P2262 | BENCH
Predictors and prognostic value of biomarkers in patients and an intermediate or low risk grace score

I. Markava, A. Miadzvedzeva, L. Helis, I. Lazareva. *Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Purpose: To assess the prevalence, predictors and prognostic value of biomarkers underlying the pathological process of atherothrombosis in patients with known or suspected coronary artery disease having an intermediate or low risk Grace Score.
Methods: Eight biomarkers [myeloperoxidase (MPO), von Willebrand factor (vWf), high-sensitivity C-reactive protein (hsCRP), homocysteine, cardiac troponin T (cTnT), B-type natriuretic peptide (BNP), antithrombin III (AT III), D-dimers] and mean platelet volume (MPV) were measured in 150 patients presenting on admission with symptoms of unstable angina (M/F=120/60, 61±12.2 years) and having an intermediate or low risk according to Grace Score. MPV measurements were obtained from the admission blood work. All samples were obtained in standardized dipotassium ethylenedinitrotetraacetic acid (EDTA) tubes. The measurements were performed using automated hemograms (Bayer Advia 2120, Bayer Diagnostics, NY). End points were all-cause mortality and major cardiac events (MACE, i.e., cardiac death or myocardial infarction).
Results: Over a mean follow-up of 18±3.4 months 30 MACE occurred. MPO >283,7pmol/ml (OR 1.01, 95% CI 1.00-1.02, p <0.001), MPV> 8,8 fl (OR 5.84, 95% CI 3.41-7.20, p <0.002), D-dimers > 250mcmol/l (OR 1,3, 95% CI 1.00-1.57, p <0.05) were predictors of MACE. Even after log transformation, these biomarkers remained independent predictors. In multivariate analysis
Conclusions: MPV, MPO and D-dimers can be used as a risk biomarker in prognosticating the 12 months outcomes for unstable angina and help in decision making in intermediate and low risk patients.

P2263 | BENCH
Associations of myeloperoxidase, as a marker of oxidative stress and plaque instability, with coronary artery disease and cardiovascular event

I. Markava, A. Miadzvedzeva, L. Helis, I. Lazareva. *Republican Scientific and Practical Centre of Cardiology, Minsk, Belarus*

Background: Myeloperoxidase (MPO) may be a useful marker for oxidative stress and plaque instability. Recent studies have shown that plasma MPO is elevated in patients with unstable angina and acute myocardial infarction. However, its prognostic value remains unclear. The aim of this study was to investigate associations of MPO with coronary artery disease and cardiovascular event.
Methods and results: 215 patients (mean age 66±10 years) undergoing coronary angiography (CAG) were enrolled and divided into three groups: acute coronary syndrome (ACS, n=144), stable angina pectoris (SAP, n=49) and healthy people (Control, n=22) in the cross-sectional study. Each coronary risk factors and patients characteristic were evaluated. Plasma MPO level were determined by immunoassay Abbott Architect and other laboratory data were measured by standard laboratory methods. These Data were examined statistically. A cardiac event, which was defined as cardiac death, rehospitalization for ACS, rehospitalization for worsening heart failure, or coronary restenosis, was monitored for 12 months after admission. Statistically, plasma MPO levels were higher in ACS patients (284.6±14.3 pmol/ml) than in SAP (155.2±12 pmol/ml) and healthy control (50±1.5 pmol/ml) (P<0.05). HsCRP (high sensitive C-reaction protein) and BNP (brain natriuretic peptide) were significantly increased in ACS patients over SAP patients and Control patients. Additionally, adrenalin induced aggregation levels were significantly decreased in ACS patients over other groups (80±3.5%, 60±4.8% vs. 41.8±4.3%, P<0.05). Furthermore, a total of 50 (34.7%) cardiovascular events occurred during the 1 year follow-up period. The cardiovascular event rate was higher in patients with increased MPO. A Kaplan-Meier analysis revealed that patients with increased MPO had a higher risk for cardiac events than those without (P<0.05).
Conclusion: This study shows that measurement of plasma MPO may be considered to be a sensitive and specific biomarker for diagnosis of ACS and may substantially improve the early risk stratification of patients with coronary artery disease, and suggests a possibility that plasma MPO level may become one element which predicts a cardiovascular event.

