·临床研究·

治疗性内镜逆行胰胆管造影取石术前后校正的QT离散度变化及影响因素

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【摘 要】 **目的** 探讨治疗性内镜逆行胰胆管造影(ERCP)取石术前后校正的QT离散度(QTcd)变化及影响因素。**方法** 连续入选2018年6月至2019年1月在南京医科大学第二附属医院行治疗性ERCP取石术的患者61例作为研究对象。分别在术前、术后3 h、术后24 h记录静息12导联心电图。术后3 h QTcd较术前增加者纳入QTcd增加组,反之纳入QTcd降低组。采用SPSS 23.0统计软件进行统计学分析。依据数据类型,组间比较分别采用t检验或χ^2检验。多因素logistic回归分析筛选ERCP取石术后3 h QTcd增加的危险因素。**结果** 61例患者中1例行ERCP取石术后即刻出现室颤,最终获得60例完整数据。ERCP取石术前、术后3 h及术后24 h的QTcd分别为(29.05±11.09)、(36.00±13.46)及(21.81±10.52) ms,术后3 h QTcd较术前及术后24 h均升高,差异具有统计学意义(P<0.05)。多因素logistic回归分析结果显示,女性(OR=15.895, 95%CI 2.505~100.853)和估算肾小球滤过率(eGFR)(OR=1.039, 95%CI 1.003~1.077)是ERCP取石术后3 h QTcd增加的危险因素。**结论** 治疗性ERCP取石术后短期(3 h)内可出现一过性QTcd增加,提示术后短期(3 h)内的恶性心律失常风险增加。女性和eGFR是术后3 h QTcd增加的危险因素。

【关键词】 心律失常;内镜逆行胰胆管造影;校正的QT离散度
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Change of corrected QT dispersion before and after stone removal by therapeutic endoscopic retrograde cholangiopancreatography and its influencing factors

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【**Abstract**】 **Objective** To investigate the change of corrected QT dispersion (QTcd) before and after stone removal by therapeutic endoscopic retrograde cholangiopancreatography (ERCP) and the related influencing factors. **Methods** A total of 61 patients who underwent therapeutic ERCP for stone removal in our hospital from June 2018 to January 2019 were consecutively enrolled as subjects. Resting 12-lead electrocardiography (ECG) was performed before and in 3 h and 24 h after operation. The patients with QTcd in 3 h after operation higher than the value before were assigned into QTcd-increased group, otherwise were into QTcd-reduced group. Statistical analysis was performed using SPSS 23.0. Student t test or Chi-square test was used for comparison between groups on different data types. Multivariate logistic regression analysis was applied to screen the risk factors of QTcd increase at 3 h post-ERCP. **Results** Among the 61 patients, 1 of them experienced ventricular fibrillation immediately after ERCP, and so complete data were obtained from the left 60 patients. The average QTcd value was (29.05±11.09), (36.00±13.46) and (21.81±10.52) ms respectively, before and at 3 h and 24 h post-ERCP. The value at 3 h after ERCP was significantly higher than those at the other 2 time points (P<0.05). Multivariate logistic regression analysis showed that female (OR=15.895, 95%CI 2.505-100.853) and estimated glomerular filtration rate (eGFR, OR=1.039, 95%CI 1.003-1.077) were the risk factors for QTcd increase at 3 h post-ERCP. **Conclusion** Therapeutic ERCP can lead to QTcd increase in a short time (3 h) after stone removal by ERCP, which suggesting increased risk for malignant arrhythmia at that duration. Female and eGFR are the risk factors for QTcd increase at 3 h post-ERCP.

