

## ·实验研究·

# 骨骺损伤对发育性髋关节发育不良大鼠术后髋外翻的影响研究

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**【摘要】目的** 髋外翻(coxa valga)是发育性髋关节发育不良(Developmental dysplasia of the hip, DDH)患儿术后并发症之一,术中大转子骨骺受损被推测是可能因素,但尚无实验证实,本研究拟证实股骨大转子骨骺损伤与髋外翻的关系。**方法** 在建立大鼠DDH模型后,通过切开复位左侧髋关节同时损伤大转子骨骺的方法,探讨DDH术中骨骺损伤因素对预后颈干角、前倾角的影响。将43只新生SD大鼠下肢伸直襁褓位固定10 d,待出生1个月时行骨盆正位X线片,确诊其中41个左侧髋关节发生脱位(41/43)。将41只DDH大鼠随机分为骨骺损伤组(21只)和对照组(20只)。对照组于大鼠出生1个月时切开复位左侧髋关节,骨骺损伤组在切开复位左髋的同时用1 mm克氏针钻孔损伤左股骨大转子骨骺。术后1个月处死并取得左股骨标本,使用超微立体扫描仪(Epson)测取颈干角及前倾角。**结果** 骨骺损伤组颈干角为 $130.56^\circ \pm 3.44^\circ$ ,前倾角为 $28.57^\circ \pm 9.25^\circ$ ;对照组颈干角为 $126.57^\circ \pm 6.04^\circ$ ,前倾角为 $28.83^\circ \pm 7.85^\circ$ 。骨骺损伤组颈干角显著大于对照组( $P = 0.015$ ),前倾角比较差异无统计学意义( $P = 0.925$ )。**结论** 术中大转子骨骺受损的DDH大鼠颈干角更大,提示该损伤可能是发生DDH术后髋外翻的因素之一。手术中减少对大转子骨骺的干扰和损伤,或可改善术后颈干角的变化,减少髋外翻的发生。

**【关键词】** 骨骺/损伤; 髋关节/生长和发育; 髋外翻; 大鼠

**Influence of greater trochanter drilling on neck-shaft angle and femoral anteversion after open reduction for developmental dysplasia of the hip in rats.** Li Chao, Huang Luyu, Xu Huifa, Yan Yabo, Liu Zhichen, Wang Hong. Department of Orthopedics, Xijing Hospital, Fourth Military Medical University, Xi'an 710032, China. Corresponding author: Huang Luyu, Email: huangly@fmmu.edu.cn

**【Abstract】Objective** Sometimes coxa valga occur as a surgical complication for developmental dysplasia of the hip (DDH). Its cause is assumed to be intraoperative damage to trochanteric growth plate at the time of operation, but no experiment has confirmed it. The aim of this study was to corroborate the relationship between transphyseal damage and coxa valga. **Methods** By operating open reduction and transphyseal drilling on DDH in 43 neonatal Sprague Dawley (SD) rats and measuring neck-shaft angle and femoral anteversion, this study explored the effect of transphyseal damage on neck-shaft angle and femoral anteversion after open reduction. The legs and hips were fixed by adhesive tape in an extension and adduction position for 10 days. 41 left dysplastic hips (41/43), verified on anteroposterior pelvic radiographs, were randomized, 21 left hips underwent transphyseal drilling and open reduction at the age of 1 month while 20 in control group underwent open reduction. All rats were sacrificed after 1 month raising in the same condition. Forty-one left femoral specimens were scanned and input into computers for measuring to calculate neck-shaft angle and femoral anteversion. **Results** Mean neck-shaft angle in transphyseal trauma group was larger than in control group ( $130.56^\circ \pm 3.44^\circ$  vs  $126.57^\circ \pm 6.04^\circ, P = 0.015$ ). No differences existed between groups in femoral anteversion ( $P = 0.925$ ). **Conclusion** Intraoperative damage to trochanteric growth plate during operation for DDH is associated with larger neck-shaft angle. Improved understanding of these relationships may help to reduce the incidence of coxa valga and improve the prognosis of DDH in children.

**【Key words】** Epiphyses/IN; Hip Joint/GD; Coxa Valga; Rats

DOI:10.3969/j.issn.1671-6353.2018.04.012

基金项目:国家自然科学基金项目(编号:81171735)

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发育性髋关节发育不良(developmental dysplasia of the hip, DDH)是指从髋关节的轻微发育异常到完全脱位的一系列疾病<sup>[1]</sup>。DDH在新生儿中发

