

· 基础研究 ·

低强度游泳运动对自发性高血压大鼠左心室重构的影响

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【摘要】目的 观察运动训练对自发性高血压大鼠(SHR)左心室重构的影响。**方法** 将 20 只 8 周龄雄性 SHR 按随机数字表法分为高血压对照组和高血压运动组,每组 10 只;另选取 8 周龄健康雄性 Wistar 大鼠 10 只作为正常对照组。高血压运动组大鼠进行为期 12 周低强度的无负重游泳运动,每周 6 次、每次 60 min;高血压对照组和正常对照组大鼠仅常规饲养,不进行任何训练。3 组大鼠每周测量 1 次血压,运动 12 周后 ELISA 检测血清中去甲肾上腺素(NE)和血管紧张素 II (ANG II)水平。组织学检测左心室心肌形态学的变化及心肌细胞直径,天狼星红染色检测左心室胶原沉积,半定量逆转录-聚合酶链反应(RT-PCR)和免疫印迹检测重塑的左心室心肌组织中肿瘤坏死因子- α (TNF- α),白介素-6(IL-6),白介素-1 β (IL-1 β)和转化生长因子 β 1(TGF- β 1)的表达。**结果** 入组 12 周后,高血压运动组的收缩压和舒张压分别为(150.6 $\pm$ 6.7) mmHg 和(91.6 $\pm$ 7.1) mmHg,与组内入组后当天和高血压对照组入组 12 周后比较,均显著下降($P < 0.05$),但与正常对照组比较,差异仍有统计学意义($P < 0.05$)。入组 12 周后,高血压运动组的 LVW/BW、NE 和 ANG II 水平显著低于高血压对照组大鼠($P < 0.05$),但仍显著高于正常对照组大鼠($P < 0.05$);高血压运动组和高血压对照组大鼠的左心室心肌细胞直径均显著大于正常对照组($P < 0.05$),而高血压对照组的左心室心肌细胞直径亦大于高血压运动组($P < 0.05$);高血压运动组和高血压对照组大鼠的胶原容积分数(CVF)值均显著高于正常对照组($P < 0.05$),而高血压对照组的 CVF 值亦显著高于高血压运动组($P < 0.05$)。入组 12 周后,高血压运动组和高血压对照组重塑的左心室心肌中 TNF- α 、IL-6、IL-1 β 和 TGF- β 1 的 mRNA 及蛋白的表达均显著高于正常对照组($P < 0.05$);高血压运动组重塑的左心室心肌中 TNF- α 、IL-6、IL-1 β 和 TGF- β 1 的 mRNA 及蛋白的表达均显著低于高血压对照组($P < 0.05$)。**结论** 游泳运动可显著降低 SHR 的血压水平,改善 SHR 大鼠的左心室重构,其改善左心室重构的机制不仅与降低交感神经与肾素-血管紧张素系统的活性有关,还与降低细胞因子 TNF- α 、IL-6、IL-1 β 和 TGF- β 1 的表达有关。

【关键词】 运动; 高血压; 心室重构; 大鼠

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【Abstract】 Objective To investigate the effects of swimming exercise training on left ventricular (LV) remodeling and its possible mechanism in spontaneous hypertensive rats (SHR). **Methods** Twenty eight-week-old male SHRs were divided into SHR control (SC) group and SHR exercise training (ST) group, with 10 rats in each group. Ten eight-week-old male Wistar rats were used as normal control (WC) group. The ST group was subject to 60-min moderate swimming exercise without loading once daily, 6 times a week, for a total of 12 weeks; while the SC and WC group had no special intervention. The blood pressure was examined once weekly. After 12 weeks, the norepinephrine (NE) and serum angiotonin II (ANG II) levels were determined by ELISA. The LV hypertrophy was assessed by analysing the ratio of LV weights to body weights (LVW/BW) and cardiomyocyte diameter. The collagen deposited in LV was detected by sirius red staining. The expressions of tumor necrosis factor- α (TNF- α), interleukin-6 (IL-6), interleukin-1 β (IL-1 β) and transforming growth factor- β 1 (TGF- β 1) in LV were determined by semi-quantitative real time-polymerase chain reaction (RT-PCR) and Western blotting. **Results** After 12 weeks, the blood pressure, serum NE and ANG II levels, LVW/BW ratio, cardiomyocyte diameter and collagen volume fraction (CVF) increased significantly in SC group compared

