

CARDIOVASCULAR DISEASE CLINICAL RESEARCH

ISCHEMIC HEART DISEASE

GW26-e4457

Associations among genetic variants in *ccl17*, serum CCL17 levels, and coronary artery disease in Chinese Han population

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OBJECTIVES Our previous study has indicated that serum chemokine ligand 17 (CCL17) levels are associated with coronary artery disease (CAD) and atherosclerosis severity. This study is to further determine the relationship among genetic variants in *ccl17*, serum CCL17 levels, and CAD in Chinese Han population.

METHODS Nine hundred and forty seven patients (153 patients with non-CAD and 794 patients with CAD) presenting to our center for coronary angiography were recruited consecutively. Five tag single-nucleotide polymorphisms (SNPs) including rs223895, rs4784805, rs9302690, rs223899, and rs223828 were identified using HapMap Project data and determined by TaqMan genotyping. Serum CCL17 levels were determined by enzyme-linked immunosorbent assay. With an additive genetic model, both linear and logistic regression models (adjusted for covariates of age, gender, body mass index, hypertension, diabetes, lipid profile, smoking status, and family history of CAD) were used to investigate the relationship among tag SNPs, serum CCL17 levels, and CAD.

RESULTS Minor allele T at rs223828 was significantly associated with higher serum CCL17 levels ($\beta = 18.92$ per effect allele of SNP, 95% confidence interval 2.16~35.68, $p = 0.027$). Besides, minor allele T at rs223828 was also associated with increased risk of CAD (Odds ratio = 2.39 per effect allele of SNP, 95% confidence interval 1.43~4.02, $p = 0.001$). There is no significant association among other SNPs, serum CCL17 levels, and CAD risk.

CONCLUSIONS rs223828 in *ccl17* is linked to both serum CCL17 levels and risk of CAD in Chinese Han population.

GW26-e5419

Does heart failure cause ischemia?

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OBJECTIVES New onset of heart failure (HF) is indication for investigation of significant coronary artery disease (CAD), including stress test or coronary angiogram. In many cases, the angiogram results showed mild CAD with mild to moderate left ventricular dysfunction and the management was suggested to continue medical treatment without indication for percutaneous coronary interventions (PCI) or open heart surgery (CABG). In these cases, did CAD cause HF or did HF cause ischemic changes on EKG and chest pain? Did the elevation of the left ventricular (LV) end diastolic pressure (representing the systolic and diastolic dysfunction) cause any EKG changes suggestive ischemia?

METHODS 20 patients were consecutively selected with the following criteria: (1) history of new onset of HF on presentation to the emergency room (shortness of breath, rales in lungs, treated with intravenous diuretics) (2) having chest pain in the index admission, (3) EKG changes of ischemia (only ST depression or T wave inversion) (no ST segment elevation) AND (4) negative coronary angiogram not requiring PCI or CABG. All patients underwent coronary angiogram and LV angiogram. Electrocardiogram (EKG) changes were classified as type 1 (mild nonspecific ST T changes) type 2 (ST depression (>1mm) and deep symmetrical T wave inversion (type 3). Ejection fraction (EF), aortic systolic (AOS) and diastolic pressure (AOP) were recorded. The key formula is the coronary perfusion pressure (CPP) = AOD-LVEDP. How was the CPP in patients with HF and no severe CAD?

RESULTS The results showed all patients had high LVEDP. However, the AO Diastolic (AOD) pressure was lower during the index events. In patient with elevated LVEDP and significant low AOD, with CPP<20 mmHg, the EKG changes with deep T waves inversion (type 3) were very obvious even the coronary angiograms were negative. If the CPP was between 20-30 mmHg, the EKG changes were more of type 2 of mild ST depression. If the CPP> 30 mmHg, there were normal EKG or only type 1 non specific STT changes. It is clearly that CPP< 30 mmHg caused ischemia on patients and in EKG. Once the elevated LVEDP was treated to a lower level or when the OAD pressure improved (no more hypotension), the EKG changes disappeared (from type 3 to type 1) and the chest pain improved.

CONCLUSIONS In patients presenting with HF associated with chest pain and EKG changes suggested of ischemia, a combination of low aortic diastolic pressure (AOD) and elevated LVEDP was associated with ischemia in patients with no significant lesions in coronary arteries. The reason is that the coronary perfusion pressure (CPP) is the difference between AOD and LVEDP and the CPP could be decreased and cause ischemia (due to low perfusion pressure) even the coronary arteries are patent. These results are important to understand that LV dysfunction could cause ischemia in selected patients and could be the cause of death in patient with elevated LVEDP (e.g. CAD with LV dysfunction or aortic stenosis) undergoing PCI.

