NORSKE ABSTRAKTER PÅ HEART FAILURE

P337 Comparing one-year change in symptoms in operated versus non-operated patients with severe aortic valve stenosis

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Introduction: Assessment of symptoms plays a key role in patient evaluation. However, little is known about how symptoms change after aortic valve replacement (AVR), and how they evolve over time in non-operated patients with severe aortic stenosis (SAVS).

Purpose: To describe changes in prevalence of symptoms from inclusion to one year after AVR or refusal of intervention in patients with SAVS. Method: Of 480 patients with SAVS evaluated for AVR, 389 patients were operated (351 surgical, 38 trans catheter) (OP) and 91 were declined surgery (NON-OP). We collected data on symptoms at inclusion and follow-up using a self-reported questionnaire. We present paired analysis.

Results: Operated patients were younger than non-operated (mean 74 vs. 81 years) and a higher proportion were men (59 % vs. 48 %).

Conclusion: AVR reduces prevalence of symptoms in patients with SAVS. Patients declined for operation experience an increase in prevalence of dyspnoea, chest pain and dizziness, but a reduction in syncope during one year of observation. Our results advocate AVR in patients with SAVS.

See table.

P342 The association between hs-CRP, hs-TnT and NT-proBNP, and all-cause mortality in operated versus non-operated patients with severe aortic valve stenosis.

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Introduction: A proper evaluation and risk stratification is important in patients with severe aortic stenosis (SAVS) as operation is associated with improved survival and quality of life, while refusal is associated with high mortality. We investigated whether use of high sensitivity C-reactive protein (hs-CRP), high sensitivity troponin T

Symptoms at inclusion and at one-year fo						
OP Inclusion		NON-OP Follow-up p		Inclusion	Follow-up p	
Dyspnoea n (%)	n = 282		<0,001	n = 45		< 0.001
Not the last two weeks	65 (22)	176 (60)		21 (47)	15 (33)	
Not daily	107(37)	75 (26)		7 (16)	10 (22)	
Daily	120 (41)	41 (14)		17 (38)	20 (44)	
Chest pain n (%)	n = 282		<0,001	n = 43		< 0.001
Not the last two weeks	140 (49)	231 (80)		28 (65)	24 (56)	
Not daily	115 (40)	52 (18)		11 (26)	16 (37)	
Daily	33 (12)	5 (2)		4 (9)	3 (7)	
Dizziness n (%)	n = 295		<0,001	n = 45		0.006
Not the last two weeks	147 (50)	173 (59)		27 (60)	24 (53)	
Not daily	100 (34)	99 (34)		12 (27)	16 (36)	
Daily	48 (16)	23 (8)		6 (13)	5 (11)	
Syncope n (%)	n = 297		<0,001	n = 45		0.003
Not the last three months	275 (93)	279 (93)		36 (80)	41 (91)	
Not monthly	12 (4)	14 (5)		5 (11)	3 (7)	
Monthly	10 (3)	4 (1)		4 (9)	1 (2)	

(hs-TnT) and N-terminal pro brain natriuretic peptide (NT-proBNP) and could be useful in risk stratification in patients with SAVS.

Purpose: To examine the prognostic value of hs-CRP, hs-TnT, and NT-proBNP lev- els in relation to all-cause mortality in patients with SAVS

Method: Of 480 patients with SAVS evaluated for AVR, 351 had surgical- and 38 transcatheter-AVR (OP), while 91 were declined operative treatment (NON-OP). On day of operation for OP and day of inclusion in the study for NON-OP, plasma levels of hs-CRP, hs-TnT and NT-proBNP were analyzed by enzyme immunoassay.

Results: During a median follow-up of 418 (103) days, 45 (9,4%) patients died. At inclusion, all patients had echocardiographic evidence of SAVS. The strongest conventional predictors of death were AVR (Hazard ratio, HR [95% CI] 0.29 [0.16-0.54] p < 0.001), diabetes (2.53 [1.29-4.96] p = 0.007), NYHA class (1.84 [1.19-2.84] p = 0.006) and LVEF (2.20 [1.11-4,36] p = 0.024). Analyzed separately and adjusting for these covariates in multivariable analysis revealed that hs-CRP (HR 1.38 [1.05-1.80] p = 0.021), NT-proBNP (HR 1.67 [1.16-2.41] p = 0.002) and hs-TnT (HR 1.30 [1.01-1.67] p = 0.042) were independently associated with death. However, NT-proBNP was the only biomarker that remained in the model when all three biomarkers were included in a stepwise approach. When analyzed separately, NT-proBNP gave similar prognostic information in patients who had AVR (HR 2.04 [1.30-3.22] p = 0.002) or not (HR 2.16 [1.30-3.59] p = 0.003) in univariate analysis. None of the 60 patients with all three biomarkers in the normal range (i.e. hs-CRP 2.0, hs-TnT 14 and NT-proBNP 35) died during follow up.