P2264 | BEDSIDE
Peripheral and coronary vascular function in patients with variant angina

R. Parrinello, A. Villano, G. Russo, A. Di Franco, P. Tarzia, R. Nerla, S. Figliozzi, A. Sestito, G.A. Lanza, F. Crea. *Catholic University of the Sacred Heart, Institute of Cardiology, Rome, Italy*

Purpose: Coronary artery spasm responsible for variant angina (VA) is usually focal and involves one or more segments of epicardial coronary arteries. However, it is not clear whether a more diffuse vascular abnormality can be present in these patients. In this study we investigated whether VA patients present abnormalities in coronary microvascular (CMV) function and/or in peripheral arterial function.
Methods: We studied 23 VA patients (i.e., angina at rest, ST-segment elevation during angina attacks and documented occlusive coronary spasm at angiography; age 67±7 years, 17 men), and 15 sex- and age-matched healthy controls (age 64±7 years, 7 men). In all subjects we assessed endothelium-dependent and endothelium-independent CMV function, by measuring coronary blood flow (CBF) response to adenosine and to cold-pressor test (CPT), respectively, in the left anterior descending artery by trans-thoracic Doppler echocardiography. Endothelium-dependent and endothelium-independent peripheral vascular function was assessed by measuring flow-mediated dilation (FMD) following forearm post-ischemic hyperaemia and nitrate-mediated dilation (NMD) of the brachial artery, respectively.
Results: The results are summarized in the table. In VA patients, CBF response to adenosine, CBF response to CPT and peripheral FMD were lower, whereas NMD was higher (p<0.01) compared to healthy controls. The differences persisted statistically significant after adjustment for cardiovascular risk factors and drug therapy.

	Variant angina (n=23)	Healthy controls (n=15)	p
CBF response to ADO	1.7±0.3	2.8±0.5	<0.01
CBF response to CPT	1.7±0.2	2.5±0.6	<0.01
FMD (%)	3.9±2.1	7.5±1.6	<0.01
NMD (%)	16.7±1.8	12.7±2.2	<0.01

Conclusions: Our data show that patients with VA have a generalized vascular dysfunction that involves both systemic arteries and coronary microcirculation.

P2265 | BEDSIDE
The impact of a short psychological intervention on quality of life and angina control in patients with chronic refractory angina

M. Khan[1], S. Thappar[1], S. Taylor[1], A. Scally[2], P. Sainsbury[1]. *[1]Bradford Royal Infirmary, Bradford, United Kingdom; [2]University of Bradford, Bradford, United Kingdom*

Introduction: Patients with refractory angina (RA) have chronic disabling chest pain that significantly impacts upon their quality of life. The prevalence of RA is thought to effect in excess of 5% of patients diagnosed with angina. The focus of angina management in this patient group has traditionally revolved around symptom management through medication, angioplasty and surgery. However, there is a clear lack of a structured pathway of care that addresses their maladaptive psychological response. As a result patients feel that they have no control over their angina leading to high utilization of medical services, anxiety, depression and poor quality of life.
Methods: Bradford Refractory Angina Service (BRAS) has designed a short psychological intervention based upon an angina education program combined with a course of cognitive behavioral therapy. It is delivered in four two hour sessions over the course of one month by a Clinical Nurse Specialist and a Clinical Psychologist. The impact of this intervention was examined in 33 consecutive patients attending the BRAS between 20011-2012 (25 males, 6 females median age=63). Quality of life scores were assessed by the SF36 questionnaire and angina frequency/GTN use by the Seattle Angina Questionnaire (SAQ) pre and post intervention. Both questionnaires are well recognized and have been previously validated. Two additional questions were asked of each patient pre and post intervention. "How much control do you feel you have over your angina?" (No control =0, full control 10) and "How much does angina restrict what you do? (Not at all 0, extremely restricted 10). Data were analysed using Wilcoxon paired testing and are presented as medians.
Results: Over the 4 week period of the psychological intervention, SF36 Quality of Life scores increased significantly (30 vs 44 P=0.0001) whilst levels of anxiety and depression decreased (8 vs 8 p=0.0049 and 9.5 vs 8 p=0.0152). In response to the question "How much control do you feel that you have over your angina" scores rose significantly (5 vs 7 p=0.0031) and in response to "How much does angina restrict what you do" scores fell significantly (8 vs 5 p=0.001). No significant change was noted in either angina frequency or GTN use.
Conclusion: A short psychological intervention combining education with cognitive behavioral therapy is effective in increasing patient's sense of control over their angina and improves their quality of life. This appears to be achieved independently of any improvement in angina frequency. Further research is required to see if this effect is maintained in the longer term.

