Abstracts of the Scientific Spring Congress of the Netherlands Society of Cardiology
6-7 April 2017

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 6 and 7 April 2017 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
THE RELATIONSHIP BETWEEN CONTRAST-FLOW QUANTITATIVE FLOW RATIO AND ISCHEMIA ASSESSED BY SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY MYOCARDIAL PERFUSION IMAGING

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Purpose:
A new method has been developed to calculate fractional flow reserve (FFR) from invasive coronary angiography, the so-called “contrast-flow quantitative flow ratio (cQFR)”. Recently, cQFR was compared to invasive FFR in intermediate coronary lesions showing an overall diagnostic accuracy of 85%. The purpose of this study was to investigate the relationship between cQFR and ischemia assessed by single-photon emission computed tomography myocardial perfusion imaging (SPECT MPI).

Methods:
Patients who underwent SPECT MPI and coronary angiography within 3 months were included in the study. cQFR computation was performed offline, using a software package. cQFR computation was based on 3D quantitative coronary angiography (QCA) and computational fluid dynamics. The standard 17-segment model was used to determine the vascular territories. Myocardial ischemia was defined as a summed difference score ≥2 in a vascular territory.

Results:
224 coronary arteries were analysed in 85 patients who underwent SPECT MPI and coronary angiography. Overall accuracy of cQFR to detect ischemia on SPECT MPI was 90%. In multivariable analysis, cQFR was independently associated with ischemia on SPECT MPI (OR 1.10; 95% CI 1.04-1.18), whereas clinical and QCA parameters were not. Furthermore, cQFR showed significant incremental value for the detection of ischemia compared to clinical and QCA parameters (global chi square 48.7 to 62.6; p <0.001).

Conclusion:
A good relationship between cQFR and SPECT MPI was found. Before cQFR can be adopted online in the catheterization laboratory as a potential alternative for invasive FFR, larger validation and outcome studies are needed.
AUTOMATED SPECT ANALYSIS COMPARED TO EXPERT VISUAL SCORING FOR THE DETECTION OF CORONARY ARTERY DISEASE

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Purpose:
Traditionally, the interpretation of myocardial perfusion imaging (MPI) is based on visual analysis. A computer-based automated analysis might be a simple alternative obviating the need for extensive reading experience. Therefore, the aim of the present study is to compare the diagnostic performance of automated analysis with expert visual reading for the detection of obstructive coronary artery disease (CAD) taking invasive coronary angiography with fractional flow reserve (FFR) as a reference.

Methods:
206 Patients (64% men, age 58.2 ± 8.7 years) with suspected CAD were prospectively included. All patients underwent stress-rest 99mTc-tetrofosmin single-photon emission computed tomography (SPECT) and invasive FFR measurements. Noncorrected (NC) and attenuation-corrected (AC) SPECT images were analyzed both visually by a blinded expert as well as automatically by commercially available SPECT software. Automated analysis comprised a segmental summed stress score (SSS), summed difference score (SDS), stress total perfusion deficit (S-TPD), and ischemic total perfusion deficit (I-TPD), representing the (reversible) extent and severity of hypoperfused myocardium. Subsequently, software was optimized with an institutional normal database and thresholds.

Results:
Visual reading sensitivity (56.5%) did not differ significantly from automated scoring parameters, except for SDS, which was significantly higher (p <0.001). Specificity, however, was significantly higher for visual reading (93.9%) as compared to any of the automated scoring (p <0.001 for all). Diagnostic accuracy was significantly higher for visual scoring (77.2%) in comparison with all NC images (p <0.05), although not in comparison with SSS AC and S-TPD AC (69.8% and 71.2%, p = 0.063 and p = 0.134). After the automated software optimization, diagnostic accuracies in the validation cohort were equal for visual (73.8%) and automated analysis. Among the automated parameters, S-TPD AC revealed the highest accuracy (73.5%, p = 1.000).

Conclusion:
Automated analysis of myocardial perfusion SPECT can be as accurate as visual interpretation by an expert reader for the detection of significant CAD defined by FFR.
SCAR TRANSMURALITY AND COMPOSITION DERIVED FROM LGE MRI PREDICTS VT IN POST-INFARCT PATIENTS

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Purpose:
Patients after myocardial infarction (MI) are at risk for reentrant VTs facilitated by inhomogeneous scar tissue, which may not be restricted to the infarct borderzone. We hypothesize that a higher degree of inhomogeneity of the total scar is associated with VT. We propose a new LGE MRI derived method to evaluate scar composition.

Methods: Consecutive pts with LGE MRI prior to ICD implantation were enrolled. From MRIs, total scar, scar borderzone, transmurality, and composition were derived. Scar composition is characterized by the entropy of probability distribution of signal intensity within tissue. Pts were followed for ICD therapy and mortality.

Results:
A total of 174 pts (64 ±10 yrs, 85% male, EF 31±9%) were enrolled. Appropriate ICD therapy occurred in 54 pts (31%); during a median follow up of 53 (IQR40-72) months 44 pts died. Multivariate Cox hazard analysis showed that 50-75% scar transmurality (HR2.3; CI 1.3-4.0; P=0.003), and higher entropy of scar (HR2.2; CI1.2-4.1; p=0.008) but not scar borderzone were associated with VT, independent of total scar and EF. Pts who died had a lower EF, broader QRS, more often prior CABG, renal failure and diabetes. In multivariate analysis renal failure (HR 2.7; CI 1.4-5.0; p=0.003) and, of interest, the entropy of the LV remote from scar (HR 1.8; CI 1.1-2.9; p= 0.03) were associated with mortality, independent from borderzone and LVEF.

Conclusion:
Post MI scars with 50%-75% transmurality and high tissue inhomogeneity assessed by SI entropy are associated with VT, independent of EF. High entropy of remote myocardium is associated with mortality.
Figure 1: Examples of a short-axis MRI slide and signal intensity histogram in a pt with VTs (A) and without VTs (B) with a matching scar size and transmurality. Histograms displaying the distribution of signal intensity within the myocardium. Signal intensities derived from scar areas are outlined in grey. The entropy within the scar is 8.5 for the pt with VT and 7.9 for the pt without VT.
Purpose:
Left atrium (LA) dilatation is predictive for complications in a multitude of cardiac diseases, therefore adequate assessment is essential. Technological advances have made it possible to quantify LA function with Speckle Tracking Echocardiography (STE) however, there are currently no recommendations for normal values with regard to LA function. This study aimed to establish reference ranges for LA myocardial and volumetric function and investigated correlations with baseline characteristics.

Methods:
In 147 (aged 20 to 72) healthy individuals LA reservoir function was assessed using peak strain in LA relaxation (LA-strain), conduit function using peak strain rate in early LA contraction (LA-SRe) and pump function using peak strain rate in late LA contraction (LA-SRa) with the QRS-onset as reference point. LA volumetric function was calculated with the Method-of-Disk summation technique.

Results:
Mean LA-strain was 39.7±6.2%, LA-SRe -2.78±0.62s-1 and LA-SRa -2.56±0.62s-1. Subjects were divided in 5 age-groups (each 50% female). LA-strain and LA-SRe were lower in the older age groups, whereas LA-SRa was higher (figure 1). Age proved to be an independent predictor for LA-SRa after correcting for blood pressure and heartrate. LA expansion index and passive emptying fraction decreased with age, while active emptying fraction increased with age.

Conclusion:
This study provides echocardiographic reference ranges for the three phasic functions of the LA, assessed with STE and volumetric measurements. Influences of age have been analyzed and emphasize the need for age-specific reference ranges, which have been provided accordingly.
Figures:
LA: Left atrium, STE: Speckle tracking echocardiography, Sre: early strain rate peak, Sra: active strain rate.
Purpose:
Coronary calcium score (CCS) accurately risk stratifies stable patients with acute chest pain. Zero CCS (ZCCS) is associated with an excellent long-term outcome. However cardiac events do occur in these patients. To evaluate the prevalence of significant coronary artery diseases (CAD) in patients with a ZCCS and to explore risk factor predicting significant CAD in patients with a ZCCS.

Methods:
Retrospective single-centre cohort study of 935 patients with a ZCCS. In all patients routinely a coronary computer tomography angiography (CCTA) was also performed.

Results:
Based on CCTA findings a total of 46 patients (5%) underwent invasive coronary angiography (CAG). Compared to the 889 patients who did not undergo CAG, patients were more often male and had a positive family history for premature CAD. Other (traditional) risk factors did not differ between groups. A total of 27 patients (59%) out of the 46 patients referred for CAG had significant CAD and underwent a revascularisation strategy. This subgroup only differed in BMI.

Conclusion:
In our study population about 3% of patients with ZCCS had a clinical indication for revascularization. When compared to patients who were not referred for CAG, revascularized patients differed in gender and family history, not in traditional risk factors. CCTA is valuable in detecting significant CAD in patients ZCCS.
TRICUSPID REGURGITATION REDUCES SUBSTANTIALLY AFTER PERCUTANEOUS ATRIAL SEPTAL DEFECT CLOSURE IN YOUNGER PATIENTS WITHOUT ATRIAL ARRHYTHMIAS

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Purpose:
In adults with secundum atrial septal defect (ASD) functional tricuspid regurgitation (TR) can occur due to right atrial and -ventricular dilatation by left-to-right shunting. Simultaneous tricuspid valve repair is often considered in ASD patients with TR who are candidates for surgical ASD closure. Successful percutaneous ASD closure causes significant reverse remodeling, however it remains unknown in which patients this reduces TR severity.

