Norske abstracts presentert på AHA

Best Original Resuscitation Science, Moderated Poster Session

Abstract P156: Elderly Laypersons Can Perform Ten Minutes of Cardiopulmonary Resuscitation on Manikins with Human-like Chest Properties

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Introduction: Many cardiac arrest witnesses are elderly, who previous studies indicate have difficulties performing CPR. We studied elderly laypersons randomized to perform ten minutes of either continuous chest compression CPR (CCC) or standard 30 compressions 2 ventilations CPR (30:2), and we studied if verbal and visual feedback could prevent fatigue.

Materials and methods: Participants were recruited 5–7 months after classes and randomized to perform either standard 30:2 or CCC with (FB) or without (nFB) feedback in a factorial design. CPR quality was recorded from a manikin with human-like chest properties (Laerdal Medical, Stavanger, Norway). Correlation between age and compression depth and rate were analyzed using bivariate regression. Fatigue was assessed using repeated measures ANOVA. Compression depth (c.depth) and rate (c.rate) are reported as mean±SD, ventilation variables as median with 25–75-percentiles.

Results: Sixty-four persons aged 50 to 76 (median 63) were included. The groups were similar with regards to age, gender, height and weight. All were able to perform ten minutes of CPR. Overall c.depth and c.rate was 46±4 mm and 94±20, respectively. C.depth or c.rate did not differ for CCC vs. 30:2 (mean difference (95 % confidence interval) 2 (–1, 4) p=0.13 and 5 (–5, 15) p=0.35), and age had no effect (R=0.16, p=0.90 and R=0.13, p=0.31). Mean c.depth was within guideline limits for ten minutes with a slight decrease with time from 48 mm to 45 mm, mean change 3.7 (2.8, 4.6), p<0.0005, steeper the first five than the last five minutes. Similar pattern was found with and without feedback. C.rate increased from 92±18 the first minute to 103±8 in the tenth minute (p=0.006) with feedback. C.rate did not change with time for nFB and mean was lower than with feedback, 86±26 vs. 101±6, p=0.002. The FB group delivered 4 (4, 5) ventilations per minute, while the nFB group delivered 2 (0, 4), p=0.026. Six of 32 study subjects in the 30:2 group were unable to deliver any ventilations, all were in the nFB group.

Conclusions: Laypersons aged 50 + can do 10 minutes of CPR with satisfactory quality. Age does not influence chest compression depth or rate. Compression depth decreased (fatigue) most the first five minutes, but remained well within guideline recommendations.

Abstract 1334: Living Alone Predicts Long-term Mortality in Older Women After Myocardial Infarction

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Background: Research on long term survival after acute myocardial infarction (MI) in older women is scarce. Living with someone has shown a protective effect, but in cardiac populations reported mainly in men. The aim of this study was to determine whether 10-year survival in older women after MI is related to living arrangements.

Methods : We included all women aged 60 – 80 years suffering an MI during 1992–1997, and treated at one university hospital in Norway. In 1998, 145 (60% of those alive) completed a questionnaire package including socio-demographics, the Sense of Coherence Scale (SOC-29) and the World Health Organization Quality of Life Instrument Abbreviated (WHOQOL-BREF). Clinical information was based on self-reports and hospital medical records data. Patients were followed-up for 10 years (1998 –2008). End points were all-cause death, and adverse cardiac and cerebral events (MACCE); a composite of cardiac death, reinfarction and stroke.

Results: The all-cause mortality rate during 10 years of follow-up of all patients was 41%. Mean age was 72 years, and 41% were living alone. The majority of those living with someone lived with a spouse or partner (85%), whereas 12% lived with their children. In univariate analysis, women living alone had more than a twofold increased risk of all-cause death (HR 2.87, 95%CI 1.70 – 4.86, p<0.001) and MACCE (HR 2.12, 95%CI 1.22–3.66, p=0.007). After adjusting for age, time since MI, conventional predictors like creatinine and left ventricular ejection fraction, and a number of patient reported outcomes, living alone proved to be a robust, independent predictor of all-cause death (HR 6.24, 95%CI 2.68 –14.51, p<0.001) and MACCE (HR 6.07, 95%CI 2.69 –13.69, p<0.001). There was no significant difference between women living alone and women living with someone as to self-reported health, quality of life, and sense of coherence.

Conclusion : Living arrangements has prognostic importance for long-term outcome, and need to be taken into account when planning aftercare of older female MI patients.

Abstract 1964: A Genome-Wide Association Study in Icelanders Identifies a Novel Sequence Variant on Chromosome 16q22 That is Additive to 4q25 Variants for Atrial Fibrillation Risk

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Introduction. Atrial fibrillation (AF) is a common arrhythmia in humans and a major cause of morbidity and mortality. We have previously reported a genome-wide study identifying sequence variants on chromosome 4q25 that confer risk of AF. We have now expanded our cohort for genome-wide association stud, in the attempt to discover additional variants that associate with the common forms of AF.

Methods. A sample set of 2,385 Icelandic patients with AF and/or atrial flutter (AFl) and 33,752 Icelandic population controls were genotyped with the Illumina HumanHap300 and HumanHapCNV370 bead chips, yielding 304,226 SNPs that were tested individually for association. Of the top ten SNPs, seven represented the previously discovered signal on chromosome 4q25. The remaining three SNPs were genotyped in three replication cohorts of European descent, from Iceland (989 cases and 2,027 controls), Norway (725 cases and 725 controls) and the United States (735 cases and 729 controls).

Results. One SNP, rs7193343, on chromosome 16q22, showed genome-wide significant association with AF in the combined Icelandic sample set and this association was replicated in the non-Icelandic samples, with an odds ratio (OR) for AF of 1.21 (95% CI: 1.14–1.29) for all four sample sets combined. This variant does not associate with hypertension, coronary artery disease, or obesity, all known risk factors for AF. The at-risk allele of this variant has a population frequency of 20% in controls of European descent and was independent of the two independent variants near the PITX2 gene on 4q25. The data support the use of a multiplicative model- all 3 variants combined define AF risk relative to the general population ranging from 0.6 fold to 4 fold.

Conclusions. A sequence variant on chromosome 16q22 associates with common AF in populations of European descent and adds to the risk from the two variants previously discovered on 4q25. This is the third independent common sequence variant with association to AF that has been replicated in several populations and is further evidence of an important genetic contribution to the pathogenesis of this complex arrhythmia.

Thomas Smith Memorial Lecture: Signaling Pathways and Heart Failure

Abstract 3395: The Homeostatic Chemokine CXCL13 and Its Receptor CXCR5 Are Regulated in Heart Failure and Are Involved in Cardiac Remodelling

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The chemokine CXCL13 and its receptor CXCR5 are crucial for lymphocyte trafficking, also in non-lymphatic tissue. Since inflammatory mechanisms have been suggested to play a role in the development of heart failure (HF), we hypothesized that CXCL13/CXCR5 could be involved in this process. We found increased plasma levels of CXCL13 in HF patients corresponding to NYHA class (n=110), accompanied by enhanced mRNA levels of CXCR5 in circulating T cells (14%, $p<0.01$). In an experimental mouse model of HF secondary to pressure overload (aortic banding, AB), we found a threefold increase ($p<0.01$) in gene expression of CXCR5 in the hypertrophic left ventricle (LV) compared to sham-operated mice. To further examine the role of CXCL13 and CXCR5 in myocardial remodelling and development of HF, we exposed CXCR5 deficient (CXCR5 KO) and wild type (WT) mice to AB for 3 weeks. Echocardiography demonstrated substantially increased LV inner diameter in CXCR5 KO as compared to WT mice (5.00±0.24 mm vs. 4.31±0.12 mm, $p<0.05$). Heart weight was similar in the two groups, but the thickness of the LV posterior wall (0.70±0.06 mm vs. 1.10±0.09 mm, $p<0.05$) and interventricular wall (0.77±0.06 vs. 0.98±0.07 mm, $p<0.05$) was significantly reduced in CXCR5 KO compared to WT mice. The dilatation of the LV in CXCR5 KO mice was accompanied by a significant increase in gene expression of ANP, BNP and α-MHC ($p<0.05$ for all), reflecting enhanced wall stress and possibly accelerated remodelling. Moreover, we found increased infiltration of CD45R+ cells in AB CXCR5 KO mice together with increased total MMP activity (24%, $p<0.01$) and decreased TIMP 3 levels (47%, $p<0.01$), suggesting enhanced matrix degradation in CXCR5 KO mice. Microarray analysis (Affymetrix) revealed altered expression of a large number of genes encoding proteins found in the extracellular matrix. In conclusion, our data demonstrate that the homeostatic chemokine CXCL13 and its receptor CXCR5 are regulated in experimental and human HF. Furthermore, we show that lack of CXCR5 leads to LV dilatation and wall thinning, possibly via altered infiltration of inflammatory cells and alterations in the composition of the extracellular matrix.

Abstract 3735: Secretogranin II is Closely Regulated in the Murine Myocardium and Increased in the Circulation of Heart Failure Patients

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Background: Secretogranin II (SgII) and chromogranin (Cg) A and B are members of the granin protein family. While CgA and B recently have been found associated with heart failure (HF) development, the regulation of SgII has not been investigated.

Aim: To examine SgII levels in the myocardium and circulation during HF development, and investigate the potential for SgII as a HF biomarker.

Methods: SgII production in the myocardium was evaluated in a post-MI HF mouse model with animals characterized by echocardiography before being sacrificed one week post-MI. Gene expression was measured with qRT-PCR, localization of SgII production examined by immunohistochemistry, and protein levels measured by RIA. In 80 HF patients recruited mainly from an outpatient HF clinic, circulating SgII levels were measured and compared to 20 age- and gender-matched healthy control subjects.

Results: Compared to sham-operated animals, SgII mRNA levels were 11.5 fold upregulated in the left ventricle (LV) ($p<0.001$). This was a greater relative increase than observed for LV BNP gene expression (5.8 fold increase). LV SgII protein levels were increased during HF development by 35 and 85% in the non-infarcted and infarcted region, respectively. Production of SgII in the myocardium was confined to the cardiomyocytes. SgII protein levels were unaltered in other tissues investigated (pulmonary, renal, spleen, GI-tract, and skeletal muscle). Patients with HF of mainly moderate severity had clearly increased circulating SgII levels compared to control subjects (0.17±0.01 vs. 0.12±0.01 nmol/L, $p<0.001$), and SgII levels were superior to CgA, an established HF biomarker, for diagnosing HF (ROC-AUC 0.84 vs. 0.61, $p=0.001$).

Conclusion: SgII is produced by cardiomyocytes during HF development and increased in the LV. Circulating SgII levels are also closely regulated and increased in HF patients, indicating that SgII may represent a novel cardiac biomarker.

Abstract 429: Prediction of Ventricular Arrhythmias by Mechanical Dispersion in Patients After Myocardial Infarction

Kristina H Haugaa[1]; Marit Kristine Smedsrud[1]; Torkel Steen[2]; Erik Kongsgaard[3]; Jan Pål Loennechen[4]; Terje Skjaerpe[5]; Jens-Uwe Voigt[6]; Rik Willems[6]; Gunnar Smith[7]; Otto A Smiseth[8]; Jan P Amlie[8]; Thor Edvardsen[8]. [1] Rikshospitalet Univ Hosp and Univ of Oslo, Oslo, Norway, [2] Ullevaal Univ Hosp, Oslo, Norway, [3] Rikshospitalet Univ Hosp, Oslo, Norway, [4] St Olavs Univ Hosp and Univ of Science and Technology, Trondheim, Norway, [5] St Olavs Univ Hosp, Trondheim, Norway, [6] Univ Hosp Gasthuisberg, Catholic Univ, Leuven, Belgium, [7] Ullevaal Univ Hosp, Oslo, Norway, [8] Rikshospitalet Univ Hosp and Univ of Oslo, Oslo, Norway

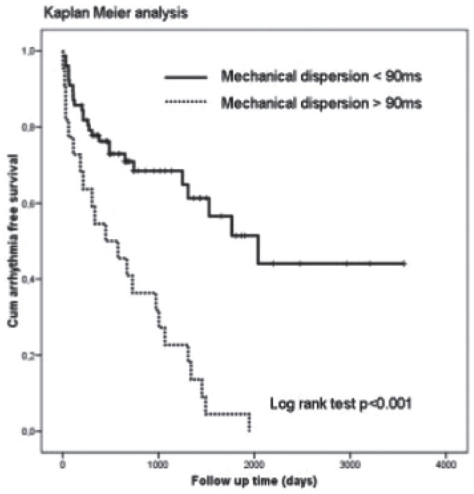
Background Left ventricular ejection fraction (EF) is insufficient in selecting patients for ICD therapy after MI. Electrical dispersion in infarcted myocardium facilitates malignant arrhythmia. Myocardial strain by echocardiography can quantify detailed regional and global myocardial function. We hypothesized that electrical abnormalities in patients after MI will lead to LV mechanical dispersion which can be measured as regional heterogeneity of contraction by myocardial strain.

Methods We included 104 patients post MI, 45 meeting primary and 59 meeting secondary ICD prevention criteria. Strain measurements were assessed by echocardiography. Contraction duration was measured as the time from ECG Q to maximum LV shortening by strain. Standard deviation (SD) of contraction duration in a 16 LV segment model was calculated as a parameter of mechanical dispersion.

