NORSKE ABSTRAKTER PÅ AHA

14644 Impact of Time to Return of Spontaneous Circulation on Neuro-protective Effect of Target Temperature Management at 33 and 36 Degrees in Comatose Survivors of Out of Hospital Cardiac Arrest

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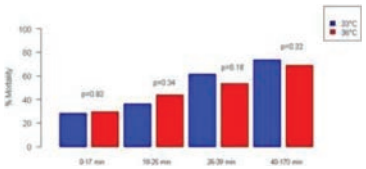
Introduction Prolonged time to Return of Spontaneous Circulation (ttROSC) after Out of Hospital Cardiac Arrest (OHCA) has consistently been associated with adverse outcome by a plausible direct relation to severity of anoxic injury. Hypothesis: Target temperature management (TTM) is assumed effective against anoxic brain injury and we hypothesized that TTM at 33 degrees would be more beneficial with prolonged time to ROSC compared to 36 degrees.

Methods In a post hoc analysis of the TTM trial, which showed no overall benefit of targeting 33 °C over 36 in 939 patients (NEJM 2013), we investigated the relation of time to ROSC and mortality and neurological outcome as assessed by the Cerebral Performance Category (CPC) and Modified Ranking Scale (mRS) after 180 days.

Results: Prolonged ttROSC was significantly and independently associated with increased mortality, p<0.001 (figure), with Hazard Ratio (HR) of 1.02 (95% CI 1.01-1.02, p<0.001) per minute increase and level of TTM did not modify this association, pinteraction=0.85. In survivors prolonged ttROSC was associated with increased odds of surviving with an unfavorable neurological outcome for CPC (p=0.008 for CPC 3-4) and a similar trend, albeit not statistically significant was observed for mRS (p=0.17, mRS 4-5). Odds for unfavorable neurological outcome (CPC>2, mRS>3) was not modified by levels of TTM overall.



Conclusion Time to ROSC remains a significant prognostic factor in comatose patients resuscitated from OHCA with regards to risk of death and risk of adverse neurological outcome in survivors. TTM at 33 degrees offers no advantage over targeting 36 degrees with regards to mortality or neurological outcome in patients with prolonged time to ROSC

20414 Cardiac Resynchronization Therapy Reduces Septal Contribution to Right Ventricular Work

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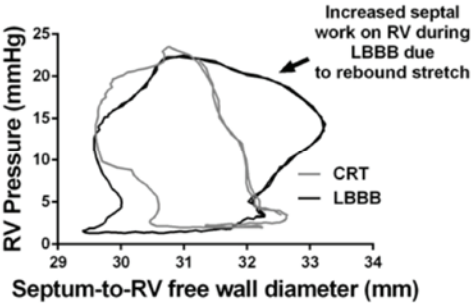
Introduction: During left bundle branch block (LBBB) there is abnormal motion of the interventricular septum (IVS) with early systolic beaking into the left ventricle (LV), followed by rebound stretch into the right ventricle (RV).

Hypothesis: We hypothesize that septal rebound stretch contributes to RV function, and therefore cardiac resynchronization therapy (CRT) which removes rebound stretch, may have a negative effect on RV systolic performance.

Methods: In 6 anesthetized dogs, LBBB was induced by radio frequency ablation. CRT was applied with electrodes on the IVS and the LV lateral wall. RV pressure (RVP) was measured by a micromanometer, and septum-to-RV free wall diameter and RV free wall long axis segment length by sonomicrometry. RV short-axis work was calculated as the area of RVP-diameter loop and long-axis work as area of the RVP-segment length loop. Results: Induction of LBBB increased RV short axis work from 36 ± 20 to 62 ± 18 mmHg*mm (± SD, p<0.05), but decreased RV long-axis work from 40 ± 13 to 30 ± 14 mmHg*mm (p<0.05). With CRT these changes were reversed; RV short-axis work decreased to 35 ± 21 (p<0.05) and long-axis work increased to 41 ± 15 mmHg*mm (p<0.05). This was associated with an increase in RV dP/dt max (p<0.05).



Conclusions: Application of CRT during LBBB caused a marked reduction in RV short-axis work, indicating reduced septal contribution to RV work. This was compensated by an increase in RV free wall long-axis work, and RV dP/dt max increased. Thus, a non-failing RV has the ability to compensate and even increase its function during CRT, but emphases the importance of RV function to achieve response of CRT treatment.

13617 Cardiac Resynchronization Therapy Increases Workload of the Right Ventricular Free Wall

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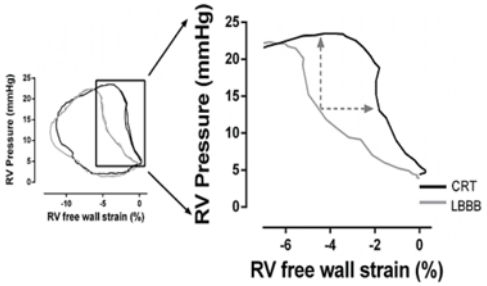
Introduction: Right ventricular (RV) dysfunction is a predictor of reduced response to cardiac resynchronization therapy (CRT) in heart failure with left bundle branch block (LBBB). There is, however, limited insight into potential direct interactions between CRT and RV function. Hypothesis: To investigate the effect of CRT on RV free wall function.

Methods: In 7 anesthetized dogs, LBBB was induced by radio frequency ablation. CRT was applied with septal and left ventricular lateral wall electrodes. RV pressure was measured by micromanometer and longitudinal strain in the RV free wall by sonomicrometry. Regional RV free wall work was calculated as the area of the RV pressure-strain loop.

Results: Induction of LBBB reduced RV free wall work from 39 ± 13 to 28 ± 14 mmHg*mm (± SD, $p<0.05$) and there was pronounced preejection shortening of total shortening (43 ± 11%). CRT restored RV free wall work to 39 ± 15 mmHg*mm ($p<0.05$) which was attributed to a reduction in preejection shortening to 17 ± 11% of total shortening ($p<0.05$, vs. LBBB). As illustrated in the figure, the increase in work was explained by an upward shift of the early systolic portion (preejection) of the RV pressure-strain loop ($p<0.05$). CRT increased RV dP/dtmax from 395 ± 69 to 467 ± 74 mmHg/s ($p<0.05$).



Conclusions: Induction of LBBB reduced RV free wall work and there was observed a substantial preejection shortening. CRT restored RV contraction pattern and work, consistent with a beneficial effect on RV function. However, in hearts with reduced RV function the CRT-induced increase in workload may not be well tolerated. Further studies are needed to explore if this interaction explains why RV dysfunction is a predictor of poor response to CRT.

17131 Diastolic Dysfunction in Asymptomatic Patients With Moderate to Severe Aortic Regurgitation is Strongly Related to Increased Longitudinal Fiber Stress and Subsequent Non-uniform Myocardial Relaxation

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Introduction: Diastolic dysfunction in aortic regurgitation (AR) is present at an early stage of the disease. Yet, the mechanisms are not clearly understood.

Hypothesis: We hypothesized that diastolic dysfunction in AR patients is caused by increased longitudinal (meridional) fiber stress and subsequent impaired relaxation of the corresponding subendocardial (longitudinal) fibers.

Methods: Thirty asymptomatic patients with moderate to severe aortic regurgitation (AR) and 17 age matched healthy controls (C) where analyzed (32 ± 7 and 35 ± 4 (SD) years, respectively, p=NS) with 3D speckle tracking echocardiography. We measured early diastolic longitudinal- (LSRe) and circumferential (CSRe) strain rate (1/s) as the time derivative of strain (%) and the peak difference (LSRe — CSRe) during isovolumic relaxation (IVR). Early diastolic flow rate (sec-1) was estimated as the time derivative of the LV volume curve normalized to end-diastolic volume (EDV). Finally, we calculated end-systolic meridional fiber stress (mmHg).

Results: LV ejection fraction in C and AR was 61 ± 2 and 62 ± 3 %, respectively (p=NS). AR patients had signs of impaired LV filling with lower early diastolic flow rate (Table 1). During IVR, the strain rate curves consistently departed (Figure 1, arrow), indicating a non-homogenous relaxation. A negative correlation was shown between meridional fiber stress and the IVR strain rate gradient (y= -0.0123x + 1.0921, r=0.61, p<0.001).

Table 1	Healthy Controls	Aortic Regurgitation	p-value
LV end-diastolic volume (ml)	146 ± 21	239 ± 43	p<0.01
LV end-systolic volume (ml)	58 ± 9	91 ± 18	p<0.01
LV stroke volume (ml)	88 ± 13	147 ± 27	p<0.01
Peak early diastolic flow rate (sec^{-1}) (Normalized to EDV)	2.8 ± 0.6	2.2 ± 0.5	p<0.01
Early diastolic LS strain rate (1/s)	1.10 ± 0.19	0.81 ± 0.20	p<0.01
Early diastolic CS strain rate (1/s)	0.92 ± 0.17	0.68 ± 0.14	p<0.01
Peak IVR LSRe – CSRe gradient (1/s)	-0.02 ± 0.20	-0.27 ± 0.21	p<0.01
End-systolic meridional fiber-stress (mmHg)	91.1 ± 7.1	108.8 ± 9.3	p<0.01

Conclusions: We have demonstrated a non-homogenous relaxation of subendocardial- relative to circumferential fibers in AR patients that strongly correlated with longitudinal fiber stress, suggesting a causal relationship.

19035 Exercise Intolerance in Heart Failure Patients With Preserved Ejection Fraction (HFpEF) - Not Only a Diastolic Problem

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Introduction: Potential mechanisms of exercise intolerance in HFpEF patients were investigated.

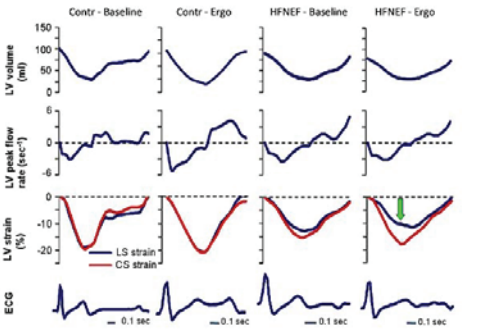
Hypothesis: We hypothesized that HFpEF patients have reduced capacity to increase left ventricular (LV) cardiac output (CO) during exercise due to subendocardial (longitudinal) dysfunction. Patients were compared to healthy controls (C) by threedimensional speckle tracking echocardiography.

Methods: Thirteen patients and 5 age matched controls (age: 74 ± 5 (SD) and 69 ± 6 years, respectively, p=NS) were compared. All were examined with 2D and 3D echo at baseline and immediately after ergometric testing until exhaustion. Left ventricular diastolic function was assessed by transmitral flow velocities (E and A) and average of tissue velocities from basal septal and lateral walls by Doppler (e'). LV systolic measures including EF, cardiac output, peak systolic flow rate (time derivative of 3D volume trace normalized to end-diastolic volume) and peak systolic longitudinal and circumferential global strains (LS and CS, respectively) were obtained.

Results: Table 1 summarizes results at baseline and after exercise. As predicted, impaired filling was detected in the HFpEF group. There were no differences in systolic measures between HFpEF and C at baseline (Table 1). During exercise, HFpEF patients were unable to increase their cardiac output and peak systolic flow rate. A concomitant reduction of systolic longitudinal strain was observed while circumferential strain was unchanged (Figure 1, arrow).

Table 1	Control-Baseline	Control-Ergo	HFpEF - Baseline	HFpEF-Ergo
HR (bpm)	59 ± 8	94 ±16 *	64 ± 11	92 ± 17*
EF (%)	65 ± 4	67 ± 3	67 ± 5	61 ± 14
CO (l/min)	3.9 ± 0.5	6.2 ± 1.3*	4.4 ± 0.6	5.3 ± 2.1
Peak syst. LS (%)	-17.4 ± 1.5	-16.1 ± 2.1	-15.1 ± 2.0	-12.2 ± 2.2*†
Peak syst. CS (%)	- 18.2 ± 0.8	-17.8 ± 1.9	-16.8 ± 2.2	-15.8 ± 2.9
Peak syst. flow rate (s^{-1})	3.4 ± 0.1	4.5 ± 0.7*	3.6 ± 0.6	3.6 ± 1.1
E/A	1.17 ± 0.25	1.27 ± 0.4	0.97 ± 0.30	1.11 ± 0.37
E/e'	8.0 ± 2.4	10.3 ± 1.9*	12.5 ± 4.1†	13.8 ± 3.9

* p<0,05 (within group), †p<0,05 (between groups)



Conclusion: In conclusion, exercise intolerance in HFpEF patients may be explained by subendocardial dysfunction that was revealed during ergometric testing.

12760 Left Ventricular (LV) Remodeling in Aortic Regurgitation Differs From Athlete's Heart With Similar LV Volumes and is Closely Related to Different Fiber Stress Distribution

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Introduction: Elite endurance athletes often develop left ventricular dilatation comparable to that observed in aortic regurgitation (AR).

Hypothesis: We hypothesized that the LV remodeling observed in athlete's heart differs from that seen in AR, and that the difference may be attributed to different fiber stress distribution.

Methods: Thirty asymptomatic patients with moderate to severe AR, 15 age matched elite endurance athletes (Athl) and 17 age matched healthy controls (C) where analyzed with 3D speckle tracking echocardiography. We calculated the ratio between peak systolic circumferential (CS) - and peak systolic longitudinal strain (LS) and end-systolic (ES) circumferential (ESSc) and meridional (ESSm) fiber stress.

Results: LV ejection fraction in C, Athl and AR patients was (61 ± 2, 61 ± 3 and 62 ± 3%, respectively, p=NS). LV enddiastolic volume was 78 ± 11, 112 ± 13 and 117 ± 20 ml/m2 in C, Athl and AR, respectively, (C vs AR and Athl, p<0.01, AR vs Athl, p=NS). A non-uniform contraction pattern with a rightward shift of the LS strain curve was observed in AR (Figure 1). The CS/LS ratio was 0.91 ± 0.11, 0.91 ± 0.16 and 1.12 ± 0.24 in C, Athl and AR, respectively, (AR vs C and Athl, p<0.01, C vs Athl, p=NS). Consistently, the ESSc/ESSm ratio was similar in C and Athl (1.75 ± 0.08 and 1.74 ± 0.07, respectively, p=NS) and lower in AR patients (1.67 ± 0.07, AR vs C and Athl, p<0.01), indicating a relative increase in meridional fiber stress in the AR group (Figure 2).