Methods:
A total of 106 patients (25% male, mean age 49±16 years) with successful percutaneous ASD closure had complete transthoracic echocardiography at both baseline and median follow-up (FU) of 6-months. TR was qualitatively assessed (grade 1-4). Quantitative right heart volumes/ function and end-diastolic TV annulus diameter (TAD) were measured blinded to the outcome. All parameters were revised by an independent investigator.

Results:
Pre-procedural TR was present in 48/106 patients (45%; n=25 mild, n=16 moderate, n=7 severe). At follow-up TR remained in 41 patients (39%; n=27 mild, n=9 moderate, n=5 severe). 15/48 (31%) patients resolved to no TR at follow-up (p<0.001). Overall, mean TR severity significantly reduced at FU (p<0.05) and TR grades 3-4 reduced ≥1 grade in 11/23 patients (48%). TR prevalence at FU was related to presence of atrial arrhythmia (χ²=7.3; p<0.01) and age ≥60 years (χ²=9.3; p<0.01). TAD significantly decreased at FU independent of TR severity, however ΔTAD was less prominent in TR grade 3-4 vs grade 1-2 (1.2% resp. 7.3%; p<0.05).

Conclusion:
Our data show that TR reduces substantially in all post-closure ASD patients regardless of pre-procedural TR severity, however less likely in patients with atrial arrhythmia or age ≥60 years. Hence, patients with secundum ASD below 60 years of age and without atrial arrhythmias should be considered for percutaneous closure as first line of treatment.
Session II: Electrofysiology

SIX YEAR FOLLOW-UP OF THE INITIAL DUTCH SUBCUTANEOUS IMPLANTABLE CARDIOVERTER-DEFIBRILLATOR COHORT: LONG TERM COMPLICATIONS AND BATTERY LONGEVITY

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Purpose:
The purpose of this study is to present the first long term data on S-ICD performance.

Methods:
Follow-up (FU) data of all patients implanted between December 2008 and April 2011, and previously described in the initial Dutch S-ICD cohort, were collected. Complications were defined as device related complications requiring surgical intervention. Kaplan-Meier estimates for complication rates, with corresponding confidence intervals (CI), were calculated.

Results:
All 118 patients of the initial Dutch cohort were included. Median FU was 6.0 years (IQR 5.6-6.5 years) in this cohort. Short term complication rate (0-30 days) was 3% (CI 0-6%). Long term complication rate (>30 days) was 12% (CI 6-18%), corresponding with an annual complication rate of 2%. One patient in this cohort needed a transvenous ICD (TV-ICD) in order to provide bradycardia pacing (1%). Six patients were implanted with a TV-ICD after experiencing an S-ICD complication for which extraction was necessary. Eleven patients, continued with S-ICD therapy after a complication. Eight patients had a local ICD related infection. No lead failures occurred. The majority, 74 (63%) patients, received an elective generator replacement. Two patients had a complication related to generator replacement requiring surgical intervention. Median battery longevity in this cohort was 5.7 years (IQR 5.3-6.0).

Conclusion:
This S-ICD cohort represents the longest follow-up to date and shows a low annual complication rate without lead failures or systemic infections. Battery longevity of the first S-ICD generation results in relative early generator replacement. Outcomes in this initial cohort include the early phase of the implanters learning curve.
RISK STRATIFICATION IN PATIENTS WITH CATECHOLAMINERGIC POLYMORPHIC VENTRICULAR TACHYCARDIA

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Purpose:
Patients with catecholaminergic polymorphic ventricular tachycardia (CPVT) are at risk for life-threatening cardiac events (CEs). Here, we evaluate the incidence of and risk factors for CEs at follow-up in a large cohort of CPVT patients.

Methods:
Baseline and follow-up (FU) data of all CPVT patients from 21 centers worldwide were collected and analyzed. CEs included syncope, appropriate ICD shock, aborted cardiac arrest (ACA), and sudden cardiac death. Fatal or near fatal events (nFEs) included all CEs except for syncope.

Results:
We included 727 patients (46% male, 41% proband), of whom 350 (48%) were symptomatic at baseline. Median age at diagnosis was 16.6 years (IQR 9.5-38.1). One hundred one patients (14%) had a CE and 68 patients (9%) a nFE during a median FU of 5.3 years (IQR 2.1-9.5). Yearly incidences of CEs and nFEs were 2.6% and 1.4%, respectively. Among asymptomatic patients at baseline, 11 (1.5%) had a CE and six (0.8%) a nFE (yearly incidences of 0.6% and 0.3%, respectively). Independent risk factors for CEs and nFEs were being a proband (HR 2.4, p=0.02; and HR 3.7, p=0.02, respectively), and ACA before diagnosis (HR 3.3, p=0.01; and HR 4.6, p=0.02, respectively). Age at diagnosis was a significant independent predictor for CEs only (HR 0.98 per year, p=0.04).

Conclusion:
The risk of cardiac events after diagnosis was significant for symptomatic patients (2.6%/year), but low in non-probands and asymptomatic patients (<1%/year). Probands and patients diagnosed at an early age or after an ACA are at highest risk of CEs.
LED-BASED TERMINATION OF VENTRICULAR ARRHYTHMIAS IN THE ADULT RAT HEART UPON OPTOGENETIC ENGINEERING: TOWARDS BIOLOGICAL SHOCKLESS DEFIBRILLATION

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Purpose:
Current treatment options for ventricular tachyarrhythmias (VTs) rely on modulation of cardiac electrical function through drugs, ablation or electroshocks, which are all rather unspecific, irreversible or traumatizing interventions. Optogenetics, in contrast, is a novel biological technique allowing electrical modulation in a specific, reversible and trauma-free manner using light-gated ion channels. The purpose of this study was to determine the feasibility and requirements for termination of monomorphic and polymorphic VTs in the whole heart.

Methods:
Cardiotropic adeno-associated virus (AAV) vectors encoding the light-gated ion channel red-activatable channelrhodopsin (ReaChR) were systemically injected in the tail vain of adult Wistar rats (n=11). Four weeks later, VTs were induced in the optogenetically modified hearts by electrical burst pacing in a Langendorff setup, followed by programmed, local epicardial LED illumination.

Results:
Systemic delivery of AAV vectors encoding ReaChR resulted in cardiomyocyte-restricted transgene expression with an average ventricular transduction rate of 93±4%. A single 470-nm light pulse (1000 ms, 2.97 mW/mm²), illuminating 125 mm² of the ventricular surface, terminated 96% of monomorphic and 52% of polymorphic VTs vs 0% without illumination. Optogenetic termination rate of polymorphic VTs increased to 89% (p=0.029) when the ventricular illumination area was enlarged to 250 mm², while light pulse intensity and duration remained unchanged.

Conclusion:
Brief epicardial LED illumination of the optogenetic modified heart evoked depolarizing photocurrents which were sufficient to terminate both monomorphic and polymorphic VTs in an effective and repetitive manner. Optogenetic arrhythmia termination could open the way to pain-free cardiac defibrillation, as it would make extraneous high-voltage shocks obsolete.

Figure 1:
Intra-cardiac electrogram readout demonstrating successful termination of a polymorphic VT with a single 1000-ms local light pulse (blue line) onto the epicardial surface.
Purpose:
Patient selection in cardiac resynchronisation therapy (CRT) currently relies on QRS duration and left bundle branch block (LBBB) morphology. Significant non-response rates imply suboptimal patient selection. The purpose of this study is to compare the value of a new ECG-parameter; QRS area to that of traditional QRS duration and LBBB morphology.

Methods:
In a multicentre cohort of 1,946 patients implanted with a CRT device between 2001 and 2015, baseline and outcome data was collected. QRS area was calculated by converting the digital 12-lead ECG to a vectorloop and taking the root of the sum of squared QRSAREA in X-, Y-, and Z-direction. Primary endpoint (LVAD, cardiac transplantation, all-cause mortality) was available in 1,486 patients. Secondary endpoints were Heart failure hospitalisation and echocardiographic reverse remodelling.

Results:
Kaplan Meier curves for survival free from the primary event show significant differences for patients stratified according to both QRS duration, LBBB morphology and QRS area. QRS area showed the strongest association with the primary endpoint; HR 0.45, 95%CI [0.36, 0.56]. (Figure 1.) Multivariable cox regression analyses proved QRSAREA to be the only independent electrocardiographic determinant associated to the occurrence of the primary endpoint (HR 0.52; 0.37-0.75) HF hospitalisation and echocardiographic reverse remodelling were also significantly associated with QRS area, and QRS area was the only independent determinant associated after multivariable correction.

Conclusion:
Baseline QRS area is strongly associated to clinical and echocardiographic outcome to CRT. Moreover its distinctive character seems better than that of traditional ECG parameters.
TISSUE HEAT SHOCK PROTEIN 27 BECOMES LOWER IN LONGSTANDING PERSISTENT ATRIAL FIBRILLATION, WHILE SERUM LEVELS BECOME HIGHER IN PERSISTENT AF

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Purpose:
Atrial Fibrillation (AF), the most common age-related cardiac arrhythmia, is a persistent and progressive disease. It initially presents as short, self-terminating episodes and progresses into long-lasting episodes that unlikely convert to sinus rhythm spontaneously. The exact mechanism underlying this progressive nature of AF is still unknown, but there is strong evidence that disease progression is caused by derailment of proteostasis, resulting in structural remodeling and contractile dysfunction of cardiomyocytes. Structural remodeling of the cardiomyocytes is sustainable and impairs electrical coupling and the functional recovery to sinus rhythm (electropathology), explaining the limited efficacy of current therapies. Previously, we showed that exhaustion of heat shock proteins (HSPs), which are important cardio-protective chaperones involved in the maintenance of proteostasis, contribute to structural damage in AF patients. In addition, compounds the induce HSP expression protected against AF initiation and progression in experimental AF models. In human AF, it is still unclear whether high HSP levels in tissue play a role in the success rate of cardioversion. Therefore, the aim of the present study is to examine whether HSP levels in the blood and atrial tissue correlate and can predict the stage of AF.