病率约1‰~3‰<sup>[2-3]</sup>,是影响儿童健康常见的下肢疾病之一<sup>[4]</sup>。治疗越早,疗效越好。手术是治疗DDH的有效方法,但长期随访发现,部分经手术复位后的患儿会出现髋外翻(coxa valga)<sup>[5-7]</sup>。这种迟发型髋外翻会影响对髋关节发育的矫正<sup>[8]</sup>,是术后股骨头出现异常的主要原因<sup>[9]</sup>。Mau等<sup>[10]</sup>提出大转子骨骺在术中的损伤可能是导致髋外翻的原因,但尚无实验验证。本研究在建立大鼠DDH模型后,通过切开复位左侧髋关节同时用克氏针钻孔损伤股骨大转子骨骺的方法,探讨DDH手术治疗时骨骺损伤因素对预后的颈干角、前倾角的影响。

## 材料与方法

### 一、实验动物

取SD新生幼鼠共43只(雌性23只,雄性20只),由第四军医大学实验动物中心提供,起始体重6.0~7.0g。

### 二、实验方法

1. DDH模型制作及分组:依据随机数字表对43只幼鼠编号,将每只幼鼠双侧髋关节及膝关节用医用胶带缠绕,固定于伸直襁褓位<sup>[11]</sup>。注意轻柔操作,以免暴力脱位。每日松解胶带1min后重新缠绕固定,避免出现胶带浸湿松脱,或下肢因生长而受胶带过度挤压。襁褓位固定10d后取下胶布,正常饲养,自由活动。出生30d拍骨盆正位X线片,确诊其中41只出现左侧髋关节发育不良(41/43)(图1,2)。将41只左侧髋脱位大鼠随机分为骨骺损伤组(21只)和对照组(20只)。



图1 正常大鼠的骨盆正位X线片,箭头所示为正常股骨头。图2 双侧DDH大鼠骨盆正位X线片,箭头所示为脱位股骨头。

**Fig. 1** Anteroposterior pelvic radiographs of normal rats, showing normal femoral head (arrow head). **Fig. 2** Bilateral dislocation, showing dislocated femoral head (arrow head).

2. 左侧髋关节切开复位及骨骺损伤:两组大鼠均行左侧髋关节切开复位术。将大鼠置于仰卧位,在全麻及无菌条件下,消毒左后肢及半侧腹部皮肤。于左髋关节屈曲90°、外展90°确定髋臼位置,并判断股

神经血管束大致位置。于股骨头正上方牵拉皮肤并纵向切开一长约1.5cm手术切口,钝性分离皮下组织。沿肌纤维走行方向纵向分离骨薄肌。向下牵开内收大肌,切断内收长肌、内收短肌及耻骨肌。轻柔向外上方牵开股神经血管束,保护髂内动脉,钝性分离、显露髋关节囊。在关节囊前内侧做一与髋臼前缘平行的小切口,可见股骨头及大量软组织、关节囊液存留髋臼中(图3)。清除髋臼内所有填塞组织,将股骨头复入真臼内(图4),切除多余关节囊壁,用显微缝合针(宁波成和,显8/0\*3/8 1.5\*6)间断缝合关节囊。松开左后肢,进行髋关节正常范围的活动,试验复位稳定性。用大量生理盐水冲洗切口,连续缝合深筋膜,间断缝合皮肤。骨骺损伤组大鼠在切开复位左髋关节囊手术中,于缝合关节囊后,钝性分离显露大转子,用克氏针(AINUO,1.0\*250)垂直穿透股骨头大转子损伤骨骺(图5),冲洗缝合如前述。

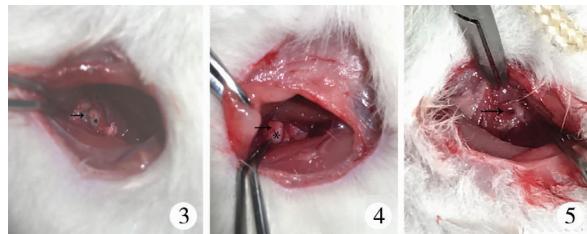


图3 打开脱位髋臼,星号所指为脱位股骨头,箭头所示为髋臼。图4 复位髋关节。图5 箭头所示为钻孔损伤大转子骨骺。

**Fig. 3** After opening acetabulum, femoral head (asterisk) and acetabulum (arrow).

**Fig. 4** Reduction of dislocated hip.

**Fig. 5** Injury of great trochanter (arrowhead).

3. 标本取材及颈干角、前倾角测量:两组大鼠均于术后30d(2月龄)处死,取得完整股骨标本。  
①颈干角测量:超微立体扫描仪(EPSON Perfection V370 Photo)扫描<sup>[12]</sup>:保持小转子及内外踝于同一平面上,置股骨于扫描仪上。将扫描图片导入电脑,确定经大转子及内外踝中点的连线为股骨干轴线,确定经股骨颈基底部中点和股骨头中心点的连线为股骨颈轴线,两轴线在此投影平面下的夹角为股骨颈干角<sup>[13]</sup>。用精确到0.1°的B-Ruler软件测量角度。  
②前倾角的测量:将股骨头置于玻璃板上,并将大转子朝下置于扫描仪上。调整摆放角度,使股骨颈基底部中心位于两股骨踝最外部连线的中点处,此时踝平面垂直扫描仪。股骨颈轴为股骨头中心与股骨颈基底部连线,前倾平面由股骨的长轴和股骨颈轴所确定的平面,此时前倾平面也垂直于扫描仪。前倾角为前倾平面与踝平面所成的

