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不同消融方式对心房颤动患者凝血参数、心肌损伤以及生活质量的影响*

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摘要 目的:探讨不同消融方式对心房颤动患者凝血参数、心肌损伤以及生活质量的影响。**方法:**回顾性分析 2018 年 1 月至 2019 年 7 月在我院心血管内二科住院拟行消融手术的心房颤动患者 200 例的临床资料, 根据消融方式分为射频消融 (RFCA) 组 (n=99) 和冷冻消融 (CBA) 组 (n=101), 比较两组患者围术期指标、凝血参数、心肌损伤以及生活质量, 记录两组术后并发症发生情况。**结果:**CBA 组手术时间、消融时间短于 RFCA 组, 冷冻最低温度低于 RFCA 组 ($P<0.05$)。两组术后 24 h 活化部分凝血活酶时间 (APTT) 降低, 但 CBA 组高于 RFCA 组 ($P<0.05$), 两组术后 24 h 血管性假血友病因子 (vWF)、D-二聚体 (D-D) 升高, 但 CBA 组低于 RFCA 组 ($P<0.05$)。两组术后 24 h 肌酸激酶 (CK)、肌酸激酶同工酶 (CK-MB)、肌钙蛋白 I (TnI) 较术前升高, 且 CBA 组高于 RFCA 组 ($P<0.05$)。两组术后 3 个月情感职能、躯体疼痛、生理机能、精神健康、活力、生理职能、健康状况、社会功能维度评分较术前升高, 且 CBA 组高于 RFCA 组 ($P<0.05$)。两组并发症发生率对比未见统计学差异 ($P>0.05$)。**结论:**与 RFCA 相比, CBA 治疗心房颤动, 可缩短手术时间、消融时间, 减轻对凝血功能的影响, 提高患者生活质量, 且不增加并发症发生率, 但 CBA 对机体心肌损伤影响更大, 临床应视患者具体情况选择合适的手术方法进行治疗。

关键词:射频消融; 冷冻消融; 心房颤动; 凝血参数; 心肌损伤; 生活质量

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Effects of Different Ablation Methods on Coagulation Parameters, Myocardial Injury and Quality of Life in Patients with Atrial Fibrillation*

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ABSTRACT Objective: To investigate the effects of different ablation methods on coagulation parameters, myocardial injury and quality of life in patients with atrial fibrillation. **Methods:** The clinical data of 200 patients with atrial fibrillation who were hospitalized in Second Department of Internal Medicine-Cardiovascular of our hospital from January 2018 to July 2019 were analyzed retrospectively. According to the ablation methods, they were divided into radiofrequency ablation (RFCA) group (n=99) and cryoablation (CBA) group (n=101). The perioperative indexes, coagulation parameters, myocardial injury and quality of life of the two groups were compared. The postoperative complications of the two groups were recorded. **Results:** The operation time and ablation time of CBA group were shorter than those of RFCA group, and the lowest freezing temperature was lower than that of RFCA group ($P<0.05$). The activated partial thromboplastin time (APTT) decreased at 24 hours after operation in both groups, but CBA group was higher than RFCA group ($P<0.05$). The von Willebrand factor (vWF), D-Dimer (D-D) increased at 24 hours after operation in both groups, but CBA group was lower than RFCA group ($P<0.05$). The creatine kinase (CK), creatine kinase isoenzyme (CK-MB), troponin I (TNI) at 24 hours after operation in both groups were higher than those before operation, and CBA group was higher than RFCA group ($P<0.05$). The scores of emotional function, physical pain, physiological engineering, mental health, vitality, physiological function, health status and social function in both groups were higher than those before operation, and CBA group was higher than RFCA group ($P<0.05$). There was no significant difference in the incidence of complications between the two groups ($P>0.05$). **Conclusion:** Compared with RFCA, CBA is used to treat atrial fibrillation, can shorten the operation time and ablation time, reduce the influence on coagulation parameters, improve the quality of life of patients, and do not increase the incidence of complications, but CBA has a greater impact on the body myocardial injury, so we should choose the appropriate operation method according to the specific situation of patients.

