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彩色多普勒超声联合性激素对性早熟女童的诊断价值及其相关性分析*

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摘要 目的:探讨彩色多普勒超声联合性激素对性早熟女童的诊断价值及其相关性分析。**方法:**选择2017年10月至2019年10月我院收治的性早熟女童80例,根据促性腺激素释放激素(GnRH)激发试验结果将其分为中枢性性早熟(CPP)组($n=31$),外周性性早熟(PPP)组49例($n=49$)。比较两组女童的彩色多普勒超声检查结果及性激素水平,分析卵巢容积、子宫容积与性激素的相关性,并分析子宫容积、卵巢容积及FSH峰值、LH峰值、LH峰值/FSH峰值在性早熟女童中的鉴别诊断价值。**结果:**CPP组女童卵巢容积、卵泡个数、最大卵泡直径、子宫容积、子宫内膜厚度、乳腺低回声团厚度均显著高于PPP组女童($P<0.05$)。CPP组女童促卵泡生成素(FSH)基础值、FSH峰值、促黄体生成素(LH)基础值、LH峰值、LH峰值/FSH峰值均显著高于PPP组女童($P<0.05$)。CPP组女童卵巢容积、子宫容积与LH峰值、LH峰值/FSH峰值呈正相关($P<0.05$),PPP组女童卵巢容积、子宫容积与性激素水平无相关性($P>0.05$),两组LH峰值与LH峰值/FSH峰值均呈正相关($P<0.05$)。ROC曲线分析显示,子宫容积、卵巢容积、LH峰值、FSH峰值、LH峰值/FSH峰值鉴别诊断性早熟女童的曲线下面积分别为0.834,0.804,0.753,0.802,0.873。**结论:**彩色多普勒超声和性激素能够为性早熟女童病情的鉴别提供重要的临床信息,两者结合应用有助于提高性早熟女童的诊断价值。

关键词:彩色多普勒超声;性激素;中枢性性早熟;外周性性早熟;鉴别诊断价值

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The Diagnostic Value and Correlation Analysis of Color Doppler Ultrasound Combined with Sex Hormone in Girls with Precocious Puberty*

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ABSTRACT Objective: To explore the diagnostic value of color Doppler ultrasound combined with sex hormone in girls with precocious puberty. **Methods:** 80 girls with precocious puberty who were admitted to our hospital from October 2017 to October 2019 were selected, the patients were divided into central precocious puberty (CPP) group ($n=31$) and 49 cases into peripheral precocious puberty (PPP) group according to gonadotropin releasing hormone (GnRH) stimulation test, the results of color Doppler ultrasound and sex hormone levels of the two groups of girls were compared, analyzed the correlation between ovarian volume, uterine volume and sex hormones and to analyze the early differential diagnosis value of uterine volume, ovarian volume and FSH peak value, LH peak value, LH peak value/FSH peak value in girls with precocious. **Results:** The ovarian volume, the number of follicles, the diameter of the largest follicle, the volume of uterus, the thickness of endometrium and the thickness of low echo mass of mammary gland in CPP group were significantly higher than those in PPP group ($P<0.05$). The basic values of Follicle stimulating hormone (FSH), FSH, Luteinizing hormone (LH), LH and LH/FSH in CPP group were significantly higher than those in PPP group ($P<0.05$). There was a positive correlation between the ovarian volume, uterine volume and LH peak, LH peak/FSH peak in CPP group ($P<0.05$). There was no correlation between the ovarian volume, uterine volume and sex hormone levels in PPP group ($P>0.05$). There was a positive correlation between LH peak and LH peak/FSH peak in both groups ($P<0.05$). ROC curve analysis showed that the area under the curve of differential diagnosis of girls with precocious puberty by uterus volume, ovary volume, LH peak value, FSH peak value, LH peak value/FSH peak value was 0.834, 0.804, 0.753, 0.802, 0.873 respectively. **Conclusion:** Color doppler ultrasound and sex hormone can provide important clinical information for girls with precocious puberty and the combination of the two can improve the diagnostic value of girls with precocious puberty.

Key words: Color doppler ultrasound; Sex hormone; Central precocious puberty; Peripheral precocious puberty; Differential diagnostic value