夹角,即扫描图像中股骨颈轴与髋轴所呈夹角<sup>[14,15]</sup>。

### 三、统计学处理

采用 IBM SPSS 21 统计软件对两组大鼠左股骨头的颈干角、前倾角进行统计分析,数据以均数±标准差( $\bar{x} \pm s$ )来表示。骨骺损伤组与对照组间颈干角及前倾角的比较采用两组独立样本资料的 *t* 检验,以  $P < 0.05$  为差异有统计学意义。

## 结 果

DDH 建模大鼠共计 43 只,建模成功 41 只,伸直襁褓位建模成功率 95.3%。两组大鼠左股骨颈干角、前倾角情况详见表 1。骨骺损伤组大鼠股骨颈干角大于对照组,差异有统计学意义( $t = 2.582$ ,  $P = 0.015$ )。两组间前倾角比较,差异无统计学意义( $t = 0.095$ ,  $P = 0.925$ )。

表 1 两组大鼠左股骨颈干角、前倾角的差异( $\bar{x} \pm s$ )

Table 1 *t* test results of left neck-shaft angle and femoral anteversion between two groups

分组	n	颈干角	前倾角
骨骺损伤组	21	$130.56 \pm 3.44^a$	$28.57 \pm 9.25$
对照组	20	$126.57 \pm 6.04$	$28.83 \pm 7.85$
<i>P</i> 值		0.015	0.925

注:与对照组比较,<sup>a</sup> $P < 0.05$

## 讨 论

目前 DDH 的治疗方案日趋成熟,治疗年龄越早,预后越好<sup>[16]</sup>。我们应用 Pemberton 方法治疗 61 例低龄 DDH 患儿(平均 7.9 岁),经 2 年以上随访临床优良率达 88.57%,影像学优良率达 91.43%<sup>[17]</sup>。部分 DDH 患儿在随访中会出现髋外翻畸形。Jones DA 等<sup>[18]</sup>报道了 6 例 DDH 患儿在平均 9 年的随访中出现髋外翻畸形。Hess T<sup>[19]</sup>等在对 33 例 DDH 患儿平均 26 年的随访中发现,术中虽将颈干角纠正至 120°,但在术后 5 年的随访中颈干角逐渐增大。在 Thielemann F<sup>[6]</sup>等治疗的 DDH 患儿中,也有髋外翻病例的出现,并有再次接受内翻截骨的需要。

DDH 术后髋外翻出现的原因之一是 Kalamchi-MacEwen II型 AVN<sup>[20]</sup>,表现为股骨头二次骨化中心发生改变,伴外侧生长板破坏所致股骨颈外侧生长延迟、髋外翻、短颈<sup>[21]</sup>。但在临床中发现,部分患儿没

有 AVN 症状,却在长期随访中出现髋外翻畸形。

针对此类未出现 AVN 的髋外翻情况,很多学者提出了其他假说。Mau H<sup>[10]</sup>最先提出了术中大转子骨骺受损可能是导致髋外翻的主要因素。Yamaguchi I<sup>[22]</sup>在对 46 名患儿(51 髋)的随访中发现:①术中螺钉通过大转子的患儿,出现髋外翻的比例更大;②术后出现股骨头坏死的病例中,均未出现髋外翻畸形。Kim HW<sup>[23]</sup>通过对 58 例 DDH 患者进行回顾性分析,发现股骨头骨骺在术中受损虽是造成股骨头生长停滞的主要原因,但和术后颈干角的变化或髋臼畸形并无统计学上的相关性。Langenskiöld A<sup>[24]</sup>报道两名因外伤致大转子骨骺损伤的病例出现髋外翻畸形。Schofield CB<sup>[25]</sup>对 14 例患儿(16 髋)的随访发现,螺钉穿过大转子骺板的患儿颈干角明显大于对照组。Yamaguchi 等人的临床研究支持 Mau 的大转子骨骺损伤假说,但目前尚缺乏实验支持,因此我们通过在大鼠身上建立 DDH 模型和大转子骨骺损伤模型来研究大转子骨骺损伤和髋外翻的相关性。

