Abstracts of the Scientific Spring Congress of the Netherlands Society of Cardiology 5-6 April 2018

Conference Center Leeuwenhorst, Noordwijkerhout
Dear reader,

We are pleased to present here the abstracts of the Scientific Spring Congress of the Netherlands Society of Cardiology which will be held on 5 and 6 April 2018 in Conference Center Leeuwenhorst in Noordwijkerhout.

We hope that you will enjoy reading the abstracts.

On behalf of the Chief Editorial Board,

Prof. dr. J.J. Piek
Editor in Chief Netherlands Heart Journal
Session I: General Cardiology

KEY ROLE FOR AMBULANCE PARAMEDICS IN SUSPECTED NON-ST ELEVATION MYOCARDIAL INFARCTION

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Purpose:
Yearly, numerous patients are presented to the emergency department with suspected non-ST elevation Myocardial Infarction (non-STEMI). Many of them have non-cardiac complaints, and hospitalization is unnecessary. Paramedics can play a more important role in risk stratification of suspected non-STEMI. This study aims to investigate whether risk stratification by paramedics, using the HEART score including pre-hospital troponin assessment, is accurate in predicting major adverse cardiac events (MACE).

Methods:
A prospective observational cohort study, including 700 patients with suspected non-STEMI. Risk stratification was performed by paramedics, low-risk was defined as HEART score ≤3. Primary endpoint was occurrence of MACE within 45 days. Secondary endpoint was myocardial infarction or death.

Results:
A total of 172 patients (24.6%) were stratified as low-risk, 528 patients (75.4%) as intermediate to high-risk. Mean age was 53.9 years in the low-risk group, 66.7 years in the intermediate to high-risk group (p<0.001), 50% was male in the low-risk group versus 60% in the intermediate to high-risk group (p=0.026). MACE occurred in 5 patients in the low-risk group (2.9%) and in 111 (21.0%) patients at intermediate to high-risk (p<0.001). There were no deaths in the low-risk group. The occurrence of myocardial infarction in this group was 1.2%. In the high-risk group 6 patients died (1.1%). 77 Patients had myocardial infarction (14.6%).

Conclusion:
In suspected non-STEMI, pre-hospital risk stratification by paramedics, including troponin measurement, is accurate in differentiating between low and intermediate-high risk. Future studies should investigate whether transport of low-risk patients to the hospital can be avoided.
THE ENDOCARDITIS TEAM; A TERTIARY CENTRE EXPERIENCE

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Purpose:
In 2015 the European Society of Cardiology (ESC) introduced the multidisciplinary infective endocarditis (IE) team to improve diagnostics, treatment and outcome in patients with IE. This study evaluates the clinical implementation of an IE team in a high-volume surgical center.

Methods:
Retrospective cohort of all IE patients diagnosed between 2012-2016 in a tertiary center. Clinical characteristics, data on imaging techniques, surgical procedures, IE-related complications and all-cause mortality were collected. Differences before and after installation of the IE team in 2015 were analyzed.

Results:
Overall, 218 IE patients were included with a minimal follow-up of 1 year. No significant differences in baseline characteristics or imaging method were observed. The annual incidence of IE gradually increased over time from 36 cases in 2012 to 50 cases in 2016. This was caused by an increase in native IE cases. No difference in cumulative mortality was observed before and after 2015 (30% vs 33%, p=0.67). Initially, early surgery led to a higher mortality but over the long-term survival improved compared to late surgery (Figure 1). After 2015, a reduction in median time from first symptoms to IE diagnosis was observed (14 vs. 8 days; p=0.14) and median time to surgery had significantly decreased (21 vs. 9 days; p=0.02). Furthermore, a downtrend in IE-related complications namely acute renal failure (25% vs 11%, p=0.02) and embolic events (27% vs 19%, p=0.18) were observed.

Conclusion:
This study demonstrated that IE incidence increased from 2012 to 2016. The introduction of a multidisciplinary IE team led to earlier surgical intervention and lower IE-related complications. These results are important in view of designing novel clinical trials.
**Figure:**
Survival Early vs. Late Surgery
PREVALENCE AND OUTCOME OF INFECTIVE ENDOCARDITIS AFTER TRANSCATHETER AORTIC VALVE REPLACEMENT

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Purpose:
Trans-catheter Aortic Valve Replacement (TAVR) is increasingly being used as an alternative to surgical valve replacement but data on infective endocarditis (IE) prevalence and outcome is scarce.

Methods:
A multi-centre study was performed identifying patients who underwent TAVR and developed IE using the in hospital database for TAVR and the IE insurance database.

Results:
A total of 3968 patients who underwent TAVR were screened for IE. A total of 16/3698 (0.4%) developed IE. The majority of patients was male ((9/16 (56.3%)) with a median age of 81 (60-91) years. The effected prosthetic valves were a Corvalve CRS® in 25% (4/16), Sapien XT® in 44% (7/16), Evolute R® in 13% (2/16) and a Direct Flow® in 19% (3/16). The implantation was trans-femoral in 81% (13/16), via the subclavian artery in 13% (2/16) and one patient received a trans-apical approach. All patients had positive cultures. In the follow up period of 15 months (1-42months) mortality was 31% (5/16) with 25% dying during hospital admission. Concomitant mitral valve endocarditis was present in 25% (4/16). All patients were treated conservatively with intravenous antibiotics alone. Complications of IE occurred in 31% (5/16) and consisted of cerebral infarction due to a dislodged vegetation in one patient, aortic root abscess formation in 2/16 patients and decompensated heart failure in 2/16 patients.

Conclusion:
In this multi-centre study infective endocarditis in patients receiving trans-catheter aortic valve implantation is a relatively rare with rates lower than in conventional surgical valve implantation. Outcome is better than after surgical valve implantation despite conservative treatment.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>N=16</th>
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<tr>
<td>Mortality</td>
<td>5 (31%)</td>
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<table>
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<tr>
<th>Complications of endocarditis</th>
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<tbody>
<tr>
<td>Cerebral embolization</td>
<td>6%</td>
</tr>
<tr>
<td>Root abscess</td>
<td>13%</td>
</tr>
<tr>
<td>Decompensated heart failure</td>
<td>13%</td>
</tr>
<tr>
<td>None</td>
<td>69%</td>
</tr>
<tr>
<td>Infected pacemaker</td>
<td>0</td>
</tr>
<tr>
<td>Concomitant mitral valve endocarditis</td>
<td>25%</td>
</tr>
<tr>
<td>Time to Infective Endocarditis (days)</td>
<td>451 (21-2837)</td>
</tr>
<tr>
<td>Patients with IE within one year of TAVR</td>
<td>56%</td>
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<tr>
<td>Mean length of hospitalisation (days)</td>
<td>31.8 (7-49)</td>
</tr>
</tbody>
</table>

Table 2: Outcome. (Abbreviations: IE=Infective Endocarditis, TAVR=Trans-catheter Aortic Valve Replacement)
TRENDS IN OPTIMAL MEDICAL THERAPY PRESCRIPTION AND MORTALITY AFTER ADMISSION FOR ACUTE CORONARY SYNDROME: A 9-YEAR EXPERIENCE IN A REAL-WORLD SETTING

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Purpose:
Optimal medical therapy (OMT) is recommended in acute coronary syndrome (ACS) patients. Few studies present temporal trends of OMT prescription and its impact on outcomes in a real-world setting. We aimed to evaluate OMT prescription in a real-world ACS population and its relation to mortality during almost a decade.

Methods:
Consecutive STEMI and NSTEMI patients (n=9202) admitted to a single Dutch tertiary hospital between 2006-2014 were included and followed for drug prescription and mortality up to 1 year. OMT was defined as prescription of aspirin, P2Y12inhibitors, statin, beta-blockers, and angiotensin converting enzyme inhibitors or angiotensin receptor blockers (ACEi/ARB).

Results:
OMT prescription was 43.7% at discharge, 46.6% at 30-days, and 25.5% at 1-year. OMT prescription at discharge was lower among NSTEMI patients (34.5% vs. 49.2%, p<0.001). OMT prescription at discharge, 30-days and 1-year and mortality outcomes did not change during the study period. After adjustment for baseline and admission characteristics, OMT at discharge was associated with a reduction in mortality in patients who survived hospitalisation for the index event [adjusted hazard ratio: 0.66, 95% confidence interval (0.46-0.93)].

Conclusion:
In this single-centre observational registry with >9000 patients reflecting almost a decade of ACS care, <50% of patients were on OMT at discharge. Prescription of OMT and mortality outcomes remained stable during the study period. After adjustment, OMT prescription at discharge was associated with reduced mortality in ACS survivors. Further contemporary randomised studies are warranted to determine the role of beta-blockers and ACEi/ARBs in ACS patients with preserved LVEF.
Figure:
Trends in Optimal Medical Therapy and Mortality over the course of 9 years.
Differences in Heart Failure Treatment Between Age Groups in the Netherlands: A Subgroup Analysis of the CHECK-HF Registry

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Purpose:
The poor prognosis of chronic heart failure (HF) can be optimized by adherence of medical therapy according to the guidelines. The rate of drug prescription and dosage are often used as benchmark of quality of care. Data on age differences in HF treatment are scarce. The purpose of this study was to evaluate age differences in HF treatment in the Netherlands.

Methods:
The current analysis is part of a cross-sectional registry of 10,910 chronic HF patients at 34 Dutch outpatient clinics in the period of 2013 until 2016 (CHECK-HF). Demographic parameters, laboratory and echocardiographic values as well as medication use (type, dosage and frequency and total daily dose) were recorded.

Results:
We studied 8,360 patients with HF with reduced ejection fraction (HFrEF; 78.7%), with a mean age of 72.3 years (y). In elderly, we observed more hypertension (<60y 29.1%, 60-69y 38.0%, 70-79y 42.4%, >80y 43.0%, \( p < 0.01 \)) and diabetes (20.0%, 24.9%, 28.9%, 24.6%, \( p < 0.01 \)) as well as lower eGFR (79.3, 67.3, 58.1, 48.2 ml/min/1.73 m², \( p < 0.01 \)) between groups. Current HF medication use is described in Table 1. Elderly patients received less beta-blocker, RAS-inhibitors, MRA and ivabradine, but more diuretics (all \( p < 0.01 \)). Furthermore, we observed less ICD and CRT, but more pacemaker therapy in elderly (\( p < 0.01 \)). Elderly were more often treated with lifestyle treatment (\( p < 0.01 \)).

Conclusion:
In this large registry of HFrEF patients, we observed significant differences in medical, device and lifestyle therapy between age-groups.

<table>
<thead>
<tr>
<th>Table 1. Age and HF therapy in HFrEF</th>
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<tr>
<td></td>
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<tr>
<td>Pharamcotherapy</td>
</tr>
<tr>
<td>Beta-blocker, ( % (n=8218) )</td>
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<tr>
<td>RAS-inhibitors, ( % (n=8218) )</td>
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<tr>
<td>MRA, ( % (n=8218) )</td>
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<tr>
<td>Ivabradine, ( % (n=8960) )</td>
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<tr>
<td>Diuretics, ( % (n=8218) )</td>
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<tr>
<td>Device therapy</td>
</tr>
<tr>
<td>ICD, ( % (n=6666) )</td>
</tr>
<tr>
<td>CRT-D, ( % (n=6666) )</td>
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<tr>
<td>Pacemaker, ( % (n=6666) )</td>
</tr>
<tr>
<td>Lifestyle therapy</td>
</tr>
<tr>
<td>Fluid restriction, ( % (n=6758) )</td>
</tr>
<tr>
<td>Sodium restriction, ( % (n=6752) )</td>
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EFFECT OF LIFELONG PHYSICAL ACTIVITY ON PHENOTYPE EXPRESSION IN HYPERTROPHIC CARDIOMYOPATHY

V.L. Aengevaeren (Radboudumc, Nijmegen); V.L. Aengevaeren (Radboudumc, Nijmegen); D.H.F. Gommans (Radboudumc, Nijmegen); H-J. Dieker (Radboudumc, Nijmegen); J. Timmermans (Radboudumc, Nijmegen); F.W.A. Verheugt (Radboudumc, Nijmegen); J. Bakker (Albert Schweitzer Hospital, Dordrecht); M.T.E. Hopman (Radboudumc, Nijmegen); M-J. de Boer (Radboudumc, Nijmegen); M.A. Brouwer (Radboudumc, Nijmegen); P.D. Thompson (Hartford Hospital, Hartford CT); M.J.M. Kofflard (Albert Schweitzer Hospital, Dordrecht); G.E. Cramer (Radboudumc, Nijmegen); T.M.H. Eijsvogels (Radboudumc, Nijmegen)

Purpose:
Hypertrophic cardiomyopathy (HCM) is characterized by inappropriate left ventricular (LV) wall thickness. Adaptations to exercise can occasionally mimic the HCM phenotype. However, it is unclear whether physical activity (PA) affects HCM genotype expression and disease characteristics. Consequently, we compared the volume of lifelong PA between HCM gene carriers with and without HCM phenotype, and compared disease characteristics among tertiles of PA in HCM patients.

Methods:
HCM genotype positive individuals who were either HCM phenotype positive (G+/P+) or negative (G+/P-), as well as genotype negative HCM patients (G-/P+) were included. Lifelong PA volumes were calculated. PA volumes were compared between G+/P+ and G+/P- participants. Secondly, clinical parameters of cardiac magnetic resonance imaging, echocardiography and Holter monitoring were compared across tertiles of PA volumes among all P+ participants.

Results:
We included n=109 subjects (51±15 years, 51% male), including 44 G+/P+ HCM patients, 22 G+/P- HCM gene carriers, and 43 G-/P+ HCM patients without a (known) genetic mutation. Lifelong PA volumes were not different (p=0.33) between G+/P+ and G+/P- subjects. Secondly, there was no difference in LV function, wall thickness, mass, and LGE across PA tertiles, but the most active HCM patients were younger at the time of diagnosis and had more often experienced non-sustained ventricular tachycardia.

Conclusion:
Lifelong PA volumes did not differ between HCM gene carriers with and without HCM phenotype. Interestingly, the most active HCM patients were younger at the time of diagnosis and had a higher arrhythmic burden. These observations warrant further exploration of the role of exercise in HCM.
CARDIAC REHABILITATION IN YOUR NEIGHBOURHOOD: THE SPAARNE MODEL OF CARDIAC REHABILITATION

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Purpose:
By an active approach and possibility to have cardiac rehabilitation in the neighbourhood of patients we pursued a better accessibility and a higher participation of cardiac rehabilitation.