Conclusion: Results from this study show that for patients with SAVS, NT-proBNP is associated with all-cause mortality at 14 months in adjusted analysis. High sensitivity CRP or hs-TnT gave no additional prognostic information. This suggest that the level of NT-proBNP should be considered when deciding whether to operate or not in patients with SAVS

P526 Study of a mouse with proximal titin A-band truncation reveals disease mechanisms and modifiers of titin dilated cardiomyopathy

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Purpose: 20% of dilated cardiomyopathy (DCM) patients carry heterozygous truncating mutations in the giant protein titin (TTNΔ). Titin spans the cardiomyocyte sarcomere from Z-disc to M-line and regulates sarcomere assembly, contraction, relaxation and signaling. Truncating mutations are overrepresented in the A-band. We engineered mice with titin A-band truncation (TTNΔA) and assessed cardiac phenotype and transcriptional profile.

Results: TTNΔA mice were generated by introducing lox-P sites flanking exons 276-277 and crossing with EIIa-Cre mice, causing a frameshift and a premature stop codon in the TTN proximal A-band. 28 heterozygous intercrosses produced 120 pups: none were homozygous TTNΔA. Genotyping (n = 125) revealed homozygous embryos at E8.5 - E10.5, with fetal demise at E10.5. Heterozygous male and female mice (age 6-80 weeks) were viable, fertile and not different from wild type (WT) in appearance, activity, or echocardiographic phenotype. Pregnant heterozygous females showed no echocardiographic phenotype and produced similar litter size as WT. Transcriptional changes (RNA sequencing) and local sarcomere lesions (electron microscopy) at baseline (age 6-8 weeks, males) suggested that TTNΔA pre-disposed to disease. Voluntary cage-wheel running (two months) (n = 5-8 per study, males), angiotensin II or isoproterenol infusion (two weeks) evoked no echocardiographic differences in TTNΔA compared to WT. Double heterozygous TTNΔA LMNA knock-out, TTNΔA MYH6 F764L knock-in and TTNΔA PLN R9C transgenic mutation mice showed no exacerbation of DCM. Interestingly, upon thoracic aortic constriction (TAC, four weeks) TTNΔA mice showed exacerbated DCM and congestive heart failure. RNA sequencing of TTNΔA vs. WT TAC hearts showed differential expression (fold

change>1.5/ < 0.67, p < 0.001) of 1465 transcripts. Total TTN transcripts were reduced and mutant transcripts half that of WT transcripts (digital PCR) in TTNΔA TAC hearts, with no detection of mutant protein (titin gels and titin immunoblotting). rAAV9 delivery to WT pups in vivo (n = 12-15) of TTN RNAi targeting the TTN exon 276-277 junction, reduced TTN mRNA and protein to 30%and resulted in mortality and severe DCM, with degradation of myofibrils (electron microscopy). Pathway analyses of differentially expressed transcripts in TTNΔA TAC and TTN RNAi, i.e. titin DCM, implicated cardiotoxic pathways. Calcineurin-NFAT and TGFβ/Smad signaling were identified as central players in titin DCM, along with titin-associated mechanosensors FHL1 and ANKRD1 (pathway analyses and immunoblotting).

Conclusions: Homozygous TTNΔA mutation is embryonically lethal, while heterozygous mice show overt DCM upon pressure overload. TTNΔA transcripts are expressed but do not yield detectable mutant protein, suggesting haploinsufficiency as disease mechanism. Reduced titin level is sufficient to cause DCM.

P571 Low ambient temperature induces increased mortality, cardiac autonomic nervous system dysregulation and heart dysfunction in endotoxemic mice

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Purpose: Induced therapeutic hypothermia is documented to be organ-protective including neuro- and cardiac protection. In contrast, spontaneously occurring hypothermia provokes several negative effects that rise concerns regarding potential detrimental effect of induced hypothermia, particularly during inflammation. Whereas septic patients with hypothermia suffer from higher incidence of organ dysfunction and increased mortality, underlying molecular mechanisms are barely elaborated.

Methods: Mice were acclimatized either to neutral ambient temperature of 30∘C (normal ambient temperature group, NORM) or reduced ambient temperature of 26∘ C (reduced ambient temperature group, COOL). Thereafter, mice received LPS (10mg/g bw i.p.) and effects on survival, cardiac autonomic regulation (ANS, telemetry), left ventricle performance (Pressure-Volume-conductance) and stress-associated tissue injury and cell death in heart were studied at control, 3h, 24h, 3days & 7days post injection.

