

宫颈锥切术至妊娠间隔时间对未足月胎膜早破和新生儿结局的影响及预测分析^{*}

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【摘要】 目的 探讨宫颈锥切术至妊娠间隔时间对未足月胎膜早破和新生儿结局的影响和预测作用。方法 回顾性分析我院 2019 年 6 月—2022 年 6 月收治的 86 例既往宫颈锥切术病史单胎初产妇临床资料, 收集患者宫颈锥切术至妊娠间隔时间, 绘制受试者工作特征(ROC)曲线分析宫颈锥切术至妊娠间隔时间对未足月胎膜早破和新生儿结局的预测作用, 采用单因素和 Logistic 回归模型分析未足月胎膜早破和新生儿结局的影响因素。结果 未足月胎膜早破发生率为 38.37%(33/86), ROC 曲线分析宫颈锥切术至妊娠间隔时间预测未足月胎膜早破的曲线下面积(AUC)为 0.856, 约登指数的最大值为 0.603, 截断值为 10.5 个月, 灵敏度为 0.906, 特异度为 0.697, 95%CI 为 0.772~0.940。胎膜早破组流产史、妊娠期高血压、羊水过多、冷刀锥刀术(CKC)、胎位异常、宫颈锥切术至妊娠间隔时间<10.5 个月发生率高于非胎膜早破组, 差异有统计学意义($P<0.05$)。多因素分析发现 CKC($OR=6.596, 95\%CI:1.287\sim33.795$)、宫颈锥切术至妊娠间隔时间<10.5 个月($OR=28.769, 95\%CI:5.761\sim143.671$)是未足月胎膜早破独立影响因素($P<0.05$)。新生儿不良结局发生率为 26.74%(23/86), ROC 曲线分析宫颈锥切术至妊娠间隔时间预测新生儿不良结局的 AUC 为 0.804, 约登指数的最大值为 0.568, 截断值为 12.5 个月, 灵敏度为 0.698, 特异度为 0.870, 95%CI 为 0.704~0.905。单因素分析发现, 新生儿不良结局组流产史、妊娠期高血压、宫颈锥切术至妊娠间隔时间<12.5 个月、未足月胎膜早破发生率高于非新生儿不良结局组, 差异有统计学意义($P<0.05$)。多因素分析发现流产史($OR=4.834, 95\%CI:1.094\sim21.367$)、妊娠期高血压($OR=16.068, 95\%CI:2.081\sim124.046$)、宫颈锥切术至妊娠间隔时间<12.5 个月($OR=10.968, 95\%CI:2.254\sim53.377$)是新生儿不良结局的独立影响因素($P<0.05$)。结论 对于初产妇, 当宫颈锥切术后至妊娠间隔小于 10.5 个月和 12.5 个月, 分别是未足月胎膜早破和新生儿不良结局的独立危险因素, 具有一定的预测作用。

【关键词】 宫颈锥切术; 未足月胎膜早破; 妊娠结局; 初产妇; 宫颈疾病

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The effect and prediction of the time interval from cervical conecotomy to pregnancy on premature rupture of membranes and neonatal outcomes

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【Abstract】 Objective To investigate the effect and predictive effect of the interval from cervical conecotomy to pregnancy on premature rupture of membranes and neonatal outcome. **Methods** The clinical data of 86 single primiparas with a history of cervical conecotomy admitted to the 909th Hospital of Joint Logistics Support Force from June 2019 to June 2022 were retrospectively analyzed. The time interval from cervical conecotomy to pregnancy was collected. The predictive effect of the time from conecotomy and pregnancy on premature rupture of membranes to neonatal outcome was analyzed by the ROC curve. Univariate and Logistic regression models were used to analyze the influencing factors of premature rup-

