A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

IPSG

STUDY IDENTIFIER
Perthes’: Late Stage Cohort

FULL STUDY TITLE
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes disease

LAY STUDY TITLE
Prospective study of the role of containment in children with late stage Legg-Calvé-Perthes disease

CONFIDENTIAL
This document is confidential and the property of the International Perthes’ Study Group. No part of it may be transmitted, reproduced, published, or used without prior written authorization.

STATEMENT OF COMPLIANCE
This document is a procedural outline for a clinical research study. The study will be conducted in compliance with all stipulations of this outline and the conditions of ethics committee approval of each of the participating institutions.

Last Updated: March 2017
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

TABLE OF CONTENTS

1. INVESTIGATORS AND FACILITIES
   1.1 Study Locations
   1.2 Study Management
      1.2.1 Principal Investigator
      1.2.2 Statistician
   1.3 Funding and resources

2. INTRODUCTION AND BACKGROUND
   2.1 Background Information
   2.2 Research Question
   2.3 Rationale for Current Study

3. STUDY OBJECTIVES
   3.1 Primary Objective
   3.2 Secondary Objectives

4. STUDY DESIGN
   4.1 Type of Study
   4.2 Study Design Diagram
   4.3 Number of Subjects
   4.4 Expected Duration of Study
   4.5 Primary and Secondary Outcome Measures

5. STUDY TREATMENTS
   5.1 Treatment Arms
      5.1.1 Description

6. SUBJECT ENROLLMENT
   6.1 Recruitment
   6.2 Eligibility Criteria
      6.2.1 Inclusion Criteria
      6.2.2 Exclusion Criteria

7. STUDY VISIT AND PROCEDURE SCHEDULE

8. CLINICAL AND RADIOGRAPHIC ASSESSMENTS

9. STATISTICAL METHODS
   9.1 Sample Size Estimation
   9.2 Population to be analyzed
   9.3 Statistical Analysis Plan
   9.4 Interim Analyses

10. DATA MANAGEMENT
    10.1 Data Collection

Last Updated: March 2017
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

**IPSG**

10.2 Data Storage
10.3 Study Record Retention

11. ADMINISTRATIVE ASPECTS
11.1 Confidentiality
11.2 Independent HREC Approval

12. USE OF DATA AND PUBLICATIONS POLICY
13. REFERENCES
14. APPENDICES

**PROTOCOL SYNOPSIS**

<table>
<thead>
<tr>
<th><strong>Title</strong></th>
<th>A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late stage Legg-Calvé-Perthes disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Objectives</strong></td>
<td>The primary objective of the study is: To evaluate the impact of containment treatment (surgical or bracing) in children with LCPD in the late stages of disease on the shape of the femoral head compared with no containment.</td>
</tr>
<tr>
<td><strong>Design</strong></td>
<td>Prospective hospital-based multi-centre non-randomized study.</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>The primary outcome measure is the shape of the femoral head at 2 and 5 years, and at skeletal maturity. Secondary outcome measures include functional and quality of life scores.</td>
</tr>
<tr>
<td><strong>Study Duration</strong></td>
<td>Twelve years</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Containment (nonsurgical and surgical)</td>
</tr>
<tr>
<td><strong>Number of Subjects</strong></td>
<td>65 patients in each arm of the study; 200 total patients</td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Children diagnosed with Legg-Calvé-Perthes disease in the late stages of the disease (stage IIb or IIIa) at presentation; Hospital based</td>
</tr>
</tbody>
</table>
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes' disease

1. INVESTIGATORS AND FACILITIES

1.1 Study Locations

This study will be conducted by willing and able institutions across the globe. The lead site, Texas Scottish Rite Hospital for Children, is located in Dallas, Texas, United States of America and will be the storehouse of all IPSG data.

For a list of individual centers participating in the IPSG, please see Appendix VIII.

1.2 Study Management

The study will be conducted by research teams at each of the participating centers. Each center will have a Principal Investigator who will coordinate the study.

1.2.1 Principal Investigator

Harry Kim, Texas Scottish Rite Hospital for Children, 2222 Welborn Street, Dallas, Texas 75219
Phone: 214-559-7877
Email: Harry.kim@tsrh.org

Harry Kim, MD is the IPSG Chair. For a list of individual Principal Investigators from participating institutions, please see Appendix VIII.

1.2.2 Statisticians

i) ChanHee Jo, PhD, Statistician, Texas Scottish Rite Hospital for Children, Dallas, Texas, USA

1.3 Funding and Resources

Upon inclusion into the IPSG, the participating centers and Principal Investigators agree to contribute and participate in the IPSG without funding.