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with WC group; while those in ST group decreased significantly. In addition, in ST group the mRNA and protein expressions of TNF- α , IL-6, IL-1 β and TGF- β 1 also decreased significantly. **Conclusions** The swimming exercise could reduce the blood pressure of SHR and improve LV remodeling. This effect was mediated not only by improving the hemodynamics, but also by decreasing sympathetic nerve and renin-angiotensin system (RAS) activities, decreasing the gene expressions of cytokines. The swimming exercise may be an effective strategy for improving LV remodeling in hypertension.

【Key words】 Exercise; Hypertension; Ventricular remodeling; Rat

高血压病常引起严重的心、脑、肾并发症,可导致死亡,其中左心室肥厚是高血压最常见的并发症之一^[1]。目前,高血压病的发生机制尚未完全阐明,关于高血压的防治还存有许多问题,如临床药物治疗高血压的效果常不够满意,且具有各种不良反应^[2]。有学者研究了运动疗法对高血压的疗效,研究表明,适量的运动具有降低人和动物血压,同时预防高血压的发生的作用^[3]。本研究采用低强度运动干预自发性高血压大鼠,旨在探讨低强度运动对高血压大鼠心室重构的影响,及其保护机制。

材料与方法

一、实验动物与分组

选取 8 周龄雄性高血压 Wistar 大鼠 20 只和 8 周龄、雄性 Wistar 大鼠 10 只,均购于北京维通利华动物中心,将高血压大鼠 20 只采用随机数字表法分成高血压运动组和高血压对照组,每组 10 只,10 只 Wistar 大鼠则作为正常对照组。所有大鼠均在清洁、通风、温度 20 ~ 22 °C、相对湿度 40% ~ 70% 环境下单只分笼喂养。

二、运动方法

高血压运动组于入组后当天即进行游泳运动,游泳缸体积为 150 cm × 60 cm × 高 70 cm,水温 30 ~ 32 °C,第 1 周进行适应性运动,按循序渐进原则,第 1 天 10 min,第 2 天 20 min,第 3 天 30 min,第 4 天 40 min,第 5 天 50 min,第 6 天 60 min,以后每次游泳 60 min,每周 6 次,连续训练 12 周。正常对照组和高血压对照组仅常规饲养,不进行任何训练。

三、血压的测定

采用大鼠血压和心率测定仪检测 3 组大鼠入组当天和入组后清醒状态下的尾动脉收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)和心率,每周测量 1 次,每次重复 3 次,取平均值,比较 3 组大鼠不同时间点血压和心率的变化。

四、血清学分析

3 组大鼠均于入组 12 周后,从颈静脉抽取静脉血 5 ml,分别注入内含 10% 乙二胺四乙酸二钠的试管,离心半径 10 cm,3000 r/min,离心 5 min,分离血清,然后采用 ELISA 法测定血浆去甲肾上腺素(norepineph-

rine, NE)和血管紧张素 II(angiotensin II, ANG II)的水平。

五、左心室重量/体重的测定

3 组大鼠均于入组 12 周后进行左心室重量(left ventricular weight, LVW)/体重(body weight, BW)测定,先测量体重,然后经腹腔注射戊巴比妥 40 mg/kg 体重麻醉,迅速开胸,取出心脏,沿主动脉根部剪去大血管,冰生理盐水充分灌洗,滤纸吸干,沿房室交界处去除心房及脂肪、血管等组织,紧贴室间隔右侧剪下右心室游离壁,将剩余部分采用磷酸盐缓冲液(phosphate buffered saline, PBS)冲洗,用滤纸吸干水分后称重,然后计算出 LVW/BM 比值,作为观察左心室肥厚的指标。