Results: Intriguingly, an enhanced sympathetic tone verified by heart rate (HR), HRV (heart rate variability), sympathetic tone activity and cardiac catecholamine release was found in mice kept at 26∘ C. Mortality rate of the COOL group was significantly increased (> 50%) after LPS-induced SIRS, compared to the NORM group (mortality rate < 10%). The evaluation of body temperature revealed a LPS-dependent induction of hypothermia in both groups, which was more pronounced in the COOL group by about 4∘ C. We further revealed that the cardiac contractility was transiently impaired in mice kept at 30∘C with complete recovery after 7days, whereas animals of the COOL group developed a pronounced and prolonged myocardial dysfunction with reduced contractility compared to the NORM group. The reduced contractility of the COOL group was further confirmed by a reduced beta adrenergic pathway activity of heart tissue. Surprisingly, the level of inflammation in cardiac tissue from both groups was comparable, whereas the stress maker (HSP90) for tissue and organ injury known to be upregulated under catecholamine overstimulation was abundantly increased in COOl group. In addition, further evaluation of cardiac tissue revealed a higher level of stress-related inflammatory response (iNOS expression with enhanced nitrotyrosine formation), stress-induced damage (PARP) and cell death (Tunel positive) in mice from the COOL group.

Conclusion: Enhanced sympathetic activation induced by unsuitable ambient tem- perature provokes in LPS-induced SIRS mice significant effects including mortality rate and sustained heart failure.

674 Plasma fibroblast growth factor 23 is associated with poor outcome and unsuccessful uptitration of guideline-recommended pharmacotherapy in patients with worsening heart failure

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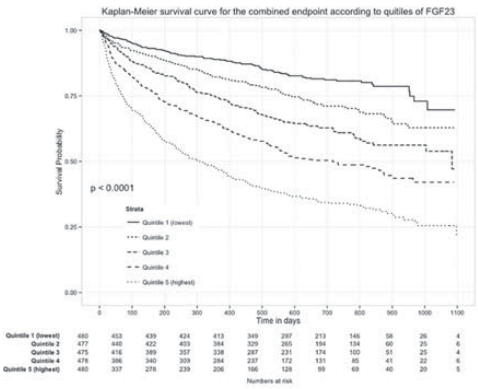
Background: Recent studies suggest that fibroblast growth factor (FGF) 23 pro- motes sodium retention yet its potential value in worsening heart failure (WHF) has not been explored.

Purpose: To investigate the relation between FGF23 and clinical outcomes in patients with WHF.

Methods: We measured plasma C-terminal FGF23 levels in 2,399 of the 2,516 patients included in the BIOlogy Study to Tailored Treatment in Chronic Heart Failure (BIOSTAT-CHF) trial, in which patients with WHF were to be uptitrated to guideline recommended doses of angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB). The association between FGF23 and out- come was evaluated by Cox regression analysis adjusted for potential confounders, such as renal function.

Results: Median FGF23 was 218.0 [117.1-579.3] RU/ml, and patients with higher FGF23 levels had a worse NYHA class and more signs of congestion (all P < 0.005). Patients with higher baseline FGF23 levels were less likely to use ACEi or ARB therapy at baseline and less likely to reach target dose after 3 months of uptitration. In multivariable Cox regression analysis, log transformed FGF23 was independently associated with all-cause mortality (1.25 (1.14-1.37) per log increase, P < 0.001), and the combined endpoint of all-cause mortality and heart failure hospitalization (1.20 (1.11-1.29) per log increase, P < 0.001). The predictive value of FGF23 for all-cause mortality was significantly greater than that for BNP (Univariable Harell's c-statistic: 0.689 vs. 0.649, respectively, P<.001).

Conclusion: Higher plasma FGF23 levels are independently associated with less successful uptitration of guideline recommended therapies and an increased risk of all-cause mortality and heart failure hospitalization in patients with WHF.



Survival curve per quintiles of FGF23

P971 Comparing one-year outcomes beyond mortality in operated versus non-operated patients with severe aortic valve stenosis

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Introduction: Aortic valve replacement (AVR) improves survival and quality of life in patients with severe aortic valve stenosis (SAVS). Few clinical studies compare outcomes beyond mortality-rates in operated versus non-operated patients.

Purpose: To compare functional- cognitive- and morbidity-outcomes in the year following AVR or not in patients with SAVS. Method Of 480 patients with SAVS evaluated for AVR, 351 had surgical- and 38 transcatheter-AVR (OP), while 91 were declined operation (NON-OP). At inclusion and one year follow-up, we obtained data on Six-Minute Walk test (6MWT), New York Heart Association-scale (NYHA) and Canadian Cardiovascular Society-scale (CCS). Cognitive function was assessed by the mini-mental state examination (MMSE). Questionnaires and medical records provided information on home situation, level of independence and hospitalizations.