GW26-e1326

Exercise induced myocardial but not peripheral muscle ischemia is associated with rise in plasma macrophage migration inhibitory factor (MIF)

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OBJECTIVES Early diagnosis is critical for the management of acute myocardial infarction (AMI). Beside ECG, circulating cardiac biomarkers are routinely used for the early detecting myocardial necrosis including CK, CK-MB, troponins (Tns) or hsTn, and myoglobin. These traditional biomarkers have not been helpful for diagnosing AMI until 3-6 after symptoms, when their blood levels rise and some have poor cardiac-specificity. Recent studies demonstrated macrophage migration inhibitory factor (MIF) rose in early MI, and, unlike hsTn, predicted infarct size. It is unknown whether ischemia without infarction is also associated with MIF. In this study, MIF and hsTn were examined in patients experiencing myocardial ischemia. The possibility of MIF released from ischemic skeletal muscle was also examined in patients with peripheral artery obstructive disease (PAOD).

METHODS There were 2 patient cohorts. The first (n=83) comprised chest-pain patients referred for possible myocardial ischemia by either stress echocardiography or nuclear images after exercise. The second cohort comprised patients with known PAOD (n=10) who underwent a 6 minutes walk test (6MWT) and developed claudication. In both groups blood samples were obtained before (baseline) and at 5 and 15 mins after excise. All blood was stored at -80°C prior to analysis for MIF (ng/ml), hsTn ($\mu\text{g/l}$) and hsCRP (mg/L). In the first cohort subjects with exercise induced onset of symptoms and regional wall motion abnormality or reversible perfusion were classified as positive whilst those without such changes and without ECG changes were classified as negative. In addition, protein and mRNA expressions of MIF in mice hearts and leg muscles (n=5 for each) were also studied.

RESULTS In the chest-pain cohort there were 19 positive (63±10.6 years old) and 64 negative (62.5±10.6 years). No differences were in baseline hsCRP (2.7±2.0 and 4.3±12.7) or MIF (59.9±33.4 and 52.5±21.5) between positive and negative groups. No changes were with exercise for hsTn or hsCRP in either group. However, in the positive group, the 5 and 15 min MIF difference from baseline were 16.5±5.5 and 7.7±4.5 respectively while in the negative group they were 0.37±2.33 and -4.8±2.33. Both changes of MIF at 5 and 15 min from the baseline in positive group are significantly different ($p < 0.01$, $P < 0.05$ respectively) comparing with them in negative group. In contrast circulatory MIF levels in PAOD patient showed no statistically changes at 5min (63.4±55.6) and 15 min (41.4±14.7) after 6MWT compared with baseline (45.7±19.9). The MIF protein and mRNA were 3.05 ±0.38 vs. 1.00±0.53 and 29.6±15.3 vs. 1.4±0.4 in mice hearts and leg muscles respectively which are significant different between two tissues ($p < 0.001$).

CONCLUSIONS Plasma MIF elevation responding to myocardial ischemia indicates different mechanisms of release between MIF and

hsTn, and MIF might be a useful early and specific diagnostic biomarker for myocardial ischemia.

GW26-e1236

Early intravenous low/high doses of Metoprolol in myocardial infarction dogs on the effects of cardiac sympathetic activity and electrophysiological properties

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OBJECTIVES Observed effects of early intravenous low/high doses of Metoprolol in myocardial infarction dogs on cardiac sympathetic activity and electrophysiological properties.

METHODS 32 mongrel dogs were randomly divided into three groups, low-dose group (n=12), high-dose group (n=12) and control group (n=8). Three groups were all ligating the first diagonal branch of LAD to establish the myocardial infarction model. After ligation the low-dose group was given metoprolol 0.6mg/kg immediately by intravenous, the high-dose group was given 1.6mg/kg, while the control group was injected with normal saline. Norepinephrine (NE) and epinephrine (E) levels in the coronary sinus blood, the ventricular effective refractory period (ERP), The incidence of VA were all measured during the experiments. The pathological detection of infarction and infarct area were also performed.

RESULTS 1. The NE and E concentrations in three groups were all increased comparing with the previous measurement before ligation (NE: Control group 589.7 ± 14.6 ng/L vs 199.5 ± 27.4 ng/L, $p < 0.05$; Low-dose group 396.6 ± 68.8 ng/L vs 192.3 ± 17.4 ng/L, $p < 0.05$; High-dose group, 422.8 ± 26.1 ng/L vs 201.8 ± 27.8 ng/L, $p < 0.05$); Changes in the control group was the biggest increase compared with the other two groups (NE variation values: control group 390.18 ± 26.9 ng/L vs low-dose group 204.25 ± 73.2 ng/L, the high-dose group 220.99 ± 38.0 ng/L, $p < 0.05$); The low-dose and high-dose group performs no significant difference, (204.25 ± 73.2 ng/L vs 220.99 ± 38.0 ng/L, $p > 0.05$);

2. ERP values after myocardial infarction were significantly shorter in all three groups compared with the first measurements, (Control group, 137.5 ± 1.2 ms vs 154.9 ± 0.8 ms, $p < 0.05$, Low-dose group, 139.2 ± 1.0 ms vs 153.9 ± 1.0 ms, $p < 0.05$, High-dose group 139.0 ± 1.2 ms vs 154.2 ± 1.5 ms, $p < 0.05$); The low-dose group and high dose group shortened ERP approximately, there was no statistically significance, (14.7 ± 1.4 ms vs 15.2 ± 1.3 ms, $p > 0.05$); Three groups all exhibited uneven shortness of ERP among different regions, infarct area was significantly shortened ($p < 0.05$);

3. In control group there was 4 dogs (50%, n=8) induced polymorphic ventricular tachycardia or ventricular fibrillation, the low-dose group had 5 dogs (41.7%, n=12) induced polymorphic ventricular tachycardia or ventricular fibrillation, the high-dose group had 4 dogs (33.3%, n=12). There was no significant difference among all groups ($p > 0.05$);

4. Pathology in all groups showed regional myocardial infarction changes such as dark red myocardium, coagulation necrosis, edema, hemorrhage and neutrophil infiltration. TH staining showed the injured sympathetic fibers. GAP43 staining did not see a positive result, failed to observe the effects on regeneration of sympathetic nerve fibers.

