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Original Article

Ossification in developmental dysplasia of the hip can be evaluated by accurate volume measurement on 3D CT: a retrospective study

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Abstract: Background: The present study aimed to develop an accurate method for evaluating hip-bone development in DDH. Methods: CT scans were performed on 15 phantoms and 16 unilateral hips with developmental dysplasia. The validity of the three-dimensional reconstruction (3DR) method and ellipsoid model (EM), as well as ossification volumes (OVs) and ossification-volume ratios (OVRs), were analyzed. Results: Mean ± SD EM- and 3DR- absolute-errors were 20.02 ± 23.67 mL and 0.25 ± 2.72 mL. The SNR of the 3DR method was 0.129, 50 times greater than that of the EM. The OVs of hips in the dislocated group (8.62 ± 4.09/cm^3, 3.93 ± 1.94/cm^3, and 20.21 ± 8.93/cm^3 for the ischium, pubis and proximal femur) were significantly smaller (*P* = 0.008, 0.002, 0.006) than those in the normal group (11.61 ± 5.63/cm^3, 4.93 ± 2.73/cm^3, and 23.42 ± 12.48/cm^3, respectively) and for the ilium (32.84 ± 17.36/cm^3 and 31.14 ± 16.25/cm^3, respectively; *P* = 0.018). OVRs in the young group (age < 44 months; 1.03 ± 0.33, 0.91 ± 0.15, and 0.93 ± 0.05 for the ischium, pubis and proximal femur, respectively) were significantly higher (*P* = 0.010, 0.018, and 0.023, respectively) than those in the old group (participants aged ≥ 44 months; 0.60 ± 0.24, 0.75 ± 0.09, and 0.84 ± 0.08, respectively), except for the ilium (1.09 ± 0.17 and 1.06 ± 0.08, respectively, *P* = 0.644). Conclusion: The accuracy of the 3DR method is higher than that of EM. OVs of dislocated hips are smaller. OVRs are associated with age but not dislocation distance. Bone development is delayed in dislocated hips and tends to reduce with age.

Keywords: Three-dimensional computed tomography, DDH, ossification, dislocation distance, phantom study

Introduction

Developmental dysplasia of the hip (DDH) is a common joint disease leading to complex pathmorphology features affecting the acetabulum, proximal femur, hip articular capsule, and surrounding ligaments and muscles [1, 2]. DDH is a primary cause of osteoarthritis at an early age [3, 4]. Incidence of DDH has been reported as 1.5-20 per 1,000 births [5]. Residual DDH is likely to develop when receiving improper treatment. It is important to detect the development of residual DDH and give intervention early to avoid of progress to severe hip osteoarthritis (OA), which requires total hip arthroplasty (THA).

Typically, DDH is diagnosed and evaluated via both ultrasonography and radiography. The most important indicators of DDH in radiographies are acetabular index(AI), Shenton's line, center edge angle of Wiberg, Hilgenreiner's line, and Perkin's line [6]. Additionally, computed tomography (CT) and magnetic resonance imaging (MRI) provide valuable information on bone defects, enabling the design of soft tissue implants and treatment plans in children older than 6 months of age. Radiography, CT, and MRIs enable evaluation of the development of DDH via the following parameters: acetabular cartilaginous angle [7] and thickness [8], bone mineral density [9], alternation of femoral head shape/morphology [10], and other angle measurements [11]. Key issues for evaluation of bone development of DDH are ossification of hips after treatment. X-rays were applied in evaluation of bone development of DDH by AI. Plain radiographic assessment may have limited reliability and miss deformities depending on the location. There remains a lack of methods to detect it sensitively and quantitatively. The present study developed a novel quantitative CT assessment method, calculating the bone mineral volume of hips, to describe the morphological characteristics of DDH.

Recently, three-dimensional measurements and augmented virtual reality have been widely used in clinical practice, offering more abundant and detailed anatomic information [12-14]. The present study applied a three-dimensional model to assess the development of ossification in DDH and evaluated the validity of this new method.