六、组织学检测左心室重构

取 3 组大鼠左心室,用 10% 甲醛固定,石蜡包埋,切取 5 μ m 厚的截面标本后行苏木精-伊红(hematoxylin-eosin, HE)染色,观察心肌形态结构变化并计算心肌细胞直径,天狼星红染色检测左心室心肌胶原沉积。光镜下观察,心肌细胞呈黄色,胶原呈红色。采用光学显微镜测定,每个心肌切片取 6 个视野,用计算机图像分析系统定量分析切片中每个视野的胶原容积分数(collagen volume fraction, CVF), CVF = 胶原面积/全视野面积 × 100%。

七、半定量逆转录-聚合酶链反应检测

采用半定量逆转录-聚合酶链反应(reverse transcription-polymerase chain reaction, RT-PCR)法检测 3 组大鼠左心室心肌肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、白细胞介素-6(interleukin-6, IL-6)、白细胞介素-1 β (interleukin-1 β , IL-1 β)和转化生长因子- β 1(transforming growth factor- β 1, TGF- β 1)的信使核糖核酸(messenger ribonucleic acid, mRNA)的表达,取大鼠左心室心肌剪碎,参照 Trizol RNA 提取试剂说明书提取组织总 RNA。应用 RT-PCR 法进行脱氧核糖核酸(complementary deoxyribonucleic acid, cDNA)的合成及聚合酶链式反应(polymerase chain reaction, PCR)扩增。引物设计如下:TNF- α (360 bp)为上游 5'-TGG CCC AGA CCC TCA CA-3',下游 5'-TGC CCG GAC TCC GTG AT-3'; IL-6(295 bp)为上游 5'-AGA GCA ATA CTG AAA CCC TA-3',下游 5'-CAA CAT AAT TTA

GAT ACC CAT C-3'; IL-1 β (508 bp) 为上游 5'-CCC ATA CAC ACG GAC AAC TAG A-3', 下游 5'-ATC CCA AAC AAT ACCC AAA GAA-3'; TGF- β 1 (396 bp) 为上游 5'-GCC TCC GCA TCC CAC CTT TG-3', 下游 5'-GCG GGT GAC TTC TTT GGC GT23'; 甘油醛-3-磷酸脱氢酶 (glyceraldehyde-3-phosphate dehydrogenase, GAPDH) (213 bp) 做内参, 其引物为上游 5'-TAT GAT GAC ATC AAG AAG GTG G-3', 下游 5'-CAC CAC CCT GTT GCT GTA-3'。PCR 扩增产物用 1.5% 琼脂糖凝胶电泳, 用凝胶成像系统 (美国 BIO-RAD 公司) 扫描采图, 用 Quantity-one 4.4.0 版软件进行图像分析和半定量分析, 以各细胞因子与内参 GAPDH 的核糖核酸 (complementary deoxyribonucleic acid, cDNA) 条带的灰度值比值来评定各细胞因子 mRNA 表达水平。

八、蛋白质印迹法检测

采用蛋白质印迹法检测 3 组大鼠左心室心肌 TNF- α , IL-6, IL-1 β 和 TGF- β 1 的蛋白的表达。左心室心肌组织于三 (羟甲基) 氨基甲烷缓冲液 (50 mmol/L) 中匀浆提取蛋白, 以牛血清白蛋白做标准曲线, 采用考马斯亮蓝法 (Bradford) 法测定蛋白浓度。每孔取 30 μ g 蛋白行十二烷基硫酸钠-聚丙烯酰胺凝胶电泳 (sodium dodecyl sulfate-polyacrylamide gel electrophoresis, SDS-PAGE), 转移电泳至硝酸纤维素膜。转膜后采用 5% 脱脂奶粉封闭 2 h, 加入适当稀释于 2.5% 脱脂奶粉中的一抗 [山羊抗大鼠 IL-6、TNF- α (美国 R&D 公司), 小鼠抗大鼠 IL-1 β (英国 Serotec 公司), 兔抗鼠 TGF- β 1 (美国 Santa Cruz 公司), 0.2 μ g/ml], 4 $^{\circ}$ C 孵育过夜。三 (羟甲基) 氨基甲烷缓冲液洗涤后加入辣根过氧化物酶标记相应二抗 (1:10 000) 37 $^{\circ}$ C 环境下孵育 1 h。TBS 洗涤后应用化学发光法显色, 采用英国 UVP 公司产 GSD 8000 版密度扫描分析系统进行图像分析, 以各细胞因子与 β -肌动蛋白扩增条带的吸光面积积分比值来评定各细胞因子蛋白表达水平。

