扩张型心肌病患者中解聚素金属蛋白酶及其抑制因子的表达改变

背景：解聚素金属蛋白酶(ADAM)或许可通过改变细胞表面的基质受体(整合素)、激活有效的生物分子而促进心脏结构重构。作者比较了具有不同结构重构模式的人心脏组织中ADAM及其内源性抑制物金属蛋白酶组织抑制因子(TIMP)－3以及整合素的表达情况。方法和结果：获取扩张型心肌病(DCM)患者($n=20$)、肥厚型梗阻性心肌病患者(HOCM，$n=5$)以及无心衰的供体($n=7$)的心肌组织。在插入左室辅助器械之前及心脏移植时获得配对样本($n=10$)。采用定量免疫印记法测定ADAM10、ADAM12、ADAM15、ADAM17、TIMP－3以及整合素受体β1D、β3的表达。计算整合素分裂产物与完整蛋白的丰度比值来评估整合素脱落情况。并使用了共聚焦显微镜进行检查。DCM的特征是ADAM10和ADAM15表达升高，而TIMP－3表达下降。整合素β1D分裂比增高，这表示受体脱落加剧。ADAM10和ADAM15表达与分裂比相关。共聚焦显微镜发现ADAM10与整合素β1D共存。ADAM10的表达与心腔扩张和收缩功能不全的临床指标相关。减轻血流动力学负荷可减少ADAM10和ADAM12的表达，增加整合素β1D表达。HOCM样本中ADAM12和整合素β1D表达增高。而ADAM17在DCM和HOCM中均增高。结论：在人的心肌组织中，解聚素金属蛋白酶表达差异较大，这反映了结构重构的潜在模式。ADAM10和ADAM15可能减少细胞－基质作用(通过整合素脱落的途径)而促进心脏扩张。或许可采用基于基因或细胞的治疗来补充所缺乏的TIMP－3，这种将ADAM作为治疗靶点的方法将可能防止DCM患者的进行性心腔扩张。

0631. Increased peripheral chemoreceptors sensitivity and exercise ventilation in heart transplant recipients

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Background - Heart failure is characterized by increased ventilation during exercise, which is positively related to increased peripheral and central chemoreceptor sensitivity. Heart transplantation does not normalize the ventilatory response to exercise, and its effects on the chemoreflex control of ventilation remain unknown. We tested the hypothesis that chemoreceptor sensitivity is increased in heart transplant recipients(HTRs) and linked to exercise hyperpnea. Methods and Results - We determined the ventilatory, muscle sympathetic nerve activity(MSNA), and circulatory responses to isocapnic hypoxia and hyperoxic hypercapnia 7 ± 1 years after transplantation in 19 HTRs with a normal left ventricular ejection fraction of 60 ± 2%. Results were compared with those of 11 closely matched referent subjects. Sixteen patients and 10 referent subjects also underwent cycle ergometer exercise tests. HTRs compared with referent subjects presented higher MSNA(52 ± 4 versus 34 ± 3 bursts/min; $P < 0.01$) and heart rates (83 ± 3 versus 68 ± 3 bpm; $P < 0.01$) during room air breathing. The ventilatory response to hypoxia was higher in HTRs than in referent subjects($P < 0.01$, ANOVA). The increase in MSNA also was more marked during hypoxia in the HTRs than in the referent group($P < 0.05$, ANOVA). Responses to hyperoxic hypercapnia did not differ between the HTRs and the referent group. The ventilatory response to exercise, characterized by the regression slope relating minute ventilation to CO_2 output, was steeper in HTRs than in referent subjects(38 ± 2 versus 29 ± 1 L/mm Hg; $P < 0.01$). Exercise ventilation in HTRs was related to the ventilatory response to isocapnic hypoxia($r = 0.57$; $n = 16$; $P < 0.05$) and to the ventilatory response to hyperoxic hypercapnia($r = 0.50$; $n = 16$; $P < 0.05$). Conclusions - Peripheral chemoreceptor sensitivity is increased in HTRs and is related to exercise hyperpnea after heart transplantation.

心脏移植受者中外周化学感受器的敏感性和运动通气量均增加

背景：心力衰竭的特征之一是运动过程中通气量增加，这与外周和中枢化学感受器的敏感性增强呈正相关。心脏移植并不能使运动时的通气反应正常化，而且其对通气相关化学反射控制的影响作用尚不清楚。本研究拟验证如下假说：心脏移植受者(HTR)的化学感受器敏感性增强，并与运动时呼吸加强有关。方法和结果：检测了19例左室射血分数正常(60% ±2%)的HTR(心脏移植后7 ± 1年)对等二氧化碳性缺氧及高氧性高碳酸血症的通气、肌肉交感神经活性(MSNA)及循环方面反应。将检测结果与11例严格匹配的参照个体进行比较。16例患者和10例参照个体还进行了踏车测力运动试验。与参照者相比，HTR在室内空气呼吸中表现出更强的MSNA(52 ± 4脉冲/min *vs* 34 ± 3脉冲/min，$P < 0.01$)和更快的心率(83 ± 3次/min *vs* 68 ± 3次/min，$P < 0.01$)。HTR对缺氧的通气反应也更强于参照者($P < 0.01$，ANOVA)。HTR在缺氧过程中表现出的MSNA增

