

论著·临床研究

宫颈机能不全孕妇早、中孕期盆底结构变化初探

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[摘要] **目的**·通过超声检查探究有宫颈机能不全(cervical incompetence, CIC)史的孕妇早、中孕期盆底结构的变化特点。**方法**·收集2022年8月至2023年1月在同济大学附属第一妇婴保健院建卡的早、中孕期孕妇,所有孕妇均有且仅有1次早产,或者中孕流产、引产史,按照前次妊娠有无CIC病史将其分为CIC组和对照组。比较2组孕妇的年龄、体质指数(BMI)、孕周、尿道内口漏斗形成率、尿失禁发生率。运用二维、三维及四维盆底超声对静息状态、盆底肌收缩(pelvic floor muscle contraction, PFMC)状态和瓦尔萨尔瓦动作(Valsalva maneuver, VM)状态下2组女性盆底结构进行测量;测量参数包括:膀胱颈位置、尿道倾斜角、尿道旋转角、膀胱后角、膀胱颈移动度、宫颈位置、直肠壶腹部位置、肛提肌裂孔面积(area of urogenital hiatus, HA)、肛提肌裂孔左右径、肛提肌裂孔前后径。采用一般线性回归模型校正混杂因素影响,分析CIC病史与盆底结构差异指标的相关性。**结果**·共纳入早、中孕期孕妇76例,其中CIC组39例,对照组37例。2组孕妇年龄差异无统计学意义, C组BMI、孕周均显著大于对照组,差异均有统计学意义(均 $P<0.05$)。静息状态和PFMC状态下,2组孕妇盆底结构参数差异均无统计学意义(均 $P>0.05$);VM状态下,CIC组HA($P=0.016$)和肛提肌裂孔前后径($P=0.014$)显著增大,其他指标差异无统计学意义。一般线性回归模型校正2组孕妇的孕周及BMI后发现,CIC病史与VM状态下HA($P=0.038$)和肛提肌裂孔前后径($P=0.049$)均存在相关性。CIC组和对照组尿道内口漏斗形成率分别为10.25%和0,压力性尿失禁发生率分别为23.07%和13.51%,差异均无统计学意义(均 $P>0.05$)。**结论**·有CIC病史的孕妇VM状态下,HA和肛提肌裂孔前后径明显增大,肛提肌裂孔的形态改变以纵轴增加更为明显。

[关键词] 宫颈机能不全; 超声检查; 盆底; 孕期; 盆底功能障碍性疾病**[DOI]** 10.3969/j.issn.1674-8115.2023.04.008 **[中图分类号]** R445.1 **[文献标志码]** A

Preliminary study of pelvic floor structural changes in early and middle pregnant women with cervical incompetence

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[Abstract] **Objective**·To explore the changes of pelvic floor structure in the early and middle pregnant women with the history of cervical incompetence (CIC) by ultrasound. **Methods**·The pregnant women during early and middle trimesters were collected from Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine from August 2022 to January 2023. All the pregnant women had only one history of premature delivery, abortion or induced labor in the middle trimester, and were divided into CIC group and control group according to whether having the history of CIC in the previous pregnancy. Age, body mass index (BMI), gestational age, the prevalence of funneling of internal urethral orifice and the prevalence of urinary incontinence were compared between the two groups. Two-dimensional, three-dimensional, and four-dimensional pelvic floor ultrasound was used to measure the pelvic floor structures of the women in the states of resting, pelvic floor muscle contraction (PFMC) and Valsalva maneuver (VM). The parameters of pelvic floor structure included bladder neck position, urethral inclination angle, urethral rotation angle, posterior angle of bladder, bladder neck mobility, cervix position, position of ampulla of rectum, area of urogenital hiatus (HA), hiatal transverse diameter, and hiatal anteroposterior diameter. General linear regression model was used to correct the influence of confounders and to analyze the association between the history of CIC and the different indexes of pelvic floor structure. **Results**·A total of 76 pregnant women in early and middle trimesters were collected, including 39 women in the CIC

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group and 37 women in the control group. There was no significant difference in the age between the two groups, while BMI and gestational age in the CIC group were significantly greater than those of the control group, and the differences were significant (both $P < 0.05$). At the states of resting and PFMC, there were no significant differences in structural parameters (all $P > 0.05$); at the state of VM, HA ($P = 0.016$) and hiatal anteroposterior diameter ($P = 0.014$) increased in the CIC group, while other parameters did not change significantly. It was found that the CIC history was associated with HA ($P = 0.038$) and hiatal anteroposterior diameter ($P = 0.049$) at VM after adjusting gestational age and BMI by the general linear regression model. The incidence rates of funneling of internal urethral orific in the CIC group and the control group were 10.25% and 0, respectively; the incidence rates of stress incontinence were 23.07% and 13.51%, respectively. Neither of the differences were significant (both $P > 0.05$). **Conclusion** In the pregnant women with the history of CIC, HA and hiatal anteroposterior diameter at VM increase, and the morphological change of the levator ani hiatus is more obvious with the increase of the vertical axis.