九、统计学方法

采用 SPSS 16.0 版统计软件进行统计学分析处理。数据以 ($\bar{x} \pm s$) 表示, 采用单因素方差分析对组间差异进行统计学比较分析, 两两之间的比较采用 LSD 检验。以 $P < 0.05$ 为差异有统计学意义。

结 果

一、3 组大鼠不同时间点血压的变化

入组 12 周后, 高血压运动组的收缩压和舒张压分别为 (150.6 ± 6.7) mmHg (1 mmHg = 0.133 kPa) 和 (91.6 ± 7.1) mmHg 与组内入组后当天和高血压对照组入组 12 周后比较, 均显著下降 ($P < 0.05$), 但与正

常对照组比较, 差异仍有统计学意义 ($P < 0.05$), 详见表 1。

表 1 3 组大鼠不同时间点血压比较 (mmHg, $\bar{x} \pm s$)

组别	只数	入组后当天	入组 5 周后	入组 9 周后	入组 12 周后
正常对照组					
SBP	10	117.3 $\pm$ 4.2	121.1 $\pm$ 5.3	120.1 $\pm$ 3.3	116.1 $\pm$ 4.8
DBP	10	71.3 $\pm$ 4.2	75.1 $\pm$ 5.6	73.1 $\pm$ 5.3	73.1 $\pm$ 5.3
高血压对照组					
SBP	10	161.2 $\pm$ 7.3 ^a	186.1 $\pm$ 9.5 ^{ac}	194.1 $\pm$ 9.2 ^{ac}	221.1 $\pm$ 15.2 ^{ac}
DBP	10	101.2 $\pm$ 7.3 ^a	115.1 $\pm$ 7.2 ^{ac}	130.1 $\pm$ 9.2 ^{ac}	145.1 $\pm$ 11.4 ^{ac}
高血压运动组					
SBP	10	162.5 $\pm$ 8.9 ^a	178.6 $\pm$ 5.6 ^{abc}	172.6 $\pm$ 5.6 ^{abc}	150.6 $\pm$ 6.7 ^{abc}
DBP	10	102.5 $\pm$ 8.9 ^a	110.6 $\pm$ 5.7 ^a	105.6 $\pm$ 4.8 ^{ab}	91.6 $\pm$ 7.1 ^{abc}

注: 与正常对照组同时点比较, ^a $P < 0.05$; 与高血压对照组同时点比较, ^b $P < 0.05$; 与组内入组后当天比较, ^c $P < 0.05$

二、血清学分析与左心室肥厚检测

入组 12 周后, 高血压运动组的心率、LVW/BW、NE 和 ANG II 水平显著低于高血压对照组大鼠 ($P < 0.05$), 但仍显著高于正常对照组大鼠 ($P < 0.05$), 详见表 2。