Materials and methods

Subjects

This retrospective self-control study was approved by the Institutional Review Board. The requirement for informed consent was waived. All patients treated with surgery in Tongji Hospital, between Dec 2010 and Dec 2014, with unilateral DDH, were enrolled in this study. Inclusion criteria were as follows: 1) Radiography-based diagnosis of unilateral DDH; 2) Aged < 12 years; and 3) Pre-operative CT examinations performed. Exclusion criteria were as follows: 1) Neuromuscular disease; and 2) Previous surgery.

Sixteen patients (12 females and 4 males; mean ± standard deviation (SD) age 4.42 ± 2.59 [range, 1 to 9] years; affected hip: 6 right-side and 10 left-side) were included in this study. All underwent spectral CT examinations for both the affected and healthy limbs. Thus, 32 hips were allocated to either the dislocated group (n = 16) or control (healthy) group (n = 16). The patients were further grouped according to their age (young group: aged < 44 months; old group: aged ≥ 44 months) and degree of hip dislocation (low-dislocation group: dislocation length < 2 cm; high-dislocation group: dislocation length ≥ 2 cm).

Fifteen randomly selected irregularly-shaped potatoes (2 to 17 cm in length; bought from the supermarket, Qiaokou District, Wuhan, China) were used as phantoms. The phantoms were identified with serial numbers (1 to 15), according to their length.

Computed tomography protocol

Three-dimensional CT scans were performed using a General Electric 128 slice volume CT scanner (General Electric Company, USA). The scanning technique consisted of 80-100 kV and 80-100 mA, at a signal-to-noise ratio (SNR) of 7-11. Patients lied in a supine position, with their hips extended and thighs horizontal and parallel. Their feet were placed slightly apart, with their knees and ankles fixed when necessary. Contiguous slices (0.625 mm) were obtained from the upper rim of the acetabulum to proximal femur. Phantoms were examined via same method.

Image post-processing

Retrieved data was transferred to a personal computer (Lenovo, Windows 8.1, Intel® Core™ i7-4720HQ CPU) and 3DR was performed using Mimics software (version 10.0, Materialise, Leuven, Belgium). A bone threshold of 226-maximum HU was applied to extract the skeletal components of the CT image. The proximal femur, ilium, ischium, and pubis of each hip were selected and isolated, creating four separate masks for each hip [15]. Next, step-by-step thresholding, region-growing, 3D calculations, and outputs were applied. Three-dimensional calculation masks of the proximal femur, ilium, ischium, and pubis generated a 3D model for each bone, which were smoothed to reduce bumps from pixilation [15]. All imaging data was formatted as STL+ files and saved. Smoothed 3D models were then exported as STL+ files to the reverse-engineering image software (Geomagic Studio, version 12.0, Raindrop company, USA) to generate solid 3D models of the hip joints for further anatomical/morphological measurement [15].

Determination of dislocation length

Central points of the acetabula and femoral head models were obtained from 3D digital models (where established) to evaluate dislocation lengths (DLs), defined as the distance between these two central points. Central points of the acetabula and femoral head models were the same point in concentric hips (DL = 0), defined as the hip rotation center. Conversely, in dislocated hips, these central points were separated (DL ≠ 0). To define the