Results After 3.4±2.6 years follow up, 53 had no and 51 patients had one or more recorded arrhythmias requiring appropriate ICD therapy. Mechanical dispersion was more pronounced in patients with recurrent arrhythmias during follow up com-

pared to those without (90±31ms vs. 57±14ms, p<0.001). By Cox regression analysis, mechanical dispersion >90ms was a strong and independent predictor of arrhythmias (HR 3.7, 95%CI 2.1– 6.6, p<0.001). Kaplan Meier analysis showed more arrhythmic events in patients with mechanical dispersion>90ms (Log rank p<0.001) (Figure). EF did not discriminate those with follow up arrhythmias from those without (36±10% vs. 35±11%, p = 0.59.

Conclusions Mechanical dispersion predicted ventricular arrhythmias in post MI patients independently of EF.



Abstract 1655: Diuretic Doses and Mortality in 3632 Patients With Stable Chronic Heart Failure

Morten Grundtvig[1]; Lars Gullestad[2]; Dan Atar[3]; Berit Flønæs[4]; Torstein Hole[5]; Arne S Westheim[6]. [1] Innlandet Hosp Trust, Div Lillehammer, Lillehammer, Norway, [2] Oslo Univ Hosp Rikshospitalet, Oslo, Norway,[3] Oslo Univ Hosp Aker, Oslo, Norway, [4] Asker and B Ærum Hosp Health Authority, Asker, Norway, [5] Sunnmøre Hosp Trust, Ålesund Hosp, Ålesund and Norwegian Univ of Science and Technology (NTNU), Ålesund, Norway, [6] Oslo Univ Hosp Ullevål, Oslo, Norway

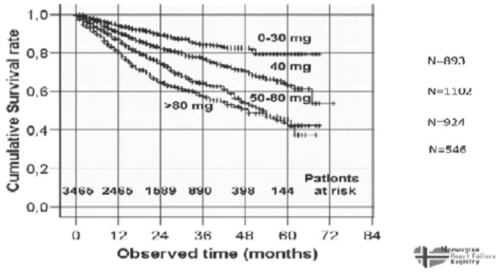
Background: Diuretics are widely used in patients with congestive heart failure (HF). However, their effect on mortality has not been evaluated in large clinical trials.

Aim: To determine the dose-dependent relations between diuretic (D) doses and mortality in outpatients with chronic HF included in the nationwide Norwegian Heart Failure Registry.

Methods: The HF outpatient clinics are run by specially trained nurses in close cooperation with cardiologists. They constitute a network linked through a web-based HF database establ. in 1998. The daily dose of D was expressed in frusemide equivalents (bumetanid 1mg = frusemide 40 mg). An additional 10 mg was added if the patients also used a thiazide. The patients were divided into quartiles of equivalence of total daily dose of D. Data on mortality were obtained from the National Statistics Bureau.

Results: A total of 3632 patients, 70% males, mean age 71±12 yrs and mean ejection fraction of 33±12% were included. Betablockers were prescribed to 83%, angiontensin-converting enzyme inhibitors or angiotensin receptor blockers to 87% and spironolactone to 33% of the patients. The mean daily dose equivalence of D was 58± X mg. In multivariate analysis examining a host of variables, the dose equivalence of D showed the strongest correlation to mortality (hazard ratio 1.83; 95% confidence interval 1.48 to 2.27, p<0.001), i.e., a decrease in survival was observed with increasing diuretic dose (Fig).

Conclusion: In patients with chronic HF, we observed a strong dose-dependent association between use of diuretics and mortality. Thus, the highest dosage of diuretics seems to be marker of HF patients at particularly high risk for reduced survival.



Survival in patients heart failure related to the daily dose frusemide equivalents – grouped according to 25 percentiles

Abstract 3782: Does Regional Electromechanical Delay in the Left Ventricle Contribute to Dyssynchrony During Left Bundle Branch Block?

Kristoffer Russell[1]; Espen W Remme[1]; Ola Gjesdal[2]; Anders Opdahl[3]; Helge Skulstad[3]; Erik Kongsgård[4]; Thor Edvardsen[5]; Otto A Smiseth[5]. [1] Institut for Surgial Rsch, Rikshospitalet Univ Hosp, Oslo, Norway, [2] Oslo Univ Hosp, Rikshospitalet, Oslo, Norway, [3] Institut for Surgial Rsch, Rikshospitalet Univ Hosp, Oslo, Norway, [4] Oslo Univ Hosp, Rikshospitalet, Oslo, Norway, [5] Institut for Surgial Rsch, Rikshospitalet Univ Hosp, Oslo, Norway

Background: Previous studies have suggested that the latest activated segments during left bundle branch block (LBBB) display prolonged electromechanical delay (EMD). In the present study we investigated EMD by two different methods in the septum and lateral LV wall during baseline, LBBB and biventricular pacing (BVP).

Methods: In 5 anesthetized dogs with LV micromanometers we measured intramyocardial electromyograms (IM-EMG) and myocardial segment lengths by sonomicrometry. As reference method for onset of mechanical activation we used onset of regional active force generation (AFG), defined as the time when the myocardial pressure-segment length coordinate deviated upward from its passive-elastic curve (Fig. 1). In addition we measured onset of mechanical activation as first onset of shortening (FOS). EMD was calculated as time from regional electrical activation (onset R in IM-EMG) to onset AFG and FOS during baseline, LBBB and BVP.

Results: Electrical activation delay of the lateral wall relative to septum was 3±5 ms (±SEM) at baseline, 53±4 ms during LBBB, and –5±2 ms during BVP. EMD measured by AFG was essentially constant in both walls during all interventions (13±1ms Fig. 2). EMD assessed by FOS showed an increase in the lateral wall from baseline (17±2 ms) to LBBB (43±8 ms, $p<0.05$) but was near normalized by BVP (25±24 ms).

Conclusions: Electromechanical delay assessed by onset AFG was constant during all interventions and did therefore not contribute to dyssynchrony. The large changes between interventions in electromechanical delay assessed by first onset of shortening in the lateral wall suggest that this is an inaccurate measure of mechanical activation.

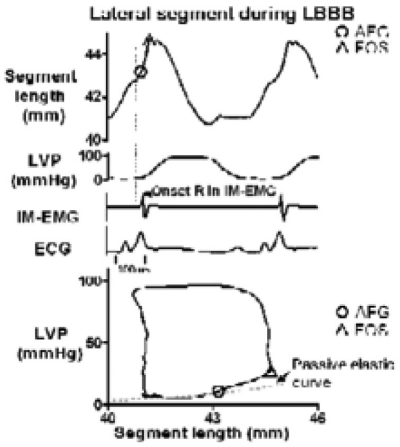


Fig. 1

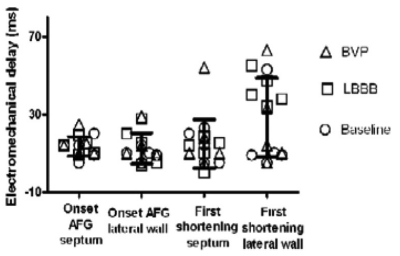


Fig. 2

Abstract 3783: Non-uniform Left Ventricular Work Load in Left Bundle Branch Block -Improved, but Not Equalized With Biventricular Pacing

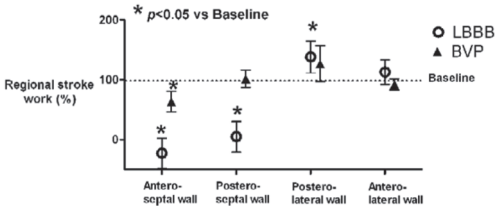
Kristoffer Russell[1]; Ola Gjesdal[2]; Espen W Remme[3]; Anders Opdahl[3]; Helge Skulstad[3]; Erik Kongsgård[4]; Thor Edvardsen[5]; Otto A Smiseth[5]. [1] Institut for Surgial Rsch, Rikshosptalet Univ Hosp, Oslo, Norway, [2] Oslo Univ Hosp, Rikshospitalet, Oslo, Norway, [3] Institut for Surgial Rsch, Rikshosptalet Univ Hosp, Oslo, Norway, [4] Oslo Univ Hosp, Rikshospitalet, Oslo, Norway, [5] Institut for Surgial Rsch, Rikshosptalet Univ Hosp, Oslo, Norway

Background: For bi-ventricular pacing (BVP) to be most efficient and cause reverse remodeling in patients with left bundle branch block (LBBB), there should be electrical resynchronization as well as equalization of work distribution within the left ventricle. In the present study we investigate regional work distribution during LBBB and how it was modified by BVP.

Methods: In 5 anesthetized dogs with micromanometers we measured dimension changes with sonomicrometry. Regional electrical activation was defined as onset R in intramyocardial electromyograms (IM-EMG). Segmental work was calculated as area of the pressure-segments length loops. Measurements were performed during baseline, LBBB by RF ablation and BVP.

Results: During LBBB segmental work was markedly reduced in the early-activated antero-septal (net passive) and posteroseptal walls (Fig 1). In the late-activated postero-lateral wall, however, segmental work was increased relative to baseline. BVP during LBBB reduced the heterogeneous timing of electrical activation of the LV free wall from 37±22 to 17±15ms (mean±SD). Segmental work became more evenly distributed, but there was still substantial non-uniformity, with a 27% increase of segmental work in the postero-lateral wall and a 36 % reduction in the anteroseptal wall relative to baseline (Fig 1).

Conclusion: BVP leads to a greater degree of LV electrical and mechanical synchrony in LBBB. However, segmental work during BVP still shows an uneven distribution.



Abstract 662: Outcome of Asymptomatic Patients With Low Gradient "Severe" Aortic Valve Stenosis and Preserved Ejection Fraction - Results From the Prospective SEAS Study

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Background: Low gradient "severe" aortic valve stenosis (LGSAS) is observed in up to 30% of patients with normal left ventricular ejection fraction (EF) with a constellation of severe stenosis based on aortic valve area (AVA) <1.0 cm^2 and non-severe stenosis based on mean pressure gradient (MPG) ≤40mmHg. The natural history is not known. We evaluated the outcome of patients with LGSAS in the prospective SEAS (Simvastatin and Ezetimibe in Aortic Stenosis) study.

Methods: 1525 asymptomatic patients (mean age 67.3±9.6 years, 39 % women) with mild to moderate aortic stenosis (AS), (peak velocity ≥2.5 and ≤ 4.0 m/s, prospectively followed for a mean of 51.8 months) and normal EF were analysed. Outcome was determined by the occurrence of major cardiac events (MACE), which include death from cardiovascular causes, aortic valve replacement, nonfatal myocardial infarction, hospitalisation for unstable angina pectoris, heart failure, coronary artery bypass grafting, percutaneous coronary intervention and nonhemorrhagic stroke. Furthermore aortic valve related events (AVE) including aortic valve replacement, heart failure due to progression of AS, and cardiovascular death were compared between patients with LGSAS, moderate AS (AVA 1–1.5cm^2 and MPG 25–40mmHg) and patients with consistently graded severe AS (AVA<1.0cm^2 and MPG > 40mmHg).

Results: At baseline 435 of the 1525 patients (29%) had LGSAS, 184 (12%) had moderate AS and 35 (2%) had consistently graded severe AS. The remaining patients had mild AS. During follow up MACE occurred in 50.9% (CI 40 –57%) of patients with LGSAS and 48.4% (CI 42–59%) of patients with moderate AS (p=0.58). Similarly, there was no significant difference in AVE or cardiovascular death between the two groups (48.5% (CI 36 –53%) vs. 44.6% (CI 40 –57%), p=0.37 and 7.8% (CI 1–9%) vs. 4.9% (CI 4 –12%), p=0.19, respectively). In contrast, patients with consistent-

ly graded severe AS suffered a MACE in 74.3 % ($p<0.01$).

Conclusion: Asymptomatic patients with low gradient "severe" AS and normal left ventricular ejection fraction appear to have a relatively good outcome similar to patients with moderate AS and significantly better than those with consistently graded severe AS.

Abstract 4529: Partial Thrombosis of the False Lumen is Not a Predictor of Follow-up Mortality in Patients With Acute Type A Aortic Dissection

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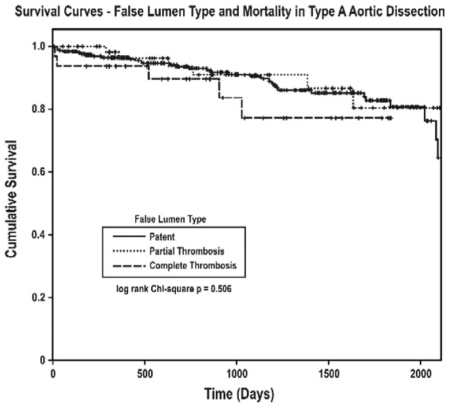
Background: Prophylactic interventions in patients with chronic aortic dissections are based on serial control images of the aortic wall. Previous assessments in patients with type B dissections have indicated that a partially thrombosed false lumen is an independent predictor of intermediate and/or long term mortality. In the present study, we assessed the hypothesis that a partially thrombosed false lumen also is a predictor of increased mortality in patients with acute type A dissections.

Methods: The International Registry of Acute Aortic Dissection (IRAD) is a large database containing patients from 24 hospitals world-wide. Patients with acute type A aortic dissection with registered follow-up data (n=379) were divided into three groups according to the status of the dissected aortic wall (patent flow in the false lumen, n=281 (74.1%), complete thrombosis of the false lumen, n=32 (8.4%), partial thrombosis of the false lumen, n=66 (17.4%). In these three groups follow-up mortality was compared using Kaplan-Meier survival analysis and log rank tests.