2. INTRODUCTION AND BACKGROUND

2.1 Background Information

The theory of containment, while lacking rigorous scientific support, has been the prevailing concept in the treatment of Perthes since it was described in 1929. The concept is simple - “if the head is contained within the acetabular cup, then like jelly poured into a mold the head should be the same shape as the cup when it is allowed to come out after reconstitution¹.” The primary assumption is that containment offers the best known method for promoting a round femoral head that will be less symptomatic in adulthood. Non-operative methods of containment include casting and many versions of abduction bracing. Operative methods include a proximal femoral varus osteotomy, Salter pelvic osteotomy, shelf acetabuloplasty or a combination.

While there is no consensus, treatment is often broken down by age – less than 6 years of age, 6 to 8 years of age, and over 8 years of age. This stems from two prospective level 2 studies that evaluated the effectiveness of surgical containment²,³. These were two landmark studies that
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes' disease

have changed the treatment of LCPD. However, these studies did not standardize operative and non-operative treatments or the timing of intervention (i.e. pre-collapse versus post-collapse). This resulted in heterogeneity of the study populations and treatments. In addition, neither study specifically addressed how to treat the many patients who present for treatment who already have femoral head collapse and are in the later stages of fragmentation.

There have been retrospective studies looking at the timing of varus osteotomy. Axer et al found that 9% of patients treated in the initial stages of disease had a poor outcome compared to 56% in the later stages of disease. Joseph et al also reported improved results for patients treated early. There is a relatively renewed interest in non-operative containment using an A-frame orthosis. Rich et al reported good outcomes in a retrospective study. Prospective evaluation of the treatment of late-stage LCPD is needed.

2.2 Research Question
2.2.1. Will nonsurgical or surgical containment of the hip in children with LCPD presenting in late fragmentation or early reossification (Appendix I) increase the success rate of restoring the spherical shape of the femoral head than if no containment treatment is offered?

2.3 Rationale for Current Study
Currently there is no consensus regarding the optimal treatment for children after femoral head collapse. If the results of this study show no benefit of containment treatment over non-containment, then those who currently offer containment will likely be inclined to change their practice.

3. STUDY OBJECTIVES

3.1 Primary Objective
The primary objective of the study:

3.1.1. To evaluate the impact of containment treatment (surgical or bracing) in children with LCPD in the late stages of disease on the shape of the femoral head compared with no containment.

3.2 Secondary Objectives
The secondary objectives of the study are:

3.2.1 To evaluate the impact of containment in children with LCPD in the late stages of disease on the shape of the femoral head.

3.2.2 To assess whether hip abduction as measured on radiographs correlates with long-term outcome.

3.2.3 To evaluate whether hip range of motion during the late stages of disease correlates with final femoral head shape.

3.2.4 To assess whether QOL outcome measures correlate with radiographic outcome.
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

4. STUDY DESIGN
4.1 Type of Study

This is a prospective, non-randomized, multicenter study of patients presenting in the late stage of disease (modified Waldenström stage IIb or IIa) (Appendix I). There are three arms to this study.

Arm 1: Symptomatic treatment
Arm 2: Non-surgical containment with a brace
Arm 3: Surgical containment

Participating surgeons will choose treatments based on their current clinical practice and the options of treatment includes treatment regimens currently considered standard of care which includes symptomatic treatment, bracing or surgical containment. Since hip range of motion, especially hip abduction, at the time of presentation is considered by most surgeons as an important variable for treatment selection, patients will be stratified into poor hip motion (≤20 degrees) vs. adequate motion (>20 degrees) based on hip abduction measured on a maximum leg abduction x-ray (see flow chart on 4.2 and Appendix II). In those patients with ≤20 degrees hip abduction on x-ray, Petrie casting with or without adductor tenotomy can be performed based on surgeon preference and does not exclude a patient from any treatment group. Symptomatic treatment can include periods of non-weight-bearing, anti-inflammatories, and/or physical therapy. This group will serve as the control. Bracing patients will be treated with a prolonged A-frame brace similar to the method of Rich et al\textsuperscript{7} or the method used by Kim at TSRH (see Appendix III). Patients will be braced for a minimum of 6 months or at least until ossification of the lateral pillar. The brace serves as a form of non-surgical containment. The surgical containment can include femoral or pelvic osteotomy per the surgeon’s routine practice. A greater trochanteric epiphysiodesis can be performed per the surgeon’s current practice.

Patients presenting with adequate motion, defined as abduction >20° on radiograph, will be treated with either symptomatic treatment or surgical containment.

The choice of management will be solely governed by the current practice of the participating surgeons (i.e. the current practice of the individual surgeon will be followed within the broad framework of the study).