Methods:
In this prospective observational study, patients are recruited at the Department of Cardiothoracic Surgery or Cardiology at the Erasmus Medical Center, Rotterdam. In the study group, 100 patients, older than 18 years, who were scheduled for elective cardiothoracic surgery for structural heart disease with or without a history of AF are included. Before cardiothoracic surgery blood was obtained from the patient for HSP measurements. During surgery tissue samples of the right and/or left atrial appendage were obtained for HSP determination. HSP27 and HSP70 was determined in blood samples by commercially available ELISA’s and in tissue by Western blot analysis. HSP levels in tissue were intra experimentally corrected for GAPDH and inter experimentally with a reference sample. The HSP levels in AF patients were compared to HSP levels in sinus rhythm patients.

Results:
We included 100 patients scheduled for elective cardiothoracic surgery for structural heart disease. 38 patients underwent CABG surgery, 31 valve surgery, 21 a combination of valve and CABG surgery, 4 Maze procedure and 6 patients had coronary heart disease. 27 of the patients were female and 73 male, with a mean age of 67,7 +/- 10,8. 47 patients did not have a history of AF, 53 did have a history of AF, of which 14 have paroxysmal, 23 persistent and 16 longstanding persistent AF. Compared to tissue HSP27 levels in sinus rhythm patients (0,606 +/- 0,249), tissue HSP27 were significantly lower in patients with longstanding persistent AF (0,429 +/- 0,212) (p=0,020), indicating an exhaustion of tissue HSP27 levels in higher stage of AF. For HSP70 this was not significant (0,620 +/- 0,284 and 0,544 +/- 0,409, resp.) (p=0,45). Furthermore, tissue HSP27 and HSP70 levels significantly correlate (p=3,5*10-9). Serum HSP70 levels and tissue HSP70 levels inversely correlate (p=0,020), which may indicate that HSP70 is released from the cardiomyocytes into the blood. For serum HSP27 we only observed significant inverse correlation with tissue HSP27 levels in the persistent AF group (p=0,003).

Conclusion:
Tissue HSP27 is lower in longstanding persistent AF. Serum and tissue HSP27 and HSP70 levels inversely correlate, indicating that HSPs are released from tissue into the blood. Serum HSP27 levels predict AF the stage of AF and may serve as a potential biomarker for the stage of AF.
SUCCESS AND COMPLICATION RATES OF LEAD-EXTRACTION WITH THE FIRST VERSUS THE SECOND GENERATION EVOLUTION MECHANICAL SHEATH

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Purpose:
The Evolution sheath (Cook, USA) is a power sheath frequently used for chronic lead extraction. In 2013 a novel type (bidirectional) of Evolution sheath (the RL type) was introduced. We evaluated differences in success and complication rates of the two types.

Methods:
From 2009-2015 all lead extractions requiring the use of an Evolution sheath were prospectively examined. According to the current guidelines, complete procedural success was defined as the removal of all targeted lead material. Clinical success was the retention of a small portion of the lead and failure was the inability to achieve either complete procedural or clinical success, or the development of any permanently disabling complication.

Results:
The Evolution sheath was used to extract 149 leads in 103 patients. The first 56 leads were extracted with the original uni-directional sheath, and 93 leads were extracted with the novel bi-directional R/L type. The median age of the lead at time of extraction was 6.8 years versus 9.1 years (p=0.007). Complete procedural success was higher for the Evolution R/L (80.0% versus 98%, p=0.0004). Clinical success rate was 98% versus 99%. There were no major complications and 6 (12.0%) versus 2 (3.8%) minor complications (p=0.153). We did not observe changes in success rates or complications over time, meaning that the difference can’t be explained by learning curve.

Conclusion:
Use of the novel Evolution R/L sheath versus the original Evolution sheath was associated with significant higher complete success rates, without major complications and with a trend towards reduction of minor complications.
Session III: Intervention Cardiology, part I

FRACTIONAL FLOW RESERVE BASED DEFERRAL OF CORONARY REVASCULARIZATION: LONG-TERM CLINICAL OUTCOME IN A LARGE REAL WORLD POPULATION

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Purpose:
After 15 years of follow-up the DEFER-trial showed positive results for non-revascularized patients with a fractional flow reserve (FFR) above 0.75. We sought to investigate if similar results can be obtained in a large real world population.

Methods:
This study is a single-center retrospective cohort study. Between 2009 and 2015 FFR was determined in 1139 cases in our hospital. Patients were included in case FFR was above 0.80 and revascularization was deferred. Study endpoint was occurrence of major adverse cardiac events (MACE) defined as a composite of acute coronary syndrome, revascularization and all-cause mortality.

Results:
In total 515 patients with FFR measurements >0.80 were identified for analysis. Mean follow-up was 26.8±17.9 months. MACE were observed in 85 (16.5%) patients. Revascularization occurred in 34 patients (6.6%), followed by all-cause mortality in 28 patients (5.4%), and acute coronary syndrome in 23 patients (4.5%). The MACE rate displayed a gradual inclining course. FFR did not differ significantly between patients with and patients without MACE (89.8 ± 5.4 vs 89.9±5.1, p=0.733). Patients with FFR close to the cut off value of 0.80 were not at higher risk for revascularization. Cox-regression analysis showed that both age and history of CABG are predictors of MACE (respectively p=0.016 and p=0.014).

Conclusion:
In a large real-world population long-term outcome of deferral of revascularization in FFR controlled haemodynamically non-significant coronary artery disease confirms long-term results of the DEFER-trial. A sudden increase in event rate over time is not detected. In general, it can be acknowledged that FFR based deferral of coronary revascularization is safe on the long-term.
Figure 1: Event-free survival (%)
N.D. Fagel (OLVG, Amsterdam); M. Maarse M (OLVG Amsterdam); T. Slagboom (OLVG, Amsterdam); J.P. Herrman (OLVG, Amsterdam); R.J. van der Schaaf (OLVG, Amsterdam); G. Amoroso (OLVG, Amsterdam); M.S. Patterson (OLVG, Amsterdam); M.J. Suttorp (St. Antonius ziekenhuis, Nieuwegein); F.C. van Nooijen (Waterland ziekenhuis, Purmerend); M.A. Vink (OLVG, Amsterdam)

Purpose:
The purpose of this study was to evaluate the long-term outcome of multivessel percutaneous coronary intervention (MV-PCI) versus culprit vessel PCI (CV-PCI) only in patients with multivessel coronary disease (MVD). In patients with MVD and an identified culprit lesion who undergo percutaneous revascularization for stable angina or non-ST-elevation myocardial infarction, MV-PCI may reduce the need for additional evascularization, but may also involve an increased risk of late stent-related adverse events.

Methods:
In this dual-center, prospective, randomized study a total of 215 patients with ≥70% stenosis in two or more native epicardial vessels were randomly assigned to MV-PCI or CV-PCI using drug eluting stents. The identification of the culprit vessel was based on non-invasive testing and/or angiography. The primary endpoint was the occurrence of major adverse cardiac events (MACE) including death, myocardial infarction (MI), and repeat revascularization. Secondary endpoints were the combined endpoint of death or MI, the individual components of the primary endpoint, and the occurrence of stent thrombosis.

Results:
At 5 year follow up, complete data on vital status was available of 94% of all patients. The occurrence of the primary endpoint was comparable at 30% versus 32% (HR 0.87, 95% CI: 0.53 to 1.44, p = 0.60) in the MV-PCI and CV-PCI group, respectively. The incidence of death or MI was 14% in the MV-PCI group and 8% in the CV-PCI group (HR 1.95, 95% CI 0.78 to 4.88, p = 0.16). The need for repeat revascularization was 15% versus 24% (HR 0.57, 95% CI 0.31 to 1.07, p = 0.080), whereas the rate of definite or probable stent thrombosis was 2% versus 0% (p=0.44) in the MV-PCI and CV-PCI group, respectively.

Conclusion:
In this randomized study including patients with stable angina or non-ST-elevation MI with MVD, there was no difference in the occurrence of MACE up to 5 years after MV-PCI, as compared with CV-PCI only. We observed a higher incidence of death or MI and a lower rate of repeat revascularization after MV-PCI, although this difference was not statistically significant.

Figure 1:
MACE rate 5 year follow-up
DOES FRACTIONAL FLOW RESERVE OVERESTIMATE THE SEVERITY OF LAD LESIONS?

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Purpose:
Fractional Flow Reserve (FFR) is increasingly used to estimate severity of coronary stenoses, prior to coronary revascularization. However, it has been suggested that FFR may overestimate severity of Left Anterior Descending (LAD) lesions. Our aim was to assess whether in patients without ischemia with Myocardial Perfusion Imaging, FFR of the LAD is more often abnormal compared to FFR of other coronary arteries.