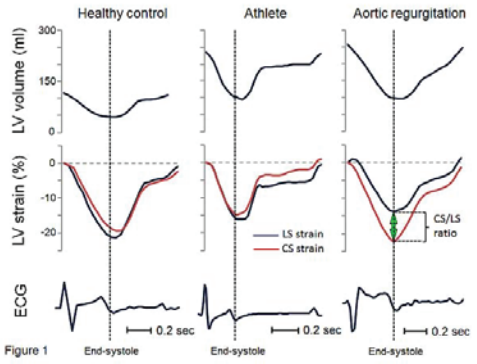

Figure 1

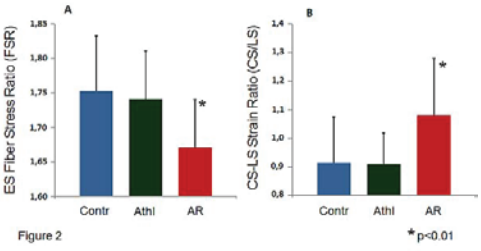

Figure 2

Conclusions: We have demonstrated that LV remodeling in AR patients differs from athlete's heart with similar LV volumes, and may be attributed to a shift in the circumferential-meridional fiber stress ratio in AR patients.

12717 Improvement of Longitudinal Function is Closely Related to Reverse Remodeling in Cardiac Resynchronization Therapy

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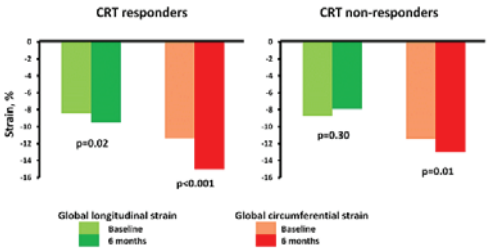
Introduction Response to cardiac resynchronization therapy (CRT) is often defined as reverse remodeling as a reduction in left ventricular (LV) end systolic volume (ESV). How myocardial mechanics are affected by biventricular pacing is not fully clarified. We tested the hypothesis that longitudinal and circumferential function are affected differently by biventricular pacing.

Methods Echocardiography (two dimensional) was performed before and 6 months after CRT implantation in heart failure patients with LV ejection fraction (EF) ≤ 35% and QRS ≥ 120 ms. LV function was assessed by EF and by global longitudinal (GLS) and global circumferential (GCS) strain from 16 LV segments by speckle tracking technique. CRT responders were defined as patients with reverse remodeling with a reduction in ESV ≥ 15% at 6 months.

Results We included 138 heart failure patients (65±10 years, 22% women, NYHA functional class 2.8±0.4, 48% ischemic cardiomyopathy). In the total population, GLS did not change (-8.5±3.9% to -8.9±4.7%, p=0.31) after 6 months with biventricular pacing, while GCS (-11.3±3.3% to -14.2±4.5%, p<0.001) and EF (27±9% to 36±12%, p<0.001) improved. Analyzing CRT responders (62%) and non-responders separately, GLS improved in responders (-8.4±3.8% to -9.5±3.8%, p=0.02) but not in non-responders (-8.7±4.1% to -7.9±4.5%, p=0.30) (Figure). GCS improved in both groups (-11.3±3.0% to -15.0±4.3%, p<0.001 and -11.4±3.8% to 13.0±4.7%, p=0.01). ΔGLS was a predictor of CRT response (OR 0.84 (0.75-0.95), p=0.009) and of ΔESV (1.62 (0.45-2.79), p=0.007) independently of ΔGCS.

Conclusions Biventricular pacing by CRT generally induced less changes in GLS than in GCS and EF. Importantly, GLS improved only in CRT responders with reverse remodeling. We suggest

that reverse remodeling is more dependent on improved longitudinal function than circumferential function.



12891 Mitral Valve Analysis Adding a Virtual Semi-Transparent Annulus Plane for Improved Visualization of Prolapsing Segments

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Introduction: Three-dimensional echocardiography has improved the preoperative evaluation of mitral valve disease. Though, better tools to quantify the amount of prolapsing tissue is warranted. A novel 3D holographic display (Setred AS, Oslo, Norway) offer a 3-dimensional echocardiographic presentation without the need for stereo glasses. We have developed a semi-transparent annulus plane presentation that may better quantitate the prolapsing tissue.

Hypothesis: We assessed the hypothesis that it is feasible to create a semi-automatic, semi-transparent annulus plane visualized on the holographic display, demonstrating the prolapsed segment that crosses the virtual mitral valve plane.

Methods: Eight patients with degenerative mitral valve disease were analysed. Three-dimensional transthoracic echocardiography was obtained from an apical view and data was converted to the holographic display for further analysis. Findings were compared with visual inspection during surgery. A semi-automated tool was used to detect the annulus; placement of annulus points was done by clicking out points at small rotation intervals around a rotation center point while rotating around the long axis. After a full rotation, the plane was triangulated using a delaunay triangulation process and the annulus plane was visualized as a semi transparent blue surface. The dataset could then be shown from surgeons view in order to see where the valve crosses the visualized valve plane.

Results: A total of 48 segments were analysed. We were able to obtain an annulus plane in all and by adding the annulus mitral valve plane, the prolapsing segments could be reproduced in all cases. Figure 1 shows representative recordings (surgeons view) demonstrating a P2 prolapse in the upper panel and a large A2 prolapse in the lower panel.

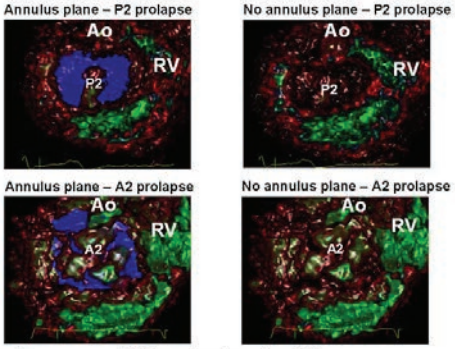

Figure 1 Mitral annulus plane coloured blue

Conclusion: In conclusion, the presentation of a semi-transparent annulus plane was feasible and the findings correlated well with that observed during surgery.

18422 NLRP3 Inflammasome Promote Myocardial Remodeling During Diet-Induced Obesity

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Introduction: Type 2 diabetes (T2D) is a risk factor for heart failure. We have demonstrated that NLRP3 inflammasome is functional in the heart and may regulate cardiac dysfunction and cell death.

Hypothesis: This led us to hypothesize that the NLRP3 inflammasome may play a role in development of cardiomyopathy in T2D. The present project aims to explore this hypothesis by examining NLRP3 and ASC deficient mice in a model of metabolic stress-induced cardiomyopathy.

Methods: Wt (C57Bl/6J), NLRP3-/- and ASC-/- male mice were fed a high-fat diet (HFD; 60%cal from fat) or control diet for 52 weeks. Echocardiography and measurements of fasting plasma

glucose were performed during the study period. Systolic and diastolic blood pressures were measured using the tail-cuff method.

Results: HFD induced increase in body weight in all mice, but Wt mice gained significantly more. Wt mice on HFD also had significantly higher fasting plasma glucose levels. Long-term exposure to HFD induced elevation in left ventricle (LV) mass in all mice. Wt-HFD mice had a three-fold increase in liver weight indicating liver steatosis; this was reduced in NLRP3-/- mice but not significant in ASC-/- mice. Cardiac structure and function were evaluated using echocardiography. Wt-HFD mice had significantly increased LV wall thickness, diameter and relative wall thickness (RWT), indicating concentric hypertrophy. These structural changes were much less pronounced in NLRP3-/- and ASC-/- mice on HFD, with no significant changes in wall thicknesses and RWT. Both systolic and diastolic blood pressure were increased in mice fed a HFD, and Wt-HFD mice showed a significantly greater increase in comparison to the NLRP3-/- HFD mice, but not significant in ASC-/- mice on HFD. This may explain the cardiac hypertrophic response in Wt-HFD mice. LV fractional shortening (FS), was not reduced in Wt-HFD mice, but significantly reduced in NLRP3-/- and ASC-/- mice. However, FS values were maintained within the normal range, indicating preserved myocardial function.

Conclusions: Long-term HFD induces development of LV concentric hypertrophy. We did not observe these changes in NLRP3 or ASC deficient mice, suggesting that the NLRP3 inflammasome plays a role in development of diabetic cardiomyopathy.

18507 Icosabutate, a Novel Structurally Enhanced Fatty-acid Increases Hepatic Uptake of Cholesterol and Triglycerides in Conjunction With Increased Hepatic LDL Receptor Expression

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Background: At a tenth of the dose of unmodified omega-3 fatty acids, Icosabutate (a structurally modified omega-3 fatty acid) achieves potent lowering of both plasma triglycerides (TG) and non-HDL cholesterol (C) in APOE*3Leiden.CETP transgenic mice. The mechanism/s by which Icosabutate exerts its hypolipidemic effect was investigated.

Methods: Male APOE*3Leiden.CETP mice were fed a semi-synthetic Western-type diet (WTD, 15% cocoa butter, 40% sucrose and 0.25% cholesterol; all w/w) without or with Icosabutate (112 mg/kg bw/day). Hepatic production and clearance of lipids/lipoproteins, lipolytic activity, hepatic lipids and expression of LDL receptor protein (LDLr) were assessed.

Results: After 4 to 6 weeks of treatment Icosabutate lowered both plasma TG and C, confined to the non-HDL particles, by 68% ($p<0.001$ vs. control). No significant effects were seen in lipoprotein lipase and hepatic lipase activity. However, hepatic uptake of VLDL-like 14C-cholesteryl oleate particles (as marker for VLDL-CE) and 3H-triolein (as marker for VLDL-TG) were significantly increased vs. control by 72% and 87%, respectively (both $p<0.001$). Icosabutate tended to decrease hepatic TG (38%, $p=0.083$) and significantly decreased CE (25%, $p<0.05$). Hepatic expression of LDLr was increased 1.9 fold ($p<0.05$). In contrast to fenofibrate, there was no increase in hepatic VLDL-TG production rate with Icosabutate.

Conclusion: Icosabutate lowers plasma lipids primarily via a markedly increased hepatic uptake and is associated with a significant increase in hepatic LDLr expression. Despite the increased hepatic TG uptake, no compensatory increase in hepatic lipid storage or TG production was observed. Icosabutate thus offers a promising new approach to lowering plasma TG and non-HDL cholesterol.

11889 Phase Ib Study of Icosabutate, a Novel Structurally Enhanced Fatty Acid, in Subjects With Hypercholesterolemia

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Introduction: Icosabutate, an orally active structurally enhanced fatty acid (SEFA), has demonstrated reductions in triglycerides (TG) and cholesterol in several rodent models of dyslipidemia and diabetes. In clinical single and multiple ascending dose studies, icosabutate was well tolerated and significantly lowered LDL-C, non-HDL-C, and TG in subjects with mixed dyslipidemia. This phase 1b study explored the lipid-lowering effects of icosabutate in subjects with hypercholesterolemia.

Methods: This was a randomized, double-blind, placebo-controlled study. Subjects with hypercholesterolemia treated with a statin for at least 3 months were screened. Statins were temporarily discontinued for at least 28 days prior to dosing and for the duration of the study. To qualify for the study, subjects were required to have an LDL-C ≥ 2.5 mmol/L (97 mg/dL) at the secondary screening visit and an increase in LDL-C of at least 20 % between the primary and secondary screening. Twenty four subjects were randomized to icosabutate 600 mg once daily or matching placebo in a 3:1 fashion and treated for 28 days. Safety and pharmacodynamics were evaluated. Results are reported as placebo-adjusted median percentage change from baseline (average of visit 2-4) to 24 hours after last dose (day 29).

Results: Six subjects received placebo and 18 subjects received icosabutate. Median baseline lipid values (mg/dL) placebo/ icosabutate: TC: 270 and 240; LDL-C: 174 and 166; and TG: 204 and 168. Compared to placebo, icosabutate reduced total cholesterol (17.4 %, $p < 0.05$), LDL-C (29.3 %, $p<0.05$), non-HDL-C (25.4 %, $p<0.05$), and apo B (22.8 %, $p< 0.05$). There was a non-significant increase in HDL-C. TG reductions were not statistically significant (12.6 %, ns), but both placebo and icosabutate subjects experienced large reductions from baseline (29 % versus 42 %).

Conclusions: In this randomized, double-blind, placebo-controlled phase Ib study in subjects with hypercholesterolemia, icosabutate demonstrated placebo-adjusted reductions in total cholesterol, LDL-C, non-HDL-C, and apo B. TG levels were also substantially reduced, but not statistically significant in placebo-adjusted analyses.

20310 Cardiovascular Risk Markers in a Large Cohort of Children With Genetically Verified FH Show No Inheritance-Related but LDL Receptor Mutation-Type and Family History of CVD-related Variance

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Introduction: Familial hypercholesterolemia (FH) is an autosomal dominant disease caused primarily by mutations in the low density lipoprotein (LDL) receptor gene. FH patients have increased total- and LDL cholesterol leading to accelerated atherosclerosis and premature cardiovascular disease (CVD). In an FH pregnancy the absolute rise in lipid levels are often much higher than in healthy pregnancies, and this maternal hypercholesterolemia may thus contribute to an unfavorable in utero environment potentially increasing susceptibility of adult CVD. Few studies have investigated whether maternal FH is associated with an unfavorable phenotype in offspring compared with paternal FH inheritance.

Hypothesis: The aim of the present study was to investigate the impact of maternal vs. paternal FH on pre-treated plasma lipids. In addition, the effect of LDL receptor mutation types and Family history of early CVD in FH children was evaluated Methods: We included 1063 children with FH (0-19 years) in the study. Five-hundred had inherited FH maternally and 563 paternally. Furthermore, 624 children with FH had an LDL receptor negative mutation and 332 of the FH children had an FH grandparent suffering from early CVD whereas the remaining children had an FH grandparent with late or no CVD. Differences were tested for using a random intercept mixed model taking account for between-family variation.

Results: Children with maternal FH did not have different levels of total-, LDL- or HDL-cholesterol, triglycerides, apoA1, apoB, lipoprotein (a) compared with children With paternal FH. Moreover, children with LDL receptor negative mutations had higher levels of total- and LDL cholesterol in addition to apoB, and concomitantly lower levels of HDL-cholesterol and apoA-1 than children with other LDL receptor mutations. Finally, children with an FH grandparent with early CVD had significant higher LDLcholesterol levels than children without.