Results: The mean follow-up for these patients was 1064 days (+/– 662). We did not observe any difference in survival according to the status of the false lumen in the aortic wall (log rank test p=0.86 in patients with patent false lumen, p=0.28 in thrombosed and p=0.59 in partially thrombosed false lumen).

Conclusion: Status of the false lumen does not seem to influence mortality in patients with type A dissection admitted to an IRAD center follow-up program. Risk factors for death in the follow up period after aortic dissection need further characterization and analysis of their prognostic value.



Abstract 668: 2D Longitudinal Myocardial Strain: A More Sensitive Parameter of Left Ventricular Dysfunction in Aortic Valve Stenosis?

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Background: In aortic stenosis (AS), ejection fraction (EF) might be preserved despite reduced left ventricular (LV) function. Stress-corrected midwall shortening (scMWS) has been suggested to be a better marker of early LV dysfunction and a pre-

dictor of symptom onset. Less is now about myocardial deformation assessed as 2D strain in AS.

Methods: Conventional and 2D speckle tracking echocardiography was performed in 70 patients (40 asymptomatic) with AS (mean age 73±10 years, 54% women). LV function was assessed as peak systolic longitudinal strain (LS), biplane EF and scMWS. Severity of AS was assessed from the energy loss index. LS measurements were also averaged to obtain a global LV strain value.

Results: Severe AS was present in 30 patients (43%) (mean energy loss index 0.44 cm^2/m^2), 22 symptomatic. LS was lower in the basal septum (–11±6 vs. –8±6%), and in the lateral wall (–16±5 vs. –14±6%) in patients with severe vs. mild/moderate AS, and lower in the lateral wall in symptomatic vs. asymptomatic patients (–16±5 vs. –13±6%) (all $p<0.05$). Symptomatic patients had lower average LS (–16±4 vs. –14±4%, $p<0.05$). In univariate analysis, average LS was significantly correlated with scMWS (r=–0.43, $p<0.001$). In multivariate regression analysis, lower average LS was associated with lower scMWS, EF and energy loss index, and with male gender (all $p<0.05$) ($R^2=0.72$) (Table).

Conclusions: In patients with AS, lower regional and average LS is associated with more severe AS and presence of symptoms. Average LS is independently associated with EF, and even stronger with scMWS, supporting its use as a marker of global LV dysfunction.

Dependent variables	ß	t	p
Age (yrs)	-0.113	-1.491	0.141
Male gender	0.204	2.904	0.005
Hypertension	-0.041	-0.588	0.559
EF (%)	-0.148	-2.066	0.043
ScMWS (%)	-0.176	-2.279	0.026
Energy loss index (cm^2/m^2)	-0.196	-2.670	0.010
Average longitudinal displacement (cm)	-0.713	-9.914	<0.001

Table. Predictors of lower average LS

Abstract 2961: CCN2/CTGF - Connective Tissue Growth Factor - Reduces ß-Adrenergic Receptor Responsiveness and Catecholamine-Induced Cardiotoxicity by Upregulation of Cardiac Myocyte G Protein-Coupled Receptor Kinase-5

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Background: Myocardial CTGF is dramatically induced in CHF, a condition associated with diminution of β-adrenergic receptor (βAR) responsiveness. Accordingly, we aimed to investigate if CTGF is mechanistically involved in desensitization of βARs in this condition.

Methods and results: Transgenic mice with cardiac-restricted overexpression of CTGF (Tg-CTGF) were generated and compared with nontransgenic control mice (NLC). Stimulation of ventricular muscle strips with increasing concentrations of βAR agonist isoproterenol (ISO) revealed substantial attenuation of maximal inotropic response of muscle fibers from Tg-CTGF vs. NLC mice (increase of force [(dF/dt)max] 123±14% vs. 427±27%, $p<0.01$). Concentration-effect curves of ISO-stimulated cAMP generation in adult cardiac myocytes from Tg-CTGF hearts revealed reduced efficacy of ISO compared with cardiac myocytes from NLC hearts. Indeed, similar reduction of efficacy of ISO was observed in ventricular muscle strips of Tg-CTGF hearts. Furthermore, no differences in maximal contractile responses upon stimulation with cAMP analogue dibutyryl-cAMP were detected; excluding affection of downstream signalling pathways or contractile proteins. Analysis of [^{125}I]-iodocyanopindolol binding did not disclose alterations in βAR densities on cardiac myocytes from Tg-CTGF versus NLC mice. Real time qPCR analysis revealed a three fold upregulation of cardiac myocyte G-protein receptor kinase 5 (GRK5) in Tg-CTGF hearts, while levels of other cardiac GRKs (2, 3 and 6) were unaltered among the groups. ISO-stimulated cardiac myocytes from Tg-CTGF mice also displayed enhanced ERK-phosphorylation (Thr202/Tyr204), indicating activation of GRK5 dependent β-arrestin-mediated cytoprotective pathways. Chronic exposure to ISO for 14 days delivered through mini-osmotic pumps, revealed attenuated myocardial hypertrophy in Tg-CTGF versus NLC mice, and preserved cardiac function as evaluated by echocardiography.

Conclusion: CTGF desensitizes βAR signaling in the heart through induction of myocardial GRK5. Desensitization of βAR on cardiac myocytes may contribute to cytoprotection and maintenance of cardiac function. CTGF might be an important mediator of reduced βAR responsiveness in CHF.

Abstract 3536: Circulating Markers of Collagen Turnover Following ST-Segment Elevation Myocardial Infarction and Primary Percutaneous Coronary Intervention Predict Infarct Size and Left Ventricular Volumes, Estimated by Serial Cardiac Magnetic Resonance Imaging for up to 1 Year

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We investigated the time profile and predictive value of circulating markers of collagen turnover (CTO) for infarct size (IS), ejection fraction (EF) and left ventricular (LV) volumes, determined by serial cardiac magnetic resonance imaging (cMRI) in patients undergoing primary percutaneous coronary angioplasty for ST-elevation myocardial infarction (STEMI).

Methods: Forty-two patients with first time STEMI, 1-vessel disease, and successful revascularization of the proximal occluded infarct related artery were included. Serum samples were obtained at admission, 2 days, 7 days, 2 months and 1 year post-STEMI. We analyzed CTO-markers of collagen synthesis: N-terminal procollagen type I (PINP), N-terminal procollagen type III (PIIINP), and collagen degradation: C-terminal telopeptide of type I collagen (ICTP); established markers of outcome: Troponin-T (TnT), C-reactive protein (CRP), and N-terminal pro brain natriuretic peptide (NT-proBNP). Late enhancement and cine cMRI was performed on day 2, day 7, 2 months and 1 year post-STEMI.

Results: Median time from symptom debut to admission was 145 minutes (range: 25–720). CTO-marker analyses from admission samples were available in 35 patients. Significant time-dependent changes occured for all 3 CTO-markers and the PINP/ICTP ratio ($p<0.001$ for trend for all markers). In multivariable analysis including markers of CTO, TnT, CRP and NT-proBNP at admission, PINP was the only independent predictor of IS, EF and LV volumes at all imaging time-points (R^2 ranging from 0.17 for LV end systolic volume index at 2 months [$p<0.05$], to 0.36 for EF at 1 year [$p<0.001$]). For serum samples drawn at 2 days, a model containing PINP/ICTP ratio, CRP, TnT and NT-proBNP was highly predictive for LV volumes, infarct size and EF at all imaging time-points, explaining up to 80 % of the variance of cMRI findings ($R^2=0.80$ for IS at 2 months, $p<0.0001$).

Conclusions: Following STEMI, PINP appears to be a very early predictor of infarct size and LV-volumes, while the combination of PINP/ICTP ratio, CRP, NT-proBNP and TnT at 2 days post-STEMI is highly predictive for cMRI findings for up to 1 year. Our findings support the potential role of circulating markers of CTO as surrogates for subsequent extracellular cardiac matrix remodeling.

Abstract 3888: Exercise-induced Increase in Cardiac Efficiency: The Impact of Intensity

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There is growing evidence that exercise has beneficial effects in patients with cardiovascular disease. Although the importance of the intensity, duration and modality of the exercise training is debated, recent studies have indicated more beneficial cardiovascular effects of high- as compared to low- and moderate-intensity levels. The significance of exercise intensity with respect to myocardial substrate metabolism, oxygen consumption (MVO_2) and cardiac efficiency is, however, not known. Thus, the aim of the study was to compare cardiometabolic effects of high-intensity interval training (HIT) vs. moderate-intensity continuous training (MIT). Male C57BL/6J mice were subjected to high-intensity (85–95% of VO_{2max}) interval treadmill running or moderate-intensity (50 –70% of VO_{2max}) continuous running for 10 wks (5 days/wk), as described by Kemi et al. (*J Applied Physiol,* 2002), both groups covering the same running distance. Age-matched sedate mice served as controls. Myocardial substrate utilization (radioisotope technique), cardiac efficiency (regression analysis of cardiac work -MVO_2 relationships) and the oxygen cost for basal metabolism and E-C coupling were measured in isolated perfused hearts. HIT increased max running speed by 60%, which was accompanied with an 18% increase in aerobic capacity (VO_{2max}). The corresponding numbers for

MIT were 30% and 10%. Both modes of exercise were associated with a 10% increase in heart weight to body weight ratio, but altered cardiac substrate utilization was observed only in the HIT group, as revealed by a 36% increase in glucose oxidation and a concomitant reduction in fatty acid oxidation. In addition, only HIT significantly increased cardiac efficiency, due to a decrease in the oxygen cost for basal metabolism. In conclusion, high, but not moderate intensity training was associated with a shift in myocardial substrate utilization in favour of glucose oxidation, combined with increased cardiac efficiency. Improvement of cardiac metabolism and efficiency may in part explain the superiority of high-intensity exercise training with regard to cardioprotection in patients with cardiovascular disease, an issue that should be followed up with further investigations.

Abstract 2690: Myocardial Contraction Duration is Longest in the Interventricular Septum in Patients With Long QT Syndrome With Arrhythmic Events

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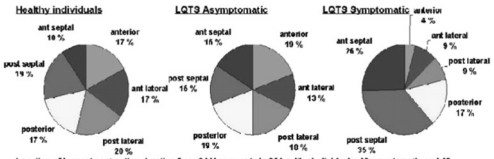
Background Long QT syndrome (LQTS) is due to inherited cardiac ion channel defects leading to prolonged action potential duration (APD). Purkinje cells have longer APD than cardiac myocytes and are predominantly located in the interventricular septum. Prolonged APD in LQTS may cause prolonged cardiac contraction which can be assessed by strain echocardiography. We hypothesized that myocardial contraction is inhomogeneously prolonged throughout the LV in LQTS patients.

Methods We included 88 genotyped LQT1 and LQT2 mutation carriers and 35 healthy individuals. A history of cardiac arrest or syncope was present in 42 mutations carriers and 46 were asymptomatic. Myocardial contraction duration was assessed by strain echocardiography as time from ECG Q to peak strain in 6 LV segments. Location of longest contraction duration was recorded.

Results Contraction duration in septum was longer in symptomatic compared to both asymptomatic LQTS mutation carriers and healthy individuals (475±65 vs. 435±65 vs. 385±50ms, $p<0.001$, respectively). Longest contraction duration was located in septum in 61% of the symptomatic mutation carriers compared to 31% of asymptomatic and 29% of healthy ($p<0.001$). In asymptomatic mutation carriers and healthy, longest contraction duration was evenly distributed throughout the LV (Fig).

Conclusions Contraction duration in healthy individuals and asymptomatic LQTS mutation carriers was uniformly disseminated in LV. Contraction duration in symptomatic LQTS mutation carriers, however, was longer and more frequently located in septum. This might reflect that ion channel dysfunction in septal cells play a role in arrhythmogenesis in LQTS patients.



Location of longest contraction duration from 6 LV segments in 35 healthy individuals, 46 symptomatic and 42 symptomatic LQTS mutation carriers.

Abstract 2944: Activation of Heat Shock Proteins and Shifts in Cytoskeleton Composition in a Cardiac-specific SERCA2 KO Mouse

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Background: Depressed contractility is a key feature of the failing heart and has been linked to reduced Ca^{2+} availability due to decreased activity of the sarcoplasmic reticulum Ca^{2+} ATPase 2 (SERCA2). Yet, surprisingly, a conditional, cardiac specific SERCA 2 knock out (KO) mouse, has sustained cardiac contractility for several weeks despite dramatically altered cytosolic Ca^{2+} handling and SR function. The molecular mechanism behind this intriguing contractile compensation is not clear.

Aim: To examine the protein alterations in the cytosolic sub-proteome and identify the biological

processes altered in the KO myocardium that can compensate for the loss of SERCA2 in the heart.

Methods and results: SERCA2 KO and age matched control mice analyzed 9 days after induced gene excision showed no differences in cardiac function (left atrial diameter, echocardiography), even though the quantity of SERCA2 protein was reduced to 30±5% in the left ventricles in KO vs. control mice (western blot). The cytosolic-enriched protein extracts from KO and control hearts (n=6) was analyzed by two dimensional gel electrophoresis (pH 4–7 and 6–11) and 33 cytosolic proteins were identified as being altered (Redfin, Ludesi). The majority of the proteins were identified (tandem mass spectrometry, MS^2) and analyzed further using seeded Bayesian networks. The main changes occurred to the cytoskeleton composition with alterations in vinculin, actin, gelsolin and coffilin-2. These were accompanied by regulation of a subset of heat shock proteins (HSPs), HSPB1, alpha-B-crystallin and HSPA5. Further analysis of the HSPs (Immobilized metal affinity chromatography and MS^2) showed an increased level of the phosphorylated (activated) forms. Finally, these results were compared to effects in acute thapsigargin-treated neonatal cardiomyocytes to examine whether the observed proteomic changes in SERCA2 KO hearts occur *in vivo* as a direct consequence of altered Ca^{2+} homeostasis.