[Key words] cervical incompetence (CIC); ultrasound examination; pelvic floor; pregnancy; pelvic floor dysfunction (PFD)

宫颈机能不全 (cervical incompetence, CIC) 指宫颈解剖结构或功能异常, 可导致患者在足月妊娠前出现进行性、无痛性宫颈缩短、扩张、展平及漏斗状宫颈, 妊娠中晚期无法维持妊娠^[1]。CIC在孕妇中的发生率约为1%^[2]。CIC是复发性中晚期妊娠流产及早产的重要原因。正常宫颈由富含胶原蛋白的结缔组织组成, 只有15%的肌肉细胞。结缔组织疾病或者埃勒斯-当洛斯综合征可使宫颈组织中羟脯胺酸含量显著下降, 胶原纤维合成受阻或者功能障碍, 进而破坏宫颈的完整性, 诱发CIC^[3]。

我国成年女性盆底功能障碍性疾病 (pelvic floor dysfunction, PFD) 主要表现包括压力性尿失禁和盆腔脏器脱垂, 发生率高达30.9%, 因此PFD被称为严重影响女性生活质量的五大慢性病之一^[4]。盆腔肌肉及结缔组织的完整性对于保持盆底解剖位置至关重要, 它主要由纤维细胞外基质成分来维持。盆腔脏器脱垂的患者子宫骶韧带中的胶原蛋白减少^[5], 推测CIC和PFD可能有着相似的组织学变化, 那么这两者之间是否存在潜在的关联?

一项对多家机构电子健康记录的研究^[6]发现, 有CIC史的患者远期发生压力性尿失禁和盆腔脏器脱垂的风险显著升高。女性孕期腹腔压力增大, 盆底结构变化, 压力性尿失禁发生率升高^[7]。另有研究^[8]发现, 三维超声可以在仅有轻微PFD症状但体格检查结果正常的女性中发现轻度的盆底结构改变, 推测超声下盆底形态的改变早于临床症状的出现。本研究拟通过盆底超声检查, 探究有CIC病史的孕妇孕期盆底结构变化的特点。

1 对象与方法

1.1 研究对象及分组

收集2022年8月至2023年1月在同济大学附属第

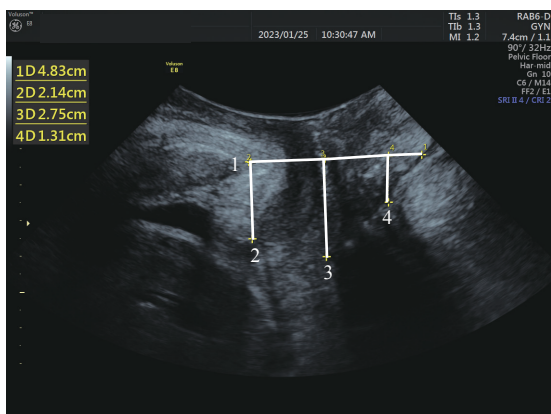
一妇婴保健院建卡的孕妇, 孕周为8周~28周。按是否有CIC病史, 将孕妇分为CIC组和对照组。CIC组纳入标准: 曾有1次CIC病史, 即在孕37周前出现进行性、无痛性宫颈缩短、扩张、展平及漏斗状宫颈, 导致中孕流产或早产, 并排除孕中期出血、感染、破膜等明确的病理因素^[1]; 此次孕前有且仅有1次中孕流产史, 或早产史。对照组纳入标准: 此次孕前有且仅有1次中孕流产/引产史, 或早产史, 无其他分娩史, 不符合CIC诊断标准。排除标准: ①有先天性子宫畸形。②有妇科手术史。③有心脏病、高血压等其他脏器或系统疾病。④有泌尿系统感染或白带检查异常。⑤体质指数 (BMI) $> 30 \text{ kg/m}^2$ 。⑥有吸烟史。⑦盆底超声检查发现孕妇有肛提肌撕裂, 或者肛门内、外括约肌断裂。中孕流产或引产的孕周范围为孕12周~孕27周6d, 早产的孕周范围为孕28周~孕36周6d。