Conclusions: Maternal FH does not lead to a more unfavorable phenotype in untreated FH children. However, both FH children with LDL receptor negative mutation and FH children with early CVD in family had a more unfavorably phenotype. Hence statin treatment should potentially be initialized earlier in this group.

9613 Randomized Evaluation of Anacetrapib Lipid-modifying Therapy in Patients with Heterozygous Familial Hypercholesterolemia (REALIZE Study)

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Introduction: Anacetrapib, a cholesteryl ester transfer protein inhibitor, has been shown to robustly reduce atherogenic lipoproteins, including low-density lipoprotein cholesterol (LDL-C), and Apo B, and raise high-density lipoprotein cholesterol (HDL-C) as well as Apo A-1.

Hypothesis: This 1-year, Phase 3, multicenter, randomized, double-blind, placebo-controlled study assessed the lipid-modifying efficacy and safety profile of anacetrapib added to optimized LDL-C lowering therapy in patients with heterozygous familial hypercholesterolemia (HeFH).

Methods: Patients with a genotype-confirmed or clinical diagnosis of HeFH, treated with an optimal dose of statin ± other lipid-modifying medication(s) and having an LDL-C ≥100 mg/dL without history of cardiovascular disease or LDL-C ≥70 mg/dL with a history of CVD, were randomized in a ratio of 2:1 to anacetrapib 100 mg (n=204) or placebo (n=102) for 52 weeks followed by a 12-week reversal phase. The primary end points were the percent change from baseline in LDL-C (beta-quantification method) and the safety profile of anacetrapib. This trial is registered in ClinicalTrials.gov, NCT01524289.

Results: A total of 306 patients were enrolled at 25 sites in 9 countries. At baseline, most patients were on high-dose statin therapy and >70% also were on ezetimibe. Baseline LDL-C and HDL-C were 129.4 and 53.3 mg/dL, respectively. At Week 52, anacetrapib vs placebo significantly reduced LDL-C by 39.7% and increased HDL-C by 102.1% (p<0.001 for both). Significant placebo-adjusted reductions in Apo B (24.8%) and increases in Apo A-1 (32.9%) also were observed. Significantly more patients in the anacetrapib vs placebo group achieved LDL-C <100 (82% vs 18%; p<0.001) and <70 mg/dL (44% vs 5%; p<0.001). Sustained effects on LDL-C (21.9%; p<0.001) and HDL-C (53.0%; p<0.001) were seen 12 weeks after cessation of anacetrapib therapy. No clinically important between-group differences were seen in the proportions of patients with abnormalities in liver enzymes, CK, blood pressure, electrolytes, adverse experiences, and adjudicated CV events.

Conclusion: In patients with HeFH, treatment with anacetrapib for 1 year was generally well tolerated and resulted in substantial reductions in LDL-C and increases in HDL-C.

15135 The Cardioprotective Effect of the Modern Farmed Atlantic Salmon -Dietary Spillover from Fish

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Introduction: Omega-3 (n-3) long-chain polyunsaturated fatty acids (PUFAs) and in particular DHA and EPA from oily fish have beneficial cardiovascular effects. To meet the demands for sustainability and reduce production cost parts of the marine ingredients in the "modern" Atlantic salmon diet have been replaced by vegetable oil (VO) increasing the monoene fatty acid levels and to some extent the linoleic and linolenic fatty acids on the expense of n-3 PUFAS in the filet. The nutritional as well as cardio protective benefit of the modern farmed Atlantic salmon is therefore under discussion.

Hypothesis: Filets of salmon fed VO with a reduced n-3/n-6 ratio has reduced anti atherosclerotic properties compared to filets of salmon fed FO.

Methods: Fillets of Atlantic salmon fed diets with fish oil (FO) or diets where FO was partly replaced (80%) with rapeseed (RO) or soy oil (SO) were used to prepare western style diets high in fat, sucrose and cholesterol for use in a mouse trial. Three groups of male apoE knock out (KO) mice were fed either of the three western style diets with FO (n=14; alpha-linolenic acid (ALA) level: 1.6 mg/g), SO (n=13; ALA: 2.6 mg/g) or RO (n=13; ALA: 4.0 mg/g) salmon replacing 50% of the dietary protein.

Results: Replacement of FO with SO and RO in the salmon diet led to a significant accumulation of fat in mice livers. Higher red blood cell n-6 levels were detected in SO (1.40 ± 0.18 mg/g) and RO (1.16 ± 0.08 mg/g) fed mice when compared to the FO (0.68 ± 0.05 mg/g) fed

groups. Interestingly the HDL cholesterol was higher in RO and SO whereas the LDL cholesterol was high in SO when compared to FO. Despite these metabolic changes, atherosclerotic lesion were reduced in the arch and abdominal region in RO (12 ± 1% and 4 ± 1% respectively) fed mice compared to the FO (18 ± 2% and 10 ± 2% respectively) fed mice.

Conclusions: The dietary spillover from salmon fed VO induced systemic metabolic changes, but also cardio protection in apoE KO mice fed a diet with filets from RO fed salmon. The level of ALA in RO and its potential anti atherosclerotic effect warrants further investigation.

17245 The Effect on Vitamin D Levels of Long-term High-dose Treatment With a Concentrated Omega-3 Compound (Omacor®/Lovaza®) in Patients Hospitalized With a Myocardial Infarction

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Background: Several studies have demonstrated an inverse relationship between cardiovascular risk and levels of vitamin D and omega-3.

Objectives: To assess the impact of high-dose treatment of concentrated omega-3 (ethylester form) on serum vitamin D measured as 25-hydroxyvitamin D [25(OH)D] in 288 patients hospitalized with a myocardial infarction who were randomly assigned into a daily dose of either 4 g highly concentrated omega-3 fatty acids (114 patients) or corn oil (114 patients), administered in a double-blind manner over 12 months. Four mg of alfa-tocopherol was added to each capsule to protect against fatty acid oxidation. Supplementation with other fish-oil products was discontinued. 25(OH)D was measured at baseline, at 6 weeks and 12 months follow-up. Changes in 25(OH)D were compared statistically.

Results: Median 25(OH)D levels in the two groups are shown in Table 1. The increase in 25(OH)D was statistically significant in both treatment groups at 12 months; $p < 0.001$ for n-3 polyunsaturated fatty acids (PUFAs) and $p = 0.011$ for corn oil. A statistical significant rise in 25(OH)D was already apparent in the n-3 PUFA patients at 6 weeks follow-up ($p < 0.001$). There was no significant difference between intergroup changes after 6 weeks intervention ($p = 0.867$) or after 12 months intervention ($p = 0.267$) (Mann-Whitney Rank Sum Test).

Table 1. 25(OH)D levels at baseline, after 6 weeks and 12 months supplementation with high dose of n-3 PUFAs as compared to corn oil.

	25(OH)D levels; Median (25% - 75% percentile)		
	Baseline	6 weeks	12 months
n-3 PUFAs	49.0 nM (40.2 nM - 62.1 nM)	51.8 nM (42.2 nM - 61.3 nM)	53.0 nM (44.9 nM - 69.5 nM)
Corn Oil	51.6 nM (42.9 nM - 63.5 nM)	52.8 nM (41.5 nM - 67.1 nM)	54.2 nM (45.2 nM – 65.0 nM)

Conclusion: A statistical significant early rise in vitamin D at 6 weeks follow-up was noted in the omega-3 group of patients, persisting at 12 months, but these changes were not reflected as compared to corn oil, probably due to the fact that both compounds are biologically active.

18541 Gastric Bypass Surgery is Associated with a Marked Reduction in Circulating High Sensitivity Cardiac Troponin I Concentrations: Comparison with Intensive Lifestyle Intervention

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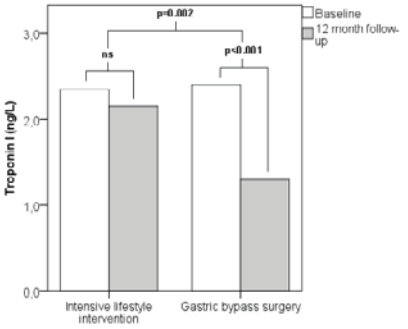
Introduction: Morbid obesity is associated with increased cardiac mass and cardiovascular risk. Circulating high sensitivity cardiac troponin I (hs-TnI) concentrations reflect cardiac mass and hemodynamic stress and are strongly predictive of subsequent risk of heart failure and premature death. The impact of weight loss induced by gastric bypass surgery (GBS) and intensive lifestyle intervention (ILI) on circulating hs-TnI is unknown.

Hypothesis: Weight loss induced by GBS and ILI is associated with reduced circulating hs-TnI concentrations.

Methods: The Morbid Obesity treatment, Bariatric surgery versus Intensive Lifestyle intervention study was a controlled clinical trial conducted from December 2005 to June 2009 at the Morbid Obesity Centre, Vestfold Hospital Trust, Tønsberg, Norway. A group of 139 morbidly obese subjects were treated either with GBS or ILI. Biochemical and clinical indices of cardiovascular and metabolic health were assessed at baseline and after 12 months of follow-up. Blood samples for hs-TnI analyses were available from 136 participants (94 female), out of whom 74 received GBS.

Results: At baseline median hs-TnI levels were 2.35 (1.38-4.40) ng/L in the ILI group and 2.40 (1.28-3.95) ng/L in the GBS group (ns). After 12 months of follow-up, hs-TnI had decreased significantly more in the GBS group than in the ILI group (1.10 ng/L vs. 0.20 ng/L; p=0.002) (see

Figure). Variables associated with the change in hs-TnI concentrations by univariate analyses included intervention group (p=0.002), changes in body mass index (p=0.002), body weight (p=0.003), waist circumference (p=0.04), serum total cholesterol (p=0.009), serum triglycerides (p=0.002) and HbA1c (p=0.017).



Conclusions: In patients with morbid obesity, GBS was associated with a significantly greater reduction in hs-TnI than ILI, suggesting that bariatric surgery and/or large weight loss unloads the stressed heart and may lead to reduced cardiac mass and hemodynamic stress.

16518 The Sodium Glucose Co-Transporter 2 Inhibitor (SGLT2i) Empagliflozin Reduces Weight and Markers of Visceral Adiposity (VA) in Type 2 Diabetes (T2D) in Short- and Intermediate Term

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Excess VA is associated with increased risk of T2D and cardiovascular (CV) disease. Empagliflozin (EMPA), a SGLT-2i, increases urinary glucose excretion, and reduces blood pressure (BP) and body weight. We explored the impact of EMPA versus placebo on surrogate markers of VA in two T2D study cohorts with short- and intermediate-term exposure with analyses performed on individual patient data from the full analysis set (FAS). Cohort 1 had 823 patients with hypertension participating in a 12-week randomized ambulatory BP monitoring trial with mean (SD) age 60.2 (9.0) yrs, HbA1c 7.9 (0.7)%, office systolic BP (SBP) 142 (12) mmHg and BMI 32.6 (5.1) kg/m2. Cohort 2 pooled 2476 patients from four 24-week phase III randomized trials with age 55.6 (10.2) yrs, HbA1c 8.0 (0.9)%, office SBP 129 (15) mmHg and BMI 28.7 (5.5) m/kg2. Changes from baseline to study-end for HbA1c, body weight and three validated markers of VA (waist circumference (WC), index of central obesity (ICO; ratio WC/height), visceral adiposity index (VAI) (VAImen: (WC/[39.68 + (1.88 x BMI)] x (TG/1.03) x (1.31/HDL)); VAIwomen: (WC/[36.58 + (1.89 x BMI)] x (TG/0.81) x (1.52/HDL)), and changes in estimated total body fat (eTBF) using the YMCA-formula (eTBFmen: 100*(-98.42 + [4.15*WC] - [0.082*weight])/weight; eTBFwomen:100*(-76.76 + [4.15*WC] - [0.082*weight])/weight), were assessed. In both cohorts HbA1c was significantly reduced with EMPA (mean [SE]):-0.64% (0.04)/-0.65% (0.03); both p < 0.001). There were significantly greater reductions in body weight and markers of VA in the EMPA groups compared with placebo (Table); changes in eTBF did not reach statistical significance. These findings suggest that EMPA may directly reduce VA and potentially alter TBF beyond its effects on glycemia. The ongoing EMPA-REG OUTCOME™ trial (NCT01131676) will provide further insights into whether changes in body composition induced by EMPA are associated with CV risk reduction.

18574 Empagliflozin Reduces Systolic Blood Pressure in Dipper and Non-Dipper Patients with Type 2 Diabetes and Hypertension

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In a Phase III randomized trial (EMPA-REG BP™), patients with type 2 diabetes (T2DM) and hypertension (defined as mean seated office systolic blood pressure [SBP] 130-159 mmHg and diastolic BP [DBP] 80-99 mmHg at screening) received empagliflozin (EMPA) 10 mg (n=276), EMPA 25 mg (n=276) or placebo (PBO; n=271) once daily in the morning for 12 weeks (mean [SD] age 60.2 [9.0] yrs, HbA1c 7.90 [0.74] %, 24-h SBP 131.4 [12.3] mmHg, 24-h DBP 75.0 [7.8] mmHg). We assessed changes from baseline in SBP (mean 24-h, awake-time, sleep-time) via ambulatory BP monitoring at week 12 in patients categorized as dippers (sleep-time mean SBP ≤90% of awake-time mean; n=417) or non-dippers (sleep-time mean SBP >90% of awake-time mean; n=350). Baseline mean (SD)

24-h SBP (mmHg) was 129.9 (11.6) in dippers and 133.1 (12.4) in non-dippers. Adjusted mean (SE) changes from baseline in mean 24-h SBP (mmHg) in dippers were -0.2 (0.7) with PBO vs -3.8 (0.6) and -3.9 (0.7) with EMPA 10 and 25 mg, respectively (both p<0.001), and in non dippers were 1.0 (0.7) with PBO vs -1.6 (0.7) with EMPA 10 mg (p=0.013) and -3.8 (0.7) with EMPA 25 mg (p<0.001). Hourly mean SBP patterns over 24 h for dippers and non-dippers were maintained with EMPA 25 mg (Figure) and 10 mg. Adjusted mean (SE) changes from baseline in awake-time SBP (mmHg) in dippers were -0.5 (0.7) with PBO vs -4.6 (0.7) with EMPA 10 and 25 mg (both p<0.001), and in non dippers were 1.3 (0.8) with PBO vs -2.2 (0.8) with EMPA 10 mg (p=0.002) and -4.2 (0.7) with EMPA 25 mg (p<0.001). Adjusted mean (SE) changes from baseline in sleep-time SBP (mmHg) in dippers were 0.4 (0.8) with PBO vs -2.6 (0.8) with EMPA 10 mg (p=0.007) and -2.2 (0.8) with EMPA 25 mg (p=0.022), and in non-dippers were 0.1 (0.9) with PBO vs -0.5 (0.9) with EMPA 10 mg (p=0.603) and - 3.2 (0.8) with EMPA 25 mg (p=0.006). There were no apparent differences in heart rate with EMPA vs PBO in dippers or nondippers. In patients with T2DM and hypertension, EMPA 10 mg and 25 mg significantly reduced SBP vs PBO in dippers and nondippers.