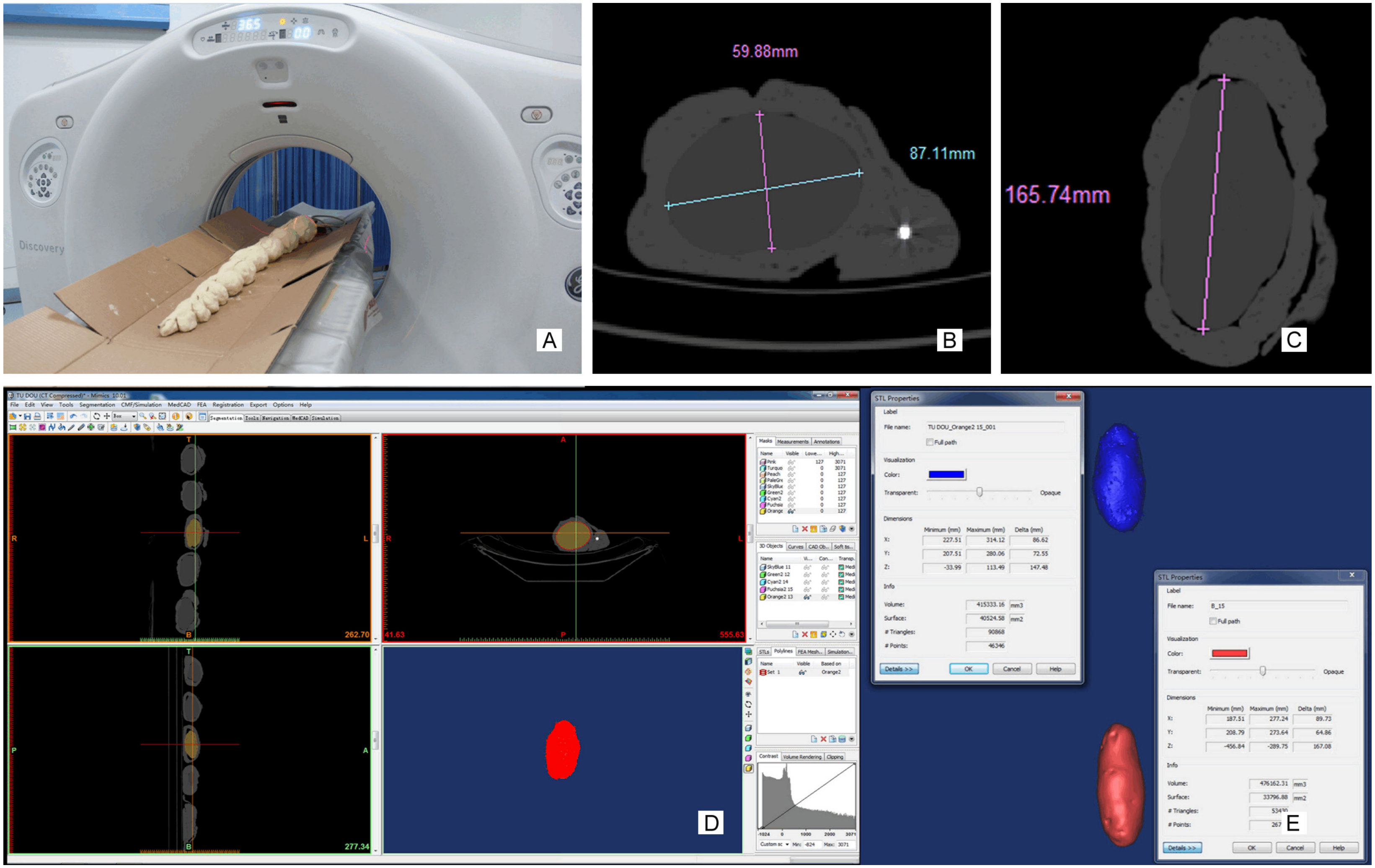

Figure 1. The phantom study (A. CT examination, B and C. Measurement of phantom, D. 3D reconstruction, E. 3D measurement).

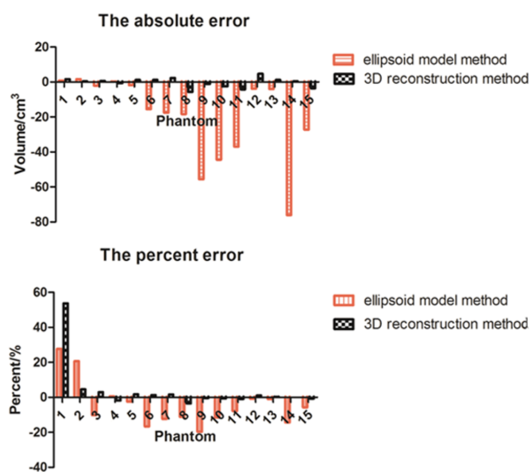

Figure 2. Comparison of volumes measured by different methods.

position of these central points, a Cartesian coordinate system was created. Starting from a referential X-Y-Z coordinate system, the central points of the femoral head model and acetabula models were identified. A "fit sphere" function button was applied to establish a solid sphere model that best mimicked the acetabula or femoral head model. The solid sphere model was established based on the cupped articular surface of the acetabula model and the secondary ossification center of the femoral head model. The central point was fixed as the center of the solid sphere model and the dislocation length was calculated according to the following formula: d = √ [(x1-x2)2 + (y1-y2)2 + (z1-z2)2], where A (x1, y1, z1) was defined as the central point of the acetabula model and B (x2, y2, z2) was defined as the central point of the femoral head model.