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ture of membranes before term and neonatal outcome. **Results** The incidence of premature rupture of membranes before term was 38.37% (33/86). The area under the curve (AUC) of ROC curve analysis for predicting preterm premature rupture of membranes was 0.856, the maximum Youden index was 0.603, the optimal cut-off value was 10.5 (month), the sensitivity was 0.906, and the specificity was 0.697. 95%CI was 0.772~0.940. The incidence of abortion history, gestational hypertension, hyperamniotic fluid, CKC, fetal position abnormality, cervical conectomy and gestation interval <10.5 months in the premature rupture group was higher than that in the non-premature rupture group ($P<0.05$), and the difference was statistically significant. Multivariate analysis showed that CKC(OR: 6.596, 95%CI: 1.287~33.795) and the interval from cervical conectomy to gestation <10.5 months (OR: 28.769, 95%CI: 5.761~143.671) were independent influencing factors for premature rupture of membranes ($P<0.05$). The incidence of adverse outcomes in neonates was 26.74% (23/86). The area under the curve (AUC) of ROC curve analysis for predicting neonatal adverse outcomes was 0.804, the maximum Youden index was 0.568, the cut-off value was 12.5 (months), and the sensitivity was 0.698. The specificity was 0.870 and 95%CI was 0.704~0.905. Univariate analysis showed that the incidence of abortion history, gestational hypertension, interval time from cervical conectomy to gestation <12.5 months, and premature rupture of membranes before term in the adverse neonatal outcome group was higher than that in the non-adverse neonatal outcome group ($P<0.05$), and the difference was statistically significant. Multivariate analysis found history of abortion (OR: 4.834, 95%CI: 1.094~21.367), gestational hypertension (OR: 16.068, 95%CI: 2.081~124.046), and interval from cervical conectomy to gestation <12.5 months (OR: 10.968, 95%CI: 2.254~53.377) were independent influencing factors of neonatal adverse outcomes ($P<0.05$). **Conclusion** For primiparous women, when the interval from cervical conectomy to gestation is less than 10.5 months and 12.5 months, respectively, it is an independent risk factor for premature rupture of membranes before term and adverse neonatal outcome, which has a predictive effect.

【Key words】 Cervical conectomy; Premature rupture of membranes before term; Pregnancy outcome; Primipara; Cervical disease

子宫颈上皮内瘤变(Cervical intraepithelial neoplasia, CIN)是育龄期女性常见的妇科疾病,近年来发病率呈逐年上升趋势^[1-2]。其中Ⅱ级和Ⅲ级 CIN 有进展为宫颈癌的可能,需要进行宫颈锥切术^[3]。目前宫颈锥切术常采用的方法有宫颈冷刀锥切术(Cold knife conization, CKC)和宫颈环形电切术(Loop electrosurgical excision procedure, LEEP)^[4]。由于宫颈锥切术改变了宫颈长度,因此其增加了孕产妇未足月胎膜早破发生率,并且是新生儿低体重、窒息、肺炎等不良结局的影响因素^[5-6]。当前关于宫颈锥切术至妊娠间隔具体时间对未足月胎膜早破和新生儿结局影响的报道相对较少。因此,本研究通过分析单胎初产妇宫颈锥切术至妊娠间隔时间对未足月胎膜早破和新生儿结局的影响,旨在为该人群的临床风险评估提供预测依据。

1 资料与方法

1.1 一般资料 回顾性分析我院 2019 年 6 月—2022 年 6 月收治的 86 例既往有宫颈锥切术病史的单胎初产妇临床资料,年龄为(31.88±4.84)岁,宫颈锥切术至妊娠时间(即患者行宫颈锥切术至末次月经时间)为(12.57±4.76)个月。本研究经我院伦理委员会审批同意。

1.2 纳入、排除标准 纳入标准:①我院建档并规律产检。②既往接受宫颈锥切术,病理诊断明确为 CIN

Ⅱ~Ⅲ级。③单胎妊娠。④初产妇。⑤阴道分娩。⑥临床资料完整。排除标准①恶性肿瘤患者。②子宫、阴道畸形患者。③免疫系统疾病患者。④凝血功能障碍患者。

1.3 观察指标 年龄、BMI、流产史、入院孕周、瘢痕子宫、妊娠期糖尿病、妊娠期高血压、前置胎盘、羊水过多、胎位、未足月胎膜早破(指产妇孕周末满 37 周而发生胎膜自发性破裂)发生情况。新生儿结局包括窒息、肺炎、呼吸窘迫综合征(Neonatal respiratory distress syndrome, NRDS)、低体重、黄疸、败血症、死亡。

1.4 统计学分析 采用 SPSS 24.0 软件统计分析处理数据。符合正态分布的计量资料以($\bar{x} \pm s$)表示,组间比较采用 t 检验;计数资料以(%)表示,组间比较采用 χ^2 或 Fisher 精确检验;绘制受试者工作特征(Receiver operating characteristic, ROC)曲线,计算曲线下面积(Area under curve, AUC),用最大约登指数法确定截断值,并计算灵敏度和特异度;采用单因素及多因素 Logistic 回归分析宫颈锥切术至妊娠间隔时间对未足月胎膜早破和新生儿不良结局的影响因素。以 $P<0.05$ 表示差异有统计学意义。