Methods:
Between 2010 and 2014 a total of 133 patients underwent within 6 months after normal Myocardial Perfusion Imaging, invasive angiography and FFR measurement because of persistent or worsening of angina complaints. FFR of a graft or diagonal branch were excluded. In these patients, a total of 167 FFR measurements were performed including 85 (50.9%) in the LAD. A FFR ≤0.80 denoted a significant stenosis.

Results:
Mean age of the patients was 64.8 ± 10.5 years, 40% were women. There were no differences in baseline characteristics between LAD and non-LAD measurements. An abnormal FFR was observed in 35.3% of the LAD measurements, compared to 9.8% in the non-LAD measurements (p=0.001). Also after adjusting for age and gender, the FFR was more often abnormal in the LAD with OR 5.2 (95% CI 2.2 – 12.3). Of the abnormal FFR LAD measurements, 70% had no angiographic severe stenosis.

Conclusion:
In selected patients with normal MPI, FFR measurement of the LAD was significantly more often abnormal, the majority of these patients had no significant lesions on invasive angiography. Possibly, FFR may overestimate severity of LAD lesions.
THE PREVALENCE OF RELEVANT CORONARY STENOSES AS DEFINED BY ABNORMAL FRACTIONAL FLOW RESERVE FOLLOWING NORMAL SPECT

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Purpose:
Previous studies raised concern about low sensitivity of myocardial perfusion imaging (MPI). However, these studies were performed without fractional flow reserve measurements (FFR), while MPI has been improved, including better (CZT) cameras and routine use of attenuation correction. Our aim was to study the prevalence of relevant coronary disease based on functional assessment in symptomatic stable patients with normal SPECT.

Methods:
We identified a total of 133 patients who underwent invasive angiography and FFR measurements within 6 months after normal SPECT. In these patients, a total of 180 FFR measurements were performed. A FFR ≤0.80 denoted a significant stenosis.

Results:
Mean age of the patients was 64.8 ± 10.5 years, 40% were women. Functionally relevant coronary disease based on FFR was depicted in only 13% of stenoses. No differences in baseline characteristics, symptoms, coronary history or pre-test likelihood could be identified for the prediction of functionally relevant coronary disease.

Conclusion:
In selected patients with normal SPECT and persisting complaints, the prevalence of functionally relevant coronary artery disease is low.
FUNCTIONAL ASSESSMENT OF CORONARY STENOSES BY QUANTITATIVE FLOW RATIO: A NON-INVASIVE ALTERNATIVE FOR STANDARD FRACTIONAL FLOW RESERVE

T.K.K.Liu (HagaZiekenhuis, Den Haag); S. Somi (HagaZiekenhuis, Den Haag); G. Bleeker (HagaZiekenhuis, Den Haag); C.E. Schotborgh (HagaZiekenhuis, Den Haag); M.J.W. Götte (HagaZiekenhuis, Den Haag)

Purpose:
Fractional Flow Reserve (FFR) is the gold standard for clinical decision making in patients with coronary artery disease. However, performing FFR is time consuming, expensive and not always available in non-PCI centers. This leads to limited clinical use of FFR. Recently, Quantitative Flow Ratio (QFR) has been proposed as a new technique to derive a FFR. QFR does not require an intracoronary pressure wire or the use of drugs to obtain hyperemia. The aim of this study was to assess the feasibility and reliability of QFR in clinical practice in a high-volume heart center.

Methods:
Patients with stable angina underwent coronary angiography and conventional FFR measurements. QFR calculation was applied on the diagnostic coronary angiograms, with optimized projection angles for assessment of QFR (figure 1). Both, fixed flow QFR (fQFR) and contrast flow QFR (cQFR) analyses were performed and compared with state-of-the-art FFR measurements.

Results:
In total 51 patients were included. From the 56 coronary arteries with intermediate lesions and FFR measurements, 45 were suitable for QFR analysis. Good agreement of QFR with FFR was found in 79% for fQFR and 93% for cQFR, with a clinical acceptable correlation between FFR and cQFR of r=0.678 [p=<0.001], figure 1.

Conclusion:
QFR is shown to be a good alternative for FFR in daily practice with a good correlation, providing functional assessment of lesions without procedural risk and additional costs involved in FFR procedures. QFR allows for a wider adoption of functional assessment even in non-PCI centers, which presumably improves clinical outcome for patients otherwise deprived from functional assessment.
Figure 1:
SEPARATE ASSESSMENT OF HYPERAEMIC EPICARDIAL AND MICROVASCULAR CONDUCTANCE USING CORONARY PRESSURE AND FLOW VELOCITY

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Purpose:
Invasive assessment of the coronary circulation has been largely based on the use of pressure ratios (epicardial-) and resistance (micro-vessels). Simultaneous assessment of epicardial- (CEPI) and microvascular conductance (CMICRO), might provide a more coherent (same units for both compartments) and intuitive (expressing deliverability of blood) approach.

Methods:
Validation of this new approach was performed in a total of 403 both obstructive and non-obstructive coronary vessels interrogated with intracoronary Doppler and pressure in 261 patients with stable angina pectoris. Hyperaemic mid-late diastolic pressure and flow velocity (PV) relationships were calculated from PV loops using an automated algorithm. The slope of the linear PV relationship was first calculated from both aortic and intracoronary pressures and, subsequently, used to derive separately CEPI, CMICRO and zero-flow pressure (Pzf).

Results:
Median CEPI and CMICRO were 4.56 (IQR 2.18 – 8.64) and 1.28 (IQR 0.95-1.73) cm/s-1/mmHg-1 respectively. Concordance in stenosis severity classification of two validated indices of stenosis severity (FFR and hyperemic stenosis resistance) was used as a robust reference standard to validate CEPI. ROC curves demonstrated an excellent ability of CEPI to characterize significant epicardial stenoses indicating a cutoff of 1.69 (AUC 0.93) with a sensitivity of 93% and a specificity of 82%. Validation of CMICRO (previously reported in endomyocardial biopsies) was not feasible in this population given the lack of a reference standard. Mean Pzf was 29.89 ± 14.16 mmHg.

Conclusion:
A comprehensive assessment of the coronary circulation, based on separate calculation of epicardial- and microcirculatory conductance, is feasible and provides a clear, coherent depiction of coronary haemodynamics in ischaemic heart disease. As part of this novel approach, calculation of zero flow pressure (an index of extravascular compression) can also be performed. The findings should foster the development of simple, reliable methods for its calculation in the clinical arena.
IMPROVED RECOVERY OF REGIONAL LEFT VENTRICULAR FUNCTION AFTER PERCUTANEOUS CORONARY INTERVENTION OF CHRONIC TOTAL OCCLUSION IN ST-ELEVATION MYOCARDIAL INFARCTION PATIENTS.

THE IMPACT OF PERCUTANEOUS CORONARY INTERVENTION FOR CONCURRENT CHRONIC TOTAL OCCLUSION ON LEFT VENTRICULAR FUNCTION IN ST ELEVATION MYOCARDIAL INFARCTION (EXPLORE) CARDIAC MAGNETIC RESONANCE IMAGING STUDY

J. Elias (AMC, Amsterdam); L.P.C. Hoebers (AMC, Amsterdam); I.M. van Dongen (AMC, Amsterdam); B.E.P.M. Claessen (AMC, Amsterdam); T. Råmunddal (Sahlgrenska, Gotenburg); P. Laanmets (North Estonia Medical Center, Tallinn); E.Eriksen (Haukeland, Bergen); R.J. van der Schaaf (OLVG, Amsterdam); R. Nijveldt (VUMC, Amsterdam); J.G. Tijssen (AMC Amsterdam); A. Hirsch (AMC, Amsterdam) and J.P.S. Henriques (AMC, Amsterdam) on behalf of the EXPLORE investigators.

Purpose:
The EXPLORE trial did not show a significant benefit of percutaneous coronary intervention (PCI) of the concurrent chronic total occlusion (CTO) in ST-segment elevation myocardial infarction (STEMI) patients on left ventricular (LV) function at 4 months follow-up. Therefore we aimed to study the effect of CTO PCI compared to no-CTO PCI on the recovery of global and regional LV function, particularly in the CTO territory.

Methods:
We studied 180 of the 302 EXPLORE patients randomized to CTO PCI or no-CTO PCI. Cardiac Magnetic Resonance imaging was performed at baseline and 4 months follow-up. Global LV function and segmental wall thickening (SWT) were quantified on cine images. Imaging analyses were performed by an independent core laboratory. Dysfunctional segments were defined as SWT<45%. Dysfunctional segments were further analyzed by transmural extent of infarction (TEI). All outcomes were stratified for randomization treatment.

Results:
Recovery of SWT was better after CTO PCI compared to no-CTO PCI. This recovery was most pronounced in the dysfunctional segments in the CTO territory (ΔSWT 17±27% vs 11±23%, p=0.03). Furthermore, CTO PCI compared to no-CTO PCI resulted in a better recovery in the dysfunctional segments with TEI>25%. However, this regional effect did not translate in a better recovery of global LV function after CTO PCI compared to no-CTO PCI.