Assessment of method validity

The volume measurement method was validated by a phantom study. Three-dimensional CT scans were performed on 15 phantoms (potatoes encapsulated with semolina). Three-dimensional reconstructions, mimic analyses, and 3D volume measurements were performed, as previously described. The 3DR method and EM were employed to measure phantom-volumes. Validities of the measurements were then compared. Actual volume was measured via the gold standard water-displacement method. All measurements were repeated three times and mean values were recorded.

Archimedes' principle was employed to measure the actual volume of the phantoms via the water-displacement method. A phantom was put in a beaker full of water and the volume of overflowing water was measured. The actual volume of the phantom was equal to the volume of overflowing water. After CT examinations, radiographic images were downloaded in a DICOM format. Materialise Mimics software (Materialise's interactive medical image control system, version 10.0, Belgium) was used to measure phantom: a) length, b) width, and c) height. Volume was calculated according to the following formula: $V = \pi * a * b * c/6$.

Statistical analysis

Continuous variables are expressed as means ± SDs. SNRs were calculated to evaluate the validity of the two volume-measurement methods. Pearson's correlation coefficients (r) were calculated and linear regression analyses were used to establish a linear model of the measurement results for the two measurement methods. When assessing hip development, ossification radius, dislocation distance, and associations with age and dislocation distance were analyzed. Paired-samples t-tests were performed with Statistical Package for Social Science 17.0 software (SPSS; Chicago, Illinois). Probability values (P) < .05 indicate statistical significance.

Results

Phantom volumes

Figure 1 provides volumes of the 15 phantoms. Mean ± SD volumes were 238.29 ± 201.88 (range, 3 to 530) mL, 218.26 ± 187.71 (range, 3.83 to 453.96) mL, and 238.04 ± 201.39 (range, 4.61 to 530.45) mL, when evaluated via the water-displacement model, EM, and 3DR method, respectively. The average absolute and percent errors for the EM and 3DR methods were 20.02 ± 23.67 mL and 4.31 ± 13.10% and 0.25 ± 2.72 mL and 3.95 ± 13.89%, respectively. The absolute and percent errors of 3DR method were smaller than the EM, except for phantom 1, 4, and 12. Volume measurements correlated significantly with those of the water displacement method. Linear regression analysis demonstrated that volumes measured by the EM and 3DR method were 2.09 +

Table 1. The measurement of ossific volumes of hips

No.	Sex	Age	Side	ADL	AIL	AIS	APU	APF	NIL	NIS	NPU	NPF
1	Girl	5y3m	L	25.72	25.59	4.47	2.36	12.88	23.89	9.57	3.44	17.34
2	Girl	4y5m	L	20.21	38.93	7.56	4.23	20.85	38.98	12.66	6.40	23.86
3	Girl	7y8m	L	35.29	30.76	6.51	3.22	24.81	33.61	16.04	4.13	28.83
4	Girl	1y8m	L	20.76	19.06	6.05	2.52	11.77	20.83	6.23	2.94	13.00
5	Girl	3y7m	R	23.73	15.99	7.67	2.19	14.62	10.91	7.27	2.82	14.83
6	Boy	2y5m	R	12.20	19.79	8.66	3.35	11.10	17.43	8.74	3.49	12.97
7	Girl	3y3m	L	35.08	45.43	13.09	5.70	25.59	43.68	13.05	6.66	29.00
8	Boy	9y9m	R	8.64	46.50	15.86	7.41	43.05	42.11	22.29	11.62	59.84
9	Girl	3y9m	L	20.63	41.94	4.64	2.90	17.89	41.33	12.68	3.61	19.82
10	Girl	5y8m	L	21.91	20.10	6.05	3.20	20.00	16.77	12.51	4.63	21.74
11	Boy	1y9m	L	13.40	22.07	3.66	2.04	13.05	21.16	6.91	2.55	14.70
12	Girl	5y2m	L	15.09	45.61	14.35	5.74	30.17	43.58	12.97	6.70	32.69
13	Girl	2y	R	12.91	22.13	7.71	3.16	17.53	22.61	7.83	3.54	18.31
14	Boy	9y3m	L	15.84	83.79	16.58	8.61	31.35	76.31	24.61	10.12	38.67
15	Girl	3y5m	R	19.60	28.37	8.34	3.70	18.12	26.40	8.56	4.14	18.37
16	Girl	1y9m	R	10.56	19.37	6.71	2.57	10.60	18.55	3.88	2.05	10.83