Methods:
We reorganised the concept of the accessibility of cardiac rehabilitation by active clinical approach of patients who qualify for this form of post cardiac event therapy. Eligible patients are signed up before hospital discharge or at our outpatient clinic and included <1-2 weeks. Goals are set with an interview, a computer program (CARDS) and an X-ECG by a special team during the entrance consult. The physical part of rehabilitation is started as soon as possible (<1 week if appropriate) and done in 14 dedicated (fixed) physiotherapy partners in our region as close as possible to the address of patients. Complex cases are rehabilitated in the two fysio-departments in our hospital locations. All patients receive an extended information module and if necessary psychological support. Reducing weight and stop smoking together with an active lifestyle is active promoted. Progress of the cardiac rehabilitation an possible physical and psychological problems is monitored weekly with an telephonic conference meeting.
Every 3 months there is an evaluation and education program for all the members the Spaarne Model cardiac rehabilitation team.

Results:
Participation augmented form 40% to over 60% in patients eligible for cardiac rehabilitation with an increasing tendency. Non-participants were mostly to old and/or physical not capable to participate. Only a smal part of the patients refused to participate. Most patients show significant physical improvement. Less than 10% of patients doesn't complete the program. None serious events were recorded during the cardiac rehabilitation program. All team members are highly motivated by this program.

Conclusion:
Participation in cardiac rehabilitation is augmented with an active approach of eligible patients with the use of a dedicated in-hospital and external team. Most patients can safely have their cardiac rehabilitation in their neighbourhood which promote participation.
REPEATED MEASUREMENTS OF CARDIAC BIOMARKERS FOR DYNAMIC RISK PREDICTION IN PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONGENITAL HEART DISEASE: RESULTS AFTER A 10-YEAR FOLLOW-UP

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Purpose:
Pulmonary arterial hypertension (PAH) is a chronic, fatal complication of congenital heart disease (CHD). The underlying pathophysiology is complex and characterized by multiple biological pathways. Our aim was to investigate the utility of repeated cardiac biomarkers measurements for risk prediction.

Methods:
In a prospective multi-cohort of 98 PAH-CHD patients, four biomarkers (NT-proBNP, cardiac troponin T, cystatin C and galectin-3) were repeatedly measured at outpatient clinic visits. The primary outcome of interest was death. We fitted a linear mixed effect model and a Cox model, correcting for age and sex. The relationship between repeated measurements and survival was assessed using flexible joint modelling.

Results:
In total, 40 of 98 patients (age 43±16 years; 34% male; 69% Eisenmenger) died during a follow-up of 7.1±3.6 years. Repeated measurements were more strongly related to the risk of death than baseline measurements, with 50% increase of NT-proBNP resulting in a 1.43-fold (95%CI:1.26-1.62, p<0.0001), 50% increase of troponin T in a 1.63-fold (95%CI:1.34-1.98, p<0.0001), 50% increase of galectin-3 in a 1.82-fold (95%CI:1.17-2.82, p=0.0447) and 50% increase of cystatin C in a 2.62-fold (95% CI:1.63-4.19, p=0.0001) increase. Repeated NT-proBNP, troponin T and cystatin C also achieved high discriminatory abilities for 10-year mortality (c-index 0.78, 0.89 and 0.91), as compared with galectin-3 (c-index 0.59).

Conclusion:
Repeated measurements of NT-proBNP, troponin T and cystatin C provides important prognostic value for risk stratification of PAH-CHD patients, beyond a conventional risk model with baseline measurements. Regular assessment of these biomarkers therefore may play an important role in the monitoring and management of these patients.
Figure:
Examples of dynamic survival predictions for a single subject: the probability that patient A (left) with repeated NT-proBNP measurements (*) up to 9.8 years follow-up (dotted vertical line) will survive the next 2.5 years is 10% vs. the probability that patient B (right) with repeated NT-proBNP measurements (*) up to 11.1 years follow-up (dotted vertical line) will survive the next 2 years is 97%.
Session II: Intervention Cardiology

ROBOT-ASSISTED MINIMALLY INVASIVE CORONARY ARTERY BYPASS GRAFTING: THE ZWOLLE EXPERIENCE

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Purpose:
Robot-assisted coronary artery bypass grafting has been developed to minimize surgical trauma, to enhance post-operative recovery and patient satisfaction, but has not been performed in The Netherlands. To determine the safety and feasibility of this procedure in the Netherlands, we evaluated the first 50 patients who underwent minimally invasive LIMA-LAD bypass grafting at Isala Hospital, Zwolle.

Methods:
From October 2016 to January 2018, 50 consecutive patients underwent a robotically assisted left internal mammary artery (LIMA) to LAD procedure utilizing the da Vinci surgical system (Intuitive Surgical, Inc., Mountain View, CA). This study analyzed conversion rates, surgical complications, major adverse cardiac events (MACE; defined as mortality, myocardial infarction, target vessel revascularization (TVR)) and length of hospital-stay.

Results:
There was no perioperative mortality. Conversion to sternotomy occurred in 3 patients (6%). The cumulative incidence of MACE was 3/50 (6%), driven by the rate of TVR. All 3 patients who needed repeat (percutaneous) revascularization were part of the first 5 cases. Furthermore, there were no reoperations for bleeding (0%), 1 neurologic complication (TIA; 2%), new-onset atrial fibrillation in 12 patients (24%), 1 superficial wound infection (2%), ventilation greater than one day in 3 patients (6%). The amount of blood loss was low, with only 4 (8%) patients receiving a transfusion. The average postoperative length of stay was 6.24 days. One year survival was 100%.

Conclusion:
Our early results suggest that after a relatively short learning curve robot-assisted CABG is a safe and feasible method of myocardial revascularization.
ADDISON OF ROUTINELY MEASURED BLOOD BIOMARKERS SIGNIFICANTLY IMPROVES GRACE RISK STRATIFICATION IN PATIENTS WITH MYOCARDIAL INFARCTION

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1. Department of Cardiology, Northwest Clinics, Alkmaar
2. Department of Cardiology, Erasmus MC, Rotterdam
3. Netherlands Heart Institute, Utrecht
5. Department of Public Health, Erasmus MC, Rotterdam
*Shared first authorship

Purpose:
To investigate whether blood biomarkers measured routinely at hospital admission in myocardial infarction (MI) patients can improve the admission GRACE score for the composite endpoint of all-cause mortality and non-fatal MI at 6 months.

Methods:
2055 patients treated for MI in the Northwest clinics, the Netherlands, between 2013 and 2016 were examined. As part of the prevailing MI treatment protocol, 19 biomarkers were measured and the GRACE score was ascertained. Information on the composite endpoint was derived from municipal registries and electronic medical records. We applied elastic net logistic regression (LR) analysis to select biomarkers that had statistically significant additive prognostic value on top of the GRACE score. We then studied the prognostic performance of the LR model containing the GRACE score and the selected biomarkers.

Results:
At 6 months follow-up 143 (6.96%) reached the composite endpoint. Nine variables were included in the final LR model: GRACE score, urea, sodium, potassium, alkaline phosphatase, LDL cholesterol, glucose, hemoglobin and C-reactive protein. This extended GRACE score model showed improved discrimination (C-statistic 0.76 vs 0.70, \( p=0.0008 \)) and classification (continuous net reclassification index 0.49, \( p<0.0001 \)) compared with the GRACE score only.

Conclusion:
The ability of the GRACE score detecting MI patient at high risk for mortality or MI within 6 months, was significantly improved by adding several biomarkers measured routinely at admission.
Figure:

AUC from the Biomarker model versus the original GRACE risk model
LONG-TERM IMPACT OF CHRONIC TOTAL OCCLUSION RECANALIZATION IN ST-ELEVATION MYOCARDIAL INFARCTION PATIENTS

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Purpose:
During primary percutaneous coronary intervention(PCI) a concurrent chronic total occlusion(CTO) is found in 10% of ST-elevation myocardial infarction(STEMI) patients. Long-term benefits of CTO-PCI have been suggested, however randomized data are lacking. Our aim was to determine mid- and long-term clinical outcome of CTO-PCI versus CTO-No PCI in STEMI patients with a concurrent CTO.

Methods:
The Evaluating Xience and left ventricular function in PCI on occlusions after STEMI(EXPLORE) was a multicenter randomized trial that included 302 STEMI patients after successful primary PCI with a concurrent CTO. Patients were randomized to either CTO-PCI or CTO-No PCI. The primary endpoint was occurrence of major adverse cardiac events (MACE); cardiac death, coronary artery bypass grafting and MI. Other endpoints were one-year left ventricular function(LVF); LV-ejection fraction and LV-end diastolic volume, and angina status.

Results:
The median long-term follow-up was 3.9[2.1-5.0] years. MACE was not significantly different between both arms(13.5% vs. 12.3%, HR=1.03, 95%CI;0.54-1.98; p=0.93). Cardiac death was more frequent in the CTO-PCI arm (6.0% vs. 1.0%, p=0.02) with no difference in all-cause mortality (12.9% vs. 6.2%, HR=2.07, 95%CI;0.84-5.14; p=0.11). One-year LVF did not differ between both arms. However there were more patients with freedom of angina in the CTO-PCI arm at 1-year (94% versus 87%, p=0.03).

Conclusion:
In this randomized trial involving STEMI patients with CTO, CTO-PCI was not associated with a reduction in long-term MACE compared to CTO-No PCI. One-year LVF was comparable between both treatment arms. The finding that there were more patients with freedom of angina after CTO-PCI at 1-year FU needs further investigation.
Long-term MACE

Cumulative event rate (%)

Follow-up (years)

CTO-PCI

CTO-No PCI

No. at risk

CTO-PCI 148 132 115 94 59 34

CTO-No PCI 154 143 110 85 63 38

p=0.93
Purpose:
Coronary contrast-flow quantitative flow ratio (cQFR) is a recently developed technique to calculate fractional flow reserve (FFR) based on 3-dimensional quantitative coronary angiography and computational fluid dynamics, obviating the need for an invasive pressure-wire and hyperaemia induction. The aim of the current study was to investigate the feasibility to use cQFR to appropriately select patients for FFR referral.

Methods:
Patients who underwent invasive coronary angiography in a hospital where FFR and percutaneous coronary intervention (PCI) could not be performed, and were referred to our hospital for invasive FFR measurement, were included. Angiogram images from the referring hospitals were retrospectively collected for cQFR analysis. cQFR was calculated offline, using a dedicated software package. Based on cQFR cut-off values of 0.77 and 0.86 (derived from the FAVOR II Europe-Japan Study), our patient cohort was reclassified to “no referral” (cQFR ≥0.86), referral for “FFR” (cQFR 0.78-0.85) or “direct PCI” (cQFR ≤0.77).

Results:
In total, 290 patients were included in the study. Overall accuracy of cQFR to detect an invasive FFR of ≤0.80 was 86%. Based on a cQFR cut-off value of 0.86, a 50% reduction in patient referral for FFR could be obtained, while only 5% of these patients had an invasive FFR of ≤0.80 (thus, these patients were incorrectly reclassified to the “no referral” group). Furthermore, 22% of the patients that still need to be referred could undergo direct PCI, based on a cQFR cut-off value of 0.77.

Conclusion:
cQFR is feasible to use for the selection of patients for FFR referral. Large, prospective trials are needed to confirm the results of our study.
Figure:
Reclassification of patients according to cQFR value

ICA and FFR within 6 months (n = 290)

↓

No direct PCI without FFR measurement and no coronary arteries excluded (n = 120)

↓

Reclassification to “referral” group

Reclassification to “no referral” group

- cQFR < 0.86
- cQFR ≥ 0.86

- cQFR ≤ 0.77
- cQFR 0.78-0.85

Reclassification to “direct PCI” group

Reclassification to “FFR” group

Number of true and false negatives compared to FFR

Number of true and false positives compared to FFR
EVALUATION OF THE IMPACT OF A CHRONIC CORONARY TOTAL OCCLUSION ON VENTRICULAR ARRHYTHMIAS AND LONG-TERM MORTALITY IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY AND AN IMPLANTABLE CARDOVERTER-DEVICE FOR PRIMARY OR SECONDARY PREVENTION (THE ECTOPY-IN-ICD STUDY)

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Purpose:
Previous studies report conflicting results about a hypothetical higher incidence of ventricular arrhythmias (VA) in patients with a chronic coronary total occlusion (CTO). We aimed to investigate this association in a large cohort of implantable cardioverter defibrillator (ICD) patients with long-term follow-up.

Methods:
All consecutive patients from 2002-2014 who underwent ICD implantation for ischemic cardiomyopathy (ICM) at the Leiden University Medical Center were evaluated. Coronary angiography films were reviewed for the presence of a CTO. The occurrence of VA and survival status at follow-up were compared between patients with and patients without a CTO.

Results:
Our total cohort consists of 722 patients (age 66 ± 11 years; 84% males; 74% primary prevention, median left ventricular ejection fraction (LVEF) 30% [25-37], 44% received a cardiac resynchronization therapy defibrillator). At baseline, 240 patients (33%) had a CTO, and the CTOs were present for at least 44 [2-127] months on average. The median follow-up duration was 4 [2-6] years. The 10-year survival rate was lower, and the appropriate device therapy rate was higher for CTO patients (figure 1A+B). Corrected for baseline characteristics including LVEF, the presence of a CTO was an independent predictor for appropriate device therapy.

Conclusion:
Compared to their peers without a CTO, the presence of a CTO in ICD patients was associated with worse prognosis and more appropriate device therapy at long-term follow-up.
Figure:

**1A**

Freedom from Death (%)

- Non-CTO patients
- CTO patients

Years of Follow-Up

Log-rank p<0.01

Number at risk
- CTO patients: 239, 96, 13
- Non-CTO patients: 477, 205, 29

**1B**

Appropriate Therapy (%)

- Non-CTO patients
- CTO patients

Years of Follow-Up

Log-rank p<0.01

Number at risk
- CTO patients: 237, 50, 5
- Non-CTO patients: 478, 141, 22
NO INFLUENCE OF IMPLANTATION TECHNIQUE (PRE-DILATATION, SIZING, AND POST-DILATATION) ON THE INCIDENCE OF SCAFFOLD THROMBOSIS AND REVASCULARIZATION IN LESIONS TREATED WITH AN EVEROLIMUS-ELUTING BIORESORBABLE VASCULAR SCAFFOLD: AN AIDA SUBSTUDY

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Purpose:
Absorb BVS specific implantation strategies have been proposed to optimize outcomes. We analyzed whether the occurrence of definite scaffold thrombosis (ScT) and target lesion revascularization (TLR) in Absorb-treated AIDA patients was influenced by scaffold implantation techniques.

