

Spatial Relation of QRS-T Vectorcardiogram is a Good Predictor of Coronary Disease in Patients with Normal Rest 12-Leads ECG

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Background: Many people with normal rest 12-leads ECG (NE) have underlying significant coronary disease (CAD). We describe a new method to detect CAD in this population.

Methods: 101 patients with NE underwent coronary angiography due to routine indications. Prior to angiography a computerized simultaneous multi-leads ECG was recorded and using a new dedicated algorithm for 3D electrical activity reconstruction we plotted the horizontal vectorcardiogram (VCG) of the whole ECG cycle. We defined two configurations of spatial relation for the QRS and T VCG loops: 1) T inside QRS (T in), 2) T outside or overlapping QRS (T out). Following angiography patients were categorized as having normal coronary arteries (NC), or coronary disease (CD) if >50% lumen diameter narrowing was found in one of the arteries.

Results:

	Number	T in	T out
NC	31	20	11
CD	70	7	63

The positive predictive value of “T outside QRS” to reveal CD is 85% and the negative predictive value is 74% with 90% sensitivity and 65% specificity, $p < 0.0001$.

Conclusions: Using a regular simultaneous multi-leads ECG, we found a very high predictive value to reveal coronary disease in cases where the T VCG is outside the QRS VCG among patients with NE. This new feature can serve as a simple, low cost, easy to perform tool with no side effects for a global screening of coronary disease.

Weak Magnetic Field is Cardio Protective Following Chronic Coronary Occlusion but Not Following Reperfusion

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Background: Previous study has shown that pre exposure the heart to weak magnetic field (WMF) reduces infarct size shortly after induction of myocardial ischemia. **Aim:** To further investigate the role of WMF on left ventricular remodeling following chronic coronary occlusion and short episode of ischemia reperfusion (I/R). **Methods:** The study was conducted on rats using two sets of experiments: (1) acute myocardial infarction (AMI) followed by a 4 week recovery period, and (2) 60 minutes of ischemia followed by 120 minutes reperfusion. Half of each group was subjected to WMF comprising of 15.95Hz and 80nT. Left ventricular function was measured with echocardiography before AMI or I/ R and while sacrificed. In the I/ R model, infarct size was determined as a percentage of the area at risk using triphenyltetrazolium chloride (TTC) staining. **Results:** AMI resulted in a significant 13.4%±1.7% reduction in SF compared with 6.1%±2.8% decrease in animals exposed to WMF (p<0.04). Exposing the heart to WMF prior to reperfusion did not show any preservation neither on SF (17.4%±6.7 decrease in SF in the treated group vs. 18.6 ±6.7% reduction in the non treated group, p=NS) nor on the infarct size. **Conclusion:** WMF was cardiac protective in the AMI model but not in the I/ R model. The mechanisms underlying cardiac protection following chronic injury is currently under investigation.

Short-term Exercise Training Induces Cardiac Protection Through Molecular Stimulation of the Remodeled Left Ventricle

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Background: We have previously shown that long-term exercise training induces favorable morphological changes that play a major role in the deteriorated left ventricle following acute myocardial infarction (AMI). **Aim:** To investigate the effect of prior exercise training and duration on the molecular and gene expression alterations and their relation to cardiac repair during remodeling. **Methods:** SD male rats (n=188) underwent 3 or 7 weeks of swimming exercise training (90 min, 5 days/wk), or remained sedentary, and then subjected to AMI, followed by a 4-week sedentary period. At sacrifice, hearts were harvested, weighted, dissected the viable left ventricle, and flashed frozen for RNA extraction. Biotin-labeled cRNA were hybridized to a high-density oligonucleotide array (Affymetrix) and analyzed. **Results:** Based on a hierarchy of expression similarity, global analysis of all the expressed genes distinguished the experimental groups according to AMI (p<0.05): 486 and 533 genes from the 3 vs. 7 weeks, respectively. Criterion of 2 fold change in the average difference for each probe set divided to up/down regulated genes in 3 vs. 7 weeks, respectively (up: 33 vs. 160 genes; down: 93 vs. 41 genes). Bioinformatics web tools enabled to identify 45 genes that fall in functional categories of angiogenic, antiapoptotic, antifibrotic, and metabolic role in the injured heart, which were significantly altered by 7 weeks and even by 3 weeks of exercise prior to AMI. **Conclusion:** Short-term exercise training conducted prior to AMI induces sufficient cardiac protection of the remodeled myocardium through variety of gene family expression and alteration.

Transmyocardial Revascularization Does Not Increase the Efficacy of Endothelial Cell Transplantation

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Background:

We have reported that transmyocardial revascularization (TMR) of infarcted hearts prior to bone marrow cell (BMC) transplantation increases BMC survival and angiogenesis.

Hypothesis:

We hypothesized that endothelial cell (EC) transplantation would supply the optimal cell population to enhance TMR-induced angiogenesis.

Methods:

Female rats underwent LAD ligation 3 weeks before TMR (2 groups: EC+TMR and TMR), or no TMR (2 groups: EC and CONTROL), followed **after 15 minutes** by transplantation of 3×10^6 male EC, or medium. After 2 and 4 weeks, we evaluated regional perfusion by microspheres, vascular densities by histology, cell survival by PCR, and LVEF by echocardiography.