The method of surgical containment will again be as per the choice of the individual participating surgeon. Thus, if the surgeon’s current practice is to achieve containment by performing a shelf operation, the same procedure will be followed during the study. A greater trochanteric epiphysiodesis can be performed per the surgeon’s current practice.

If surgical treatment is the preferred treatment option for a participating surgeon but the patient’s parents opt for a non-osteoectomy treatment, the patient will be enrolled into the study with notation. At the end of the study, outcome analysis will be performed with and without this patient’s data.

For the surgical group it is desirable that all the investigators adhere to a common post-operative regimen during the study in order to reduce confounding variables related to the duration of casting and/or non-weight-bearing. Petrie casting can be used for up to two months postoperatively.

Last Updated: March 2017
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes' disease

4.2 Study Design Diagram

**IPSG Late Stage Protocol Flowchart**

- **Child w/ LCPD**
  - Ages ≥6 to <11 years old
  - Stage IIb or IIIa

- **Abduction on XR ≤20°**
  - Bracing
  - Symptomatic treatment
  - AP & frog pelvis
    - Every 3 months x 1 year

- **Abduction on XR >20°**
  - Surgical Containment
  - Hinge Abduction
    - Treatment per surgeon
  - AP & frog pelvis
    - Every 6 months x 1 year

- **2 years**
  - AP & Frog pelvis
  - Deformity Index

- **5 years & maturity**
  - Standing AP & Frog pelvis
  - Head sphericity
  - Stulberg
  - QOL questionnaires
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

IPSG

4.3 Number of Subjects
Approximately 200 patients total based on power analysis calculations. See section 9.1. This assumes a 15% patient lost-to-follow-up due to study duration.

4.4 Expected Duration of Study
The duration of the disease is between two to five years. Each child will be followed up till skeletal maturity (age 14 for girls and age 16 for boys).

The expected recruitment period is 24 months, though the recruitment period ends when the goal number of subjects has been reached.

The study will run for a period of ten years following the recruitment period (in order to follow up all recruited children till skeletal maturity).

4.5 Primary and Secondary Outcome Measures
The primary outcome measure will be the shape of the femoral head. The shape of the femoral head will be measured at three points (at 2 years, 5 years, and skeletal maturity).

The first measure would be undertaken two years after enrollment by applying the Deformity Index.

At the 5 year follow-up visit and at skeletal maturity, a quantitative measure of the sphericity of the femoral head (the Sphericity Deviation Score) and Stulberg classification will be applied. These assessments will be performed by a team that is blinded to the treatment arm.

At five years and skeletal maturity the function and quality of life will be assessed with the PROMIS questionnaire (Appendix IV) and the modified Harris Hip Score (Appendix V).

5. STUDY TREATMENTS
5.1 Treatment Arms
There are three arms to the study.
First arm - Symptomatic treatment: patients presenting with poor motion, defined as abduction ≤20° on initial radiograph, or adequate range of motion, defined as abduction >20° on initial radiograph, and can include periods of non-weight-bearing, anti-inflammatories, range of motion exercises and/or formal physical therapy. This group will serve as the control.
Second arm - Bracing: patients presenting with poor motion, defined as abduction ≤20° on initial radiograph, treated with a prolonged A-frame brace following Petrie cast treatment similar to the method of Rich et al or Kim (see Appendix III). Bracing treatment lasts for a minimum of six month or at least until re-ossification of the lateral pillar is established. The brace serves as a non-surgical containment.
Third arm - Surgical containment: patients presenting with poor motion, defined as abduction ≤20° on initial radiograph, or adequate range of motion, defined as abduction >20° on initial radiograph, treated with surgical containment. Surgical containment can include femoral or pelvic procedures per the surgeon’s routine practice. A greater trochanteric epiphysiodesis can be performed per the surgeon’s current practice.

Investigators are asked to commit to one arm or the other.
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes' disease

5.1.1 Description
The choice of treatment arms will be solely governed by the current practice of the participating surgeons.

The method of surgical containment may vary from surgeon to surgeon (femoral osteotomy, pelvic osteotomy or shelf acetabuloplasty).

Details of the protocol for each treatment arm is summarized in the diagram in section 4.2.

If a patient/family chooses to enroll in the study but chooses not to proceed with the their surgeon’s recommended treatment (e.g. a patient chooses non-operative management despite a surgical recommendation), the patient can still be enrolled and followed as a study patient with a notation indicating the alternate selection in the database. The above stated scheduled follow-up, radiographic and clinical measures will continue to apply.

6. SUBJECT ENROLLMENT
6.1 Recruitment
Identification and recruitment of potential subjects is from the respective clinics of the participating investigators.

Relevant information regarding the study will be given to prospective subjects and their legally acceptable representatives in a language that they comprehend.