Results: Mean (SD) age was 74 (10) and 81 (9) years, and gender (% women) was 41 and 52 for OP and NON-OP, respectively. At inclusion, all patients had echocardiographic evidence of SAVS. One-year mortality was 6% for OP- and 19% for NON-OP. Any cause hospitalization (at least an overnight stay) this year was in days and incidence rate per million patient years (IR): 2364 (46) and 362 (142) for OP and NON-OP, respectively. Number (IR) of any cause hospitalization (3 times or more) was for OP 39 (0,8) and 15 (5,8) for NON-OP (p=0,08). Table displays paired analyses for additional outcomes.

Conclusion: The present study demonstrates that aortic valve replacement for severe aortic stenosis is associated with improved functional outcome, while being declined AVR is associated with high mortality, more hospitalizations, unaltered functional status and a tendency to loss of independence.

See table

Additional						outcomes
Operated (OP), n = 389 Inclusion		Follow-up	p-value	Non-operated (NON-OP), n = 91 Inclusion	Follow-up	p-value
Six-Minute Walk test, meter	465	442	< 0.01	412	369	0.05
NYHA functional class						
I/II/III or IV (%)	5/49/46	67/24/9	< 0.01	30/42/28	33/33/33	0.08
CCS functional class						
0, I, II, III or I (%)	54/13/27/6	95/3/1/1	0.01	80/6/8/6	86/8/6/0	0.08
No help or home nurse, n(%)	298(98)	276(96)	0.15	44(100)	41(93)	0.08
MMSE, mean total score	28.5	28.1	0.03	27.4	26.9	0.11

P972 Comparing one-year patient reported outcomes (PROs) in operated versus non-operated patients with severe aortic valve stenosis (SAVS)

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Introduction: Advancements in surgical techniques make high risk and progressively older patients with SAVS eligible for aortic valve replacement (AVR). Current guidelines emphasize the importance of improving PROs as an outcome after AVR. Purpose: To compare PROs at inclusion and one year for operated versus non-operated patients with SAVS.

Method: Of 480 patients with SAVS evaluated for AVR, 351 had surgical- and 38 transcatheter-AVR (OP), while 91 were declined operation (NON-OP). We collected data on SF-36v2; Physical-(PCS) and Mental-(MCS) Component Summary, EuroQol-5 Dimensions (EQ-5D), visual analogue scale (EQ-VAS), and Hospital Anxiety and Depression Scale (HADS).

Results: Mean (SD) age was 74 (10) and 81 (9) years, and 41 and 52 % were women for OP and NON-OP patients, respectively. Physical- and general health increased for OP patients, while anxiety decreased. In the NON-OP group there was a tendency towards decreased physical health. Table displays paired analyses of selected PROs.

Conclusion: Aortic valve replacement improves PROs assessed as perception of overall health and physical health, and reduces anxiety in patients with SAVS. Patients with SAVS declined for operation tend to experience a decrease in physical health over a one-year period. Our results advocate AVR in patients with SAVS.

P1097 The long term effects of high intensity exercise; a 5 years follow-up of a randomized controlled trial in heart transplant recipients

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Background: High-intensity interval training (HIT) has repeatedly proven to be superior to moderate continuous exercise regarding improvement of aerobic capacity in normal subjects and patients with established heart disease. Heart transplanted (HTx) patients has traditionally not been exposed to HIT because of chronotropic incompetence, but we have recently shown that HIT is safe and efficient also in this group. We now report 5 yr long-term effects of this intervention.

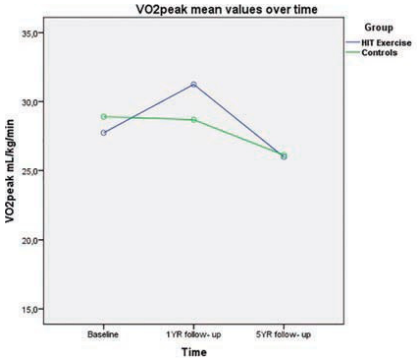
Purpose: To evaluate the long- term effects of HIT.

Method: 48 HTx patients completed a randomized control trial at our hospital in 2009-2011, comparing a 12-month HIT intervention with usual care. Four years after completed intervention, 41 patients were eligible for follow-up testing, to evaluate long-term effects of HIT. The patients underwent cardiopulmonary exercise testing, blood sampling, echocardiography, intravascular ultrasound (IVUS) in coronary arteries, health-related quality of life questionnaires (QoL), measurement of body composition and isokinetic testing of muscle strength.