2 结果

2.1 宫颈锥切术至妊娠间隔时间对未足月胎膜早破 ROC 曲线分析 86 例患者中,33 例发生未足月胎膜

早破,发生率为 38.37%(33/86)。ROC 曲线分析宫颈锥切术至妊娠间隔时间预测未足月胎膜早破的 AUC 为 0.856,约登指数的最大值为 0.603,截断值为 10.5 个月,灵敏度为 0.906,特异度为 0.697,95%CI 为 0.772~0.940,见图 1。

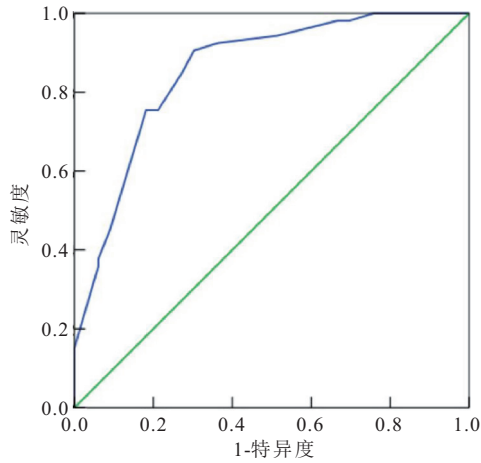


图 1 宫颈锥切术至妊娠间隔时间预测未足月胎膜早破的 ROC 曲线

Figure 1 ROC curve analysis for predicting preterm premature rupture of membranes by time interval from cervical conecotomy to pregnancy

2.2 未足月胎膜早破单因素分析 单因素分析结果显示,胎膜早破组流产史、妊娠期高血压、羊水过多、CKC、胎位异常、宫颈锥切术至妊娠间隔时间<10.5 个月发生率高于非胎膜早破组,差异有统计学意义($P < 0.05$);两组患者年龄、BMI、瘢痕子宫、妊娠期糖尿病、前置胎盘对比差异无统计学意义($P > 0.05$),见表 1。

2.3 未足月胎膜早破多因素分析 多因素分析结果显示,CKC($OR = 6.596, 95\%CI: 1.287 \sim 33.795$)、宫颈锥切术至妊娠间隔时间<10.5 个月($OR = 28.769, 95\%CI: 5.761 \sim 143.671$)是未足月胎膜早破的独立影响因素($P < 0.05$),见表 2。

2.4 宫颈锥切术至妊娠间隔时间对新生儿不良结局 ROC 曲线分析 86 例患者中,23 例发生新生儿不良结局,发生率为 26.74%(23/86),ROC 曲线分析宫颈锥切术至妊娠间隔时间预测新生儿不良结局 AUC 为 0.804,约登指数的最大值为 0.568,截断值为 12.5 个月,灵敏度为 0.698,特异度为 0.870,95%CI 为 0.704~0.905,见图 2。

2.5 新生儿不良结局单因素分析 单因素分析结果显示,新生儿不良结局组流产史、妊娠期高血压、宫颈锥切术至妊娠间隔时间<12.5 个月、未足月胎膜早破发生率高于非新生儿不良结局组,差异有统计学意义($P < 0.05$);两组患者年龄、BMI、瘢痕子宫、妊娠期糖尿病、前置胎盘、羊水过多、手术方式、胎位异常对比差异无统计学意义($P > 0.05$),见表 3。

表 1 86 例患者未足月胎膜早破单因素分析 $[\bar{x} \pm s, n]$

Table 1 Single factor analysis of 86 patients with preterm premature rupture of membranes

一般资料	胎膜早破组 (n=33)	非胎膜早破组 (n=53)	t/ χ^2	P
年龄(岁)	31.63±4.82	32.04±4.88	-0.372	0.711
BMI(kg/m ²)	23.48±0.98	23.66±0.76	-0.962	0.339
流产史			11.742	0.001
是	11	3		
否	22	50		
瘢痕子宫			0.33	0.855
是	1	2		
否	32	51		
妊娠期糖尿病			1.135	0.287
是	4	3		
否	29	50		
妊娠期高血压			4.787	0.029
是	7	3		
否	26	50		
前置胎盘			2.171	0.141
是	5	3		
否	28	50		
羊水过多			6.213	0.013
是	11	6		
否	22	47		
手术方式			6.972	0.008
CKC	15	10		
LEEP	18	43		
胎位异常			10.847	0.001
是	8	1		
否	25	52		
宫颈锥切术至妊娠 间隔时间(月)			33.636	<0.001
<10.5	23	5		
≥10.5	10	48		