Methods:
Absorb BVS implantation in 1074 lesions was graded according to definitions of optimal implantation based on pre-dilatation, sizing, and post-dilatation (PSP). Lesion-oriented outcomes (definite ScT and TLR) that occurred during a median follow-up of 707 days were related to the presence or absence of PSP. We also tested the relationship between the occurrence of ScT or TLR and the individual components of PSP.

Results:
Of 1074 lesions, 158 (14.7%) lesions met PSP. The most prevalent reason for not meeting PSP was inadequate sizing: 863 (94.2). Definite ScT occurred in 4 of 158 PSP treated lesions against 27 of 916 non PSP treated lesions, with 2-year KM-estimates of 3.0% vs. 4.1% and a HR of 1.14; (p=0.811). TLR occurred in 8 of 158 PSP treated lesions against 61 of 916 non PSP treated lesions, with KM-estimates 5.6% vs. 7.1% and a HR of 1.29; (p=0.492).

Conclusion:
In AIDA, lesions that underwent scaffold implantation according to an optimized Absorb BVS implantation technique did not have lower rates of ScT and TLR, compared to scaffold treated lesions that did not meet PSP criteria.
INFLUENCE OF CORONARY ARTERY CALCIFICATION ON RESPONSE TO ADENOSINE DURING FRACTIONAL FLOW RESERVE MEASUREMENTS

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Purpose:
During invasive fractional flow reserve (FFR) measurements adenosine is regularly used to obtain maximal hyperemia. Severe coronary artery calcification (CAC) is associated with impaired vasodilation. We investigated whether the response to adenosine during FFR measurements differ between vessels with mild versus severe CAC.

Methods:
Retrospectively we obtained CAC-scores in 236 consecutive patients. In 304 vessels with intermediate coronary artery stenoses FFR was performed. FFR before the administration of adenosine minus FFR after the administration of adenosine was used to investigate the response to adenosine ('FFR Difference'). Furthermore, pressure-bounded coronary flow reserve (pb-CFR) was calculated.

Results:
Mean age was 65 ±10 years, 65% was male. Median CAC score was 510 (range 0 to 6141). Mean FFR before the administration of adenosine was comparable in vessels with mild versus severe calcifications. Severe CAC was associated with FFR ≤0.80 after the administration of adenosine (p=0.045). A large FFR Difference was seen in younger patients (p=0.05). FFR Difference was not influenced by the severity of CAC. In 49% of all FFR measurements, pb-CFR could be categorized into pb-CFR <2.0 or pb-CFR ≥2.0. Linear regression analysis demonstrated that Pb-CFR was not influenced by severe CAC (p= 0.83).

Conclusion:
We did not find an association between the severity of CAC and the response to adenosine during FFR / pb-CFR measurements in intermediate coronary artery stenoses.
AN INCREASED FFR IN NON-CULPRIT VESSELS IN THE ACUTE MOMENT OF STEMI DUE TO DECREASED ADENOSINE RESPONSIVENESS: A COMPARISON WITH THE ADENOSINE FREE IFR

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Purpose:
Primary percutaneous intervention (PPCI) of non-culprit vessels in ST-segment elevation myocardial infarction (STEMI) patients is associated with improved clinical outcome. Fractional flow reserve (FFR) can guide revascularization of these non-culprit lesions. Recently instantaneous wave-free ratio (iFR) was introduced as a non-hyperemic alternative to FFR. In the acute setting of STEMI, coronary hemodynamics are altered, potentially influencing both FFR and iFR. The aim of the present study was to assess changes in coronary hemodynamics in non-culprit vessels of STEMI patients from index event to 1 month follow-up.

Methods:
We included 73 STEMI patients with multivessel disease. Following successful PPCI, resting and hyperaemic intracoronary pressure measurements were performed and repeated at 1-month follow-up. iFR, FFR, coronary flow reserve (CFR) and the index of microcirculatory resistance (IMR) were calculated for both time-points.

Results:
FFR significantly decreased (0.88±0.07 versus 0.86±0.09, p=0.001) and iFR remained stable between baseline and follow-up (0.93±0.06 versus 0.94±0.06, p=0.118). CFR significantly increased from baseline to follow-up (2.9±1.4 versus 4.1±2.2, p<0.001). IMR showed a trend towards a decrease over time (18 [14-27] versus 15 [11-21], p=0.06). There was a significantly lower pressure drop after adenosine at the acute moment versus follow-up (10.6±11.2 versus 14.1±14.2 mmHg, p=0.010).

Conclusion:
In STEMI, non-culprit hyperemic coronary hemodynamics alter from index event to 1 month follow up as demonstrated by an increased CFR, decreased resistance and decreased FFR. This could be explained due to a blunted adenosine responsiveness at the acute moment. Non-hyperemic iFR is less affected, showing no significant change from baseline to 1 month follow up.
Figure:
The effect of adenosine on intracoronary pressures measured at baseline versus follow-up

A.

B.
Pressure drop after adenosine i.v.

Δ Pd
Resting pressures

Hyperemic pressures
NORMALIZATION OF QRS DURATION TO LEFT VENTRICULAR DIMENSION IMPROVES PATIENT SELECTION FOR CARDIAC RESYNCHRONIZATION THERAPY

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Purpose:
In patients with left bundle branch block (LBBB), QRS duration (QRSd) is dependent on both myocardial conduction velocity and conduction path length. Although left ventricular (LV) dilation causes QRSd lengthening which is expected to result in cardiac resynchronization therapy (CRT) benefit, it is truly associated with poor outcome. Previously, we demonstrated that normalizing QRSd to LV dimension, to adjust for conduction path length, improved prediction of hemodynamic response to CRT. This study evaluates the effect of QRSd normalization on the prediction of CRT survival.

Methods:
We studied 250 heart failure patients (67 years, 66% male) with LV ejection fraction ≤35% and LBBB with QRSd ≥120ms who underwent CMR imaging before CRT implantation. CMR derived LV end-diastolic volumes (LVEDV) were used for QRSd normalization (i.e. QRSd/LVEDV). The primary endpoint was a combined endpoint of death, LVAD or HTx.

Results:
During a median follow-up of 3.9 years, 79 (32%) patients reached the primary endpoint. In univariable Cox regression, unadjusted QRSd was unrelated to CRT outcome (p=0.116). In contrast, normalized QRSd was a strong predictor of outcome (HR 0.13 per ms/ml, p=0.008). In an adjusted model (age, gender, diabetes mellitus, atrial fibrillation, kidney function, strict LBBB morphology, LVEDV, LV end-systolic volume and etiology on CMR), normalized QRSd remained a predictor of survival together with age, atrial fibrillation, kidney function and etiology on CMR.

Conclusion:
Normalization of QRSd to LV dimension improves prediction of survival after CRT implantation. QRSd normalization is a relatively simple method that might improve patient selection for CRT.
Figure:
Guideline recommendations for CRT depend on QRS duration with a higher class of recommendation for patients with QRSd ≥150ms. Unadjusted QRSd, however, showed poor differentiation in CRT survival between groups (figure A). Normalization of QRSd to LV dime
PATIENTS IN NEW YORK HEART ASSOCIATION FUNCTIONAL CLASS I BENEFIT FROM PRIMARY PREVENTION IMPLANTABLE CARdioverter DEFibrillator THERAPY

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Purpose:
Current ESC guidelines recommend implantable cardioverter defibrillator (ICD) therapy for primary prevention of sudden cardiac death in patients with a left ventricular ejection fraction (LVEF) ≤35% and New York Heart Association (NYHA) class II or III. According to the ESC guidelines update in 2015, primary prevention ICD therapy for NYHA I patients is no longer recommended. The aim of the study was to evaluate the potential benefit of primary prevention ICD therapy in NYHA class I patients with a LVEF ≤35%.

Methods:
122 patients (84% men, age 66 ± 9 years, 75% ischemic cardiomyopathy [CMP], mean LVEF 28 ± 7%) who received an ICD for primary prevention according to pre-2015 guidelines were included (thus including NYHA class I patients). Data were collected from ongoing prospective studies. Exclusion criteria were resynchronization therapy, patients with hypertrophic CMP or arrhythmogenic right ventricular CMP. NYHA class was assessed at the time of ICD implantation. A subgroup of 45 (37%) patients received annual NYHA class assessment. During follow-up, appropriate device therapy (ADT) and mortality were evaluated in NYHA I and NYHA II-III patients. ADT was defined as anti-tachycardia pacing or shock for ventricular tachyarrhythmia.

Results:
51 patients (42%) were in NYHA I, 64 (53%) NYHA II and 7 (6%) NYHA III. During a mean follow-up of 3.52±3.93 years, 28 (23%) patients received ADT and 16 (13%) died. NYHA I patients received significantly more ADT compared to NYHA II-III patients, 33% versus 16%, respectively (HR 2.2, p=0.04, 95% CI 1.03-4.78). No differences were observed in mortality between NYHA I and NYHA II-III patients, 12% versus 14%, respectively (HR 0.9, p=0.86, 95% CI 0.32-2.55). In the subgroup of NYHA I patients with an annual NYHA assessment during follow-up (n=17), 5 patients received ADT (29%) and 4 (80%) out of these 5 patients were still in NYHA I at time of ADT.

Conclusion:
During follow-up, NYHA class I primary prevention ICD patients experienced significantly more ADT compared to primary prevention NYHA II-III ICD patients. These results indicate that primary prevention NYHA I patients might benefit from ICD therapy and challenges the current ESC guidelines for ICD therapy.
Figure:

HR 2.2; p=0.04

Appropriate ICD therapy (%)

Time (days)

NYHA class I

NYHA class II-III
EVALUATION OF A NEW AUTOMATED SCREENING TOOL FOR THE ASSESSMENT OF THE ELIGIBILITY FOR A SUBCUTANEOUS IMPLANTABLE-CARDIOVERTER DEFIBRILLATOR

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Purpose:
The eligibility for subcutaneous implantable defibrillator (S-ICD) system relies on a pre-implant ECG-screening. The manufacturer has developed a new ECG screening tool, automatic screening tool (AST), which may render manual ECG-screening unnecessary. The aim of the study was to determine the eligibility for S-ICD system using both methods (conventional manual ECG-screening versus AST) in different patient categories including patients with cardiomyopathy, congenital heart disease and inherited primary arrhythmia syndrome in an academic center.

Methods:
We prospectively evaluated the ECG suitability for an S-ICD in consecutive patients at our outpatient clinic between February and June 2017. The primary endpoint of our study was ECG eligibility defined as at least 1 successful vector in both supine and sitting postures.

Results:
A total of 254 patients (167 men; mean age 45±16 years) were screened using both methods. Overall, there was a high ECG eligibility using either method (93% versus 92%, p=0.45). Overall agreement between both methods was 94%. Patients with hypertrophic cardiomyopathy (HCM) had a higher risk to have a failed screening test using either test in comparison to the total population (manual: odds ratio [OR] 3.3, 95% confidence interval [CI] 1.2-9.3, p=0.02; AST: OR 3.0, 95% CI 1.2-7.6, p=0.02). Figure 1 demonstrates discrepancy in ECG suitability between manual measurements and AST in a HCM patient.

Conclusion:
AST showed a high agreement with manual ECG-screening for S-ICD. Overall there was a high ECG eligibility for a S-ICD, although patients with HCM seem to have a lower passing rate in comparison to the total population irrespective of the screening method.

Figure
Discrepancy between manual ECG-screening and AST.
LOCAL GENE THERAPY ENABLES AUTOGENOUS AND PAIN-FREE TERMINATION OF ATRIAL FIBRILLATION IN VIVO

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Purpose:
Maintenance of sinus rhythm is the primary goal for symptomatic AF patients but remains difficult to achieve because of suboptimal treatment options. Despite being effective, the use of implantable atrial defibrillators is limited due to patients intolerance to repeated shocks. Shock-related adverse effects can hypothetically be overcome by allowing the heart itself to produce the electrical current needed for arrhythmia termination. Therefore, the purpose of this study was to evaluate the feasibility of autogenous AF termination through light-controlled generation of atrial currents following optogenetic gene therapy.

Methods:
AAV-vectors encoding ReaChR were locally delivered to the right atrium (RA) of adult rats by gene painting (n=10). Four weeks later, episodes of AF were induced in vivo by electrical burst pacing during carbachol infusion, followed by programmed RA epicardial illumination through a small opening of the 4th right intercostal space.

Results:
Gene painting of the RA resulted in transmural ReaChR-transduction with minimal transgene expression of the left atrium and ventricles. Following in vivo induction of sustained AF, a single 1s light pulse targeting 20mm² of the RA, terminated AF in all rats tested, with an average termination efficiency of 94±4% vs 0% when no light was applied (p<0.01).

Conclusion:
Our study proofs that the heart can be enabled to autogenously terminate AF with high efficiency by adding light-gated ion channels to its bioelectric capacity. This way, the heart relies on endogenous current production for arrhythmia termination rather than high-voltage shocks used in conventional electrical cardioversion. These findings may lay the foundation for development of pain-free device therapy for AF through biomedical engineering.

Figure:
Typical body-surface ECG trace demonstrating successful in vivo light-induced AF termination and subsequent restoration of sinus rhythm by a single 470-nm light pulse (1000 ms, 3.5 mW/mm²).
DETECTION OF RECURRENCES AFTER CRYO-ABLATION FOR ATRIAL FIBRILLATION: TOWARDS OPTIMAL YIELD AND MINIMAL MONITORING TIME

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Purpose:
Intensive holter monitoring increases the chance of recurrence detection, but also the burden on available resources. We evaluated the proportion of detected recurrences with a reduced monitoring time in a cohort of atrial fibrillation (AF) patients that underwent cryo-ablation.

Methods:
We studied consecutive patients who underwent a first cryo-ablation for AF between March 2010 and December 2016 with holter recording performed in the first year after ablation. Follow-up comprised both one-year symptom-driven clinical follow-up as well as protocol-driven six-day holter recordings at 6, 12, 26 and 52 weeks after the procedure. Arrhythmia recurrence was defined as the composite of AF and atrial flutter.

Results:
Patients (n=404) had a median age of 60 years (IQR 54-66) and predominantly paroxysmal AF (82%). We analyzed a total of 1246 holter recordings, with a median of 3 (IQR 2-4) per patient. Overall one-year success rate after a 3-month blanking period was 70%, of which 65% was initially detected on holter recording. With a reduced monitoring interval, 70% and 92% of the recurrences were detected after 2 and 4 days, respectively.