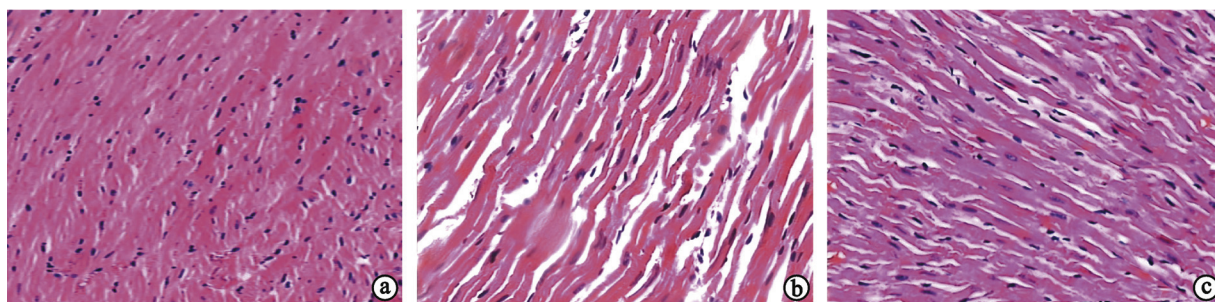
表 2 3 组大鼠入组 12 周后 LVW/BW 及血清 NE 和 ANG II 的比较 ($\bar{x} \pm s$)

组别	只数	心率 (次/min)	LVW/BW (mg/g)	NE (pg/ μ l)	ANG II (ng/ml)
正常对照组	10	392.5 $\pm$ 5.3	2.3 $\pm$ 0.2	17.5 $\pm$ 2.1	90.2 $\pm$ 3.8
高血压对照组	10	433.4 $\pm$ 9.5 ^a	4.2 $\pm$ 0.3 ^a	71.3 $\pm$ 6.8 ^a	131.7 $\pm$ 7.3 ^a
高血压运动组	10	409.1 $\pm$ 7.3 ^{ab}	3.1 $\pm$ 0.2 ^{ab}	30.4 $\pm$ 4.5 ^{ab}	110.1 $\pm$ 5.5 ^{ab}

注: 与正常对照组比较, ^a $P < 0.05$; 与高血压对照组比较, ^b $P < 0.05$

三、组织学检测左心室重构

左心室心肌组织学检测结果显示: 正常对照组大鼠心肌细胞排列整齐, 无增粗, 细胞核大小均一, 胞质染色均匀; 高血压对照组大鼠心肌排列稀疏、紊乱, 肌纤维明显增粗; 高血压运动组大鼠心肌可见心肌纤维稍有增粗, 排列较整齐紧密, 较高血压对照组明显改善 (图 1); 高血压运动组和高血压对照组大鼠的左心室心肌细胞直径均显著大于正常对照组 ($P < 0.05$), 而高血压对照组的左心室心肌细胞直径亦大于高血压运动组 ($P < 0.05$) (图 2)。图 3 可见, 高血压运动组和高血压对照组的心肌胶原成分较正常对照组均明显增多, 高血压运动组和高血压对照组大鼠的 CVF 值均显著高于正常对照组 ($P < 0.05$), 而高血压对照组的 CVF 值亦显著高于高血压运动组 ($P < 0.05$), 详见图 2。



注:A 为正常对照组,B 为高血压对照组,C 为高血压运动组

图 1 3 组大鼠入组 12 周后左心室心肌组织图(HE 染色, ×200)

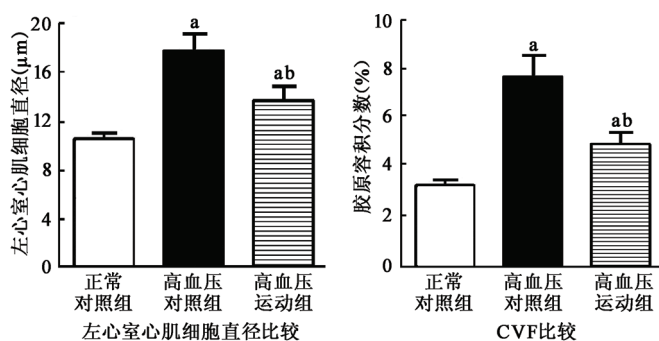
注:与正常对照组比较,^a $P < 0.05$;与高血压对照组比较,^b $P < 0.05$