Conclusions and perspectives: Altered Ca^{2+} homeostasis induces activation of HSPs and shifts in cytoskel-eton protein composition. This indicates that Ca^{2+} changes can induce phenotypical effects beyond the contractile apparatus, also involving the architecture of the cardiomyocytes.

Abstract 2954: CCN2/CTGF, Connective Tissue Growth Factor, Prevents Heart Failure and Improves Survival After Myocardial Infarction

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Background: Myocardial CCN2/CTGF is robustly induced in heart failure (HF). Yet, its role in the pathophysiologic mechanisms of HF remains unresolved.

Methods and Results: To elucidate the role of myocardial CTGF in HF, transgenic mice with cardiac-restricted overexpression of CTGF (Tg-CTGF) were employed and compared with non-transgenic controls (NLC). Myocardial infarction was induced by ligation of the LAD in Tg-CTGF (n=22) and NLC mice (n=21). Sham-operated animals underwent the same procedure without ligation of the artery. Area at risk was estimated in a separate group of animals sacrificed immediately after ligation of the left coronary artery and perfusion with Evans blue dye. Area at risk was similar among Tg-CTGF and NLC mice (42.7±1.6%, n=8 versus 40.4±2.1%, n=8, p=0.39). During follow-up, significant increase of survival was found in Tg-CTGF mice (63.6% versus 38.1%, $p<0.05$). In vivo pressure-volume analysis performed after 4 weeks displayed preserved cardiac performance in Tg-CTGF vs. NLC mice. End-point analysis revealed attenuation of cardiac hypertrophy in Tg-CTGF vs. NLC mice (Heart weight/body weight ratio; 5.3±0.2mg/g, n=14 versus 8.0±0.9mg/g, n=9, $p<0.05$). Consistently, markers of myocardial remodeling, i.e. BNP and β-myosin heavy chain mRNA levels were significantly less upregulated in Tg-CTGF hearts than NLC hearts. Consistently, markers of myocardial remodeling, i.e. BNP and β-myosin heavy chain mRNA levels, were significantly lower in Tg-CTGF than in NLC hearts. Interestingly, induction of myocardial collagen contents four weeks after myocardial infarction, determined by quantitative HPLC of myocardial hydroxyproline, was lower in Tg-CTGF than in NLC mice. Selective upregulation of GRK5 in cardiac myocytes of Tg-CTGF hearts were found and confirmed as mediator of β-adrenergic receptor desensitization. Tg-CTGF hearts also displayed increased phosphorylation of AKT(Ser473) and GSK-3β (Ser9).

Conclusion: This study uncovers novel, unexpected cardioprotective properties of CTGF in ischemic HF. Myocardial CTGF prevents development of HF and improves survival after myocardial infarction, possibly due to activation of salvage kinase pathways and inhibition of sympathetic β-adrenergic stimulation of the heart.

Abstract 4964: Tnf-α Antagonists Improve Arterial Stiffness in Patients With Inflammatory Arthropathies: Results From a One Year Controlled Study

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Introduction: The chronic inflammatory state of rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) contributes to the accelerated atherosclerosis associated with these diseases.

Hypothesis: We assessed the hypothesis that one year treatment with TNF-α antagonists would improve arterial stiffness in patients with RA, AS and PsA.

Methods: A total of 52 patients with RA, AS or PsA and clinical indication for anti-TNF-α therapy were included. 36 patients started with anti-TNF-α therapy and were compared with a non-treatment group of 16 patients. Aortic pulse wave velocity (aPWV) and augmentation index (AIx) were measured at baseline and after one year (Sphygmocor). Each visit also included blood samples and assessment of disease activity.

Results: Values are given as mean± SD. Age of the patients in the treatment/control group was 46.2±12.2/49.0±14.1 years (p=0.21), 42.9/50.0 % (p=0.63) were females and disease duration was 11.0±9.6/11.6±10.1 years (p=0.56). Patients who started anti-TNF-α therapy had a significant decrease in aPWV (–0.53±0.13 m/s) whereas the patients in the control group had no change (+0.08±0.10 m/s, p=0.001 for between groups changes). Between groups differences for AIx were not observed (change 0.1±6.1 % and 0.2±5.7 %, p=0.95). There was no change in blood pressures, lipid levels or kidney function in any of the groups. A significant reduction in CRP and DAS28 (RA patients) was observed in the treatment group, but we did not find any significant bivariate correlations between the changes in aPWV and CRP (ρ =0.11, p=0.55) or between changes in aPWV and DAS28 in the RA group (ρ= –0.21, p=0.44).

Conclusion: The present study shows for the first time in a comparative design that long term anti-TNF-α therapy improves aPWV in patients with RA, AS and PsA. This finding supports the idea that atherosclerosis is partly driven by inflammation, and that this process is amenable to pharmacologic intervention.

	baseline			change		
	anti-TNF (n=36)	control (n=16)	p-value	anti-TNF (n=36)	control (n=16)	p-value
aPWV m/s	7.5±1.3	7.3±1.3	0.64	-0.53±0.1	0.08±0.1	0.001
AIx %	20.5±11.4	23.0±12.3	0.41	0.1±6.1	0.2±5.7	0.95
CRP mg/l	12.5±20.7	10.9±12.2	0.73	-8.63±15.3	0.88±10.2	0.001
DAS28'	3.92±1.47	4.20±1.26	0.47	-1.10±0.91	-0.20±1.04	0.02
MAP** mmHg	98.5±13.2	95.9±12.9	0.78	-3.2±7.8	-2.7±7.8	0.85
HR b/min	64.0±10	65.0±10	0.93	-0.3±7.1	1.4±8.2	0.45

Baseline value and change in key variables

Abstract 1651: Is Obstructive Sleep Apnea Associated With Endothelial Dysfunction? The Akershus Sleep Apnea Project

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Introduction: Severe obstructive sleep apnea (OSA) has been associated with increased risk of cardiovascular events. Whether OSA of mild to moderate severity in subjects drawn from the general population is associated with endothelial dysfunction, a precursor of atherosclerosis, is unknown.

Hypothesis: We wanted to assess the hypothesis that there is an association between endothelial dysfunction, as measured by peripheral arterial tonometry, and the apnea-hyponea index (AHI) in a large population-based sample of subjects.

Methods: From a Norwegian, population-based cohort of 30 000 subjects aged 30 – 65 years we invited 518 subjects to attended, in-hospital polysomnography. Oversampling of subjects classified as being at high risk of OSA was performed. Endothelial function studies were performed the following morning on 484 subjects (mean age 48 years, 57 % male). Endothelial function was assessed by measuring the digital pulse wave amplitude reactive hyperemic response, expressed as the reactive hyperemia index (RHI), using the EndoPAT 2000 (Itamar Medical, Caesarea, Israel).

Results: Out of the 484 subjects, 349 subjects were classified as being at high risk of OSA, whereas 135 subjects were classified as low risk. Subjects were categorized according to AHI cutoffs that correspond to mild, moderate and severe degrees of OSA. The RHI was significantly lower in subjects with AHI >30 than those with AHI<5 (Table). In a multivariable linear regression model, adjusting for conventional cardiovascular risk factors, the association between AHI and RHI was attenuated and no longer significant.

Conclusions: Severe, but not mild to moderate OSA, is associated with an impaired digital pulse wave amplitude reactive hyperemic response in a population-based cohort. However, this association can be explained by a clustering of traditional

cardiovascular risk factors in subjects with severe OSA.

	AHI<5 (n=216)	AHI 5–14.99 (n=121)	AHI 15–29.99 (n=71)	AHI ≥30(n=76)
RHI Mean (±SD)	2.08 (±0.59)	2.06 (±0.53)	2.04 (±0.43)	1.93 (±0.44)
P vs. AHI<5		NS	NS	0.02

Table: Endothelial function assessed by peripheral arterial tonometry in categories of AHI

Abstract 5862: Development of Systolic Dysfunction Not Related to Myocardial Infarction in Treated Hypertensive Patients With Left Ventricular Hypertrophy: The LIFE Echo Substudy

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Background: While it is commonly thought that left ventricular (LV) systolic function deteriorates insidiously in hypertensive patients (burnt-out hypertensive heart), few prospective data are available to support this notion. Accordingly, the aim of this study was to identify echocardiographic predictors of reduced EF in a population of hypertensive patients.

Methods: We evaluated 703 hypertensive patients (66±7 years; 45% women) enrolled in the LIFE echo-substudy. Only patients free of prevalent cardiovascular disease and with baseline ejection fraction (EF)<55% were included. Echocardiographic exams were performed annually for 5 years during anti-hypertensive treatment. Development of reduced systolic function was defined as incident EF<50%.

Results: During a mean follow up of 5±1 years, 37 patients developed reduced EF without an intercurrent myocardial infarction. Patients who developed reduced EF were more often men (p<0.05). In analysis of covariance, patients who developed reduced EF had greater baseline LV diameter and LV mass, lower mean EF (all p<0.05), and similar diastolic function indices as compared to patients who did not develop reduced EF. As shown in the Table, at last available exam before EF reduction, patients with reduced EF showed a significant increase in left atrial size, LV diameter, end-systolic stress and mitral E/A ratio, as compared to those who did not develop reduced EF (all p<0.05). In time-varying Cox regression analysis, also controlling for baseline EF, predictors of developing reduced EF were higher in-treatment LV diameter (HR=5.2; 95%CI:2.6 –10.4; p<0.001) and higher in-treatment mitral E/A ratio (HR=2.4; 95%CI:1.6 –3.6; p<0.001).

Conclusions: In treated hypertensive patients, incident reduced EF is associated with the development of dilated LV chamber and signs of increased LV filling pressure. Higher in-treatment LV diameter and mitral E/A ratio are the strongest echocardiographic predictors of reduced EF.

	Normal EF (N=662)		Reduced EF (N=37)		
	observed	delta %	observed	delta %	P values
LV diameter (cm)	5.31±0.45	+3.8	5.73±0.59	+7.2	**0.022**
Relative wall thickness	0.33±0.05	-20.3	0.30±0.05	-24.3	NS
LV mass index (g/m$^{2.7}$)	45.9±8.8	-15.8	51.3±11.3	-11.2	NS
Ejection Fraction (%)	62.9±5.1	-3.0	57.9±4.6	-6.9	0.05
LA diameter (cm)	3.80±0.55	-1.00	4.14±0.7	+7.86	**0.001**
Mitral E/A ratio	0.91±0.32	+15.5	1.24±0.98	+48.4	**0.001**
E deceleration time (msec)	250.2±66.1	+20.4	234.8±81.9	+1.0	**0.011**
Isovolumic relaxation (msec)	95.0±21.0	-13.2	96.4±21.3	-13.1	NS

Echocardiographic Findings on Last Available Exam Before Reduced EF Documented

Abstract P43: A Hemodynamic Study of Hybrid Mechanical Chest Compression Patterns, Discriminating the Effect of Accelerated Compression from Accelerated Decompression in a Porcine Model of Cardiac Arrest

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Introduction: Effective chest compressions to reestablish sufficient cerebral and coronary perfusion are crucial during cardiac arrest. Piston based mechanical chest compression devices deliver accelerated compressions and decompressions,

resulting in superior hemodynamics compared to manual compression in animal studies. We have, in a porcine model of cardiac arrest, compared the hemodynamic effects of two different hybrid compression patterns with a standard pattern used in modern mechanical chest compression devices.

Methods: In 12 anesthetized domestic pigs in ventricular fibrillation, we monitored coronary perfusion pressures (CPP), cerebral cortical blood flow (CCBF), and cardiac function using transesophageal echocardiography (TEE). Three chest compression curves with similar rate and depth were tested in randomized crossover experiments using a custom build servo controlled mechanical chest compression device. Two hybrid compression curves, one with accelerated trapezoid compression and sinusoidal decompression (TrS), and one with sinusoidal compression and accelerated trapezoid decompression (STr), were tested against a standard accelerated trapezoid compression/decompression pattern (TrTr). Statistical comparisons were done with paired t tests and data presented as difference in means with 95% CI.

Results: We found 7% (1, 14, p=0.046) lower CCBF and a 3 mmHg (1, 5, p=0.017) reduction in CPP with the TrS method compared to TrTr, whereas there were only non-significant reduction in CCBF, 6% (–3, 15, p=0.176), with the STr method compared to TrTr, and no difference in CPP, 0 mmHg (–2, 3, p=0.703). TEE imaging revealed that direct cardiac compression was the major mechanism generating forward blood flow in our experimental model.

Conclusion: Both cardiac and cerebral perfusion benefited from rapid decompression, while rapid compression in itself caused no significant improvement in hemodynamics. The evolution of mechanical CPR is dependent on further exploring the physiology behind forward blood flow during external chest compressions.

Best Original Resuscitation Science, Moderated Poster Session

Abstract P81: Transthoracic Impedance During Real Cardiac Arrest Defibrillation Attempts: Are Stacked-Shocks Appropriate?