【**Key words**】 arrhythmia; endoscopic retrograde cholangiopancreatography; corrected QT dispersion
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目前,内镜逆行胰胆管造影(endoscopic retrograde cholangiopancreatography,ERCP)是诊治胆胰疾病,尤其是胆总管结石的首选方法[1]。治疗性 ERCP 取石术的并发症复杂,其中恶性心律失常是最严重的一种,死亡率极高[2]。校正的 QT 离散度(QT corrected dispersion,QTcd)能准确地反映心室复极差异性,对预测恶性心律失常具有重要意义[3]。但治疗性 ERCP 取石术对 QTcd 的影响如何,尚鲜有文献报道。笔者旨在探讨治疗性 ERCP 取石术前后 QTcd 的变化及相关影响因素。

1 对象与方法

1.1 研究对象

连续入选 2018 年 6 月至 2019 年 1 月在南京医科大学第二附属医院行治疗性 ERCP 取石术的患者 61 例作为研究对象。入选标准:(1)大于 18 周岁;(2)术前提示存在胆总管结石;(3)自愿参加该研究并签署知情同意。排除标准:(1)严重肾功能不全[估算肾小球滤过率(estimated glomerular filtration rate,eGFR<30 ml/(min · 1.73 m^2)];(2)近期服用影响心室复极的药物;(3)心房颤动或束支传导阻滞;(4)严重心电图记录伪差。本研究通过南京医科大学第二附属医院伦理委员会批准[(2017)KY 第 100 号]。

1.2 方法

术前行常规检查,禁食 8 h。给予右美托咪定联合瑞芬太尼静脉麻醉。检查时均吸氧、心电监护。于术前、术后 3 h、术后 24 h 行常规 12 导联心电图检查(aECG-12PW 心电图机,厦门纳龙科技有限公司,纸速 25 mm/s,灵敏度 10 mm/mv),记录心电图有无 T 波改变(低平、双向或倒置)。由同 1 名心电专业人员行手工分规测量。选择心电图 V_2 导联进行测量,得到心率、最大 QT 间期(QT_{max})、最小 QT 间期(QT_{min})。测量确定 QT 间期时以 Q 波起点水平为等电位线。终点判断方法:(1)T 波回到等电位线;(2)T 波与 u 波之间的切迹;(3)双相 T 波最后回到等电位线的交点。按 Bazett 公式校正心率后得到校正的 QT_{max}、校正的 QT_{min},计算 QTcd,连续测量 3 次取平均值。术后 3 h QTcd 较术前增加者纳入 QTcd 增加组,反之纳入 QTcd 降低组,同时测量术前及术后 3 h Ca^{2+}、K^+、肌钙蛋白 I(cardiac troponin I,cTnI)等相关血清指标变化。

1.3 统计学处理

采用 SPSS 23.0 统计软件进行统计学分析。计量资料用均值±标准差($\bar{x}\pm s$)表示,组间比较采用 t 检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。将单因素分析 $P<0.10$ 的变量纳入多因素 logistic 回归分析,筛选出独立的危险因素。$P<0.05$ 为差异具有统计学意义。

2 结 果

2.1 2 组患者基线资料比较

61 例患者中,1 例患者(女性,31 岁)术后即刻出现室颤,无法完成本研究,最终获得 60 例完整数据。ERCP 取石术前、术后 3 h 及术后 24 h 的 QTcd 分别为(29.05±11.09)、(36.00±13.46)及(21.81±10.52)ms,术后 3 h QTcd 较术前及术后 24 h 均升高,差异具有统计学意义($P<0.05$)。2 组患者的基线资料进行比较,差异均无统计学意义($P>0.05$;表 1)。

表 1 2 组患者基线资料比较

Table 1 Comparison of baseline data between two groups

Item	QTcd increased group (n=41)	QTcd reduced group (n=19)	t/χ^2	P value
Age(years, $\bar{x}\pm s$)	65.56±13.92	68.16±11.77	0.704	0.484
Female[n(%)]	23(56.10)	6(31.58)	3.126	0.077
BMI(kg/m^2, $\bar{x}\pm s$)	22.99±3.63	23.92±2.06	1.043	0.301
History of smoking[n(%)]	13(31.71)	8(42.11)	0.617	0.432
Frequency of ERCP history[n(%)]				
0	29(70.73)	13(68.42)	0.495	0.781
1	6(14.63)	2(10.51)	0.410	0.783
>1	6(14.63)	4(21.05)	0.167	0.683
History of abdominal surgery[n(%)]	26(63.40)	8(42.11)	2.401	0.121
Hypertension[n(%)]	17(41.52)	10(52.62)	0.654	0.419
Diabetes mellitus[n(%)]	3(7.32)	3(15.79)	0.308	0.579
Coronary heart disease[n(%)]	3(7.32)	4(21.05)	1.231	0.267
Total cholesterol(mmol/L, $\bar{x}\pm s$)	4.80±1.35	4.47±1.61	−0.836	0.407
Triglycerides(mmol/L, $\bar{x}\pm s$)	1.39±0.60	1.60±0.78	1.165	0.249
eGFR[ml/(min · 1.73 m^2), $\bar{x}\pm s$]	94.21±22.75	83.66±21.03	−1.710	0.093