Results: Mean age (SD) of the patients at baseline was 49 (16) yr, 68 % men and mean years after HTx was 4 (2) yr. During 12 months of HIT, VO2peak increased significantly from 27.7 (5.7) to 31.2 (5.3) and thereafter decreased to 26.0 (6.2) ml/kg/min at 5 yr follow-up, while it remained slightly decreased during the whole period in the control group: 28.9(6.7), 28.7 (6.3) and 26.1 (7.1) mL/kg/min at baseline, 12 mo and 5 yr respectively. The HIT-group also had significantly higher muscular capacity and less coronary artery vasculopathy (CAV) at 12 mo. Analysis of variance (baseline, 12 mo, 5 yr)

showed no changes between groups in VO2peak, muscular capacity, body composition, weight, chronotropic responses during exercise, glucose tolerance or lipid profile. The indifferences in aerobic performance between groups, was in line with the similar everyday activity frequency and intensity measured by senseWear armband at 5 yr follow-up.

Conclusion: Patients who had completed a 12 month HIT-intervention were not able to maintain their high post-exercise VO2peak levels and muscle capacity during long-term follow up. There were no significant differences in VO2peak levels between the two groups at 5 yr follow-up and they reported similar activity frequency and intensity. Despite the reduced VO2peak other positive effects may have sustained: for example the reduced CAV progression, which currently is being analyzed. However, our findings so far suggest that moderate levels of exercise and intensity are insufficient in order to maintain the achieved VO2peak levels. Intermittent periods of HIT are probably necessary to maintain high VO2peak levels.



1242 Statins attenuate but not eliminate the reverse epidemiology of total serum cholesterol in patients with non-ischemic chronic heart failure

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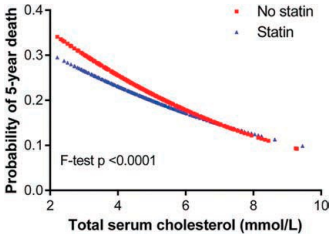
Background: As opposed to general cohorts, in patients with heart failure (HF) increasing levels of total serum cholesterol are associated with improved survival termed reverse epidemiology. The potentially confounding impact of statin treatment thereon is unclear.

Purpose: To investigate the impact of statin treatment on the reverse epidemiology of cholesterol in patients with HF.

Methods: 2,992 consecutive patients with non-ischemic systolic HF were studied from three European HF registries. 1,736 patients were individually double-matched on both cholesterol levels and the individual propensity scores for statin treatment. All-cause mortality was analysed as a function of baseline cholesterol and statin use in both the general and the matched sample.

Results: 1,209 patients (40.4%) received a statin. During a follow-up of 13,740 patient-years, 360 statin users (29.8%) and 573 (32.1%) statin non-users died. When grouped according to cholesterol levels as low (3.6mmol/L), moderate (3.7-4.9mmol/L), high (5.0-6.2mmol/L), and very high (6.3mmol/L), we found improved survival with very high as compared with low cholesterol levels. This association was present in statin users and non-users in both the general and matched sample ($p < 0.05$ for each group comparison). The negative association of TC and mortality persisted when cholesterol was treated as a continuous variable (HR 0.83, 95%CI 0.77-0.90, $p < 0.001$ for matched patients), but it was less pronounced in statin users than in non-users (HR 0.85, 95% CI 0.77-0.95, $p = 0.004$ and HR 0.81, 95%CI 0.73-0.90, $p < 0.01$ for matched statin users and non-users, respectively).

Conclusion: Statins attenuate but not eliminate the reverse epidemiology of total serum cholesterol in patients with non-ischemic HF.



Probability of 5-year death plot

P1590 Adverse events in operated and non-operated patients with severe aortic valve stenosis

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Background/Introduction: Aortic valve replacement (AVR) in patients with severe aortic valve stenosis (SAVS) provides considerable improvement of survival and quality of life. Postoperative adverse events are not negligible, but little is known about the total burden when compared with patients refused for AVR.