Note: Side = affected side, L = left side, R = right side, ADL = dislocation length of affected hip, AIL = ilium of affected hip, AIS = ischium of affected hip, APU = pubis of affected hip, APF = proximal femur of affected hip, NIL = ilium of normal hip, NIS = ischium of normal hip, NPU = pubis of normal hip, NPF = proximal femur of normal hip.

0.92* standard volume (r = 0.995; $P < .001$) and 0.53 + 0.99* standard volume (r = 1.000; $P < .001$), respectively, where standard volume was measured via the water displacement method.

Validity of the three-dimensional reconstruction method

Compared to measurements obtained via the water-displacement method, the mean absolute and percent errors of the 3DR method (0.25 ± 2.72 ml and 3.95 ± 13.89%, respectively) were significantly smaller than those of the EM (20.02 ± 23.67 ml, t_a = 3.355, P = 0.005 and 4.31 ± 13.10%, t_p = 3.129, P = 0.007, respectively; **Figure 2**). SNR of the 3DR method was 0.129, nearly 50 times the SNR of traditional EM (0.00238).

Three-dimensional reconstruction of hips

Three-dimensional reconstruction and measurements were completed on all 16 patients (**Table 1**). **Figure 3A-D** provides 3D-reconstruction results. **Figure 3E** provides measurements of dislocation length and **Figure 3F** provides 3D measurements of volume for each bone component.

Ossification volumes of dislocated versus normal hips

Comparisons between dislocated and normal (healthy) hips are provided in **Figure 4**. Mean ± SD OVs of the ilium, ischium, pubis, and proximal femur were 31.14 ± 16.25/cm^3, 11.61 ± 5.63/cm^3, 4.93 ± 2.73/cm^3, and 23.42 ± 12.48/cm^3, respectively, in the normal group, and 32.84 ± 17.36/cm^3, 8.62 ± 4.09/cm^3, 3.93 ± 1.94/cm^3, and 20.21 ± 8.93/cm^3, respectively, in the dislocated group. Ossific-ation volumes (OVs) of the ischium, pubis, and proximal femur (but not the ilium [t_{ilium} = 2.660; P = 0.018]) were smaller in the dislocated versus normal group ($t_{ischium}$ = 3.041, t_{pubis} = 3.776, t_{femur} = 3.158, respectively; all P =0.008, 0.002, and 0.006, respectively).

Association between ossification-volume ratio and age

Mean ± SD ossification-volume ratios of the young and old groups were 1.09 ± 0.17 and 1.06 ± 0.08 (t = 0.472; P = 0.644), respectively, for the ilium, 1.03 ± 0.33 and 0.60 ± 0.24, respectively, for the ischium (t = 2.993; P = 0.010), 0.91 ± 0.15 and 0.75 ± 0.09 (t = 2.691; P = 0.018), respectively, for the pubis, and 0.93