1.2 研究方法

收集2组孕妇的一般临床资料, 统计孕期有无咳嗽漏尿、憋气漏尿等压力性尿失禁症状。

采用GE Voluson E8超声诊断仪, RAB6-D探头, 频率4~8 MHz。受检查者排空膀胱和直肠, 取截石位。将探头置于两侧大阴唇之间, 获得正中矢状切面。盆底标准正中矢状切面要求: 以耻骨联合后下缘为参考点, 从前往后主要包括耻骨联合、尿道、膀胱颈、阴道、宫颈、直肠、直肠壶腹部和肛管。在受检者平静呼吸 (静息状态) 时测量参数: 使用二维超声测量膀胱颈位置、尿道倾斜角、宫颈位置、直肠壶腹部位置 (图1); 使用四维超声测量肛提肌裂孔面积 (area of urogenital hiatus, HA)、肛提肌裂孔左右径及前后径。

孕妇盆底肌收缩 (pelvic floor muscle contraction, PFMC) 状态下使用三维超声观察肛提肌和肛门内、



Note: 1—The reference line is a horizontal line placed at the inferoposterior margin of the symphysis pubis; 2—vertical distance of bladder neck; 3—vertical distance of cervix; 4—vertical distance of rectal ampulla position.

图1 孕妇静息状态下盆底超声测量膀胱颈位置、宫颈最低点位置和直肠壶腹部位置

Fig 1 Measurements of bladder neck position, lowest edge of cervix and rectal ampulla position by pelvic floor ultrasound in pregnant women at rest

外括约肌完整性；四维超声测量HA、肛提肌裂孔左右径及前后径。

孕妇做瓦尔萨尔瓦动作（Valsalva maneuver, VM）最大程度时，冻结图像。使用二维超声测量膀胱颈位置、膀胱后角、尿道旋转角、膀胱颈移动度、宫颈位置、直肠壶腹部位置，以及尿道内口有无漏斗

形成（图2A）；再使用四维超声测量HA、肛提肌裂孔左右径及前后径（图2B）。

1.3 统计学分析

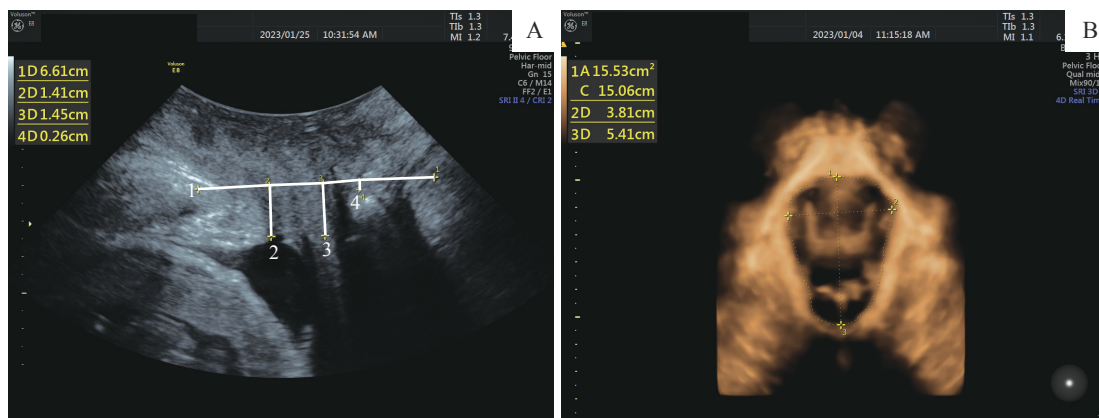
应用SPSS 20.0软件处理数据。定量资料用 $\bar{x} \pm s$ 表示，组间比较采用独立样本 t 检验；定性资料用频数（百分比）表示，组间比较采用 χ^2 检验；用一般线性回归模型校正混杂因素影响，对参数间的相关性进行分析。 $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 研究对象一般资料

研究共纳入76例孕妇，其中CIC组39例，对照组37例。2组孕妇的年龄差异无统计学意义（ $P > 0.05$ ）；CIC组BMI、孕周均显著大于对照组，差异有统计学意义（均 $P < 0.05$ ）。

CIC组孕妇尿道内口漏斗形成4例（10.25%），对照组无尿道内口漏斗形成，差异无统计学意义（ $P = 0.064$ ）。CIC组压力性尿失禁9例（23.07%），对照组压力性尿失禁5例（13.51%），差异无统计学意义（ $P = 0.219$ ）。详见表1。



Note: A. Bladder neck position, lowest edge of cervix and rectal ampulla position observed by ultrasound at VM. 1—The reference line is a horizontal line placed at the inferoposterior margin of the symphysis pubis; 2—vertical distance of bladder neck; 3—vertical distance of cervix; 4—vertical distance of rectal ampulla position. B. HA measured by 4-dimensional ultrasound at VM.