Results:

At both timepoints, vascular densities were increased by EC transplantation and by TMR ($p < 0.05$), but TMR prior to EC transplantation had **no** additive effect.

At 2 weeks, regional perfusion was lowest in the control, intermediate in EC+TMR and TMR, and greatest in the EC group ($p < 0.05$).

Fewer than 5% of EC survived to 2 and 4 weeks, and survival was not increased by prior TMR.

At 4 weeks, LVEF was increased by EC transplantation ($57 \pm 4\%$ to $65 \pm 4\%$ in EC+TMR and $57 \pm 5\%$ to $63 \pm 3\%$ in EC, both $p < 0.05$), but was not improved by TMR alone or in controls.

Conclusions:

While TMR increases the survival and angiogenic effect of BMC transplantation, this effect is cell-type specific, as no such effect is seen with EC. Combined TMR and cell transplantation may enhance treatment effects in infarcted hearts, but further studies defining optimal cell type and time interval between therapies are mandatory.

Human Serum Corin Level as a Predictor of Major Adverse Cardiovascular Events Post Percutaneous Coronary Intervention

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Background: Corin is a Type II transmembrane protease responsible for the cleavage of Pro-ANP to ANP and Pro-BNP to BNP.

ANP and BNP have vasodilatory and antiproliferative functions, and may confer protective effect against atherosclerosis.

In a previous study we found that plasma corin level is significantly higher in atherosclerotic patients compared to healthy volunteers (Abstract 3741: Human serum corin levels in healthy and atherosclerosis. *Circulation* 2007;116:II_850-II_851).

Hypothesis: Plasma corin level measured pre-PCI can predict major adverse cardiovascular events in long term follow up.

Methods and results: 98 atherosclerotic patients in whom plasma corin levels was measured pre-PCI were followed between two to three years for MACE. Forty six patients suffered from MACE (mortality, re-infarction, angina pectoris, recurrent revascularization, CVA/TIA). Plasma corin level was significantly lower in the MACE group compared to the non-MACE group (729 pg/ml, Std error 39 vs 849 pg/ml, Std error 45, $P=0.05$ by unpaired t test). By multivariate analysis corin was an independent predictor of MACE

Conclusion: Plasma corin level can predict long term MACE in coronary artery disease patients post-PCI.

Plaque Rupture: Look Out to the Other Side

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Back ground: Rupture of atherosclerotic plaque occurs when it cannot withstand the strain induced by the pulsating blood. Increase in circumferential strain will increase the risk of rupture.

Aim: To study the strain of the normal looking coronary artery arc (CA) opposing eccentric plaque.

Methods: We used Intravascular ultrasound to measured the ratio between the systolic and diastolic length of the normal arc of non culprit left main CA. Arteries were divided according to the atherosclerotic plaque arc: none, $90^0\pm 30^0$, $180^0\pm 30^0$ and $270^0\pm 30^0$. We used Young's modulus to describe tissue semi-compliance.

Results: In an artery with a plaque occupying $270^0\pm 30^0$ of CA, a significant systolic distension, was found between the plaque (0.960 ± 0.049) and normal arcs (1.04 ± 0.101), $p<0.00001$. Such finding was not documented for an artery with a plaque occupying $90^0\pm 30^0$ of CA. We calculated the Young's modulus; the higher the value, the stiffer the artery is. A significant difference was found between the stiffness of the free arc of a CA with a plaque of $270^0\pm 30^0$ (1.35 ± 1.75) and that of CA with a plaque of $90^0\pm 30^0$ (3.78 ± 3.11), $p<0.0002$, or with no plaque at all (5.25 ± 3.77) $p<0.0001$, suggesting that the larger the occupied arc, the less stiffer the normal part is.

Conclusion: The normal looking arc of eccentric plaque becomes more distensible as the arc becomes smaller. This enables on hand to allow sufficient cross-sectional area to maintain flow, but on the other hand increases the strain on the cap shoulder, rendering it for plaque rupture.

Caloric Restriction Attenuates Cardiac Injury after Ischemia-Reperfusion Injury in Mice.

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Background: Caloric restriction (CR) is currently the only therapeutic intervention that delays age-related diseases and extends longevity in mammals. Our goal is to investigate whether CR can confer cardioprotection against ischemia-reperfusion (I/R) injury inflicted in murine models *in vitro* (isolated heart preparation) and *in vivo* (left anterior descending coronary artery -LAD- ligation).

Methods & Results: Wild type (WT) mice fed *ad libitum* were compared to life-time calorically restricted transgenic mice. Mice underwent LAD ligation at the age of 4 (young) or 18 (old) months (n=5-9 in each experimental group). Echocardiography conducted before and one week after ligation indicated that after ligation the fractional shortening was significantly higher in all calorically restricted mice (46±1.2% vs. 39±5.2% for young; 48±0.4% vs. 37±0.2% for old; p<0.05). In addition, hearts excised from young mice (n=5 in each group) were subjected to global ischemia followed by reperfusion (30 min each). Cardiac analyses showed that the calorically restricted mice exhibited smaller infarct sizes compared to WT (11±1.6% vs. 16±1.8%, p<0.05), superior left ventricular pressure recovery (56±4.5% vs. 42±5%, p<0.05), and lower leakage of creatine kinase into the coronary effluent.