16474 BP Reduction With the Sodium Glucose Co-Transporter 2 Inhibitor Empagliflozin in Type 2 Diabetes is Similar in Treatment Naïve as in Those on One or ≥ 2 Antihypertensive Agents - Further Insights From a Dedicated 24h ABPM Study

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In patients with type 2 diabetes (T2D) hypertension is accompanied by an increase in CV risk which can be substantially attenuated if BP is lowered by drug treatment. Empagliflozin (EMPA) is a new glucose-lowering agent of the sodium glucose co-transporter 2 inhibitor (SGLT2i) class, which has been shown to reduce body weight and also lower BP. It is not known, however, whether the EMPA-related BP lowering effect is preserved in patients under background antihypertensive treatment. We investigated the effect of 12 weeks with EMPA on 24 hour (h) mean BP in 823 T2D patients (age 60.2 ± 9.0 years, HbA1c 7.9 ± 0.7%, office systolic (S)/diastolic (D) BP 142.1 ± 12.3/83.9 ± 7.0 mmHg, mean ± SD) in a study with a randomized design. EMPA was given at 10mg (n=276) or 25mg (n=276) daily; 271 patients were randomized to placebo. Patients were under no, 1 or ≥ 2 antihypertensive drugs (n= 62, 353 and 408, respectively) such as an ACE inhibitor (ACEI), an angiotensin receptor antagonist (ARB) or a diuretic (D). HbA1c and weight were significantly reduced with EMPA 10 mg (mean [SE] -0.62% [0.05], -1.5 kg [0.2]) and EMPA 25 mg (-0.65 [0.05], -2.0 [0.2]) relative to placebo (all p < 0.001). As shown in the Table, compared to placebo, EMPA at the lower or higher dose reduced 24h mean SBP and DBP in all groups. With the lower dose the BP reduction was somewhat less pronounced in patients with ≥ 2 antihypertensive drugs whereas with the higher dose the BP effect was similar irrespective of the presence and intensity of background antihypertensive treatment. The antihypertensive effect of EMPA was preserved also irrespective of the type of treatment (D and ACEIs or ARBs), especially at the higher dose. Thus, EMPA reduces BP in patients with T2D regardless of whether they are untreated or more or less intensively treated for hypertension.

16709 Contrasting Influences of Renal Function on Blood Pressure and HbA1c Reductions With Empagliflozin in Patients With Type 2 Diabetes and Hypertension

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The sodium glucose cotransporter 2 inhibitor empagliflozin (EMPA) reduces HbA1c, weight and blood pressure (BP) in patients with type 2 diabetes (T2D). While glucose lowering with EMPA is dependent on renal function, the impact of chronic kidney disease (CKD) on BP reduction with EMPA is less well understood. Our aim was to determine if impaired renal function attenuates antihypertensive effects of EMPA. A Phase III randomized placebo (PBO)-controlled trial (EMPA-REG BP™) investigated the efficacy and safety of EMPA in patients with T2D and

hypertension (defined as mean seated office systolic BP [SBP] 130-159 mmHg and diastolic BP [DBP] 80-99 mmHg at screening). Patients (mean [SD] age 60.2 [9.0] years, HbA1c 7.90 [0.74] %, 24-hour SBP 131.4 [12.3] and 24- hour DBP 75.0 [7.8] mmHg) received EMPA 10 mg (n=276), EMPA 25 mg (n=276) or PBO (n=271) once daily for 12 weeks. We assessed changes from baseline in mean ambulatory 24-hour SBP and HbA1c in subgroups by baseline eGFR (MDRD equation), adjusting for differences in baseline mean 24-hour SBP (for SBP analyses only), HbA1c, region, number of antihypertensive medications, treatment, eGFR and treatment by eGFR interaction between groups. In patients with normal renal function, or stage 2 or 3 CKD, EMPA significantly reduced HbA1c and mean 24-hour SBP vs PBO (Table). As expected, PBO-corrected HbA1c reductions with EMPA appeared to decrease with decreasing eGFR (Table). In contrast, PBO-corrected reductions in mean 24-hour SBP with EMPA mostly appeared to increase with decreasing eGFR (Table). Unlike HbA1c, mean 24-hour SBP reductions with EMPA in patients with T2D and hypertension appear to be greater in patients with lower eGFR, indicating that SBP modulation with EMPA may involve pathways other than urinary glucose excretion such as diuretic effects, weight loss, improved glycemic control, reduced arterial stiffness or direct vascular effects.

13659 Development of a Trans-Atlantic Cardiovascular risk Calculator for Rheumatoid Arthritis (ATACC-RA)

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Introduction: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular disease (CVD), which is not accurately predicted by risk calculators designed for the general population. Hypothesis: To develop a RA specific CVD risk calculator.

Methods:The study population included RA patient cohorts from 8 centres in 7 countries. In all cases, data had been collected prospectively on CV outcomes (MI, revascularization, angina, stroke, TIA, PAD and CV death). At baseline RA characteristics (duration, seropositivity, disease activity (DAS28) and CRP/ESR) were collected in addition to traditional CV risk factors. Cox models stratified by centre were used to develop a CVD risk calculator considering traditional CV risk factors and RA characteristics. Model performance was assessed using measures of discrimination and calibration.

Results: In total 3176 RA patients who did not have prior CVD were included (mean age: 55 [SD: 14] years, 73% female). During a mean follow-up of 7.8 years (24733 person years), 314 had a CVD event. The multivariable risk score modelling revealed 2 models including either seropositivity or DAS28 along with age, sex, current smoking, presence of hypertension, and ratio of total cholesterol to high-density lipoprotein (table). Both 10-fold cross validation and multiple imputation analyses confirmed these findings with little change to the estimated coefficients. Both models demonstrated good discrimination (c-statistic: 0.76 and 0.74) and calibration (observed/predicted ratio: 1.00; 95% confidence interval: 0.89, 1.12). The ATACC-RA (mean: 11.5%, SD 14.1%) showed significantly improved discrimination compared to either Framingham (c-statistic: 0.71, p<0.001) or SCORE (cstatistic: 0.72, p<0.001) risk algorithms.

Variable	ATACC-RA with seropositivity		ATACC-RA with DAS28	
	Hazard ratio (95% CI)	p-value	Hazard ratio (95% CI)	P-value
Age (per 10 years)	1.91 (1.70 – 2.15)	<0.001	1.71 (1.49 – 1.96)	<0.001
Sex (male)	1.70 (1.32 – 2.19)	<0.001	1.52 (1.13 – 2.06)	0.005
Current smoking	1.76 (1.35 – 2.29)	<0.001	1.66 (1.22 – 2.25)	0.001
Hypertension	1.47 (1.12 – 1.94)	0.006	1.64 (1.19 – 2.24)	0.002
TC:HDL lipid ratio	1.27 (1.13 – 1.42)	<0.001	1.31 (1.14 – 1.50)	<0.001
seropositivity	1.45 (1.06 – 2.00)	0.022		
DAS28			1.14 (1.03-1.27)	0.009

Conclusions: Development of an RA-specific CVD risk calculator is feasible by pooling resources from many centres. Further development including external validation is underway.

15603 Does Repeat Measurement of High Sensitivity Troponin I Improve Prediction of Cardiovascular Events in Atrial Fibrillation?

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Background: Troponin levels predict stroke and other cardiovascular events in patients with atrial fibrillation (AF). This study investigates if repeat measurement using a high-sensitivity cardiac troponin I (cTnI) assay improve the prognostication of outcomes in patients with AF treated with anticoagulation.

Methods: Levels of cTnI were measured in samples obtained at study entry and after 2 months with the Abbott ARCHITECT high sensitivity assay in 4 648 patients in the ARISTOTLE trial. Repeated measures ANOVA were used to assess intraclass correlation. Patients were grouped according to ±20% change at follow-up relative to baseline levels. The associations between cTnI levels and outcomes were evaluated with Cox and C index adjusted for baseline levels.

Results: Median cTnI level at entry was 5.1 ng/L. Intraclass correlation was 0.87 and within subject variance 19%. The proportions with decreasing and increasing cTnI levels were 21.6% and 29.2%, respectively. During follow-up, median 1.9 years, the group with increasing levels at 2 months indicated an elevated risk for cardiovascular events with hazard ratio (HR) (95% CI) up to 1.93 (1.04-3.59) for stroke/systemic embolism, and HR 2.53 (1.49-4.31) for cardiovascular death as compared with patients with decreasing cTnI levels at follow-up. Based on continuous levels repeated measurements significantly improved C index for cardiovascular mortality (0.738 to 0.754, p<0.0005) but not for stroke/systemic embolism on top of established risk factors.

Outcome	Change from baseline	n	Events (%/year)	Hazard Ratio (95% CI)	p-value
Stroke or systemic embolism	<-20%	1006	18 (1.01)	Reference	0.1159
	±20%	2284	47 (1.13)	1.51 (0.86-2.66)	
	>20%	1358	29 (1.17)	1.93 (1.04-3.59)	
Cardiovascular death	<-20%	1006	23 (1.28)	Reference	0.0019
	±20%	2284	58 (1.38)	1.57 (0.95-2.59)	
	>20%	1358	44 (1.74)	2.53 (1.49-4.31)	

Conclusions: In patients with AF, increasing troponin levels are associated with a raised risk of adverse cardiovascular outcomes. The variability of troponin levels during 2 months is limited. Thus, repeat measurement may contribute to refining cardiovascular risk assessment at an individual level.

16157 Single Measurement of GDF-15 Provides Reliable Prognostication of Stroke and Major Bleeding in Atrial Fibrillation

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Background: GDF-15 level was recently shown to predict stroke, mortality and bleeding in anticoagulated patients with atrial fibrillation (AF). However, the variability in GDF-15 levels over time and the robustness of the risk prediction in a single individual have not been investigated in this population. We investigated the value of repeated measurements of GDF-15 concerning prognostication of new events in patients with AF.

Methods: GDF-15 levels were determined with the Elecsys GDF-15 pre-commercial assay (Roche Diagnostics) in plasma samples obtained in 4,548 pts both at randomization and at 2 months follow-up in pts with AF included in the ARISTOTLE trial. The reliability of the two measurements was investigated by intraclass correlation obtained from repeated measures ANOVA. The associations between GDF-15 levels at baseline, at 2 months and the changes between the two measurements and the occurrence of cardiovascular events after 2 months until the end of follow-up were evaluated by Cox models.

Results: Median level at baseline was 1361 ng/L (Q1, Q3: 973, 2015) and increased by 2.8% reaching 1410 ng/L (1003, 2069) (p<0.0001) at 2 months. The median change was 1.4% (Q1, Q3: -12.2, 16.6). The intraclass correlation was 0.86 between the two measurements and the within subject coefficient of variance was 3%. GDF-15 levels at baseline and at 2 months showed similar significant (p<0.0001) relations to stroke, total mortality and major bleeding occurring during the follow-up period after the 2 months visit. The c-statistics at baseline and after adding the 2 months results to the Cox model were for stroke 0.652 and 0.660 (p=0.2490), death 0.688 and 0.699 (p<.0001) and major bleeding 0.627 and 0.633 (p=0.0654). Mortality increased by an increasing GDF-15 level at 2 months corresponding to a HR of 1.60 (95% CI 1.40-1.83) per 50% increase of GDF-15 (adjusted for the level at baseline).

Conclusions: A single measurement of the level of GDF-15 provides a reliable estimate of the risk of stroke, death and major bleeding in patients with AF during anticoagulant treatment. Repeated measurement after 2 months provides no significant incremental information concerning the risk of stroke and major bleeding but a somewhat better prognostic information on the risk of death.

18326 Heart Rate-independent Qt Variability in Congenital Long Qt Syndrome

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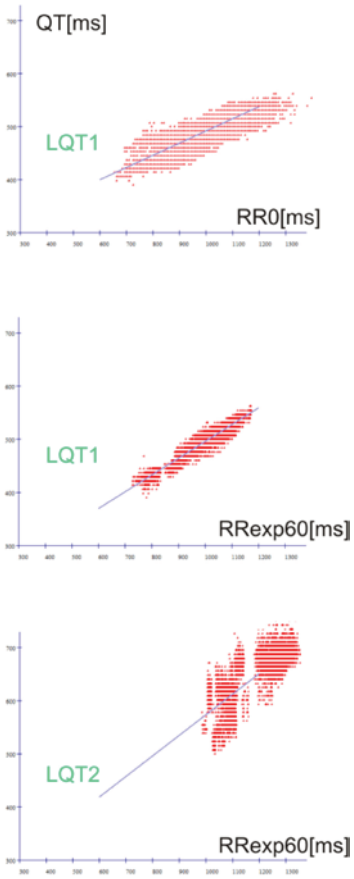
Introduction Heart rate is a major factor affecting QT interval duration. In normal ambulatory subjects, modeling QT interval as a linear function of preceding RR intervals weighted with an exponential function with 60 s time-constant reproduces gradual QT accommodation and provides a better fit than any function of instantaneous RR interval. QT accommodation in LQTS is not well understood.

Methods Digitized Holter recordings (24 hrs) from 63 genotyped LQTS patients (47 LQT1, 13 LQT2, 2 JLN, 1 unknown) were analyzed. LQTS-related symptoms (syncope, ventricular tachycardia, cardiac arrest, or appropriate device shock) were present in 21 patients. RR and QT intervals were automatically determined with custom software; all data were manually edited. QT was modeled as a linear function of preceding RR interval, or of the RR intervals in preceding 180 s weighted with a 30 s or 60 s time-constant exponential function. QTc was determined for each patient from the 60 s time-constant model.