Conclusion:
We observed a 70% success rate after a first cryo-ablation in the setting of intensive protocol-driven holter monitoring and symptom-driven clinical follow-up. Over 90% of the recurrences on holter recordings were observed within four days of monitoring, suggesting that the duration of holter monitoring can be significantly reduced.
OPTIMAL GUIDELINE ADHERENCE IN ATRIAL FIBRILLATION CARE BY USING THE QUALITY SYSTEM OF THE NETHERLANDS HEART NETWORK

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Purpose:
In order to improve patient relevant outcomes, guidelines need to be followed. Guideline adherence in atrial fibrillation (AF) care is suboptimal and therefore urgently needs improvement. To achieve certain improvements, transmural standards of AF-care accompanied with active quality systems may offer a solution. This study aims to assess whether quality systems are a feasible and effective approach to improve guideline adherence and outcome registration in AF-care.

Methods:
Data for this research were used from 4 hospitals that jointly developed and implemented transmural standards for AF-care within the Netherlands Heart Network (NHN). In September-October 2017 audits were performed to assess AF guideline adherence in which process and structural measures were indicated based on (inter)national guidelines on AF treatment and diagnosis. Completeness of outcome measures for AF-patients, based on the Netherlands Heart Registration medical sets, were evaluated by performing descriptive statistics using SPSS 21.0.

Results:
A total of 270 AF-patients (67.7 years) were included in the present study (58.1% male). Most (38.9%) AF-patients were diagnosed with paroxysmal AF, with a mean CHA2DS2-VASc of 2.73 and HASBLED-score of 1.45. Regarding guideline adherence, process measures (n=11) were followed for 96.4% whereas structural measures (n=7) for 97.7% were implemented as intended. Furthermore, the registration density of the 6 AF-patient relevant outcomes measures ranged between 96.7–98.5%.

Conclusion:
Optimal guideline adherence in AF-care is a feasible target when transmural standards of care are accompanied with active quality systems. Within the NHN studies are ongoing to demonstrate the effects of optimal guideline adherence on long-term outcomes in this population.
GANGLION PLEXUS ABLATION FOR ADVANCED ATRIAL FIBRILLATION: 2-YEARS RESULTS OF THE AFACT STUDY

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Purpose:
The randomized AFACT study showed no effect of additional ganglion plexus (GP) ablation in patients with advanced AF undergoing thoracoscopic AF surgery at one year. However, GP ablation was associated with more major bleeding, sinus node dysfunction and pacemaker implantation. We now determined efficacy and safety of additional GP ablation to thoracoscopic AF surgery during 2 years follow-up in the AFACT trial.

Methods:
The AFACT study randomized 240 patients with advanced AF undergoing thoracoscopic pulmonary vein isolation 1:1 to no GP ablation or epicardial ablation of the four major GPs and Marshall’s ligament. In persistent AF patients a roof and trigone line were also made. Follow-up visits were every three months until 18 months and one at 2 years. After an initial 3-month blanking period, all antiarrhythmic drugs (AAD) were discontinued.

Results:
At two years information was available of 231 patients (age 59±8 years, 27% women, 65% enlarged left atrium, 60% persistent AF). Freedom of AF recurrence did not differ statically between the GP and no GP group (n=60, 54% vs. n=64, 54%; p=0.97), regardless of paroxysmal (p=0.66) or persistent AF (p=0.95). Twenty four percent of patients in both groups had >3 recurrences during follow up (figure). At 2 years 78% were off AADs. GP ablation was not associated with late complications.

Conclusion:
GP ablation during thoracoscopic AF surgery does not affect mid-term freedom of AF recurrence. As it causes more major procedural complications, ablation of the GPs should not routinely be performed.
Figure:
Number of recurrences during 2 year follow-up in AF patients undergoing GP ablation versus no GP ablation.
Purpose:
Percutaneous pulmonary valve implantation (PPVI), with Melody or Edwards Sapien valves, is used to resolve right ventricular outflow tract obstruction (RVOT) and/or regurgitation. However, long term outcomes of PPVI are fairly unknown. This study aims to investigate the long-term clinical and hemodynamic outcomes.

Methods:
A multicenter retrospective, observational study was performed including all consecutive patients from May 2004 until November 2017 at the Erasmus Medical Center or Radboud Medical Center. All clinical data, ECG and echocardiographic data were collected and analyzed using linear mixed effects models.

Results:
Of 82 attempts (Melody 91%, Sapien 9%) at a mean age of 28±10 years (range 12-54 years), 75 (91%) were successful. The most common original diagnosis was tetralogy of Fallot (n=24; 32%). Mean transvalvular gradient decrease was 38 mmHg, and 71 patients (95%) were discharged with none/mild regurgitation. During a median follow up of 4.1 years (total follow up duration: 322 years), there were two patients who died due to end stage heart failure. Sixteen events of endocarditis occurred in 14 patients (linearized occurrence rate (LOR) 5%/year), of which two died. Four patients needed pacemaker/ICD implants (LOR 1.2%/year), not related to the PPVI procedure. Eight patients had Melody/Sapien valve replacements after an estimated mean follow-up of 9.8 years due to endocarditis (n=5), progressive heart failure (n=1) and restenosis (n=2). At 5 years, the mean peak gradient was 41 mmHg and 68 patients (91%) had none/mild regurgitation.

Conclusion:
PPVI is an excellent relieve of RVOT obstruction and regurgitation. However, yearly substantial endocarditis risk of 5% and restenosis limit durability of the valves.
Figure:
Average trend of transvalvular pulmonary gradient (mmHg)
INCREASED PULMONARY INHALANT USE IN ADULTS WITH ATRIAL SEPTAL DEFECTS EVEN LONG AFTER REPAIR

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Purpose:
Background: Patients with secundum atrial septal defects (ASDs) may present late during adulthood due to symptom overlap with pulmonary diseases and consequently often use bronchodilators. We studied pulmonary inhalant use in adults with open and repaired ASDs compared to matched references.

Methods:
Methods: In this cohort study, ASD patients from the national CONgental CORvitia registry were linked to the national Dispensed Drug Registry. The use of all pharmacy-dispensed pulmonary inhalants was determined yearly between 2006-2014 using the Anatomical Therapeutic Chemical classification system for pulmonary inhalants. Patients were compared with an age-and sex-matched reference cohort from the general population (1:10 ratio) using generalized estimation equations.

Results:
Results: This study comprised 1,959 adult patients (66% female, mean age 42±17y). 1223(62%) underwent ASD repair a median 22[10-37] years ago. Overall, more ASD patients used inhalants than matched references (OR=1.81[95%CI 1.62-2.03]; p<0.001). No differences were seen between open and repaired ASD patients (p=0.56) or patients repaired at age ≤25y versus >25y when corrected for sex and current age (p=0.87). Still, patients repaired at age ≤25y used significantly more inhalants than matched references.

Conclusion:
Conclusion: This study shows a twofold higher pulmonary inhalant use in adult ASD patients compared to matched references, suggesting pulmonary functional impairment even post-closure. Together with the lifetime risk of post-repair pulmonary hypertension, this may warrant lifelong post-repair follow-up.
Figure:
Pulmonary inhalant use. Proportion of ASD patients (closed and repaired) receiving pulmonary inhalants compared to age- and sex-matched references (A), and in patients repaired at age ≤25 years vs. >25 years compared to their matched references.
Purpose:
Currently used prognostic factors struggle to identify patients with a systemic right ventricle (sRV) who are at risk for late cardiac complications. This study aims to identify prognostic factors, derived from echocardiographic and blood biomarkers, that are associated with cardiovascular events.

Methods:
Prospectively recruited clinically stable patients with congenitally corrected transposition of the great arteries (ccTGA) and patients who underwent an atrial switch operation (M-TGA), were included between 2011-2013. All patients underwent venous blood sampling and echocardiography. The primary endpoint was a composite of death and heart failure, the secondary endpoint was arrhythmia. Associations between variables and endpoints were assessed with Cox-regression analysis, event-free survival with Kaplan-Meier curves.

Results:
Sixty-five patients with M-TGA and 21 ccTGA patients were included (age: 37±9 years, 65% male). Both groups were equal regarding age or sex, but there was less loss of sinus rhythm in the M-TGA group (77% vs 43%, p-value: 0.004). Median follow-up time was 5.3[4.8-5.7] years. The primary and secondary endpoint occurred 21 and 26 times, respectively. Survival did not differ between ccTGA and M-TGA. Cox-regression analysis, adjusted for age, showed that all biomarkers were significantly associated with death and heart failure. For arrhythmia, some but not all of these associations were found (Figure). None of the strain parameters were significantly associated with both endpoints.

Conclusion:
Strain parameters were not able to identify patients at risk for death and heart failure, or arrhythmia, while blood biomarkers from several pathophysiological axes were. There was no difference in survival between patients with ccTGA and M-TGA.
Figure:

Death or heart failure

<table>
<thead>
<tr>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>eGFR</td>
<td>0.87 (0.66, 1.15)</td>
<td>P = 0.257</td>
</tr>
<tr>
<td>Hb</td>
<td>8.30 (5.93, 11.90)</td>
<td>P = 0.096</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>2.30 (1.52, 3.51)</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>High serum CRP*</td>
<td>2.00 (1.27, 3.18)</td>
<td>P = 0.029</td>
</tr>
<tr>
<td>N-terminal proBNP*</td>
<td>2.45 (1.35, 4.48)</td>
<td>P = 0.029</td>
</tr>
<tr>
<td>GFR ≥ 50%</td>
<td>2.80 (1.78, 4.39)</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>O2-saturation</td>
<td>1.16 (1.21, 1.32)</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>UV-index</td>
<td>1.19 (1.01, 1.42)</td>
<td>P = 0.05</td>
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</tbody>
</table>

Arrhythmia

<table>
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<th>Hazard ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
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<tbody>
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<td>0.64 (0.54, 0.78)</td>
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<tr>
<td>Hb</td>
<td>7.30 (5.67, 9.47)</td>
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<tr>
<td>White blood cell count</td>
<td>1.30 (0.89, 1.92)</td>
<td>P = 0.001</td>
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<tr>
<td>High serum CRP*</td>
<td>1.47 (1.15, 1.93)</td>
<td>P = 0.001</td>
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<tr>
<td>N-terminal proBNP*</td>
<td>1.11 (0.83, 1.47)</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>GFR ≥ 50%</td>
<td>1.25 (0.90, 1.74)</td>
<td>P = 0.22</td>
</tr>
<tr>
<td>O2-saturation</td>
<td>1.50 (1.20, 1.90)</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>UV-index</td>
<td>1.40 (0.93, 2.15)</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>LV-Strain</td>
<td>1.73 (1.09, 2.75)</td>
<td>P = 0.05</td>
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</table>

*Variables are adjusted by age.
For interpretation purposes, only statistically significant variables are used.
NON-VITAMIN K ANTAGONIST ORAL ANTICOAGULANTS (NOACS) FOR THROMBOEMBOLIC PREVENTION, ARE THEY SAFE IN CONGENITAL HEART DISEASE? A PROSPECTIVE WORLDWIDE OBSERVATIONAL STUDY

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Purpose:
Adults with congenital heart disease (ACHD) and non-valvular atrial arrhythmia (AA) have higher annual incidence of major bleeding (4.4%) under the use of vitamin K antagonists (VKA) than adults with acquired heart disease. The Non-vitamin K antagonist oral anticoagulants (NOACs) for thromboembolic prevention (NOTE) registry was designed to evaluate the incidence of thromboembolic and bleeding events in consecutive ACHD patients using NOACs.

Methods:
In this international multicenter prospective registry of ACHD using NOACs for the prevention of thromboembolism, clinical data were collected at baseline and at follow-up of 6 months, 1 year and 2 years. The primary endpoints were thromboembolic events and major bleeding. Secondary endpoint was minor bleeding. Incidence was determined by Poisson regression.

Results:
In total, 408 adults (mean age 45±16 years, 55% male) with various congenital heart defects (CHD) (11% complex, 43% moderate, 46% simple) using NOACs (34% apixaban, 5% edoxaban, 11% dabigatran, 44% rivaroxaban) have been included. Indication of NOACs were atrial arrhythmias (88%), primary prevention (7%) and secondary prevention (5%) of thromboembolism. During a mean follow-up of 1.3±0.8 years of follow-up, all three thromboembolic events occurred in patients with complex CHD (annual incidence 0.8% [95%CI 0.2-2.2]) and four major bleedings occurred in patients with moderate or complex CHD (annual incidence 1.1% [95%CI 0.3-2.6]). The annual incidence of minor bleeding was 10.1% [95%CI 7.1-13.8] (n=35).

Conclusion:
Our annual incidence of thromboembolism and major bleeding under NOACs are lower than previously reported in ACHD patients using VKA, mostly occurring in patients with moderate or complex defect.
Figure:
Kaplan-Meier curves for survival free from thromboembolic event, major bleeding and minor bleeding in adult with congenital heart disease using NOACs.
STRESS ECHOCARDIOGRAPHY IDENTIFIES PATIENTS WITH CLINICAL BENEFIT FROM PERCUTANEOUS MITRAL VALVE REPAIR

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Purpose:
Percutaneous mitral valve repair (PMVR) with the MitraClip is an option for high-risk patients with symptomatic moderate-severe to severe mitral regurgitation (MR), but not all patients have clinical benefit after a successful procedure. The aim of our study was to investigate whether stress echocardiography can improve the selection of patients who will have clinical benefit from PMVR.

Methods:
39 patients selected for MitraClip implantation underwent a preprocedural low-dose stress (dobutamine or handgrip) echocardiography with determination of stroke volume, ejection fraction and MR grade. Clinical benefit after MitraClip implantation was determined by New York Heart Association classification and the RAND Short Form-36 Quality of Life questionnaire.

Results:
36 patients with a technical successful procedure were included in the analysis, (mean age 79±8 years, 47% male, 50% functional MR). All patients (7/7) with a decrease of MR during the stress phase of the preprocedural stress echocardiography remained in NYHA III or IV or died within 6 months, while in the case of a stable or increase of MR during stress 62% (18/29) were alive and in NYHA I or II at follow-up (p=0.008). A raise in stroke volume (>40%) during stress echocardiography (present in 10/36 patients) was associated with a significant increase in Quality of Life on 4/8 subscales of the questionnaire: Physical Functioning (p<0.001), Social Functioning (p<0.001), Mental Health (p=0.022) and Vitality (p=0.026).