图2 孕妇VM状态下盆底超声图像及测量指标

Fig 2 Ultrasonic images and measurements of pelvic floor in pregnant women at VM

2.2 2组孕妇在静息状态下盆底结构超声测量指标的比较

2组孕妇在静息状态下膀胱颈位置、宫颈位置、直肠壶腹部位置、尿道倾斜角、HA，以及肛提肌裂孔左右径、上下径差异均无统计学意义（均 $P > 0.05$ ，表2）。

2.3 2组孕妇在PFMC状态下盆底结构超声测量指标的比较

2组孕妇在PFMC状态下HA、肛提肌裂孔左右径和肛提肌裂孔前后径差异均无统计学意义（均 $P > 0.05$ ，表3）。

表 1 2 组孕妇的临床特征比较

Tab 1 Comparison of clinical characteristics between two groups of pregnant women

Item	CIC group (n=39)	Control group (n=37)	t/χ ² value	P value
Age/year	32.10±3.62	32.19±4.29	0.077	0.939
BMI/(kg·m ⁻²)	25.29±3.76	22.44±3.13	-3.040	0.004
Gestational age/week	22.68±5.07	16.11±6.56	-4.207	0.000
Urinary incontinence/n(%)	9 (23.07)	5 (13.51)	1.156	0.219
Funneling of internal urethral orifice/n(%)	4 (10.25)	0 (0)	4.006	0.064

表 2 2 组孕妇在静息状态下盆底结构超声测量指标的比较

Tab 2 Comparison of ultrasound measurements of the pelvic floor structure between two groups at rest

Item	CIC group (n=39)	Control group (n=37)	t value	P value
Position of bladder neck/mm	27.76±3.44	27.74±2.71	-0.021	0.983
Urethral inclination angle/(°)	19.93±12.16	21.37±11.88	0.448	0.656
Cervical position/mm	35.69±6.60	33.26±8.91	-1.166	0.249
Position of ampulla of rectum/mm	23.66±8.64	22.04±7.33	-0.753	0.455
HA/cm ²	12.76±3.24	11.70±2.22	-1.413	0.163
Hiatal transverse diameter/mm	33.83±5.56	34.07±4.08	0.188	0.852
Hiatal anteroposterior diameter/mm	51.66±7.89	49.07±6.38	-1.340	0.186

表 3 2 组孕妇在PFMC状态下盆底结构超声测量指标的比较

Tab 3 Comparison of ultrasound measurements of the pelvic floor structure between two groups at PFMC

Item	CIC group (n=39)	Control group (n=37)	t value	P value
HA/cm ²	9.90±2.01	9.89±1.95	-0.014	0.988
Hiatal transverse diameter/mm	30.59±4.21	31.22±3.78	0.593	0.555
Hiatal anteroposterior diameter/mm	44.34±6.53	44.74±5.67	0.241	0.810

2.4 2 组孕妇在VM状态下盆底结构超声测量指标的比较

在VM状态下，CIC组孕妇的HA（P=0.016）和肛提肌裂孔前后径（P=0.014）较对照组均显著增大，

而膀胱颈位置、膀胱后角、尿道旋转角、膀胱颈移动度、宫颈位置、直肠壶腹部位置、肛提肌裂孔左右径与对照组之间的差异均无统计学意义（P>0.05，表4）。

表 4 2 组孕妇在VM状态下盆底结构超声测量指标的比较

Tab 4 Comparison of ultrasound measurements of the pelvic floor structure between two groups at VM

Item	CIC group (n=39)	Control group (n=37)	t value	P value
Position of bladder neck/mm	15.62±5.60	18.00±6.25	1.449	0.154
Posterior angle of bladder/(°)	138.48±18.17	139.04±17.47	0.114	0.910
Urethral rotation angle/(°)	30.92±15.52	24.38±18.33	-1.388	0.171
Bladder neck mobility/mm	12.15±5.64	9.62±5.98	-1.575	0.122
Cervical position/mm	19.92±8.84	19.27±9.48	-0.257	0.798
Position of ampulla of rectum/mm	8.35±11.28	13.35±8.06	1.840	0.072
HA/cm ²	16.19±3.80	13.85±3.03	-2.485	0.016
Hiatal transverse diameter/mm	37.69±4.65	35.85±3.77	-1.587	0.119
Hiatal anteroposterior diameter/mm	57.92±9.29	52.19±6.93	-2.555	0.014