Results The 60 s time-constant model provided a better fit of data than preceding RR interval or 30 s time-constant model ($p<0.001$ for both; see Figure for an example). Residual variability (the QT variability not explained by the 60 s time-constant model) correlated positively with QTc ($r=0.53$; $p<0.001$) and was higher in LQT2 than in LQT1 subjects ($p<0.005$; Figure). There was a trend to higher residual QT variability in symptomatic subjects ($p=0.058$). QTc did not differ between LQT1 and LQT2 or between symptomatic and asymptomatic patients.

Conclusions In ambulatory LQTS patients, QT interval depends on heart rate in the preceding 3 minutes and is well described by an exponential weight function with 60 s time-constant. Residual QT variability is higher in LQT2 than LQT1 and may be higher in symptomatic subjects. Additional research is required to determine if residual QT variability improves risk-stratification in LQTS.



Figur 1: QT intervals from a LDT1 patient (top and middle panel), are plotted as a function of preceding RR interval (top) or as a function of RR intervals in the preceding 3 minutes weighted with an exponential function with 1 min. time-constant. Tighter clustering of data points along the regression line in the middle panel indicates better fit. An example of similar plot from a LQT2 patient (bottom) demonstrates high residual QT variability, not explained by heart rate.

15199 Nadolol Decreases Incidence and Severity of Ventricular Arrhythmias at Exercise Compared to Metoprolol SR in Patients with Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT)

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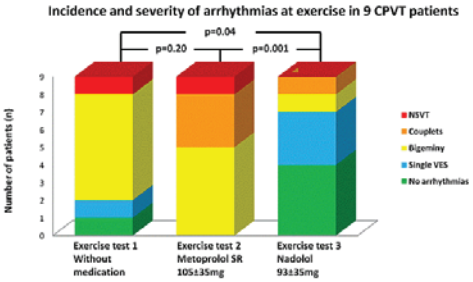
Introduction Catecholaminergic polymorphic ventricular tachycardia (CPVT) is an inheritable cardiac disease predisposing to malignant ventricular arrhythmias at exercise. Beta blockers are mainstay of treatment, but not all beta blockers are equally effective. We explored the incidence and severity of exercise induced arrhythmias in CPVT patients on metoprolol SR, on nadolol medication and without medication.

Methods In this cross over study, 9 CPVT patients were included and completed the study (age 30±15, 56% female, 8 RYR2 mutation positive). We performed 3 bicycle exercise stress tests (50W+25W increase every 2. minute until exhaustion) in each patient; 1) before start of beta blocker treatment, 2) >6 weeks on maximum tolerated dose of metoprolol SR and 3) >6 weeks on maximum tolerated dose of nadolol. We recorded resting and maximum heart rate (HR) and the most severe arrhythmia occurring. Severity of arrhythmias was scored as: no arrhythmias (0), single ventricular extra systoles (1), bigemini (2), couplets (3) and non-sustained VT (4).

Results HR was similar on metoprolol SR and nadolol at rest (53±13bpm vs. 54±9bpm, p=0.72), while maximum HR was lower on nadolol (147±23bpm vs. 120±24bpm p=0.004). The incidence of arrhythmias was lower on nadolol compared to both metoprolol SR (5/9 (56%) vs. 9/9 (100%)) and no medication (8/9 (89%)). There was a shift towards less severe arrhythmias during exercise on nadolol compared to metoprolol SR (0.9±1.1 vs. 2.6±0.7, p=0.001) and compared to no medication (0.9±1.1 vs. 1.9±1.1, p=0.04) but not on metoprolol SR compared to no medication (2.6±0.7 vs 1.9±1.1, p=0.20) (Figure).

Conclusion Incidence and severity of ventricular arrhythmias at exercise decreased on nadolol compared to metoprolol SR. Metoprolol SR did not change occurrence of arrhythmias compared to no medication. Our results indicate that nadolol is superior to metoprolol SR in arrhythmia control in CPVT patients.



18631 Increase in Left Ventricular Mass and Decrease in 3d Global Strain After Right Delayed Recognition of Cardiac Arrest in Emergency Medical Dispatch - Best Source of Key Information for System Improvement?

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Background: Measuring emergency medical dispatch performance is important for both quality control and clinical outcome. Recognition of cardiac arrest is one of the key metrics when evaluating performance as it is essential for initiation of bystander CPR. It is commonly reported as either recognized or not recognized without any benchmarked definition or time limit. Little is known about the extent of delayed recognition, and if these initial delays lead to clinically relevant delays in CPR.

Methods: Prospective, observational study of cardiac arrest calls during a 1 year period in Oslo and Akershus Emergency Services. Dispatch logs, ambulance records and audio files were analyzed. Recognition of cardiac arrest was reported as (1) recognized, (2) not recognized and (3) delayed recognition. Delayed recognition was defined as failure to initially clarify consciousness or abnormal breathing before moving on to further questioning regarding other symptoms or patient history. Calls across all three groups were purposefully selected, and respective dispatchers invited for interviews based on the calls they had experienced.

Results: 500 cardiac arrest calls were processed of which 289 calls were included for further analysis as the dispatcher had the opportunity to recognize cardiac arrest and initiate CPR instructions. 74% of cases were recognized, 13% were not recognized and in 13% recognition was delayed. Median time to bystander CPR (first compression performed) was 2,6 (range 0.9,12.3) minutes when cardiac arrest was recognized

and 5,1 (range 2.9,9.7) minutes when recognition was delayed. Interviews after calls where cardiac arrest was not recognized or delayed in recognition yielded insight into challenging areas for the dispatchers such as agonal breathing, handling health care workers as callers and non-compliance with protocol that have impacted future training and education.

Conclusion: Delayed dispatch recognition of cardiac arrest is common and leads to significant delays in chest compressions. Emergency medical dispatch systems committed to improving cardiac arrest outcomes need to identify and explore all calls that challenge the system, not only those where cardiac arrest is not recognized.

18847 Secretoneurin Provides Independent Prognostic Information in Patients with Heart Failure and Cardiac Arrest, and has a Direct Inhibitory Effect on Diastolic Ca 2+ Leak and Arrhythmogenic Ca2+ Waves via CaMKIId Inhibition

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Background: Secretoneurin (SN) levels are increased in patients with heart failure (HF), but whether SN provides prognostic information in cardiovascular disease (CVD) and influences cardiomyocyte function are not known.

Methods and Results: Circulating SN was measured <24 h of hospitalization in 134 patients with acute HF and <6 h of hospitalization in 155 patients with ventricular arrhythmias and out-of-hospital cardiac arrest (OHCA-VF). SN levels were associated with mortality in acute HF patients (median follow-up 776 days, 66 deaths) after adjusting for established risk factors, including hs-TnT and NT-proBNP levels: HR [logSN] 4.27 (95% CI 1.83-9.94), p=0.001. SN levels were also associated with short-term mortality after OHCA-VF (30 days, 51 deaths) after adjusting for established risk factors and biomarkers: HR [logSN] 3.33 (1.83-6.05), p<0.001. Perfusing hearts with SN increased myocardial SN levels and SN was internalized into cardiomyocytes via endocytosis. Intracellularly, SN was found to directly bind to calmodulin (CaM) and Ca 2+/calmodulin (CaM)- dependent protein kinase II δ (CaMKIIδ). SN attenuated CaMKIIδ activity, reduced CaMKIIδ-dependent ryanodine receptor (RyR) phosphorylation, lowered diastolic Ca 2+ leak at different concentrations, and increased sarcoplasmic reticulum Ca 2+ content. These results were also consistent with results from cardiomyocytes of HF animals, as SN reduced RyR leak in HF reflected by less Ca 2+ sparks and waves. SN also reduced basal and isoproterenol (ISO)-induced frequency and dimensions of Ca2+ sparks and the development of arrhythmogenic Ca 2+ waves, attenuated ISO-induced CaMKIIδ autophosphorylation, and reduced CaMKIIδ-induced RyR phosphorylation in the presence of ISO.

Conclusions: SN is a novel CV biomarker that provides independent prognostic information to established risk indices and reduces diastolic Ca2+ leak and arrhythmogenic Ca2+ waves via direct CaMKIIδ inhibition, which identifies high SN levels as a compensatory mechanism in the most severely ill patients.

17498 Prognostic Importance of Novel Cardiac and Renal Biomarkers in Patients With Heart Failure, Reduced Ejection Fraction and Anemia

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Background: B-type natriuretic peptides add further prognostic information to standard risk

markers in heart failure. Whether other biomarkers provide additional predictive information is uncertain. We tested the incremental prognostic value of novel cardiac and renal biomarkers in the Reduction of Events by Darbepoetin Alfa in Heart Failure trial (RED-HF).

Methods: NT-proBNP, copeptin, cystatin-C, high-sensitivity CRP, mid-regional pro adrenomedullin (MR proADM), and troponin T (TnT) were measured in 2278 patients in RED-HF. The incremental predictive value of each biomarker added to standard clinical risk markers (age, sex, LVEF, NYHA class, diabetes, systolic BP etc. - "basic clinical model") was calculated using Cox multivariable regression and c-statistics for all-cause mortality (ACM). The value of a multimarker prognostic strategy was also assessed using all biomarkers together.

Results: The hazard ratio (HR) for ACM per log standard deviation (SD) difference for each biomarker was as follows: NTproBNP 2.31 (95%CI 2.04, 2.61), copeptin 1.65 (1.43, 1.89), cystatin C 1.73 (1.51, 1.98), hs-CRP 1.25 (1.14, 1.38), MR proADM 1.87 (1.68, 2.08), and TnT 2.08 (1.86, 2.31) (all p<0.001). The c-statistic increased from 0.652 for the basic clinical model to 0.699, 0.666, 0.666, 0.657, 0.682 and 0.694, respectively, with each biomarker added individually. When all biomarkers were considered together, the HRs per log standard deviation (SD) difference were: NT-proBNP 1.60 (1.38, 1.86), copeptin 1.09 (0.94, 1.27), cystatin C 1.05 (0.90, 1.22), hs-CRP 1.04 (0.97, 1.12), MR proADM 1.26 (1.09, 1.47) and TnT 1.48 (1.29, 1.69); only NT-proBNP and TnT (both p<0.001) and MR proADM (p=0.003) remained significant. The c-statistic for the multimarker model was 0.715 which was significantly greater than for the basic clinical model plus NT proBNP alone (P=0.002).

Conclusion: In RED-HF, novel cardiac and renal biomarkers individually added prognostic information to conventional risk predictors. In a multimarker strategy only NT-proBNP troponin T and MR proADM provided incremental information. The multimarker model was superior to the basic clinical model plus best individual biomarker (NT proBNP).

16551 Throttle and Brake - A Novel Therapeutic Strategy in Post-Ischemic Acute Heart Failure by Combined Use of Dobutamine and Ivabradine

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Introduction: Compensatory tachycardia can potentially be deleterious in ischemic and post ischemic acute heart failure. We tested a therapeutic strategy by combining inotropic support and slowing the sinus node using ivabradine.

Methods: In an open-chest pig model (n=12) with left ventricular (LV) ischemic reperfusion injury, cardiac performance was assessed by LV pressure catheter and sonometric crystals for LV volumetry. Coronary flow probes and blood samples from the coronary sinus supplied data for myocardial oxygen combustion (MVO2).

Results: Dobutamine (5 ug/kg/min) restored cardiac output in the post ischemic heart by increasing heart rate from 102 ± 21 to 131±16 bpm. Adding ivabradine (0.5 mg/kg) to dobutamine-support slowed heart rate back to 100 ± 9 bpm and increased stroke volume (SV) from 29 ± 5 to 35 ± 3 ml while maintaining cardiac output (CO) and mean arterial pressure (MAP). Ivabradine had a neutral effect on post ischemic LV energetics compared to dobutamine alone at a wide range of workloads.

Conclusion: There was no surplus oxygen consumption in post-ischemic hearts when combining ivabradine with dobutamine , Furthermore, addition of ivabradine to dobutamine restored the hemodynamics to pre-ischemic levels by reducing the heart rate and increasing the SV and stroke work while maintaining MAP and CO.

17939 Lack of the Alpha-11 Integrin in the Heart is Associated With Progressive Diastolic Dysfunction, Myofibrillar Disarray and Impaired Cardiomyocyte Growth

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Background: Integrins, transmembrane receptors, play crucial roles in diverse cellular and developmental processes due to critical interactions with the extracellular matrix (ECM). During fetal development and towards adulthood, heart growth and function is suggested to depend on forming and remodeling the ECM and its con-

nection to the myocyte. Currently however, the role of integrins in cardiovascular development (CVD) is poorly defined. Thus, we hypothesized that the α11 integrin (α11), which is expressed by fibroblasts and binds preferentially to type I collagen fibers, plays a vital role in CVD.

Methods: α11 KO and wildtype littermate mice (both n = 8) were examined at 4 weeks and 8 weeks of age. Animals underwent function assessments, including echocardiography and invasive pressure volume (PV) loop analysis, and structural examination via histological and electron microscopy (EM) analysis.

Results: At 4 weeks, heart weight (HW) and HW indexed to tibial length were decreased in α11 KO mice ($P < 0.05$), which were normalized at 8 weeks. Echocardiography revealed reduced end-diastolic area (EDA) at 4 weeks ($P < 0.05$). Despite normalization of EDA at 8 weeks, PV loop revealed impaired diastolic function as evidence by increased EDP, prolonged Tau and steeper EDPVR (all $P < 0.05$). No differences in HR or systolic parameters were evident. α11 KO mice also demonstrated structural changes. WGA staining revealed evidence of myofibrillar disarray. Connexin 43 and desmin staining showed increased Z-disk and intermediate filament clustering, respectively. LV myocyte size was also reduced ($P < 0.05$). Similarly, EM analysis showed reduced cardiomyocyte thickness and distance between end plates (both $P < 0.05$).

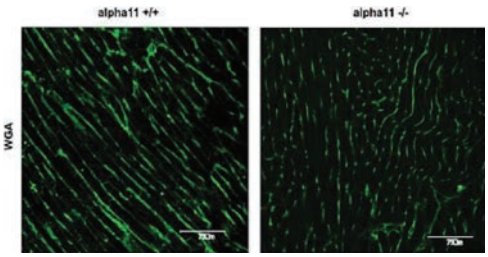

Figure 1. WGA staining showing evidence of myofibrillar disarray in the hearts of the a11 integrin KO (-/-) mice at 8 weeks.

