

Purpose: We investigated the association between different classes of antihyperglycemic drugs and NAF.

Methods: This was a nested case-control study performed using the database of National Health Insurance Program in Taiwan. Each participant aged 20 years and older who were NAF from 2005 to 2013 were assigned to the NAF group, whereas case was sex-, age-, diabetes duration-, index date-matched, and Charlson Comorbidity Index score-matched randomly selected participant without NAF were assigned to the non-NAF group. Multivariable logistic regression model was used for the estimation of odds ratios (ORs) and 95% confidence intervals (CIs) of NAF associated with use of different classes of antihyperglycemic agents. Non-users served as the reference group.

Results: We identified 2882 cases and 11528 controls. The risk of NAF after adjusting for sex, age, comorbidities, and concurrent medication was higher among the users of insulin than among the non-users (OR, 1.19, 95% CI, 1.06–1.35). Patients who took biguanides and thiazolidinediones were at lower risk of developing NAF than the non-users (OR, 0.81, 95% CI, 0.71–0.95; OR, 0.72, 95% CI, 0.63–0.83). Acarbose, glinides, sulfonylureas, and dipeptidyl peptidase 4 inhibitors were not associated with the risk of NAF.

Conclusions: In this population, use of biguanides and thiazolidinediones were associated with a low risk of NAF during the long-term follow-up. The results of this study may provide important clinical implications to the mechanistic links between anti-hyperglycemic drugs and NAF in diabetes mellitus.

Acknowledgement/Funding: Chung Shan Medical University Hospital

P4458 | BEDSIDE

Glycemic variability influences to bring left ventricular positive and reverse remodeling in patients with ST-segment elevation acute myocardial infarction

Y. Minamoto¹, N. Iwahashi¹, J. Kirigaya¹, H. Takahashi¹, Y. Matsuzawa¹, M. Konishi¹, N. Maejima¹, K. Hibi¹, M. Kosuge¹, T. Ebina¹, K. Kimura¹, K. Tamura². ¹Yokohama City University Medical Center, Cardiovascular center, Yokohama, Japan; ²Yokohama City University Hospital, Department of Medical Science and Cardiorespiratory Medicine, Yokohama, Japan

Background: Although the relationship between glycemic variability (GV) and left ventricular remodeling (LVR) has been reported, the mechanism of leading left ventricular reverse remodeling (LVRR) and LVR in patients with ST-segment elevation acute myocardial infarction (STEMI) remains unclear.

Methods: We investigated 126 patients with STEMI who underwent reperfusion therapy within 12h onset. We analyzed GV, as determined by a continuous glucose monitoring system (CGMS; iPro2, Medtronic, USA), and the LV by cardiac magnetic resonance imaging (CMR). All patients were equipped with CGMS in a stable phase after admission. CMR were performed 7days and 7 months repeatedly. The mean amplitude of glycemic excursions (MAGE) was calculated. LVR was defined as an absolute increase in LVESVI of >20%, and LVRR as an absolute decrease in LVESVI of >10%. Patients were divided into 3 groups which were occurred LVRR (Group RR; n=36) or LVR (Group PR; n=35) or not changed (Group NR; n=55).

Results: Group RR had more frequently with culprit LAD (75% vs. 54% vs. 36%, p=0.001). MAGE were significantly lowest in group RR (35.2±17.3 vs. 51.5±20.1 vs. 44.8±25.0mg/dl, p=0.006). Multivariate analysis revealed that MAGE were independent predictor of LVRR (p=0.008) and LVR (p=0.023).

Conclusion: The difference of glycemic variability may be the main factors of the change of LV function after STEMI.

P4459 | BEDSIDE

Ranolazine reduces repolarization heterogeneity in symptomatic patients with diabetes, non-obstructive coronary artery disease, and impaired coronary flow reserve

E. Evaristo¹, F.G. Stocco¹, N.R. Shah², M.K. Cheezum³, J. Hainer³, C. Foster³, B.D. Nearing⁴, M. Di Carli³, R.L. Verrier⁴. ¹University of Sao Paulo, Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil; ²Brown University, Department of Medicine, Providence, United States of America; ³Brigham and Women's Hospital, Department of Medicine, Boston, United States of America; ⁴Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, United States of America

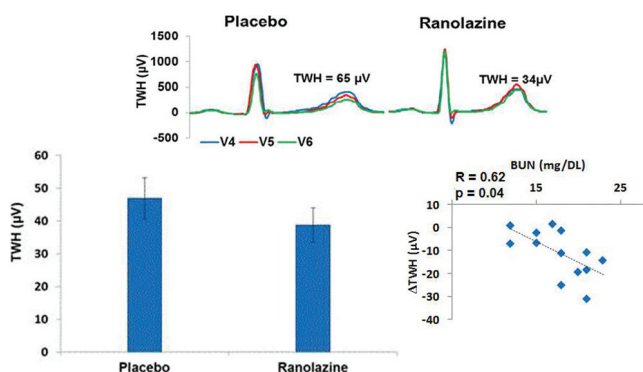
Background/Introduction: Experimental evidence suggests that ranolazine decreases susceptibility to ischemia-induced arrhythmias independent of an effect on coronary flow.