Key words: Radiofrequency ablation; Cryoablation; Atrial fibrillation; Coagulation parameters; Myocardial injury; Quality of life

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前言

心房颤动是临床上常见的心律失常,由于心房节律不规整,引起主观心悸、胸闷等不适感受^[1,2]。药物治疗是以往治疗心房颤动的主要方法,但此类治疗方式无法彻底根治该疾病^[3,4]。射频消融(RFCA)是药物治疗无效的心房颤动的一线治疗方法,其成功率已经得到临床普遍认可^[5,6]。而冷冻消融(CBA)近年来也逐渐受到国内外的广泛关注^[7,8]。现临床有关 RFCA、CBA 在心房颤动中的具体疗效优劣尚存在一定的争议,本研究就此展开分析,探讨上述两种消融方式对心房颤动患者凝血参数、心肌损伤以及生活质量的影响,以期为临床治疗心房颤动提供参考。

1 资料与方法

1.1 临床资料

回顾性分析 2018 年 1 月至 2019 年 7 月在我院心血管内科住院拟行消融手术的心房颤动患者 200 例的临床资料,纳入标准:(1)同步导联心电图或 24 小时动态心电图明确诊断为心房颤动;(2)持续性心房颤动患者病史在 2 年以内;(3)均符合治疗指征,择期行消融手术;(4)抗心律失常药物治疗效果差;(5)消融手术均由同一组医师完成。排除标准:(1)患有精神疾病不能配合;(2)预期寿命短于 1 年;(3)患有心脏瓣膜病、心肌病、心衰等一系列器质性心脏病;(4)患有凝血功能严重异常、肝肾功能衰竭、肿瘤等消耗性疾病;(5)其他原因引起的房颤,如甲亢、酒精或药物中毒等;(6)无法进行随访的患者。上述患者根据消融方式分为 RFCA 组($n=99$)和 CBA 组($n=101$),其中 RFCA 组男 52 例,女 47 例,年龄 40~73 岁,平均(57.52 ± 4.38)岁;病程 3~16 月,平均(9.46 ± 2.15)月;体质量指数 $20 \sim 27 \text{ kg/m}^2$,平均(23.58 ± 0.96) kg/m^2 。CBA 组男 55 例,女 46 例,年龄 38~75 岁,平均(56.97 ± 3.98)岁;病程 4~18 月,平均(9.81 ± 1.67)月;体质量指数 $21 \sim 27 \text{ kg/m}^2$,平均(23.72 ± 0.88) kg/m^2 。两组一般资料对比无差异($P>0.05$)。

1.2 方法

(1)RFCA 组:给予 RFCA 治疗,患者取平卧位,常规消毒、铺巾,局麻,于右、左股静脉分别置入 8F 和 6F 鞘管,并将可调弯冠状窦电极送入至冠状窦远端。穿刺房间隔成功后,采用导管(8.5F SL 1)进行左、右肺静脉造影。Lasso 导管于 CARTO3 引导下左房建壳及电压标测。桔把或蓝把 ST 消融导管(强生公司)行双肺静脉隔离,盐水功率模式 43°C 、30-35 W。Lasso