Dana E Niles[1]; Robert M Sutton[1]; Sara Brunner[2]; Mette Stavland[3]; Peter Meaeny[4]; Akira Nishisaki[4]; Kristy Arbogast[4]; Matthew Maltese[4]; Aaron Donoghue[4]; Sujatha Devale[4]; Robert A Berg[4]; Vinay Nadkarni[4]. [1] Childrens Hosp Philadelphia, Philadelphia, PA, [2] Laerdal Med, Stavanger, Norway, [3] Lerdal Med, Stavanger, Norway, [4] Childrens Hosp Philadelphia, Philadelphia, PA

Introduction: In 2005, AHA changed recommendations to treat ventricular fibrillation from 3 transthoracic stacked-shocks to 1 shock followed by immediate chest compressions. Prior stacked-shocks were recommended based on low first-shock efficacy of monophasic waveforms and theoretical decrease in TransThoracic Impedance (TTI) following each shock. Recent data shows poor first-shock efficacy of biphasic defibrillation in children. Our *objective* was to characterize TTI following failed biphasic defibrillation attempts in children during real cardiac arrest, and assess whether a stacked-shock approach is appropriate.

Hypothesis: Transthoracic impedance (TTI) is lower immediately post-shock compared to pre-shock in children ≥8 years during real cardiac arrest. However, the duration of decreased TTI is too short to expect stacked shocks to improve defibrillation success.

Methods: TTI was collected via standard Anterior-Apical defibrillator electrode pads during consecutive in-hospital cardiac arrest defibrillation attempts in children ≥8yrs. TTI (Ohms) was measured continuously, and specifically documented at 0.5 second intervals pre and post-shock. TTI variables analyzed with descriptive summaries/ paired t-test.

Results: Analysis yielded 13 evaluable shock events during 5 cardiac arrests (mean age 14.3±5 yrs, weight 47.4±7.3 kg,) between September 2006-May 2009. Compared to pre- shock values (56.6±23.5 Ohms), TTI was significantly lower immediately post-shock at 0.1sec post (55.2±22.2 Ohms, $p<0.01$), 0.5 sec post (55.4±22.3 Ohms, $p<0.01$), and 1 sec post (54.3±22.9 vs. $p<0.02$). No difference was demonstrated by 2 sec post-shock (54.7±23.3 vs. 55.5±24.2 Ohms, $p<0.07$).

Conclusions: TTI was significantly lower for <2 seconds immediately post-shock, compared to pre-shock, in children during real cardiac arrest. However, TTI reduction quickly dissipates (<2 sec), suggesting limited feasibility and low likelihood that stacked-shocks would improve defibrillation success.

Abstract 5419: Hypokalemia Blunts Left Ventricular Mass Regression in Hypertensive Patients During Losartan- or Atenolol-Based Treatment: The LIFE Echo-substudy

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Background: It has been reported that hypokalemia (HypoK) is associated with persistent ECG left ventricular (LV) hypertrophy in treated hypertensive patients. The aim of the present study was to assess the impact of HypoK on echocardiographic LV mass regression during aggressive antihypertensive treatment.

Methods: We analyzed data from 863 patients in the LIFE echo substudy (age 66±7 years, 41% women) with available serum K^+ levels. Patients were dichotomized according to presence of HypoK (i.e. <3.90mmol/L, lowest quartile). LV mass regression after one year of treatment was compared among groups.

Results: Patients with HypoK had similar mean age and gender distribution to patients with normal K^+ (all p=ns), but higher systolic and diastolic blood pressure (BP) and heart rate (all p<0.05). After one year, similar reduction among groups in both systolic and diastolic BP (p=ns) was found. In multivariate analysis controlling for differences in age, gender, baseline LV mass, hydroclorothiazide use before or during the study, baseline BP, and BP change, patients with HypoK had a significantly lower regression of LV mass as compared to the normal K^+group (p<0.001). Furthermore, while in patients randomized to Losartan (n=434) reduction in LV mass was not significantly different in the absence or presence of HypoK (p=ns), in the Atenolol group HypoK was associated with a nearly 60% lower LV mass reduction (Figure; p<0.001).

Conclusions: Despite similar blood pressure reduction with treatment, patients with HypoK have a lower LV mass regression. While Losartan is able to offset the negative impact of HypoK, its presence markedly affects LV mass reduction on Atenolol-based therapy.

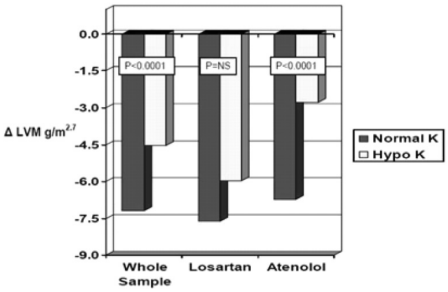

Figure. Left ventricular mass reduction after one year of anti-hypertensive treatment according to serum K^+ levels and treatment arm.

Abstract 5533: Gender Differences in Outcome During Antihypertensive Therapy in Relation to Regression of Electrocardiographic Left Ventricular Hypertrophy: The LIFE Study

Peter M Okin[1]; Eva Gerdts[2]; Darcy A Hille[3]; Sverre E Kjeldsen[4]; Jonathan M Edelman[5]; Björn Dahlöf[6]; Richard B Devereux[7]. [1] Weill Cornell Med College, New York, NY, [2] Univ of Bergen and Haukeland Univ Hosp, Bergen, Norway, [3] Merck Rsch Labs, West Point, PA, [4] Univ of Oslo, Ullevål Hosp, Oslo, Norway, [5] Merck & Co., Inc., Whitehouse Station, NJ, [6] Sahlgrenska Univ Hosp/Östra, Göteborg, Sweden, [7] Weill Cornell Med College, New York, NY

Background: Men and women have well-established differences in the magnitude of ECG amplitudes and durations and women have less regression of ECG left ventricular hypertrophy (LVH) in response to blood pressure lowering, even after adjusting for gender differences in baseline severity of LVH, treatment effects and blood pressure changes. However, whether women ex-

perience less prognostic benefit from their lesser regression of ECG LVH has not been examined.

Methods and Results: Cardiovascular (CV) outcomes were examined in relation to regression of Sokolow-Lyon voltage (SLV) in 4963 women and 4230 men randomly assigned to losartan- or atenolol-based treatment. ECGs were performed at baseline, 6 months and then yearly until study end. Regression of LVH was dichotomized using sex-specific median decreases in SLV ≥3.0 mm in women and ≥4.5 mm in men. Women had significantly lower 5-year event rates for CV death (3.8 vs 6.2%, p<0.0001), MI (3.3 vs 6.0%, p<0.0001), stroke (5.5 vs 7.3%, p=0.003) and the LIFE study composite endpoint of these three events (9.8 vs 15.6%, p<0.0001). In Cox regression analyses performed separately in women and men, women and men had similar reductions in risk of all events associated with regression of SLV defined by decreases in SLV exceeding the sex-specific median entered as time-varying covariates (Table). The absence of gender differences in predictive value of regression of SLV LVH was confirmed by the absence of any significant interaction term between gender and change in SLV, with analyses performed treating SLV as either a sex-specific median decrease or as a continuous variable with no adjustment for gender.

Conclusions: Despite lesser regression of ECG LVH than men, women have lower event rates than men and appear to derive the same degree of risk reduction as men from greater regression of SLV, independent of treatment effects, in-treatment blood pressure and the impact of possible gender differences in other risk factors on outcomes.

		Women			Men		
Cox Analysis	Endpoint	Hazard Ratio	95% CI	P Value	Hazard Ratio	95% CI	P Value
Univariate		0.52	0.43–0.63	<0.001	0.61	0.51–0.71	<0.001
	Cardiovascular Death	0.55	0.41–0.73	<0.001	0.53	0.40–0.69	<0.001
	MI	0.54	0.39–0.76	<0.001	0.65	0.50–0.85	0.002
	Stroke	0.48	0.37–0.63	<0.001	0.61	0.48–0.77	<0.001
Multivariate*	Composite Endpoint	0.60	0.48–0.74	<0.001	0.68	0.56–0.82	<0.001
	Cardiovascular Death	0.56	0.40–0.79	0.001	0.53	0.39–0.72	<0.001
	MI	0.55	0.38–0.79	0.001	0.88	0.65–1.20	0.420
	Stroke	0.62	0.46–0.83	0.001	0.65	0.49–0.86	0.003

Outcomes in Relation to Sex-Specific Median Regression of Sokolow-Lyon Voltage LVH

Abstract 1449: Racial Differences in Incident Heart Failure Among Hypertensive Patients During Antihypertensive Therapy: The LIFE Study

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Background: Blacks have a higher prevalence of heart failure (HF) than non-blacks, possibly reflecting a greater burden of HF risk factors, including hypertension. Although recent data have shown that incident HF is significantly higher in blacks during 20 year follow-up of young adults and in elderly population cohorts, the relationship of incident HF to race among hypertensive patients undergoing aggressive blood pressure lowering has not been examined.

Methods and Results: Incident HF was examined in 497 black and 8199 non-black hypertensive patients with no history of HF who were randomly assigned to losartan- or atenolol-based treatment. Compared with non-blacks, blacks were younger, more obese, more likely to smoke and have diabetes, have a history of ischemic heart disease and stroke, had higher baseline serum creatinine and albuminuria and a higher baseline prevalence of the ECG strain pattern. During 4.7±1.1 years mean follow-up, HF hospitalization occurred in 265 patients (3.0%); 5-year HF incidence was significantly greater in black than non-black patients (7.0 vs 3.1%, p<0.001). In univariate Cox analyses, black race was associated with a 132% increased risk of new HF (HR 2.32, 95% CI 1.58 –3.42). In Cox multivariate analyses adjusting for randomized treatment, incident MI, in-treatment heart rate, diastolic and systolic pressure, Cornell product and Sokolow-Lyon voltage criteria for left ventricular hypertrophy (LVH), age, sex, body mass index, prevalent and history of atrial fibrillation and diabetes, history of MI, ischemic heart disease, stroke, peripheral vascular disease, smoking status, baseline serum total and HDL cholesterol, creatinine,

glucose, urine albumin/creatinine ratio and for the presence of the strain pattern on the baseline ECG, black race remained associated with an 85% increased risk of developing new HF (HR 1.85, 95% CI 1.01–3.38).

Conclusions: Incident HF is substantially more common among black than white hypertensive patients. The increased risk of developing new HF in black patients persists after adjusting for the higher prevalence of HF risk factors in blacks, for treatment effects and in-treatment blood pressure and for the known predictive value of in-treatment ECG LVH for incident HF in this population.

Abstract 3477: Prognostic Value and Serial Changes of Plasma Adiponectin Concentration in Patients With Chronic Heart Failure. Data From the GISSI-HF Trial

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Aims: Adiponectin, an adipocyte-specific cytokine abundant in plasma, is a marker of poor outcome in chronic heart failure (HF). We assessed the prognostic value of a single determination and serial changes in adiponectin concentration in HF and the effect of n-3 PUFA or statin.

Methods: Adiponectin (Delphia, Perkin Elmer) and NT-proBNP (Roche) were assayed at baseline and after 3 months in 1234 patients with chronic HF enrolled in the GISSI-HF trial, and randomized to n-3 PUFA (1 g/d) or rosuvastatin (10 mg/d) vs. placebo. Association between markers and mortality (follow-up 3.9 yrs) was tested with Kaplan-Meier curves and Cox models.

Results: Baseline adiponectin was inversely related to BMI (r=–0.28, $p<0.0001$), directly proportional to NT-proBNP (r=0.47, $p<0.0001$) and higher in the 333 patients who died (11.37 [7.43–17.73] mg/L) compared to the 901 survivors (8.43 [5.94 –12.25 mg/L], $p<0.0001$). Patients in the upper tertile of baseline adiponectin (>11.83 mg/L) had a higher risk of mortality compared to lower tertile ($p<0.05$) but not after adjustment for NT-proBNP. Patients with relative increase in adiponectin over 3 months had higher mortality (29.1%) than those with stable levels (21.7%, HR [95%CI] = 1.46 [1.09 –1.96], p=0.011). By univariate analysis, median adiponectin levels predicted mortality in normal and overweight but not in lean or obese patients (Table). Adiponectin predicted mortality in the 172 patients with a non-intentional loss of body mass ≥2kg in the previous 6 months (p=0.0018), but not in those with intentional loss (n=194, p=0.34); NT-proBNP was predictive in both groups ($p<0.0005$). Compared to matching placebos, 3-month changes in adiponectin concentration were not different in the two arms.

Conclusions: Single measurement and serial changes in adiponectin are weak predictors of mortality in this large cohort of patients with chronic HF. Neither n-3 PUFA nor rosuvastatin had an effect on adiponectin plasma concentration.

BMI (kg/m^2)	N. patients	Adiponectin (median [Q1-Q3], mg/L)	Mortality (%)		Log-rank test (K-M)
			<median	>=median	
<22	137	13.8 [9.7–18.4]	27.1	37.3	0.16
22–24.9	302	10.2 [7.0–15.0]	21.6	37.6	0.0016
25–29.9	535	8.4 [6.0–12.1]	16.6	34.4	<0.0001
>=30	260	7.7 [5.2–11.7]	20.0	28.5	0.08

Univariate prognostic value of baseline adiponectin according to body-mass index

Abstract 3526: Biphasic Preejection Septal Deformation in Left Bundle Branch Block -"Tug Of War" Between Early-activated Septum and Late-activated Lateral Wall

Ola Gjesdal; Espen W Remme; Anders Opdahl; Helge Skulstad; Kristoffer Russell; Erik Kongsgård; Thor Edvardsen; Otto A Smiseth. Rikshospitalet, Oslo, Norway

Introduction: Abnormal septal motion in LBBB has been assumed to represent passive motion related to reversal of the end-diastolic left-to-right transseptal pressure gradient (TSG). Recently, we

demonstrated contribution of active septal contraction to this motion during preejection. We now investigate how active septal and LV free wall contractions contribute to septal deformation in LBBB.

