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EFFECTS OF RAT ANTSENSE AT_{1B} GENE TRANSFER BY ADENOVIRAL VECTOR MEDIATED ON NEOINTIMA PROLIFERATION AFTER RAT CAROTID ARTERY INJURY

P. Ouyang, DL Xu, YL Liu, YQ Hou , HL Huang, HY Song, David S. W. Ho* . Department of Cardiology, Nanfang Hospital,Guangzhou. * Department of Medicine, The University of Hong Kong, Hong Kong

Objective: Angiotensin II is a growth factor for vascular smooth cells in culture and in the intact animal. The physiologic effects of angiotensin are elicited through binding to specific receptors on cell membranes. In this study, we evaluated the effects of rat antisense AT_{1B} gene transfer on neointimal proliferation using a rat carotid artery injury model. **Method:** Rat carotid artery injury model was established and antisense AT_{1B} gene was transducted into six SD rats carotid artery at the time of injury using adenovirus as a vector. Six rats receiving unilateral carotid artery injury acted as control. For both groups, neointima to media area ratio at the site of arterial injury was measured at 21 days after balloon injury ± gene transfer. **Results**: Neointima to media area ratio in the treatment group was significantly reduced compared with the control group at 21 days after gene transfer (0.555±0.078 vs 1.004±0.052, $P < 0.01$). **Conclusion:** The results suggest the possibility of antisense AT_{1B} gene transfer as a potential therapeutic approach to prevent neointimal hyperplasia. Further evaluation of this technique in a large study group or in other animal models (e.g. rabbit and pig) are underway.

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Implantable Atrial Defibrillator Prevented Atrial Stunning and Improved Ventricular Function after Cardioversion from Atrial Fibrillation

Qiong Wang, Cheuk-Man Yu, Hung-Fat Tse, Vella Tsang, Cathy Lam, Sum-Kin Leung, Gregory Ayers, Chu-Pak Lau. Division of Cardiology, Department of Medicine, Queen Mary Hospital, University of Hong Kong, Hong Kong

Background: Atrial stunning occurs after external cardioversion from of atrial fibrillation (AF), though the effect of cardioversion on ventricular function is largely unexplored. This study investigated whether early termination of AF by an implantable atrial defibrillator (IAD) IAD may affect atrial and ventricular function.

Methods: Eleven patients (mean age 59±12 years, 9 male) with lone AF received an IAD capable of delivering low energy (<5J) biatrial shocks (Metrix, InControl). Serial atrial and ventricular mechanical function was studied by pulse Doppler and tissue Doppler echocardiography (TDI) at 1 min, 20 min and 4 hours after restoration to sinus rhythm.

Results: The left atrial size was 3.9±0.5cm by M-mode measurement. There were 38 episodes of AF (63% spontaneous and 37% induced) and the mean AF duration was 93±138 hrs (range: 1 minute to 600 hrs). Thirty-two episodes were restored by internal defibrillation, 4 spontaneously and two by anti-arrhythmic agents. Atrial contraction occurred immediately after restoration to sinus rhythm. The TDI measured atrial contraction velocity (TDI-A) was significantly higher in both left and right atrial free wall at 1 min when compared to 20 min and 4 hours (LA: 4.0±2.4 Vs 2.8±1.5 Vs 3.2±2.3 cm/s, $p<0.05$; RA: 6.8±3.2 Vs 5.0±2.5 Vs 4.9±2.2 cm/s, $p<0.05$). There was no change in diastolic early and atrial filling velocities as measured by transmitral and transtricuspid inflow pattern. However, there was better initial atrial relaxation as reflected by a shorter pulmonary vein atrial reversal time (94±42 Vs 118±25 Vs 125±19 ms, $p<0.05$) and higher pulmonary vein systolic velocity (42.2±5.8 Vs 33.3±9.5 Vs 36.6±10.1, $p<0.05$). For left ventricular systolic function, TDI derived systolic velocity at mitral annulus was also significantly increased at 1 min and 4 hour when compared to 20 min (5.1±1.2 Vs 4.5±0.6, $p<0.05$). In addition, the left ventricular fractional shortening (30±6 Vs 37±6%, $p=0.02$) and ejection fraction (66±7 Vs 74±7%, $p=0.02$) increased significantly at 4 hours. The above parameters did not change by a maximal energy shock (300V) at sinus rhythm indicating that the changes were related to atrial mechanical remodeling rather than the shock itself.

Conclusion: Early restoration of sinus rhythm by IAD will not result in atrial stunning, but rather atrial mechanical function is enhanced. This may explain the improved ventricular function.