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前言

正常情况下,人在进入青春期后性激素水平逐渐提高,促进人体第二性征出现。而性早熟是指女童在8岁前,男童在9岁前出现第二性征,是儿童内分泌常见疾病之一^[1]。近年来,随着人们生活水平的提高及保健食品服用不当的情况频发,儿童性早熟发生率呈升高趋势,尤其是女童性早熟发生率显著升高^[2,3]。临床中根据发病机制将性早熟分为中枢性性早熟(Central precocious puberty, CPP)和外周性性早熟(Peripheral precocious puberty, PPP),其中CPP属于促性腺激素释放激素(Gonadotropin releasing hormone, GnRH)依赖性,又称为真性早熟;而PPP为非GnRH依赖性,又称为假性早熟,两者的鉴别诊断对于临床治疗女童性早熟具有重要的意义^[4,5]。目前临床上主要通过GnRH激发试验对CPP和PPP进行鉴别诊断,但该方法需要对患儿多次抽血,患儿依从性较差,且不能直观地观察儿童内生殖器官发育情况^[6]。促卵泡生成素(Follicle-Stimulating Hormone, FSH)和促黄体生成素(Luteinizing hormone, LH)为垂体生成的激素,可以促进子宫和卵巢的发育,对于性早熟女童CPP和PPP的鉴别有较好的价值。子宫和卵巢可以直观反映女童的发育水平,对于性早熟诊断具有重要的价值。因此本研究通过分析彩色多普勒超声联合性激素对性早熟女童的诊断价值及其相关性,旨在为女童性早熟的诊断提供依据,现报道如下。

1 资料与方法

1.1 一般资料

选择2017年10月至2019年10月我院收治的性早熟女童80例。纳入标准:(1)所有患儿均符合《性早熟诊疗指南(试行)》中女童性早熟的诊断标准^[7]:女童在8岁前出现乳房发育、阴毛出现、阴道分泌物增多等第二性征;经GnRH激发试验, LH>3.3~5.0IU/L,同时 LH/FSH>0.6 诊断为CPP;(2)患儿入院后接受彩色多普勒超声检查和GnRH激发试验;(3)患儿初次发病,病历资料齐全;(4)患儿家属对研究知情同意。排除标准:(1)合并中枢神经系统感染性疾病、中枢神经系统肿瘤、中枢神

经系统先天性异常引起的性早熟;(2)合并外周生殖器官器质性病变;(3)因甲状腺功能低下等引起性激素异常者。根据GnRH激发试验结果将患儿分为CPP组31例,PPP组49例。CPP组:年龄4~7岁,平均年龄(5.25±1.21)岁;PPP组:年龄5~7岁,平均年龄(5.17±1.25)岁。本研究经医院伦理委员会批准。两组患儿一般资料比较无统计学差异($P>0.05$),具有可比性。

1.2 方法

1.2.1 彩色多普勒超声检查 应用西门子 Acuson Sequoia 512 彩色多普勒超声诊断仪(上海寰熙医疗器械有限公司)检查患儿子宫、卵巢和乳腺,受检患儿排空膀胱,取仰卧位,使用扇形探头对患儿腹部和乳腺进行检查,探头频率3.5~5MHz,记录受检患儿卵巢容积、卵泡个数、最大卵泡直径、子宫容积、子宫内膜厚度、乳腺低回声团厚度。

1.2.2 GnRH 激发试验 所有受检患儿均于入院次日上午8~9时静脉注射GnRH激发试验类似物醋酸曲普瑞林[厂家:丹东医创药业有限责任公司,批准文号:国药准字H20054645,规格:1 mL:0.1 mg(以曲普瑞林计)],注射剂量为2.5 μ g/kg,最大剂量不超过100 μ g。分别于开始注射前0 min及注射后30 min、60 min、90 min抽取患儿外周静脉血2 mL,应用Roche E601全自动电化学发光分析仪(瑞士罗氏公司)测定以上时间点患儿的LH、FSH水平,记录FSH基础值、FSH峰值、LH基础值、LH峰值、LH峰值/FSH峰值。

1.3 统计学方法

应用SPSS24.0软件进行统计学分析,计量资料以($\bar{x}\pm s$)表示,两组间比较采用配对t检验,应用Pearson相关性分析患儿彩色多普勒超声检测结果与性激素水平的相关性,应用ROC曲线分析子宫容积、卵巢容积及性激素在性早熟女童中的早期诊断价值。 $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组女童彩色多普勒超声检查结果比较

CPP组女童卵巢容积、卵泡个数、最大卵泡直径、子宫容积、子宫内膜厚度、乳腺低回声团厚度均显著高于PPP组女童($P<0.05$),见表1。

表1 两组女童彩色多普勒超声检查结果比较($\bar{x}\pm s$)

Table 1 Comparison of color Doppler ultrasound results between two groups of girls($\bar{x}\pm s$)

Groups	n	Ovarian volume(mL)	Number of follicles(n)	Maximum follicle diameter (mm)	Uterine volume (mL)	Endometrial thickness (mm)	Thickness of low echo mass of breast (mm)
CPP group	31	3.68±0.46	7.91±1.88	0.81±0.25	4.31±0.82	3.05±0.61	5.39±0.88
PPP group	49	2.35±0.55	3.21±0.98	0.42±0.18	3.51±0.87	2.71±0.86	3.13±0.65
t		11.204	14.665	8.104	4.096	1.915	13.185
P		0.000	0.000	0.000	0.000	0.059	0.000