Methods: In 8 anesthetized dogs with ventricular manometers we measured myocardial deformation (strain) by sonomicrometry and echocardiography and electrical conduction time by intra-myocardial EMG. LBBB was induced by RF-ablation.

Results: During LBBB electrical activation of the LV free wall was delayed 51±4 ms (±SEM) relative to septum. The free wall segment was stretched 2.2±0.5% prior to onset of shortening. Preejection septal deformation was biphasic with 6.1±4.5% ($p<.01$) shortening followed by 3.9±2.8% ($p<.01$) lengthening which continued into the ejection phase (Fig). The interruption of septal shortening (ISS) coincided with onset of free wall shortening (4±3 ms after). At this time the radius of curvature was increased for septum (35±5%), but reduced for the free wall (–6±2%, $p<0.1$), implying higher wall stress in septum.

Conclusions: In LBBB, septal preejection deformation is biphasic with active shortening followed by lengthening. The results suggest that the septal wall lengthens due to forces generated in the late-activated freewall. Presystolic stretching increases free-wall force development via the Frank-Starling mechanism, whereas increased septal radius of curvature increases septal wall stress, and both mechanisms contribute to septal lengthening.

Abstract 3573: Protection of Hypothermia-induced Contractile Dysfunction in Mice With Cardiac Specific Expression of Slow Skeletal Troponin I

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Rewarming the intact heart from hypothermia is associated with reduced contractile function, decrease in myofilament response to Ca^2, and increased cardiac troponin I (cTnI) phosphorylation. To further investigate the functional significance of increased TnI phosphorylation in this setting, we tested the hypothesis that transgenic murine hearts with a complete stoichiometric replacement of cTnI with the isoform slow skeletal TnI (TG-ssTnI) results in improved myocardial function after deep hypothermia followed by rewarming (H/R). This isoform lacks PKA-induced phosphorylation sites and myofilaments show increased Ca^{2+} sensitivity. A group of non-transgenic littermates (NTG, n=7) were used for controls. Hypothermia (3 h at 22°C) was induced in anesthetized NTG and TG-ssTnI mice (n=7), followed by rewarming to normothermia (37°C). Cardiac function was determined in close chest animals using a 1.4F pressure-volume Millar catheter placed inside the left ventricle (LV) via the right carotid artery. Change in core temperature, measured by esophageal thermocouple, was achieved by surface cooling and rewarming. At baseline, cardiac output (CO) was similar between groups. During deep hypothermia, CO remained significantly reduced in NTG animals compared to TG (3.4±0.9 vs. 4.2±1.2 $ml \bullet min^{-1}$, $p<0.05$). After rewarming, significant differences ($p<0.05$) were found in CO (NTG 6.6±0.7 vs. TG-ssTnI 8.8±0.7 $ml \cdot min^{-1}$), stroke work (SW) (NTG 796±112 vs. TG-ssTnI 1208±67 $mmHg \cdot \mu l^{-1}$), and preload recruitable stroke work (PRSW) (NTG 38.3±4.9 vs. TG-ssTnI 68.8±8.2 mmHg). The isovolumic relaxation constant (Tau) was prolonged in TG-ssTnI both at baseline conditions (NTG=7.0±0.5 and in TG-ssTnI=8.6±0.4, $p<0.05$). However, after H/R, end diastolic pressure volume relationship remained unaltered in both groups. We conclude that TnI phosphorylation plays a significant role in the systolic dysfunction observed after H/R. Further, the expression of the ssTnI isoform results in functional preservation in hearts subjected to deep hypothermia followed by normothermia.

Abstract 3733: Inhibiting Phosphorylation of SMAD2 Preserves Cardiac Function During Pressure Overload

Johannes L Bjørnstad; Biljana Skrbic; Henriette S Marstein; Ivar Sjaastad; Geir Christensen; Theis Tønnessen. Oslo Univ Hosp Ulleval, Oslo, Norway

The TGF-beta superfamily has been postulated to play a role in regulating myocardial remodelling. SMAD2 mediates intracellular signalling by TGF-beta family members, and phosphorylation of SMAD2 might induce both deleterious and cardioprotective effects. We hypothesized that inhibiting phosphorylation of SMAD2 in pressure overload preserves left ventricular (LV) function by reducing myocardial fibrosis and cardiomyo-

cyte remodelling. C57BL/6 mice were randomized to one of the following four groups: one week of banding of the ascending aorta (AB) or sham procedure and receiving chow without (STD) or with an inhibitor of SMAD2 phosphorylation (SM16). SM16 treatment improved fractional shortening (FS) (31.8±2.6 % AB SM16 vs. 23.6±2.0 % AB STD, n=11–12, p=0.02) and mitral deceleration slope (Mdec) (25.6±2.2 m/s2 AB SM16 vs. 35.5±2.4 m/s2 AB STD, n=11–12, p<0.01), indicating improvement of both systolic and diastolic function. This was further supported by a negative correlation between p-SMAD2 and systolic and diastolic peak tissue velocity (R=0.47, p=0.04 and R=0.56, p=0.01, respectively, n=19). AB induced 37 % increased LV weight in both AB groups (n=32–40) and LV end diastolic diameter was equal in the four groups (n=6–12). However, markers of cardiomyocyte remodelling were reduced by SM16 as demonstrated by RT-PCR (n=5–8); the increased expression of alpha skeletal actin (7.3-fold up-regulation in AB) and myosin heavy chain beta (5.5-fold) was significantly lower in mice receiving SM16. The reduction in expression of SERCA2 in AB mice (1.8-fold down-regulation) was inhibited in the SM16 group. Moreover, the increased expression of collagen genes was dramatically reduced by SM16. There was, however, no difference in LV collagen protein between the four groups (n=10), as demonstrated by HPLC of hydroxyproline. This indicates beneficial cardiac effects of SM16 beyond inhibition of fibrosis. We conclude that inhibiting phosphorylation of SMAD2 preserves cardiac function in LV pressure overload. The improved systolic and diastolic function, as measured by improved FS and Mdec, might be explained by mechanisms beyond inhibition of myocardial fibrosis, possibly by effects on contractile proteins and Ca++ handling in the cardiomyocytes.

Best Original Resuscitation Science, Moderated Poster Session

Abstract P31: Out-of Hospital Advanced Cardiac Life Support With or Without a Physician: Effects on Quality of CPR and Outcome

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Background: The presence of physicians is believed to facilitate optimal management of out-of-hospital cardiac arrest, but has not been sufficiently documented.

Methods: Adult non-traumatic cardiac arrests treated by Oslo and Follo EMS between May 2003 and April 2008 were prospectively registered. Patients were categorized according to being treated by the physician manned ambulance (PMA) or by regular paramedic manned ambulances (non-PMA). Patient records and continuous electrocardiograms (ECGs) with impedance signals were reviewed. Quality of cardiopulmonary resuscitation (CPR) and clinical outcomes were compared.

Results: Resuscitation was attempted in 1128 cardiac arrests, of which 151 treated by non-PMA and PMA together were excluded from comparative analysis. Of the remaining 977 patients, 232 (24%) and 741 (76%) were treated by PMA and non-PMA, respectively. The PMA-group was more likely to have bystander witnessed arrests and initial VF/VT, and received better CPR quality with shorter hands-off intervals and pre-shock pauses, and having a greater proportion of patients being intubated. Despite uneven distribution of positive prognostic factors and better CPR quality, short-term and long-term survival were not different for patients treated by the PMA vs. non-PMA, with 34% vs. 33% (p=0.74) achieving return of spontaneous circulation (ROSC), 28% vs. 25% (p=0.50) being admitted to ICU and 13% vs. 11% (p=0.28) being discharged from hospital, respectively.

Conclusions: Survival after out-of-hospital cardiac arrest was not different for patients treated by the PMA and non-PMA in our EMS system.

Abstract 227: Normalized Global Systolic Circumferential Strain Can Detect Incipient Myocardial Dysfunction in Patients With Chronic Aortic Regurgitation

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Introduction: This study assessed whether global circumferential strain could disclose incipient myocardial dysfunction due to chronic aortic regurgitation (AR) with a consequent potential of being a means for optimal timing of valve surgery in patients with AR.

Methods: Thirty-four patients with chronic severe AR referred for aortic valve replacement were studied along with 31 healthy controls. Myocardial circumferential strain was measured by 2-dimensional speckle tracking echocardiography (2D-STE) in addition to standard assessment of LV volumes and ejection fraction (LVEF). Strain was normalized by end-diastolic volume in order to correct for the volume dependency of deformation.

Results: Global systolic circumferential strain was similar in the AR patients before surgery as compared to the healthy controls (–22.4±2.9 % vs. –22.6±2.5 %, p=0.74). This was the case also for LVEF (58±5 % vs. 59±6 % p=0.52). In contrast, normalized global circumferential strain was significantly lower in the AR patients (–0.10±0.05 vs. –0.24±0.08, p<0.01). Moreover, normalized strain increased after surgery indicating improved LV function (–0.13±0.07, p<0.01), although still reduced as compared to controls (p<0.01).

Conclusions: The study demonstrated markedly reduced normalized global circumferential strain in chronic AR patients with still preserved LVEF. Thus, normalized circumferential strain seems to be more sensitive in identifying myocardial impairment in AR patients than traditional measures and might consequently be of importance for improved timing of valve surgery.

Abstract 551: Left Ventricular Lengthening Load and Shear Strain Are Important and Independent Determinants of Rate of Diastolic Untwist

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Background: Previous studies suggest that peak rate of LV untwist (UTR) is determined by rate of LV relaxation. We tested the hypothesis that circumferential-longitudinal shear strain (S_{CL}) representing restoring forces and LV *lengthening load*, defined as LV pressure at onset of filling, are two other independent determinants of UTR.

Methods: In 8 anesthetized dogs we measured LV *lengthening load* as LV pressure at mitral valve opening (LVP_{MVO}). End-systolic S_{CL} and peak diastolic UTR were measured by sonomicrometry and UTR also by speckle tracking echocardiography (STE) at different levels of contractility induced by dobutamine and LAD-occlusion, and different lengthening loads induced by volume loading and caval constriction.

Results: Changes in UTR during dobutamine and ischemia correlated well with changes in *tau* (R = 0.81; *P*<0.01), and with S_{CL} (Fig 1), confirming a strong relationship between UTR and relaxation and restoring forces, respectively. Elevation of LVP_{MVO} by 5.4± 3.1 mmHg (mean ± SD, *P*<0.01) was associated with an increase in UTR from 59±10 to 82±27 °/s (*P*<0.05) and reduction of LVP_{MVO} by 6.4±1.3 mmHg (*P*<0.01) with a decrease in UTR to 45±12 °/s (*P*<0.05). Changes in UTR during loading interventions were associated with minor changes in *tau* and S_{CL}. Therefore, neither relaxation nor restoring forces could account for these changes in UTR, whereas LVP_{MVO} correlated well with UTR (Fig 2), suggesting a causal relationship. Similar changes in UTR were found using STE.

Conclusion: The present findings indicate that in the non-failing ventricle shear strain and lengthening load are important determinants of UTR, in addition to LV relaxation.

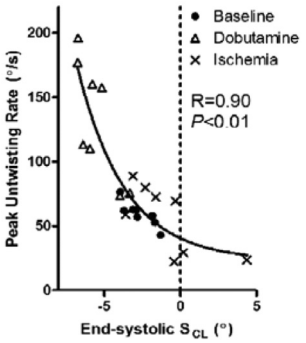


Figure 1: Restoring forces vs. untwisting rate

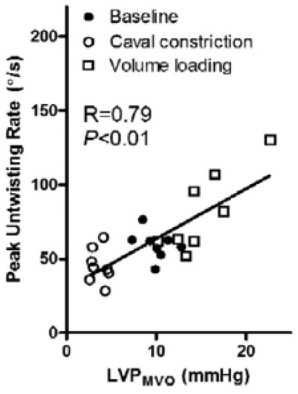


Figure 2: Lengthening load vs. untwisting rate

Abstract 552: How Twisted is the Left Ventricle?

Anders Opdahl; Espen W Remme; Thomas Helle-Valle; Thor Edvardsen; Otto A Smiseth. Rikshospitalet Univ Hosp, Oslo, Norway

Background: Conventional twist (RTwist) is calculated relative to end-diastolic (ED) LV configuration. The degree of diastolic untwisting may depend on the ED pressure. Hence, peak RTwist may not reflect how twisted the systolic LV configuration is. By calculating absolute twist (ATwist) relative to a fixed LV configuration we investigated the preload dependent untwisting of LV. We further investigated the influence of preload on peak RTwist and ATwist.

Methods: In 8 anesthetized dogs we assessed ED LV pressure (LVEDP) and measured LV twist by sonomicrometry which allowed assessment of twist relative to a fixed LV configuration. Both ED and peak ATwist was calculated relative to this configuration at baseline, during volume loading and caval constriction.