Conclusion:
Our study reveals that CTO PCI compared with no-CTO PCI is associated with a greater recovery of regional function, especially in dysfunctional segments in the CTO territory. However, there was no effect of CTO PCI on global LV function.
Figure 1:
Change in percentage segmental wall thickening (SWT) in all segments (A) and dysfunctional segments (B) and in all segments and dysfunctional segments in the CTO territory (C and D). Recovery of SWT was compared between baseline and 4 month follow-up in segments and between CTO PCI and no-CTO PCI (*).
EXPLORATORY STUDY OF THE ADDED VALUE OF PATIENT-SPECIFIC COMPUTER SIMULATION IN THE PLANNING AND EVALUATION OF TRANSCATHETER AORTIC VALVE IMPLANTATION

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Purpose:
Increase in experience and improvements in device technology have resulted in improved outcome after transcatheter aortic valve implantation (TAVI). Due to the increasing number of valve types and sizes, outcome of TAVI will depend more on device-host interactions which necessitates a patient-tailored approach. Therefore the aim of this study was to explore the added value of patient-specific computer simulation to predict outcome.

Methods:
55 patients underwent TAVI between November 2005 and May 2013 with the Medtronic CoreValve System. In all patients patient-specific computer simulation was performed after TAVI. The objective was to assess to what extent optimal valve size according to computer simulation differs from the MD driven decision based upon multi-slice computer tomography (MSCT) pre-TAVI that was also used for computer simulation. Since simulation may propose different valves sizes and depth of implantation in relation to paravalvular leakage (PVL), the proposed (i.e. computer simulation) valve size that was associated with the least amount of PVL was chosen as optimal valve size according to computer simulation.

Results:
32 patients (58%) received the same valve size as proposed by the simulation. In 23 patients (42%) the simulation proposed another size than the implanted size. In 20 out of these 23 patients, the simulation proposed a larger valve size and in 3 a smaller one. In 4 out of the 32 and 6 out of the 23 patients, echocardiography disclosed ≥ moderate aortic regurgitation. The computer simulation observed less PVL when the valve would have been implanted at a mean depth of 8.1 ± 3.0mm at the left coronary cusp and 7.9 ± 3.3mm at the right coronary cusp.

Conclusion:
In a substantial proportion of patients (42%) computer simulation proposed a different valve size that is associated with less PVL, thereby underscoring its potential added clinical value and support for patient-specific treatment planning.

Figure 1:

<table>
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<td>n=55</td>
<td>n= 32 (58%)</td>
<td>n= 23 (42%)</td>
</tr>
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ABSORB BIOABSORBABLE SCAFFOLD: A SINGLE-CENTER REAL LIFE EXPERIENCE

W.S. Remkes (Isala, Zwolle); M.W. Kennedy (Isala, Zwolle); J.P. Ottervanger (Isala, Zwolle); E. Fabris (Isala, Zwolle); J.H. Dambrink (Isala, Zwolle); A.T.M. Gosselink (Isala, Zwolle); V. Roolvink (Isala, Zwolle); A.W. van ‘t Hof (Isala, Zwolle); E. Kedhi (Isala, Zwolle).

Purpose:
Recently, there has been concern about safety of the Absorb bioabsorbable scaffold (Abbott Santa Clara CA, USA). Our purpose was to evaluate incidence of cardiovascular adverse events after implantation of this stent in a real life situation.

Methods:
All Absorb treated patients in our center were included in this retrospective analysis. The primary endpoint was the incidence of stent thrombosis (ST), myocardial infarction (MI), target lesion and target vessel revascularization (TLR and TVR) and all-cause and cardiac death.

Results:
Between October 2013 and January 2017 a total of 105 patients were treated with the Absorb scaffold. Mean age was 60 years (SD +/-11), (30) 28.6% were females, (40) 38% had diabetes mellitus (DM). Mean follow-up duration was 20.2 months, no patients were lost to follow-up. Intravascular imaging guidance during scaffold implantation was used in (38) 36.2%. All-cause and cardiac mortality were respectively (2) 2% and (0) 0%. Stent thrombosis was observed in 1 patient who was treated with a combination of Absorb and metallic drug eluting stents. ST was intraprocedural and occurred after stenting a bifurcation with metallic stents. MI rate was (2) 2% both intraprocedural; one due to ST (see above) and the other due to catheter dissection in de LM- LAD (not scaffold related). TLR was (2) 2% both coronary artery bypass grafting (CABG) immediately post index PCI, as explained above, due to peri-procedural complications. No further TLR cases during follow-up were observed. Target vessel revascularization was performed in 7.6%. Even in DM patients there was no TLR observed.

Conclusion:
In this relatively small single center study, patients treated with the Absorb biodegradable scaffold had an excellent prognosis, with low risk of death, myocardial infarction, stent thrombosis or target vessel revascularization.
THE LEFT SUBCLAVIAN ARTERY AS PRIMARY ACCESS SITE IN TRANSCATHETER AORTIC VALVE IMPLANTATION: FEASIBILITY, SAFETY AND CLINICAL OUTCOME

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Purpose:
In Transcatheter Aortic Valve Implantation (TAVI), the standard primary transfemoral access is not feasible in about one-third of candidates. Major vascular complications and life-threatening bleeding are observed in more than one out of ten transfemoral treated TAVI patients. Our center adopted the left subclavian artery (LSA) as primary access site. We report on vascular complications, bleeding and clinical outcome.

Methods:
Retrospective cohort of all 327 consecutive (first generation, Medtronic CoreValve) TAVI patients treated at the Radboudumc (December 2008 - February 2015). A dedicated heart team allocated TAVI to patients. LSA eligibility (anatomy, diameter and tortuosity) was assessed by means of angiography. Procedures were performed by an interventional cardiologist and a cardio-thoracic surgeon, under general anesthesia with surgical-cutdown of the LSA. Vascular complications, bleeding and clinical outcome (mortality, stroke and new pacemaker) were assessed at discharge according to the standardized VARC definitions.

Results:
LSA access was feasible in two hundred and ninety-seven patients (90.8%). Median age was 80 [76-84] years and Logistic Euroscore 14.0% [9.2 – 22.6]. Overall, major vascular complications were observed in 4.0%, 1.7% were LSA-related. Life-threatening or major bleeding during hospitalization were observed in 1.0% and 10.1%, respectively. Additional clinical outcome is described in table 1.

Conclusion:
The left subclavian artery as primary access for TAVI is highly feasible with more than 90% of patients eligible for subclavian access. This approach is safe with relatively low incidence of vascular complications, bleeding and good clinical outcome during index hospitalization.

Table 1: Clinical outcome

<table>
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<th>Procedure/mortality</th>
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<tbody>
<tr>
<td>New pacemaker</td>
<td>33 (11.1)</td>
</tr>
<tr>
<td>Stroke</td>
<td>5 (1.7)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>14 (4.7)</td>
</tr>
<tr>
<td>1-year mortality</td>
<td>60 (20.2)</td>
</tr>
</tbody>
</table>
Purpose:
Recent studies show that microvascular injury consists of microvascular destruction and intramyocardial hemorrhage (IMH). Patients with IMH after ST-elevation myocardial infarction (STEMI) have a poorer prognosis compared to patients without IMH. Knowledge on the predictors for the occurrence of IMH after STEMI is lacking. The current study aimed to investigate the prevalence and extent of IMH in STEMI and its relation with periprocedural and clinical variables.

Methods:
A multi-center observational cohort study was performed in successfully reperfused STEMI patients with cardiovascular magnetic resonance (CMR) exam after 5.5±1.8 days post-PCI. IMH was assessed using T2-weighted CMR. The median was used as cutoff value to divide the study population with presence of IMH into mild or extensive IMH. Clinical and periprocedural parameters were studied in relation to occurrence of IMH and extensive IMH, respectively.

Results:
Of the 410 patients, 54% showed IMH. The presence of IMH was independently associated with anterior infarction (OR 2.96, p<0.001) and periprocedural glycoprotein IIb/IIIa-inhibitor treatment (OR 2.67, p<0.001) (Table 1). Extensive IMH was independently associated with anterior infarction (OR 3.76, p<0.001), and negatively associated with hypertension (OR 0.60, p=0.045). Presence and extent of IMH was associated with larger infarct size, greater extent of microvascular obstruction (MVO), larger left ventricular (LV) dimensions and lower LV ejection fraction (all p<0.001).

Conclusion:
Over half of reperfused STEMI patients showed IMH, which was associated with anterior infarction and glycoprotein IIb/IIIa-inhibitor treatment. Extensive IMH was associated with anterior infarction and (negatively) with hypertension. IMH was associated with more severe infarction and worse short-term LV function. These findings warrant further investigation of the optimal application of aggressive antithrombotics, especially in the current era of adequate dual antiplatelet preloading. Furthermore, the identified predictors might prove useful in future risk stratification in the acute phase of STEMI.
Figure 1: Univariable and multivariable logistic regression analysis for presence of IMH
COMPARISON OF CLINICAL RISK SCORES TO PREDICT SURVIVAL AFTER MITRACLIP IMPLANTATION


Purpose:
Selecting patients for the MitraClip implantation remains challenging. Several surgical risk scores are available, although not intended for, may also be used for assessing long-term survival. The aim of this study was to determine which risk score performs best for predicting one-year survival in patients undergoing percutaneous mitral valve repair using the MitraClip.

Methods:
Nine relevant risk scores, namely the STS score, EuroSCORE I, EuroSCORE II, ACEF, Charlson Comorbidity Score, Elixhauser Comorbidity Score, Guaragna Score, OBSERVANT Score and Ambler Score were calculated and compared to the observed survival. The tertiles consisted of roughly even numbers and categorized as high-risk, intermediate-risk, and low-risk group based on their score. Multivariate Cox regression, using stepwise forward selection, was performed to analyze the association of risk scores with one-year survival rates.