导管验证双肺静脉均隔离成功。术后拔除鞘管,纱布包扎。(2)CBA 组:给予 CBA 治疗,患者取平卧位,常规消毒、铺巾,局麻,于左、右股静脉置入鞘管,并将电极送入至冠状窦远端。穿刺房间隔成功后,采用导管(8.5F SL 1)进行左、右肺静脉造影。采用美敦力公司生产的 28 mm 的二代冷冻球囊(温度 $-55^\circ\text{C} \sim -40^\circ\text{C}$)依次对左上、左下、右下、右上等肺静脉进行 CBA。Achieve 电极验证双侧肺静脉均隔离成功。消融右侧肺静脉时监测膈肌运动,如膈肌运动减弱或消失立即停止消融。术中给予芬太尼止痛、咪达唑仑镇痛,维生素 B6 止吐。术后拔出静脉鞘管,纱布包扎。(3)围术期处理:术前口服华法林或新型抗凝药,手术当天停用药物。房间隔穿刺成功后即刻予以肝素,按照 100 U/Kg 体重计算,术中监测 ACT,维持在 250-300 s。术后心电图监测至少 24 小时。术后 6 小时给予达比加群酯[正大天晴药业集团股份有限公司,国药准字 H20203097,规格:75 mg(以达比加群酯计)]110 mg/次,2 次/d 抗凝。术后加用胺碘酮片(江西制药有限责任公司,国药准字 H36020916,规格:0.2 g),200 mg/次,3 次/d,维持口服 3 个月。

1.3 观察指标

(1)记录两组围术期指标情况:消融时间、手术时间、冷冻最低温度。(2)记录术后并发症发生情况。(3)术后对患者进行为期 3 个月的随访,随访方式为门诊复查。于术前、术后 3 个月采用 36 条简明健康状况调查表(SF-36)^[9]评价患者生活质量,其中 SF-36 包括情感职能、躯体疼痛、生理机能、精神健康、活力、生理职能、健康状况、社会功能这 8 个维度,每个维度均为 100 分,分数越高,生活质量越好。(4)抽取两组患者术前、术后 24 h 空腹静脉血 3 mL,采用 ACL3000 血凝仪(美国贝克曼-库尔特公司生产)进行活化部分凝血活酶时间(APTT)、血管性假血友病因子(vWF)、D-二聚体(D-D)水平的检测。采美国雅培公司生产的 i2000 发光免疫分析仪和原装试剂盒检测肌酸激酶(CK)、肌酸激酶同工酶(CK-MB)、肌钙蛋白 I (TnI)水平。

1.4 统计学方法

研究数据采用 SPSS25.0 进行统计分析。观测数据中的计量资料用均数 $\pm$ 标准差($\bar{x} \pm s$)描述,行 t 检验。计数资料采用率(%)描述,采用 χ^2 检验。检验标准设置为 $\alpha=0.05$ 。

2 结果

2.1 两组围术期指标比较

CBA 组手术时间、消融时间短于 RFCA 组,冷冻最低温度低于 RFCA 组($P<0.05$),详见表 1。

表 1 两组围术期指标比较($\bar{x} \pm s$)

Table 1 Comparison of perioperative indexes between the two groups($\bar{x} \pm s$)

Groups	Operation time(min)	Ablation time(min)	Lowest freezing temperature($^\circ\text{C}$)
RFCA group($n=99$)	16.76 ± 1.63	11.97 ± 1.26	-44.15 ± 5.21
CBA group($n=101$)	13.03 ± 1.02	8.06 ± 1.13	-48.86 ± 6.24
t	19.440	13.114	5.789
P	0.000	0.000	0.000

2.2 两组凝血参数指标比较

两组术前 APTT、vWF、D-D 比较差异无统计学意义($P>0.05$)。

两组术后 24 h APTT 降低,但 CBA 组高于 RFCA 组($P<0.05$),两组术后 24 h vWF、D-D 升高,但 CBA 组低于 RFCA 组($P<0.05$)。

05), 详见表 2。

2.3 两组心肌损伤指标比较

两组术前 CK、CK-MB、TnI 比较差异无统计学意义 ($P>0.05$)。

05)。两组术后 24 h CK、CK-MB、TnI 较术前升高, 且 CBA 组高于 RFCA 组 ($P<0.05$), 详见表 3。

表 2 两组凝血参数指标比较($\bar{x} \pm s$)

Table 2 Comparison of coagulation parameters between the two groups($\bar{x} \pm s$)

