Heart Failure

GW25-e1578
Obesity paradox in patients with atrial fibrillation and heart failure
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Objectives: An obesity paradox, a "paradoxical" decrease in morbidity and mortality with increasing body mass index (BMI), has been shown in patients with cardiovascular diseases. However, whether this phenomenon exists in atrial fibrillation (AF) patients with concomitant heart failure (HF) is not known.

Methods: This study consecutively enrolled AF patients presenting to an emergency department at 20 hospitals in China from Nov 2008 to Oct 2011. AF concomitant HF patients were categorized as underweight (BMI<18.5), normal (BMI 18.5 to <24), overweight (BMI 24 to <28), and obese (BMI ≥28 kg/m²). Multivariate Cox proportional hazards regression was used on all the patients. End points of the analyses were all-cause mortality and cardiovascular mortality.

Results: A total of 806 AF patients with concomitant HF were included in the analysis, mean BMI was 23.3±4.1 kg/m². A total of 153 deaths occurred during the 12-month follow-up, all-cause mortality was 19% in the whole patients, in underweight patients, normal weight, overweight, obese categories were 28.7%, 23.6%, 10.4%, and 11.8% respectively (P<0.001). The cardiovascular mortality in whole patients was 14%, in underweight, normal weight, overweight, obese categories were 21.8%, 17.2%, 7.8% and 8.8% respectively (P<0.001). On multivariate analysis, as a continuous variable, BMI was not a risk factor for all-cause mortality (HR 0.91, 95% CI 0.87-0.95; P<0.001), and for cardiovascular mortality (HR 0.91, 95% CI 0.86-0.96; P<0.001); as a category variable, obesity (HR 0.50, 95% CI 0.26-0.94, P=0.032) and overweight (HR 0.40, 95% CI 0.25-0.63, P<0.001) were significantly associated with a lower risk of all-cause mortality, and overweight also with a lower cardiovascular death (HR 0.45, 95% CI 0.26-0.76, P=0.003) compared to normal weight patients.

Conclusions: Our study showed an "obesity paradox" exists in AF patients with concomitant HF. Obesity was not a risk factor for 12-month mortality in AF and HF patients. Overweight AF patients have better survival and outcomes than normal weight (BMI 18.5-24.9 kg/m²) patients.

GW25-e2316
Sildenafil is effective in the treatment of heart failure patients with reduced ejection fraction: a meta-analysis of randomized controlled trials
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Objectives: Several clinical trials have evaluated the PDE5 inhibitors sildenafil as a potential adjunct in the treatment of heart failure (HF) with mixed results. Thus, we conducted this meta-analysis to evaluate the clinical viability of sildenafil in the treatment of HF.

Methods: Relevant studies were searched and identified in the MEDLINE and EMBASE databases. Randomized clinical trials (RCT) comparing sildenafil to placebo, in heart failure patients, reporting at least one outcome of interest were included. Data were extracted regarding the characteristics and clinical outcomes.

Results: We identified 9 RCTs enrolling 612 HF patients. There were no significantly different in adverse events between sildenafil group and placebo group (RR=1.10, 95% CI 0.74-1.65, P=0.41), whereas sildenafil therapy was associated with a marked improvement in hemodynamics parameters peak VO2 (MD=3.25, 95% CI 2.07-4.42, P<0.0001) in HF with reduced ejection fraction (HF-REF patients) but not in HF with preserved ejection fraction (HF-Preserved fraction). Also, sildenafil therapy improved VO2 at anaerobic threshold (AT) (MD=3.47, 95% CI 1.68-5.27, P=0.0002), VE/VO2 slope (MD=7.06, 95% CI 8.93-5.19, P<0.0001) and LV ejection fraction (MD=3.43, 95% CI 3.66-7.20, P<0.0001) than placebo in HF patients, which had no impact on blood pressure and heart rate. For quality of life (emotional function, fatigue and breathlessness), there was no significant difference between the two groups.

Conclusions: Sildenafil improved hemodynamic parameters particularly in HF-REF patients comparing with placebo, yet with no increase in adverse events. Sildenafil treatment was well tolerated and had no impact on quality of life.

GW25-e3541
miR21* contributes to sildena-induced cardiac dysfunction
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Objectives: Sildenafil-induced cardiac dysfunction is characterized by myocardial infarction and cardiac dysfunction (RD). The mechanism of non-coding RNAs, has been reported to play important roles in a wide range of cell functions including cell proliferation, differentiation, and apoptosis, making them novel contributors for many human diseases. However, the role of miRNAs in sildena-induced cardiac dysfunction is unclear. This study aims at investigating the role of miR21* in sildena-induced cardiac dysfunction.