Results:
A total of 152 patients (age: 75 ± 11 years, male: 52%) who received a MitraClip were included. The estimated overall 30-day, one-year, and two-year survival after MitraClip implantation were 97%, 80%, and 71% respectively. Of all included scores, the Elixhauser comorbidity score had highest global discriminative performance (area under the curve (AUC): 0.71; 95% confidence interval (CI): 0.62-0.79; hazard ratio (HR)=4.5; p-value=0.006).

Conclusion:
The Elixhauser Comorbidity Score showed the best discriminative performance for predicting one-year survival. Therefore the Elixhauser Comorbidity Score could be used for assistance in patient selection.

Figure 1:
Kaplan-Meier estimate of overall cumulative survival of patients treated with MitraClip categorized for Elixhauser comorbidity score tertiles (<11, 11-15, and >15), log-rank: p-value=0.006.
Session V: Congenital Cardiology

PROGNOSTIC VALUE OF SERIAL N-TERMINAL PRO-B-TYPE NATRIURETIC PEPTIDE MEASUREMENTS IN ADULTS WITH CONGENITAL HEART DISEASE

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Purpose:
A single measurement of N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a strong independent prognostic factor in patients with adult congenital heart disease (ACHD). The aim of this study was to investigate the temporal evolution of NT-proBNP within individual patients with ACHD and to relate this to cardiovascular events.

Methods:
Patients with ACHD who routinely visited the outpatient clinic between 2011 and 2013 were prospectively enrolled. NT-proBNP was measured at study inclusion and at four annual follow-up visits. The association between repeated log2 NT-proBNP measurements and events (death, heart failure, arrhythmia, hospitalizations, thromboembolic events, re-interventions) was assessed using Cox regression, linear mixed models and joint models.

Results:
In total, 595 patients were included (median age 33 [25-41] years, 58% male, 90% NYHA I). During a median follow-up of 53 [46-58] months, 2024 NT-proBNP measurements were collected. The NT-proBNP level at any point in time, calculated using a joint model, was stronger associated with cardiovascular events (n=199, 34%) than the baseline NT-proBNP level, calculated using Cox regression (adjusted HR per doubling of NT-proBNP 1.52 [1.33-1.72] compared with 1.38 [1.23-1.55], respectively). In addition, the slope of the NT-proBNP trajectory was significantly associated with cardiovascular events (adjusted HR per annual doubling 1.12 [1.07-1.17]).

Conclusion:
NT-proBNP levels increased prior to the occurrence of an event; whereas patients without any cardiovascular event exhibited stable and low NT-proBNP levels. An increase in NT-proBNP level over time indicated a worse prognosis. Serial NT-proBNP measurements could therefore be of additional value in the annual follow-up of high-risk patients.

Figure 1:
The average annual increase in patients who died or developed heart failure was 21.7 pmol/L, compared with 0.3 pmol/L in patients without death or heart failure (P for interaction <0.001).
IMPACT OF PVR ON FREEDOM FROM DEATH AND SUSTAINED VENTRICULAR TACHYCARDIA IN PATIENTS WITH REPAIRED TETRALOGY OF FALLOT: RESULTS FROM THE INDICATOR COHORT

J.P. Bokma (Academic Medical Center, Amsterdam); T. Geva (Boston Children's Hospital, Boston); L.A. Sleeper (Boston Children's Hospital, Boston); S.V. Babu-Narayan (Royal Brompton Hospital, London); R.M. Wald (Peter Munk Cardiac Centre, Toronto); K. Hickey (Boston Children's Hospital, Boston); M. Lu (Boston Children's Hospital, Boston); M.A. Gatzoulis (Royal Brompton Hospital, London); B.J.M. Mulder (Academic Medical Center, Amsterdam); A.M. Valente (Boston Children’s Hospital, Boston)

Purpose:
To determine the association between pulmonary valve replacement (PVR) and major adverse clinical outcomes in patients with repaired tetralogy of Fallot (rTOF) and to determine whether there is prognostic benefit of PVR according to consensus guidelines.

Methods:
Subjects with rTOF and cardiac magnetic resonance (CMR) from the multicenter INDICATOR registry were included. A propensity score for PVR was created to adjust for baseline differences between PVR and non-PVR subjects. Proactive and conservative consensus guidelines were pre-defined as a pulmonary regurgitation >25% and at least ≥2 of the criteria listed in figure 1. The primary outcome included death, aborted sudden death, and sustained ventricular tachycardia (VT). A composite secondary outcome included heart failure, non-sustained VT, and supraventricular tachycardia.

Results:
A total of 977 subjects (age 26±15 years, 45% PVR) were included. During follow-up of 5.3±3.1 years after CMR, the primary and secondary outcome occurred in 41 and 88 subjects, respectively. The hazard ratio (HR) for subjects with versus without PVR was 0.65 (95% CI:0.31-1.36; p=0.25) for the primary outcome and 1.43 (95% CI:0.83-2.46; p=0.19) for the secondary outcome after adjusting for PVR propensity and other factors. There was potential harm when PVR was performed without meeting pre-defined proactive guidelines criteria (HR for primary and secondary outcome 2.53 (95% CI:0.79-8.06) and 2.31 (95% CI:1.07-4.97), respectively).

Conclusion:
In this large multicenter rTOF cohort, there was no statistically significant prognostic benefit of PVR. Additionally, there may be harm performing PVR in patients not yet meeting proactive criteria.
Figure 1: Event rates of PVR according to proactive/conservative criteria status. Event rates according to PVR status and pre-defined proactive/conservative PVR criteria. Hazard ratio of event in PVR compared to no PVR within subgroups are displayed in Forest plot. Patients meet guidelines if PR is more than 25% and at least two of the criteria listed in the figure are present. Abbreviations: EDV: end-diastolic volume, EF: ejection fraction, ESV: end-systolic volume, HR: hazard ratio, LV: left ventricle, PR: pulmonary regurgitation, PVR: pulmonary valve replacement, RV: right ventricle.
OUTCOME IN TURNER PATIENTS WITH AORTIC DILATION

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Purpose:
The risk of aortic dissection in Turner syndrome (TS) patients is presumed high. To prevent dissection, aortic surgery is advised when aortic size index (ASI) exceeds 27 mm/m². This study evaluates the risk of complications in TS patients with a dilated ascending aorta defined as ASI >20mm/m².

Methods:
All TS patients seen in our specialized outpatient clinic since begin 2004 until August 2016 with no previous medical history of aortic dissection or ascending aorta surgery, were analysed. Patients with an ASI >20mm/m2 on first MR-scan were included and follow up was evaluated.

Results:
In 56 (21.4%) of the 262 patients the inclusion criteria were met (table 1). Bicuspid aortic valve (BAV) and hypertension was more common in the dilated group. During a median follow up of 5.9 (IQR 4.1-8.0) years, 3 patients died of which 1 due to a type A aortic dissection (ascending aorta diameter 65 mm (ASI 39mm/m2) in which surgery was delayed by patient and 2 non-cardiac deaths (Cancer, depression with anorexia). Ascending aorta surgery criteria were met and was performed in 3 patients during follow up.

More than one MR-scan was performed in 41 of 56 patients (73%). In this subset, median ascending aorta diameter increase was 0.0 (IQR -0.22-0.31) mm/year, ASI 0.038 (IQR -1.87-0.22) mm/m2/year.

Conclusion:
In adult TS patients with a dilated ascending aorta no unexpected dissections occurred and ascending aorta increase was slow, which underscores that the present guidelines adequately prevent aortic dissection in TS patients.

Figure 1: Baseline characteristics Turner patients cohort

CONGENITALLY CORRECTED TRANSPOSITION OF THE GREAT ARTERIES, UP TO 81 YEARS FOLLOW-UP

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Purpose:
Patients with congenitally corrected transposition of the great arteries (ccTGA) have substantial associated comorbidities. The aim of this study is to get an adequate picture of the long-time course of the disease.

Methods:
In a retrospective study 23 patients with ccTGA (48% male) were included with a mean follow-up (fu) of 47 years (SD±15.4). The patient reports were analysed with the main focus on their anatomical status at birth, right ventricular (RV) function, tricuspid valve (TV) function, cardiac arrhythmias and functional class. Patients were divided into complicated (ccTGAC) or non-complicated (ccTGANC) ccTGA.

Results:
Table 1 describes the main outcomes. 15 patients had ccTGAC (fu 42y (23-81)) and 8 were categorised as ccTGANC (fu 58y (38-71)). 1 patient with ccTGAC died a cardiac death at the
age of 25. TV regurgitation in ccTGAC showed a more severe course than in ccTGANC 
(p=0.042). In the ccTGAC 8 patients had TVR or TVP (Hazard-ratio 9.053 (p=0.046)) in contrast to 1 ccTGANC patient, who underwent TVR. Also ccTGAC patients have a higher incidence in ICD and/or pacemaker implantation (hazard-ratio 3.245 (p=0.135)).

**Conclusion:**
Long-term survival in ccTGA is excellent. However, in both groups a high incidence of cardiac arrhythmias, TV regurgitation and reduced systemic RV function is found. In most patients a sudden clinical deterioration is observed, which presents earlier in life in patients with ccTGAC. Overall, patients with ccTGAC show a worse course of the disease during lifetime.