Groups	APTT(s)		vWF(%)		D-D(mg/L)	
	Before operation	24 hours after operation	Before operation	24 hours after operation	Before operation	24 hours after operation
RFCA group(n=99)	28.44± 3.02	22.31± 3.35*	132.24± 14.21	169.23± 17.19*	0.14± 0.04	0.32± 0.08*
CBA group(n=101)	28.63± 4.19	25.05± 3.13*	131.01± 12.74	146.99± 15.23*	0.15± 0.07	0.24± 0.07*
t	0.367	5.978	0.645	9.689	1.237	7.530
P	0.714	0.000	0.520	0.000	0.218	0.000

Note: compared with before operation, * $P<0.05$.

表 3 两组心肌损伤指标比较($\bar{x} \pm s$)

Table 3 Comparison of myocardial injury indexes between the two groups($\bar{x} \pm s$)

Groups	CK(U/L)		CK-MB(U/L)		TnI(μ g/L)	
	Before operation	24 hours after operation	Before operation	24 hours after operation	Before operation	24 hours after operation
RFCA group(n=99)	93.75± 12.04	122.86± 15.52*	14.83± 3.46	18.81± 3.59*	0.04± 0.01	1.12± 0.18*
CBA group(n=101)	92.48± 13.57	158.74± 14.75*	14.26± 4.65	23.75± 2.62*	0.04± 0.01	2.23± 0.21*
t	0.700	16.761	0.982	11.132	0.000	38.462
P	0.485	0.000	0.367	0.000	1.000	0.000

Note: compared with before operation, * $P<0.05$.

2.4 两组生活质量比较

两组术前情感职能、躯体疼痛、生理机能、精神健康、活力、生理职能、健康状况、社会功能比较差异无统计学意义 ($P>0.05$)。

两组术后 3 个月情感职能、躯体疼痛、生理机能、精神健康、活力、生理职能、健康状况、社会功能维度评分较术前升高, 且 CBA 组高于 RFCA 组 ($P<0.05$), 详见表 4。

表 4 两组生活质量比较($\bar{x} \pm s$, 分)

Table 4 Comparison of quality of life between the two groups($\bar{x} \pm s$, scores)

Groups	Time	Emotional function	Health status	Social function	Physiological function	Vitality	Mental health	Physiological enginery	Physical pain
RFCA group(n=99)	Before operation	48.26± 7.11	51.74± 6.82	51.76± 7.61	53.92± 7.98	49.15± 6.12	49.67± 5.18	52.38± 7.06	49.74± 6.82
	3 months after operation	69.94± 7.92*	72.76± 7.73*	73.43± 7.66*	69.08± 7.48*	68.24± 7.48*	66.81± 7.23*	73.75± 6.72*	74.63± 6.79*
CBA group(n=101)	Before operation	47.96± 6.24	51.39± 8.27	51.12± 6.23	54.18± 6.31	49.97± 7.64	50.21± 6.76	52.87± 7.73	49.19± 6.26
	3 months after operation	82.03± 7.29*#	81.85± 6.33*#	83.79± 8.29*#	82.62± 7.27*#	82.04± 7.36*#	81.45± 6.52*#	84.73± 6.64*#	83.26± 7.41*#

Note: compared with before operation, * $P<0.05$; compared with RFCA group, # $P<0.05$.

2.5 并发症发生率比较

两组并发症发生率对比未见统计学差异 ($P>0.05$), 详见表 5。

3 讨论

据以往报道统计^[10], 心房颤动在人群中的总体发病率约为 0.4%~1.0%, 且随着年龄的增长而上升, 随着我国人口老龄化进程的加快, 心房颤动已成为严重的公共卫生安全问题之一^[11]。