Conclusion: Loss of α11 resulted in progressively worsening diastolic function that was associated with myofibrillar disarray and impaired cardiomyocyte growth. These findings suggest that α11 is required for the development of normal heart structure and function.

18460 Asymmetric Septal Hypertrophy as a Prognostic Indicator During Progression of Aortic Valve Stenosis

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Objective: Asymmetric septal hypertrophy (ASH) in patients with severe aortic stenosis (AS) has been associated with increased perioperative morbidity and mortality in smaller studies with severe aortic stenosis (AS). This association has not been tested in a large, longitudinal study.

Methods: Clinical, echocardiographic and outcome data from 1730 patients with asymptomatic AS, participated in the Simvastatin Ezetimibe in Aortic Stenosis study (SEAS), a randomized placebo controlled study evaluating the effect of lipid lowering medications on progression of AS, were used. ASH was considered present if interventricular septal/posterior wall thickness ratio exceeded 1.5. The association of ASH with rate of major cardiovascular (CV) events was tested in time-dependent coxregression analysis.

Results: During a median of 4.3 years follow-up, ASH developed in 17.0 % of patients, and was associated with higher left ventricular mass (LVM) and body mass index (BMI) compared to non-ASH patients (all $p<0.05$). In time-varying Cox regression analysis, ASH predicted a 50% greater incidence of ischemic CV events (ICE), a 63% greater incidence in the need for coronary artery bypass grafting (CABG) at the time of aortic valve replacement, and a 2-fold higher incidence of hospitalization for heart failure due to progression of AS (CHFAS) independent of important confounders (all $p<0.05$) (Table).

	ICE(n=321)	CABG (n=165)	CHFAS(n=47)
Asymmetric septal hypertrophy	1.45(1-11-1.88)*	1.63 (1.13-2.34)*	2.25(1.20-4.21)*
Aortic valvular velocity (m/sec)	1.25(1.08-1-44)*	1.75(1.43-2.14)‡	1.92(1.33-2.78)*
Simvastatin/Ezetimibe treatment	0.77(0.62-0.96)*	0.66(0.46-0.90)*	1.03(0.58-1.82)
Left ventricular mass (g)	1.00(1.00-1.00)*	1.00(0.99-1.00)	
Hypertension	1.95(1.35-2.81)‡	2.14(1.26-3.64)*	

P-value: *<0.05, ‡<0.001

Conclusions: Development of ASH during progression of AS was a strong predictor of major CV events in patients participating in the SEAS-study. Table. Results are presented as Hazard ratio (95% Confidence Interval).

19120 Preoperative Symptoms Predict Improvement in Health-related Quality of Life After Surgery for Severe Aortic Stenosis, While Preoperative Echocardiographic Parameters Do Not

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Introduction Symptoms and echocardiographic assessment of the heart and the aortic valve are key factors in the pre-operative decisionmaking process in patients with severe aortic stenosis (AS). Improved survival and HRQoL are primary goals after surgical aortic valve replacement (SAVR). In this study, we report changes in HRQoL one year after SAVR and study the association between symptoms, echocardiographic measures, and change in HRQoL.

Methods In a prospective cohort study of 480 patients with severe AS, 327 patients have been to follow-up at one year, and of these 276 patients have had SAVR. Mean age was 74 years, and 40 % (111) were female. HRQoL was measured using Short-Form 36 (SF-36). Response rate was > 90%. Patients` answers on type (fatigue, dyspnea, chest pain or dizziness) - and frequency (last week) of cardinal AS-symptoms were used to create three patient groups based on estimated total symptom load. We used valve area, mean pressure gradient, cardiac output, ejection fraction, and estimated systolic pulmonary artery pressure as echocardiographic measures of heart function and AS characteristics.

Results Mean valve area was 0.7 cm2, mean pressure gradient was 53 mmHg, mean maximum valve velocity 4.5 m/s, mean estimated systolic pulmonary artery pressure 36 mmHg, cardiac output 5,2 m/s, and 89 % had normal ejection fraction. There was a statistically significant improvement in HRQoL one year after SAVR in six of the eight SF-36 scales. Physical Functioning: (mean pre-operative - mean post-operative score) 61 - 72 p < 0.001, Role-physical Functioning: 52 - 62 p < 0.001, Bodily Pain: 65 - 74 p < 0.001, General Health: 58 - 71 p < 0.001, Vitality: 48 - 56 p < 0.001, Social Functioning: 78 - 81 p = 0.2, Role-emotional Functioning: 77 - 80 p = 0.2, Mental Health: 77 - 80 p = 0.02. There was no association between the echocardiographic parameters and change in HRQoL.

Conclusions There was a substantial gain in HRQoL after SAVR. Despite their importance in the pre-operative assessment, echocardiographic measures did not predict change in HRQoL. After SAVR, patients with more symptoms experience the greatest yield in HRQoL, and amount of AS-symptoms is a strong predictor of intermediate HRQoL

9397 Prognostic implications of small aortic root in aortic valve stenosis

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Background: In aortic stenosis (AS), having a small aortic root influences assessment of AS severity as well as treatment strategy. The aim was to test the prognostic implications of having a small aortic root in patients with AS

Methods: Data from 1563 patients with initially asymptomatic mild-moderate AS enrolled in the Simvastatin and Ezetimibe in Aortic Stenosis study was used. Small aortic root was defined as an aortic diameter <2.60 cm at the sinotubular junction.

Results: A small aortic root was found in 32.6% of patients and twice as frequent among women. In multivariate logistic regression, having small aortic root was associated with lower body height, smaller left ventricular dimensions and wall thickness, higher arterial stiffness and female sex (all p<0.05). In multivariate Cox

Table 1. Small aortic root as predictor of different cardiovascular events in multivariate analyses.

Variables	OR	95% CI	p-value
Aortic valve event	1.29	1.05-1.58	0.014
Cardiovascular death	2.17	1.35-3.51	0.001
Hospitalization for HF due to AS progression	2.08	0.96-4.54	0.064
Ischemic cardiovascular events	1.66	1.27-2.18	<0.001
Non-haemorrhagic stroke	2.21	1.27-3.83	0.005
Total mortality	1.45	1.02-2.06	0.037
Combined total mortality and hospitalization for HF due to AS progression	1.46	1.05-2.02	0.025

AS= aortic stenosis, HF= heart failure

regression analyses, having a small aortic root at baseline predicted increased cardiovascular morbidity and mortality independent of age, sex, AS severity by energy loss index, hypertension and study treatment (all p<0.05, Table 1).

Conclusion: In AS patients without known cardiovascular disease, having a small aortic root is an independent predictor of higher cardiovascular morbidity and mortality.

19354 Management and Outcomes of Acute Type B Dissection in IRAD Treated with Open Surgery, Endovascular Flap Fenestration or TEVAR

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Background: The debate for the optimal treatment of complicated Type B Acute Aortic Dissection (TBAAD) is primarily focused upon open surgical intervention versus thoracic endovascular aortic repair (TEVAR). The technique of fenestration with stenting has been proposed to resolve malperfusion. This study evaluated post-procedural outcomes of all three approaches for TBAAD.

Methods: TBAAD patients enrolled in the International Registry of Acute Aortic Dissection were stratified by management type: TEVAR, fenestration and stenting, and surgery.

Results: Of the 552 patients with TBAAD, 231 (41.8%) underwent TEVAR, 214 (38.8%) standard open surgery, and 107 (19.4%) fenestration and stenting. TEVAR or fenestration and stenting were more likely to be performed in classic double barrel aortic dissection when compared to open surgery (73.2%, 76.6%, 52.8% respectively; p<0.001). Patients treated with open repair were less likely to have distal extension into the abdominal aorta than those with TEVAR or fenestration and stenting (47.7%, 62.7%, 86.4%, respectively; p<0.001). In-hospital mortality was similar between groups (11.7% TEVAR, 14.0% fenestration and stenting, 15.9% surgery). At five years, Kaplan-Meier post-discharge all-cause survival estimates were highest for TEVAR, followed by endovascular fenestration and finally open surgical intervention (85.2%, 78.3%, 67.2%, respectively; p=0.039).

Conclusion: Patients treated by endovascular approaches, whether with flap fenestration or thoracic endovascular aortic repair, had lower five year mortality when compared to patients who required open repair in the setting of TBAAD. Either endovascular approach may be helpful in the treatment of TBAAD. Further research is needed to determine how much of the observed difference represents patient selection versus differential effects of treatment.

20255 Risk Factors of Mortality in Patients Undergoing Surgical Management of Acute Type a Dissection: A Multivariate Analysis From the International Registry of Acute Aortic Dissection (IRAD)

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Background: Acute type A dissection remains a challenging clinical problem. Contemporary surgical outcomes of acute type A aortic dissection along with independent risk factors for mortality are evolving. This study investigates the relationship between postoperative complications and mortality in a large multi-national cohort.

Methods: Of 2741 Type A patients enrolled in IRAD from January 1996-February 2013, 1207 were surgically managed and included in the final model. Univariate correlation between in-hospital mortality and clinical variables used the Chi-squared test or two-sided Fisher test when applicable. Multivariate analysis was performed using iterative binary logistic regression.

Results: 1207 patients with acute type A aortic dissection underwent surgical intervention with an overall in-hospital mortality of 18.1%. Average age was 60.6±13.8, and the cohort was 69.8% male. Independent predictors of operative mortality were age greater than 70 years (OR 1.94), prior cardiac surgery (OR 2.39), presentation with coma/altered consciousness (OR 2.61) and coronary artery compromise (OR 2.06). Post-operative complications associated with hospital death were post-operative coma (OR 11.71), mesenteric ischemia or infarction (OR 9.46), hypotension (OR 8.05), and limb ischemia (OR 4.86).

	Odds Ratio	95% CI	p-value
Pre-Operative Predictors			
Female gender	0.936	(0.597-1.466)	0.771
Age > 70 years	1.940	(1.252-3.008)	0.003
Prior cardiac surgery	2.392	(1.351-4.233)	0.003
Presenting coma/altered consciousness	2.608	(1.481-4.593)	0.001
Coronary artery compromise	2.063	(1.232-3.453)	0.006
Post-Operative Predictors			
Coma	11.705	(5.389-25.423)	<0.001
Mesenteric ischemia/infarction	9.462	(3.942-22.713)	<0.001
Hypotension	8.053	(5.275-12.294)	<0.001
Limb ischemia	4.864	(2.030-11.656)	<0.001

Conclusions: There are 8 independent predictors of mortality: 4 pre-operative factors and 4 complications. The overall mortality model predicts 84.7% of the outcome. These data may guide decisions about planning treatment and or evaluating outcomes.

20187 Type a Aortic Dissection in Bicuspid Aortic Valve and Marfan Syndrome Patients: Differences and Similarities

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Background: Bicuspid aortic valve (BAV) and Marfan Syndrome (MFS) are associated with deleterious changes in the aortic media that predispose patients to Type A acute aortic dissection (TAAAD). Little comparison has been done regarding how TAAAD manifests itself in these different diseases.

Methods: Type A patients enrolled in the International Registry of Acute Aortic Dissection with recorded history of either condition were compared (N=2320). BAV was noted in 93 patients (4.0%) and MFS in 84 (3.6%).

Results: MFS patients presented younger (36.7±11.7 v 52.7±16.1, p<0.001). BAV patients were more commonly of white race (95.6% v 85.4%, p=0.033). Regarding patient history, BAV was more often associated with hypertension (60.4% v 28.9%, p<0.001), atherosclerosis (24.7% v 2.4%, p<0.001), and aortic valve stenosis or insufficiency (41.6% v 19.3%, p=0.002). Conversely, patients with MFS more frequently demonstrated prior aortic dissection (15.9% v 4.3%, p=0.019), prior aneurysm or dissection surgery (19.0% v 5.5%, p=0.006), and family history of aortic disease (44.1% v 3.2%, p<0.001). Patients with MFS were more likely to present with pain (96.4% v 86.8%, p=0.030); no other differences in presenting symptoms were noted. Annulus, root, sinotubular junction, arch, and descending aortic diameters were similar between groups. The ascending aorta was larger in BAV patients (median diameter 5.5 cm (4.8-6.4) v 4.8 (4.0-6.0), p=0.008). BAV patients were more likely to have periaortic hematoma at presentation (23.3% v 9.1%, p=0.024). Surgery was performed frequently in both groups (91.4% BAV v 90.5% MFS, p=NS) with BAV patients undergoing more aortic valve replacement (59.7% v 37.7%, p=0.008). In-hospital mortality was similar (16.1% BAV v 13.1% MFS, p=NS), and no other differences were seen in in-hospital complications or 5-year survival estimates. MFS patients were much more likely to require a subsequent aortic intervention on 5-year Kaplan-Meier analysis (0% in BAV v 51.4% MFS; p=0.003).

Conclusions: Differences in patient history and ascending aortic size were noted between groups, while presentation, management and outcomes were similar. Notably, patients with MFS were much more likely to require an aortic operation 5 years post-discharge.

20107 The Matricellular Protein CCN2/CTGF Attenuates Ventricular Remodeling by Enhancing Scar Healing after Myocardial Infarction

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We have previously shown that left ventricular (LV) remodeling after myocardial infarction (MI)

is attenuated in transgenic mice with cardiac-restricted overexpression of CCN2 (Tg-CCN2) regardless of reperfusion of the ischemic area or not. Thus, the aim of this study was to resolve to what extent the role of CCN2 in scar healing may mechanistically contribute to attenuation of LV dilatation after MI. MI was induced by ligation of the left coronary artery in Tg-CCN2 and in non-transgenic control (NTC) mice. Area of necrosis and LV dimensions were determined by cardiac MRI. Primary cultures of cardiac fibroblasts (cFBs) were prepared from NTC mice and stimulated with or without recombinant CCN2 (rCCN2; 200 nmol/L). Area of necrosis 24 hours after induction of MI was similar in Tg-CCN2 and NTC mice. Serial cardiac MRI examinations at day 1, 7, 14, and 42 after induction of MI revealed that CCN2 engendered robust inhibition of LV dilatation during the first week after MI, i.e. the period of infarct dilatation (LV end-diastolic volume at day 7: 97±9 vs. 136±7 μL in Tg-CCN2 vs. NTC mice; $p<0.01$). Concurrently, we found enhanced deposition of collagen in the developing scar tissue of Tg-CCN2 mice from day 5 after MI (21.3±0.4 vs. 16.6±0.8 μg/mg dry weight in Tg-CCN2 vs. NTC; $p<0.01$). This decreased LV dilatation and accelerated collagen deposition also reflected in reduced incidence of infarct rupture in Tg-CCN2 vs. NTC mice (2/41 vs. 10/39, $p<0.05$) during the first week after MI. Stimulation of cFBs with rCCN2 in vitro evoked robust increase of collagen synthesis (+66±3%, $p<0.05$, $n=6$) corroborating the in vivo finding of Tg-CCN2 mice. Gene set enrichment analysis of rCCN2-stimulated cFBs also revealed increased expression of NFkB target genes and induction of an inflammatory phenotype (false discovery rate <0.05) that was capable of mediating caspase-1-dependent, paracrine senescence of cFBs.

