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心肺康复训练对脑卒中患者的康复效果及对血清 BDNF、NT-3、MMP-9 及心肺功能的影响 *

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摘要 目的：探讨心肺康复训练对脑卒中患者的康复效果及对血清脑源性神经生长因子（BDNF）、神经营养因子 -3（NT-3）、基质金属蛋白酶 -9（MMP-9）及心肺功能的影响。**方法：**选择 2020 年 01 月 -2021 年 01 月在我院接受治疗的 129 例脑卒中患者，采用抽签法分为试验组（n=65）和对照组（n=64）。对照组给予常规康复治疗，试验组给予心肺康复训练治疗。比较两组患者的临床疗效、血清 BDNF、NT-3、MMP-9、左心室射血分数（LVEF）、左心室收缩末期内径（LVESD）、最大心率、静息心率、峰值摄氧量（VO_{2peak}）、无氧阈（AT）、峰值能量代谢当量（MET_{peak}）、每分峰值通气量（VE_{peak}）及 Fugl-Meyer 评定量表（FMA）、改良 Barthel 指数（MBI）评分变化情况。**结果：**治疗后，两组总有效率比较差异显著（$P<0.05$）；治疗前，试验组和对照组血清 BDNF、NT-3、MMP-9 比较无显著差异；治疗后，试验组和对照组血清 BDNF 随着时间的推移而升高，且试验组均高于对照组，NT-3、MMP-9 随着时间的推移而降低，且试验组均低于对照组，差异显著（$P<0.05$）；治疗前，试验组和对照组 LVEF、LVESD、最大心率及静息心率比较无显著差异；治疗后，试验组和对照组 LVEF、最大心率随着时间的推移而升高，且试验组均高于对照组，LVESD、静息心率随着时间的推移而降低，且试验组均低于对照组，差异显著（$P<0.05$）；治疗前，试验组和对照组 VO_{2peak}、AT、MET_{peak} 及 VE_{peak} 比较无显著差异；治疗后，试验组和对照组 VO_{2peak}、AT、MET_{peak} 及 VE_{peak} 随着时间的推移而升高，且试验组均高于对照组，差异显著（$P<0.05$）；治疗前，试验组和对照组 FMA、MBI 评分比较无显著差异；治疗后，试验组和对照组 FMA、MBI 评分随着时间的推移而升高，且试验组均高于对照组，差异显著（$P<0.05$）。**结论：**在脑卒中患者中应用心肺康复训练临床效果更好，可有改善患者血清 BDNF、NT-3、MMP-9 及心肺功能。

关键词：心肺康复训练；脑卒中；康复效果；脑源性神经生长因子；神经营养因子 -3；基质金属蛋白酶 -9；心肺功能

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Effect of Cardiopulmonary Rehabilitation Training on Cerebral Apoplexy Patients and Its Effect on Serum BDNF, NT-3, MMP-9 and Cardiopulmonary Function*

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ABSTRACT Objective: Effect of cardiopulmonary rehabilitation training on cerebral apoplexy patients and its effect on serum Brain-derived nerve growth factor (BDNF), neurotrophic factor-3 (NT-3), matrix metalloproteinase-9 (MMP-9) and cardiopulmonary function. **Methods:** 129 stroke patients treated in our hospital from January 2020 to January 2021 were selected and divided into experimental group (n=65) and control group (n=64) by drawing lots. The control group was given routine rehabilitation treatment, and the experimental group was given cardiopulmonary rehabilitation training treatment. Clinical efficacy, serum BDNF, NT-3, MMP-9, left ventricular ejection fraction (LVEF), left ventricular end-systolic diameter (LVESD), maximum heart rate, resting heart rate, peak oxygen uptake (VO_{2Peak}), anaerobic threshold (AT), peak energy metabolic equivalent (MET) were compared between 2 groups Peak), Ve_{Peak}, Fugl-Meyer Rating Scale (FMA) and Modified Barthel Index (MBI) scores. **Results:** After treatment, the total effective rate between the two groups was significantly different ($P<0.05$). Before treatment, there were no significant differences in serum BDNF, NT-3 and MMP-9 between the experimental group and the control group. After treatment, serum BDNF in experimental groups and control group increased with time, and NT-3 and MMP-9 decreased with time, and the difference was significant ($P<0.05$). Before treatment, there were no significant differences in LVEF, LVESD, maximum heart rate and resting heart rate between the experimental group and the control group. After treatment, LVEF and maximum heart rate in experimental and control groups increased over time, and those in experimental groups were higher than those in control group, while LVESD and resting heart rate decreased over time, and those in experimental