图 2 3 组大鼠入组 12 周后左心室心肌细胞直径和 CVF 比较

四、RT-PCR 检测

入组 12 周后,高血压运动组和高血压对照组重塑的左心室心肌中 TNF- α , IL-6, IL-1 β , TGF- β 1 的 mRNA

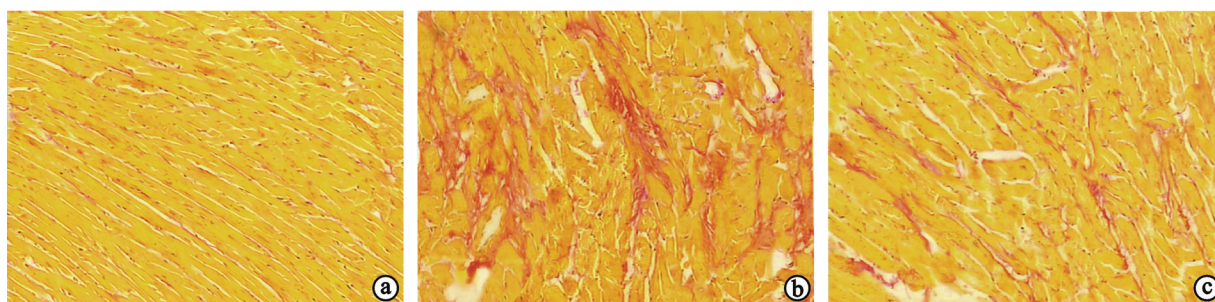
表达均显著高于正常对照组 ($P < 0.05$);高血压运动组重塑的左心室心肌中 TNF- α , IL-6, IL-1 β , TGF- β 1 的 mRNA 表达均显著低于高血压对照组 ($P < 0.05$),详见图 4。

五、蛋白质印迹法检测左心室心肌细胞因子蛋白表达

入组 12 周后,蛋白质印迹法检测结果显示:高血压运动组和高血压对照组重塑的左心室心肌中 TNF- α , IL-6, IL-1 β 和 TGF- β 1 的蛋白的表达均显著增加 ($P < 0.05$),而高血压运动组重塑的左心室心肌中 TNF- α , IL-6, IL-1 β 和 TGF- β 1 的蛋白的表达均显著低于高血压对照组 ($P < 0.05$),详见图 5。

讨 论

心室重构是指心室由于心肌损伤或负荷增加所产



注:A 为正常对照组,B 为高血压对照组,C 为高血压运动组

图 3 3 组大鼠入组 12 周后心肌胶原沉积图(天狼星红染色, ×200)

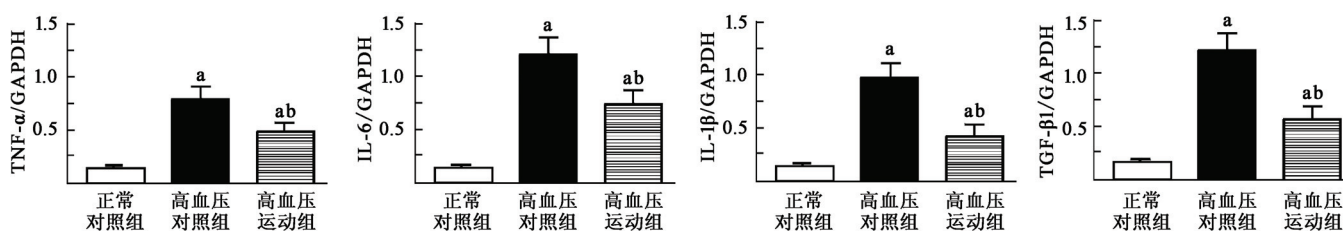
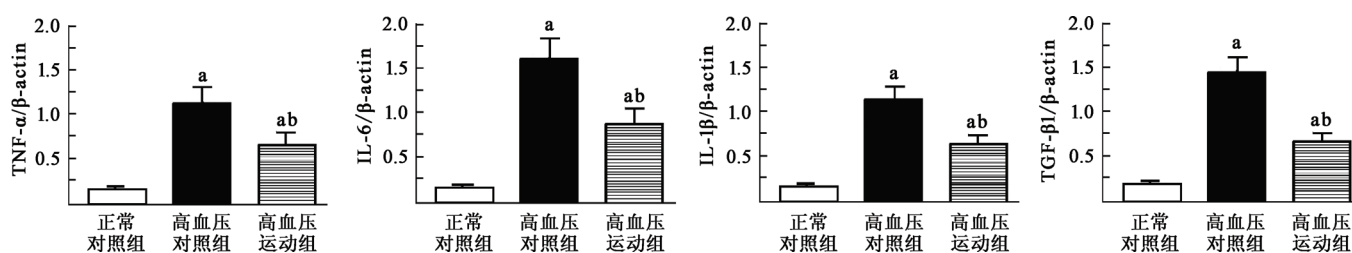
注:与正常对照组比较,^a $P < 0.05$;与高血压对照组比较,^b $P < 0.05$