在 DDH 模型动物的选择上,兔、鸡、鼠等均可建立可靠的 DDH 模型,且兔类操作更为便捷。但我们在选择动物模型时,还基于以下方面的考量:①鸡和兔的股骨头外形和人类差距较大,兔的股骨颈较短,其受力和人类有较大区别。鸡的股骨颈更短,颈干角明显大于人类。②大鼠的股骨头,有着与人类更为相似的前倾角和颈干角,在力学性能上更接近人类。③DDH 模型的传统制作方法有很多种,如切断股骨头圆韧带、切除髋臼软骨等<sup>[26]</sup>。大鼠襁褓位 DDH 模型相较于外科手术致 DDH 模型,具有创伤小、操作易的特点。我们从出生起将大鼠伸髋伸膝襁褓位固定,至第 10 天大鼠断奶,与人类婴幼儿成长的规律更类似。大鼠襁褓位 DDH 模型建立方法成熟可靠,效果明确,且在建模阶段不需要给予药物或其他介质,创伤更小。综上考虑,我们最终选择了襁褓位大鼠 DDH 这一动物模型。

骨骺损伤模型的制备方法有磨钻法、克氏针钻孔法、刮除法、成角法等<sup>[27-29]</sup>。克氏针钻孔法是一个成熟的骨骺损伤模型,其损伤效果明确并具有如下优点。首先克氏针光滑,产生碎屑少,对周边骺板软骨损伤较小;其次是无明显轴向加压作用,可进行单一致伤因素的研究;最后是钻孔时无需辅助固定,对动物实验本身影响小<sup>[30]</sup>。Janarv PM<sup>[31]</sup>和石峰<sup>[32]</sup>等对克氏针钻孔法损伤骨骺的研究证实:有 7%~9% 的克氏针骺板损伤面积即可导致骨生长抑

制。我们在动物实验中发现了术中大转子骨骺损伤和股骨颈干角之间的相关性。但其机理如何,大转子骨骺受损后发生了什么样的继发改变,最终导致颈干角的变化尚不清楚。

骨盆正侧位X线片为DDH模型建立是否成功的评价指标。依据影像学资料,股骨头影和髋臼影无重叠,关节间隙明显增大可判定为髋关节脱位,正常髋关节其股骨头和髋臼在影像学上连续<sup>[11]</sup>。但是缺少术前股骨头颈干角和脱位程度等指标,我们曾试图用micro CT对大鼠术前髋臼进行扫描,但过长的麻醉时间对幼龄大鼠的存活而言是个很大的问题,因此我们试图在同品系、同批次大鼠中建立DDH模型,在X线确诊DDH后,通过严格的随机分组方法,尽量排除因个体间差异所致的术后颈干角的统计学差异。本实验的不足之处在于缺乏DDH术后转归的影像学观察指标,仅通过大鼠处死后大体标本的研究,观察其复位情况。因而无法从影像学上排除因股骨头外侧损伤所致的Ⅱ型AVN,虽然我们在术中尽量避免了对股骨头的损伤或干扰。

本实验发现大转子骨骺在术中受损的大鼠,其颈干角显著大于对照组。大转子骨骺损伤后,股骨颈外侧生长受限,可能是其导致颈干角增大的原因。大转子骨骺在术中的损伤可能是导致DDH术后髋外翻的因素之一。虽然在临床DDH切开复位的手术中,很少损伤大转子骨骺。但DDH的病因及术后转归都是一个非常复杂的过程。通过此次研究,一方面可以对我们进一步认清DDH术后髋外翻这一复杂疾病有所助益,另一方面提示我们在DDH切开复位的手术中,我们应更加谨慎的处理股骨头大转子,尽最大可能减少对股骨头大转子的损伤干扰,减少因大转子骨骺受损而出现髋外翻的情况,获得更好的临床效果。然而距离解决这一问题还有一段距离。一方面,除大转子骨骺损伤和股骨头外侧骺板损伤机制外,还有很多假说尚待探讨,包括髋臼覆盖不足<sup>[18]</sup>、内收肌损伤<sup>[33]</sup>、术后疼痛、关节活动度等多种假说和推测。另一方面,目前我们在动物实验中发现了大转子骨骺术中损伤和股骨颈干角之间的相关性。但其机理究竟为何,在损伤后大转子骨骺发生了什么样的继发改变,如骨骺早闭或骨桥形成等,这些都将是下一步实验研究的重点。

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(收稿日期:2017-11-14)

**本文引用格式:**李超,严亚波,徐会法,等.骨骺损伤对发育性髋关节发育不良大鼠术后髋外翻的影响研究[J].临床小儿外科杂志,2018,17(4):290-294. DOI:10.3969/j. issn. 1671-6353. 2018. 04. 012.

**Citing this article as:** Li C, Huang LY, Xu HF, et al. Influence of greater trochanter drilling on neck-shaft angle and femoral anteversion after open reduction for developmental dysplasia of the hip in rats [J]. J Clin Ped Sur, 2018, 17(4): 290-294. DOI: 10.3969/j. issn. 1671-6353. 2018. 04. 012.