A signed consent form will be obtained for each subject from a parent or legal guardian. The consent form will describe the purpose of the study, the procedures to be followed, and the risks and benefits of participation. When possible, a research coordinator or a nurse will conduct the informed consent discussion and will check that the legally acceptable representative comprehends the information provided and answers any questions about the study. This is to avoid parent/caregivers feeling pressured to participate if the consent is obtained by the treating physician. Consent will be voluntary and free from coercion.

6.2 Eligibility Criteria
6.2.1 Inclusion Criteria (all criteria must be met)
i) A child with LCPD (confirmed by plain radiographs or MRI) between the ages of 6 and 11 years old (i.e. between the 6th and 11th birthday) at time of presentation to an IPSG member or their group.

ii) Child in the stage of late fragmentation (Stage Iib or IIIa) at the time of presentation to an IPSG member or their group. The stage of disease will be confirmed by two independent observers prior to enrolment.

iii) Supine AP pelvis radiograph with maximum abduction of legs (supervised by the physician participating in the study).
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

6.2.2 Exclusion Criteria

i) Children with known causes of osteonecrosis
   a. Children with a hemoglobinopathy (confirmed by haemoglobin electrophoresis if suspected), coagulopathy, or leukemia.
   b. Children who have been treated with systemic steroids for a period of 30 consecutive days or more.

ii) Children with endocrine dysfunction (e.g. hypothyroidism)

iii) Children with a previous history of congenital or acquired hip disease on the affected hip (e.g. DDH, traumatic dislocation or fracture neck of the femur) with the exception of transient synovitis

iv) Children with any form of skeletal dysplasia

v) Children with Down syndrome

vi) Children with previous surgery on the affected hip
   a. This does not include limited procedures such as adductor tenotomy, limited Petrie casting or bracing

7. STUDY VISITS AND PROCEDURES SCHEDULE

Each of the children recruited for the study will be followed regularly as part of standard of care. All children will be reviewed every three months for the first 2 years and every 6 months thereafter till complete healing of the disease and skeletal maturity, which is considered standard of care.

At each visit the child will undergo a clinical examination and have radiographs as outlined in the following section.

8. CLINICAL AND RADIOLOGICAL ASSESSMENTS

On inclusion, a SUPINE AP and Lauenstein frog-lateral radiograph of the pelvis showing both hips and a supine maximal abduction radiograph will be obtained. The patient will be positioned for the maximal abduction radiograph in the supine position with the patella straight forward (see Appendix II).

On each three-monthly follow-up visit, the child will also have a SUPINE AP and Lauenstein frog-lateral radiograph of the pelvis showing both hips. Note that all radiographs should be taken with the child supine.

At each clinic visit, hip abduction will be measured by clinical examination. At 5 years and skeletal maturity, a detailed clinical evaluation of hip function and a quality of life assessment (QOL) will be performed.

At five years and skeletal maturity the function and quality of life will be assessed with the PROMIS questionnaire (Appendix IV) and the modified Harris Hip Score (Appendix V).

On each radiograph **taken at every 3-monthly visit** the following features will be noted:

i) The stage of evolution of the disease (modified Waldenstrom staging)

ii) The extent of collapse of the lateral pillar (applicable at mid-fragmentation stage)

iii) The degree of extrusion of the femoral head (by measuring the Reimer’s migration index)
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

IPSG

In addition:
On radiographs obtained on the 8th three-monthly follow-up visit (i.e. 24 months after inclusion in the study)
   i) The Deformity Index will be measured (details of method is included in Appendix VI) by image analysis subcommittee

On the radiographs after complete healing of the disease (5 year follow-up visit and at skeletal maturity), the following measurements will be made by the image analysis subcommittee:
   i) The Sphericity Deviation Score (A quantitative measure of sphericity of the femoral head - details in Appendix VII)
   ii) The neck-shaft angle
   iii) The size of the femoral head
   iv) The articulo-trochanteric distance
   v) The acetabular angle
   vi) Limb length discrepancy
   vii) Stulberg radiographic outcome

At the 5-year and the final follow-up visit (skeletal maturity) in addition to the AP and frog-lateral radiographs a full-length standing radiograph of both the lower limbs will be obtained to measure limb-lengths and to assess the alignment of the limb by drawing the mechanical axis and measuring mechanical axis deviation, if present.

9. STATISTICAL METHODS
9.1 Sample Size Estimation

1) Abduction<=20
Our primary outcome is the sphericity deviation score (SDS). For simplicity, the power analysis is based on the comparison between Group 1 (No Sx) and Group 2 (Surgery). Using historical data, 27.1 ± 15.6 for their mean and standard deviation, a sample size of 40 per group will achieve at least 80% power to detect a difference of 10 of SDS score at alpha = 0.05, using a two-sided t-test.