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groups were lower than those in control group, with significant differences (P<0.05). Before treatment, there were no significant differences in VO_{2peak}, AT, Met peak and VE_{peak} between the experimental group and the control group. After treatment, VO_{2peak}, AT, Met_{peak} and VE_{peak} in experimental group and control group increased with time, and the difference was significant (P<0.05). Before treatment, there were no significant differences in FMA and MBI scores between the experimental group and the control group. After treatment, the scores of FMA and MBI in experimental group and control group increased with the passage of time, and those in experimental group were higher than those in control group, with significant differences (P<0.05). **Conclusion:** The clinical effect of cardiopulmonary rehabilitation training is better in patients with cerebral apoplexy, which can improve the patients' serum BDNF, NT-3, MMP-9 and cardiopulmonary function.

Key words: Cardiopulmonary rehabilitation training; Stroke; Rehabilitation effect; Brain-derived nerve growth factor; Neurotrophic factor-3; Matrix metalloproteinase-9; Cardiopulmonary function

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前言

脑卒中是神经内科常见疾病,发病率较高,据数据统计,全球每年约 1500 万人患脑卒中,其中我国约为 150~200 万人,其中大约 1/3 患者遗留功能障碍,影响患者的日常生活[1]。脑卒中后可引起诸多功能障碍,常见的有偏瘫、认知障碍等,其中偏瘫最为常见,引起活动受限,导致有氧代谢能力下降,心肺适能减弱,增加再发心脑血管等意外,因此对脑卒中患者给予有效地康复训练可改善患者生活质量[2-4]。心肺康复训练可通过有计划的康复方案，提高脑卒中患者心肺功能，提高运动耐力[5]。BDNF 是神经营养因子家族的成员,在脑缺血过程中具有保护神经元及促进神经修复的作用;NT-3 是一类重要的生长因子,有助于刺激和控制神经的发生，在脑卒中等疾病中变化异常;MMP-9 属于基质金属蛋白酶家族，能降解和重塑细胞外基质的动态平衡,能分解呼吸道和肺内的结构复合物[6-8]。有研究显示,血清 BDNF、NT-3、MMP-9 参与了脑卒中的发展,可作为诊治疾病的重要指标[9]。本研旨在探讨心肺康复训练对脑卒中患者的康复效果，并分析其对血清 BDNF、NT-3、MMP-9 及心肺功能的影响。

1 资料与方法

1.1 一般资料

选择 2020 年 01 月 -2021 年 01 月在我院接受治疗的 129 例脑卒中患者。采用抽签法分为 2 组,试验组 65 例:男 45 例,女 20 例,年龄 41~72 岁,平均(61.51±3.47)岁,病程 1~9 月,平均(4.41±1.15)月,其中脑干 23 例,基底节 22 例,大脑半球 20 例;对照组男 48 例,女 16 例,年龄 43~73 岁,平均(61.67±3.58)岁,病程 1~10 月,平均(4.47±1.11)月,其中脑干 20 例,基底节 25 例,大脑半球 19 例。两组基线资料无显著差异(P>0.05),存在可比性。

参照《中国急性缺血性脑卒中诊治指南》[10],(1)经影像检查确诊;(2)情绪低落、精力、精神均减退、思考能力下降,睡眠障碍,食欲、性欲减退,具有其中四项即可确诊纳入标准:(1)符合上述诊断标准;(2)继发卒中后;(3)近期未进行抗抑郁治疗;(4)具有沟通能力;(5)患者可耐受心肺运动试验,可进行踏车运动;(6)签署知情同意书。排除标准:(1)合并严重脏器疾病;(2)呼吸、血液感染疾病者;(3)卒中疾病期间者;(4)失语、精神异常者;(5)拒绝治疗,严重自杀倾向者;(6)中途退出者。

