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盆底超声参数预测剖宫产后压力性尿失禁的效能及其与盆底组织E-cadherin和Vimentin表达的关系研究*

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摘要 目的:研究盆底超声参数预测剖宫产后压力性尿失禁(SUI)的效能及其与盆底组织钙粘附蛋白E(E-cadherin)和波形蛋白(Vimentin)表达的关系。**方法:**选取2020年1月~2021年1月湖南省妇幼保健院收治的124例剖宫产患者。将其按照是否发生SUI分为SUI组18例以及无SUI组106例。对所有患者均进行盆底超声检查,比较两组静息期(R)、张力期Valsalva动作(V)的膀胱尿道后角(PUA)以及膀胱颈到耻骨联合下缘水平垂直距离(BNS),膀胱颈移动度(BND)、尿道旋转角度(UR)。通过受试者工作特征(ROC)曲线分析盆底超声参数预测剖宫产后SUI的效能。另外,对比两组盆底组织E-cadherin和Vimentin mRNA水平,采用Pearson相关性分析各项盆底超声参数和盆底组织E-cadherin、Vimentin mRNA表达的相关性。**结果:**SUI组R-PUA、V-PUA、BND以及UR均高于无SUI组,而R-BNS以及V-BNS均低于无SUI组(均P<0.05)。ROC曲线分析结果:各项盆底超声参数联合预测剖宫产后SUI的效能均优于各项参数单独预测。SUI组盆底组织E-cadherin mRNA水平低于无SUI组,而Vimentin mRNA水平高于无SUI组(均P<0.05)。经Pearson相关性分析发现,R-PUA、V-PUA、BND、UR均和盆底组织E-cadherin mRNA水平呈负相关关系,与Vimentin mRNA水平呈正相关关系;而R-BNS、V-BNS均和盆底组织E-cadherin mRNA水平呈正相关关系,与Vimentin mRNA水平呈负相关关系(均P<0.05)。**结论:**盆底超声参数预测剖宫产后SUI的效能较高,且和盆底组织E-cadherin、Vimentin表达有关。

关键词:压力性尿失禁;盆底超声;钙粘附蛋白E;波形蛋白

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Efficacy of Pelvic Floor Ultrasound Parameters in Predicting Stress Urinary Incontinence after Cesarean Section and its Relationship with E-cadherin and Vimentin Expression in Pelvic Floor Tissues*

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ABSTRACT Objective: To study the efficacy of pelvic floor ultrasound parameters in predicting stress urinary incontinence (SUI) after cesarean section and analyze its relationship with the E-cadherin and Vimentin expression in pelvic floor tissue. **Methods:** 124 patients with cesarean section who were admitted to Hunan Maternal and Child Health Hospital from January 2020 to January 2021 were selected. According to the occurrence of SUI, they were divided into SUI group with 18 cases and non-SUI group with 106 cases. Pelvic floor ultrasonography was performed in all patients, and the posterior Angle of bladder and urethra (PUA), the horizontal and vertical distance from bladder neck to the lower margin of pubic symphysis (BNS), bladder neck mobility (BND) and urethra rotation Angle (UR) were compared between the two groups during rest (R) and tension (V) Valsalva movements. The efficacy of pelvic floor ultrasound parameters in predicting SUI after cesarean section was analyzed by receiver operating characteristic (ROC) curve analysis. In addition, the mRNA levels of E-cadherin and Vimentin in pelvic floor tissues were compared between the two groups, and the correlation between various pelvic floor ultrasound parameters and the E-cadherin and Vimentin expression in pelvic floor tissues was analyzed by Pearson correlation. **Results:** R-PUA, V-PUA, BND and UR in SUI group were higher than those in non-SUI group, while R-BNS and V-BNS were lower than those in non-SUI group (all P<0.05). ROC curve analysis results: the combined efficacy of various pelvic floor ultrasound parameters in predicting SUI after cesarean section was better than that of various parameters alone. The mRNA level of E-cadherin in the pelvic floor tissues of SUI group was lower than that of the non-SUI group, while the mRNA level of Vimentin was higher than that of the non-SUI group (all P<0.05). Pearson correlation analysis showed that R-PUA, V-PUA, BND, UR were negatively correlated with E-cadherin mRNA levels in pelvic floor tissues, and positively correlated with Vimentin mRNA levels. While R-BNS and V-BNS were positively correlated with E-cadherin mRNA level in pelvic floor tissue, and negatively correlated with Vimentin mRNA level (all P<0.05). **Conclusions:** Pelvic floor ultrasound parameters are highly effective in predicting SUI after cesarean section, and are

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related to the E-cadherin and Vimentin expression in pelvic floor tissues.

