Original Article
Spatial changes of the peri-acetabular pelvic in developmental dysplasia of the hip—a combined 3-dimensional computed tomography (3D-CT) study in patients and experimental study in rats

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Abstract: Few previous studies noticed the three bony structures that formed the acetabulum in developmental dysplasia of the hip (DDH). This study aimed at investigating the spatial changes of the peri-acetabular pelvis in developmental dysplasia of the hip through radiological evaluation of the patients and experimental observations in rat models. 115 unilateral DDH patients were studied through 3D-CT. In reconstruction workstation, the iliopubic inner plate angle, ilioischial inner plate angle and ischialpubic inner plate angle were measured and compared. 58 neonatal Wistar rats were divided into two groups and the rats in experiment group were swaddled to establish DDH models. The hips were sectioned, stained. The same three angles were measured and compared. The ilioischial inner plate angle of the affected hip decreased while the ischialpubic inner plate angle increased compared to those of the contralateral side. The iliopubic inner plate angle showed no difference between the affected and unaffected hips. In animal models we observed the same pathological pattern. The three angles measured on the sections showed similar tendency as those in the patients with DDH. The ischium rotates up and forwardly around the posterior and vertical limbs of the triradiate cartilage complex in DDH, just as a lifted piece of Pizza.

Keywords: Developmental dysplasia of the hip, triradiate cartilage complex, 3D-CT, animal model, ischium

Introduction
The acetabulum of young children is mainly comprised of the triradiate cartilage complex (TCC), a conjunct cartilage that lies among the three osseous components of the pelvis (the ilium, ischium, and pubis) [1, 2]. In the natural history of DDH, not only the shape but also the direction of the acetabulum changes in untreated dislocated hip in children [3-5]. Considering the osteogenesis role of the TCC, changes in the TCC or (and) relevant bony changes may contribute to this phenomenon.

Relevant articles mainly focused on the acetabulum, through either radiological studies in patients or histological studies in experimental animals. Few of them noticed the three-dimensional relationship between the ilium, pubis and ischium in DDH, let alone the TCC in conjunction of them. In our previous study, we observed both in patients and rat models of DDH that excessive lateral rotation of the ischium resulted in increased acetabular anteverision [6-8]. So we hypothesized that the position of the ischium might display some changes within the hemipelvis of the dislocated hip in DDH.

This study combines clinical evaluation of DDH patients through 3D-CT with experimental observation of rat DDH models, aiming at finding out the features of spatial change in ischium in DDH. We hope our study can provide further insight to the pathology of DDH.

Materials and methods
Radiologic study on clinical subjects
We investigated all the patients who had been diagnosed unilateral DDH in our hospital from
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January 2007 to August 2010. The inclusion criteria were as follows: (1) the affected hip was diagnosed DDH and the unaffected hip presented no radiographic abnormalities; (2) no treatment before admission to our hospital and (3) complete 3D-CT image data of the patient can be obtained. Before September 2010, 3D-CT was used in our institution to evaluate the femoral neck anteversion (FNA) of the patients with DDH preoperatively. After that, MRI has been utilized instead of CT to evaluate FNA. Patients with neuromuscular diseases or hip dislocation complicated by other congenital malformations were excluded. A total of 115 cases met the criteria, including 76 left dislocations and 39 right dislocations; 16 were male and 99 were female. Age range was from 2 to 9 years, averaging 3 years and 6 months. 40 cases were classified as Tönnis II, 43 cases as Tönnis III and 32 cases as Tönnis IV. The unaffected hips were used as control.

The patients were examined with the U. S. Marconi Company’s Mx8000 type CT. The scan range was from the iliac crest to the lesser trochanter of the femur. Scan parameters: tube voltage ball 120 Kv, current 70-100 MA, slice thickness 1.0 mm, the interlayer spacing 1.0 mm and pitch 0.875 mm. Reconstruction and measurement were done in the spiral CT workstation applications (Extended Brilliance [Tm] Workspace) and Display image associated measurement systems (Figure 1). For the ilio-pubic inner plate angle, the measurement was performed on the plane through the midpoint of the anterior branch of TCC perpendicular to the inner plate of ilium and pubis concurrently. Tangent lines of the inner panel of the ilium and the pubis formed the ilio-pubic inner plate angle. Similarly, the measurement of the ilioischial inner plate angle and the ischialpubic inner plate angle (Figure 2) were performed and compared. Reconstruction and measurement were performed by two different experienced doctors of department of radiology in our hospital to assess the interobserver variation. One of the observers reconstructed and measured the data the second time a month after the first time to assess the intraobserver variation. And the average of the three results of measurement was used as the final data of each angle to be analyzed.