2.5 CIC史与VM状态下HA、肛提肌裂孔前后径的相关性分析

用一般线性回归模型校正孕周和孕妇BMI,对是否有CIC史与VM状态下HA和肛提肌裂孔前后径这2个参数进行相关性分析。结果发现,是否有CIC病史与这2个参数均存在相关性(表5、表6)。

表5 VM状态下HA的一般线性回归结果

Tab 5 General linear regression results of HA at VM

Variable	β	<i>t</i> value	<i>P</i> value
Constant	9.044	2.999	0.004
CIC history	2.135	2.133	0.038
BMI	0.182	1.320	0.193
Gestational age	0.045	0.567	0.573

表6 VM状态下肛提肌裂孔前后径的一般线性回归结果

Tab 6 General linear regression results of hiatal anteroposterior diameter at VM

Variable	β	<i>t</i> value	<i>P</i> value
Constant	40.115	5.854	0.000
CIC history	4.830	2.020	0.049
BMI	0.369	1.165	0.249
Gestational age	0.234	1.249	0.217

3 讨论

妊娠期盆底受到激素变化和胎儿机械性压力影响出现明显的变化,尿道和盆腔脏器活动度增大,HA增大,经阴道分娩的女性较剖宫产女性盆底结构变化更为显著^[9]。有过1次生育史的女性再次妊娠,其盆底结构变化较首次妊娠的女性更为明显^[10]。已有研究^[11]发现与无分娩史的未孕女性比较,妊娠晚期静息状态和VM状态下的HA分别增加了27%和41%;随着孕周逐渐增大,膀胱颈、宫颈及直肠壶腹部位置都明显下降,HA逐渐增加;晚孕期静息状态和VM状态下HA较早孕期分别增加了15%和25%。膀胱颈位置下降、HA增大与压力性尿失禁相关,HA增大还与盆腔脏器脱垂症状相关^[10,12]。在产后1~3年的随访中,顺产的女性HA及肛提肌裂孔左右径、前后径明显大于剖宫产女性,膀胱颈位置低,在VM状态下变化更明显,并且膀胱颈移动度也增大^[13];产后3~5年,顺产女性膀胱颈、宫颈和直肠壶腹部位置更低,HA更大,并且胎次越多,HA越大^[14-15]。目前孕期盆底的研究对象大多是正

常妊娠孕妇,有关CIC女性孕期盆底结构变化的研究少见报道。

有CIC病史的女性,至少有过1次中孕流产史或者早产史,因此对照组也选择了曾有1次中孕流产、中孕引产或早产的女性,流产或早产的原因为胎膜早破、胎盘早剥等病理因素。本研究应用盆底超声对有CIC病史的女性和有早产、中孕流产或引产史的无CIC病史女性再次妊娠时的早、中孕期盆底结构进行观察,发现在静息状态和PFMC时,2组孕妇盆底结构参数均无明显差异;VM状态下,CIC组孕妇HA和肛提肌裂孔前后径显著大于对照组。2组孕妇均有中孕流产史或者早产史,虽然产程时间长度较足月顺产短,宫缩强度也相对较小,但是仍会对盆底肌产生一定影响。静息状态下,盆底肌肉和筋膜等结构受到外力影响较小;PFMC时,盆底肌收缩增厚,2组盆底肌形态变化相近;VM时,盆底肌受到大力牵拉,CIC组孕妇HA和肛提肌裂孔前后径表现出差异,提示盆底结构的变化可能与CIC病史有关。

有研究发现膀胱颈位置下降、HA增大与压力性尿失禁相关^[4,10,12,16]。也有研究^[17]认为HA与压力性尿失禁相关性低。本研究中,CIC组VM状态下HA明显大于对照组,而关于压力性尿失禁,CIC孕妇的发生率为23.07%,对照组的发生率为13.51%;虽然2组压力性尿失禁发生率差异无统计学意义,但是由于本研究的样本量较小,可能存在统计误差。因此还需要进一步加大样本量,并随访孕妇孕期盆底及压力性尿失禁的后续进展,为产后盆底康复咨询提供依据。