QTcd: QT corrected dispersion; BMI: body mass index; ERCP: endoscopic retrograde cholangiopancreatography; eGFR: estimated glomerular filtration rate.

2.2 2组患者手术资料比较

2组患者术中资料比较,差异均无统计学意义($P>0.05$;表2)。

2.3 2组患者手术前后血清指标比较

2组患者术后3 h的Ca^{2+}较术前均显著降低,差异具有统计学意义($P<0.05$;表3)。

2.4 多因素logistic分析

将女性、eGFR、T波改变纳入多因素logistic回归分析发现,女性和eGFR是ERCP取石术后3 h QTcd增加的危险因素(表4)。

3 讨 论

目前,治疗性ERCP取石术的心肺并发症受到了内镜工作者的高度重视。Andriulli等[4]纳入14项前瞻性研究进行荟萃分析发现,心肺并发症发生率约1%。Christensen等[2]报道,在ERCP取石术相关的死亡患者中,16.7%~50.0%是由心肺并发症引起的,并指出恶性心律失常发生率约为0.2%。尽管ERCP取石术后恶性心律失常发生率较低,但一旦发生,死亡率高,这已成为行ERCP取石术的首要顾虑。

心脏自主神经功能失调在心血管疾病的发生及发展中起着重要作用。其中心脏副交感神经张力降低以及交感神经张力增加是恶性心律失常猝死的重要诱因[5]。既往研究表明治疗性ERCP取石术可致心脏自主神经系统失调。Petelenz等[6]研究发现,在ERCP过程中,对比剂刺激正常直径的胆总管可引起心脏自主神经功能波动。此后,Christensen等[7]证实了ERCP取石术的"去迷走"现象,发现其与心脏自主神经失调有关,并能增加患者发生恶性心律失常的风险。另有大量研究表明QTcd可反映心脏自主神经功能失调。Langen等[8]发现,QTcd改变可能与心脏交感神经分布不均匀有关。Ishida等[9]发现,交感神经张力增加及迷走神经张力降低均能增大健康受试者的QTcd。Perkiomaki等[10]发现,QTcd的增加及心率变异性改变与心室颤动相关,进一步证实了上述观点。

本研究结果显示,ERCP取石术后3 h QTcd较术前及术后24 h增加,提示治疗性ERCP手术后短期(3 h)内心室肌复极差异性增大,恶性心律失常风险增加。治疗性ERCP取石术后出现一过性QTcd增加的原因考虑如下:(1)结石对胆总管的刺激可致患者迷走张力亢进[11];(2)ERCP取石术中"去迷走"现象所致的交感张力亢进;(3)术后解除结石所致的迷走亢进。

表2 2组患者手术资料比较

Table 2 Comparison of operation data between two groups

Item	QTcd increased group ($n=41$)	QTcd reduced group ($n=19$)	t/χ^2	P value
Operation procedure(min, $\bar{x}\pm s$)	50.71±20.72	51.42±28.28	0.110	0.913
Vagal reflex[n(%)]	1(2.44)	0(0.00)	0.735	0.391
Remifentanil (μg, $\bar{x}\pm s$)	203.33±87.28	193.33±78.71	−0.383	0.703
Dexmedetomidine(μg, $\bar{x}\pm s$)	18.17±14.85	19.47±17.10	0.272	0.786
Meperidine[n(%)]	5(12.20)	3(15.79)	0.000	1.000
Stone[n(%)]				
Mud-like stone	8(19.51)	4(21.05)	0.019	0.890
One stone	12(29.27)	7(36.83)	0.344	0.557
Several stones	21(51.22)	8(42.11)	0.432	0.511
Biliary/pancreatic duct stent implantation[n(%)]	4(9.76)	2(10.53)	0.008	0.927
T wave change at 3 h post-ERCP[n(%)]	11(26.83)	2(10.53)	2.245	0.134