**Figure 1:** Baseline characteristics, TV function, NYHA functional class, cardiac arrhythmias and RV function. SVT: supraventricular tachycardia, VT: ventricular tachycardia, EF: ejection fraction.

<table>
<thead>
<tr>
<th></th>
<th>Complicated</th>
<th>Non-complicated ccTGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>ccTGA 15</td>
<td>8</td>
</tr>
<tr>
<td>Male(%)</td>
<td>47%(n=7)</td>
<td>50% (n=4)</td>
</tr>
<tr>
<td>Mean follow-up (range)</td>
<td>42y (23-81)</td>
<td>58y (38-71)</td>
</tr>
<tr>
<td>Mean TV surgery free survival</td>
<td>51y (SE 6,9)</td>
<td>68y (SE 2, 3)</td>
</tr>
<tr>
<td>Patients with TVR or TVP</td>
<td>N=8</td>
<td>N=1</td>
</tr>
<tr>
<td>NYHA functional class at last</td>
<td>2,2 (SD±1 ,O)</td>
<td>1, 9 (SD±1 ,O)</td>
</tr>
<tr>
<td>Patients with heart block, SVT, (±SD)</td>
<td>87%±35</td>
<td>75%±46</td>
</tr>
<tr>
<td>Heart block (%)</td>
<td>8 (53%)</td>
<td>4 (50%)</td>
</tr>
<tr>
<td>SVT (%)</td>
<td>12 (80%)</td>
<td>5 (63%)</td>
</tr>
<tr>
<td>VT (%)</td>
<td>4 (27%)</td>
<td>1 (13%)</td>
</tr>
<tr>
<td>Device free survival</td>
<td>39y (SE 3,7)</td>
<td>53y (SE 5,8)</td>
</tr>
<tr>
<td>Mean age at device</td>
<td>30y (SD±1)</td>
<td>40y (SD±1 8,1 ) (n=3)</td>
</tr>
<tr>
<td>Mean RV EF (%)</td>
<td>31% (SD±9,7)</td>
<td>38% (SD±15,3)</td>
</tr>
</tbody>
</table>

**GENDER DIFFERENCES IN MICROVASCULAR FUNCTION, FICTION OR FACT?**

T.I. Aipassa *(Radboudumc, Nijmegen)*, T. ten Cate, *(Radboudumc, Nijmegen)*, R. van Kimmenade *(Radboudumc, Nijmegen)*, M.J. de Boer *(Radboudumc, Nijmegen)*

**Purpose:**
It is suggested that women with complaints of chest-pain without significant obstructive coronary disease more often suffer from microvascular dysfunction than men. Therefore we describe gender specific microvascular function in patients with complaints of chest-pain without a epicardial origin.

**Methods:**
All patients in the period November 2015-December 2016 that underwent coronary angiography with microvascular function assessment were analysed. Those with a previous acute coronary syndrome or significant valvular disease were excluded. To assess gender specific values we describe the values in males and females as well as for the complete group. A CFR <2.0 and an IMR >25 was considered abnormal.

**Results:**
We analysed 47 vessels in 28 patients, 19 (40.4%) vessels in 13 (44.8%) females, mean age 65.1 yr; BMI 27.4 kg/m2. Hypertension or diabetes mellitus type 2 was present in 66.0% and 14.9% patients respectively. The mean FFR was 88.8, the mean CFR 1.9 and the mean IMR 30.8 respectively. For females the mean CFR was 2.4 and IMR 22.7U. Whereas for males these figures were 2.0 resp 32.7U. Both an abnormal CFR and IMR was present in 3 (23.1%) females and 6 (37.5%) males.
Conclusion:
Although it is proposed that microvascular dysfunction shows a gender specific distribution, with females being more at risk, our results show otherwise.
Purpose: To evaluate the diagnostic yield and consequences of an ILR in a tertiary referral center.

Methods: This single-center study included all consecutive patients (n=94) who received an ILR between March 2013 and December 2016. Follow-up was until diagnosis or for at least 6 months of follow-up. Patients were stratified according to the primary indication: syncope (n=35), palpitations (n=25) and high-risk group (n=34). The high-risk group consisted of patients with cardiomyopathy, primary electrical disease or congenital heart disease who were at risk for developing VA according to the treating physician. All patients had remote monitoring with daily transmissions.

Results: The cohort consisted of 94 patients (mean age 45±17 years, female 57%). During a median follow-up time of 10 months (interquartile range, 3-17 months), 42 patients (45%) had an ILR-guided diagnosis. The diagnostic yield was 46% in the syncope group, 48% in the palpitations group and 41% in the high-risk group. The arrhythmogenic diagnosis was different per indication group (Figure). The most common diagnosis was sinus arrest; supraventricular tachycardia; and (non)sustained ventricular tachycardia in the syncope, palpitations, and high-risk group, respectively. As expected, there was a high percentage of pacemakers and catheter ablations in the syncope and palpitations group, respectively. In the high-risk cohort, 14% of patients with a diagnosis received an implantable-cardioverter-defibrillator, however, the majority were treated with anti-arrhythmic drugs.

Conclusion: The current study confirms the role of an ILR in patients with syncope and palpitations. A new finding is the high diagnostic yield in the high-risk cohort which seems useful for risk stratification.
Session VI: Heart Failure

PROGNOSIS OF PATIENTS WITH ACUTE HEART FAILURE: THE INFLUENCE OF RENAL FUNCTION AND ANAEMIA, SEPARATELY AND IN COMBINATION

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Purpose:
The prognostic value of the combination of anaemia and renal dysfunction in patients with acute heart failure (AHF) has been studied less well. We therefore assessed the prognostic impact of renal function and anaemia in such patients, both separately as well as in combination with each other.

Methods:
This prospective registry included all patients who were consecutively admitted at the (Intensive) Coronary Care Unit in the period of 1985-2008 for AHF. Renal dysfunction was defined as eGFR <60 mL/min/1.73 m2. Anaemia was defined as haemoglobin <7.5 mmol/L in women and <8.2 mmol/L in men. Total mortality was the main outcome measure.

Results:
We included 1783 patients, of whom 1095 (61%) had renal dysfunction and 850 (48%) had anaemia. Patients with a severely impaired renal function had the worst prognosis (Figure 1A). The outcome of patients with anaemia was worse compared to patients without anaemia (Figure 1B). Moreover, anaemia was a strong predictor of short-term mortality among both patients with and without renal dysfunction (Figure 1C). After longer follow-up, anaemia had additive prognostic value among patients with renal dysfunction (HR 1.27 [95% CI 1.10-1.47]) but not among those without renal dysfunction (HR 1.13 [95% CI 0.93-1.36]).

Conclusion:
Both renal dysfunction and anaemia were strong predictors of mortality among patients with AHF. Furthermore, anaemia was associated with increased short-term mortality in patients with and without renal dysfunction. With longer follow-up duration, presence of anaemia was related to increased mortality in patients with renal dysfunction but not in patients without renal dysfunction.
Figure 1: Kaplan-Meier curves according to different groups
Purpose:
Patients with cardiac sarcoidosis (CS) appear to be at high risk of (ventricular) arrhythmias and ICDs are recommended in some patients for prevention of sudden cardiac death. However, there is little known about the incidence of ventricular arrhythmic events in CS patients. In this study, we report the incidence of ventricular arrhythmias in CS.

Methods:
All new CS patients who underwent a cardiac device implantation between 01-2009 and 07-2016 in the St. Antonius Hospital, a tertiary expertise centre for sarcoidosis, were included. The diagnosis of CS was made by a multidisciplinary team and based on multi-modality imaging and clinical criteria described in the international consensus statement. An ICD was recommended in the presence of left ventricular (LV) dysfunction or as secondary prevention. An internal loop recorder (ILR) was advised in the presence of a normal LV function and absence of significant conduction disorders, otherwise a pacemaker (PM) was recommended. Ventricular arrhythmias were classified as: ventricular fibrillation (VF), sustained or non-sustained ventricular tachycardia (sVT or nsVT). All devices were evaluated every six months or in case of an event.

Results:
In total 66 newly diagnosed CS patients underwent cardiac device implantation. Two patients were lost to follow-up; therefore 64 patients could be included (mean age 52.2±10.4 years, 73.4% male, mean LV ejection fraction 52.1%). An ICD was implanted in 29 patients, an ILR in 33 patients, and a PM in 2 patients. During a mean follow-up of 21.2 months, 34.4% of CS patients suffered a ventricular arrhythmia (VF 6.3% and sVT 10.9%, all within ICD carriers). Within the ILR and PM carriers only nsVT occurred in 4 out of 35 patients (11.4%). One patient died due to respiratory failure in presence of pneumonia. None of the CS patients died due to ventricular arrhythmias.

Conclusion:
The incidence of ventricular arrhythmias in patients suffering cardiac sarcoidosis is high. Therefore careful evaluation and treatment of all CS patients is important. Further studies are necessary to evaluate CS specific predictors for ventricular arrhythmias.
12-LEAD ECG ALGORITHM TO DIFFERENTIATE BETWEEN ARVC AND CARDIAC SARCOIDOSIS

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Purpose:
Cardiac sarcoidosis (CS) can mimic ARVC. CS is characterized by granuloma formation creating confluent, transmural scars which may result in local conduction block and late activation of RV areas with preserved voltages. ARVC is characterized by fibrofatty replacement progressing from epicardium to endocardium which may result in gradual activation delay and late activation of low voltages RV areas. Therefore we sought to develop a specific 12-lead ECG algorithm to distinguish CS from ARVC.