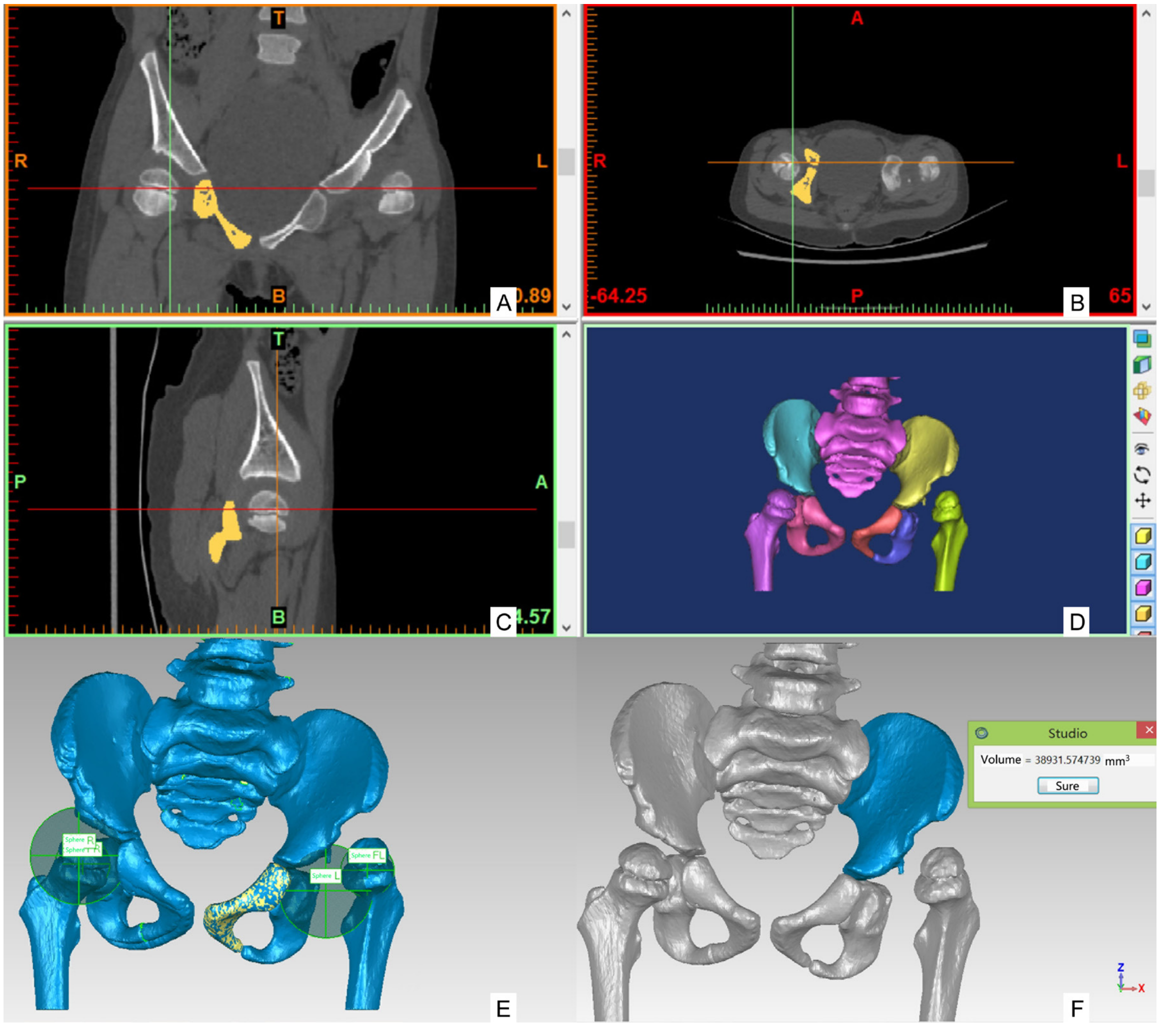

Figure 3. Volume measurement of ossify hips in DDH by 3D-CT (A. Coronal plane, B. The axial plane, C. The sagittal plane, D. The 3D figure, E. The figure of dislocation length, F. The 3D measurement of volume).

± 0.05 and 0.84 ± 0.08 (t = 2.558; *P* = 0.023), respectively, for the proximal femur. Ossification-volume ratios (OVRs) of the old group were significantly smaller than those of the young group for the ischium, pubis, and proximal femur, but not the ilium.

Association between ossification-volume ratio and degree of hip dislocation

OVRs of the ilium, ischium, pubis, and proximal femur in the low-dislocation group (1.07 ± 0.05, 0.96 ± 0.37, 0.89 ± 0.17, 0.89 ± 0.09, respectively) were not significantly different (*P* = 0.862, 0.098, 0.076, and 0.890, respectively) from those in the high-dislocation group (1.08 ± 0.18, 0.67 ± 0.29, 0.76 ± 0.08, 0.88 ± 0.07, respectively).

