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## 超声微泡介导H-FABP基因改善慢性心衰大鼠的心功能(PDF)

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Title: Ultrasound microbubble-mediated heart fatty acid binding protein in treatment of chronic heart failure rats

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**摘要:** 目的 研究超声靶向破坏微泡 (ultrasound targeted microbubble destruction, UTMD) 技术转染H-FABP基因对心肌梗死后心功能的影响。方法 通过结扎成年雄性Wistar大鼠46只, 体质量 (220±20) g, 冠状动脉前降支建立心肌梗死模型。于心肌梗死8周后, 将存活的31只心衰大鼠随机分为4组: ①H-FABP+超声+微泡组 (H-FABP+US/MB组, n=8), 用超声破坏携H-FABP基因微泡转染大鼠心肌; ②超声+微泡组 (US/MB组, n=8), 用超声破坏不含基因的微泡; ③H-FABP+生理盐水组 (H-FABP+NS组, n=8), 由颈静脉输入含基因的生理盐水; ④单纯手术组 (SA组, n=7), 仅由颈静脉输入生理盐水; ⑤假手术组 (SS组, n=6)。基因转染14 d后测定各组大鼠心功能, Western blot检测左心室非梗死区H-FABP表达, ELISA法检测静脉血及非梗死区心肌游离脂肪酸 (FFA) 含量, 硫代巴比妥酸反应物 (TBARS) 法检测非梗死区心肌组织脂质过氧化水平, 免疫组织化学法检测非梗死区心肌诱导型一氧化氮合酶 (iNOS) 表达。结果 心肌梗死大鼠各组与假手术组比较心功能明显下降 ( $P<0.05$ ), H-FABP表达明显下降 ( $P<0.05$ ), 静脉血及心肌FFA含量明显升高 ( $P<0.05$ ), 丙二醛 (MDA) 水平明显升高 ( $P<0.05$ ), iNOS表达明显升高 ( $P<0.05$ )。H-FABP+超声+微泡组与心肌梗死大鼠中的另外3组比较心功能明显改善 ( $P<0.05$ ), H-FABP表达升高 ( $P<0.05$ ), 心肌FFA含量降低 ( $P<0.05$ ), MDA水平降低 ( $P<0.05$ ), iNOS表达受抑制 ( $P<0.05$ )。结论 超声微泡介导的H-FABP转染可改善大鼠慢性心衰时心功能。可能与通过提高H-FABP表达、降低心肌FFA含量、改善心肌氧化应激水平、进而抑制iNOS的表达有关。

**Abstract:** Objective To determine the effect of heart fatty acid binding protein (H-FABP) transfected by ultrasound targeted microbubble destruction (UTMD) technology on cardiac function after post-infarction. Methods Myocardial infarction (MI) was induced in Wistar male rats ( $n=46$ ,  $220\pm 20$  g) by ligating the left anterior descending coronary artery. After 8 weeks, the 31 surviving rats with heart failure were randomly divided into 4 groups, H-FABP+ultrasound+microbubble group (H-FABP+US/MB group,  $n=8$ , ultrasound-targeted destruction microbubble loaded with H-FABP gene was transfected to rat heart), ultrasound+microbubble group (US/MB group,  $n=8$ , ultrasonic destruction of microbubbles loaded without gene), H-FABP+normal saline group (H-FABP+NS group,  $n=8$ , normal saline containing gene were infused from jugular vein), surgery alone group (SA group,  $n=7$ , only normal saline were infused from jugular vein), and sham-operation group (SS group,  $n=6$ ). In 14 d after transfection, the cardiac function of all the rats were measured, H-FABP expression in non-infarct region of left ventricular was detected by Western blotting, free fatty acid (FFA) content of venous blood and non-infarct region myocardium were detected by ELISA, lipid peroxidation in non-infarct region of left ventricular was detected by thiobarbituric acid reactive substances (TBARS) method, and the iNOS expression in non-infarct region of left ventricular was detected by immunohistochemical assay. Results Compared with sham-operation group, left ventricular ejection fraction (LVEF) and the H-FABP expression were decreased significantly ( $P<0.05$ ), free fatty acid content and malondialdehyde (MDA) level and the iNOS expression were obviously increased ( $P<0.05$ ) in the MI groups. Compared with US/MB, H-FABP+NS and SA groups, LVEF and the H-FABP expression were apparently increased ( $P<0.05$ ), free fatty acid content of myocardium and MDA level were obviously decreased ( $P<0.05$ ) and the iNOS expression was markedly inhibited ( $P<0.05$ ) in H-FABP+US/MB group. Conclusion Ultrasound microbubble-mediated H-FABP transfection improves cardiac function via upregulating H-FABP, reducing myocardial FFA, ameliorating myocardial oxidative stress and inhibiting iNOS expression.

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