由于各种抗心律失常的药物治疗效果欠佳, 经导管消融治疗已被推荐为治疗心房颤动的主要方式之一^[12]。RFCA 作为治疗心房颤动的主要介入术, 利用导管头端电极对患者心肌病灶局部产生热效应, 当心肌局部上升到一定的温度后, 可导致该处心肌细胞脱水并且坏死, 达到阻止疾病进展的目的^[13-15]。但其也存在一定的弊端, 由于病人对疼痛的耐受性不同, 导致消融线不彻底, 易产生肺静脉隔离的漏点, 增加微折返性房性心律失常

的发生风险;同时 RFCA 操作难度高、手术人员培训时间较长,临床广泛应用受限^[16,17]。CBA 作为一种替代 RFCA 治疗心房颤动的新型术式,主要利用迅速降温方式使局部心肌细胞发生病理改变,导致组织产生不可逆损伤,阻止异常信号的传递,从

而发挥治疗作用^[18-20]。该介入术操作技术难度较低,国外临床经验已较为成熟,但国内相关临床应用效果仍需进一步的研究以明确。

表 5 两组并发症发生率比较 [例(%)]

Table 5 Comparison of the incidence of complications between the two groups [n(%)]

Groups	Phrenic nerve paralysis	Pericardial effusion	Left atrial esophageal fistula	Cerebrovascular accident	Pulmonary vein stenosis	Total incidence rate
RFCA group(n=99)	2(2.02)	3(3.03)	2(2.02)	1(1.01)	1(1.01)	9(9.09)
CBA group(n=101)	2(1.98)	1(0.99)	1(0.99)	2(1.98)	1(0.99)	7(6.93)
χ^2						0.317
<i>P</i>						0.573

本次研究结果显示,CBA 组手术时间、消融时间短于 RFCA 组,冷冻最低温度低于 RFCA 组,主要是因为 CBA 操作难度较低,手术时间相对缩短,且冷冻最低温度更低,可有效缩短消融时间^[21]。本研究结果显示,两组介入术均对机体凝血参数有一定影响,但 CBA 的影响效果明显更轻。APTT 为内源性凝血系统相对敏感指标,其水平下降一般见于血高凝状态^[22]。D-D 为纤维蛋白单体,其水平升高可引起体内高凝状态或者继发性纤溶亢进现象^[23]。vWF 可促进血小板黏附并且活化,导致凝血酶的生成,最终引起血栓^[24]。RFCA 治疗具有边界不清特点,成锯齿状,可对机体内皮细胞造成损伤,导致抗凝作用减弱,最终导致血栓形成^[25]。应用 CBA 治疗,该术式的损伤边界清晰,对内皮下组织以及细胞外结构可发挥一定的保护作用,减小血栓风险^[26]。同时,进行 CBA 时,导管头端附近可将血液冻结为血液球,发挥保护血细胞的效果^[27]。心肌损伤是 RFCA、CBA 治疗期间均不可避免的损害,以往有研究提示两者对心肌细胞的损伤程度相似^[28]。但也有报道显示 CBA 对机体心肌细胞的损伤程度更为严重^[29]。本次研究结果中,与 RFCA 相比,CBA 对机体心肌损伤影响更大。CK、CK-MB、TnI 均是临床常见的心肌指标,可有效反映心肌损伤严重程度。可能是因为进行 CBA 可导致心肌即刻坏死,而 RFCA 升高温度需一定的时间,心肌坏死发展相对缓慢^[30]。另两组并发症发生率对比未见明显差异,可见两种术式治疗均安全可靠。同时本研究随访 3 个月结果发现,CBA 治疗者的生活质量改善情况优于 RFCA 治疗者,CBA 治疗者即使受到的心肌损伤更为严重,但属于一过性伤害,CBA 治疗者的其他机能受到的影响相对较轻,利于患者术后恢复,使患者尽早回归正常的工作生活中,有效提高其生活质量。

综上所述,与 RFCA 相比,CBA 治疗心房颤动,可缩短手术时间、消融时间,减轻对凝血参数的影响,提高患者生活质量,且不增加并发症发生率,但 CBA 对机体心肌损伤影响更大,临床应视患者具体情况选择合适的手术方法进行治疗。

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