QTcd: QT corrected dispersion; Vagal reflex: heart rate and blood pressure drop more than 20% during procedure; ERCP: endoscopic retrograde cholangiopancreatography.

表3 2组患者手术前后血清指标比较

Table 3 Comparison of serum indicators before and after operation between two groups ($\bar{x}\pm s$)

Group	n	Ca^{2+}(mmol/L)		K^{+}(mmol/L)		cTnI(ng/ml)	
		Before operation	After operation	Before operation	After operation	Before operation	After operation
QTcd increased	41	2.22±0.12	2.05±0.19*	3.86±1.40	4.01±0.42	0.006±0.007	0.007±0.008
QTcd reduced	19	2.24±0.27	2.06±0.10*	3.85±0.51	4.04±0.50	0.007±0.006	0.006±0.008

QTcd: QT corrected dispersion; cTnI: cardiac troponin I. Compared with before operation, * $P<0.05$.

表 4 ERCP 术后 3 h QTcd 增加的多因素 logistic 回归分析

Table 4 Multivariate logistic regression analysis of QTcd increase at 3 h post-ERCP

Factor	*Wald*	*P* value	*OR*	95%*CI*
Female	8.609	0.003	15.895	2.505-100.853
eGFR	4.504	0.034	1.039	1.003-1.077

QTcd: QT corrected dispersion; ERCP: endoscopic retrograde cholangiopancreatography; eGFR: estimated glomerular filtration rate.

QTcd 的影响因素较多,主要包括抗心律失常药物应用、心肌缺血及电解质水平改变等[12]。本研究纳入的患者近期均没有服用影响心肌复极的药物,并通过 T 波改变及 cTnI 检测心肌缺血,结果显示,60 例患者 T 波改变的发生率为 21.7%,与既往研究相符[13]。本研究结果显示,2 组患者的 T 波改变发生率及 cTnI 水平间差异均无统计学意义,提示 ERCP 取石术后患者均无明显心肌缺血,考虑 T 波改变与 ERCP 取石术致心脏自主神经失调有关。本研究结果表明,2 组患者术后 3 h 的 Ca^{2+} 较术前均显著降低,差异具有统计学意义($P<0.05$),但比较 2 组间 Ca^{2+} 差异无统计学意义,提示术后 Ca^{2+} 下降与 QTcd 增加无明显关系。考虑术后 Ca^{2+} 降低与术前禁食、术后未及时补充 Ca^{2+} 及手术应激引起 Ca^{2+} 胞内转移有关。

既往研究显示[14],人类心肌电活动存在着明显的性别差异,尤其在长 QT 间期综合征中,女性较男性更易发生恶性心律失常,这可能与性激素参与调节心脏离子通道的表达相关。本研究中发现,女性是 ERCP 取石术后 QTcd 增加的危险因素,与既往研究结果一致。再者,本研究中有 1 例青年女性患者发生了室颤,进一步佐证了上述观点。但考虑样本量较小,偶然性大,需扩大样本量深入研究。

研究表明,肾功能不全并发心律失常常发生于终末期肾功能不全阶段[15]。对于轻中度肾功能不全患者,eGFR 是否为 QTcd 增加的危险因素至今尚不明确。本研究结果显示,eGFR 是术后 QTcd 增加的危险因素,提示有望通过改善肾功能来降低 ERCP 取石术后 QTcd 增加。

总之,本研究初步提示治疗性 ERCP 取石术后短期(3 h)内的恶性心律失常风险可能不降反升。其中,女性和 eGFR 是术后 3 h QTcd 增加的危险因素。

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