强也更为明显($P < 0.05$,ANOVA)。HTR 和参照者对高氧性高碳酸血症的反应无差异。可反映运动时通气反应的特征是每分通气量与 CO_2 产生量之间的回归斜率。该斜率在 HTR 中较参照者中更为陡直(38 ± 2 L/mmHg *vs* 29 ± 1 L/mmHg,$P < 0.01$)。HTR 中,运动通气量与对等二氧化碳性缺氧($r = 0.57$,$n = 16$,$P < 0.05$)和高氧性高碳酸血症($r = 0.50$,$n = 16$,$P < 0.05$)的通气反应均相关。结论:HTR 的外周化学感受器敏感性增强,这与心脏移植后的运动时呼吸增强有关。

0632. Sustained reverse left ventricular structural remodeling with cardiac resynchronization at one year is a function of etiology: Quantitative Doppler echocardiographic evidence from the Multicenter InSync Randomized Clinical Evaluation(MIRACLE)

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Background - Cardiac resynchronization therapy(CRT) is an effective therapy for patients with moderate to severe heart failure and prolonged QRS duration. The purpose of this study was to determine whether reverse left ventricular (LV) remodeling and symptomatic benefit from CRT were sustained at 12 months, and if so, in what proportion of patients this occurred. Methods and Results - Serial Doppler echocardiograms were obtained at baseline and 6 and 12 months after CRT in 228 patients enrolled in the Multicenter InSync Randomized Clinical Evaluation (MIRACLE) trial. Measurements were made of LV end-diastolic(EDV) and end-systolic(ESV) volumes, ejection fraction, LV mass, severity of mitral regurgitation (MR), peak transmitral velocities during early(E wave) and late(A wave) diastolic filling, and myocardial performance index. At both 6 and 12 months, respectively, CRT was associated with reduced LV EDV(P < 0.0001 and P = 0.007) and LV ESV(P < 0.0001 and P < 0.0001), improved ejection fraction(P < 0.0001 and P < 0.0001), regression of LV mass(P = 0.012 and P < 0.0001), and reduced MR(P < 0.0001 and P < 0.0001). LV filling time, transmitral E/A ratio, and myocardial performance index all improved at 12 months compared with baseline (P < 0.001, P = 0.031, and P < 0.0001). Reverse LV remodeling with CRT occurred in more patients at 6 than at 12 months(74% versus 60%, respectively; P < 0.05) and was greater in patients with a nonischemic than an ischemic etiology. Conclusions - Reverse LV remodeling and symptom benefit with CRT are sustained at 12 months in patients with New York Heart Association class III/IV heart failure but occur to a lesser degree in patients with an ischemic versus a nonischemic etiology, most likely owing to the inexorable progression of ischemic disease.

心脏再同步化治疗 1 年后左室结构重构持续逆转是一个病因函数:来自 MIRACLE(多中心 InSync 再同步化治疗随机临床评估)的定量多普勒超声心动图证据

背景:对于中至重度心力衰竭及 QRS 波群时间延长的患者来说,心脏再同步化治疗(CRT)是一项有效方法。本研究旨在确定 CRT 所致的左室(LV)重构逆转和症状减轻是否可持续到术后 12 个月,如果可持续,则确定这种持续效应发生的患者比例。方法和结果:对入选 MIRACLE(多中心 InSync 再同步化治疗随机临床评估)试验的 228 例患者在基线时和 CRT 后 6 个月、12 个月连续采集多普勒超声心动图资料。测量 LV 舒张末(EDV)及收缩末(ESV)容积、射血分数、LV 质量、二尖瓣反流(MR)的严重程度、舒张充盈早期(E 波)及晚期(A 波)的跨二尖瓣流速峰值以及心肌功能指数。在 6 个月和 12 个月时,CRT 均与 LV EDV($P < 0.000\ 1$、$P = 0.007$)及 LV ESV($P < 0.000\ 1$、$P < 0.000\ 1$)减小、射血分数改善($P < 0.000\ 1$、$P < 0.000\ 1$)、LV 质量复原($P = 0.012$、$P < 0.000\ 1$)以及 MR 减小($P < 0.000\ 1$、$P < 0.000\ 1$)相关。与基线时相比,12 个月时的 LV 充盈时间、跨二尖瓣 E/A 比值以及心肌功能指数均有改善($P < 0.001$、$P = 0.031$ 及 $P < 0.000\ 1$)。CRT 后 6 个月时发生 LV 重构逆转的患者多于 12 个月时(74% *vs* 60%,$P < 0.05$);与缺血性病因引起 LV 重构者相比,重构逆转更多发生于非缺血性病因引起者中。结论:NYHA 分级为 III/IV 级的心力衰竭患者其 CRT 后 LV 重构逆转以及症状改善可持续至 12 个月,但与非缺血性病因引起 LV 重构者相比,缺血性病因引起者逆转的程度较低,这可能是因缺血性疾病的不可逆性进展所致。

(0626 ~ 0632 杜 媛 译 刘少伟 校)

0633. Gender differences in outcomes after hospital discharge from coronary artery bypass grafting

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