1.2 方法

对照组给予常规康复:肢体良肢位摆放、关节松动训练、偏瘫肢体综合训练、平衡功能训练、日常生活活动训练及理疗等,训练强度依据患者个体状况而调整。试验组在常规康复的基础上给予心肺康复训练:患者坐位,口唇紧闭,鼻子吸气至最大极限后,将口唇缩拢如吹口哨状呼气;卧位,上腹部放置沙袋(患者可承受),鼻持续缓慢吸气上腹部达最大隆起 ,缩唇缓慢呼气,使腹部下陷并收缩腹肌;有氧运动:充分热身后按不同患者测试所得无氧阈所对应的运动负荷进行运动康复训练 20-30 min,训练结束后继续 5 min 缓慢踏车;运动方式:踩功率自行车。

1.3 观察指标

采集空腹静脉血 5 mL，以 3000 r·min^{-1} 的速度进行离心，时间 10 min,提取上层血清后,采用双抗体夹心酶联免疫吸附法测定 BDNF、NT-3、MMP-9 水平；使用下肢功率车行心肺运动试验(CPET)结果,包括 VO_{2peak}、AT、MET peak 及 VE_{peak}。常规脉搏血氧仪监测心率。

疗效评定标准：显效:NIHSS 评分降低 90~100%；有效：NIHSS 评分降低 45%~89%;无效:临床症状无明显改善甚至加重。

1.4 统计学分析

以 spss18.0 软件包处理，符合正态分布计量资料用均数±标准差($\bar{x}\pm s$) 表示,组间比较使用独立样本 t 检验,计数资料以率表示,χ^2 检验，P＜0.05 表示差异具有统计学意义。

2 结果

2.1 两组治疗效果评价

治疗后,两组总有效率比较差异显著(P<0.05)见表 1。

2.2 两组血清 BDNF、NT-3、MMP-9 检查结果比较

治疗前，试验组和对照组血清 BDNF、NT-3、MMP-9 比较无显著差异;治疗后,试验组和对照组血清 BDNF 随着时间的推移而升高，且试验组均高于对照组,NT-3、MMP-9 随着时间的推移而降低,且试验组均低于对照组,差异显著(P<0.05),见表 2。

2.3 两组心功能检查结果比较

治疗前,试验组和对照组 LVEF、LVESD、最大心率及静息

心率比较无显著差异；治疗后，试验组和对照组 LVEF、最大心率随着时间的推移而升高，且试验组均高于对照组，LVESD、静息心率随着时间的推移而降低，且试验组均低于对照组，差异显著（P<0.05），见表 3。

表 1 两组治疗效果评价[n(%)]

Table 1 Treatment effect evaluation of the two groups[n(%)]

Groups	n	Excellent	valid	Invalid	Total effective rate
Experimental group	65	39(60.00)	21(32.31)	5(7.69)	60(92.31)
Control group	64	28(43.75)	16(25.00)	20(31.25)	44(68.75)
χ^2 value			11.455		
P value			0.000		

表 2 两组血清 BDNF、NT-3、MMP-9 检查结果比较($\bar{x}\pm s$)

Table 2 Comparison of serum BDNF, NT-3 and MMP-9 test results between the two groups($\bar{x}\pm s$)

Groups	n	BDNF(ng/mL)		NT-3(ng/L)		MMP-9(μg/L)	
		Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	65	24.45±2.14	35.06±3.14	227.56±40.14	131.05±22.14	262.15±31.17	141.25±14.23
Control group	64	24.51±2.32	30.11±2.75	228.01±39.89	175.46±30.59	261.09±32.05	220.16±35.16
t value		0.153	9.519	0.064	9.457	0.190	16.755
P value		0.879	0.000	0.949	0.000	0.849	0.000

表 3 两组心功能检查结果比较($\bar{x}\pm s$)

Table 3 Comparison of cardiac function examination results between the two groups($\bar{x}\pm s$)