Frequencies of adverse clinical events

	OP, n = 389	NON-OP, n =91	p-value	
	During postoperative stay	One year	One year	
One-year mortality, n (%)	-	22 (6)	17 (19)	< 0.01
Myocardial infarction, n (%)	4 (1.1)	6 (1.5)	9 (9.9)	< 0.01
Stroke, n (%)	14 (3.5)	27 (6.9)	3 (3.3)	0.2
Transient ischemic attack, n (%)	2 (0.5)	9 (2.3)	0	0.1
New permanent pacemaker, n (%)	1 (0.2)	26 (7)	6 (7)	0.9
Endocarditis, n (%)	1 (0.2)	11 (2.8)	2 (2.2)	0.7
Myocarditis, n (%)	4 (1.0)	5 (1.2)	0	0.3
Pneumonia, n (%)	65 (17)	82 (21)	12 (13)	0.09
Urinary tract infection (UTI), n (%)	24 (6.2)	38 (9.8)	8 (9)	0.8
Wound infection, n (%)	11 (2.8)	22 (5.7)	1 (1.1)	0.3
Minor bleeding, n (%)	29 (7.1)	-	-	-
Major bleeding, n (%)	23 (5.7)	-	-	-
Post-operative hospital stay, median days (SD)	10 (9)	-	-	-
At least one hospitalization, % patients	-	52	54	0.7
Overnight hospitalizations, median days (IQR)	-	6 (11)	14 (18)	< 0.01
Hospital contacts, total number (rate/patient)	-	382 (0.98)	99 (1.09)	< 0.01

SD = standard deviation, p-value compares one year results in OP vs NON-OP

Purpose: To report adverse clinical events one year following AVR and one year after refusal for AVR, in patients with SAVS.

Methods: Of 480 patients with SAVS evaluated for AVR, 389 underwent operation (OP) and 91 were declined operation (NON-OP). Mean (SD) age was 74 (10) and 81 (9) years, and percentage women was 41 and 52 for OP- and NON-OP respectively. Counting one year from the operation day, or time of evaluation for non-operated patients, all available medical records were reviewed. The outcomes of interest were predefined as clinically relevant.

Results: See table

Conclusion: This study demonstrate a significant number of adverse events among OP patients, but not being operated for SAVS is associated with significantly more myocardial infarctions, new hospital admissions as well as significantly increased one-year mortality. These results advocate AVR in patients with SAVS.

P1660 Reproducibility and value of quantitative computed tomography to diagnose heart failure in patients with non-ST-elevation myocardial infarction

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Background: Assessing pulmonary congestion from cardiac CT images in patients is poorly investigated. Animal models have showed Quantitative CT (QCT) is correlated to pulmonary congestion and we therefore hypothesized it also has potential to improve a diagnosis of heart failure in patients with non-ST-elevation myocardial infarction (NSTEMI)

Purpose: To test if QCT assessed from cardiac-CT images in patients with NSTEMI can differentiate between patients and without a clinical heart failure (HF).

Methods: Patients were identified from a previously examined cohort of 371 patients with NSTEMI who underwent 64-slice cardiac-CT. Two groups were defined: A HF group defined as Killip class>1 within 5 days prior to CT, at least 1 significant stenosis on coronary angiogram, and LVEF <45%. A control group was defined as Killip class 1, no stenosis on angiogram, and LVEF > 55 %. Patients with inappropriate image quality, signs of emphysema or pneumonia were excluded.

Results: 25 patients (12 HF, 13 control) were identified from the previously examined cohort of 371 patients.15 patients fulfilled the criteria for the HF group. 3 were excluded because of incomplete lung delineation, bullae and pneumonia. 30 patients fulfilled the criteria for the control group. 17 were excluded because of incomplete lung delineation (n = 12), motion artifacts (n = 2), bullae (n = 2) and pneumonia (n = 1). Mean lung density was significantly decreased in the HF group (-732 ± 31 vs -653 ± 48, p < 0.0001). The ROC area under the curve was 0.93 (0.84-1.00). The Intra observer variability and inter observer variability (CV) among examiners was 0.8 % and 0.6 % respectively.

Conclusion: QCT is highly reproducible, objective and accurately discriminates NSTEMI patients with and without overt heart failure

P1748 Echocardiography predicts right ventricular size and function in patients with dilated cardiomyopathy: a comparison with magnetic resonance imaging

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Introduction: Right ventricular (RV) size and function can be difficult to estimate by echocardiography due to the complex geometric shape of the right ventricle. Magnetic resonance imaging (MRI) is the gold standard when assessing RV size and function, but is costly and resource demanding.

Purpose: We aimed to assess echocardiographic indices of RV size and function in a prospectively recruited population of patients with dilated cardiomyopathy (DCM). We compared results with those obtained by MRI.

Methods: In 44 patients with idiopathic DCM and an LV ejection fraction (EF) <40%, we performed echocardiography and cardiac MRI. Image analysis was performed blinded to patient characteristics and to the results of the other image modality. The echocardiograms were analysed off-line according to current recommendations with particular focus on RV function. For the MRI measurements, RV endocardial borders were traced manually, and volumes and ejection fractions were calculated by short axis slice summation.