图 4 3 组大鼠入组 12 周后左心室心肌细胞因子的 mRNA 表达



注:与正常对照组比较,^a $P < 0.05$;与高血压对照组比较,^b $P < 0.05$

图5 3组大鼠入组12周后3组大鼠左心室心肌中细胞因子的蛋白表达

生的大小、形状、室壁厚度和组织结构等一系列变化,是病变修复和心室整体代偿及继发的病理生理反应过程^[4-5]。心肌负荷过重是导致高血压引起左心室重构的主要因素之一,其发病机制与血流动力学负荷过重及神经内分泌等因素密切相关,体液和细胞因子参与了其发生和发展的过程^[6-8]。在左心室重构的过程中,心肌细胞、胞外基质、胶原纤维网等均有相应变化。组织学上表现为左心室肥厚和心肌纤维化。通过检测LVW/BW及心肌细胞直径可以检测左心室肥厚,检测胶原容积分数则可以检测心肌纤维化^[2,9-11]。本研究结果显示,入组12周后,高血压运动组的LVW/BW、左心室心肌细胞直径及胶原容积分数与高血压对照组比较均显著降低($P < 0.05$),提示游泳运动可降低高血压大鼠的LVW/BW、心肌细胞直径及胶原容积分数,即改善了高血压大鼠的心室重构。本研究结果还显示,入组12周后,高血压运动组大鼠的收缩压、舒张压和心率与高血压对照组比较均显著改善($P < 0.05$),游泳运动显著降低了高血压大鼠的收缩压、舒张压和心率,提示游泳运动改善心室重构的机制与降低血流动力学负荷有关。

Agarwal等^[12]的研究显示,运动可降低大鼠血清中NE和ANG II的浓度。本研究也证实了这点。本研究结果显示,入组12周后,高血压对照组与正常对照组大鼠比较,血清NE和ANG II均显著增加,高血压运动组大鼠NE和ANG II与高血压对照组比较均显著降低($P < 0.05$),提示交感神经系统及RAS系统活性的增高在自发性高血压大鼠心室重构过程中具有重要作用,且游泳运动改善心室重构的机制与降低交感神经系统及RAS系统的活性有关。

临床研究和动物实验均证实,细胞因子对调节心脏结构和功能具有重要作用^[6-8],TNF-α,IL-1β,IL-6和TGF-β1在心力衰竭患者循环和心肌组织中的水平明显升高,并且与疾病的严重程度密切相关。上述研究指出,TNF-α,IL-1β和IL-6等炎性细胞因子可以抑制心肌收缩力,介导心肌细胞凋亡,促进心室重塑,还可体外诱导心肌细胞肥大,促进细胞胚胎基因及蛋白的

表达。另外,IL-6和IL-1β还可以促进胶原合成^[13],且TGF-β1是胶原纤维和其他细胞外基质成分合成和沉积的始动因子,可刺激培养的心肌成纤维细胞合成分泌胶原,增加纤维合成和糖蛋白的合成,导致心室重塑^[14]。本研究结果显示,入组12周后,高血压对照组大鼠左室心肌TNF-α,IL-1β,IL-6和TGF-β1的表达均高于正常对照组,高血压运动组大鼠左室心肌TNF-α,IL-1β,IL-6和TGF-β1的表达均显著低于高血压对照组($P < 0.05$),提示细胞因子参与了高血压诱导的左心室重构的过程,而游泳运动可降低高血压大鼠IL-1β,IL-6和TGF-β1的表达,即游泳运动可通过降低细胞因子的表达来改善高血压大鼠的左心室重构。