Groups	n	LVEF(%)		LVESD(mm)		Maximum heart rate (next /min)		Resting heart rate(next /min)	
		Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	65	46.13±7.87	58.11±4.78	53.61±2.48	50.10±0.91	125.41±15.61	144.16±17.87	92.62±12.48	82.14±11.78
Control group	64	46.09±7.81	49.68±6.35	53.58±2.53	52.46±0.59	126.08±15.58	134.18±16.51	92.57±12.51	88.59±12.23
t value		0.029	8.527	0.068	17.448	0.244	3.293	0.023	3.051
P value		0.977	0.000	0.946	0.000	0.808	0.001	0.982	0.003

2.4 两组心肺功能检查结果比较

治疗前，试验组和对照组 VO_{2peak}、AT、MET_{peak} 及 VE_{peak} 比较无显著差异；治疗后，试验组和对照组 VO_{2peak}、AT、MET_{peak} 及 VE_{peak} 随着时间的推移而升高，且试验组均高于对照组，差异显著（P<0.05），见表 4。

表 4 两组心肺功能检查结果比较($\bar{x}\pm s$，mL/kg/min)

Table 4 Comparison of pulmonary function test results between the two groups($\bar{x}\pm s$, mL/kg/min)

Groups	n	VO_{2peak}		AT		MET_{peak}		VE_{peak}	
		Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	65	13.10±1.79	16.79±1.28	11.58±2.14	14.79±1.78	4.07±1.01	5.13±0.81	33.61±7.54	41.79±6.78
Control group	64	13.08±1.47	14.12±1.08	11.63±2.18	13.08±1.82	4.09±1.05	4.28±0.83	33.28±7.63	36.58±7.48
t value		0.069	12.795	0.131	5.395	0.110	5.887	0.247	4.146
P value		0.945	0.000	0.896	0.000	0.912	0.000	0.805	0.000

2.5 两组 FMA、MBI 评分比较

治疗前，试验组和对照组 FMA、MBI 评分比较无显著差异；治疗后，试验组和对照组 FMA、MBI 评分随着时间的推移而升高，且试验组均高于对照组，差异显著（$P<0.05$），见表 5。

表 5 两组 FMA、MBI 评分比较（$\bar{x}\pm s$，points）

Table 5 Comparison of FMA and MBI scores between the two groups（$\bar{x}\pm s$, points）

Groups	n	FMA		MBI	
		Before the intervention	After the intervention	Before the intervention	After the intervention
Experimental group	65	40.51±11.71	69.78±20.13	44.34±17.78	75.14±15.18
Control group	64	41.16±11.68	55.14±13.20	44.61±18.19	65.28±22.10
t value		0.316	16.109	0.085	2.958
P value		0.753	0.000	0.932	0.004

3 讨论

脑卒中是由脑血管疾病引起的综合征，是我国主要致命性疾病之一，多数发生于 40 岁以上中老年人群，主要是由于脑细胞缺血缺氧等导致患者出现认知、情绪等障碍，部分患者还可出现不同程度神经功能障碍，导致患者不能自理，对患者心理造成压力[11]。有研究显示，脑卒中后偏瘫是脑卒中后最常见的并发症，可导致患者出现运动障碍，同时还会导致其呼吸肌无力伴有胸廓扩张受限，影响患者心肺功能，严重者甚至会出现肺部感染，再发心脑血管意外等，严重影响患者预后[12]。有研究显示，尽早给予脑卒中患者康复训练可促进脑部功能的恢复，加速脑部微循环，挖掘相关脑组织和器官的潜能，帮助患者恢复基本的运动功能，改善患者生活质量[13,14]。

