritis	6 (7.6)	6 (2.3)	0.21
	Diabetes	6 (7.6)	6 (2.3)	0.21
	HIV	1 (1.3)	1 (0.5)	ND
	Anticoagulant	1 (1.3)	2 (1.1)	ND
	Dialysis	0	1 (0.5)	ND
	Kidney transplant	6 (7.6)	2(1.1)	**0.015**
	Transplantation	4	2 (1.1)	ND
	Cushing syndrome	1 (1.3)	0	ND
Age at inclusion	Mean ± SD	45.2 ± 11	41.2 ± 14	**0.015**
	Minimum / Maximum	16.5 / 68	60.7 / 20	
BMI	Mean ± SD	25.6 ± 3.6	26.4 ± 5.9	0.19
	Minimum / Maximum	15.4 / 34	17.2 / 63.9	

UCLA score [19]	Mean ± SD	5.5 ± 2.2	5.5 ± 2	0.99
	Minimum / Maximum	1 / 10	1 / 10	
Devane score [22]	Mean ± SD	3.2 ± 1.2	3.2 ± 1	0.90
	Minimum / Maximum	1 / 5	1 / 5	
MDP score [20]	Mean ± SD	12.8 ± 2.2	12.8 ± 2.2	0.98
	Minimum / Maximum	8 / 18	7 / 17	
Harris Hip score [21]	Mean ± SD	63.9 ± 17.7	64 ± 14	0.97
	Minimum / Maximum	31.8 / 100	11 / 93	

ND: Not determined since count is less than 8; Bold values indicate significant differences

BMI: Body Mass Index, MDP: Merle d'Aubigné Postel score

Table 2: Type of augmented core decompression (CD)

	Number (% augmented CD)
CD + BMP + non-concentrated bone marrow	27 (13.6)
CD with cancellous autograft	84 (45.7)
CD with bone marrow stem cells	65 (35.3)
Hematopoietic stem cells and PRP	5 (2.7)
Bone marrow stem cells and PRP	3 (1.6)

PRP: Platelet-rich plasma, BMP: Bone Morphogenetic Protein 2

Table 3: Change in clinical outcome scores from preoperative to final follow-up

	Technique	Standard CD	Augmented CD	*p* value
Change in Devane score [22]	Mean	-0.19 ± 0.95	0.009 ± 1.15	
Follow−up – preop	Median (Q1;Q3)	0(−1; 0)	0(0; 1)	0.11
	Min−Max	−3; 2	−3; 3	
Change in UCLA score [19]	Mean	−0.21 ± 1.95	0.51 ± 2.10	
Follow−up – preop	Median (Q1;Q3)	0(−1; 0)	0(−1; 2)	**0.009**
	Min−Max	−6; 5	−7; 6	
Change in Harris Hip score [21]	Mean	11.56 ± 21.42	18.69 ± 20.89	
Follow−up – preop	Median (Q1;Q3)	10(−7; 28)	23(0; 32)	**0.019**
	Min−Max	−22; 53	−31; 66	
Change in MDP score [20]	Mean	1.18 ± 3.69	2.49 ± 3.14	
Follow−up – preop	Median (Q1;Q3)	2(−2; 4)	3(0; 5)	**0.020**
	Min−Max	−5; 10	−6; 10	

Bold values indicate significant differences

MDP: Merle d'Aubigné Postel score

Table 4: Postoperative complications

Complications	Standard CD (% total pop.)	Augmented CD (% total pop.)	*p* value
None	78 (98.7)	181 (98.4)	
Pulmonary embolism	0	1 (0.35)	ND
Fracture	0	1 (0.35)	ND
Superficial infection	1 (1.3)	1 (0.35)	ND

ND: Not determined since count is less than 8

Table 5: Survival free of THA at 2 years

	Methods	Standard CD n/N (%)	Augmented CD n/N (%)	*p* value
Classification Arlet & Ficat [14]	Stage 1	27/31 (87.1)	16/20 (80.0)	0.70
	Stage 2	26/43 (60.5)	107/143 (74.8)	**0.067**
	Stage 2 with crescent sign	3/5 (60.0)	15/17 (88.2)	ND
MRI volume	Less than 15°	9/12 (75.0)	28/33 (84.8)	0.66
	15-30%	25/31 (80.6)	79/90 (87.8)	0.37
	More than 30%	13/22 (59.1)	20/38 (52.6)	0.63
Kerboull angle [18]	5° to 20°	10/14 (71.4)	22/26 (84.6)	0.42
	20° to 40°	21/28 (75.0)	71/79 (89.9)	**0.063**
	40° to 60°	5/11 (45.5)	27/41 (65.9)	0.30
	More than 60°	0/1 (0.0)	14/28 (50.0)	ND