Results: RV end diastolic and end systolic volumes were 198 ± 76 ml and 124 ± 74 ml, and RV ejection fraction (EF) was 40 ± 14 % as measured by MRI. Left ventricular EF was 28 ± 12 %. End diastolic and end systolic RV area were firmly associated with corresponding RV volumes as measured by MRI ($r=79$; $p < 0.001$ and $r = 0.86$; $p < 0.001$, respectively). All pre-specified measures of RV function: fractional area change; tricuspid annular plane systolic excursion (TAPSE); and RV peak strain were associated with RV EF as measured by MRI. (Table). The association was somewhat weaker for TAPSE, even after adjusting for right ventricular long axis dimension by echocardiography. The relatively low association between TAPSE and RV EF might be due to translational movement of the right ventricle in these patients with severely dilated and dysfunctional left ventricles.

Conclusions: Indices of RV function obtained by echocardiography, in particular RV strain, correlates strongly with RV EF as measured by MRI in patients with dilated cardiomyopathy. TAPSE may be less reliable in this population.

Indices of right ventricular function			
Echo parameter	Value	Association with RV EF by MRI	
r	p		
RV fractional area change	19 ± 6	0.69	< 0.001
RV global strain	-13.5 ± 4.2	-0.76	< 0.001
RV free wall strain	-17.8 ± 5.2	-0.77	< 0.001
TAPSE (mm)	19 ± 6	0.46	0.002
Adjusted TAPSE (mm/cm)	2.2 ± 0.7	0.53	< 0.001

P1769 Complex effects of the myosin activator omecamtiv mecarbil on cardiac contractility

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Background: Omecamtiv mecarbil (OM) is a novel inotrope in evaluation for heart failure treatment. Currently, the effects of OM upon contractile function of intact cardiac tissue are relatively unknown.

Objective: The objective of the study was to characterize the contractile effects of OM.

Methods: Contractility and kinetics of the contraction-relaxation cycle (CRC) were measured in rat left ventricular strips. Sarcomere shortening and CRC were measured in isolated rat ventricular cardiomyocytes.

Results: In ventricular strips, OM (1 μM) increased contractile force (Fmax), reaching a maximum of 8 ± 1% above control. In cardiomyocytes, OM increased sarcomere shortening by 48 ± 16% above baseline. OM increased time to peak force (TPF) in ventricular strips, time to peak shortening (TPS) in unloaded cardiomyocytes and relaxation time (RT) in both preparations, with RT being substantially increased com- pared to TPF in ventricular strips. OM slowed the diastolic relengthening rate in cardiomyocytes and increased diastolic tension at stimulation frequencies greater than 2 Hz in ventricular strips at 31◦ C. Higher concentrations of OM were required to increase diastolic tension when temperature was increased to 37◦ C. OM sensitized the concentration-response relationship to Ca2+ in the lower range of [Ca2+], but reduced the maximum inotropic response (IR) to Ca2+. OM reduced the maximum IR to β-AR stimulation without altering the EC50 of β- or α1-adrenoceptors.

Conclusion: This study demonstrates that in addition to increasing Fmax and sarcomere shortening and sensitizing the myocardium to Ca2+, OM also substantially slowed the kinetics of relaxation in rat myocardium, resulting in

increased diastolic tension at higher heart rates, more at lower temperature. Finally, OM reduced maxi- mal β-AR-evoked IR. Further evaluation of the potential clinical utility of OM should take its complex effects on cardiac contractility into account.

P1888 Predictors of in-hospital mortality in a population of acutely decompensated heart failure patients

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Background: despite current therapeutic strategies organ (pulmonary, renal, hepatic) dysfunctions (AODs) are commonly encountered in the settings of ADHF patients (pts) leading to serious adverse implications on in-hospital clinical course and prognosis.

Purpose: the aim of our study was to investigate the levels of AODs in ADHF pts in a tertiary cardiology center; the main predictors of their in-hospital mortality and the influence of AODs in the complicated clinical course.

Methods: we prospectively analyzed in-hospital clinical and laboratory data on 937 ADHF pts from 2012 to November 2015: monitoring for cardio-renal syndrome type I (CRS), cadiohepatic syndrome (CHS), diuretic resistance (DR), MELD score, dyspnea severity scale (DSS) was performed on a daily basis. Patients were stratified into four levels: 1 (absence of AODs), 2 (CRS present), 3 (CRS and CHS present); 4 (CRS & CHS & DR present). A composite endpoint (use of intravenous inotropes, DR, a prolonged in-hospital treatment>a week, pulmonary edema (PE), cardiac death) was defined a complicated clinical course; Cox proportional hazards models were used to define the role of AODs on the complicated clinical course and in-hospital mortality.