Experimental animal study

58 neonatal Wistar rats from 6 litters were divided into control group (15 females, 10 males) and an experimental group (19 females, 14 males). The experimental group were swaddled with medical tape (3 M Durapore, St.Paul, Minnesota) to keep the hips and knees in extension and lower limbs together for the first ten days of life, as described by E. Wang [8]. The swaddling permitted minor hip and knee movement. The rats were released from the swaddles for thirty minutes per day and rewrapped in accommodation to the growth of their bodies. The rats all fed from their mothers, and care was taken to guarantee their normal intake. After ten days, the swaddles were removed and the rats were allowed unrestricted motion in the cage.

Figure 1. Reconstruction images were completed in three section planes. The section plane were through the midpoint of the each branch of TCC and perpendicular to the inner plates of the both adjacent bones concurrently. ___: Indicates the section plane between the ilium and the ischium. ......: Indicates the section plane between the ilium and the pubis. -----: Indicates the section plane between the ischium and the pubis.
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At the age of 1 month, all rats were euthanized by 5% chloral hydrate. All hips were dissected en bloc, fixed in neutral formalin and decalcified in 10% EDTA (ethylenediaminetetraacetic acid). Rats from two groups were used to observe the iliopubic inner plate angle, the ilioischial inner plate angle and the ischialpubic inner plate angle respectively. Then the samples were embedded in paraffin and sectioned at 4 μm thickness on the same levels as described in 3DCT image data. All the sections were stained with Safranin O-Fast Green (Sigma). Then we measured the three angles on the corresponding sections.

Statistical analysis

Statistical analysis was performed with Statistical Package for Social Science 17.0 (SPSS; Chicago, Illinois). Paired sample t-test and independent sample t-test were used to analyze differences between the control group and the experimental group. Independent sample t-test was used to analyze differences between genders. Bivariate correlate were used to study the difference among the degrees of dislocation as well as ages. P < 0.05 was regarded as statistically significant. The interobserver variation and intraobserver variation were analyzed with Bland-Altman by Medcalc 12.2.1.0 (Ostend, Belgium).

Table 1. The inner plate angles from radiographic examination of 115 children with unilateral DDH

<table>
<thead>
<tr>
<th>Inner plate angle (n = 115)</th>
<th>Affected hips</th>
<th>Unaffected hips</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iliopubic</td>
<td>129.6 ± 8.60</td>
<td>128.8 ± 8.55</td>
<td>0.109</td>
</tr>
<tr>
<td>Ilioischial</td>
<td>128.5 ± 7.48</td>
<td>135.3 ± 6.68</td>
<td>0.001*</td>
</tr>
<tr>
<td>Ischialpubic</td>
<td>178.7 ± 10.08</td>
<td>171.2 ± 8.71</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

All data were presented as mean ± standard deviation. *Indicates statistical significance compared to unaffected controls at P < 0.05.

Results

Measurement of the radiological parameters listed in Table 1 were the average of three measurements. Difference between the affected and unaffected side of unilateral DDH was significant in the ilioischial inner plate angle and the ischialpubic inner plate angle. Gender difference were insignificant in all three parameters, with p = 0.105 in the ilioischial inner plate angle, p = 0.247 in the iliopubic inner plate angle and p = 0.775 in the ischialpubic inner plate angle. Differences in the three angles between the affected and unaffected side were not correlated with age, nor the degrees of dislocation. The results of interobserver variation and intraobserver variation showed the difference between different observers and different time were small enough to be accepted. So the reconstruction and measurement from different observers and in different time were considered to be accordant and repetitive (Tables 2, 3).

In the animal study, 3 female rats in the experimental group died during the experiment. Gross observation of the remaining 60 hips rats in the experimental group showed that 48 hips were completely dislocated, 4 hips (all from female rats) were subluxation and 8 hips were normal (6 hips from male rats and 2 hips from female rats). Only the 48 completely dislocated hips were further studied. In the control group, all hips were normal and included in further study. In histological study, we found the ischium of the rats in the experimental group turned forward and upward compared to those in the control group (Figure 3). By measuring the sec-
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Table 2. The interobserver variation of 3D-CT

<table>
<thead>
<tr>
<th></th>
<th>Affected hips</th>
<th>Unaffected hips</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bias ± SD</td>
<td>Limits of agreement</td>
</tr>
<tr>
<td>Iliopubic</td>
<td>-0.2 ± 3.37</td>
<td>(-6.9, 6.4)</td>
</tr>
<tr>
<td>Ilioschial</td>
<td>-9.4 ± 8.67</td>
<td>(-26.3, 7.6)</td>
</tr>
<tr>
<td>Ischialpubic</td>
<td>-1.5 ± 5.87</td>
<td>(-13.0, 10.0)</td>
</tr>
</tbody>
</table>

All data were presented as mean ± standard deviation. Bias-average difference, ideal bias = 0. Limits of Agreement describes the range for 95% of comparison points.