ND: Not determined since count is less than 8; Bold values indicate significant differences

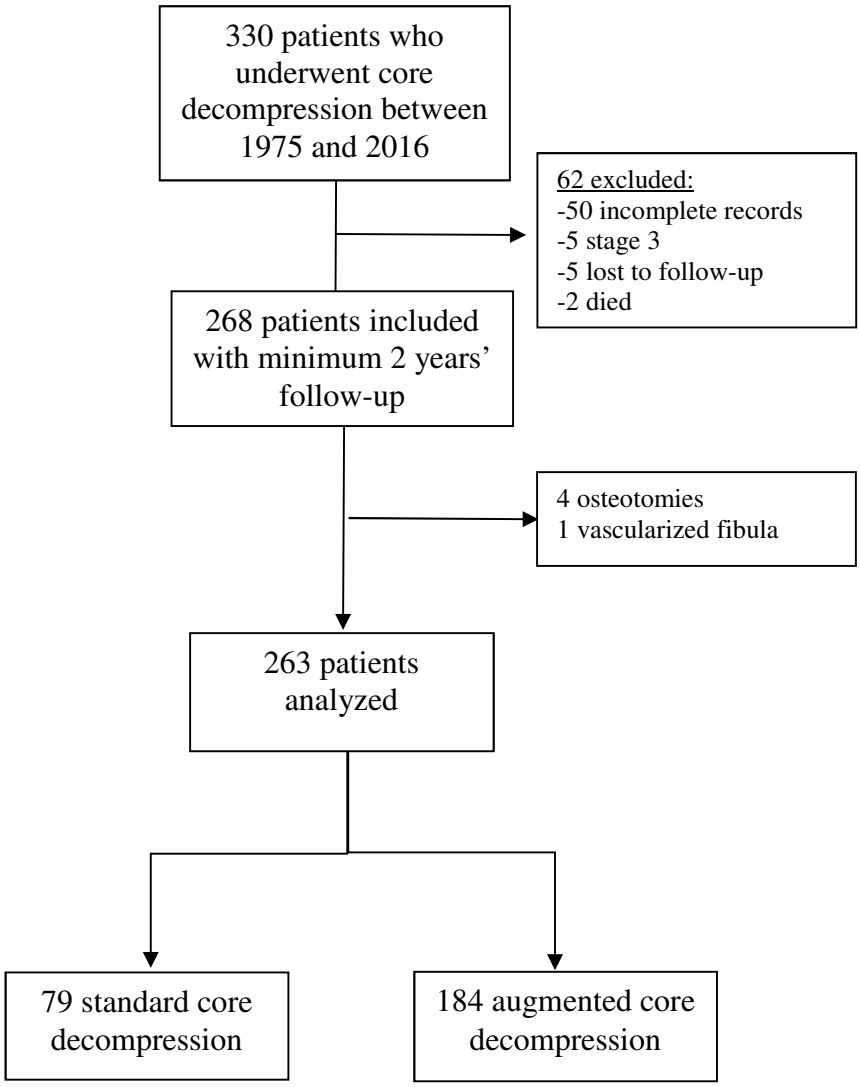
Table 6: Risk factors for revision by THA at 2 years postoperative