In conclusion, this study demonstrates that CCN2 enhances healing of MI and that the accelerated scar tissue formation during the first week after MI contributes to reduced LV dilatation and reduced incidence of infarct rupture. CCN2 stimulates an inflammatory cFB phenotype that promotes senescence of cFBs, providing a plausible mechanism for the enhanced, yet limited scar formation.

11223 Hydrochlorothiazide Use is Independently Associated With a Decreased Risk of New Atrial Fibrillation in Hypertensive Patients With Electrocardiographic Left Ventricular Hypertrophy

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Background: High and even upper-normal blood pressure (BP) are predictors of incident atrial fibrillation (AF) and we have recently demonstrated that more aggressive BP control is associated with a lower risk of new AF. Previous study has demonstrated that hydrochlorothiazide (HCTZ) use is independently associated with greater left atrial size reduction in hypertensive patients. However, whether HCTZ use is associated with a lower incidence of AF independent of BP effects is unclear.

Methods: Risk of new-onset AF was examined in relation to in-study HCTZ use in 8704 hypertensive patients with ECG LVH with no history of AF, in sinus rhythm on their baseline ECG, with baseline data on HCTZ use, who were randomly assigned to losartan- or atenolol-based treatment with additional protocol-based use of HCTZ as needed to lower BP.

Results: During 4.7±1.1 years follow-up, new-onset AF was diagnosed in 691 patients (7.9%) and 6,932 (79.6%) were treated with HCTZ at some time. In univariate Cox analysis, in-study HCTZ use, entered as a time-varying covariate, was associated with a 19% lower risk (95% CI 5-32%) of developing AF. After adjusting for other univariate predictors of new AF, including randomized treatment, age, sex, race, diabetes, history of ischemic heart disease, MI or heart failure, prior antihypertensive therapy, baseline serum creatinine, urine albumin/creatinine ratio and a logistic propensity score for HCTZ use entered as standard covariates, and for incident heart failure and in-treatment systolic and diastolic BP, Cornell product left ventricular hypertrophy, heart rate, QRS duration, HDL cholesterol, statin and calcium channel blocker use treated as time-varying covariates, in-study HCTZ use remained associated with a 21% lower risk (95% CI 7-34%) of new AF. Use of HCTZ at any time during the study, entered as a standard covariate, predicted a significantly lower 5-year incidence of AF in Kaplan-Meier analysis (7.5 vs 10.3%, $p<0.001$) and an identical 21% lower risk of new AF (95% CI 4-35%) in a parallel multivariate Cox analysis.

Conclusions: HCTZ use is associated with a lower risk of developing new-onset AF in hypertensive patients, independent of in-treatment BP, other possible AF risk factors and of the propensity to use HCTZ in this population.

11259 Lower Achieved Systolic Pressure is Associated With Increased Short-Term Mortality After Stroke in Hypertensive Patients With Electrocardiographic Left Ventricular Hypertrophy

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Background: Hypertensive patients with ECG left ventricular hypertrophy (LVH) are at increased risk of all-cause and cardiovascular (CV) mortality. Lowering blood pressure (BP) after stroke reduces the risk of recurrent stroke, but recent data suggest that lower systolic BP (SBP) measured 5 years after stroke is associated with worse long-term outcomes. Whether lower SBP is associated with increased short-term mortality after stroke in hypertensive patients is unclear.

Methods: All-cause and CV mortality were examined in relation to average in-treatment SBP in 541 hypertensive patients with ECG LVH randomly assigned to losartan- or atenolol-based treatment who had new strokes during follow-up. Patients with average SBP <144 mm Hg (lowest tertile) and SBP>157 (highest tertile) were compared with patients with average SBP between 144 and 157.

Results: During 2.02±1.65 years mean follow-up after first stroke, 170 patients (31.4%) died, 135 (25.0%) from CV causes. SBP <144 was associated with significantly higher all-cause mortality and SBP>157 with significantly higher all-cause and CV mortality rates than SBP between 144 and 157 (table), with the highest unadjusted mortality rates in patients with SBP >157. In univariate Cox analyses, compared with average SBP between 144 and 157, patients with SBP <144 had an increased risk of all-cause mortality and patients with average SBP >157 an increased risk of all-cause and CV mortality. In multivariate Cox analyses adjusting for significant univariate predictors of mortality (see table), an average SBP <144 was a significant predictor of all-cause and CV death, whereas patients who had an average SBP >157 had no significant increased risk of death.

Outcome	SBP <144 mm Hg (n=179)	SBP 144-157 mm Hg (n=183)	SBP >157 mm Hg (n=179)	Overall p value
Mortality Rates (per 100 patient-years)				
CV mortality	12.0	7.6	18.7†	<0.001
All-Cause mortality	16.4‡	9.3	22.4†	<0.001
Univariate Cox Models (Hazard Ratio and 95% CI)				
CV mortality	1.47 (0.93-2.33)	1	2.27 (1.47-3.50)	0.001
All-Cause mortality	1.66 (1.10-2.50)	1	2.26 (1.53-3.35)	<0.001
Multivariate Cox Models* (Hazard Ratio and 95% CI)				
CV mortality	1.63 (1.02-2.59)	1	1.41 (0.90-2.21)	0.040
All-Cause mortality	1.83 (1.22-2.76)	1	1.44 (0.95-2.16)	0.004

*adjusted for other univariate predictors of mortality: age, sex, history of prior stroke, heart failure or atrial fibrillation as standard covariates and in-treatment diastolic BP, heart rate and Cornell product LVH as time-varying covariates
‡ <0.05, † <0.001 vs SBP 144-157

Conclusions: Lower achieved SBP (<144) is associated with a significantly increased risk of CV and all-cause mortality after initial stroke in hypertensive patients during short-term follow-up. Further study is required to determine ideal SBP goals after stroke.

19356 Sex-differences in Left Ventricular Mass Changes in Treated Hypertensive Outpatients: The Campania Salute Network

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Introduction: In clinical trials, women achieve less regression of hypertensive LV hypertrophy (LVH) than men. Whether this is evident also in less selective hypertensive patients is uncertain.

Hypothesis: Find sex-differences in LV mass changes during hypertensive treatment.
Methods: We evaluated 6969 hypertensive patients with follow-up>12 months (43% women, 53±11 years) from the Campania Salute Network Registry, during a 4-year median follow up. Clinical and echocardiographic data from baseline and last visit during follow-up were used.

Results: At baseline, women were older, had higher systolic blood pressure (BP) and heart rate, lower diastolic BP, Framingham Risk Score and renal function, and included more patients with obesity and LVH (all p<0.001 vs. men). Despite optimal BP control in 62% of patients, LV mass increased over time in the total population, similarly in males and females, whereas relative wall thickness increased only in females (all p<0.0001). Percent change in LVM was positively related to follow-up duration and change in systolic BP, diastolic BP and body mass index (BMI) in both sexes (all p<0.0001). During follow-up, women, but not men, exhibited significant increase in BMI (both p<0.0001). After adjusting for age, follow-up duration, changes in BP and BMI, LV mass increased in the presence of both controlled and uncontrolled BP, but in men the change was less evident when BP was controlled (all p<0.001). In subgroups with baseline LVH (by sex-specific LVM normalized by

height2.7), LV mass decreased over time in men, but increased in women (p<0.001).

Conclusions: In hypertensive, Caucasian outpatients participating in the Campania Salute Network registry, lack of reduction in LV mass was particularly evident in women, independently of confounders including age, duration of follow-up, changes in BP and BMI, with negligible benefit of BP control on LVH.

16329 Small Aortic Root Dimension: A Contributor to Increased Arterial Stiffness in Hypertension (The Campania Salute Network Registry)

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Background: In preliminary analysis in a population-based study larger aortic root dimension (ARD) was associated with higher stroke volume, diastolic blood pressure (BP) and heart rate, but lower systolic BP. Thus we assessed whether ARD influences a 2-element windkessel model of arterial stiffness in the setting of arterial hypertension.

Methods: Ultrasound carotid intima-media thickness (IMT), echocardiographic ARD and pulse pressure (brachial) / stroke index ratio (PP/SVi) were measured in 12392 hypertensive patients (age 53±12 years, 43% women) free of prevalent cardiovascular (CV) disease and with ejection fraction ≥ 50% from the Campania Salute Network Registry. ARD was compared with the value predicted by age, sex and height, using an equation previously generated in 1207 normal subjects, to predict ideal sex-specific ARD. A sex-specific Z-score was thereafter calculated (ARD-z). PP/SVi was categorized in normal (lowest and middle tertiles) and high (highest tertile).

Results: High PP/SVi was slightly more common in women than in men (37% vs. 30%, p<0.01). Patients with high PP/SVi were older (55±13 vs. 52±12 years), more likely to be diabetic (12% vs. 7%) and less likely to be smokers (16% vs. 20%, all p<0.01). They had higher IMT and cholesterol level and lower BMI and GFR (all p < 0.01). ARD-z was significantly lower in the high than in the normal PP/SVi group (p<0.01). In multivariable logistic regression analysis, increased PP/SVi was associated with lower ARD-z and higher IMT (both p<0.0001), independent of significant associations with older age, female gender, low BMI, diabetes and smoking habit (Table). GFR and cholesterol levels were not independent covariates of PP/SVi.

Variables	OR	95% CI	p-value
Aortic root dimension	0.84	0.80-0-87	<0.0001
Carotid IMT (mm)	1.23	1.15-1.31	<0.0001
Age (×5 years)	1.05	1.03-1.07	<0.0001
Female gender	1.24	1.15-1.34	<0.0001
BMI (kg/m^2)	0.96	0.95-0.97	<0.0001
Diabetes	1.53	1.34-1.75	<0.0001
Smoking	0.75	0.68-0.83	<0.0001
Cholesterol (mg/dL)	1.00	1.00-1.00	0.11
GFR (mL/min/1.73 m^2)	1.00	0.99-1.00	0.12

Conclusion: Small ARD together with atherosclerotic modifications of conduit arteries are associated with increased 2- element windkessel model of arterial stiffness in hypertension, independently of significant effect of female gender and arteriosclerosis.

13994 Masked Hypertension in Ischemic Stroke Patients

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Background: Masked hypertension (MHT) is characterized by normal clinic blood pressure (BP), but elevated ambulatory BP (ABP) and associated with increased risk for target organ damage. We assessed clinical and metabolic characteristics of MHT in ischemic stroke patients.

Methods: Clinic and ABP was recorded in 219 patients (aged 15-60 years) included in the prospective Norwegian Stroke in the Young Study (NORSYS) 3 ± 1 month after the acute stroke to identify normotension (NT), white-coat hypertension (WCHT), MHT and sustained hypertension (HT).

Results: MHT was found in 10% of patients. In univariate analyses, patients with MHT had higher systolic ABP and serum triglycerides than those with HT, higher body mass index and waist circumference than those with NT and WTCH and lower serum HDL cholesterol than all other BP categories (all p<0.01) (Table). In multivariate logistic regression analysis, lower HDL cholesterol (OR 7.14[95% CI 1.61-33.33], p<0.01), lower fasting blood glucose (OR 2.44[95% CI 1.15-5.26], p<0.05) and higher systolic ABP (OR 1.07[95% CI 1.03-1.11], p<0.01), were independently associated with MHT. Adding obesity, waist circumference, alcohol consumption or fasting serum triglycerides to the model did not change the results.

Conclusion In young and middle-aged ischemic stroke patients in the NORSYS registry, combined lower HDL-cholesterol and absence of diabetes were particularly associated with presence of masked HT.

85 Defibrillation During Mechanical Chest Compressions Should Be Avoided During the Downstroke Phase of the Chest Compression Cycle

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Introduction: CPR guidelines emphasize minimizing pre-shock chest compression (cc) pauses. Animal studies indicate higher shock success rates for shocks delivered during the upstroke phase of the cc cycle. In the Circulation Improving Resuscitation Care (CIRC) trial, providers delivered shocks during mechanical cc with Load Distributing Band (LDB). This is the first clinical study investigating shock success related to different cc cycle phases.

Methods: Patients who received LDB cc were included. The first and up to three shocks were studied separately for initial shockable rhythms. Electronic defibrillator data with transthoracic impedance were used to determine when in the cc cycle (downstroke, upstroke, decompressed) a shock was delivered, and to identify control group cases with a pre-shock cc pause. Shock success was defined as termination of fibrillation/pulseless VT five seconds post-shock (TOF) and return of organized rhythm 60 seconds post-shock (ROOR). TOF and ROOR were compared between the different LDB cc cycle phases and the control group using Chi-Square tests. $P<0.05$ was considered statistically significant. Results: Of 1130 shocks during LDB cc, 164 could not be categorized to the different cc phases and were excluded. TOF was lower in the downstroke phase for all shocks and initial rhythms, and for shockable initial rhythms first up to three shocks, compared with the control group. There were no significant TOF differences for other cc phases. ROOR was independent of where in the LDB cc cycle the shock hit, irrespective of initial rhythm.

Conclusion: Defibrillation attempts should be avoided during the downstroke phase of the continuous LDB cc cycle. Shocks during continuous LDB cc do not increase shock success compared to pre-shock LDB cc pause prior to shock.

119 Bystanders Need Follow-up After Performing Cardiopulmonary Resuscitation

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Introduction: Bystanders' intervention causes a 2-3 times increased chance of survival to out-of-hospital cardiac arrest (OHCA) victims by alerting the Emergency Medical Services (EMS) and performing cardiopulmonary resuscitation (CPR). To improve community based survival in OHCA victims, health care systems are dependent on the appropriate actions of citizens. Performing CPR is, however, shown to be emotionally challenging for bystanders. We know very little about their need for formal follow-up. Aim: To clarify bystanders' need for follow-up after performing CPR.