2) Abduction>20
Our primary outcome is the sphericity deviation score (SDS). Previous data shows that Group 1 has 17.1 ± 15.6 for their mean and standard deviation. A sample size of 40 per group will achieve at least 80% power to detect a difference of 10 of SDS score at alpha = 0.05, using a two-sided t-test.

9.2 Population to be analyzed
Children in age group of 6-11 years with late stage LCPD at time of presentation to IPSG member or their group; see section 4.2.
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

IPSG

10. DATA MANAGEMENT
10.1 Data Collection

Demographic data and clinical data collection at each participating center will be on identical case report forms (CRF) available through REDCap database at https://redcap.tsrh.org.

On identification of a potential subject for inclusion in the study, soft copies of the CRF and radiographs will be transmitted to the central study coordinator at TSRH. The CRF and radiographs will be reviewed independently by two designated reviewers who will check the clinical and radiographic criteria for inclusion in the study. Once the reviewers concur, the child will be assigned a study identification number and will be included in the study. The database will be managed by the study coordinator at TSRH.

Electronic copies of the CRFs will be kept on the electronic database: https://redcap.tsrh.org. This database will be managed by the study coordinator at TSRH.

All radiographs obtained at sequential follow-up visits are uploaded and stored within the patient’s electronic CRF housed in the REDCap database.

10.2 Data Storage

The data related to each child will be coded with a study ID number allocated at the time of enrolment. Only limited individuals involved with the maintenance of the database (central study coordinator, leader of database subgroup and selected members of the subgroup, and chief organizer of IPSG) will have access to the database till the time for analysis of data, at which time the investigators involved in the analysis will have access to the data.

10.3 Study Record Retention

The data will be retained for indefinite time after completion of the study.

11. ADMINISTRATIVE ASPECTS
11.1 Confidentiality

Confidentiality of the subjects will be strictly maintained by the investigators and the IPSG. The study protocol, data and information generated from the study will be held in confidence till it is published.

11.2 Independent IRB Approval

Participating investigators will need IRB approval from their institution prior to enrolling patients.

11.3 DSMB – Data Safety Monitoring Board

The DSMB will consist of a Pediatric Orthopaedic surgeon not related to the study, a statistician and a lay person (from a patient advocacy group).

Last Updated: March 2017
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes' disease

IPSG

12. USE OF DATA AND PUBLICATIONS POLICY
The collective data is the property of IPSG. Data from this multi-center study will be published only after successful completion of the study.

Data from a single center generated during this study shall not be published separately. All the members of the participating centers will be acknowledged. Authorship will be decided by the guideline on authorship provided by AAOS and IPSG executive committee.

13. REFERENCES
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX I
DETAILS OF THE STUDY

Staging of the disease for deciding if the criteria for inclusion in the study are met

The staging of the disease is based on the plain radiographic appearances in both the AP and Lauenstein frog-lateral views. Children between the ages of 6 and 11 years at the onset of the disease in Stage IIb or IIIa, shown below, are candidates for inclusion in the study.

If fragmentation is in the early stages (I or IIa) or has progressed so that new bone is of normal texture over more than a third of the epiphyseal width, then the patient is NOT eligible for inclusion in the study.

A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX II

Protocol For Maximum Abduction Radiograph

- AP pelvis with bilateral hips in maximum straight-leg abduction, supine
- Patella pointing straight ahead

Include the proximal femoral diaphysis (in order to measure abduction)
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX III

Kim Protocol for A-frame Abduction Brace

1. The brace is custom molded in the OR just prior to the application of Petrie cast.
2. The brace is generally applied 6 weeks after initiating Petrie cast treatment. AP pelvis x-ray is obtained with patient in brace to check hip containment in the brace.
3. Instruction is given to educate parents that patient’s legs should be symmetrically abducted to prevent favoring of the affected side.
4. Brace is worn 12 hours per day for the 1st 6 months, mainly at night time and during a sleep. The brace wear does not have to be continuous 12 hours. If good hip abduction is maintained at 6 months follow up, the brace wear can be decreased to 8 hours per day and discontinued at 1 year.
5. During day time, patient uses a wheelchair, walker, or crutches to be non-weight bearing on the affected leg.
6. Patient is shown hip range of motion exercises focusing on hip rotation and abduction.
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes' disease

IPSG

APPENDIX IV

The PROMIS questionnaire is being developed to evaluate activity level in children and will have a format similar to the mobility questionnaire below. The questionnaire will be electronically administered. This questionnaire is here just for informational purposes.

