# 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 CCL 17 levels ($\beta$ = 18.92 per effect allele of SNP, 95% confidence interval 2.16~35.68, p =0.027). Besides, minor allele T at rs223328 was also associated with increased risk of CAD (Odd 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 CCL 17 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 signifcant 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 (μg/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