P2266 | BEDSIDE
Ivabradin treatment in patients with acute coronary syndrome

A.A. Shavarov, G.K. Kiyakbayev, V.S. Moiseyev, Z.D. Kobalava. *Peoples' Friendship University of Russia, Moscow, Russian Federation*

Purpose: To assess the efficacy and safety of early administration of ivabradin in addition to metoprolol in patients (pts) with acute coronary syndrome (ACS).
Methods: The study included 98 ACS pts (64% men), mean age 72 (60; 76) years, with sinus rhythm and heart failure Killip class I. Pts were randomly assigned to metoprolol+ivabradin (M+Iv) group (n=50) and metoprolol (M) group (n=48) dose up-titration for 14 days. Mean doses were 100 (75; 125) mg for M and 10 (10; 10) mg for Iv in M+Iv group pts and 100 (100; 150) mg in M group pts. We evaluated heart rate (HR) at rest, systolic and diastolic blood pressure (BP), ECG parameters, incidence and duration of myocardial ischemia during 24 hour

ECG monitoring and treadmill test, 6-minute walk test (6-MWT). The primary end point of efficacy was achievement of target HR less 60 bpm at the 14th day of treatment. The primary combined end point of safety included incidence of arterial hypotension, sinoatrial and atrioventricular conduction disturbance, bronchial obstruction and visual disturbance.
Results: At the 14th day target HR by ECG measuring was achieved in 45 (90%) pts of M+Iv group and 40 (83%) pts of M group (p=0.33). Mean HR less 60 bpm measured by 24 hour ECG monitoring was observed in 38 (76%) and 30 (63%) respectively (p=0.14). There were no significant differences in BP level, incidence and duration ischemic episodes and result of 6-MWT. The primary combined end point of safety was documented in 9 (18%) pts of M+Iv group and 18 (38%) pts of M group (p=0.03).
Conclusion: Combined treatment with metoprolol and ivabradine showed a favorable safety profile and same antiischemic activity compared with metoprolol up-titration regimen in ACS pts.

ADJUNCTIVE MEDICAL THERAPY

P2268 | BEDSIDE
Efficacy of early intensive rosuvastatin therapy in patients with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention: randomized, placebo-controlled

H. Won[1], Y.G. Ko[1], D.H. Shin[1], J.S. Kim[1], B.K. Kim[1], D. Choi[1], M.K. Hong[1], J.H. Bae[2], D.S. Lim[3], Y. Jang[1]. *[1]Severance Cardiovascular Hospital, Seoul, Korea, Republic of; [2]Konyang University Hospital, Daejeon, Korea, Republic of; [3]Korea University, Anam Hospital, Seoul, Korea, Republic of*