Methods: E.coli lipopolysaccharide (LPS) (5mg/kg) was administered to C57BL/6 mice to induce a sildena-induced cardiac dysfunction model within 5-7 h. Cardiac function was assessed by Echocardiography 5-6th post-LPS administration. Mice were then obtained on 9th day after LPS treatment for gene expression and protein analysis. A systematic analysis of cardiac miRNA profiles using an established miRNAarray was performed to assess dys-regulated miRNAs in sildena-induced cardiac dysfunction. Transmission electron microscopy analysis was undertaken by myocardium tissue. To forced expression of miR-21, miR-21 agonors were injected in the tail vein of C57BL/6 mice on 3 consecutive days with a total of 30nmol/kg agonor followed by LPS administration.

Results: LPS induced a 15% reduction in fractional shortening (%FS) and a 25% decrease in ejection fraction (%EF). In addition, LPS leads to production of inflammatory cytokines such as TNFα, IL-6 IL-1β and also reduces cardiac energy utilization including FA oxidation and glucose metabolism. miRNA arrays indicated that the expression level of miR21 was increased by 32 fold in sildena-induced cardiac dysfunction and the change of miR21 was verified by quantitative reverse transcription polymerase chain reactions (RT-PCRs). Over-expression of miR-21 with systemic delivery of agonor led to a 5% decrease in FS and a 9% decrease in EF as compared to scramble control. Transmission electron microscopic micrographs of left ventricle tissue showed significant dysfunction in mitochondria, cytoplasmic disorganization and loss and lipid droplets. HE staining and PCR result of inflammatory cytokines indicated that the aggravation of the LPS induced cardiac dysfunction by miR21 agonor was not associated with alteration in inflammation. Interestingly, elevation of miR21 was also noted when NRCMs were exposed to LPS. Western blotting indicated that the inhibition of miR21 in NRVMs by 21 -anti-sense resulted in the increase of PGC-1a. Conversely, over-expression of miR21 by 21 -mimic in NRVMs led to significant inhibition of PGC-1a. These results indicate that PGC-1a is a potential target gene for miR-21.

Conclusions: In conclusion, miR-21 contributes to sildena-induced cardiac dysfunction potentiality via targeting PGC-1a. Targeting miR-21 might be a novel therapeutic strategy for the treatment of sildena-induced cardiac dysfunction and heart failure.

GW25-e2361
prevalence, predictors and prognostic significance of early recovery of normal left ventricular ejection fraction in patients with non-ischemic dilated cardiomyopathy
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Objectives: The study was designed to determine the prevalence, predictors and prognostic significance of early recovery of normal left ventricular ejection fraction (LVEF) during in a cohort of Chinese patients with non-ischemic dilated cardiomyopathy (NIDCM).

Methods: A total of 490 consecutively hospitalized patients with NIDCM and LVEF of 40% or less by echocardiography were evaluated by retrospectively reviewing the electronic database of the institutional heart failure registry. Echocardiographic and clinical data were available for 260 patients (53%) at the early follow-up (9±4 months). Early recovery of normal LVEF was defined as an increase in LVEF to a level of 50% or greater within one year. An array of baseline variables regarded as potentially relevant to recovery was evaluated to identify predictors of early recovery using logistic regression analysis. The patients were followed thereafter for 22±14 months to evaluate the long-term prognostic value of early recovery by means of Cox hazard proportional model and receiver operating characteristic analysis.

Results: Early recovery of normal LVEF was found in 114 of 260 patients (44%) at a mean follow-up period of 7±4 months, showing a significant increase in LVEF from 30.4±5.8 % at baseline to 54.7±4.0 % at early follow-up (P<0.001), with a mean increase of 24.2±6.7 %. This increase in LVEF was associated with a marked decrease in left ventricular end-diastolic diameter (LVEDD) from 64.9±6.2 mm to 54.3±5.0 mm (P<0.001), with a mean decrease of 10.6±5.5 mm. Multivariate logistic regression analysis showed that baseline independent predictors of early recovery included a history of hypertension, shorter symptom duration, higher systolic blood pressure at presentation and smaller LVEDD on echocardiogram. When added to a prognostic baseline model including serum sodium on admission, right ventricular diameter on echocardiogram and use of a beta-blocker on discharge, the presence of non-coding RNAs, has been reported to play important roles in a wide range of cell functions including cell proliferation, differentiation, and apoptosis, making them novel contributors for many human diseases. However, the role of miRNAs in sildena-induced cardiac dysfunction is unclear. This study aims at investigating the role of miR21* in sildena-induced cardiac dysfunction.

Conclusions: Early recovery of normal LVEF, evident in up to 44% of our study patients on contemporary medication, was associated with some baseline clinical and echocardiographic parameters and significantly improved the long-term prognostic stratification of NIDCM.