Discussion

Developmental dysplasia of the hip (DDH) is a debilitating condition characterized by incomplete development of the acetabulum, femur dislocation, hip malformation, and early onset osteoarthritis. Development of a sensitive, specific, and cost-effective method evaluating hip development has remained an elusive goal. Acetabular index is typically measured manually on radiographic images and is the gold standard for DDH diagnosis and evaluation. However, the accuracy of this method is subjective (depending on physician experience) and limited by the examination position. Many studies have documented various morphological abnormalities with high dislocations, including straight or narrow femurs [16], small femoral

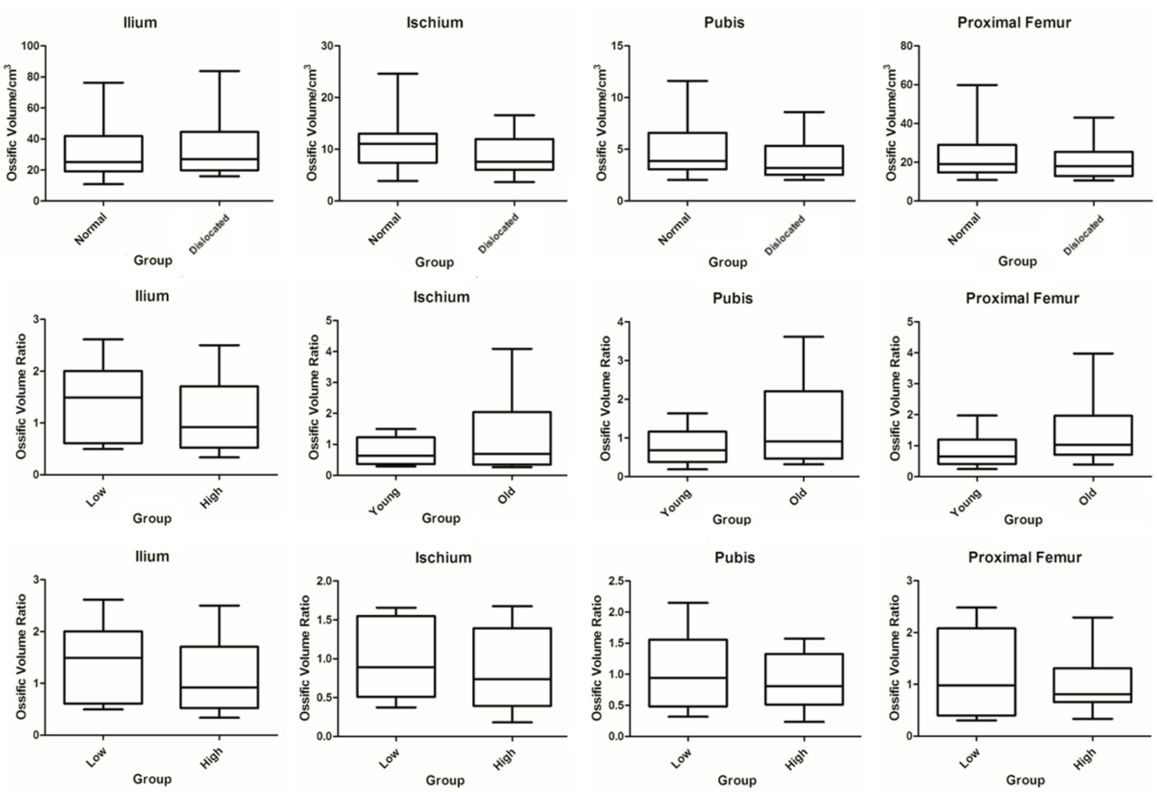

Figure 4. Comparison of volumes in different groups by age and dislocation distance.

head sizes, short neck lengths, and anteverted femoral necks [11, 17-19]. According to Wolf's law, mechanical loads affect bone architecture. Therefore, the current study presented a novel quantitative technique for DDH-morphological-characteristic evaluation, measuring bone mineralization volumes to minimize manual intervention, providing more valid and reliable results.