PROMIS™ Pediatric Item Bank v1.0 - Physical Function Mobility

© 2009-2012 PROMIS® Health Organization and PROMIS Cooperative Group Page 1 of 2

<table>
<thead>
<tr>
<th>Pediatric Physical Function Mobility</th>
<th>With no trouble</th>
<th>With a little trouble</th>
<th>With some trouble</th>
<th>With a lot of trouble</th>
<th>Not able to do</th>
</tr>
</thead>
<tbody>
<tr>
<td>Please respond to each item by marking one box per row. In the past 7 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I could do sports and exercise that other kids my age could do.</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I could get up from the floor.</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I could keep up when I played with other kids.</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I could move my legs.</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I could stand up by myself.</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I could stand up on my tiptoes.</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I could walk up stairs</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Last Updated: March 2017
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

without holding on to anything.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>I have been physically able to do the activities I enjoy most.</td>
<td></td>
</tr>
<tr>
<td>I could bend over to pick something up.</td>
<td></td>
</tr>
<tr>
<td>I could carry my books in my backpack.</td>
<td></td>
</tr>
<tr>
<td>I could get down on my knees without holding on to something.</td>
<td></td>
</tr>
<tr>
<td>I could get in and out of a car.</td>
<td></td>
</tr>
<tr>
<td>I could get into bed by myself.</td>
<td></td>
</tr>
</tbody>
</table>

Last Updated: March 2017
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX V

MODIFIED HARRIS HIP SCORE

*If you are over 10 years old, please complete:*

For each category, check the box that best describes you: *(Please check only one box.)*

1. **Which of these categories would best describe your hip pain?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>44</td>
<td>None/Able to ignore it</td>
</tr>
<tr>
<td>40</td>
<td>Slight, occasional, no compromise in activity</td>
</tr>
<tr>
<td>30</td>
<td>Mild, no effect on ordinary activity, pain after unusual activity, use aspirin/ibuprofen/Tylenol</td>
</tr>
<tr>
<td>20</td>
<td>Moderate, tolerable, make concessions, occasional pain reliever stronger than aspirin or Tylenol</td>
</tr>
<tr>
<td>10</td>
<td>Marked, serious limitations</td>
</tr>
<tr>
<td>0</td>
<td>Totally disabled</td>
</tr>
</tbody>
</table>

2. **Functional capacity (Please check only one box for each question below.)*

   a. **How much do you limp while walking?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>Slight</td>
</tr>
<tr>
<td>5</td>
<td>Moderate</td>
</tr>
<tr>
<td>2</td>
<td>Severe</td>
</tr>
<tr>
<td>0</td>
<td>Unable to walk</td>
</tr>
</tbody>
</table>

   b. **Do you need support when walking?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>Cane for long walks</td>
</tr>
<tr>
<td>5</td>
<td>Cane all the time</td>
</tr>
<tr>
<td>4</td>
<td>Crutch</td>
</tr>
<tr>
<td>3</td>
<td>2 canes</td>
</tr>
<tr>
<td>2</td>
<td>2 crutches</td>
</tr>
<tr>
<td>1</td>
<td>Walker</td>
</tr>
<tr>
<td>0</td>
<td>Unable to walk</td>
</tr>
</tbody>
</table>

   c. **How far can you walk without stopping because of hip pain?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>Unlimited</td>
</tr>
<tr>
<td>8</td>
<td>6 blocks</td>
</tr>
<tr>
<td>5</td>
<td>2—3 blocks</td>
</tr>
<tr>
<td>2</td>
<td>Indoors only</td>
</tr>
<tr>
<td>0</td>
<td>Bed and chair only</td>
</tr>
</tbody>
</table>

   d. **How do you go up and down stairs?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>Normally (1 foot on each step)</td>
</tr>
<tr>
<td>2</td>
<td>Normally with banister</td>
</tr>
<tr>
<td>1</td>
<td>Any method (both feet on each step)</td>
</tr>
<tr>
<td>0</td>
<td>Not able</td>
</tr>
</tbody>
</table>

   e. **How do you put on shoes and socks?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>With ease</td>
</tr>
<tr>
<td>2</td>
<td>With difficulty</td>
</tr>
<tr>
<td>0</td>
<td>Unable</td>
</tr>
</tbody>
</table>

   f. **How long can you sit in a chair?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Any chair, 1 hour</td>
</tr>
<tr>
<td>3</td>
<td>High chair, ½ hour</td>
</tr>
<tr>
<td>0</td>
<td>Unable to sit in any chair ½ hour</td>
</tr>
</tbody>
</table>

   g. **Are you able to use public transportation such as a bus or light rail if you wanted to?**

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Able to use</td>
</tr>
<tr>
<td>0</td>
<td>Unable to use</td>
</tr>
</tbody>
</table>
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX VI
METHOD OF MEASURING THE DEFORMITY INDEX


The method of calculating the deformity index from an AP radiograph of the pelvis is shown in the Figure 1. Using Adobe Photoshop a horizontally flipped image of the affected hip is overlaid as a semi-transparent image on that of the unaffected hip, using the medial epiphysis and the calcar to adjust for rotation and translation. The maximal orthogonal differences in height and width between the affected and normal epiphysis are measured. These data are summed and divided by the width of the normal growth plate. The last step controls for magnification differences on radiographs.