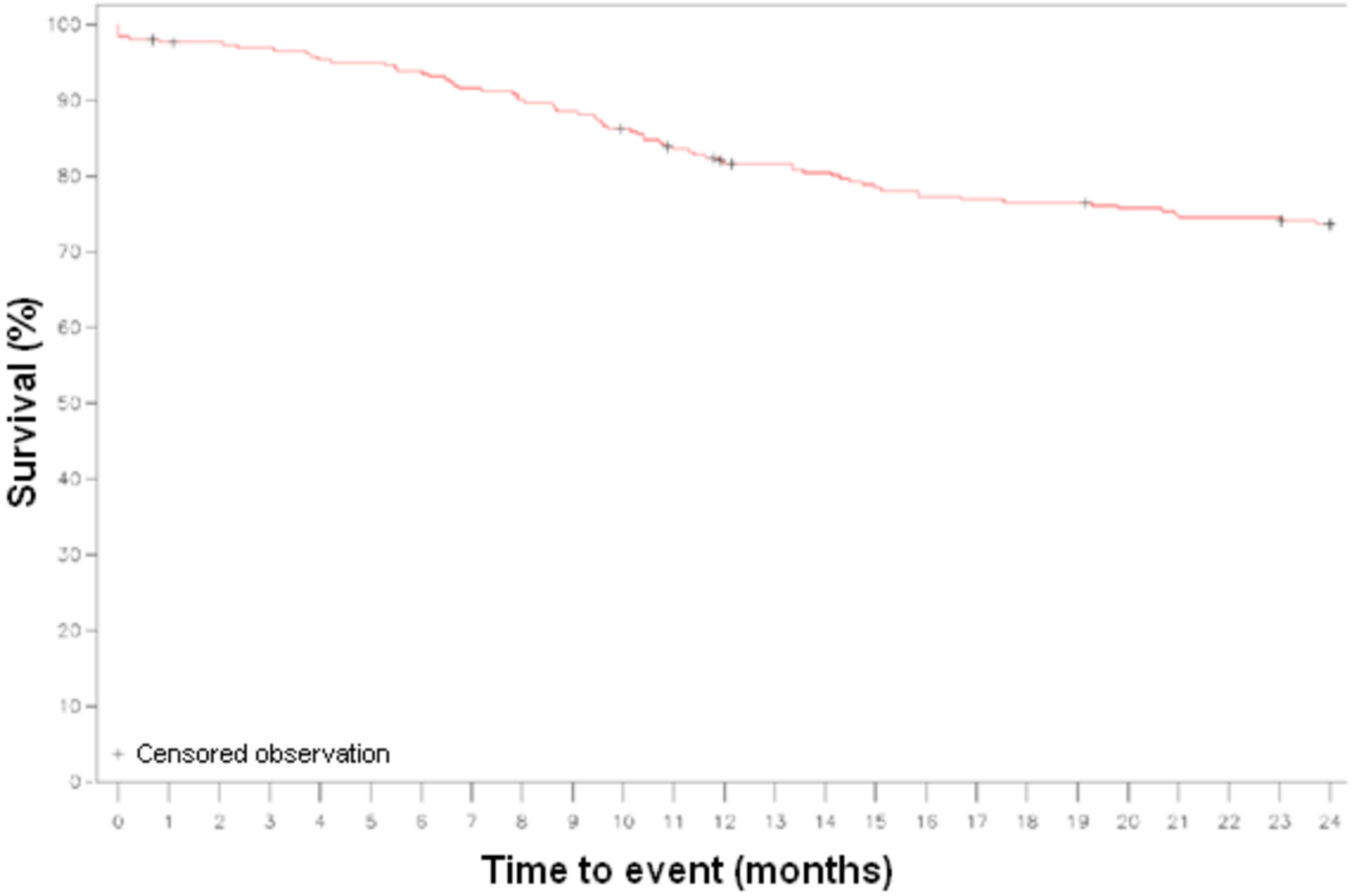
Risk factor	Hazard ratio	95% CI	*p* value
Arlet & Ficat stage [14]			
Stage 2	1.277	0.455-3.589	0.642
Stage 2 with crescent sign	0.526	0.096-2.873	0.459
Kerboull angle [18]			
20-40°	0.619	0.186-2.058	0.434
40-60°	2.431	0.8-7.388	0.117
> 60°	3.178	1.346-7.5	**0.0083**
Volume on MRI			
15-30%	0.879	0.305-2.53	0.811
> 30%	4.163	1.494-7.248	**0.0031**
UCLA score [19]	0.873*	0.775-0.983	**0.0253**
Devane score [22]	0.797*	0.637-0.997	**0.0468**
Harris score [21]	0.973*	0.959-0.988	**0.0003**
MDP score [20]	0.895*	0.803-0.997	**0.043**

Bold values indicate significant differences MDP: Merle d'Aubigné Postel score

* a low clinical score is associated with a higher probability of revision by THA at 2 years