Results: between dead an alive groups there were significant differences in: age (69.7 ± 0.6 vs 57.4 ± 0.9, p < .05); CHS (70.1% vs 43.2%, p < .0001); cardiac index < 1.5 l/min/m2 (63.6% vs 21.7%, p < .0001); MELD score (39.6 ± 7.5 vs 17.3 ± 8.5, p < .0001); DR (47.3% vs 12.4%, p < .0001); PE (81.6% vs 48.3%, p < .0001); no significant differences in sex (males)(65.7% vs 62.4%, p>.05); diabetes (32.7% vs 29.4%, p>.05); hypertension (18.7% vs 21.3%, p>.05), ischemic cardiomyopathy (67.2% vs 69.3%, p>.05). In Cox regression independent predictors of in-hospital mortality were: age HR 1.87 (95%CI: 1.15-2.34), hypotension on admission HR 2.3 (95%CI: 1.4-2.89), CRS HR1.95 (95%CI: 1.3-3.04), CHS HR 2.1 (95%CI: 1.34-2.76), DR HR 2.43 (95%CI: 1.5-3.89), cardiac index < 1.5l/min/m2 HR 2.64 (95%CI: 1.67-4.1). Comparing complicated clinical course HR (95%CI)of level 2 to 1 of ADHF pts was 1.57 (1.14-1.96), level 3 to 1 was 2.26 (1.62-3.78), and level 4 to 1 was 3.12 (1.89-4.37).

Conclusions: In our study main predictors of in-hospital mortality in ADHF patients were advanced age, hypotension on admission, cardio-renal syndrome and cardio-hepatic syndrome, diuretic resistance and low cardiac index. Presence of organ dysfunctions denotes an increased risk for complicated clinical course and should prompt adequate efforts to reduce costs, imposed by prolonged hospitalization and to improve survival.

P1992 Association of beta-blocker usage with mortality following myocardial infarction in patients with COPD: a propensity score analysis from the high-risk myocardial infarction database initiative

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Background/Introduction: Concerns that beta-blocker treatment may be harmful in patients with chronic obstructive disease (COPD) still limits their usage in this sub- set of patients, even in post-myocardial infarction (MI), where they have been shown to be highly effective in reducing mortality.

Purpose: The aim of the study was to assess the association between baseline beta-blocker intake and long-term prognosis of MI survivors with heart failure (HF) or with left ventricular dysfunction and a history of COPD.

Methods: In the 28,771 patients high risk MI collaborative database, we identified 1573 patients with a baseline history of COPD. We evaluated the association between beta-blocker usage at baseline (822 with a beta-blocker and n = 751 without) on the rate of all-cause death and cardiovascular death.

Results: By univariable Cox analysis, beta-blocker intake was associated with lower rates of both all-cause death (HR = 0.61, 0.51-0.75, p < 0.0001) and cardiovascular death (HR = 0.63, 0.51-0.78, p < 0.0001). After extensive adjustment for confounding including 24 baselines covariates, beta-blocker usage was associated with a lower risk in COPD patients (HR = 0.73, 0,60-0.90, p = 0.002 for all-cause death; HR = 0.77, 0.61-0.97, p = 0.025 for cardiovascular death) (Table). Propensity scores (PS), estimating probability of beta-blocker treatment on 24 baseline characteristics, were calculated; when entering these scores as covariate for adjustment in Cox models, the survival in the treatment group remained significantly higher. A cohort of 561 pairs of patients taking or not a beta-blocker was obtained by 1:1 nearest neighbor matching method. Among matched pairs of patients, treated group experienced less all-cause deaths (HR = 0.71, 0.56-0.89, p = 0.003) and cardiovascular deaths (HR = 0.76, 0.59-0.97, p = 0.032).

Conclusions: in the specific setting of a well-treated cohort of high-risk MI survivors, beta-blocker treatment was associated with better outcomes in patients with a history of COPD.

Cox proportional hazard models

All-cause mortality HR (95%CI)		p-value	Cardiovascular death HR (95%CI)	p-value
Univariable analysis	0.61 (0.51-0.75)	< 0.0001	0.63 (0.51-0.78)	< 0.0001
Model 1	0.66 (0.54-0.80)	< 0.0001	0.68 (0.54-0.84)	< 0.0001
Model 2	0.72 (0.59-0.88)	0.001	0.75 (0.60-0.93)	0.010
Model 3	0.73 (0,60-0.90)	0.002	0.77 (0.61-0.97)	0.025

Model 1: age and gender and smoking habits. Model 2: model 1 + Killip class≥3, co-morbidities (MI, HF, hypertension, renal failure, AF, PAD, diabetes, history of stroke), and biological variables (systolic and diastolic BP, HR, eGFR). Model 3: model 2 + LVEF and treatment (digoxin, ACE-I/ARB, diuretics, aspirin, CCB, statin).