综上所述,游泳运动可显著降低自发性高血压大鼠的收缩压、舒张压和心率,改善其左心室重构。同时,游泳运动可显著降低自发性高血压大鼠血清中NE和ANG II水平及左心室心肌细胞IL-1β,IL-6和TGF-β1的表达,提示游泳运动改善左心室重构的机制不仅与降低交感神经与RAS系统活性有关,还与降低细胞因子TNF-α、IL-6、IL-1β和TGF-β1的表达有关。

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· 外刊摘英 ·

Vitamin D as a predictor of multiple sclerosis activity

BACKGROUND AND OBJECTIVE Previous studies have demonstrated that low levels of vitamin D are associated with multiple sclerosis (MS) activity. This study was designed to determine whether vitamin D status, early in the MS disease process, influences the long-term course and progression of the disease.

METHODS Data were obtained from the participants of the Betaferon/Betaseron in Newly Emerging Multiple Sclerosis for Initial Treatment (BENEFIT) trial. Levels of 25 (OH) D were collected at baseline and at six, 12 and 24 months. The patients were followed for MS activity, with outcomes including time to definite diagnosis of MS, MS activity and MS progression. Assessments were made using the McDonald criteria (MDMS), the Poser criteria and radiologic progression.

RESULTS Over five years' follow-up, conversion to MS was documented in 81.3% to MDMS and 46.6% to clinically definite MS (CDMS). The hazard of conversion decreased with increasing serum 25 (OH) D. Among those with data at both six and 12 months, the hazard of conversion decreased by more than 50% for a 50 nmol/L increase in 25 (OH) D. The relative decrease in T2 lesion volume for a 50-nmol/L increase in 25 (OH) D was 20% per year ($P < 0.001$). The annualized change in EDSS score was lower among patients with serum 25 (OH) D levels greater than or equal to 50 nmol/L, as compared with those with less than 50 nmol/L ($P = 0.004$).

CONCLUSION This study of patients with MS found that higher levels of vitamin D predicted a lower level of multiple sclerosis activity and disease progression over five years.

【摘自:Ascherio A, Munger KL, White R, et al. Vitamin D as an early predictor of Multiple Sclerosis Activity and Progression. JAMA Neurol. 2014, 71(3):306-314.】

Vitamin D and cause-specific death

Supplementation with vitamin D has been shown to benefit skeletal conditions, with a growing body of evidence indicating that vitamin D may also reduce risks of a wide range of nonskeletal diseases. This study summarized the available evidence to determine associations of various 25-hydroxyvitamin concentrations with the risk of cause-specific mortality and quantified the effects of supplementation.

A literature search was completed using Medline, Embase and Cochrane databases. Observational cohort studies and randomized trials were considered for inclusion, which included data on associations of circulating 25-hydroxyvitamin D concentration with cause-specific or all-cause deaths in adults.

Of the studies reviewed, 95 met the inclusion criteria for the meta-analysis. For the primary prevention cohorts, pooled risk ratios comparing those in the bottom with the top third of the 25-hydroxyvitamin D concentrations were 1.25 for cardiovascular disease, 1.14 for cancer, 1.3 for other nonvascular, noncancer death and 1.35 for all-cause mortality. Each 10 ng/mL decline of 25-hydroxyvitamin D concentration was associated with a 16% increased risk of all-cause mortality. In studies focusing on vitamin D supplementation, no significant effect on mortality was medication, Tripterygium Wilfordi Hook F, is at least as effective as MTX, while the combination of both was superior to MTX for the treatment of rheumatoid arthritis.

【摘自:Lv QW, Zhang W, Shi Q, et al. Comparison of tripterygium wilfordi hook F with methotrexate in the treatment of active rheumatoid arthritis. Ann Rheum Dis. doi:10.1136/annrheumdis-2013-204807.】