Management of osteonecrosis of the femoral head in children with sickle cell disease: results of conservative and operative treatments at skeletal maturity

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Abstract

Purpose Sickle cell disease (SCD) is the most common cause of femoral head osteonecrosis (ONFH) during childhood with an overall prevalence of 10%. In children, spontaneous revascularization can occur, as in Legg-Calve-Perthes disease. Consequently, the aim of treatment is to restore proper hip containment to prevent joint arthritis. This is the first study reporting long-term results at skeletal maturity of non-operative and surgical treatments for ONFH in SCD children.

Methods All children with ONFH due to SCD were retrospectively reviewed. At initial evaluation, extension of osteonecrosis was radiographically defined using Catterall, lateral pillar Herring and Ficat classifications. Subluxation of the femoral head with Reimers migration index > 30% required surgical treatment including femoral varus osteotomy and/or pelvic osteotomies. Conservative treatment including non-weight bearing and physiotherapy was performed in the remaining cases. Outcomes were assessed at skeletal maturity using the Harris Hip Score (HHS) and the Stulberg classification. Total hip arthroplasty and Stulberg 5 were defined as failures.

Results A total of 25 hips in 17 patients were included (mean follow-up 7.5 years SD 3.4). Mean age at diagnosis was 11.4 years SD 2.9. In all, 15 hips (60%) were classified Catterall 3 and 4 and Herring B and C. A total of 13 patients (52%)

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Correspondence should be sent to C. Mallet, Pediatric Orthopedic Department, Robert Debre University Hospital, Paris Diderot University, 48 bd Serurier 75019 Paris, France. E-mail: mallet_cindy@yahoo.fr underwent surgical treatment. At skeletal maturity, mean HHS was good (81 SD 17), 12 hips (48%) were classified Stulberg 1 and 2, seven hips (28%) were classified Stulberg 3 and 4.

Conclusion Both treatments led to good functional results with 75% of congruent hips at skeletal maturity.

Level of Evidence IV

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Introduction

Sickle cell disease (SCD) is an inherited haemoglobinopathy leading to chronic anaemia and microvascular occlusion. Orthopaedic complications such as vaso-occlusive crises, osteoarticular infections and osteonecrosis of the femoral head (ONFH) can occur over time. SCD is the most common cause of ONFH in children. Milner et al¹ in a cohort of 2590 SCD patients over the age of five years reported a global prevalence of 10%. They reported a significant variation for the prevalence of ONFH, depending on age. Indeed, for three groups of patients aged between five and nine years, ten and 14 years and 15 and 24 years, the prevalence of ONFH was respectively 1.3%, 4.6% and 8.2%.¹

Risks of developing osteonecrosis are significantly correlated with the type of SCD, for example in patients affected by a homozygous form (Hb SS (Haemoglobin Sickle) genotype), who frequently develop vaso-occlusive pain crises. The main issues when dealing with ONFH in SCD children, are the occurrence of late diagnosis due to poor initial symptoms and complex perioperative precautions, such as blood transfusion exchange, that must to be planned before the surgery. The natural history of ONFH in SCD remains poorly documented in childhood.² Theoretically, spontaneous revascularization can occur in young



children, as reported in Legg-Calve-Perthes disease, so conservative and surgical treatments should improve hip containment and avoid future incongruence and prevent from arthritis.

Our institution has one of the largest paediatric SCD cohorts and multidisciplinary management, including the employment of paediatric orthopaedists, has been organized in the past 15 years.

The aim of the study was, therefore, to report longterm results of both conservative and surgical treatments in SCD children with ONFH at skeletal maturity.

Materials and methods

Patients

All SCD children with ONFH seen at our institution between January 2000 and December 2014 were retrospectively reviewed. To be eligible, patients had to be at skeletal maturity (closed triradiate cartilage on radiographs) at latest examination, with a minimum two-year follow-up. Collected data initially included gender, type of SCD (heterozygous or homozygous forms) and age at ONFH and at surgery.