Methods: Fifteen bystanders, who performed CPR to OHCA victims, took part in a qualitative interview study. We used in-depth interviews with open-ended and continuous questions, focusing on emotions, coping strategies and need for follow-up after performing CPR.

Results: All CPR bystanders reported that experiencing OHCA was an emotionally challenging experience. Most bystanders contacted health care professionals among family members and friends to receive recognition and acceptance of their CPR performance. A significant desire was to receive information on the cardiac arrest victim's outcome, and the bystanders used great efforts to obtain this information. All bystanders described a strong need to talk to health care professionals shortly after performing CPR, preferably EMS staff. It was important for them to understand the most frequently experienced emotions after performing CPR. Bystanders, who experience life threatening situations in their daily work, described less emotional stress than the others.

Conclusions: Bystanders need follow-up from health care professionals to learn about frequent emotions after CPR and to receive feed-back on patient outcome. We believe that organizing professional follow-up after CPR attempts may mitigate emotional stress among OHCA bystanders. We believe that an organized follow-up of CPR bystanders might improve the general public's future willingness to initiate CPR.

176 Assessment of Sublingual Microcirculation by Sidestream Darkfield Imaging: A Word of Caution

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Introduction: Intravital videomicroscopy of the sublingual microcirculation is used to monitor critically ill patients. Existing guidelines suggest handheld video recordings of ≥ 20 seconds from 5 areas. We tested if a fixated camera that allowed extension of the observation time could improve sensitivity in microcirculatory assessment.

Methods: Anesthetized pigs (n=8), which were equally divided to a handheld group where microcirculation was assessed continuously in 1 min in 5 areas, and a group with a fixated camera where observation time was extended to 10 min in one area. The microcirculation was challenged by infusion of arginine vasopressin (AVP). Post ischemic acute heart failure (AHF) was induced by left coronary microembolization and the AVP infusion was repeated. Recordings were divided in 20 seconds sequences and Mean Flow Index (MFI) of small vessels were then scored and averaged for each measurement point. Results: When giving 0.003, 0,006 and 0,012 IU/kg/min of AVP, MFI in the fixated 10 min group was significantly more reduced (2,03±0,38, 0,98±0,18, 0,48±0,11) compared to both the first 20 seconds (2,77±0,04, 2,06±0,04, 1,74±0,06) and the total 1 min (2,63±0,09, 1,70±0,07, 1,33±0,16) in the handheld group. Following induction of acute heart failure, cardiac output dropped to half of the pre ischemic values. Interestingly, MFI was further decreased when giving 0,001 and 0,003 IU/kg/min of AVP in AHF (1,62±0,60 and 1,16±0,38) compared to pre-ischemia (2,86±0,09 and 2,03±0,38).

Conclusion: A fixated camera with extended recording times reveals important microcirculatory changes in shock-states not detected by the guideline approach.

187 Incidence, Timing and Duration of Newborn Resuscitations: Challenges for Implementation of International Treatment Recommendations

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Introduction: International consensus recommendations for newborn resuscitation allocate <60 seconds following birth to dry, stimulate, and assess heart rate and respirations before initiating time critical interventions such as positive-pressure ventilation (PPV). However, there is scarce data on the incidence, actual timing and duration of interventions for newborn resuscitations in a normal-risk delivery room.

Methods: Prospective, observational study conducted in the delivery unit at an academic training hospital. All deliveries during selected random weekday/evening 8-hours shifts were attended by a highly trained observer. Real-time data was collected on all newborns ≥32 weeks gestational age who received PPV immediately after birth. Time was recorded as from time of birth. Descriptive summaries were compared to international recommendations for time critical assessments and interventions.

Results: Between Jan-June 2014, 295 (22%) of 1372 live deliveries were observed. PPV was required in 22/295 (7%) of those deliveries. Mean gestational age was 38 ±2.6 weeks. At 60s, heart rate was <60/m in 3 (14%), 60-100/m in 12 (55%) and >100/m in 6 (27%). Within the first 60s, 100% received suction. Pulse oximetry was eventually placed on 21 (95%), but only 2 (17%) within time critical recommended target of 60s: mean time to placement 138 ± 96s. PPV was started within 60s in 10 (45%), between 60-<120s in 7 (32%), and >120s in 5 (23%). PPV duration was <60s in 3 (14%), 60-<120s in 7 (32%), and ≥120s in 12 (54%). Time to spontaneous respirations (PPV stopped) was <120s in 6 (27%) and >5m in 7 (32%). Tracheal intubation was required in 3 (14%); mean time to intubation 5:42m ± 35s.

Conclusion: Most (93%) newborns ≥32 weeks GA spontaneously initiate respirations. Providers applied international resuscitation recommendations for assessment and treatment (e.g. suction, pulse oximetry, initiation of PPV for HR <100), but were challenged to meet time-critical targets

for assessments and interventions for newborns requiring assisted ventilation. Incidence, actual timing and duration of interventions for newborn resuscitations in normal-risk delivery rooms should inform future guidelines for simple and pragmatic resuscitation guidelines.

270 Targeted Temperature Management at 33 or 36 Degrees in Patients Resuscitated from Out-of-Hospital Cardiac Arrest with Initial Nonshockable Rhythms: Impact on Early Risk Factors

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Targeted temperature management at 33°C or 36°C in patients resuscitated from out-of-hospital cardiac arrest with initial nonshockable rhythms: impact on early risk factors OBJECTIVE Out-of-hospital cardiac arrest (OHCA) is associated with high mortality - especially with an initial non-shockable rhythm (NSR). A number of risk factors are traditionally associated with poor outcome in patients with return of spontaneous circulation (ROSC) after OHCA.

Hypothesis Prognostic information of traditional risk factors remains unaltered in relation to target temperature management of 33°C or 36°C in patients resuscitated from NSR.

Methods The Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest (TTM) trial reported similar mortality when targeting 33°C (TTM33) and 36°C (TTM36) in patients with ROSC after OHCA (NEJM 2013). We assessed the interaction of the two levels of TTM and age, time to ROSC, bystander CPR, lactate at admission and sex on mortality in the subgroup of 178 patients resuscitated from OHCA with NSR.

Results Compared to patients presenting with shockable rhythm, patients with an initial NSR had longer time to ROSC, less frequently had bystander CPR, had higher lactate levels on admission,and a higher overall mortality rate ($p<0.001$ for all 4 factors). No differential effect of TTM at the two levels was found on mortality or on the following pre-specified early risk factors of OHCA with NSR: age (risk ratio for TTM36 (RR) 1.01; confidence interval (CI) 0.98-1.05), time to ROSC (RR 0.99; CI 0.98-1.00), bystander CPR (RR 0.85; CI 0.43-1.67), lactate (RR 0.98; CI 0.91-1.04) and sex (RR 1.45; CI 0.66-3.20).

Conclusion Overall mortality rate and the prognostic information of early risk factors of mortality in patients resuscitated from NSR appear to be unaltered by level of TTM. The risk associated with these factors seems to have less importance than in shockable primary rhythm in NSR.

274 EuReCa ONE-25 Nations, ONE Europe, ONE Registry: A Prospective Data Analysis Over 1 Month in 25 Resuscitation Registries in Europe

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Background and Objectives: Cardiovascular disease is the leading cause of death throughout Europe. There is considerable variation in the incidence of out-of-hospital cardiac arrest (OHCA) between European countries and communities and the incidence of resuscitation attempts also varies widely (38-86/100,000 inhabitants /year). Reasons for variation in incidence may include differences in cardiovascular disease prevalence, lifestyle and nutritional behaviour, differences in the structure and deployment of emergency medical services and variation in treatment options in receiving

hospitals. The aim of EuReCa ONE (European Registry of Cardiac arrest Trial One) is to aid understanding of the differences in incidence and outcomes from OHCA in Europe by comparing the epidemiology, treatment and survival from OHCA across 25 European countries. Predefined research questions will focus on e. g.the incidence of OHCA throughout Europe, the initial presenting rhythm, the rate of return of spontaneous circulation (ROSC rate) and 30-day survival. The study is governed by a Steering Group from the European Resuscitation Council and is administered and conducted by a European study management team. Methods: From 1st-31st October 2014, every patient who suffers an OHCA, and is attended and/or treated by an emergency medical service and documented in one of the participating registries will be included in the study. Patients will be included regardless of arrest aetiology, first rhythm, age or gender. The study dataset was developed in accordance with Utstein criteria and was 'future-proofed' to ensure data collected will be compatible with the 2014 Utstein dataset. All data will be submitted by National Coordinators in each participating country to the EuReCa One database in anonymised format.

Conclusion: The incidence and survival rates after OHCA are heterogeneous throughout Europe. This study is the starting point for a pan-European registry of OHCA that can highlight the differences in OHCA treatment and survival throughout Europe and potentially serve as a support to quality benchmarking across the continent.

289 Effect of Elevated Legs on Hemodynamic Performance During Cardiopulmonary Resuscitation in a Porcine Model of Cardiac Arrest

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Purpose of the study: During advanced life support (ALS) end-tidal carbon dioxide (EtCO2) reflects cardiac output (CO). A recent clinical study found an association between passive leg raising (PLR) and increased EtCO2 during ALS. This may reflect a transient increase in pulmonary blood flow and CO, but might cause a detrimental decrease in coronary perfusion pressure (CPP). We evaluated the effect of PLR during experimental ALS in a randomized, factorial design.

Materials and methods: In nine anesthetized domestic pigs (30±1.8 kg) ventricular fibrillation was induced electrically. After 3 minutes of no-flow, mechanical chest compressions (5cm @ 100 min-1) were started. During four 5-minute segments of CPR we measured CO, EtCO2, perfusion pressures, carotid and cerebral cortical microcirculatory blood flow (MBF) and CPP (the average of the positive pressure difference between decompression aortic pressure (AP) and right atrial pressure (RAP)) at minute 2 and 4. Interventions were provided in a randomized sequence with PLR vs supine position, with or without epinephrine (0.5mg iv). Values are given as mean±standard deviation.

Results: PLR did not increase EtCO2 compared to supine position (3.1±0.7 vs 3.0±0.8 kPa), but CO was minimally increased from 1.1±0.3 to 1.2±0.3 Lmin-1,(p=0.003). PLR did not significantly increase AP (57±15 vs. 48±18 mmHg, p=0.3), but RAP was higher (43±10 vs. 31±7, p=0.003). However, no difference was found in CPP due to marked variation in both groups (median(range): PLR 20 (9,43) and supine 17(9,58)). The effect of epinephrine during this experimental setup was minimal.

Conclusion: We did not find a positive effect of PLR during experimental ALS, but there were no obviously detrimental effects either.

316 A Novel Video-Based Motion Analysis System to Evaluate Performance of Cardiopulmonary Resuscitation in Ambulance Transport

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Objectives: Various devices, either expensive or inconvenient, were developed to monitor the quality of CPR, which is crucial to survival for cardiac arrest. CPR performance en route of ambulance transport was hard to be measured and rarely reported. A novel videobased CPR analysis system, called "See-CPR", showing reliable CPR performance evaluation in previous manikin study, was designed to automatically analyze CPR performance in ambulance of OHCA transport.

Methods: To automatically detect chest compression (CC) movements in video documenting CPR, we first estimated the motion of objects using the motion vectors of MPEG videos. We extracted representative features and used a hierarchical detecting scheme, including frame-level detection and group-level classification, to determine the location of CC occurrence in both time and spatial domains. CC rate, CC duration, and hands-off no flow time (NFT) can be shown on video simultaneously. (Figure 1) To determine the performance of computerized video motion detection analysis, the total NFT (in seconds), the fraction of NFT (by percentage), and the CC rate (number per minute) were evaluated and compared with manual analysis of video in slow motion style. All the human faces in videos were in mosaic before analysis.

Results: Twenty video sequences of CPR in ambulance for 20 cardiac arrest patient transports by different paramedic teams were analyzed. The computerized video motion analysis versus manual analysis showed no significant difference among the total NFT (71.7±33.0 vs 61.2±37.9, p= 0.22), the fraction of NFT (33.3±5.6 vs 27.4±11.7, p= 0.13), and the chest compression rate (84.7±11.7 vs 84.9±11.8, p= 0.65).

Conclusions: A reliable video-based CPR motion detection and analysis system for automatically reporting real-time CPR performance in ambulance transport was proposed. It can be used for monitoring and real-time feedback of resuscitation en route of ambulance transport.

347 «No-Blow Time» During the First Minute of Neonatal

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Background: Most newborns manage the transition from intra- to extrauterine life without interventions. Still, approximately 5 % need positive pressure ventilation (PPV) for successful transition. Guidelines urge providers to ensure good quality PPV for at least 30 seconds before considering chest compressions and intravenous therapy. Pauses in PPV during this first minute may delay recovery of spontaneous respiration and heart rate. Objective: To find the proportion of no-blow time during the first minute of PPV in non-breathing babies.

Methods: Prospective observational study at Oslo University Hospital, Norway. All newborns (gestational age > 32 weeks) receiving PPV immediately after delivery were included. Six cameras with motion detectors were installed at every resuscitation bay capturing both expected and unexpected compromised newborns. We determined no-blow time as the cumulative number of seconds without PPV efforts and without spontaneous breathing and report fraction of no-blow time during the first minute. Data are presented as median (range). Approval was obtained from our institutional review board. All providers and parents were informed in writing about the project and could opt-out at any time.

Results: 277 of 1276 (22 %) newborns were filmed in the resuscitation bays and 49 (4 %) received PPV, weight 3.2 (1.4-4.2) kg and gestational age 40 (32-43) weeks. PPV started 44 (3-244) s after arrival at the resuscitation bay and lasted for more than one minute in 40 cases. Median duration was 128 (25-2052) s. One newborn was admitted to NICU with ongoing PPV. Nineteen infants (40 %) were ventilated continuously, or with minimal pause (< 6 seconds/10 %) during the first minute of PPV. For the remaining 30 infants no-blow fraction was 54 (13-90) %. PPV was halted due to distractions, reposition of mask or change of equipment between 1 and 5 times.

Conclusion: In 60 % of the neonatal resuscitations interruptions in ventilation are frequent with 50 % no-blow fraction during the first minute of PPV. Eliminating disruption for improved quality of PPV delivery should be emphasized when training newborn resuscitation providers.