Background: Early statin therapy before Percutaneous Coronary Intervention (PCI) reduced periprocedural myocardial infarction and improve clinical outcome in patients with stable angina pectoris or acute coronary syndrome. However, the efficacy of statin pre-treatment before PCI in patients with ST-Elevation Myocardial Infarction (STEMI) has limited information. The aim of this study was to evaluate whether high-dose statin before primary PCI in patients with STEMI affect infarct size and cardiac remodeling.
Methods: For this prospective randomized controlled study, 137 patients (117 men, age 57.6±11.5years) with STEMI were randomized to 40mg rosuvastatin pretreatment group (maintained for 7 days, n=66) before PCI or control group (placebo before primary PCI and 10mg rosuvastatin for 7 days, n=71). Both groups maintained 10mg of rosuvastatin from 8th day. Infarct size, left ventricular volume and transmural extent of infarction were assessed by Magnetic Resonance Image (MRI) within 3∼7 days after PCI and 3 months follow up. Primary endpoint was infarct volume of left ventricle by MRI.
Results: Baseline clinical and angiographic characteristics were similar between the 2 groups, except hypertension (58% in 40mg rosuvastatin group vs. 32% in control group, p=0.004). MRI at both acute and chronic phase was performed in 108 patients. On 3 months follow up, there was no difference in infarct volume between 40mg rosuvastatin group and control group (18.4±12.1 ml vs. 18.6±13.2 ml, p=0.944). Percentage of infarct volume (15.9±8.3% vs. 15.9±8.3%, p=0.943) and extent of transmural infarct (29.3±13.0% vs. 26.8±12.6%, p=0.334) were not significantly different between two groups. Clinical outcomes were similar between groups.
Conclusions: Early intensive statin pre-treatment before PCI in patients with STEMI did not reduce infarct volume at within 7 days and 3 months after PCI.

P2269 | BEDSIDE
Improvement of doppler derived coronary flow reserve in asymptomatic patients with previous percutaneous coronary intervention on left anterior descending coronary artery: effects of ranolazine

E. Tagliamonte[1], F. Rigo[2], T. Cirillo[1], C. Astarita[3], G. Quaranta[1], U. Marinelli[1], C. Romano[1], N. Capuano[1]. *[1]"Umberto I" Hospital, Operative Unit of Cardiology, Nocera Inferiore, Italy; [2]Hospital "dell'Angelo", Department of Cardiology, Mestre-Venice, Italy; [3]Santa Maria della Misericordia Hospital, Operative Unit of Cardiology, Sorrento, Italy*

Background: Ranolazine reduces the Na-dependent calcium overload via inhibition of the late sodium current, improving diastolic tone and oxygen handling. In patients with previous percutaneous coronary intervention (PCI), microvascular coronary dysfunction can be still present. Transthoracic Doppler-derived coronary flow reserve (CFR) is an index of coronary arterial reactivity and decreases under the condition with microvascular dysfunction as well as coronary artery stenosis. The aim of this study was to assess the effect of ranolazine on CFR in this patient group.
Methods: 48 asymptomatic patients (33 M, 15 F; mean age 66±11 years) with previous PCI on left anterior descending coronary artery (LAD) and no other significant coronary stenosis, was enrolled in the study. Within six weeks after PCI, they underwent baseline CFR assessment. Then they were randomly assigned to placebo or Ranolazine for 12 weeks (up-titrated from 350 to 750 mg twice, with increases every 4 weeks). CFR assessment was performed again at the end of treatment period.
Coronary flow was assessed in the left anterior descending coronary artery (LAD), and was identified as the color signal directed from the base to the apex of the left ventricle, containing the characteristic biphasic pulsed-Doppler flow signals. CFR were determined as the ratio of hyperemic, induced by intravenous dypiridamole administration, to baseline diastolic coronary flow velocity.
Results: There were no significant differences in baseline characteristics between Ranolazine and placebo group. CFR was successfully performed in all patients. Baseline CFR was not significantly different in Ranolazine and placebo group (2.23±0.59 vs. 2.19±0.55 - p = ns). After 12 weeks CFR significantly increased in Ranolazine group (2.65±0.64 vs. 2.23±0.59 - $p < 0.01$) but not in placebo group (2.24±0.58 vs. 2.19±0.55 - p = ns). No patient dropped out during 12 weeks therapy. Side effects were sinilar in both groups.
Conclusions: In asymptomatic patients with previous PCI on LAD coronary artery Ranolazine is able to improve CFR. This is probably due to improvement in microvascular coronary dysfunction. Larger studies will be able to confirm these data.