Method of measuring the Deformity Index (DI)
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX VII

METHOD OF QUANTITATIVE MEASUREMENT OF SPHERICITY OF THE FEMORAL HEAD

THE SPHERICITY DEVIATION SCORE


On the AP radiograph two reference points are marked on the medial and lateral margins of the capital femoral growth plate (Figure a) and a circle is drawn touching these reference points to match the size of the femoral head. If the circle perfectly fits the contour of the articular margin the radius of the circle is noted (r. ap). If the articular margin does not conform to the arc of the circle the size of the circle is adjusted so as to just touch the reference points and the articular margin without extending outside the femoral head (the maximum inscribed circle – MIC; Figure b). Another concentric circle is drawn to just touch the outer limits of the articular margin without extending inside the femoral head (the minimum circumscribed circle – MCC; Figure c). The radii of these circles are noted (r mic-ap & r mcc-ap; Figure d). The same measurements are performed on the Lauenstein lateral radiograph. The roundness errors which are the differences in the radii of MIC & MCC in both views are expressed as ratios:

Roundness error on the antero-posterior radiograph:

\[ \text{RE-AP} = \frac{r_{\text{mcc ap}} - r_{\text{mic ap}}}{\text{Mean of } r_{\text{mcc ap}} + r_{\text{mic ap}}} \times 100 \]

Roundness error on the lateral radiograph:

\[ \text{RE-Lat} = \frac{r_{\text{mcc lat}} - r_{\text{mic lat}}}{\text{Mean of } r_{\text{mcc lat}} + r_{\text{mic lat}}} \times 100 \]

Ellipsoid deformation of the head (ED) is considered to be present when the radius of the femoral head in the AP radiograph differs from the radius of the femoral head in the lateral radiograph. ED is computed using the following formula.

Ellipsoid deformation of the femoral head:

\[ \text{ED} = \frac{r_{\text{lat}} - r_{\text{ap}}}{r_{\text{ap}}} \times 100 \]

(If r ap was greater than r lat the formula used is:

\[ \text{Ed} = \frac{r_{\text{ap}} - r_{\text{lat}}}{r_{\text{lat}}} \times 100 \]

The extent to which the shape of the femoral head deviates from sphericity is the sum of the roundness errors in the AP and lateral view and the ellipsoid deformation (Sphericity Deviation Score (SDS) = (RE-AP) + (RE-Lat) + (ED)).

Last Updated: March 2017
The technique of measuring the roundness error of the femoral head.

Reference points are marked at the medial and lateral margins of the capital femoral growth plate.

The maximum inscribed circle is drawn and the center of the circle is marked.

The minimum circumscribed circle is drawn with its centre coinciding with the centre of the maximum inscribed circle. The difference in the radii of these two circles are calculated and expressed as a ratio.
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