用一般线性回归模型校正孕周和BMI,结果发现:CIC病史与VM时的HA、肛提肌裂孔前后径这2个参数存在相关性,提示曾经有CIC病史的孕妇再次妊娠,早、中孕期VM时的HA、肛提肌裂孔前后径这2个参数会增大,肛提肌裂孔形态以纵轴增加更明显。CIC患者一般在妊娠足月前出现进行性、无痛性宫颈缩短、扩张、展平,及漏斗状宫颈,盆底承受负担变大,可能引起盆底生物力学的改变。

此外,有研究^[5,18]发现盆腔脏器脱垂的患者,子宫骶韧带中I型胶原蛋白含量下降。而CIC患者发生I型胶原蛋白纯合突变的概率较高,该突变可导致正常合成的胶原蛋白减少^[19]。另有研究^[20]发现,PFD与基因易感性相关:患有结缔组织代谢障碍性疾

病的个体,如埃勒斯-当洛斯综合征(胶原蛋白基因缺陷)患者压力性尿失禁的发生率明显高于普通人群;此类患者胶原蛋白合成受阻,宫颈完整性被破坏,也更易发生CIC^[3]。

鉴于CIC和PFD有着相似的组织学改变,有学者推测CIC与PFD之间可能存在潜在关联。研究^[6,21]发现有CIC病史的女性发生盆腔脏器脱垂和压力性尿失禁风险更高。BENDET等^[22]报道盆腔脏器脱垂患者的CIC发生率高于无盆腔脏器脱垂组,妊娠期间宫颈环扎是随后发展为盆腔脏器脱垂的独立危险因素。本研究发现有CIC病史的孕妇在VM状态下,HA和肛提肌裂孔前后径均增大,且排除混杂因素后2个指标仍与CIC病史之间存在相关性;提示患有CIC的女性盆底结构可能发生变化,这种变化可能从孕期就存在,这为从病因学上研究PFD与CIC的关联提供了线索。

利益冲突声明/Conflict of Interests

所有作者声明不存在利益冲突。

All authors disclose no relevant conflict of interests.

伦理批准和知情同意/Ethics Approval and Patient Consent

本研究涉及的所有方法均已通过同济大学附属第一妇婴保健院医学伦理委员会的审核批准(文件号:伦字第053号)。所有过程均遵照《赫尔辛基宣言》的条例进行。受试对象已经签署知情同意书。

All protocols in this study were reviewed and approved by Ethics Committee, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine (Approval Letter No. 053), and all protocols were carried out by following the guidelines of *Declaration of Helsinki*. Consent letters have been signed by the research participants.

作者贡献/Authors' Contributions

郭丽丽、邵飞雪参与试验设计,何萍负责论文写作和修改,李克婷负责数据收集和数据分析,毛笑园、包怡榕、王磊参与患者招募。所有作者均阅读并同意了最终稿件的提交。

The study was designed by GUO Lili and SHAO Feixue. The manuscript was drafted and revised by HE Ping. Data collection and analysis were performed by LI Keting. Participant recruitment was performed by MAO Xiaoyuan, BAO Yirong and WANG Lei. All the authors have read the last version of paper and consented for submission.

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[本文编辑] 瞿麟平

学术快讯

上海交通大学公共卫生学院李辰团队合作揭示小鼠胚胎母源-合子转换过程中的RNA m⁶A动态

2023年4月6日,上海交通大学公共卫生学院单细胞组学与疾病研究中心李辰研究组,中国科学院脑科学与智能技术卓越创新中心(神经科学研究所)刘真研究组、孙怡迪研究组合作在*Genome Biology*发表题为*Reading and writing of mRNA m⁶A modification orchestrate maternal-to-zygotic transition in mice*的研究论文。该研究利用SLIM-seq技术绘制出小鼠胚胎母源-合子转换(maternal-to-zygotic transition, MZT)过程中RNA N⁶-甲基腺苷(m⁶A)修饰动态图谱,并通过与超敏蛋白质组和翻译组等进行多组学联合分析以及CRISPR/Cas13d介导的基因敲低,揭示了m⁶A的读写对于小鼠着床前胚胎发育的影响。该研究鉴定了参与着床前胚胎发育的一些m⁶A调控分子,初步阐明了YTH结构域包含蛋白1(YTH domain containing protein 1, YTHDC1)可能参与母源继承m⁶A⁺转录本的稳定性调控,体现了多组学分析在胚胎发育研究中的重要性。