Conclusion:
Stress echocardiography is feasible and useful for selection of patients in whom successful MR reduction after MitraClip implantation leads to clinical benefit.
Figure:
Patients with stroke volume raise at baseline

**Patients with stroke volume raise at baseline**

![Graph showing physical functioning metrics with baseline and 1 month data]

**Patients without stroke volume raise at baseline**

![Graph showing physical functioning metrics with baseline and 1 month data]
Regional longitudinal strain by feature tracking cardiac magnetic resonance predicts sustained ventricular arrhythmias in arrhythmogenic right ventricular cardiomyopathy

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Purpose:
Arrhythmogenic right ventricular cardiomyopathy (ARVC) is characterized by ventricular dysfunction and ventricular arrhythmias (VA). Feature tracking cardiac magnetic resonance (FT CMR) is a novel method to quantitatively assess ventricular function. While prior studies confirmed the diagnostic value of FT CMR in ARVC, its prognostic value remains unknown. Therefore, we aimed to assess whether FT CMR predicts VA in ARVC.

Methods:
Four-chamber cine CMR images of 58 definite ARVC patients (36% male, 39±16 yrs) with a desmosomal mutation and without prior sustained VA were analyzed for average and regional (subtricuspid, mid, apical) right ventricular (RV) longitudinal strain. We also performed stratified analyses by RV ejection fraction (RV EF). Primary outcome was sustained VA (sustained VT, appropriate ICD intervention, sudden cardiac arrest) in follow-up.

Results:
During 5.1±3.3 yrs follow-up, 13 (22%) patients experienced VA (cycle length 313±67 ms). Compared to patients without VA, those with VA had significantly reduced average (-14±6% vs -19±6% p=0.003) and regional (subtricuspid -23±7% vs -34±12% p=0.007; mid -14±6% vs -23±11% p=0.009) free wall strain, as well as reduced RV EF (38±10% vs 49±10% p=0.001). Worse VA-free survival was seen for reduced subtricuspid (-28% cutoff p=0.003) and mid (-20% cutoff p=0.004) free wall strain; this remained significant for mid free wall strain in patients with RV EF <45% (p=0.023).

Conclusion:
Both average and regional RV strain by FT CMR are reduced in ARVC patients with sustained VA. RV mid free wall strain predicts VA in patients with reduced RV EF, suggesting incremental value over conventional CMR measures.
Figure:
Cumulative survival free from ventricular arrhythmias (VA) stratified by cutoff values of -28% for subtricuspid strain (left) and -20% for mid free wall strain (right). Only patients with an adequate tracking of the endocardial border were included in this analysis.
DIAGNOSTIC VALUE OF LONGITUDINAL FLOW GRADIENT FOR THE PRESENCE OF HEMODYNAMICALLY SIGNIFICANT CORONARY ARTERY DISEASE

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Purpose:
Although quantitative position emission tomography (PET) perfusion imaging is considered the gold standard in non-invasive ischemia testing, reduction in hyperemic myocardial blood flow (MBF) is considered relatively non-specific as it may originate from either epicardial stenosis or microvascular dysfunction. Recently, the longitudinal MBF gradient has been suggested as a novel index for the hemodynamic consequences of an epicardial stenosis. This study therefore aimed to investigate the diagnostic value of longitudinal MBF gradient derived from PET for the presence of hemodynamically significant coronary artery disease (CAD).

Methods:
Patients with suspected CAD underwent [15O]H2O PET followed by invasive coronary angiography with fractional flow reserve (FFR) of all major coronary arteries. Longitudinal base-to-apex MBF gradients were assessed by two methods, using MBFs in the apical and mid (method 1) or the apical and basal myocardial segments (method 2) to calculate the gradient. The incremental diagnostic value of hyperemic longitudinal MBF gradient (by both methods) to hyperemic MBF alone for the presence of hemodynamically significant CAD (FFR≤0.80) was tested. Subgroup analysis was performed to determine the influence of coronary lesion location.

Results:
A total of 603 (98.5%) vessels in 204 patients were included. Hyperemic longitudinal MBF gradient was only weakly correlated with FFR (method 1: r=0.12; method 2: r=0.22). Hyperemic longitudinal MBF gradient (by both methods), had no incremental diagnostic value to hyperemic MBF alone for the presence of hemodynamically significant CAD. No significant correlation between longitudinal MBF gradient and FFR was noted in proximal lesions, whereas longitudinal MBF gradient and FFR were significantly correlated in non-proximal lesions (r=0.57).

Conclusion:
PET-measured longitudinal flow parameters had no incremental diagnostic value to hyperemic MBF for the presence of hemodynamically significant CAD. Since lesion location was found to influence the correlation of PET-measured longitudinal flow parameters with FFR, changes in longitudinal flow may be caused by normalization to relatively normal perfused areas.
Figure:
Diagnostic value of longitudinal flow parameters for the presence of obstructive CAD as defined by FFR.

Method 1

<table>
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<th>AUC</th>
<th>(95% CI)</th>
<th>p-value *</th>
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<tr>
<td>MBF</td>
<td>0.87</td>
<td>(0.84 - 0.90)</td>
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<td>Gradient</td>
<td>0.54</td>
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Method 2

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SERIAL HIGH-SENSITIVITY CARDIAC TROPONIN T MEASUREMENTS TO RULE-OUT ACUTE MYOCARDIAL INFARCTION AND A SINGLE HIGH BASELINE MEASUREMENT FOR SWIFT RULE-IN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Purpose:
To determine (I) the ability of serial high-sensitivity cardiac troponin T (hs-cTnT) measurements to correctly rule-out acute myocardial infarction (AMI) and (II) the ability of a single high baseline hs-cTnT measurement to correctly rule-in AMI in patients presenting to the emergency department with chest pain.

Methods:
Embase, Medline, Cochrane, Web of Science and Google scholar were searched for articles in English, without publication date restrictions. Prospective cohort studies that evaluated the sensitivity and negative predictive value (NPV) of serial hs-cTnT and studies that evaluated the specificity and positive predictive value (PPV) of a baseline hs-cTnT of >50 ng/L were included. Summary estimates with their 95% confidence intervals (CI) were obtained by random effects model.

Results:
The search yielded 21 studies, of which 14 were included in the meta-analysis. For rule-out, six papers presented the sensitivity and NPV of serial measurements <14 ng/L. Summary estimates of sensitivity and NPV were 96.7% (95%CI: 92.3-99.3) and 98.7% (97.0-99.7) respectively. Three studies presented the sensitivity and NPV of a 0-hour/1-hour algorithm with a baseline hs-cTnT below 12 ng/L and Δ1 hour below 3 ng/L. Summary estimates of sensitivity and NPV were 98.9% (96.4-99.96) and 99.7% (99.0-99.99) respectively. For rule-in, six studies reported the specificity and PPV of baseline hs-cTnT of >50 ng/L. Summary estimates for specificity and PPV were 94.6% (91.5-97.1) and 64.3% (40.6-84.9) respectively.

Conclusion:
Serial hs-cTnT measurement strategies to rule out AMI and a baseline hs-cTnT >50 ng/L to rule in AMI perform well. However, the PPV of a high baseline hs-cTnT is strongly influenced by disease prevalence.
Figure:
Figuur 1. Forest plots displaying the summary estimates for sensitivity and NPV of (a) serial hs-cTnT measurements < 14ng/L (99th percentile) and (b) hs-cTnT < 12 ng/L and Δ1 hour < 3 ng/L. 2: Forest plot displaying the summary estimates for specifici
CARDIAC BIOMARKERS IN AORTIC VALVE STENOSIS

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Purpose:
Natriuretic peptides were recently added in the ESC guidelines as a potential valuable biomarker in the management of aortic valve stenosis (AVS). However, little is known about the course of different cardiac biomarkers in serial measurements in AVS. Differences in serial laboratory results from a patient may reflect clinical improvement or deterioration, but may also arise from naturally occurring fluctuations. Therefore, the aim of the current study was to determine the variation of cardiac biomarkers troponin T and NTproBNP in stable and progressive AVS.

Methods:
Serial blood sampling under standardized conditions was performed in 25 subjects with (echocardiography confirmed) moderate aortic valve stenosis (7 times in 1 year). Variation of cardiac biomarkers high-sensitivity troponin T (hsTnT) and NTproBNP were determined.

Results:
Of 25 patients, 44% were female and mean(±SD) age was 66±6 years. All patients were free of acute cardiovascular events >6 months and had an echocardiogram before and after study inclusion. After 1 year, 9 patients showed progressive AVS. Concentration courses of hsTnT and NTproBNP are shown in figure 1. Variation between serial measurements in patients with AVS seemed to increase with AVS progression (stable vs progressive AVS: 11.22% vs 19.18% for hsTnT and 22.00% vs 32.56% for NTproBNP).

Conclusion:
This is the first study to determine variation of cardiac biomarkers hsTnT and NTproBNP in AVS. Our results suggest that variation of these biomarkers differ in stable versus progressive AVS. It has potential for future clinical use to identify patients at risk of AVS progression.
Figure:
Concentration courses of hsTnT and NTproBNP. Total population (black), stable AVS (grey), progressive AVS (yellow).
Session V: Electrophysiology

CORRELATION BETWEEN TERMINAL ACTIVATION DURATION AND VENTRICULAR ARRHYTHMIA IN ARRHYTHMOGENIC CARDIOMYOPATHY

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Purpose:
Prolonged Terminal Activation Duration (TAD ≥55ms) due to activation delay (AD) is a minor diagnostic revised Task Force Criterion (TFC) in arrhythmogenic cardiomyopathy (ACM). AD is a hallmark of reentrant arrhythmic mechanisms. We hypothesized an association between the absolute length of TAD and the occurrence of sustained ventricular arrhythmia (SVA) in ACM.

Methods:
We included consecutive patients fulfilling the 2010 diagnostic TFC, and underwent 12 leads ECG recording (filter setting 100-150 Hz) while off anti-arrhythmic drugs. The TAD in ms was defined as the longest interval between the nadir of the S wave and the end of all depolarization deflections in leads V1-3. Two independent investigators were blinded for patient outcomes. SVA was defined as ventricular fibrillation, sustained ventricular tachycardia or sudden cardiac arrest within 1 year before or after ECG recording. The association of TAD with SVA was evaluated by logistic regression analysis using the continuous value, as well as the dichotomous 55ms cutoff value.

Results:
TAD was measured in 190 patients (mean age 42±15, 50% males), of which 64 (34%) had experienced SVA. The overall mean TAD was 54±14ms, and ≥55ms in 35% of the patients. TAD≥55ms was not significantly associated with SVA (p=0.073). In contrast, patients with SVA had a significantly (p=0.047) higher mean TAD (56±16ms) compared to patients without SVA (52±12ms). Prolongation of TAD was associated with SVA with an odds ratio of 1.29 per 10ms (95% CI [1.004-1.049], p=0.023).

Conclusion:
Continuous prolongation of TAD was associated with a significantly higher occurrence of sustained ventricular arrhythmias. In contrast, this relation was not significant when a dichotomous cutoff value of 55ms for TAD was used. Our findings support the hypothesis of TAD as marker for arrhythmic risk in ACM.
Figure:
Purpose:
Ventricular arrhythmias (VA) are an unpredictable complication of arrhythmogenic right ventricular cardiomyopathy (ARVC). We aimed to assess the performance of the 2017 AHA/ACC/HRS guideline for management of VA recommendations for ICD implantation in ARVC.

Methods:
We categorized 549 patients (51% male, 38±15yrs) with definite ARVC by guideline ICD indication: prior sustained VA or severe ventricular dysfunction (class I, n=247); and syncope (class IIa, n=54). As per the guideline, the remaining patients (n=248) were stratified by signal averaged ECG (SAECG) and electrophysiology study (EPS) inducibility. The outcome of interest was 1) any sustained VA and 2) fast VA (cycle length [CL] ≤240ms or sudden cardiac arrest).

Results:
During 6.9 [IQR 8.8] yrs follow-up, 243 (44%) patients experienced any sustained VA (CL 287±55ms) while 61 (10%) had fast VA (CL 224±27ms). The incidence of any sustained VA was 9.3%/year (95%CI 8.2-10.6) which differed significantly among groups (p<0.001)(Figure 1A). The incidence of fast VA was 1.5%/year (95%CI 1.1-1.9), which did not differ among groups (p=0.270) (Figure 1B). In absence of ICD indication, positive SAECG or EPS inducibility were significantly associated with higher risk of any sustained VA (p=0.023, p<0.001 respectively) as well as fast VA (p=0.021, p=0.010 respectively).

Conclusion:
The 2017 AHA/ACC/HRS ICD indications accurately distinguish subjects at high risk of any sustained VA, but not fast VA. While SAECG and EPS may aid further stratification, the risk of patients without ICD indication is still considerable. This should be kept in mind when managing this high-risk population.
Figure:

Any sustained VA

Event-free survival

Overall \( p < 0.001 \)

I vs. Ila \( p = 0.2723 \)

I vs. None \( p < 0.001 \)

Ila vs. None \( p < 0.001 \)

Time (years)

Numbers at risk

<table>
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<tr>
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<th>Class I</th>
<th>247</th>
<th>64</th>
<th>26</th>
<th>12</th>
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<tr>
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<td>Class Ila</td>
<td>54</td>
<td>17</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td></td>
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<td>248</td>
<td>116</td>
<td>51</td>
<td>11</td>
<td>3</td>
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Incidence (95%CI) per year

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>16.3% (13.9-19.1)</th>
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<tr>
<td></td>
<td>Class Ila</td>
<td>11.6% (7.5-17.2)</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>4.2% (3.2-5.4)</td>
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</table>

Fast sustained VA

Overall \( p = 0.27 \)

I vs. Ila \( p = 1.00 \)

I vs. None \( p = 0.65 \)

Ila vs. None \( p = 0.47 \)

Time (years)

Numbers at risk

<table>
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<tr>
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<tr>
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<td>Class Ila</td>
<td>54</td>
<td>30</td>
<td>13</td>
<td>7</td>
<td>2</td>
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<tr>
<td></td>
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<td>248</td>
<td>128</td>
<td>60</td>
<td>15</td>
<td>6</td>
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</table>

Incidence (95%CI) per year

<table>
<thead>
<tr>
<th></th>
<th>Class I</th>
<th>1.6% (1.1-2.2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Class Ila</td>
<td>2.1% (0.9-4.2)</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>1.2% (0.8-1.9)</td>
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</tbody>
</table>
THE EFFECT OF NONINDUCIBILITY AFTER MULTI-ELECTRODE GUIDED ABLATION OF AF DRIVERS IN PATIENTS WITH FAILED PULMONARY VEIN ISOLATION OR DISEASED ATRIA

S.L. Bekker; S.L. Bekker (Isala Heartcentre, Zwolle); A. Adiyaman (Isala Heartcentre, Zwolle); A.R. Ramdat Misier (Isala Heartcentre, Zwolle); P.P.H.M. Delnoy (Isala Heartcentre, Zwolle); J.J.J. Smit (Isala Heartcentre, Zwolle).