Initial radiological evaluation

ONFH was initially diagnosed on anteroposterior and lateral radiographs, based on Ficat's classification system (Table 1).³ Catterall and Herring classifications were also used to describe the importance of epiphyseal involvement.^{4,5} Femoral head coverage was determined on anteroposterior radiographs using the Reimers migration index.⁶ MRI was systematically performed in order to confirm the diagnosis of ONFH and evaluate femoral head acetabular cartilage coverage.^{7,8}

Table 1 Ficat classification: stages of femoral head avascular osteonecrosis

Stages	Clinical signs: pain and loss of hip range of movement	Radiological signs
Early		
0 Pre-clinical	0	0
1 Pre-radiographical	+	0
2 Before flattening	+	Located or diffuse sclerosis or cysts of the femoral head
Transition		Flattening Crescent sign (subchondral fracture)
Late		
3 Collapse	++	Sequestrum of the femoral head (pathognomonic sign) Normal joint space
4 Osteoarthritis	+++	Collapse of the femoral head Decreased joint space

OFH management

After diagnosis, the initial evaluation by the orthopaedic surgeon consisted of an assessment of hip movement. In cases of painful and stiff hips, bed rest, skin traction and daily physiotherapy were performed until complete pain relief and hip abduction > 30° were achieved. For the hips that reached 30° of abduction, the Reimers index was analyzed. If the Reimers migration index was < 30%, conservative management was performed consisting of nonweight-bearing and physiotherapy. Otherwise, surgical treatment was indicated. However, hips resistant to skin traction (abduction < 30°) contraindicated surgery. Surgery consisted of a femoral varus osteotomy (FVO) and/or triple pelvic osteotomy (TPO) or shelf procedure, depending on the hip congruency (Fig. 1). Prior to surgery, blood exchange transfusion was performed within at least 24 hours preoperatively in all cases in order to obtain a rate of haemoglobin S (HbS)< 40% and hence prevent risk of acute chest syndrome. Patients were immobilized after surgery in a spica cast for six weeks and sent to a rehabilitation centre.

Clinical and radiological outcomes at skeletal maturity

Clinical outcomes were assessed at latest follow-up by measuring the hip range of movement (ROM) and by the Harris Hip Score (HHS).⁹ Radiological outcomes were assessed on anteroposterior and lateral radiographs using the Stulberg's classification.¹⁰ Hips that required a total hip arthroplasty (THA) and hips classified as Stulberg 5 were considered as treatment failures.

Clinical and radiological results were assessed within two groups: the conservative non-operative treatment group and the surgical treatment group.

Statistical analysis

Statistical analyses were performed using SPSS statistics 23.0 (SPSS Inc., Armonk, New York). A Shapiro-Wilk test was performed to assess data distribution. Continuous numerical data was expressed as mean and sd. Groups were compared with two-tailed student t-tests for variables with normal distribution. A p < 0.05 was considered significant.

Results

Patients

A total of 25 hips (17 patients) were retrospectively included, with a mean follow-up of 7.5 years sd 3.4. A total of eight patients (47%) had a bilateral involvement. There were nine males and eight females. A total of 14 patients (82%) had a SS haemoglobin type. The others had the SC haemoglobin type. ONFH was diagnosed in patients between 8.5 years and 21.1 years (mean age 11.4 years sd 2.9), with no statistical difference between girls and boys





Fig. 1 Institution proposal of treatment management for osteonecrosis of the femoral head in children with sickle cell disease (THA, total hip arthroplasty).

(respectively, 11.6 years sd 4 *versus* 11.3 years sd 2, p = 0.78). Four patients were skeletally mature at that time.

Initial radiological assessment

This is described in Table 2.

Ten hips (40%) were classified Catterall 1 and 2 and Herring A. A total of 15 were classified Catterall 3 and 4

(13 hips Catterall 3) and Herring B and C (11 hips Herring B). Initial severity of the disease classified according to the Ficat system, reported two stage 1 (8%), nine stage 2 (36%), 13 stage 3 (52%) and one stage 4 (4%).