Purpose: We analyzed whether in patients with diabetes, impaired coronary flow reserve (CFR), and non-obstructive angiographic coronary artery disease (CAD), ranolazine alters T-wave heterogeneity (TWH), a new ECG marker of repolarization abnormalities shown to predict sudden cardiac death.

Methods: We studied all 16 symptomatic patients with analyzable ECG recordings who were enrolled in a double-blind, cross-over, placebo-controlled study (NCT01754259) before and after ranolazine. TWH was quantified without knowledge of treatment assignment by second central moment analysis, which assessed the interlead splay of T waves in precordial leads about a mean waveform as the central axis.

Results: At no-drug baseline, TWH was 54±7 μV at rest and was not altered by placebo (47±6 μV, p=0.47). By comparison, following ranolazine, TWH was

significantly reduced by 28% (to 39±5 μV, p=0.002); representative example and group data are shown (figure).s Ranolazine's effects on TWH were correlated with baseline blood urea nitrogen (BUN) (p=0.02, r=0.62).



Ranolazine reduces TWH

Conclusion: Ranolazine reduces TWH, an indicator of arrhythmogenic repolarization abnormalities, in symptomatic patients with diabetes, non-obstructive CAD, and impaired CFR. The extent of the cardioprotective effect appears in part to be related to baseline BUN levels, a marker of elevated sympathetic tone. Thus, ranolazine may reduce TWH in part by suppressing adrenergically mediated enhancement of late INa.

Acknowledgement/Funding: Gilead Sciences

P4460 | BEDSIDE

Diabetes mellitus and ventriculo-arterial coupling

C. Zito¹, I. Fabiani², S. La Carrubba³, L. Carerj¹, R. Citro⁴, F. Benedetto⁵, V. Di Bello⁶, F. Antonini Canterin⁶, I. Monte⁷, S. Carerj¹, P. Colonna⁸ on behalf of Italian Society of Cardiovascular Echography. ¹U.O. Policlinic G. Martino, Cardiology, Messina, Italy; ²University of Pisa, Cardiac and Thoracic Department, Pisa, Italy; ³Ospedali Riuniti Villa Sofia, Internal Medicine, Palermo, Italy; ⁴AOU S. Giovanni e Ruggi, Cardiology, Salerno, Italy; ⁵Bianchi Melacrino Morelli Hospital (BMM), Cardiology, Reggio Calabria, Italy; ⁶Santa Maria degli Angeli Hospital, Cardiac rehabilitation, Pordenone, Italy; ⁷University of Catania, Cardiology, Catania, Italy; ⁸University of Bari, Cardiology, Bari, Italy

Background: The interaction between Cardiac Function and Arterial System, index of global cardiovascular efficiency, is defined as Ventriculo-Arterial Coupling. This relation can be mathematically expressed as the ratio between Arterial Elastance (EA) and Left Ventricular (LV) End-systolic Elastance (EES). The non-invasive equations to derive the ratio are complex but can easily be implemented in computerized algorithms, allowing the adoption of this index in the clinical arena.

Purpose: To determine, in a large sample of asymptomatic patients (Stage A and B Heart Failure), the correlation between diabetes mellitus and ventriculo-arterial coupling.

Methods: We enrolled in the study 1402 consecutive patients from a large multicenter survey on asymptomatic heart failure patients. Evaluation included a complete physical exam, with detailed history, ECG and standard Echocardiography, according to current recommendations on chamber quantification.

Ventriculo-arterial coupling has been measured as EA/EES, where EA=ESP/SV (the ratio of End Systolic pressure-Systolic Arterial Pressure * 0.9- to 2D-Echo Stroke Volume, SV) and EES=ESP/ESV (the ratio of End Systolic pressure to End-systolic Volume, ESV). Ventriculo-arterial coupling was classified as normal for values between 0.3 and 1.3, as previously described. Diabetes Mellitus and Obesity/Over-weight were defined according to standard guidelines.

Results: Of 1402 patients (Age 57.4±13.5 years), 738 were Male (52.6%) and 664 Female (47.4%). On average, patients presented an high cardiovascular risk profile (Smokers 24.5%; Family History of Cardio-vascular disease 36.2%; Diabetes 14.6%; Arterial Hypertension 55.1%; Dyslipidemia 36.8%; Over-weight/Obesity 31.5%). Ejection Fraction (EF) was 61±1%. Patients presented a variable degree of diastolic dysfunction (35.3%).

Pathological Coupling has been significantly associated to Diabetes (RR 2.2 CI 95% 1.4–3.3; p<0.001).

In multivariate analysis, Diabetes was independently associated to Pathological Coupling, also after introduction in a model of Logistic Regression of gender, age and EF as covariates (see Table).

Conclusions: Diabetes Mellitus is independently associated to pathological Ventriculo-Arterial Coupling in asymptomatic patients with Heart Failure.