2.2 两组女童 GnRH 激发试验结果比较

CPP组女童FSH基础值、FSH峰值、LH基础值、LH峰值、LH峰值/FSH峰值均显著高于PPP组女童($P<0.05$),见表2。

2.3 性早熟女童彩色多普勒超声检测结果卵巢容积、子宫容积与性激素水平的相关性

经Pearson相关分析显示, CPP组女童卵巢容积、子宫容积

与LH峰值、LH峰值/FSH峰值呈正相关($r_{\text{卵巢容积}}=0.455, 0.535, P_{\text{卵巢容积}}=0.000, 0.000; r_{\text{子宫容积}}=0.478, 0.563, P_{\text{子宫容积}}=0.000, 0.000$),与FSH基础值、FSH峰值、LH基础值无相关性($r_{\text{卵巢容积}}=0.128, 0.202, 0.176, P_{\text{卵巢容积}}=0.342, 0.328, 0.282; r_{\text{子宫容积}}=0.154, 0.187, 0.247, P_{\text{子宫容积}}=0.252, 0.324, 0.382$); PPP组女童卵巢容积、子宫容积与FSH基础值、FSH峰值、LH基础值、LH

峰值、LH 峰值 / FSH 峰值均无相关性 ($r_{\text{卵巢容积}}=0.284, 0.252, 0.176, 0.143, 0.132, P_{\text{卵巢容积}}=0.262, 0.427, 0.252, 0.342, 0.362; r_{\text{子宫容积}}=0.301, 0.212, 0.153, 0.137, 0.172, P_{\text{子宫容积}}=0.382, 0.387, 0.302, 0.314, 0.297$), 两组 LH 峰值与 LH 峰值 / FSH 峰值均呈正相关($r=0.674, 0.636, P=0.000, 0.000$)。

2.4 子宫容积、卵巢容积、LH 峰值、FSH 峰值、LH 峰值 / FSH

表 2 两组女童 GnRHa 激发试验结果比较($\bar{x}\pm s$)

Table 2 Comparison of GnRHa stimulation test results between two groups of girls($\bar{x}\pm s$)

Groups	n	FSH base value (IU / L)	FSH peak value (IU / L)	LH base value (IU / L)	LH peak value (IU / L)	LH peak value/ FSH peak value
CPP group	31	9.23±3.87	25.87±9.45	4.17±1.03	35.88±12.44	1.39±2.61
PPP group	49	3.18±1.45	8.22±2.12	1.67±0.78	2.89±0.42	0.37±2.61
t		9.926	12.625	12.315	18.616	1.703
P		0.000	0.000	0.000	0.000	0.093

表 3 各指标对性早熟女童鉴别诊断的 ROC 曲线分析

Table 3 ROC curve analysis of all indexes for differential diagnosis of girls with precocious puberty

Indexs	Best critical value	Sensitivity(%)	Specificity(%)	Area under the curve	95% CI
Uterine volume	3.93mL	92.24	82.37	0.834	0.727~0.885
Ovarian volume	2.97mL	90.23	82.65	0.804	0.709~0.873
LH peak value	3.12IU/L	90.25	86.48	0.753	0.762~0.867
FSH peak value	17.27IU/L	88.25	78.43	0.802	0.642~0.805
LH peak value/ FSH peak value	0.82	93.34	87.76	0.873	0.752~0.974

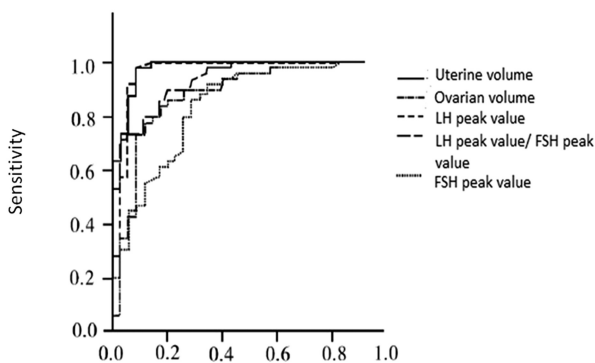


图 1 各指标对性早熟女童鉴别诊断的 ROC 曲线分析

Fig.1 ROC curve analysis of all indexes for differential diagnosis of girls with precocious puberty

3 讨论

儿童性早熟指的是儿童性器官的提前发育。有报道显示,近年来我国儿童性早熟发生率呈升高趋势,与以下因素有关:(1)儿童摄入甜食、薯条等高脂、高热量食物增加,导致儿童内分泌系统失调的发生率不断增加,引发性早熟^[8];(2)摄入含有激素的保健品和食物引发性早熟^[9];(3)学习压力过大,睡眠时间不足^[10];(4)过早且过多的接触网络、电视等大量含有性相关信息的传媒产物增加性早熟的风险^[11]。性早熟包括 CPP 和 PPP,其中 CPP 是由于下丘脑 - 垂体 - 性腺轴系统启动,引起促性腺激素释放激素分泌水平异常升高,进而导致垂体促性腺激