Conclusions: Collectively, these results indicate increased resistance to I/R injury in the calorically restricted mice, and suggest that the CR regimen could enhance clinical interventions for patients with myocardial infarction.

Early Cardiac Remodeling is Associated with Increased Myocardial Angiotensin II Expression in Normotensive Type I Diabetic Rats

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Purpose of the Study: Cardiac remodeling is a major component of both diabetic and hypertensive heart disease. Local angiotensin II plays a key role in cardiac remodeling. Its tissue levels are regulated by angiotensin converting enzymes (ACE and ACE2). We characterized myocardial changes in an animal model of hypertension and DM, with emphasis on the local renin-angiotensin system.

Methods: The male Sabra rat model (SBH/y) of salt induced hypertension was used. Control non-diabetic (C), diabetic (D) (induced by streptozotocin), and D or C rats fed with salt (DS or CS) were sacrificed after 6 weeks.

Results: Systolic BP increased in diabetic and nondiabetic rats on high-salt diets (CS and DS), and decreased in D, beginning at the third week of the experiment. Heart weight to body weight ratio was increased in CS, D and DS. Beta myosin heavy chain (β -MHC), atrial natriuretic peptide (ANP) and skeletal α -actin expression were significantly increased in D and DS compared to C and CS. A similar pattern was seen for type III collagen and TGF- β mRNA levels. Myocardial ACE mRNA levels were increased, while ACE2 mRNA levels were decreased in both D and DS groups. Cardiac AT1 receptor protein levels were unchanged but the levels of phosphorylated (p-) ERK were increased in D and DS.

Conclusion: an early cardiac remodeling phenotype is seen in normotensive DM. The increase in ACE, the decrease in ACE2 and the increase in cardiac pERK suggest a BP independent increase in free angiotensin II cardiac levels and signaling in DM.

Natural History and Clinical Significance of Tricuspid Regurgitation in Patients with Mitral Valve Prolapse and Significant Mitral Regurgitation

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Objectives The purpose of this study was to evaluate the prevalence, clinical importance and the progression of tricuspid regurgitation (TR) in patients with mitral valve prolapse (MVP).

Background Little information is currently available on the echocardiographic progression of TR in patients with MVP and significant MR.

Methods We studied 477 patients (mean age 65±15 years; 34% females) with MVP and at least moderate MR. 233 (mean age 64±15 years) of 477 patients had 2D echocardiogram with ≥1 year follow-up interval. The mean follow up was 4.04±2.4 years (range 1 to 11).

Results At entry, 85% of 477 patients had non-significant TR and only 4% had significant TR. Tricuspid valve prolapse was uncommon and found in only 4%. Over the follow-up period 200 patients (85%) had no change in TR grade. There were only 2 patients (0.85%) who had non-significant TR and developed severe TR. Twenty four patients (10 %) that had a non-significant grade TR at baseline. developed moderate or more severe TR. Overall, 14% (32) of the study patients had an increase of at least 2 levels in the severity of TR over the follow-up period.

Conclusions The study encompasses the largest reported patient group studied by echocardiography with relatively long-term follow-up. Significant TR is uncommon (4%) in patients with MVP and significant MR and the majority (85%) does not progress during follow-up.

The Impact of Tricuspid Valve Surgery on Right Ventricular Function – a single Center Experience

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Background: Severe tricuspid regurgitation (STR), either organic or functional, is associated with increased morbidity and mortality. A major consideration in fixing STR is to prevent RV dysfunction. This study sought to assess whether surgical repair of STR had indeed a positive impact on RV function.

Methods: Our database was queried for patients who underwent surgery for STR between 2004 and 2007. Data included demographic, clinical (NYHA functional class) and echocardiographic information. The diagnosis of STR and RV dysfunction were made by echocardiography. Patients must have had an echocardiographic study both before surgery and during follow-up at our center.

Results: The study included 16 patients (mean age 64 ± 14 years, 9 females). Six patients (37%) had valve replacement and 10 (63%) had valve repair. The follow-up period was 13 ± 17 months (range: 0.5-48 months). A single patient suffered from STR postoperatively (6%). However, the prevalence of RV dysfunction did not change significantly (12% before surgery vs. 25% after surgery). Data regarding functional class were available only in seven patients. Improvement was noticed in three patients (change of a single grade) but the average change for the entire group was insignificant (2.4 ± 0.5 vs. 1.9 ± 0.7 , $p=0.11$). One patient died 1 month after surgery.

Conclusions: Surgical therapy of STR was associated with significant amelioration of regurgitation. However, this was not translated into a significant improvement in RV function. The long-term impact of these opposite trends on functional class and prognosis need to be determined. Earlier surgical referral with emphasis on subtle changes in RV function, and better patient selection are advocated.