Purpose:
Improved identification of atrial fibrillation (AF) drivers marked by clusters of spatiotemporal dispersions of complex fractionated atrial electrograms (CFAE’s) using a multi-electrode catheter was recently described, allowing a patient-tailored ablation. We investigated the clinical predictors of a successful AF driver ablation.

Methods:
88 consecutive prospective patients were selected for ablation with either 1)persistent AF or 2)paroxysmal AF with structural heart disease or prior failed pulmonary vein isolation (PVI). A multi-electrode Pentaray® catheter was used to guide detection of spatiotemporal dispersions of fractionation sites during AF. After restoring sinus rhythm, AF noninducibility was tested with isoproterenol and a pacing protocol, equal to the AF induction pacing protocol. Clinical endpoint was AF free survival at 6 and 12 months.

Results:
71% of patients had (multiple) prior failed PVI(s). SR restoration was obtained in 92% and noninducibility was reached in 68% of patients. After 1,2 ablation procedures 68% of patients were free from AF recurrence. AF free survival improved in the second half of the procedures (63% vs 43%, p=0.048), using less ablation points (98 vs. 67 points, p=0.003), reaching more noninducibility (50% vs. 85%, p<0.0001). Noninducibility (CI 0.212-0.901, p=0.025) and diabetes (CI 1.088-9.996, p=0.035) were independent predictors of AF free survival. AF free survival was highest after reaching AF noninducibility (p=0.004, figure 1).

Conclusion:
Multi-electrode guided ablation targeting spatiotemporal dispersions of CFAE’s is associated with high rates of SR conversion and AF noninducibility and could be a valuable strategy in patients with diseased atria or failed PVI. Reaching noninducibility is a strong predictor of AF free survival.
Figure:

[Graph showing Kaplan-Meier survival analysis with three groups: SR restoration and non-inducibility, SR non-restoration, and SR restoration and inducibility. The graph includes a table showing patients at risk over time for each group.]
EFFECTS OF GRID VISUALIZATION OF ABLATION LESIONS ON PROCEDURE TIMES AND OUTCOME OF PULMONARY VEIN ISOLATION

M.J. Mulder (VUmc, Amsterdam); M.J. Mulder (VUmc, Amsterdam); M.J.B. Kemme (VUmc, Amsterdam); C.P. Allaart (VUmc, Amsterdam)

Purpose:
Pulmonary vein isolation (PVI) is the cornerstone of catheter ablation of atrial fibrillation (AF). Electrical reconnection of the pulmonary veins is due to insufficient lesion depth or continuity of the ablation circle. Visualizing the precise site of radiofrequency (RF) ablation using a grid (Carto3 System, VisiTag Module, Biosense Webster Inc.) may provide superior visual feedback on continuity of ablation lines, compared to conventional point-by-point visualization. This study aimed to assess the effects of grid visualization on procedural characteristics and clinical outcome.

Methods:
Two-hundred-twenty-two consecutive patients (57% paroxysmal, 43% persistent, 61% male, age 62±9 years) undergoing index PVI between January 2015 and December 2016 were retrospectively studied. Five patients were excluded due to missing procedure recordings. RF ablation was guided by either grid visualization (107 patients, 49.3%) or point-by-point visualization (110 patients, 50.7%). Recurrence was defined as any atrial tachyarrhythmia occurring after a blanking period of 3 months, lasting longer than 30 seconds.

Results:
Grid visualization was associated with a reduction in procedure time (median: 84 vs. 99 minutes, p=0.004), fluoroscopy time (median: 7.2 vs. 10.0 minutes, p<0.001) and radiation dose (median: 7.25 vs. 9.30 Gy·cm², p=0.001) compared to procedures guided by point-by-point visualization. There was no significant difference in total RF application time between the two visualization techniques (median: 46 vs. 43 minutes, p=0.118). The one-year recurrence-free rates for grid vs. point-by-point visualization were 69.2% and 63.3%, respectively (p=0.363).

Conclusion:
Grid visualization of ablation lesions during pulmonary vein isolation reduces procedure and fluoroscopy times without compromising recurrence-free rates.

Figure:
Example of grid and point-by-point visualization of ablation lesions during pulmonary vein isolation
SAFETY AND FEASIBILITY OF A FASTER ABLATION STRATEGY USING CRYO BALLOON ABLATION IN PATIENTS WITH ATRIAL FIBRILLATION

D. Mol, D. Mol (Department of Cardiology, OLVG, Amsterdam), J.R. de Groot (Department of Cardiology, Academic Medical Centre, Amsterdam), J.S.S.G. de Jong (Department of Cardiology, OLVG, Amsterdam)

Purpose:
Cryo balloon (CB) ablation is a frequently used modality to achieve pulmonary vein (PV) isolation as treatment for atrial fibrillation (AF). Recently time to isolation (TTI) was introduced as a new ablation target. This strategy is expected to result in less cryo applications per vein and higher temperatures during cryo application. We describe the safety and feasibility of a new faster ablation strategy that uses TTI.

Methods:
We describe 46 patients (30 male, age 61±8 years) who underwent PV isolation with the CB using the TTI strategy. Procedural and short-term outcomes were analysed. We compared TTI and minimal temperature between the PVs.

Results:
Eighteen (39%) patients had a history of persistent AF, LA volume index 35.5 ±11.5ml/m². Isolation of the targeted PVs using CB was achieved in 179 of 181 pulmonary veins (98.9%). PV potentials were present in 140 (77%) baseline electrograms. Isolation within the first application was achieved in 98/140 (70%). TTI and minimum temperature were comparable between all PVs, LSPV 38 ±15s LIPV 34 ±19s RIPV 47 ±35s RSPV 45 ±31s (p=161), LSPV -44.78 ± 5.59°C LIPV -41.5 ±4.26°C RIPV -45.56 ±7.8°C RSPV -42.5 ±5.92°C (p=.171). PVs were isolated using 1.7±.8 applications. Procedural time (vein puncture to sheath removal) and fluoroscopic time were 61 ±24min and 13.6 ±7.8min retrospectively. Transit phrenic nerve injury occurred in 2 patients (4.3%), vascular groin injury in 1 patient (2.2%). None of the patients developed pericardial effusion. Early recurrence of AF (within 2 months) was observed in 23% of the patients. Long term ablation results will be available in 2019.

Conclusion:
In our experience, the recently developed ablation strategy is safe and feasible to achieve PV isolation. It results in short procedural time, low number of complications and a low fluoroscopic time as a result of a low amount of applications.
EXCISED HUMAN ATRIAL TISSUE FOR IN-DEPTH DISEASE INVESTIGATION AND
DRUG SCREENING: FROM PROTEIN TO PATIENT

N. Harlaar; N. Harlaar (Leiden University Medical Center, Leiden); L. Volkers (Leiden University Medical Center, Leiden); R.J.M. Klautz (Leiden University Medical Center, Leiden); M.J. Schalij (Leiden University Medical Center, Leiden); K. Zeppenfeld (Leiden University Medical Center, Leiden); A.A.F. de Vries (Leiden University Medical Center, Leiden); D.A. Pijnappels (Leiden University Medical Center, Leiden); T.J. van Brakel (Leiden University Medical Center, Leiden)

Purpose:
Prediction of drug responses and cardiotoxicity remains difficult as generic animal models fail to reflect heterogeneity present in patient populations. Advances in human induced pluripotent stem cell and heart-on-chip technology could improve preclinical research, yet still lacks necessary complexity and validation. Patient-derived cardiac tissue, with preserved native tissue architecture and disease substrate, would provide an interesting model for studying drug (safety) effects in the actual pathological substrate.

Methods:
High-resolution optical voltage recordings were acquired of biopsies originating from appendages of patients undergoing cardiac surgery. Using a dynamic pacing protocol, action potential duration (APD) and conduction velocity (CV) were determined. Drugs were added to demonstrate modulation of these parameters. Simultaneous sharp electrode measurements of trabeculae were used to determine resting membrane potential (RMP). Biopsies were subjected to histological analyses of fibrosis, sarcomeric- and gap junctional proteins.

Results:
Right atrial biopsies (n=5) had an average RMP of -64.5 ± 7.4mV. Upon 1-Hz electrical stimulation, optical mapping revealed an APD80 of 268.8 ± 39.6ms and CV of 35.4 ± 12.5cm/s. Subsequent pharmacological modulation of the atrium-specific IK,Ach current by addition of 1μM Carbachol significantly shortened APD80 (~45% vs. baseline), whereas this effect was partly attenuated by addition of 300nM Tertiapin (~31% vs. baseline). DMSO (0.1%) as control had no significant effect on APD80. Immunohistochemistry revealed interstitial fibrosis, cross-striated cardiomyocytes stained for cardiac troponin and polar localization of connexin 43.

Conclusion:
Excised human atrial tissue can be used for complementary histological and electrophysiological studies in the context of drug screening, thereby providing new perspective for personalized disease modeling and drug therapy.
PROLONGED TPEAK-TEND INTERVAL IS A RISK FACTOR FOR SUDDEN CARDIAC DEATH IN ADULTS WITH CONGENITAL HEART DISEASE

J.T. Vehmeijer (AMC, Amsterdam); Z. Koyak (AMC, Amsterdam); W. Budts, (UZ Leuven); L. Harris (TCCCA, Toronto); B.J.M. Mulder (AMC, Amsterdam and NHI, Utrecht); J.R. de Groot (AMC, Amsterdam)

Purpose:
Adult congenital heart disease (ACHD) patients are at risk of sudden cardiac death (SCD). However, current risk stratification methods are not yet well-defined. The Tpeak-Tend interval (TpTe) is a measure of dispersion of ventricular repolarization, and a risk factor for SCD in non-ACHD patients. We analyzed the predictive value of TpTe for SCD in ACHD patients.

Methods:
From an international multicenter cohort of 25,790 ACHD patients, we identified 165 SCD cases. Cases were matched to 310 controls by age, gender, congenital defect and (surgical) intervention. TpTe was measured in one T-wave of each ECG lead on the last ECG before death in cases, and the ECG at the same age in controls. The mean (TpTe-mean) and maximum TpTe (TpTe-max) of all twelve ECG leads and TpTe dispersion were measured. Odds ratios were calculated using conditional logistic regression analysis.

Results:
ECGs were available for 146 cases (median age at death 33.5 years (quartiles 26.2, 48.0), 66% male) and 302 controls. The mean TpTe-max was 97±24ms in cases vs. 84±17ms in controls, TpTe-mean was 70±16ms vs. 63±10ms, and dispersion 51±22ms vs. 41±16ms, respectively. Assessing each ECG lead separately, TpTe in lead aVR predicted SCD most accurately. The mean TpTe in aVR was 71±23ms in SCD cases vs 61±13ms in controls. At a cutoff of 80ms, the adjusted odds ratio of a longer TpTe for SCD in aVR was 5.8 (95% CI 2.7-12.4, p<0.001). The odds ratios for SCD per 10ms increase of TpTe are presented in the figure.

Conclusion:
TpTe predicts sudden cardiac death in adults with congenital heart disease. Particularly TpTe in lead aVR, the mean TpTe and the TpTe dispersion appear to be of importance, and may add to current risk stratification methods for SCD in this young patient group.

Figure:
Figure: forest plot of univariable odds ratios for sudden cardiac death of TpTe measurements grouped per 10ms increase Mean TpTe and TpTe in aVR: <50ms, 50-59ms, 60-69ms, 70-79ms 80-89ms and ≥90ms Maximum TpTe: <70ms, 70-79ms, 80-89ms, 90-99ms, 100-109ms.

<table>
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<th>Per 10ms increase</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
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<td>TpTe in lead aVR</td>
<td>1.61</td>
<td>1.34, 1.92</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean TpTe</td>
<td>1.74</td>
<td>1.4, 2.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum TpTe</td>
<td>1.44</td>
<td>1.26, 1.65</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TpTe Dispersion</td>
<td>1.46</td>
<td>1.25, 1.72</td>
<td>&lt;0.001</td>
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<table>
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<tr>
<th>Longest vs. Shortest TpTe group</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
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<td>TpTe in lead aVR</td>
<td>9.46</td>
<td>3.13, 28.61</td>
<td>&lt;0.001</td>
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<tr>
<td>Mean TpTe</td>
<td>8.5</td>
<td>1.79, 40.28</td>
<td>0.007</td>
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<tr>
<td>Maximum TpTe</td>
<td>11.4</td>
<td>3.66, 35.52</td>
<td>&lt;0.001</td>
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<tr>
<td>TpTe Dispersion</td>
<td>4.25</td>
<td>2.07, 8.74</td>
<td>&lt;0.001</td>
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Session VI: Gender

SEX-SPECIFIC VERSUS UNIVERSAL CLINICAL DECISION LIMITS FOR TROПONIN I AND T FOR THE DIAGNOSIS OF ACUTE MYOCARDIAL INFARCTION: A SYSTEMATIC REVIEW

D.M. Kimenai; D.M. Kimenai (Maastricht UMC+, Maastricht); E.B.N.J. Janssen (Maastricht UMC+, Maastricht); K.M. Eggers (Uppsala University, Uppsala); B. Lindahl (Uppsala University, Uppsala); H.M. den Ruijter (University Medical Center Utrecht, University of Utrecht, Utrecht); O. Bekers (Maastricht UMC+, Maastricht); Y. Appelman (VU University Medical Center, Amsterdam); S.J.R. Meex (Maastricht UMC+, Maastricht)

Purpose:
The universal clinical decision limits of high-sensitivity cardiac troponin I (hs-cTnI, 26 ng/L) and T (hs-cTnT, 14 ng/L) may contribute to underdiagnosis of acute myocardial infarction in women. We performed a systematic review to investigate sex-specific and universal 99th percentiles of hs-cTnI and hs-cTnT derived from healthy reference populations.

Methods:
We searched in PubMed and EMBASE for original studies, and by screening reference lists. Reference populations designed to establish 99th percentiles of hs-cTnI(Abbott) and/or hs-cTnT(Roche), published between January 2009 and October 2017, were included. Sex-specific and universal 99th percentile values of hs-cTnI and hs-cTnT were compared with universal clinical decision ranges (hs-cTnI: 23.3-29.7 ng/L, hs-cTnT: 12.7-24.9 ng/L).

Results:
A total of 28 studies were included in the systematic review. Of 16 hs-cTnI and 18 hs-cTnT studies, 14 (87.5%) and 11 (61.1%) studies reported lower female-specific hs-cTn cut-offs than universal clinical decision ranges, respectively. Contrary, men-specific thresholds of both hs-cTnI and hs-cTnT were in line with currently used universal thresholds, particularly hs-cTnT (90% concordance). The variation of estimated universal 99th percentiles was much higher for hs-cTnI than hs-cTnT (29.4% versus 80.0% of hs-cTnI and hs-cTnT studies reported values within the current universal clinical decision range, respectively).