表 2 86 例患者未足月胎膜早破多因素分析

Table 2 Multivariate analysis of 86 cases of premature rupture of membranes

指标	β	SE	Wald χ^2	OR	95%CI	P
流产史	1.388	0.994	1.949	4.006	0.571~28.123	0.163
妊娠期高血压	2.030	1.086	3.495	7.615	0.906~63.986	0.062
羊水过多	1.128	0.997	1.280	3.090	0.438~21.816	0.258
CKC	1.886	0.834	5.121	6.596	1.287~33.795	0.024
胎位异常	2.311	1.463	2.496	10.085	0.574~177.281	0.114
宫颈锥切术至妊娠 间隔时间<10.5 个月	3.395	0.821	16.760	28.769	5.761~143.671	<0.001

2.6 新生儿不良结局多因素分析 多因素分析发现流产史($OR = 4.834, 95\%CI: 1.094 \sim 21.367$)、妊娠期高血压($OR = 16.068, 95\%CI: 2.081 \sim 124.046$)、宫颈锥切术至妊娠间隔时间<12.5 个月($OR = 10.968, 95\%CI: 2.254 \sim 53.377$)是新生儿不良结局的独立影响因素($P < 0.05$),见表 4。

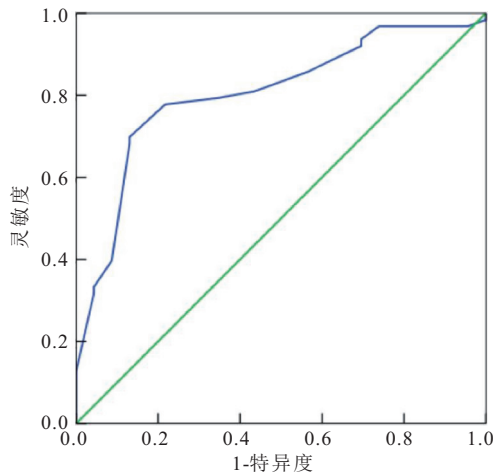


图 2 宫颈锥切术至妊娠间隔时间预测新生儿不良结局的 ROC 曲线
Figure 2 ROC curve analysis for predicting neonatal adverse outcomes by time interval from cervical conecctomy to pregnancy

表 3 86 例患者新生儿不良结局单因素分析 $[(\bar{x} \pm s), n]$

Table 3 Univariate analysis of neonatal adverse outcomes in 86 patients

指标	新生儿不良结局组 (n=23)	非新生儿不良结局组 (n=63)	t/ χ^2	P
年龄(岁)	31.39±4.73	32.06±4.90	-0.568	0.572
BMI(kg/m ²)	23.44±0.85	23.65±0.86	-1.017	0.312
流产史			12.029	0.001
是	9	5		
否	14	58		
瘢痕子宫			1.135	0.561
是	0	3		
否	23	60		
妊娠期糖尿病			0.013	1.000
是	2	5		
否	21	58		
妊娠期高血压			16.381	<0.001
是	8	2		
否	15	61		
前置胎盘			2.435	0.202
是	4	4		
否	19	59		
羊水过多			0.791	0.374
是	6	11		
否	17	52		
手术方式			1.541	0.214
CKC	9	16		
LEEP	14	47		
胎位异常			1.607	0.205
是	4	5		
否	19	58		
宫颈锥切术至妊娠间隔时间(月)			21.931	<0.001
<12.5	20	19		
≥12.5	3	44		
未足月胎膜早破			12.918	<0.001
是	16	17		
否	7	46		

表 4 86 例患者新生儿不良结局多因素分析

Table 4 Multivariate analysis of neonatal adverse outcomes in 86 patients

指标	β	SE	Wald χ^2	OR	95%CI	P
流产史	1.576	0.758	4.319	4.834	1.094~21.367	0.038
妊娠期高血压	2.777	1.043	7.091	16.068	2.081~124.046	0.008
宫颈锥切术至妊娠间隔时间<12.5个月	2.395	0.807	8.800	10.968	2.254~53.377	0.003
未足月胎膜早破	0.282	0.770	0.134	1.326	1.167~3.414	0.714