In the phantom study, 3D volumes of the smaller phantoms were less accurate than those of larger phantoms. This effect, of increasing inaccuracy with declining phantom size, has been documented previously [20, 21]. Given that percent errors are larger in smaller phantoms, this error may have resulted from inaccurate measurements. However, in this study, correlation coefficients (r) and SNRs revealed that the 3DR method was more valid than traditional EM, indicating that 3D CT-based bone-volume assessment is feasible, enabling the measurement of ossification development in the hips of children.

Most previous studies have focused on the morphological features of the acetabulum and femoral head [22-25], including asymmetry and medial twist of the pelvis, increased acetabular anteversion, and dislocation of the femoral head [22, 23, 26]. However, few studies have reported the ossification development of hip bones, including the ilium, pubis, ischium, and proximal femur. This retrospective study was performed to calculate the volume of ossification in the various bones of the hip, comparing the volumes of affected and normal limbs. Age and dislocation degrees have previously been found to relate to prognosis. Thus, patients were grouped accordingly. To facilitate analysis, hip ossification development in dislocated and normal (healthy) sides, at different developmental stages, were presumed to be synchronous in healthy children. OVR was formulated, representing the ratio of the ossification volume of dislocated versus normal hips, a standard parameter that eliminates any other related factors. OVRs were compared between the various groups (age and dislocation distance) and were found to reflect the concurrency of development.

The present study used OVs to depict the ossification development of bones and, as such, quantifiably evaluated ossification development in DDH (in humans) for the first time. OVs of bones in affected hips were smaller than those in normal hips, except for the ilium. According to Harris' principle, the development of hips is related to the concentric relationship between the femoral head and acetabulum. Therefore, ossification development of the acetabulum and femoral head are meaningful indictors of joint development. In this study, it was found that the OV of the ilium was smaller in normal versus dislocated hips. This may represent a secondary change following dislocation. However, substantial work is required to ascertain the exact mechanisms.

Given that DDH is a developmental problem, this study focused on the relationship between ossification development and age. Quantitative analysis revealed that younger age was associated with higher OVRs. Thus, alternation of ossification development increases with age, highlighting the need to receive treatment in the early stages of DDH.

Furthermore, degree of dislocation is an important indicator of femoral osteotomy for treatment of DDH. Whether bone development is related to degree of dislocation is unclear. Dislocation length was defined as the distance between the central points of the acetabulum and femoral head. Patients were divided according to dislocation length to evaluate the association with developmental retardation. Present results suggest a trend whereby lower degrees of dislocation are associated with milder developmental retardation. However, no significant differences were observed in this study.

The present study has some clear limitations. First, the sample size was small (16 patients; 32 hips), rendering some statistical analyses underpowered. Therefore, further studies are required to verify present conclusions. Second, this was a retrospective study. Thus, a mechanical study was not performed to ascertain potential mechanisms. Third, this was a supplementary evaluation determining morphological characteristics and was not intended as a replacement for other methods. The development of DDH should be assessed comprehensively and carefully. However, given that radioactivity protection should be considered and carefully handled, especially in younger children [27-30], low radiation doses associated with CT is an inherent advantage of this method.

Conclusion

In conclusion, the SNR and validity of the 3DR method is higher than those of traditional EM. Physician assessments of DDH are usually based on radiographic assessment of acetabular angles and gross appearance of secondary ossification centers. The present study developed an accurate method for measuring OV via CT. Preoperative 3D-CT successfully revealed bone development in DDH. Thus, a digital model is helpful in assessing the bone characteristics of DDH. OVs of dislocated hips are lower than those of normal (healthy) hips (including the ilium, ischium, pubis, and superior part of femur). Older age is associated with lower OVRs, but it remains unclear whether OV is related to dislocation distance.

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Written consent was obtained from the parents/guardians to publish this report.

Disclosure of conflict of interest

None.

Abbreviations

CT, computed tomography; DDH, developmental dysplasia of the hip; DL, dislocation length; 3DR, three-dimensional reconstruction; EM, ellipsoid model; OV, ossification volume; OVR, ossification-volume ratio; SNR, signal-to-noise ratio.

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