In patients that underwent conservative treatment, most of the hips (ten hips, 83%) were classified Catterall 1 and 2, Herring A. Five hips of those patients who

Table 2 Initial evaluation

	Non-surgical treatment group n = 12	Surgical treatment group n = 13	Total
Mean age at diagnosis (years)	11.4 sd 3.8	11.4 sd 1.9	11.4 sd 2.9
Catterall			
1	5	0	5
2	5	0	5
3	2	11	13
4	0	2	2
Herring			
A	10	0	10
В	0	11	11
С	2	2	4
Ficat			
1	2	0	2
2	5	4	9
3	4	9	13
4	1	0	1

underwent conservative treatment were classified Ficat 2 (42%).

In patients that required surgical treatment, epiphyseal lesions were more extensive and 85% of the hips were classified Catterall 3 or 4 and Herring B. Nine hips of those patients who required surgery were classified Ficat 3 (69%).

Treatments

Eight patients (32%) required skin traction. A total of 13 hips (52%) were operated on. Mean age at surgery was 13.0 years sd 2.9. Ten hips required FVO and two of these were combined with pelvic osteotomies (one TPO and one shelf procedure). Three hips underwent pelvic osteotomies alone (one TPO and one shelf procedure).

Clinical and radiological outcomes at skeletal maturity

All patients were reviewed with a mean follow-up of 7.5 years sd 3.4. The mean HHS was good: 81 sd 17. The mean hip ROM was satisfactory (hip flexion averaged 115° sd 11°, abduction 40° sd 13°, adduction 24° sd 7°, external rotation 27° sd 16°, internal rotation 29° sd 17°). At skeletal maturity, 12 hips (48%) were classified Stulberg 1 and 2 (Fig. 2), seven hips (28%) were classified Stulberg 3 and 4 (Fig. 3). Clinical and radiological results for both types of treatment are summarized in Table 3. Seven hips (58%) in the conservative treatment group and five (38%) in the surgical treatment group were classified Stulberg 1 and 2. Three (25%) hips in the conservative treatment group were classified Stulberg 3 and four (30%) in the surgical treatment group were classified Stulberg 3 and 4.



Fig. 2 A ten-year-old child, with bilateral osteonecrosis of the femoral head that underwent conservative treatment (right hip) and femoral varus osteotomy (left hip): (**a**) preoperative radiograph; (**b**) last follow-up (eight years) radiograph. Both hips were classified Stulberg 1.



Fig. 3 An 11-year-old child with a bilateral osteonecrosis of the femoral head that underwent femoral varus osteotomy (right hip) and conservative treatment (left hip): (**a**) preoperative radiographs; (**b**) one-year postoperative radiographs; (**c**) last follow-up (5.5 years) radiographs. Both hips were classified Stulberg 3.

Acute complications and failures

Only one patient (8%) that underwent a TPO required perioperative transfusion for acute anaemia (Hb = 7.5 g/dl). No acute chest syndrome or surgical site infection was reported.

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Table 3 Clinical and functional results at maturity					
	Conservative treatment group n = 12	Surgical treatment group n = 13			
Mean age (years)	18.9 sd 5.6	18.6 sd 3.9			
Hip range of movement (°)					
Flexion	115 sd 15	115 sd 13			
Extension	12 sd 6	12 sd 10			
Abduction	44 sd 14	37 sd 16			
Adduction	24 sd 8	24 sd 8			
External rotation	31 sd 22	23 sd 18			
Internal rotation	35 sd 22	25 sd 20			
Mean HHS	75.0 sd 21.8	87.4 sd 10.4			
Stulberg 1	4	1			
Stulberg 2	3	4			
Stulberg 3	1	1			
Stulberg 4	2	3			
Stulberg 5	1	2			
тна	1	2			

HHS, Harris Hip Score; THA, total hip arthroplasty

At last follow-up, six patients (24%) were considered as failures (three THA and three Stulberg 5). Conservative treatment failed in two hips (17%) (one THA and one Stulberg 5) and operative treatment failed in four hips (31%) (two THA and two Stulberg.