Conclusion:
Our data show substantially lower female-specific upper reference limits of hs-cTnI and hs-cTnT than universal clinical decision limits of 26 ng/L and 14 ng/L, respectively. The statistical approach strongly affects for the hs-cTnI threshold. Downwards adjustment of hs-cTn thresholds in women may be warranted, to reduce underdiagnosis of acute myocardial infarction in women.
MINOCA: THE IDENTIFICATION, CHARACTERIZATION AND PROGNOSIS OF A DUTCH COHORT

A.A. van de Bovenkamp; A.A. van de Bovenkamp, Y.V. Polyukhovych, V.J. van den Berg, M.T. Dirksen, V.A.W.M Umans

Purpose:
We aimed to identify the MINOCA’s characteristics and outcome.

Methods:
We retrospectively analyzed clinical and angiographic data of all consecutive (N)STEMI pts during a 4 year period (2013-17). We identified MINOCA’s using the definitions of 2016 ESC Position-Paper. The primary endpoint of this study was combined all-cause mortality and recurrent MI.

Results:
In 2833 consecutive (N)STEMI patients, 9 stress-cardiomyopathy, 11 myocarditis, 36 secondary and 124 (4.4%) MINOCA pts were identified. Patients with MINOCA were age-comparable (66 vs 66 years, \( p<0.05 \)) but the proportion of women was higher (62% vs 29%, \( p<0.001 \)) than the obstructive group. MINOCA group had more pts with none risk factors (25% vs 12%) and less pts with Dyslipidemia (28% vs 41%), but comparable incidence in IDDM 4% vs 5%, Hypertension 44%vs45% and Tobacco-use 30% vs 31%.

The GRACE score and creatinine levers were lower (124 vs 156 \( p<0.05 \), 73 vs 82 mol/l); the presence of ST deviation was less (19% vs 64% \( p<0.001 \)); max troponine was lower (2,9 vs 22,0 ug/l \( p<0.001 \)). Combined all-cause mortality and recurrent MI were not significantly different (figure 1).

Conclusion:
The incidence of MINOCA in the real world is high and contains a dominance of female pts. MINOCA pts appear to have a lower GRACE score and less renal impairment but their prognosis is not significantly better than pts with obstructive coronary artery disease. Further studies are necessary to offer mechanistic insights and the best management possible to those patients. We call for an extended multi-imaging modality MINOCA protocol.
Figures:
Purpose:
Depression and anxiety are more prevalent in patients with ischemic heart disease (IHD) and among women compared to men. Previous meta-analyses in populations with myocardial infarction suggest that women with IHD have higher levels of depression, but the cardiac prognosis is worse for men with depression. In our meta-analysis, we aim to assess sex and gender (S&G)-sensitive risks related to a broad range of psychosocial factors for the incidence and prognosis of a broad group of IHD outcomes. The study was funded by ZonMw and the Dutch Heart Foundation ‘Gender & Health’ program [Grant #849100001]

Methods:
A literature search was conducted using PubMed, EMBASE and PsycINFO. Studies examining psychosocial factors; depression, anxiety/panic disorder, social support, hostility (aggression, anger), personality (Type A, Type D, neuroticism), posttraumatic stress disorder, and psychological distress on the incidence or prognosis of IHD were included using Covidence. Authors of non-stratified studies are currently being asked to perform S&G-stratified analysis. The study has been registered in PROSPERO [#CRD42017067087].

Results:
The search resulted in 12,331 articles of which 669 were eligible after title-abstract, and 287 after full-text screening (figure. 1). Depression (64%) was the most examined psychosocial factor, followed by anxiety (26%). In total, 193 studies (67%) did not stratify for S&G, 33 (11%) studies reported for men only, 18 (6%) included only women, and 43 (15%) reported S&G-stratified. After contacting 158 authors (to date), we received stratified results from 32 (17%) non-stratified studies, 36 (19%) authors did not respond, and 49 (25%) were unable or unwilling to perform gender-stratified analyses. Studies examining patients with heart disease mostly focus on obstructive coronary artery disease, which are predominantly male. Data-extraction is pending.

Conclusion:
Most studies to date do not report sex and gender stratified findings, and there is a gender-bias in studies. Our findings concerning S&G-sensitive risks for IHD will contribute to increase awareness, improve prevention and healthcare, and guide S&G-sensitive interventions for incident IHD and adverse IHD progression.
Figure:
Flowchart of article selection (version January 2018)

Databases EMBASE + PubMed + PsycINFO
N = 20,460

11 Added after hand search

- 8,140 Duplicates removed

Title/abstract screening
N = 12,331

- 11,662 Non-relevant

Full-text screening
N = 669

- 382 Non-relevant:
  - Overlap with other study (126)
  - Design (94)
  - Outcome (68)
  - Predictor (51)
  - Non-English (29)
  - Population (11)
  - Duplicate (2)
  - Non-available (1)

Included
N = 287

193 (67%) Men and women not stratified
After contacting authors:
Received 32 (17%) stratified findings

43 (15%) Men and women stratified

126 (44%) Incidence IHD

161 (56%) Prognosis IHD

33 (11%) Men only

18 (6%) Women only
Purpose:
Half of adult patients with congenital heart disease (ACHD) use chronic medication. This study investigated the prevalence, risk factors, and contributing drugs to polypharmacy in ACHD, and its association with mortality.

Methods:
We identified patients from our nationwide ACHD registry and age- and sex-matched referents in a 1:10-ratio in the national Dispensed Drug Register and Cause of Death Register for the years 2006-2014. Drugs were classified according to the Anatomical Therapeutic Chemical classification, aggregated per year. Generalized estimating equations were used to determine associations between characteristics and polypharmacy, defined as ≥5 different dispensed drug types per year. Independent associations between baseline polypharmacy and mortality were analyzed using inverse probability weighted Cox regression.

Results:
Overall, 14138 ACHD patients (49% male, median age 35 years) were included, of which 29% had baseline polypharmacy, compared to 13% of referents (p<0.001). Cardiovascular drugs were most prevalent (42% vs 13%, p<0.001). Female sex (OR 1.92[1.88-1.96], p<0.001), older age (OR 1.81/10years [1.79-1.82], p<0.001), and ACHD severity, (OR 2.51[2.40-2.61], p<0.001; 3.22 [3.06-3.40], and 4.87 [4.41-5.38], p<0.001 for mild, moderate, and severe defects, respectively), were independently associated with polypharmacy during follow-up. Risk of polypharmacy increased more with age in men (Pinteraction<0.001) and severe ACHD (Pinteraction=0.001). During 7[IQR 5-8] years, 595 patients (4%) and 2375 referents (2%) died. Baseline polypharmacy was independently associated with mortality in ACHD(HR 2.87[2.53-3.25], P<0.001).

Conclusion:
Polypharmacy is common in ACHD. Female sex, defect severity, and older age, especially in men and severe ACHD, are associated with polypharmacy. Polypharmacy is associated with mortality. This underscores that these patients require care of specialists with knowledge on appropriateness of polypharmacy.
Figure:
Probability of polypharmacy by age for women (A) and men (B) during the study period, adjusted for age, sex, and congenital heart defect (CHD) severity.
DIFFERENCES IN HEART FAILURE TREATMENT BETWEEN MALES AND FEMALES IN THE NETHERLANDS: A SUBGROUP ANALYSIS OF THE CHECK-HF REGISTRY

J.J. Brugts (Erasmus MC, Rotterdam); J.J. Brugts (Erasmus MC, Rotterdam); J.F. Veenis (Erasmus MC, Rotterdam); H.P. Brunner-La Rocca (Maastricht UMC+, Maastricht); A.W. Hoes (UMC Utrecht, Utrecht); G.C.M. Linssen (Hospital Group Twente, Almelo and Hengelo); for the CHECK-HF investigators

Purpose:
The poor prognosis of chronic heart failure (HF) can be optimized by adherence of medical therapy according to the guidelines. The rate of drug prescription and dosage are often used as benchmark of quality of care. Data on gender differences in HF treatment are scarce. The purpose of this study was to evaluate gender differences in HF treatment in the Netherlands.

Methods:
The current analysis is part of a cross-sectional registry of 10,910 chronic HF patients at 34 Dutch outpatient clinics in the period of 2013 until 2016 (CHECK-HF). Demographic parameters, laboratory and echocardiographic values as well as medication use (type, dosage and frequency and total daily dose) were recorded.

Results:
We studied 8,360 patients with HF with reduced ejection fraction (HFrEF; 78.7%), of which 63.9% were male and 36.1% were female. Females were slightly older (71.6 vs. 73.4 years, male vs. female resp., \( p<0.01 \)), had more often a non-ischemic cause of HF (58.5% vs. 39.6%, \( p<0.01 \)) and hypertension (37.9% vs. 43.2%, \( p<0.01 \)), and eGFR was lower (61.4 vs. 56.6 ml/min/1.73 m², \( p<0.01 \)). Diabetes rates were equal between men and women (25.3% vs. 25.7%, \( p=0.72 \)). Current HF medication use is presented in Table 1. Females received less RAS-inhibitors and more beta-blocker, ivabradine and diuretics, independently of other factors. We observed a lower percentage of ICD and CRT-D, and more lifestyle interventions in females as compared to males.

Conclusion:
In this large registry of HFrEF patients, we observed significant differences in medical, device and lifestyle therapy between males and females.
Table 1. Gender and HF therapy in HFrEF

<table>
<thead>
<tr>
<th>Pharmacotherapy</th>
<th>Unadjusted analysis</th>
<th>Age adjusted analysis (OR [95% CI])</th>
<th>Multivariate analysis (OR [95% CI])*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
<td>Females</td>
<td>p-value</td>
</tr>
<tr>
<td>Beta-blocker, % (n=8181)</td>
<td>79.1</td>
<td>82.0</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RAS inhibitors, % (n=8181)</td>
<td>82.6</td>
<td>78.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>MRA, % (n=8181)</td>
<td>52.8</td>
<td>53.3</td>
<td>0.65</td>
</tr>
<tr>
<td>Ivabradine, % (n=6323)</td>
<td>4.2</td>
<td>5.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Diuretics, % (n=8181)</td>
<td>81.6</td>
<td>84.9</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td><strong>Device therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICD (n=6635)</td>
<td>35.5</td>
<td>22.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CRT D (n=6635)</td>
<td>18.4</td>
<td>14.5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Pacemaker (n=6635)</td>
<td>8.0</td>
<td>9.3</td>
<td>0.07</td>
</tr>
<tr>
<td><strong>Lifestyle therapy</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluid restriction (n=6724)</td>
<td>72.6</td>
<td>78.0</td>
<td>0.02</td>
</tr>
<tr>
<td>Sodium restriction (n=6728)</td>
<td>74.6</td>
<td>77.9</td>
<td>0.02</td>
</tr>
</tbody>
</table>

* Adjusted for ischemic cause of HF, age, hypertension and eGFR
DIAMETERS OF THE THORACIC AORTA: GENDER AND BODY SIZE INDEXED REFERENCE VALUES AND ASSOCIATION WITH ATHEROSCLEROTIC FACTORS

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Purpose:
Theoracic aorta dilatation is an important risk factor for aortic dissection, but it remains unclear whether its current reference values hold for both men and women. The aims of this study are to present gender and body size indexed reference values for thoracic aortic diameters and to identify atherosclerotic factors associated with aortic diameters.

Methods:
Between 2003 and 2006, adults aged ≥55 years from a population-based study underwent a non-enhanced multidetector computed tomography scan of the thorax. The diameters of the ascending aorta (AA) and descending aorta (DA) were measured double-oblique at level of the pulmonary artery bifurcation and indexed for height, weight and body surface area. Factors associated with aortic diameter were detected with use of multivariable linear regression.

Results:
A total of 2505 participants (1208 men, age 69.1±6.8 years) were included. We found a small increase with age between 55-65 and ≥75 years for the AA diameter (0.6±0.2 mm, p=0.003) and DA diameter (1.5±0.2 mm, p<0.001). The smallest difference in the aortic dimensions between men and women was found when adjusting for height (AA +1.7%; p<0.001 and DA - 0.9%; p=0.014, figure). More atherosclerotic factors (hypertension, smoking, alcohol consumption and calcification of coronaries and aortic arch) were associated with the DA compared to AA.

Conclusion:
Our results suggest that the definition currently used for aortic dilatation (≥40mm) does not account for persons ≥55 years. Because height-indexed values best correct for the difference in aortic dimensions between men and women, this could be considered as standard.
Figure:
Gender differences of absolute aortic diameter and indexed for height, weight and body surface area.

<table>
<thead>
<tr>
<th></th>
<th>Ascending aorta</th>
<th>Descending aorta</th>
</tr>
</thead>
<tbody>
<tr>
<td>95th percentile absolute diameters (mm)</td>
<td>44.0</td>
<td>41.0</td>
</tr>
<tr>
<td>95th percentile height-indexed values (mm/m)</td>
<td>25.0</td>
<td>25.4</td>
</tr>
<tr>
<td>95th percentile weight-indexed values (mm/kg)</td>
<td>0.57</td>
<td>0.64</td>
</tr>
<tr>
<td>95th percentile BSA-indexed values (mm/m²)</td>
<td>22.4</td>
<td>24.0</td>
</tr>
</tbody>
</table>
THE PROGNOSTIC VALUE OF ST-2 IN ADULTS WITH CONGENITAL HEART DISEASE

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Purpose:
Soluble suppression of tumorigenicity-2(ST-2) is upregulated as a response to myocardial stress and is associated with adverse events in chronic heart failure patients. This study aimed to investigate the association between ST-2 and adverse cardiovascular events in adults with congenital heart disease(CHD).

Methods:
This is a prospective cohort study. ST-2 and NT-proBNP was measured for research purposes in consecutive stable adults with CHD visiting the outpatient clinic between April 2011 and April 2013. Patients were prospectively followed by annual evaluation at the outpatient clinic. The study endpoint was a composite of mortality, heart failure, hospitalization, arrhythmia, thromboembolic events and re-intervention. We performed multivariable Cox proportional-hazards regression to identify the association between ST-2 level and the study endpoint, adjusted for age, sex and NT-proBNP level.