峰值对性早熟女童鉴别诊断的 ROC 曲线分析

ROC 曲线结果显示,子宫容积、卵巢容积、LH 峰值、FSH 峰值、LH 峰值 / FSH 峰值诊断 CPP 的曲线下面积分别为 0.834、0.804、0.753、0.802、0.873,最佳临界值、灵敏度、特异度、曲线下面积见表 3 和图 1。

素分泌显著升高,最终引起卵巢、子宫等发育^[12]。此外下丘脑对性激素负反馈敏感度降低也是引起 CPP 的主要原因^[13]。而 PPP 则是因为各种因素导致性激素水平升高,引发儿童第二性征提早出现,这种性早熟并无卵巢功能亢进的表现^[14]。两种性早熟治疗方法和预后不同,因此临床上能够早期判断儿童性早熟类型对性早熟儿童早期诊断具有重要的意义。

目前对于性早熟儿童的诊断主要采取 GnRH 激发试验的方法。这种方法主要是向受检儿童体内注射 GnRH 类似物,并在多个时间点检测 FSH、LH 水平,进而分析受检儿童有无下丘脑 - 垂体 - 性腺轴系统启动情况,对性早熟进行诊断^[15,16]。但这种方法存在检测手续繁琐、多次采血等缺点^[17]。而彩色多普勒超声检查是一种无创的检测方法,通过彩色多普勒超声可以观察女童的子宫、卵巢、乳腺发育情况,进而为观察 LH 水平情况提供组织影像学资料,最终对性早熟诊断提供依据^[18]。王华等人应用彩色多普勒超声检查特发性性早熟 (Idiopathic precocious puberty, ICPP) 女童和健康女童,并进行比较,结果显示性早熟女童子宫容积、卵巢容积和卵泡个数均高于健康女童^[19]。本研究结果显示 CPP 组女童卵巢容积、卵泡个数、最大卵泡直径、子宫容积、子宫内膜厚度、乳腺低回声团厚度均显著高于 PPP 组女童。正常情况下,儿童时期女童的子宫和卵巢发育非常缓慢,而进入青春期后由于下丘脑对性激素的负反馈调节敏感度下降,引起 GnRH 分泌增加,垂体促性腺激素分泌,子宫、卵巢和乳腺发育加快^[20-22]。CPP 女童身体情况与进入青春期的女性相同,因此子宫、卵巢和乳腺均加速发育^[23]。而 PPP 女童仅

为体内性激素水平异常升高,进而引发儿童第二性征提早出现,并无卵巢功能亢进的表现,因此卵巢容积、卵泡个数、最大卵泡直径、子宫容积、子宫内膜厚度、乳腺低回声团厚度低于 CPP 女童^[24-26]。

本研究结果还显示 CPP 组女童 FSH 基础值、FSH 峰值、LH 基础值、LH 峰值、LH 峰值 / FSH 峰值均显著高于 PPP 组女童。这与 CPP 女童存在下丘脑 - 垂体 - 性腺轴激活的情况,导致性激素分泌增多有关^[27,28]。而 PPP 女童不存在下丘脑 - 垂体 - 性腺轴激活的情况,因此 FSH 基础值、FSH 峰值、LH 基础值、LH 峰值、LH 峰值 / FSH 峰值升高没有 CPP 女童显著^[29,30]。本研究结果还显示, CPP 组女童卵巢容积、子宫容积与 LH 峰值、LH 峰值 / FSH 峰值呈正相关,而 PPP 组女童卵巢容积、子宫容积与性激素水平无相关性。表明彩色多普勒超声检查在评价 CPP 时与 GnRH 激发试验可能具有一致性。而各项超声检查指标和性激素相关指标的 ROC 曲线分析结果显示,子宫容积、卵巢容积、FSH 峰值、LH 峰值、LH 峰值 / FSH 峰值鉴别诊断性早熟均具有较高的敏感度和特异度,这也提示临床上可以将彩色多普勒超声与性激素检测联合,为性早熟女童早期鉴别诊断提供依据。但本研究也存在观察病例数较少,缺少对不同病情程度性早熟女童的数据观察分析的问题,这些问题有待于在后续研究中通过加大样本量、丰富样本数据的措施解决并对研究结果进一步分析。

综上所述,通过彩色多普勒超声可以观察性早熟女童的子宫、卵巢、乳腺发育情况,联合性激素诊断能够为性早熟女童病情的鉴别提供重要的临床信息,为性早熟女童的诊断提供重要依据。

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