THA

Patients that required THA had initially extensive epiphyseal lesions; two were classified Catterall 3 and Herring C and one Catterall 2 and Herring B. One of those was diagnosed at the age of 21 years with a Ficat 4 stage, and THA was indicated at that time. The two remaining patients underwent FVO associated with a shelf procedure that evolved into hip incongruency (Stulberg 5) and required a THA four years later.

Stulberg 5

Hips that were classified Stulberg 5 also had initial extensive epiphyseal lesions (Catterall 3, one Herring B and one Herring C). Surgery was contraindicated for one hip because of joint stiffness (Fig. 4). The remaining two patients underwent surgery (one TPO and one FVO) with poor results. For those patients, THA will be needed in the future.

Discussion

Outcomes at maturity

To the best of our knowledge, this study is the first to report outcomes of both conservative and operative treatments at skeletal maturity in SCD children. Our



a-preoperative

Fig. 4 A 9-year-old child with a bilateral osteonecrosis of the femoral head that underwent femoral varus osteotomy (right hip). The left hip stayed stiff despite skin traction and physiotherapy, no surgery was performed: (**a**) preoperative radiographs; (**b**) perioperative radiographs; (**c**) at last follow-up (seven years), the right hip was classified Stulberg 4, left hip was classified Stulberg 5. This hip will require total hip arthroplasty.

management was based on hip function and radiological containment (Fig. 1). Both treatments showed good functional outcomes at final follow-up with 75% of congruent hips (Stulberg 1 to 4).

Even in more severe epiphyseal lesions (Catterall 3 and 4, Herring B and Ficat 3) that required a surgical treatment, functional results at skeletal maturity were satisfactory (mean HHS = 87.4). In all, 69% of those hips were classified Stulberg 1 to 4, including 38% with spherical congruency (Stulberg 1 and 2) and 30% with aspherical congruency (Stulberg 3 and 4)¹⁰. Nevertheless, unlike Legg-Calve-Perthes disease, SCD patients are at risk of recurrence during adulthood leading to the potential risk of further arthritis.

The literature is very poor regarding management of SCD ONFH in children. Good functional results have been recently reported in advanced osteonecrosis (Ficat stages 3 and 4) treated by FVO and/or TPO. Results showed

postoperative HHS gain and 'satisfactory hip congruency in all patients'.¹¹ Athanassiou-Metaxa et al¹² compared functional and radiological improvements after subtrochanteric varus osteotomy and non-surgical treatment. However, there was a lack of assessment for initial severity and indications for surgical treatment. The current study objectively confirmed those results (mean HHS 87.4).

In adults, the literature is much more consistent. In early stages (Ficat stages 1 and 2), core decompression more or less associated with bone marrow graft is indicated.¹³⁻¹⁶ Results had showed good functionality, since the pain ceased. Furthermore, radiological progression of necrosis and femoral head collapse also stopped.

In children, less invasive surgical treatment tends to be developed. Novais et al¹⁷ reported preliminary results of multiple epiphyseal drilling and autologous bone marrow implantation in order to decrease femoral head hypertension and induce epiphyseal bone reconstruction in a SCD paediatric cohort (mean age 12.7 years). This treatment succeeded in improving hip ROM and pain and stopped the disease progression. However, these results have been evaluated with a very short-term follow-up (23 months). Furthermore, the risk of femoral head epiphysiodesis due to the multiple drillings needs to be further assessed in skeletally immature children.