Results: Changes in LVEDP from 7.9 ± 1.1 (±SD) at baseline to 14.2±2.9 and 1.4±1.5 mmHg (both $P<0.01$) during volume loading and caval constriction, respectively, were associated with an increase in ED ATwist to 3.4±2.1 and a decrease to –4.4±1.5° (both $P<0.01$), during loading and caval constriction, respectively. A close correlation was observed between LVEDP and ED ATwist (R=0.90, $P<0.01$, Fig 1). Peak ATwist demonstrated a positive correlation (R=0.61, $P<0.01$, Fig 2a), whereas peak RTwist showed a negative correlation to LVEDP (R=0.61, $P<0.01$, Fig 2b), indicating that peak RTwist and ATwist respond oppositely to preload.

Conclusion: The present study indicates that the absolute ED twist configuration is determined by preload. Hence, conventional twist does not reflect how twisted the LV really is. In our model conventional twist underestimated peak twist during caval constriction and overestimated it during loading.

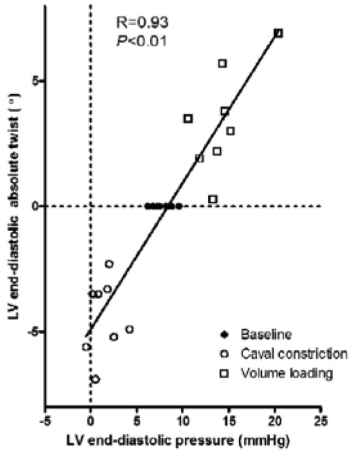


Figure 1: LVEDP vs. ED absolute twist

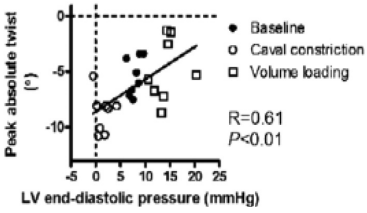


Figure 2a: LVEDP vs. peak absolute twist

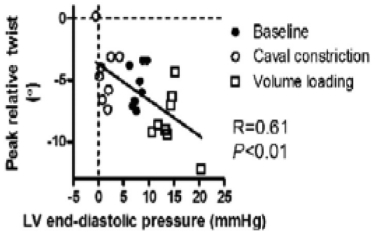


Figure 2b: LVEDP vs. peak relative twist

Abstract 711: Atrial Strain by Speckle Tracking Echocardiography: A New Non-Invasive Marker of Left Atrial Mean Pressure

Thomas Helle-Valle; Kaspar Broch; Otto Smiseth. Oslo Univ Hosp, Oslo, Norway

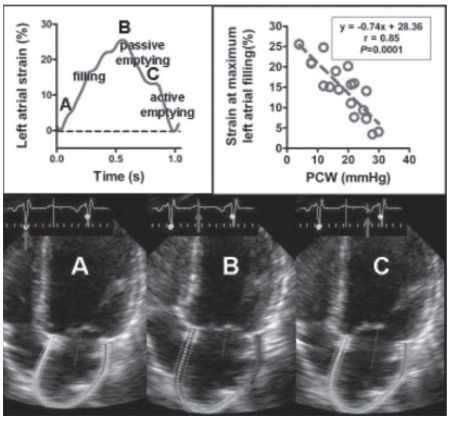
Background: Better non-invasive markers of left ventricular (LV) end-diastolic pressure (EDP) are needed. Due to the curvilinear shape of the atrial pressure-volume relationship, atrial chamber compliance will decrease when atrial pressure is elevated. Therefore, we predicted that markedly elevated atrial pressures would be associated with reduced atrial strain, and that atrial strain would be

inversely related to left atrial (LA) pressure. This hypothesis was tested in patients with congestive heart failure.

Methods: In 19 patients with idiopathic dilated cardiomyopathy, mean pulmonary capillary wedge pressure (PCWP) was measured invasively and was used as a surrogate for mean LA pressure. Using conventional 4-chamber recordings, LA strain was measured by speckle tracking echocardiography (STE) (Figure 1) and LA area by planimetry.

Results: Mean PCWP was 18.5±7.3 mmHg, LA strain at maximum filling was 14.7±6.6% and LA area was 8.4±1.9 cm^2/m^2. There was a strong correlation between PCWP and peak LA strain ($r = 0.85$, $p < 0.0001$, Figure 1), while the correlation between LA area and PCWP was not statistically significant ($r = 0.41$, $p = 0.07$).

Conclusion: We have demonstrated a close, inverse relationship between left atrial strain and left atrial pressure. These results suggest that assessment of atrial strain might be a useful supplementary clinical tool for non-invasive estimation of left atrial and LV end-diastolic pressures.



Abstract 2536: End-tidal Carbon Dioxide is Less Sensitive for Predicting Death in the Setting of Optimized Cardiopulmonary Resuscitation Quality

Jason P Alvarado[1]; Joar Eilevstjønn[2]; Brian Robertson-Dick[3]; Benjamin S Abella[4]; Terry L Vanden Hoek[5]; Dana P Edelson[5], [1] Univ of Illinois College of Medicine, Chicago, IL, [2] Laerdal Med Corp, Stavanger, Norway, [3] Univ of Chicago Med Cntr, Chicago, IL, [4] Univ of Pennsylvania, Philadelphia, PA, [5] Univ of Chicago Med Cntr, Chicago, IL

Introduction: End-tidal carbon dioxide ($ETCO_2$) is known to correlate with cardiac output and has been shown to predict death from cardiac arrest. However, $ETCO_2$ is likely affected by CPR quality, which is frequently suboptimal in clinical practice. As a result, the discrimination power of $ETCO_2$ in the setting of optimized CPR is not known.

Methods: We conducted a prospective study of consecutive in-hospital cardiac arrests at an academic medical center between 1/06 and 1/08. A CPR-sensing monitor/defibrillator which provided real-time audio visual feedback regarding CPR deficiencies was used. This device collected $ETCO_2$ via a monitor connected in line with the endotracheal tube. Patient demographics and outcomes were abstracted via chart review. Two-sided t-test and Receiver Operator Characteristics (ROC) were used to compare outcomes and assess $ETCO_2$ timepoints.

Results: $ETCO_2$ data were available for 118 patients, with a mean age of 60±16 years. Fifty-two percent were male and ROSC was achieved in 46%. Mean compression depth was 49±10 mm, with a rate of 109±10 and no flow fraction of 0.12±0.20. Ventilation rate was 13±8. The table below compares various $ETCO_2$ measurements between survivors and non-survivors. Using the previously validated 20 minute $ETCO_2$ value of $\leq$ 10 as a cutoff for predicting death yielded a sensitivity of 30%, specificity of 100%, positive predictive value (PPV) of 100%, and negative predictive value (NPV) of 7%. Increasing the cutoff to less than or equal to 25 mmHg raised the sensitivity to 65% and NPV to 13% while maintaining 100% specificity and PPV.

Conclusions: We demonstrated higher $ETCO_2$ values than have previously been reported in a setting with carefully monitored and preserved CPR quality. As a result, the sensitivity and NPV of the 20 minute $ETCO_2$ cutoff of $\leq$10 mmHg are considerably lower than previously reported, limiting its utility for predicting death. A higher cutoff may be needed to improve accuracy in the setting of optimized CPR quality.

$ETCO_2$ timepoint	Survived to Discharge [n=6]	Died in the Hospital [n=118]	p-value	ROC Area [95%CI]
Initial	42.5±10.9	18.6±14.0	0.0001	0.92 [0.86–0.98]
Final	49.8±13.7	21.0±13.1	<0.0001	0.93 [0.86–1.00]
Mean	46.5±13.3	20.1±11.7	<0.0001	0.93 [0.87–1.00]
Maximum	57.5±9.3	30.4±17.2	0.0002	0.91 [0.85–0.97]
Minimum	29.2±16.4	12.3±9.1	0.0001	0.85 [0.69–1.00]
20 minutes [n=42]	30.9±13.8 [n=2]	16.2±10.0 [n=40]	0.0004	0.78 [0.61–0.95]

Comparison of various measures of EtCO2 between survivors and non-survivors.

Abstract 2699: Mechanisms Underlying Increased Ca^{2+} Influx in SERCA2 Kockout Cardiomyocytes

William E Louch; Halvor K Mork; Karina Hougen; Ivar Sjaastad; Kristin B Andersson; Geir Christensen; Ole M Sejersted. Univ of Oslo, Oslo, Norway

In normal cardiomyocytes, contraction is predominantly dependent on Ca^{2+} release from the sarcoplasmic reticulum (SR), and reduced activity of the SR Ca^{2+} ATPase (SERCA) has been linked to heart failure. We have recently observed that mice with cardiomyocyte-specific excision of SERCA (KO) compensate for markedly reduced SR function by increasing trans-sarcolemmal Ca^{2+} flux. Here we investigated the mechanisms underlying the greater Ca^{2+} entry. At seven weeks following gene deletion, SR Ca^{2+} release was not detectable in KO cardiomyocytes. Expression of the L-type Ca^{2+} channel was increased in KO as protein levels of the pore forming subunit, α_{1C}, and regulatory subunit, α_2/δ_1, were 178% and 147% of control values, respectively. Peak L-type Ca^{2+} currents were 49% larger in KO than control, and slower Ca^{2+} current decay kinetics resulted in integrated currents which were 220% of control values. The action potential (AP) was also prolonged in KO. Treatment with 20 μM nifedipine or 0 mM Ca^{2+} in the external solution abolished this difference, indicating that the longer AP resulted from increased Ca^{2+} current. Indeed, measurements of transient outward K^+ current were similar in KO and control. Switching the voltage stimulus from the control AP to the KO AP increased the magnitude of the Ca^{2+} transient by 67% in KO myocytes. This augmentation predominantly resulted from increased integrated Ca^{2+} current. Thus, overall L-type Ca^{2+} entry in KO was increased from control values by 3–3.5 fold when AP alterations were considered. AP prolongation in control cells also increased Ca^{2+} influx, but augmentation of the Ca^{2+} transient was less marked (19%) due to reduced efficiency of Ca^{2+}-induced Ca^{2+} release. Finally, we observed that treatment with 5 μM KB-R7943 markedly reduced Ca^{2+} transients in KO cells but not in controls, indicating a greater role of reverse-mode Na^+/Ca^{2+} exchange in KO. Thus, increased expression of the Ca^{2+} channel, absence of Ca^{2+}-dependent inactivation, action potential prolongation, and augmented reverse-mode Na^+/Ca^{2+} exchange can together greatly enhance Ca^{2+} influx when SR function is reduced. These observations suggest that reduced SR function in human heart failure may be treated by strategies which augment sarcolemmal Ca^{2+} fluxes.

Abstract 4690: Impact of Thrombus Aspiration in Patients With STEMI Undergoing Primary PCI: Analysis From the HORIZONS-AMI Trial

Dennis W Nilsen[1]; Roland Wu[2]; Alexandra J Lansky[2]; Roxana Mehran[2]; Martin Fahy[2]; Eugenia Nikolsky[2]; Bernhard Witzenbichler[3]; Giulio Guagliumi[4]; Jan Z Peruga[5]; Bruce R Brodie[6]; Dariusz Dudek[7]; Martin Möckel[8]; Gregg W Stone[9]. [1] Stavanger Univ Hosp, Stavanger, Norway, [2] Columbia Univ and the Cardiovascular Rsch Foundation, New York, NY, [3] Charité Campus Benjamin Franklin, Berlin, Germany, [4] Ospedali Riuniti di Bergamo, Bergamo, Italy, [5] Silesian Cntr for Heart Disease, Lodz, Poland, [6] LeBauer Cardiovascular Rsch Foundation and Moses Cone Hosp, Greensboro, NC, [7] Jagiellonian Univ, Krakow, Poland, [8] Charité –Univ Medicine, Berlin, Germany, [9] Columbia Univ and the Cardiovascular Rsch Foundation, New York, NY

Objective: We compared epicardial flow, ST-segment resolution and clinical outcomes after primary PCI in STEMI performed with and without use of a “simple” aspiration catheter, and assessed the role of contemporary antithrombotic strategies in patients treated with thrombus aspiration.

Methods and Results: In the HORIZONS-AMI trial, at operator discretion, catheter-based thrombus aspiration prior to PCI was performed in 318 of 3233 pts (9.8%). The use of thrombus aspiration correlated with younger age, current smoking, prior history of PCI, higher incidence of thrombus on the baseline angiogram, higher rates of direct stenting and post stent dilatation. By core lab analysis, during the procedure pts with vs without thrombus aspiration had higher rates of distal embolization (9.0% vs. 3.2%, $p<0.0001$) and slow flow (5.3% vs. 3.4%, $p=0.06$) but not of dissection (6.6% vs. 5.3%, $p=0.32$). There were no significant differences in the rates of complete (>70%) STR at 60 min post procedure (48.2% vs. 50.3%, $P=0.51$). Pts with vs without thrombus aspiration had similar rates of 30-day MACE (death, reinfarction,

TVR or stroke; 4.7% vs. 4.2%, p=0.68) but higher rates of major bleeding (8.5% vs. 6.3%, p=0.13). There were no significant interactions between randomized antithrombin regimen (bivalirudin monotherapy vs. heparin + glycoprotein IIb/IIIa inhibition) and performance of thrombus aspiration on either TIMI-3 flow, 60 minute STR, or 30 day MACE (p for interaction=0.81, 0.68 and 0.62 respectively).

Conclusion: Pts treated with thrombus aspiration prior to PCI compared to conventional PCI in the HORIZONS-AMI trial had similar rates of final TIMI flow grade 3 and higher rates of angiographic complications, with similar rates of complete STR and 30-day MACE. Adjunctive antithrombotic therapy regimen had no significant impact on the outcomes of thrombus aspiration.

