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Residual hip dysplasia at 1 year after treatment for neonatal hip instability is not related to degenerative joint disease in young adulthood: a 21-year follow-up study including dGEMRIC

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SUMMARY

Objective: Developmental dysplasia of the hip (DDH) is associated with an increased risk of early hip osteoarthritis (OA). We aimed to examine the outcome at the completion of growth in a cohort of children who had residual acetabular dysplasia at age 1 year following early treatment for neonatal instability of the hip (NIH).

Design: We examined 21 of 30 subjects who had been treated with the von Rosen splint neonatally for NIH and had residual acetabular dysplasia at age 1 year. Mean follow-up time was 21 years (range 17–24). Signs of OA and acetabular dysplasia were assessed by radiography. Cartilage quality was assessed by delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC), a tool for molecular imaging of cartilage quality, at 1.5 T. Patient reported outcome (PRO) was assessed by the 12-item WOMAC score.

Results: No study participant had radiographic OA (defined as Kellgren–Lawrence grade ≥2) or minimum joint space width (JSW) ≤2 mm. The mean dGEMRIC index was 630 ms (95% CI: 600–666, range: 516–825) suggesting good cartilage quality. The mean 12-item WOMAC score was 1.2. Two of three radiographic measurements of DDH correlated positively to the dGEMRIC index.

Conclusions: Children treated neonatally for NIH have good hip function and no signs of cartilage degeneration at 21-year follow-up, despite residual dysplasia at age 1 year. Unexpectedly, radiographic signs of dysplasia were associated with better cartilage quality, as assessed with dGEMRIC. This may indicate cartilage adaptation to increased mechanical stress in mild hip dysplasia.

Introduction

Neonatal instability of the hip (NIH) is a part of the developmental dysplasia of the hip (DDH) disease spectrum, which also includes acetabular dysplasia and late hip dislocation. In DDH, the head of the femur is not fully contained in the acetabulum, leading to poor mechanical properties of the hip joint. DDH is a major underlying cause for early total hip replacement (THR)[1,2]. Despite early treatment with abduction splinting using the Frejka pillow, a Norwegian study reported that NIH leads to a 2.6 times increased risk of receiving a THR in young adulthood, compared to the rest of the population[3].

In Sweden, the most commonly used treatment for NIH is the von Rosen splint, which revealed a lower rate of treatment failure compared to the Frejka pillow in several studies[4–6]. The rationale for treatment with an abduction splint, such as the von Rosen splint or the commonly used Pavlik harness, is that hip abduction centers the head of the femur in the joint. This promotes a normal development of the acetabulum. We have previously demonstrated that children who were treated with the von Rosen splint due to NIH have a higher prevalence of acetabular dysplasia at 1 year of age compared to controls with stable hips neonatally[7].

Delayed Gadolinium Enhanced Magnetic Resonance Imaging of Cartilage (dGEMRIC) is a molecular imaging technique using an MRI scanner and a sensitive tool for detection of early cartilage

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pathology that eventually leads to osteoarthritis (OA). The technique is based on the principle that the negatively charged contrast agent $Gd(DTPA)^{2-}$ distributes in articular cartilage in an inverse relationship to the negatively charged glycosaminoglycan (GAG) after intravenous administration. GAG is essential for the biomechanical properties of the cartilage[8] and decreases early in the OA disease process[9]. Since $Gd(DTPA)^{2-}$ shortens the T_1 relaxation time of the MRI signal, a quantitative T_1 measurement within the cartilage provides a surrogate marker for cartilage GAG content. T_1 in the presence of $Gd(DTPA)^{2-}$ is often referred to as T_{1Gd}, and the dGEMRIC index is the mean T_{1Gd} in a chosen region of interest (ROI) within the cartilage. Hence, a high dGEMRIC index corresponds to higher GAG content and vice versa[10,11]. A low dGEMRIC index has been associated with failure of the Bernese periacetabular osteotomy in adult patients with DDH[12], presumably because it can differentiate the cases where the OA disease process has advanced too far from those where the cartilage composition is relatively normal. Furthermore, dGEMRIC is sensitive enough to show differences in cartilage composition between healthy subjects with different levels of physical activity[13], and has also been shown to correlate to both pain and the degree of acetabular dysplasia in DDH patients[14].

The purpose of this study was to examine the outcome after the completion of growth in subjects who had been treated neonatally with a von Rosen splint for NIH and still had residual acetabular dysplasia at age 1 year. Our hypothesis was that persistent dysplasia at the completion of growth would correlate to a low dGEMRIC index, possibly in combination with radiographic signs of OA and a worse patient reported outcome (PRO).

Subjects and methods

Study participants

All children who had been treated for NIH from 1987 to 1993 were identified from the pediatric hip register at our institution. The treatment protocol has previously been described in detail[7]. In this study, only children with a positive Barlow[15] or Ortolani[16] sign neonatally were eligible for inclusion ($n = 131$). They were treated in the von Rosen splint for 6–12 weeks. Our follow-up protocol includes a radiographic examination at age 12 months. The acetabular index (AI) was measured according to Hilgenreiner[17], on digital AP pelvic radiography films. Subjects with an AI of $\geq 28^\circ$ in either hip at age 1 year were eligible for the study.