Key words: Stress urinary incontinence; Pelvic floor ultrasound; Cadherin E; Vimentin

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前言

压力性尿失禁(SUI)属于较为常见的一种妇科疾病,患者主要表现特征为咳嗽、喷嚏以及劳作时负压剧增,进一步导致尿液难以控制漏出,但在正常状态下并无异常,极易被患者所忽视^[1-3]。目前临幊上应用于SUI诊断中的手段较多,包括超声成像、磁共振成像(MRI)及X线盆腔造影等。X线盆腔造影存在操作复杂的缺陷,且检查期间需实施导尿操作以排空膀胱,临床应用有所局限^[4-6]。MRI虽然具有一定的诊断效果,然而扫描时间较长,检查费用较高,难以在基层医院推广普及^[7,8]。超声因具有无辐射、操作简便以及重复性较好等优势,在SUI的诊断中具有一定的应用价值^[9,10]。另有研究学者发现,钙粘附蛋白E(E-cadherin)参与了细胞和细胞外基质相互黏附过程,进一步影响胶原降解过程,影响盆底组织结构完整性,增加剖宫产术后SUI发生几率^[11,12]。波形蛋白(Vimentin)属于细胞骨架蛋白之一,于正常上皮细胞中基本不表达,而在机体出现上皮-间质转化(EMT)时异常高表达,EMT会影响盆底支持结构的完整性,进一步引起盆底功能障碍的发生,增加剖宫产术后SUI发生风险^[13,14]。鉴于此,本文通过研究盆底超声参数预测剖宫产术后SUI的效能及其与盆底组织E-cadherin和Vimentin表达的关系,旨在为临幊工作提供一定支持,报道如下。

1 资料与方法

1.1 一般资料

本研究已经获得湖南省妇幼保健院伦理委员会批准,选取2020年1月~2021年1月湖南省妇幼保健院收治的124例剖宫产患者。年龄最小29岁,最大39岁,平均(33.61 ± 4.05)岁;产次1~3次,平均(1.71 ± 0.15)次;既往史:孕期饮酒7例,孕期尿失禁11例。纳入标准:(1)所有患者均行剖宫产;(2)年龄>18周岁;(3)SUI患者均有咳嗽、喷嚏以及用力时有漏尿表现,并经尿动力检查确诊;(4)既往并无泌尿系疾病史。排除标准:(1)伴有泌尿系肿瘤者;(2)因感染或(和)神经系统疾病等原因导致的尿失禁;(3)合并盆腔疾病者;(4)因故无法完成相关检查/研究者。所有患者均已签署知情同意书。

1.2 研究方法

(1)盆底超声检查:选用仪器即Resona 8 Super四维彩超(深圳迈瑞生物医疗电子股份有限公司)。探头频率为4~

8MHz。检查前告知受检者排空膀胱,并协助其取膀胱截石位。取耦合剂对探头实施涂抹,随后套上无菌隔离套,再次取耦合剂完成隔离套的涂抹。将探头置于会阴部,深度以探头距耻骨联合下缘小于1cm为宜。检测静息期(R)、张力期Valsalva动作(V)的膀胱尿道后角(PUA)以及膀胱颈到耻骨联合下缘水平垂直距离(BNS)、膀胱颈移动度(BND)、尿道旋转角度(UR)。(2)常规术中切取盆底组织,并进行总核糖核酸(RNA)的提取,以紫外分光光度计进行光密度的测定,计算D_{260/280}以及D_{260/230}。分析RNA浓度及纯度,之后采用反转录试剂盒(购自大连TaKaRa公司)进行反转录获取cDNA,以荧光定量聚合酶链反应(PCR)仪(购自德国Eppendorf公司)进行E-cadherin和Vimentin mRNA相对表达水平的检测,以 $2^{\Delta\Delta Ct}$ 计算目标基因mRNA相对表达水平。相关参数设置如下:95°C预变性2min,95°C变性15s,60°C退火20s,72°C延伸20s,共40个循环。相关引物序列如下:E-cadherin上游引物为5'-AGCAGAAAGCA-GAACCC-3',下游引物为5'-TCCTTCCACGAAACCAGTG-3'。Vimentin上游引物为5'-TCTCAAAGATGCCAGGAG-3',下游引物为5'-CACGATCCAAT-CTTCCTC-3'。以GAPDH为内参基因,上游引物为5'-TTG-ACCTCAACTACATGGTTT-3',下游引物为5'-AGATGGTGTGGGATTTC-3'。(3)分组方式:对所有患者均进行为期6个月的随访观察,采用门诊复查或电话方式进行,将其按照是否发生SUI分为SUI组18例以及无SUI组106例,比较两组盆底超声参数以及E-cadherin、Vimentin mRNA相对表达水平。

1.3 统计学方法

借助SPSS 22.0软件分析本文所得数据。计量资料均呈正态分布,以 $(\bar{x} \pm s)$ 完成表示,组间对比通过独立样本t检验实现。计数资料以例(%)予以表示,实施 χ^2 检验。通过受试者工作特征(ROC)曲线分析盆底超声参数预测剖宫产术后SUI的效能。采用Pearson相关性分析各项盆底超声参数和盆底组织E-cadherin、Vimentin mRNA表达的相关性。检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组盆底超声参数对比