临床通常使用常规康复对脑卒中患者进行康复，常规康复训练包括步态训练、日常生活能力训练等，可有效改善部分患者肢体功能，但其整体效果一般[15]。心肺康复训练是常见的一种康复治疗方法，可通过系统的康复训练，改善心功能，降低运动时的心肌耗氧量，增强运动耐力，有利于改善心肺功能[16-18]。有研究显示，心肺康复训练可提高患者呼吸肌收缩和舒张功能，降低呼吸肌疲劳，增加患者肺泡通气量，加速残气量排出，改善低氧血症，增强机体免疫力，提高患者生活质量[19,20]。本研究观察不同康复训练在脑卒中重的康复效果，结果显示，给予心肺康复训练的患者总有效率高于使用常规康复训练者，结果提示，心肺康复训练可提高脑卒中患者的康复效果，与 Hughes C [21]等研究结果相似。

有研究显示，脑卒中的发生可导致体内大量神经细胞坏死，削减神经细胞的保护作用，与疾病的发生关系密切[22]。神经细胞因子是体内重要的神经营养蛋白，能保护神经元，增强神经递质合成[23]。血清 BDNF 是神经营养因子家族的一员，被广泛分布在中枢神经系统、周围神经系统等区域内，可以对抗脑缺血性损伤，修复受损后的神经元，维持神经系统功能，有助于神经元的生长和分化[24,25]。有研究显示，血清 BDNF 在脑卒中患者中表达异常，且与神经功能受损程度呈负相关[26]。NT-3 是神经营养因子中的一个重要分类，由机体中枢神经分泌而成，有助于刺激和控制神经的发生，同时还可促进神经元存活生长，保护脑部海马神经元，刺激神经突出形成[27,28]。有研究显示，NT-3 可导致皮肤触觉及压力觉缺失，在脑卒中后神经功能缺损中表达异常[29]。MMP-9 是锌离子依赖的基质金属蛋白酶家族中的一员，可通过破坏神经血管基质加重周围细胞水肿和出血，损伤神经元，破坏血脑屏障，同时还具有导致血管重构及调节血管内蛋白含量的作用，在血管疾病的发生发展中发挥重要作用 [30-32]。较多研究显示，当发生缺血性脑卒中时患者血清 BDNF、NT-3、MMP-9 异常表达，可能参与了疾病的发生，可作为诊治疾病的重要指标 [33,34]。本研究将血清 BDNF、NT-3、MMP-9 作为参与脑卒中的重要指标，观察在不同康复训练中起水平变化，结果显示，治疗后患者血清 BDNF 水平明显升高，且给予心肺康复训练的患者高于使用常规康复训练者，NT-3、MMP-9 明显降低，给予心肺康复训练的患者低于对照组，结果提示，心肺康复训练可改善脑卒中患者血清 BDNF、NT-3、MMP-9 水平。分析其原因可能是因为当发生脑卒中时患者神经细胞因子发生异常变化，导致血清 BDNF、NT-3、MMP-9 发生变化，而给予患者心肺康复训练能够促进葡萄糖代谢，使心脏自主神经调节能力储备增大，促进神经功能的恢复，从而改善血清 BDNF、NT-3、MMP-9。本研究结果还显示，治疗后患者 LVEF、最大心率、VO_{2peak}、AT、MET_{peak} 及 VE_{peak} 明显升高，且给予心肺康复训练的患者高于对照组，LVESD、静息心率明显降低，且给予心肺康复训练的患者低于对照组，进一步提示了心肺康复训练可通过改善患者心肺功能促进患者恢复。Hsu C W [35]等研究也显示，给予脑卒中患者有氧运动可达到提高机体心肺耐力 - 机体体能的作用，从而提高患者心肺功能，与本研究结果相似。分析其原因可能是因为在心肺康复训练过程中，可通过指导患者缩唇呼吸、腹式呼吸、扩胸等使患者掌握基本的心肺康复训练，促进心肺肌肉组织的活动，有利于提高患者呼吸功能，提高患者最大吸氧量，从而改善患者心肺功能。本研究结果还显示，治疗后患者 FMA、MBI 评分升高，且给予心肺康复训练的患者高于对照组，提示，心肺康复训练可提高脑卒中患者运动功能。分析其原因可能是因为心肺康复训练可通过提高躯干的力量，改善机体运动控制能力，从而提高运动功能。

综上所述，在脑卒中患者中应用心肺康复训练临床效果更好，可有改善患者血清 BDNF、NT-3、MMP-9 及心肺功能。

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