3 讨论

近年来 CIN 患病年龄逐渐年轻化,越来越多适龄女性在尚未生育之前接受了宫颈锥切术。研究证实,宫颈锥切术是妊娠和新生儿不良结局的独立危险因素^[7]。首先,宫颈锥切术改变了宫颈的长度、形态及子宫壁的夹角,对妊娠过程产生影响^[8];其次,宫颈锥切术后子宫纤维结构发生改变,完整性受到破坏,对妊娠结局产生影响^[9];最后,宫颈锥切术改变了局部微环境,导致屏障功能减弱,逆行感染发生率增高^[10]。目前,学者普遍认为宫颈锥切术与妊娠时间间隔越长,宫颈有足够的时间进行自我微环境修复并恢复长度和结构,早产和胎膜早破发生率越低^[11]。

本研究纳入 86 例宫颈锥切术后初产妇,其中 33 例发生未足月胎膜早破,发生率为 38.37%。ROC 曲线分析发现,宫颈锥切术后至妊娠间隔对未足月胎膜早破的最佳预测值为 10.5 个月。本研究中 CKC25 例,LEEP61 例,CKC 术后未足月胎膜早破发生率(60.00%)高于 LEEP 术后(29.51%)($P<0.05$)。进一步多因素分析发现 CKC、宫颈锥切术至妊娠间隔时间小于 10.5 个月是未足月胎膜早破的独立危险因素。与 LEEP 相比,CKC 需要切除更多的组织,对子宫长度的影响更大^[12]。有学者研究也证实,CKC 术后未足月胎膜早破发生率高于 LEEP 术后,并且是未足月胎膜早破的独立危险因素^[13-14]。一项针对宫颈锥切术后子宫长度恢复时间的研究发现,LEEP 术后宫颈恢复时间至少为 6 个月,而 CKC 术后宫颈恢复时间至少为 9 个月^[15]。但是不同的个体之间,宫颈恢复程度也存在差异。本研究结果显示,宫颈锥切术后至妊娠间隔小于 10.5 个月对未足月胎膜早破的发生具有预测价值。产妇在子宫长度尚未恢复时,胎先露部位过早接触子宫下段及宫颈内口,形成机械压迫,引起宫缩,而发生胎膜早破^[16]。

本研究中共 23 例发生新生儿不良结局,发生率为 26.74%,主要以黄疸和低体重为主,为别为 11 例和 9 例。ROC 曲线分析发现,宫颈锥切术后至妊娠间隔对新生儿不良结局的最佳预测值为 12.5 月。进一步多因素分析发现流产史、妊娠期高血压、宫颈锥切

术至妊娠间隔时间 < 12.5 个月是新生儿不良结局的独立危险因素。国外学者研究也证实, 宫颈锥切术至妊娠间隔时间越短新生儿不良结局发生率越高^[17]。宫颈锥切术增加了早产和胎膜早破发生率, 早产和胎膜早破的新生儿发育尚不完全, 因此也增加了新生儿不良结局发生率^[18-19]。还有学者研究认为, 宫颈锥切术后产妇存在心理焦虑, 导致发生不规则宫缩, 对新生儿结局也有一定的影响^[20]。CKC 和 LEEP 对于新生儿不良结局是否存在影响仍存在争议^[21]。本研究中 CKC 术后和 LEEP 术后新生儿不良结局发生率分别为 36.00% 和 22.95%, 差异无统计学意义 ($P > 0.05$)。与 Zhuang 等^[22] 学者研究结论相一致, CKC 和 LEEP 均增加了新生儿不良结局发生率, 但并不是新生儿不良结局的危险因素, 原因可能是 CKC 和 LEEP 术后宫颈在短时间内尚未恢复正常的组织形态和功能, 粘液产生减少, 感染发生率增加, 新生儿不良结局发生率也增加^[23]。CKC 和 LEEP 切除范围并不相同, 宫颈需要修复的时间也不相同, 本研究认为颈锥切术至妊娠间隔时间 < 12.5 个月是新生儿不良结局的危险因素。另外, 还有学者研究认为不论是 CKC 还是 LEEP, 产妇术后会不同程度产生焦虑情绪, 对新生儿不良结局产生影响^[18]。

本研究的不足之处: 首先本研究为单中心回顾性研究, 可能存在病例选择偏倚; 其次研究结论仍需要多中心大样本量前瞻性验证。

4 结论

对于初产妇, 宫颈锥切术后至妊娠间隔对于未足月胎膜早破和新生儿不良结局具有预测作用, 当宫颈锥切术后至妊娠间隔小于 10.5 个月和 12.5 个月时, 分别是未足月胎膜早破和新生儿不良结局的独立危险因素。

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