Natural evolution of ONFH

Natural evolution is most of the time asymptomatic, which makes the diagnosis very difficult. However, screening and early detection of the pre-collapse disease is essential to propose a conservative treatment. Gupta and Adekile¹⁸ in a prospective study, reported 65% of children with significant progression of their lesion even for asymptomatic forms. Therefore, new techniques to measure risks of ONFH are required. One recent study suggested the haemoglobin to hematocrit (Hb to HCT) ratio ('mean corpuscular haemoglobin concentration') to be the strongest predictor of ONFH in children with SCD.¹⁹ The same authors reported systolic blood pressure as the second predictor of ONFH. They recommended bilateral hip MRI in case of elevated Hb/HCT ratio.

In our experience, SCD patients should be seen by an orthopaedic surgeon as soon as they become symptomatic in order to initiate physiotherapy and skin traction if required, in order to avoid hip contracture.

Multidisciplinary approach

Some of the most important advice in the management of ONFH secondary to SCD is the importance of a multidisciplinary approach by an experienced team, including paediatricians, anaesthesiologists and haematologists, to prevent perioperative general and local complications that are more important and severe than in the general population.^{21,22} General complications include blood loss requiring blood transfusion, vaso-occlusives crisis and acute chest-syndrome. Preoperative blood exchange transfusion, perioperative hyper-oxygenation and optimal analgesia are essential to avoid difficulties. Furthermore, higher rates of orthopaedic complications have been also described. Function is usually very good after THA, with very good functional recovery and loss of pain.^{21,23} However, rates of acute and late surgical site infections vary between 3% and 25%,²⁰ and a rate of 26% of aseptic loosening and hip dislocation have been reported in SCD.^{20,22} Therefore, THA should be a salvage procedure. In the present study, one general complication was reported. All the patients were managed by an experienced team who were part of the SCD reference centre and preoperative exchange transfusion was systematically performed.

Limitations

This study has several limitations, starting with the small sample size. Nevertheless, the literature is poor and the cohort is the largest with the longest follow-up of children at skeletal maturity. The second limitation was the use of Catterall, Herring and Stulberg classifications, initially described for the Legg-Calve-Perthes disease in order to determine the severity of the disease and prognosis.^{24,25} To the best of our knowledge, these have never been used for the description of the ONFH in children with SCD. Catterall and Herring classifications were essentially used in the current study to objectively describe the extension of epiphyseal lesions since there is no specific classification for ONFH in SCD children. Results showed that more extensive lesions involving the lateral pillar, required surgery because of the hip insufficient coverage. Therefore, these results showed that the disease's natural progression is very close to Legg-Calve-Perthes', even though potential recurrences are possible at adulthood.¹¹ Further studies could investigate the reliability of Catterall and Herring classifications in children with ONFH secondary to SCD.

The third limitation was the lack of statistical analyses. Nevertheless, our aim was to report the management of ONFH in SCD children as performed in our institution and the outcomes at skeletal maturity of surgical and non-surgical treatments. Group comparison was not considered as relevant since patients and disease characteristics were very different between the patients treated conservatively and those treated by surgery. Finally, the design of the study induced inevitable selection and information biases. Allocation to one type of treatment could not be randomized since the indications for one or another depended on the severity of the Reimers index. Potential radiographs and clinical outcomes scores measurements errors were also unavoidable leading to information biases.

Conclusion

The present study reported satisfactory functional and radiological outcomes at skeletal maturity in SCD children treated for ONFH by either conservative management or surgery. According to our results based on MRI, it seems that severe SCD osteonecrosis with extensive epiphyseal lesions should be surgically treated whereas with local epiphyseal lesions with intact lateral pillar (Catterall 1 and 2, Herring A), a conservative treatment must be considered in order to maintain good function. Nonetheless, these patients are at potential risk of recurrence at adulthood, which cannot be predicted.

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COMPLIANCE WITH ETHICAL STANDARDS

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ETHICAL STATEMENT

Ethical approval: All procedures performed in the study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

ICMJE CONFLICT OF INTEREST STATEMENT

K. Mazda is a consultant for Implanet. B. Ilharreborde is a consultant for Implanet, ZimmerBiomet and Medtronics. All other authors declare that they have no conflict of interest.

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