SUI组R-PUA、V-PUA、BND以及UR均高于无SUI组,而R-BNS以及V-BNS均低于无SUI组(均P<0.05),见表1。

表1 两组盆底超声参数对比($\bar{x} \pm s$)

Table 1 Comparison of pelvic floor ultrasound parameters between the two groups($\bar{x} \pm s$)

Groups	n	R-PUA(°)	R-BNS(mm)	V-PUA(°)	V-BNS(mm)	BND(mm)	UR(%)
SUI group	18	113.06±14.28	22.41±3.10	151.27±23.45	-8.12±1.34	32.41±7.12	82.25±21.37
Non-SUI group	106	102.73±12.37	27.12±3.56	136.29±21.30	3.15±0.23	22.56±6.10	66.97±17.93
t		3.202	-5.279	2.719	-81.293	6.180	3.249
P		0.002	0.000	0.008	0.000	0.000	0.002

表 4 盆底超声参数与盆底组织 E-cadherin、Vimentin mRNA 表达的相关性分析

Table 4 Correlation analysis between pelvic floor ultrasound parameters and E-cadherin and Vimentin mRNA expression in pelvic floor tissue

Pelvic floor ultrasound parameters	E-cadherin		Vimentin	
	r	P	r	P
R-PUA	-0.383	0.000	0.377	0.000
R-BNS	0.336	0.025	-0.411	0.013
V-PUA	-0.371	0.000	0.394	0.000
V-BNS	0.335	0.021	-0.323	0.006
BND	-0.356	0.001	0.420	0.000
UR	-0.402	0.000	0.431	0.000

本文结果发现,SUI 组 R-PUA、V-PUA、BND 以及 UR 均高于无 SUI 组,而 R-BNS 以及 V-BNS 均低于无 SUI 组。这表明了 SUI 以及无 SUI 剖宫产产妇的盆底超声参数存在明显的差异,考虑原因,在张力状态下的指标检测均要求受检者配合完成呼气动作,加之腹部肌肉的生理性收缩,导致腹部压力增高,最终引起上述张力状态下相关盆底超声参数的异常改变。同时,在静息状态下,尿道和人体重力方向平行,更易遭受重力以及腹内压力等因素的影响,进一步引起上述静息状态下超声参数指标的改变^[24-26]。此外,ROC 曲线分析结果:各项盆底超声参数联合预测剖宫产术后 SUI 的效能均优于各项参数单独预测。这在信吉伟等人^[27]的研究报道中得以佐证,盆底超声参数联合预测剖宫产术后 SUI 的 ROC 曲线下面积为 0.858,敏感度为 0.904,特异度为 0.812。究其原因,联合各项盆底超声参数预测可为医生诊断疾病提供更为全面的依据有关。肖汀等人^[28]的一项关于 312 例 SUI 患者的研究发现,BND 单独预测 SUI 的 ROC 曲线下面积最大,预测效能最佳。而本文结果发现六项盆底超声参数预测 SUI 的 ROC 曲线下面积差异不大,两项研究存在明显的相悖之处,而导致上述差异的原因可能和研究样本量不同有关。另外,SUI 组盆底组织 E-cadherin mRNA 水平低于无 SUI 组,而 Vimentin mRNA 水平高于无 SUI 组。这反映了剖宫产术后 SUI 患者的 E-cadherin、Vimentin 均存在表达异常,可能参与了疾病的发生、发展过程。分析原因,E-cadherin 属于上皮细胞标志性物质之一,可发挥调控细胞和细胞外基质相互黏附的作用,可阻碍胶原降解;而 Vimentin 属于间质细胞标志性物质,广泛表达于淋巴细胞以及成纤维细胞中。两者表达的异常改变,可能导致细胞黏附分子功能障碍,进一步减弱了细胞间黏附性,导致细胞骨架蛋白的异常改变,继而使得盆底组织结构完整性被破坏,最终引起 SUI 的发生^[29,30]。本文结果还显示了经 Pearson 相关性分析发现,R-PUA、V-PUA、BND、UR 均和盆底组织 E-cadherin 表达呈负相关关系,与 Vimentin mRNA 表达呈正相关关系;而 R-BNS、V-BNS 均和盆底组织 E-cadherin mRNA 表达呈正相关关系,与 Vimentin 表达呈负相关关系。这充分说明了 SUI 患者盆底超声参数和 E-cadherin、Vimentin mRNA 表达有关。其中主要原因可能是随着盆底超声参数的改变,往往反映了盆底组织结构的异常改变,继而促进了 SUI 发生、发展,进一步导致 E-cadherin、Vimentin mRNA 异常表达。

综上所述,盆底超声参数在预测剖宫产术后 SUI 的价值较高,且与盆底组织 E-cadherin、Vimentin 异常表达有关,可作为临床预测 SUI 的重要辅助指标。

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