Results:
We included 590 patients with a ST-2 measurement (median age 33[IQR 25-41] years, 42% female, 90%NYHA class 1), with a diagnosis of tetralogy of Fallot (n=176), congenital aortic stenosis (n=133), aortic coarctation (n=109), arterial switch operation (n=24), Mustard operation (n=65), congenitally corrected transposition of the great arteries (n=20), Fontan (n=36) or other (n=27). Follow-up data was available in 585 patients and 195 reached the endpoint (median follow-up 48.9[IQR 31.7-55.8] months). ST-2 was strongly associated with the incidence of the study endpoint after 5 years of follow-up: 27% patients with ST-2<18mg/mL reached the endpoint versus 40-44% in those with values >24.3mg/mL (figure). A twofold-increase in ST-2 was associated with a 32% increased risk of the study endpoint (adjusted HR 1.32, 95%CI 1.06-1.65, p=0.014).

Conclusion:
Serum ST-2 level is associated with adverse cardiovascular events in adults with CHD and provides incremental prognostic information beyond the established biomarker NT-proBNP.
Figure:
Cumulative event-free survival for ST-2 quartiles in adults with congenital heart disease.

Log rank: p=0.004

- First quartile (<18.0 mg/mL, n=145)
- Second quartile (18.0-24.3 mg/mL, n=149)
- Third quartile (24.3-32.2 mg/mL, n=147)
- Fourth quartile (> 32.2 mg/mL, n=144)
SACUBITRIL/VALSARTAN IMPROVES LEFT VENTRICULAR FUNCTION IN THE MAJORITY OF HEART FAILURE PATIENTS WITH REDUCED EJECTION FRACTION.

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Purpose:
To investigate if treatment with sacubitril/valsartan improves EF.

Methods:
This was a single centre trial. Patients received sacubitril/valsartan according to the latest ESC heart failure guideline. The EF was measured by cardiac ultrasound before the start of sacubitril/valsartan and 6-12 weeks after reaching the maximum tolerated dose of sacubitril/valsartan=optimal medical treatment (OMT).

Results:
A total of 27 patients were analysed. They had an average age of 65 years, 74% were male. Ischemic cardiomyopathy was the cause of heart failure in 59%.
After reaching OMT there was an increase of the EF in 59% of the patients, 30% had a stable EF and 11% had a decrease of the EF.
The average EF increased from 28% before starting sacubitril/valsartan to 36% after OMT ($p=0.0015$).

Conclusion:
Sacubitril/valsartan improves left ventricular function in 59% of the patients. The EF increased from 28 to 36%.
THE EFFECT OF MOBILE HEALTH ON CLINICAL MANAGEMENT IN GROWN-UP CONGENITAL HEART DISEASE PATIENTS: A PILOT STUDY

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Purpose:
Previous studies on telemonitoring in acquired heart failure (HF) have shown conflicting results with poor adherence. Grown-up congenital heart disease (GUCH) patients, prone to HF and relatively young of age, seem an appropriate population for mobile health (mHealth). Furthermore timely intervention prevents clinical deterioration. The aim of this study is to evaluate whether telemonitoring through mHealth in GUCH patients reduces HF-related emergency hospitalizations.

Methods:
Symptomatic GUCH patients were enrolled in the HeartGuard program, an mHealth telemonitoring program that evaluates blood pressure (BP) and weight twice a week. Data was matched with individualized thresholds. If data exceeded thresholds consecutively (≥2), patients were contacted by their cardiologist for treatment adjustments or reassurance. If data was missing, patients received an app notification. Adherence was registered.

Results:
So far, 24 symptomatic GUCH patients (median age 41 years (range 19-66), 42% male and CHD severity of mild (1), moderate (15) and severe (8)) were included, 14 patients experienced HF NYHA class ≥II, 15 had palpitations and arrhythmias and four had hypertension. Mean follow-up was 4.4 months, mean adherence was 96%. One patient improved in functional class by dose increase of diuretics after consecutive threshold exceeding weight measurements (2). In three patients antihypertensive treatment was successfully adjusted. During follow-up there were no HF-related emergency hospitalizations, contrary to the six months before inclusion where two patients had emergency hospitalizations (p=0.151).

Conclusion:
The first results of the HeartGuard program for GUCH patients demonstrated very good adherence compared to previous studies and suggest a tendency towards a reduction of HF-related emergency hospitalizations.
A MULTI-SITE CORONARY SAMPLING STUDY ON CRP IN NON-STEMI: NOVEL INSIGHTS ON THE INFLAMMATORY PROCESS IN ACUTE CORONARY SYNDROMES

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Purpose:
C-reactive protein (CRP) is frequently elevated in patients with non-ST elevation myocardial infarction (NSTEMI). However, controversy remains if CRP is predominantly produced or used by the heart. We therefore aimed to assess concentrations of CRP in NSTEMI patients using multiple sampling sites, to enable measurement of systemic, trans-culprit and trans-cardiac gradients.

Methods:
42 Troponin positive NSTEMI patients with significant coronary artery disease were included. Systemic arterial and venous blood was obtained, and right sided catheterization was performed to sample blood from the coronary sinus (CS). In suitable patients, an additional blood sample was collected from the culprit coronary artery distal to the culprit lesion. Six hours post procedure blood was obtained from the antecubital vein. CRP concentrations were compared between the sampling sites.

Results:
The median CRP concentrations in the arterial and venous blood were high and not significantly different. The median CRP concentrations between blood collected from the culprit coronary artery distal to the culprit lesion and the systemic arterial circulation were not significantly different (4.56mg/L to 4.59mg/L, respectively, n=14; p=NS). CRP concentrations in the CS were significantly lower (table). Systemic CRP concentrations six hours post procedure were significantly higher (5.35mg/L vs 4.97mg/L; p<0.001).

Conclusion:
In this series of patients with ongoing NSTEMI a trans-cardiac decrease in CRP to the coronary sinus was observed on a background production of systemic CRP over time. In addition, we found similar concentrations proximal and distal to the culprit lesion. These observations support an extra-cardiac source of CRP and suggest myocardial uptake.

Figure:
MEDICATION VERIFICATION USING THE LANDELIJK SCHAKEL PUNT (LSP) IN HEART FAILURE PATIENTS

M.S.A. Aertsen-van der Kuip (Diakonessenhuis, Utrecht/Zeist); C.E.E. van Ofwegen-Hanekamp (Diakonessenhuis, Utrecht/Zeist); N.A.E.M. van Lent-Evers (Diakonessenhuis, Utrecht/Zeist); L.R. Denee-Haasnoot (PharmD)

Purpose:
Pharmacological treatment improves the functional capacity, quality of life and reduces mortality in chronic heart failure. Comorbidity results in polypharmacy and multiple doctors being involved in the treatment of heart failure patients. The ‘Landelijk Schakel Punt’ (LSP), is a secured network allowing electronic data-sharing, like medication delivered by the pharmacy. The aim of our study is to investigate whether LSP is useful and reliable for improving multidisciplinary medication management in heart failure patients.

Methods:
Data were collected during regular visits at the outpatient heart failure clinic. The Electronic Patient Record (EPR) medication registration was compared to LSP information. The study analysed whether data of the LSP registration was available and whether medication registration in the EPR and LSP corresponded.

Results:
Hundred patients (n=100) were enrolled. Medication data could be retrieved in 99 patients, one patient did not consent to LSP data-sharing. In 22 patients LSP medication corresponded with EPR registration. In 77 patients discrepancies were found, in 54 patients it concerned cardiac medication. In 31 patients medication was not registered in LSP. In 19 patients medication was not registered in LSP. In 4 patients EPR data was not correct. Main reasons for inconsistencies were dose adjustment not mentioned in LSP and medication not delivered in the last 3 months being inactive in LSP.

Conclusion:
The value of the LSP for medication safety and management is promising, however improvements in the system are necessary to increase reliability.
EFFECT OF SHORT-TERM FASTING ON ELECTROCARDIOGRAPHIC PARAMETERS

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Purpose:
Electrocardiograms (ECGs) of healthy volunteers are frequently evaluated during early clinical drug development trials to screen for possible cardiac adverse reactions. Volunteers are required to be in a fasting state for multiple hours before dosing. However, the effect of the duration of fasting on electrocardiographic parameters is largely unknown. We compared the effects of a 4-h or 10-h fasting period on standard 12-lead electrocardiographic recordings.

Methods:
ECGs from 432 healthy subjects (mean age 28.5±12.5; 88.9% male) after 4 and 10-hour fasting were available. All ECGs were automatically analyzed for conduction intervals and wave amplitudes with the Marquette 12SL algorithm and compared among fasting duration. Mixed model analyses were used to identify confounding variables.

Results:
We compared two ECGs per healthy subject (n=432) respectively after 4-h and 10-h fasting. After 10-h fasting, mean P wave duration and amplitude were reduced by 1.95±1.48ms and 2.18±2.75µV, mean R wave and S wave amplitude were decreased by 25.83±31.16µV and -55.39±78.72µV, mean QRS duration was decreased by 1.84±6.61ms and mean T wave duration and amplitude were decreased by 2.06±0.72ms and 9.36±17.21µV. The mean PR interval was prolonged by 5.10±12.54ms and the mean QT interval by 4.27±20.63ms. The ventricular rate was reduced by 3.64±8.61bpm, QTcF was reduced by 3.87±14.50ms. These observations persisted after correction for demographics, electrolytes, blood pressure, heart rate variability and diurnal variation.

Conclusion:
The present study showed that several electrocardiographic parameters have changed after 10-h fasting compared to 4-h fasting, consisting of a reduced wave amplitude and duration and increased isoelectric interval duration.
LEFT VENTRICULAR REMODELLING AND PROGNOSIS AFTER DISCHARGE IN PATIENTS ADMITTED WITH ACUTE DE NOVO HEART FAILURE

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Purpose:
The aim of this study was to investigate the left ventricular (LV) remodelling and prognosis of patients admitted with de novo heart failure (HF) with ischaemic and non-ischaemic aetiology.

Methods:
We included patients that were discharged after admission for acute de novo HF in the period 2008 through 2016. Exclusion criteria were: history of cardiac disease, left ventricular ejection fraction (LVEF) >40% at admission and heart transplantation (HTx) or left ventricular assist device (LVAD) implantation during admission. LV remodelling was assessed by serial measurement of the LVEF by echocardiography. The prognosis was considered as the HTx/LVAD-free survival.

Results:
We included 112 patients (mean age 49 ± 14 years, 55% male, 39% ischemic HF) with de novo HF. During admission, 53 (47%) patients needed vasoactive medication and 25 (22%) patients needed mechanical circulatory support. The median LVEF at discharge was 28% (IQR 22-36). In patients with ischaemic HF, there was no improvement in LVEF (p=0.19) during the first six months (figure). In contrast, patients with non-ischaemic HF showed significant remodelling with improved LVEF (p<0.001; Figure) in the first half year after discharge. During the median follow-up of 4.6 years, HTx/LVAD-free survival was 90% for patients with non-ischaemic HF and 86% for patients with ischaemic HF (p=0.52).

Conclusion:
Patients with de novo HF with non-ischaemic aetiology had significant LV remodelling while this was not observed in their ischaemic counterparts. Overall, the prognosis of patients discharged after admission for acute de novo HF was better than reported in large registries including acute decompensated chronic HF.
Figure:
Trends over time of the left ventricular ejection fraction. Separate lines were plotted for patients with ischaemic heart failure and patients with non-ischaemic heart failure. Data reported in median (IQR) HF, heart failure; LVEF, left ventricular ejecti
MYOCARDIAL ADAPTATION AFTER SURGICAL THERAPY DIFFERS FOR AORTIC VALVE STENOSIS AND HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

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Purpose:
Surgical therapies in aortic valve stenosis (AVS) and hypertrophic obstructive cardiomyopathy (HOCM) aim to relief intraventricular pressure overload and improve clinical outcome. It is currently unknown to what extent myocardial adaptation concurs with restoration of intraventricular pressures, and whether this is similar in both patient groups. The aim of this study was to investigate changes in myocardial adaptation after surgical therapies for AVS and HOCM.

Methods:
Ten AVS and ten HOCM patients were prospectively enrolled and underwent cardiac magnetic resonance (CMR) cine imaging and myocardial tagging prior to, and four months after aortic valve replacement (AVR) and septal myectomy, respectively. Global left ventricular (LV) analyses were derived from cine images. Circumferential strain was assessed from myocardial tagging images at the septal and lateral wall of the mid ventricle.

Results:
Pressure gradients significantly decreased in both AVS and HOCM after surgery (p<0.01), with a concomitant decrease in left atrial volume (p<0.05) suggesting lower diastolic filling pressures. Also, LV volumes, mass and septal wall thickness decreased in both, but to a larger extent in AVS than in HOCM patients (p<0.05 for difference). AVR improved wall thickening (p<0.05) and did not change systolic strain rate. Myectomy did not affect wall thickening and reduced septal systolic strain rate (p=0.03).

Conclusion:
Both AVR and myectomy induced positive structural remodeling in line with a reduction of pressure overload. A concomitant recovery in systolic function however was found in AVR only. The systolic functional deterioration in HOCM patients seems to be inherent to myectomy and the ongoing and irreversible disease.
ADDED VALUE OF PRE-HOSPITAL TROPOGIN ASSESSMENT IN PATIENTS WITH SUSPECTED NON-ST ELEVATION MYOCARDIAL INFARCTION

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Purpose:
Pre-hospital risk stratification in patients with suspected non-ST elevation Myocardial Infarction (non-STEMI) could accelerate pre- and in-hospital logistics. The HEART score appeared to adequately identify patients at low risk and is fully assessable outside the hospital since the development of point of care (POC) troponin tests. However, the added value of troponin measurement to a pre-hospital HEART score has not yet been assessed.

Methods:
A prospective observational study including 700 patients with suspected non-STEMI. Risk stratification by using the HEART score was performed by paramedics, low-risk was defined as HEAR or HEART score ≤ 3. Troponin was measured by a Roche CARDIAC POC troponin T test on the cobas h 232 POC system. Troponin < 40 ng/L was scored 0 points, troponin ≥ 40 ng/L was scored 2 points. Primary endpoint was occurrence of MACE within 45 days after inclusion.

Results:
Mean HEAR score was 4.5 (SD 1.6), mean HEART score was 4.7 (SD 1.7). Using the HEAR score, a total of 183 patients (26.1%) were stratified as low risk, whereas using the HEART score, 172 patients (24.6%) were stratified as low risk (p<0.001). Using HEAR, in the low risk group MACE occurred in 13 patients (7.1%, p<0.001) without deaths. Using HEART, in the low-risk group MACE occurred in 5 patients (2.9%), without deaths. The use of HEART (AUC 0.74) obtained a higher predictive value compared to HEAR (AUC 0.65, p<0.001) for MACE.

Conclusion:
In patients with suspected non-STEMI, pre-hospital troponin measurement has important added predictive value.