Figure 1: Study flow chart for inclusions

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100
90
80
70
60
50
40
30
20
10
0
Censored observation
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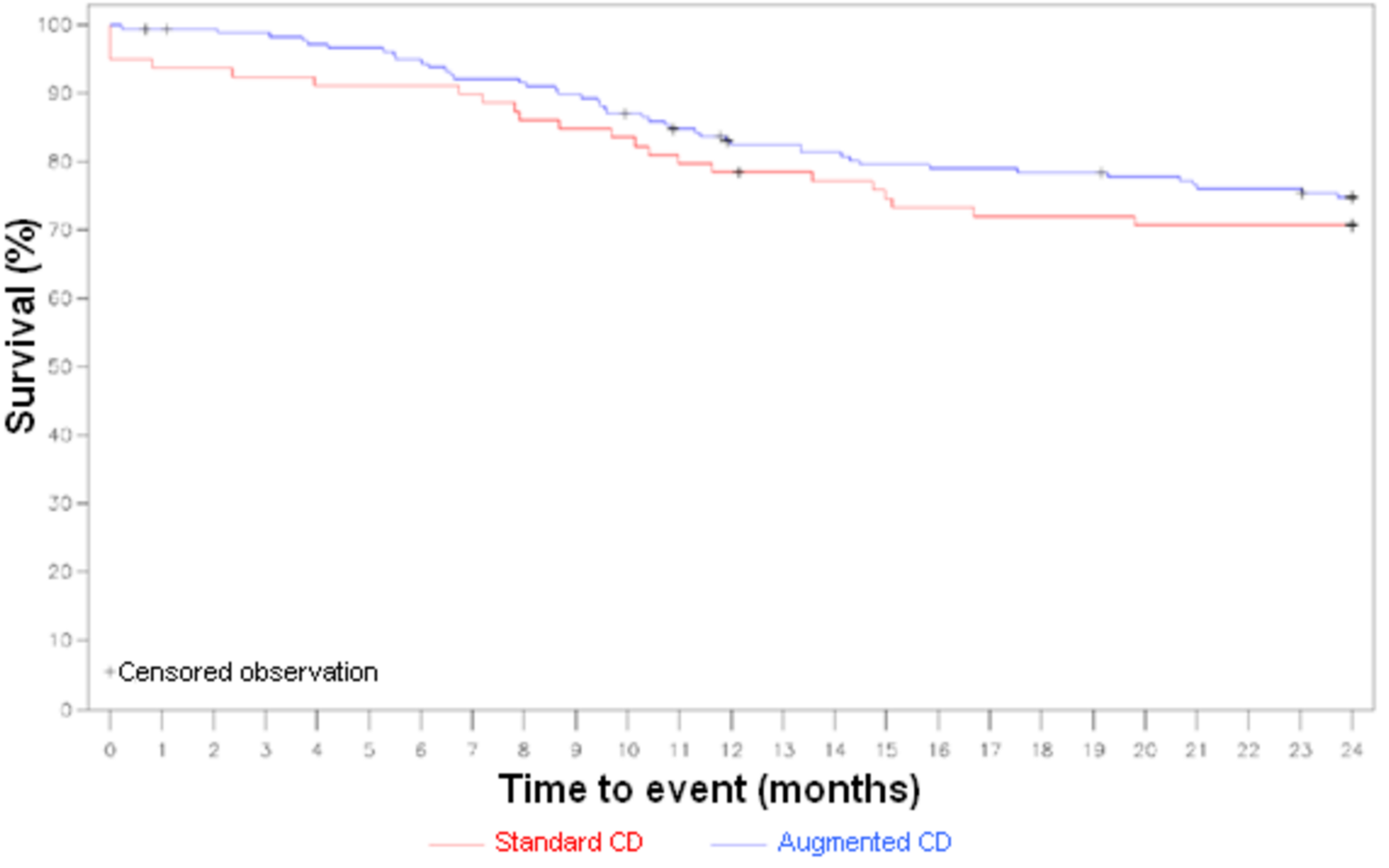
Time to event (months)