Thirty subjects had at least one hip with an AI $\geq 28^\circ$ at age 1 year. Of these, 29 could be contacted and 21 agreed to participate in the study. Eighteen of the 21 subjects were female. Mean age at treatment start was 1 day (range 0–4). Mean age at radiographic follow-up was 21 years (range 17–24). Mean age at clinical examination, answering the 12-item WOMAC and dGEMRIC examination was 21 years (range 18–24). Mean BMI was 24.7 (range: 18–53), the weight being measured on the day of the dGEMRIC examination.

Radiography

All patients had completed skeletal hip growth, i.e., had closed physes of the proximal femur and acetabulum. Radiographs were classified for OA according to Kellgren–Lawrence using AP pelvic and AP and lateral hip radiographs[18]. The minimum joint space width (JSW) was measured according to Jacobsen *et al.*[19]. Measurements assessing hip morphology were made on the AP pelvic radiographs, using three commonly used radiographic parameters of hip dysplasia:

the center-edge angle of Wiberg (CE angle)[20],
the femoral head extrusion index (FHEI)[21] and
the acetabular angle of Sharp (Sharp angle)[22].

Rotation of the pelvis in the axial plane was assessed by measuring the foramen obturator index (FOI) according to Tönnis[23]. All FOI values were within 0.7–1.8 (range 0.74–1.42) which means that errors in measurements of the CE angle and Sharp angle due to rotation of the pelvis were within $\pm 2^\circ$[24].

dGEMRIC

Subjects received a double-dose (0.2 mmol/kg) intravenously of $Gd(DTPA)^{2-}$ (Magnevist®, Schering AG, Berlin, Germany), followed by a 10 min timed walk. The walking time was based on a previously published methodological study on healthy volunteers and patients with hip dysplasia[25]. dGEMRIC imaging was performed 60 min after the injection using a standard 1.5 T MRI system (MAGNETOM Avanto, Siemens AG, Erlangen, Germany), with two flexible Body Matrix coils positioned directly over the hips[25]. Five turbo inversion recovery images with different inversion times were used to calculate T_1 relaxation times. Repetition time (TR) was 1840 ms, echo time (TE) 15 ms, field-of-view (FoV) 140×140 mm^2, and imaging matrix 256×256. Inversion times (TI) were 1650, 650, 350, 150 and 50 ms. A 3 mm thick, central slice in the coronal plane of each hip was selected for T_1 mapping. Both hips were imaged in the same imaging session with the subject lying still in the MRI machine during the whole session. The ROI in each hip was drawn manually, including both the acetabular and the femoral cartilage of the weight-bearing region of the hip joint[14] (Fig. 1). The dGEMRIC index of each hip was calculated as the mean T_{1Gd} of its ROI, excluding voxels with T_{1Gd} >1300 ms, according to standard protocol at our institution. dGEMRIC indices were then adjusted for BMI to correct for differences in distribution volume using the formula described by Tiderius *et al.*[26]. Two investigations were excluded due to motion artifacts, leaving 40 hips for dGEMRIC analysis. A standard clinical MRI scan of both hips was also performed in the same imaging session. The MRI scans were reviewed by a senior radiologist who was blinded with regards to all other outcomes of the study.

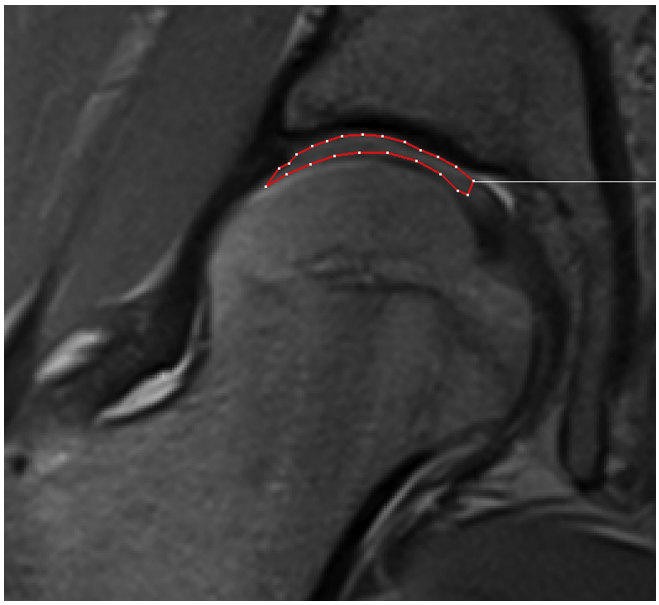

Fig. 1. The ROI is drawn manually on an anatomical MRI image. The dGEMRIC index is calculated as the mean T_{1Gd} of all voxels in the ROI.