CONCLUSIONS Low and high dose of metoprolol performed similarly in reducing the catecholamine concentrations in dogs with anterior myocardial infarction, the same effects also observed in the reduction of regional ERP, but there was no differences in induced arrhythmias.

GW26-e1337

Computed tomography angiography provides information on plaque vulnerability by identifying coronary plaque with positive remodeling and low-attenuation plaques

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OBJECTIVES The purpose of this study was to assess the relation between coronary plaques with positive remodeling (PR) and low-attenuation plaques (LAP) by computed tomography angiography (CTA) and fibrous cap thickness measured by optical coherence tomography (OCT).

METHODS 102 coronary plaques in patients with coronary artery disease were assessed by CTA and OCT (unstable angina pectoris

(UAP), n=24; stable angina pectoris, n=78). Plaque characteristics were divided into three groups: 2-feature-positive plaques (PR and LAP; n=32), 1-feature-positive plaques (PR or LAP; n=20), and 2-feature-negative plaques (neither PR nor LAP; n=50). PR was defined as remodeling index (RI) of >1.05 and LAP was defined as CT density value <50 HU.

RESULTS There were significant differences between the three plaque groups with respect to fibrous cap thickness measured by OCT: $76 \pm 24 \mu\text{m}$ in 2-feature-positive plaques, $154 \pm 51 \mu\text{m}$ in 1-feature-positive plaques, and $192 \pm 49 \mu\text{m}$ in 2-feature-negative plaques ($P < 0.001$). The RI (1.21 ± 0.06 , 1.14 ± 0.05 , $P = 0.011$) and the presence of thin cap fibroatheroma (TCFA) ($<70 \mu\text{m}$ thickness) (75%, 15%, $P = 0.001$) were significantly higher in UAP than in SAP patients with 2-feature-positive plaques, whereas fibrous cap thickness (68.9 ± 24.1 , $92.1 \pm 21.9 \mu\text{m}$, $P < 0.001$) was lower in the UAP patients. In UAP patients, the presence of ring-like enhancement showed higher accuracy of 88% for detection of TCFA.

CONCLUSIONS Coronary PR and LAP by CTA were associated with the degree of fibrous cap thickness by OCT. CTA can provide promising information on plaque vulnerability by identifying coronary plaque with PR and LAP, especially ring-like enhancement.

GW26-e1352

Bivalirudin Versus Heparin Plus Glycoprotein IIb/IIIa Inhibitors in Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention: a Meta-Analysis of Randomized Controlled Trials

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OBJECTIVES This study sought to examine the 30-day safety and efficacy of bivalirudin versus heparin plus glycoprotein IIb/IIIa inhibitors (GPI) in patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).

METHODS We included data from 12 randomized controlled trials (RCT) involving 22,912 patients. The incidence of 30-day all-cause mortality was the primary endpoint of the efficacy. Myocardial infarction and stent thrombosis were the secondary endpoints of the efficacy. The primary safety endpoint was the incidence of 30-day major bleeding.

RESULTS Compared with heparin plus GPI, anticoagulation with bivalirudin resulted in no differences in 30-day all-cause mortality (odds ratio [OR]: 0.96, 95% confidence interval [CI]: 0.77 to 1.20) and myocardial infarction (OR: 1.09, 95% CI: 0.95 to 1.24). Bivalirudin use comparing with heparin plus GPI resulted in decreased 30-day major bleeding (OR: 0.59, 95% CI: 0.46 to 0.76), but an increase in 30-day stent thrombosis (OR: 1.86, 95% CI: 1.19 to 2.91, $p < 0.05$) in patients with ACS undergoing PCI.

CONCLUSIONS In patients with ACS undergoing PCI, bivalirudin is associated with a reduction of major bleeding compared with heparin plus GPI.

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Detection of coronary artery anomalies in Chinese adults using 320-slice computed tomography

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OBJECTIVES Varied frequencies of coronary artery anomalies (CAAs) exist in different races. CAAs in Chinese were not well-documented. To investigate the frequency of CAAs in Chinese adults detected by 320-slice coronary computed tomography.

METHODS The author assessed the records of 10,457 consecutive patients (5837 males and 4620 females) who underwent 320-slice coronary computed tomography for any reason. CAAs were divided into 4 subgroups: 1) Anomalies of origination; 2) Anomalies of intrinsic coronary arterial anatomy; 3) Anomalies of termination (fistula); 4) Number anomalies. The frequency of CAAs were calculated.