APPENDIX VIII
List of participating surgeons with location

<table>
<thead>
<tr>
<th>Institution Name</th>
<th>PI /Provider</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alberta Children’s Hospital, Calgary</td>
<td>Fabio Ferri-de-Barros</td>
</tr>
<tr>
<td>BC Children’s Hospital</td>
<td>Kishore Mulpuri</td>
</tr>
<tr>
<td>Boston Children’s Hospital</td>
<td>Ben Shore</td>
</tr>
<tr>
<td>Boston Children’s Hospital</td>
<td>Eduardo Novais</td>
</tr>
<tr>
<td>Bristol Royal Children’s Hospital</td>
<td>Simon Thomas</td>
</tr>
<tr>
<td>Cincinnati Children’s</td>
<td>Chuck Mehlman</td>
</tr>
<tr>
<td>Cincinnati Children’s</td>
<td>Junichi Tamai</td>
</tr>
<tr>
<td>Connecticut Children’s Medical Center</td>
<td>Phillip Mack</td>
</tr>
<tr>
<td>Le Bonheur/Campbell Clinic</td>
<td>Derek Kelly</td>
</tr>
<tr>
<td>Children’s Hospital of Alabama, Birmingham</td>
<td>Shawn Gilbert</td>
</tr>
<tr>
<td>Children’s Colorado</td>
<td>Nancy Miller</td>
</tr>
<tr>
<td>Children’s Hospital Hamburg</td>
<td>Ralf Stuecker</td>
</tr>
<tr>
<td>Children’s Hospital Los Angeles</td>
<td>Paul Choi</td>
</tr>
<tr>
<td>Children’s Healthcare of Atlanta</td>
<td>Tim Schrader</td>
</tr>
<tr>
<td>Children's Hospital of Philly</td>
<td>Woody Sankar</td>
</tr>
<tr>
<td>Children’s National Medical Center, DC</td>
<td>Ben Martin</td>
</tr>
<tr>
<td>Columbia University</td>
<td>Josh Hyman</td>
</tr>
<tr>
<td>Alfred I duPont Hospital for Children</td>
<td>Mihir Thacker</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Jennifer Laine</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Steve Sundberg</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Susan Novotny</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Walter Truong</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Benjamin Novak</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Deborah Quanbeck</td>
</tr>
<tr>
<td>Gillette Children's Specialty Healthcare</td>
<td>Kevin Walker</td>
</tr>
<tr>
<td>Lubek, Germany University</td>
<td>Barbara Behnke</td>
</tr>
<tr>
<td>Lubek, Germany University</td>
<td>Ludwig Meiss</td>
</tr>
<tr>
<td>Johns Hopkins</td>
<td>John Tis</td>
</tr>
<tr>
<td>Kasturba Medical College</td>
<td>Ben Joseph</td>
</tr>
<tr>
<td>Kasturba Medical College</td>
<td>Hitesh Shah</td>
</tr>
<tr>
<td>Kaiser Permanente</td>
<td>Jeff Kessler</td>
</tr>
<tr>
<td>Lurie Children’s</td>
<td>Jay Janicki</td>
</tr>
<tr>
<td>Mayo Clinic</td>
<td>Noelle Larson</td>
</tr>
<tr>
<td>Monteifiore</td>
<td>Eric Fornari</td>
</tr>
<tr>
<td>Medical University of Lodz</td>
<td>Marek Synder</td>
</tr>
<tr>
<td>Nationwide Children’s</td>
<td>Kevin Klingele</td>
</tr>
<tr>
<td>NYU Langone</td>
<td>David Godfried</td>
</tr>
<tr>
<td>NYU Langone</td>
<td>Pablo Castaneda</td>
</tr>
<tr>
<td>Orlando's Arnold Palmer Hospital</td>
<td>Jose Herrero</td>
</tr>
<tr>
<td>OrthoCarolina</td>
<td>Virginia Casey</td>
</tr>
<tr>
<td>Orta Portugal</td>
<td>Nuno Lopes</td>
</tr>
<tr>
<td>Paley Orthopaedic and Spine Institute</td>
<td>David Feldman</td>
</tr>
<tr>
<td>Rady Children’s Hospital California</td>
<td>Salil Upasani</td>
</tr>
</tbody>
</table>
A prospective, multi-center, surgeon controlled, non-randomized study of the role of containment in children with late-stage Legg-Calvé-Perthes’ disease

<table>
<thead>
<tr>
<th>Institution</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheffield Children's Hospital</td>
<td>Sanjeev Madan</td>
</tr>
<tr>
<td>Shriners Hospital for Children - Northern CA</td>
<td>Vedant Kulkarni</td>
</tr>
<tr>
<td>Southampton General Hospital</td>
<td>Nick Clarke</td>
</tr>
<tr>
<td>Southampton General Hospital</td>
<td>Alex Aarvold</td>
</tr>
<tr>
<td>Seoul National University Childrens Hospital</td>
<td>WonJoon Yoo</td>
</tr>
<tr>
<td>Sao Paulo School of Medicine</td>
<td>Roberto Guarniero</td>
</tr>
<tr>
<td>Sao Paulo School of Medicine</td>
<td>Patricia Moreno</td>
</tr>
<tr>
<td>Shriners Hospital for Children, Salt Lake City</td>
<td>Theresa Hennessey</td>
</tr>
<tr>
<td>Texas Scottish Rite Hospital for Children</td>
<td>Harry Kim</td>
</tr>
<tr>
<td>Texas Scottish Rite Hospital for Children</td>
<td>Tony Herring</td>
</tr>
<tr>
<td>Texas Children</td>
<td>Scott Rosenfeld</td>
</tr>
<tr>
<td>Tianjin Center Hospital China</td>
<td>Jianping Yang</td>
</tr>
<tr>
<td>University of Arizona College of Medicine</td>
<td>Judson Karlen</td>
</tr>
<tr>
<td>Uppsala University</td>
<td>Yasmin Hailer</td>
</tr>
</tbody>
</table>

Last Updated: March 2017