P2270 | BENCH
Effect of combination therapy of ezetimibe and rosuvastatin on regression of coronary atherosclerosis in Japanese patients with stable coronary artery disease

J. Masuda[1], T. Tanigawa[1], T. Nakata[1], S. Nakamori[1], T. Sawai[1], H. Nakajima[1], N. Yamada[1], M. Nakamura[2], M. Nisikawa[3], M. Itou[1]. *[1]Mie University Graduate School of Medicine, Department of Cardiology and Nephrology, Tsu, Japan; [2]Department of Clinical Cardiovascular Research, Mie University Graduate School of Medicine, Tsu, Japan; [3]Clinical Trials Support Center, Mie University Hospital, Tsu, Japan*

Background: Recent clinical trials have demonstrated that intensive low-density lipoprotein-cholesterol (LDL-C) lowering therapy by strong statins could prevent recurrent cardiovascular event and have beneficial regressive effects on coronary plaques. Otherwise, the use of ezetimibe in combination with statin has been reported to provide greater reduction in LDL-C level than statin monotherapy. However, it is not established whether additional LDL-C lowering achieved with the addition of ezetimibe to statin monotherapy will lead to further reduction in coronary plaque volume.
Methods: In this prospective, open-label, randomized study, 40 patients with stable coronary artery disease (CAD) requiring percutaneous coronary intervention (PCI), whose LDL-C levels were higher than 100 mg/dl, were divided into combination therapy group (n=21, rosuvastatin 5mg plus ezetimibe 10mg daily) or statin monotherapy group (n=19, rosuvastatin 5mg daily). Serial volumetric intravascular ultrasound (IVUS) analysis were performed at baseline and after 6 months of follow-up for a non-PCI site.
Results: LDL-C level was significantly decreased by 54.1% in the combination group (from 132.7±31.7 mg/dl to 59.5±17.1 mg/dl, $p<0.001$) vs. 42.1% in the monotherapy group (from 122.0±15.7 mg/dl to 69.1±19.7 mg/dl, $p<0.001$). Plaque volume (PV) was significantly reduced in the combination group (14.2±12.9% decrease) compared with the monotherapy group (2.1±17.0% decrease; p=0.016). Moreover, percent change in PV showed a significantly positive correlation with percent change and nominal change of LDL-C (r=0.403, p=0.011, and r=0.418, p=0.008, respectively), and percent change of non high-density lipoprotein cholesterol (r=0.380, p=0.024). It also showed a significant positive correlation with follow-up small dense LDL level (r=0.455, p=0.006).
Conclusions: Aggressive LDL-C lowering therapy by ezetimibe in addition to statin may exert significant regression of coronary plaque volume compared with usual-dose statin monotherapy in patients with stable CAD.

P2271 | BEDSIDE
Ameliorating effects of miglitol on postprandial hyperglycemia and triglyceride/HDL ratio are associated with beneficial impact on atherosclerosis in diabetic patients with coronary artery disease

D. Terashita[1], T. Sawada[1], H. Shiotani[2], Y. Nagasawa[1], T. Mizoguchi[1], T. Mizuguchi[1], H. Okamoto[1], S. Kim[1], M. Koide[3], A. Takarada[1]. *[1]Hyogo Prefectural Awaji Hospital, Sumoto, Japan; [2]Department of Preventive Medicine, Graduate School of Health Sciences Kobe University, Kobe, Japan; [3]Koide clinic, Sumoto, Japan*

Background: Previous studies have shown that α-Glucosidase Inhibitors (α-GI), which reduce postprandial hyperglycemia without stimulating insulin secretion, may also significantly reduce the risk of Coronary Artery Disease (CAD), while glinides, which improve postprandial hyperglycemia via postprandial insulin secretion, do not appear to affect CAD. The precise reason for this disparity remains unknown.
Methods and results: A total of 104 diabetic patients with CAD were randomly divided into 2 group; patients treated with miglitol (M-group, n=52) and those treated with nateglinide (N-group, n=52). The baseline characteristics were almost the similar in the 2 groups. After 4 months' treatment, body weight and waist circumference was significantly reduced in the M-group but not in the N-group. Although both groups demonstrated a significant improvement in hemoglobinA1c, 1,5-anhydroglucitol, total cholesterol, low-density lipoprotein cholesterol and Apolipoprotein B (ApoB), only the M-group demonstrated an increase in high-density lipoprotein cholesterol (HDL-C) and reductions in the in-