Table 3. The intraobserver variation of 3D-CT

<table>
<thead>
<tr>
<th></th>
<th>Affected hips</th>
<th>Unaffected hips</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bias ± SD</td>
<td>Limits of agreement</td>
</tr>
<tr>
<td>Iliopubic</td>
<td>1.2 ± 4.85</td>
<td>(-8.3, 10.7)</td>
</tr>
<tr>
<td>Ilioschial</td>
<td>-0.4 ± 3.27</td>
<td>(-6.7, 6.0)</td>
</tr>
<tr>
<td>Ischialpubic</td>
<td>0.5 ± 4.59</td>
<td>(-8.5, 9.5)</td>
</tr>
</tbody>
</table>

All data were presented as mean ± standard deviation. Bias-average difference, ideal bias = 0. Limits of Agreement describes the range for 95% of comparison points.

In this study, we used three angles to depict the three-dimensional relationship among the three bones. The ilioschial inner plate angle of the affected hip was significantly reduced compared to the unaffected side (P < 0.01), while the ischialpubic inner plate angle of the affected side was significantly larger than the unaffected side (P < 0.01). Spatially speaking, the ischium had rotated upward around the axis of the posterior flange of TCC and forward around the axis of the anterior flange of TCC, just as a lifted piece of Pizza (Figure 5).

Acetabulum is a three-dimensional structure consisted of the acetabular TCC, articular cartilage and the three bones. These parts should develop proportionally to form a normal acetabulum. Portinaro found by measuring the thickness of epiphyseal plates that in TCC the epiphyseal plate of ischium grew the most quickly, followed by the pubis and the ilium. In other words, the ischium contributed the most to the development of acetabulum, while the ilium contributed less and the pubis the least. Changes in the three-dimensional features of the ischium will significantly influence the morphology of the acetabulum [13]. Harrison reported that the ischial epiphysis which constituted the posterior wall of the acetabulum became disturbed or even stopped growing after manual removal of the femoral head [14]. E. Delgado-Baeza et al. also found that the ilium would turn forward and outward after femoral head dislocation in an analogous animal experiment and hypothesized that it resulted from growth disorders of the triradiate cartilage [15]. But Smith et al. got different results when they investigated dogs and guinea pigs. They attributed this difference to different propor-
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We designed an animal study to further clarify this issue. Instead of manual dislocation of the femoral head, as described in most previous studies, we focused on the susceptibility of cartilage tissue in the hips and different susceptibility to deformation among spaces.

Figure 3. The gross anatomical observation of the experimental group (A) and the control group (B). Note the remarkably deviated ischium around the dislocated hips (arrows).

Figure 4. Safranin O-fast green stained sections (×20): (A, C, E) were from experimental group and (B, D, F) were from control group. (A, B) were the iliopubic inner plates angle, (C, D) were the ilioischial inner plate angle and (E, F) were the ischialpubic inner plate angle respectively. Note the difference of the ilioischial inner plate angle and the ischialpubic inner plate angle between the experimental and control groups. *Indicates ilium, #Indicates ischium, +Indicates pubis.
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Table 4. The inner plate angle measuring from the rats of the experimental and control group

<table>
<thead>
<tr>
<th>Inner plate angle</th>
<th>Dislocated hips group (n = 48)</th>
<th>Control group (n = 50)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iliopubic</td>
<td>169.6 ± 4.86</td>
<td>170.5 ± 4.15</td>
<td>0.268</td>
</tr>
<tr>
<td>Ilioischial</td>
<td>145.1 ± 6.44</td>
<td>164.4 ± 5.87</td>
<td>0.001*</td>
</tr>
<tr>
<td>Ischialpubic</td>
<td>137.5 ± 5.51</td>
<td>124.6 ± 5.92</td>
<td>0.001*</td>
</tr>
</tbody>
</table>

All data represented as mean ± standard deviation. *indicates statistical significance compared to untreated controls at P < 0.05.

Figure 5. Spatial change of the ischium. The ischium turns forward and upward slightly around the posterior and vertical limbs of the triradiate cartilage complex respectively in the hip of DDH, just as a lifted piece of Pizza. Normal hip (left) and dislocated hip (right).

Our study verified this thesis, both in patients and in animals, and thus made periacetabular osteotomies (innominate osteotomy, triple osteotomy, etc.) that redirected the acetabulum more theoretically reasonable.

The ilio-pubic inner plate angle showed no difference between the affected and unaffected hips, both in patients and in animals. We speculated that the sacroiliac joint and the pubic symphysis were firm enough to fix the ilium and pubis in their positions, while the ischium is relatively free and therefore prone to bending. Further investigation is needed to verify the mechanism of this phenomenon.

In conclusion, of the three bony components of the acetabulum, the ischium shows the most obvious spatial change in DDH, which may contribute to the change of acetabular direction. The ischium rotates up and forwardly around the posterior and vertical limbs of the TCC respectively, just as a lifted piece of Pizza.

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Disclosure of conflict of interest

None.

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