Abstract 4895: Competing Effects of Hypokalemia and Hydrochlorothiazide Treatment on Regression of Cornell Product Left Ventricular Hypertrophy in Hypertensive Patients: Implications for Development of Potassium-Sparing Diuretics

Peter M Okin[1]; Sverre Kjeldsen[2]; Lars H Lindholm[3]; Björn Dahlöf[4]; Richard B Devereux[5]. [1] Weill Cornell Med College, New York, NY; [2] Univ of Oslo, Ullevål Hosp, Oslo, Norway; [3] Umeå Univ, Umeå, Sweden; [4] Sahlgrenska Univ Hosp/Östra, Göteborg, Sweden; [5] Weill Cornell Med College, New York, NY

Background: Hydrochlorothiazide (HCTZ) treatment is associated with blood pressure reduction and regression of left ventricular hypertrophy (LVH). HCTZ is also associated with hypokalemia (hypoK), which increases blood pressure and is associated with a greater likelihood and severity of electrocardiographic (ECG) LVH. However, the competing effects of HCTZ use and concomitant hypoK on LVH regression have not been examined.

Methods: Baseline and yearly Cornell product (CP) ECG LVH levels were examined in relation to hypoK (serum K ≤3.90, the lowest quartile) and HCTZ use in 7816 patients in the LIFE study with baseline and year-1 K levels. Patients were randomized to losartan vs atenolol-based treatment and additional HCTZ as needed.

Results: Patients on HCTZ had lower serum K levels at year 1 (4.05 ± 0.38 vs 4.24 ± 0.38), year 2 (4.04 ± 0.38 vs 4.25 ± 0.38), year 3 (4.04 ± 0.39 vs 4.27 ± 0.39) and year 4 (4.05 ± 0.41 vs 4.26 ± 0.38) of the study (all p < 0.001). In 2-way analysis of covariance adjusting for age, sex, race, prior and randomized treatment, yearly body mass index, serum glucose and creatinine, and for baseline and change in diastolic and systolic pressure, hypoK was associated with less mean reduction of CP LVH whereas HCTZ use was associated with greater regression of CP LVH between baseline and years 1 to 4. Multivariate logistic regression analyses with the same covariates revealed that hypoK was associated with a statistically significant 15 to 19% lower likelihood of ≥median (236 mm·ms) reduction in CP LVH while HCTZ use was associated with an 18 to 33% greater likelihood of CP LVH regression of ≥236 mm·ms between baseline and years 1 to 4.

Conclusions: HCTZ therapy is independently associated with a greater likelihood and magnitude of LVH regression whereas concomitant hypoK is associated with a competing lower likelihood and magnitude of LVH regression during antihypertensive therapy. These findings suggest that hypoK may blunt regression of LVH during treatment.

Change in CP LVH (mm·ms)	No HCTZ & Hypokalemia (K ≤3.90)	No HCTZ & Normal K (K >3.90)	HCTZ & Hypokalemia (K ≤3.90)	HCTZ & Normal K (K >3.90)	p value* Hypokalemia	p value* HCTZ
Baseline to Year-1	-113±826	-133±726	-152±628	-213±673	0.048	0.004
Baseline to Year-2	-137±656	-194±735	-224±653	-276±762	0.017	<0.001
Baseline to Year-3	-135±860	-171±752	-237±692	-283±749	0.009	<0.001
Baseline to Year-4	-145±704	-188±784	-228±751	-261±815	0.032	0.002

Odds of CP LVH regression ≥236 mm·ms	Hypokalemia Odds Ratio	Hypokalemia 95% CI	HCTZ Odds Ratio	HCTZ 95% CI	p value* Hypokalemia	p value* HCTZ
Baseline to Year-1	0.82	0.73–0.91	1.18	1.05–1.32	<0.001	0.005
Baseline to Year-2	0.85	0.76–0.95	1.23	1.10–1.38	0.003	<0.001
Baseline to Year-3	0.81	0.73–0.91	1.33	1.19–1.49	<0.001	<0.001
Baseline to Year-4	0.87	0.78–0.97	1.20	1.07–1.35	0.012	0.002

Regression of Cornell Product LVH in Relation to HCTZ Use and Hypokalemia

Abstract 5017: Osteoprotegerin and the Risk of Recurrent Events in Patients With Non-ST elevation Acute Coronary Syndromes (NSTE-ACS): Observations From MERLIN-TIMI 36

Marc Bonaca[1]; Torbjorn Omland[2]; Marc S Sabatine[3]; Sabina A Murphy[3]; Benjamin M Scirica[3]; Lars M Rasmussen[4]; Allan Flyvbjerg[5]; David A Morrow[6]. [1] Brigham and Women's Hosp, Boston,

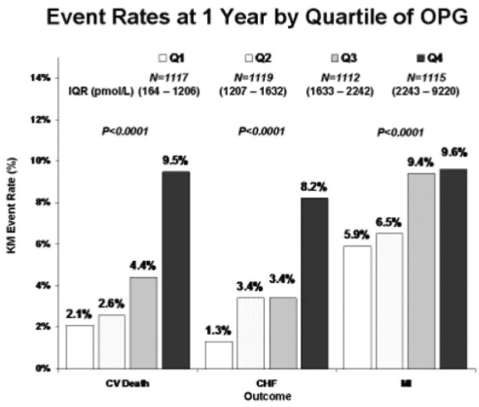
MA, [2] Univ of Oslo, Oslo, Norway, [3] Brigham and Women's Hosp, Boston, MA, [4] Odense Univ Hosp, Odense, Denmark, [5] Aarhus Univ Hosp, Aarhus, Denmark, [6] Brigham and Women's Hosp, Boston, MA

Osteoprotegerin (OPG) inhibits bone resorption and may also play a role in mediating vascular calcification. Recent studies have suggested that high plasma OPG is a strong predictor of cardiovascular disease (CV) and mortality. We hypothesized that OPG would be useful for risk assessment in patients presenting with NSTE-ACS.

Methods: We measured OPG at baseline in 4,463 pts with NSTE-ACS randomized to ranolazine or placebo in the MERLIN-TIMI 36 trial. Patients were followed for an average of one year. Endpoints were adjudicated by a blinded CEC.

Results: OPG at presentation showed a significant graded association with higher rates of recurrent CV events (Figure). OPG > median (1632 pmol/L, IQR 1206–2242) was associated with a higher risk of CV death (HR 2.9; 95% CI 2.2 – 4.0), CV death or MI (HR 1.9; 95% CI 1.6 – 2.3), and CV death or CHF (HR 2.5; 95% CI 1.9 – 3.1). After adjustment for important covariates including age, gender, diabetes, smoking, HTN, index event, cTnI, CRP and BNP, OPG remained independently associated with the risk of death (adj HR 1.7; 95% CI 1.2 – 2.4), CVD or MI (adj HR 1.4; 95% CI 1.1 – 1.7) and CVD or CHF (adj HR 1.4; 95% CI 1.1 – 1.8).

Conclusions: OPG was independently associated with long-term risk of recurrent CV events in patients with NSTE-ACS, adding to clinical predictors, cTnI, CRP and BNP. This finding in a large data set adds to the emerging evidence supporting OPG as a candidate prognostic marker in pts with ACS, and supports investigation of other therapies that might modify this risk.



Event Rates at 1 Year by Quartile of OPG

❤

Det er mogeleg at den norske gjennomsnittsintelligensen ikkje kan undervurderast; men eg trur det ikkje.

Ivar Eskeland

❤

Ulempen med politiske vitser er at noen av dem blir valgt.

Ivar Eskeland

❤

Always live within your income, even if you have to borrow money to do so.

Josh Billings

❤

To treat your facts with imagination is one thing; to imagine your facts is another.

J Burroughs

❤

I occationally play works by contemporary composers, and for two reasons: First to discourage the composer from writing any more, and secondly to remind myself how much I appreciate Beethoven.

J Heifetz

Norske abstracts presentert på TCT 2009

TCT-7

Impact of Thrombus Aspiration during Primary Percutaneous Coronary Intervention in Acute Myocardial Infarction: Analysis from the HORIZONS-AMI Trial

Dennis W.T. Nilsen[1], Roland Wu[2], Jan E Nordrehaug[3], Vernon Bonarjee[1], Vegard Tuseth[3], Jan Z Peruga[4], Bruce B Brodie[5], Dariusz Dudek[6], Martin Möckel[7], Andrzej Ochala[8], Alexandra J Lansky[2], Roxana Mehran[2], Eugenia Nikolsky[2], Martin Fahy[9], Gregg W Stone[2]
[1]Stavanger University Hospital and University of Bergen, Bergen, Norway[2]Columbia University Medical Center and the Cardiovascular Research Foundation, New York, NY;[3]Haukeland University Hospital and University of Bergen, Bergen, Norway[4]Silesian Center for Heart Disease, Lodz, Poland[5]LeBauer Cardiovascular Research Foundation and Moses Cone Hospital, Greensboro, NC;[6]Jagiellonian University, Krakow, Poland[7]Charité–University Medicine, Berlin, Germany[8]Krakow Cardiovascular Research Institute, Krakow, Poland[9]Cardiovascular Research Foundation, New York, NY

Background: Thrombus aspiration (TA) in acute ST-segment elevation myocardial infarction (STEMI) may reduce microvascular obstruction and impaired myocardial perfusion. Randomized trials of thrombectomy devices during primary PCI) have provided conflicting results regarding clinical efficacy. We therefore examined the outcomes of TA from the large-scale, multicenter HORIZONS-AMI trial.
Methods: HORIZONS-AMI prospectively randomized 3602 pts within 12h of STEMI onset to bivalirudin alone or unfractionated heparin + a glycoprotein IIb/IIIa inhibitor. Passive TA was allowed prior to PCI per investigator discretion. Rates of major adverse cardiac events (MACE; death, reinfarction, target-vessel revascularization for ischemia, or stroke) within 30 days were analyzed according to TA.
Results: Primary PCI was performed in 3345 pts in whom complete data on 3298 pts were available for analysis, including 381 pts who underwent TA and 2917 pts who underwent conventional PCI. Pts in the TA group were younger, more frequently smokers, and more commonly had a history of MI, PCI or CABG. The use of TA was associated with higher incidence of thrombus on baseline angiogram (25.6% vs. 14.3%, p<0.0001), higher rates of direct stenting (40.7% vs 29.3%, p<0.0001) and post stent dilatation (47.9% vs 35.7%, p<0.0001) and longer total stent length (28mm vs 24mm, p=0.01). Main outcomes are presented in the Table. By multivariable analysis, use of TA did not predict MACE at 30 days (hazard ratio [95% confidence interval] = 0.96 [0.56, 1.52], P=0.90) or at 1 year (1.03 [0.68, 1.55], P=0.89).

TCT-102

Angiographic Follow-up In Diabetic vs. Non-diabetic Patients In the Nordic Bifurcation Studies

Niels R Holm[1], Michael Maeng[1], Jens F. Lassen[1], Andrejs Erglis[2], Inga Narbute[2], Indulis Kumsars[2], Paal Gunnes[3], Matti Niemelä[4], Kari Kervinen[4], Terje S. Steigen[5], Jan S. Jensen[6], Helle Hoejdahl[1], Leif Thuesen[1]
[1]Dep. Cardiology B, Aarhus, Denmark[2]Paul Stradins Clinical Hospital, Riga, Latvia[3]Feiringklinikken, Feiring, Norway[4]Oulu University Hospital, Oulu, Finland[5]University Hospital of Tromsoe, Tromsoe, Norway[6]Gentofte University Hospital, Gentofte, Denmark

Background: The use of drug eluting stents (DES) reduces restenosis after percutaneous coronary intervention in diabetic and non-diabetic patients and is associated with excellent angiographic results in bifurcation lesions. However, there is limited angiographic follow-up data in coronary bifurcation lesions in diabetic patients treated with DES. Therefore, we compared the angiographical results for diabetic and non-diabetic patients included in the Nordic Bifurcation studies.
Methods: A total of 631 patients (83 diabetic and 548 non-diabetic patients) were included in the angiographic part of The Nordic Bifurcation Study and The Nordic Bifurcation Stent Technique Study. In all patients 8-month follow-up angiography was scheduled at study start. In the diabetic and the non-diabetic groups mean age were 65±9 yrs vs. 64+10 yrs, and 23% vs. 23% had female sex. Coronary angiograms obtained at baseline, at completion of the stenting procedure, and after 8 months were analyzed using a computer-based system dedicated to bifurcation analysis (QAngio XA version 7.0, Medis, Leiden, The Netherlands).
Results: Reference vessel diameter, minimal luminal diameter and late luminal loss of proximal main vessel, distal main vessel and the side branch were not significantly different in diabetic and non-diabetic patients. In-segment binary restenosis rate of the main vessel was 10.8% vs. 2.9% (p=0.003), of the side branch 12.0% vs. 10.8% (ns) and of the entire bifurcation lesion 20.5% vs. 14.3% (p=0.09) in the diabetes and in the non-diabetes groups, respectively.
Conclusion: As compared to non-diabetic patients, diabetic patients had increased main vessel binary restenosis rate following bifurcation treatment using DES.

❤

En komité er en blindgate hvor man narrer ideer inn for så å kvele dem i stillhet.
JA Lincoln

❤

Byråkrati er kunsten å gjøre det mulige umulig.
JP Salcedo