Survival (%)
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90
80
70
60
50
40
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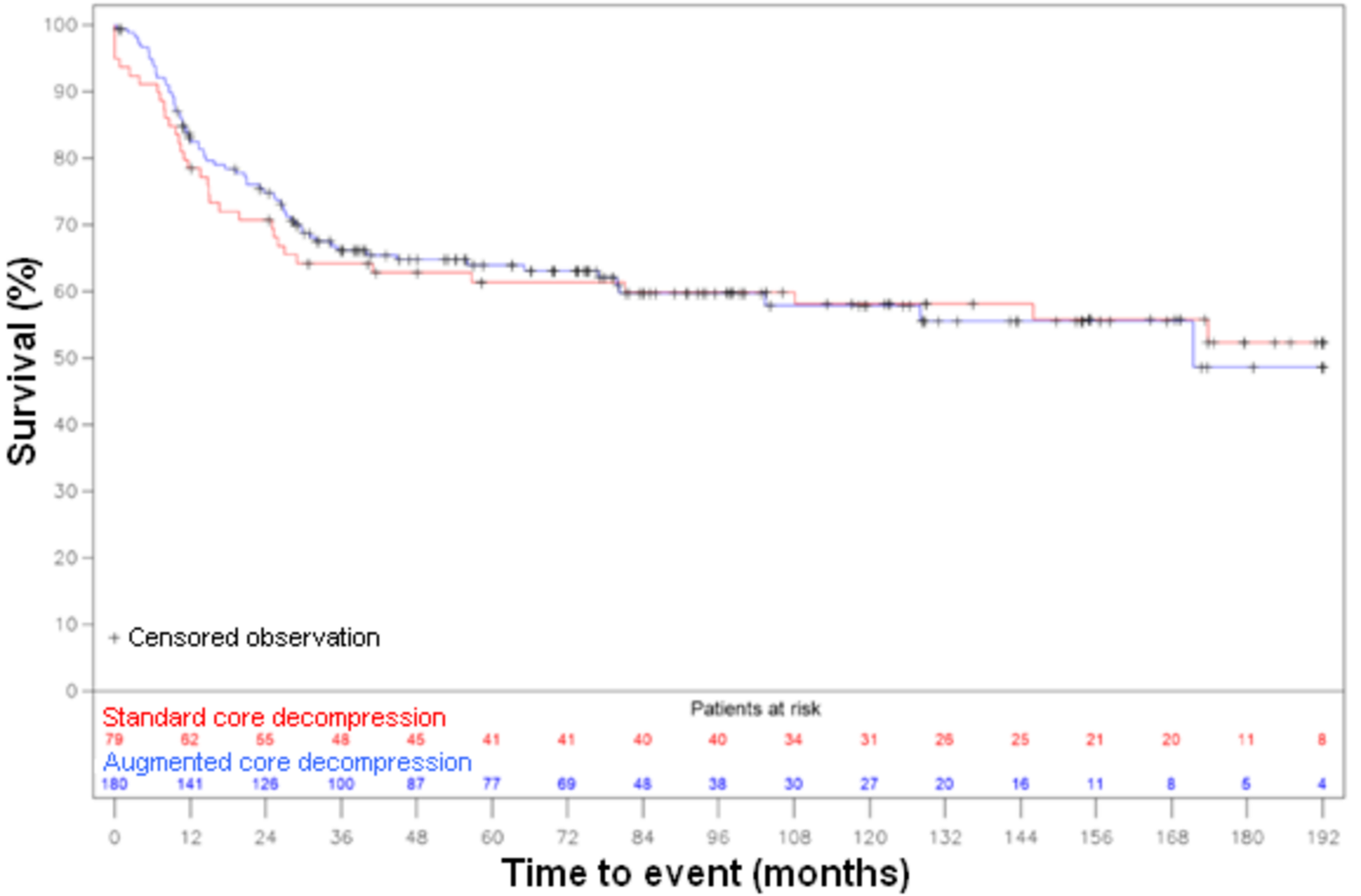
0
Censored observation
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
Time to event (months)
Standard CD
Augmented CD


Survival (%)
100
90
80
70
60
50
40
30
20
10
0
+ Censored observation
Patients at risk
Standard core decompression
79 62 55 48 45 41 41 40 40 34 31 26 25 21 20 11 8
Augmented core decompression
180 141 126 100 87 77 69 48 38 30 27 20 16 11 8 5 4
0 12 24 36 48 60 72 84 96 108 120 132 144 156 168 180 192
Time to event (months)