Methods:
Consecutive pts with ARVC (TF+ and ARVC associated mutation) and CS with dominant RV involvement undergoing VT ablation were enrolled from 2 centers (LUMC & BWH). A non-paced 12-lead ECG was obtained prior to ablation. Based on the assumption that late activated areas have preserved voltage vs. low voltage in CS and ARVC respectively, the pattern and amplitude of the terminal portion of the QRS was analyzed for the presence of (1) terminal S-wave (no r’ or R’) in V1-V3, (2) dominant R wave in V1 (R/r’ratio>1) and (3) amplitude of R’ in V1.

Results:
A total of 44 pts were included (45±17 years, 80% male; 33 [75%] ARVC, 11 [25%] CS). A terminal S-wave in V1-V3 was present in 23 (70%) ARVC pts but in no CS pt. The R in V1 was dominant (R/r’> 1) in 29 (88%) ARVC pts and in 1 pt with CS (p<0.001). The R’-wave amplitude was smaller in ARVC (0.00 (0.00-0.00) vs. 0.45 (0.25-0.53) mV, p<0.001); optimal R’ cutoff amplitude to distinguish CS from ARVC was 0.20mV (AUC 0.95). Subsequently, a 3-step algorithm was proposed with a high sensitivity and specificity for CS (figure).

Conclusion:
Our proposed, easily applicable 12 lead ECG algorithm can distinguish ARVC from CS with RV involvement. The specific ECG features likely reflect different scar patterns.

Figure 1:
PREGNANCY IN WOMEN WITH VENTRICULAR DYSFUNCTION: DATA FROM THE EUROPEAN SOCIETY OF CARDIOLOGY REGISTRY OF PREGNANCY AND CARDIAC DISEASE (ROPAC)

L. Baris (Erasmus MC, Rotterdam); A. Shotan (Hillel Yaffe Medical Center, Hadera); I.M. van Hagen (Erasmus MC, Rotterdam); M.R. Johnson (Imperial College School of Medicine, London); R. Hall (Norwich Medical School, Norwich); J.W. Roos-Hesselink (Erasmus MC, Rotterdam)

Purpose:
To describe the outcomes of pregnancy in women with impaired left ventricular function (LVF).

Methods:
Within the international, prospective, observational Registry on Pregnancy and Cardiac Disease (ROPAC), we describe cardiovascular, obstetric and fetal outcomes of pregnancy within 65 non-GUCH patients with impaired LVF (defined as left ventricular ejection fraction (LVEF) < 40%) and compare them with 805 non-GUCH patients with normal LVF.

Results:
Maternal mortality occurred in 1.5% of patients with impaired LVF and in 0.5% of patients with normal LVF (p=0.27). Heart failure complicated pregnancy in 30.8% of patients with impaired LVF, compared to 15.5% in normal LVF (p=0.003). Also, ventricular achyarrhythmias during pregnancy occurred significantly more frequently (7.7% vs. 1.2%, p=0.003). Twenty-five patients (38.5%) with impaired LVF experienced a cardiovascular event during pregnancy or within 6 months postpartum, while this was only the case in 17.3% in normal LVF (p<0.001). Especially patients with some form of cardiomyopathy were at risk: nearly half of these patients experienced a cardiovascular event during pregnancy. Preterm birth (<37 weeks) and low birthweight (<2500 g) occurred more often in patients with impaired LVF (34.5% vs. 11.9%, p <0.001; 27.7% vs. 15.7%, p = 0.012, respectively). The occurrence of emergency cesarean sections and other obstetric adverse events were not more common in patients with impaired LVF.

Conclusion:
Pregnancy in patients with impaired LVF is associated with high rates of maternal cardiovascular and fetal adverse events. Less than 62 percent of women with LVEF <40% experience a pregnancy free of cardiovascular events.
Purpose:
Regional myocardial dysfunction is the hallmark of Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC), but is only qualitatively evaluated in the clinical setting. Feature Tracking Cardiac Magnetic Resonance (FT CMR) is a novel method to measure strain, a quantitative metric of regional function. However, prior FT CMR studies in ARVC used different software methods to measure global strain. We aimed to assess global and regional strain in ARVC and to determine differences between commercially available FT CMR software packages.

Methods:
We analyzed cine CMR images of 110 subjects (39 overt ARVC [mutation+/phenotype+]; 40 preclinical ARVC [mutation+/phenotype-] and 31 control) for global and regional (subtricuspid, anterior, apical) right ventricular strain in the horizontal longitudinal axis using 3 FT CMR software methods (Medis, TomTec, MTT). Intersoftware agreement was assessed with Bland Altman plots.

Results:
For global strain, all methods showed reduced strain in overt patients vs controls (p<0.041), whereas none distinguished preclinical from control subjects (p>0.275). For regional strain, all methods showed reduced subtricuspid strain in overt patients vs controls (p<0.031). Medis additionally distinguished preclinical from control subjects by abnormal subtricuspid strain (p=0.009). Intersoftware agreement for absolute strain values was low (ICC=0.440).

Conclusion:
Despite intersoftware variability, all software methods distinguish ARVC patients from controls, suggesting robustness of FT CMR measures. Subtricuspid strain was consistently abnormal in ARVC subjects and may detect ARVC prior to overt disease expression.
Figure 1: regional strain by subgroup per software package. White, grey and black boxplots correspond to control subjects, preclinical ARVC and overt ARVC respectively. ST= sub tricuspid region; AW= anterior wall region; AP= apical region; *p<0.05; **<0.01
THE VALUE OF CARDIOVERTER-DEFIBRILLATORS IN PATIENTS WITH NONCOMPACTION CARDIOMYOPATHY COMPARED WITH THOSE WITH DILATED AND HYPERTROPHIC CARDIOMYOPATHY

E. Kaya (ErasmusMC, Rotterdam); D.A. Theuns (ErasmusMC, Rotterdam); S.C. Yap (ErasmusMC, Rotterdam); A. Schinkel (ErasmusMC, Rotterdam); A. Constantinescu (ErasmusMC, Rotterdam); M. Michels (ErasmusMC, Rotterdam); O. Manintveld (ErasmusMC, Rotterdam); T. Szili-Torok (ErasmusMC, Rotterdam); K. Caliskan (ErasmusMC, Rotterdam)

Purpose:
Implantable cardioverter-defibrillators (ICDs) are frequently used for primary and secondary prevention patients with cardiomyopathies due to different etiologies, but the long-term outcome in patients with noncompaction cardiomyopathy (NCCM) is still unknown. The aim of this study was to investigate the long-term outcome of the ICD therapy in NCCM patients, compared with those with dilated (DCM) and hypertrophic cardiomyopathy (HCM).

Methods:
Prospective data from our ICD registry was used to analyze the ICD therapy and survival in patients with NCCM (n=68 pts, 52% male, median age: 45y, IQR [35-57] compared with the cohort of DCM; n=458, 65% males, median age 57y, IQR [46-66] and HCM; n=158, 69% males, median age: 53y, IQR [42-62]).

Results:
An ICD was indicated for secondary prevention in 12 patients (18%; 50% male, median age 47y) and primary prevention in 56 patients (82%; 52% male, median age 43y) versus 15 and 85% in DCM patients and 21 and 79% in HCM patients; P=0.20). During a median follow-up of 4.2 years, IQR [2.0-6.9], appropriate and inappropriate ICD interventions were not significantly different (see figure A), while the 10-years survival was significantly better (see Figure B) in NCCM (94%) compared with DCM (69%) and HCM (79%). DCM patients were most symptomatic with NYHA class ≥ II in 90%, followed by NCCM (65%) and HCM patients (41%).

Conclusion:
At 4.2 years follow-up, appropriate and inappropriate ICD interventions in NCCM were comparable to those in DCM or HCM. In contrast, the long-term survival was significantly better in the NCCM group, probably due the younger age and less symptomatic heart failure.
INITIAL ORTHOSTATIC HYPOTENSION IS HIGHLY PREVALENT IN PATIENTS WITH UNEXPLAINED SYNCOPE – A REPORT FROM A MULTIDISCIPLINARY SYNCOPE UNIT IN A TERTIARY HEALTH CARE CENTER

D.J.L. van Twist (MUMC, Maastricht); N.H.T. Dinh (MUMC, Maastricht); E.M.E. Bouwmans (MUMC, Maastricht); A.A. Kroon (MUMC, Maastricht)

Purpose:
The prevalence of initial orthostatic hypotension (IOH) as a cause of syncope is unknown. IOH is defined as a transient decrease in blood pressure (BP) within 15 seconds after standing of >40mmHg systolic and/or >20mmHg diastolic, with symptoms of cerebral hypoperfusion, but without sustained orthostatic hypotension (BP decrease >20/10mmHg after 1-3 minutes of standing). We hypothesized that IOH is highly prevalent among patients with unexplained syncope.

Methods:
We analyzed 188 consecutive outpatients who were evaluated in our syncope-unit by two syncope-experts and who underwent a standard diagnostic protocol, including echocardiography, electrocardiography, and beat-to-beat-BP-measurement (Nexfin; BMEYE, The Netherlands). We measured BP-changes after active standing, first after lying supine for >5 minutes and then after squatting for 30 seconds. If considered indicated long-term-rhythm-monitoring, cardiac-exercise-test, head-up-tilt-table-testing, electroencephalography, or additional imaging was performed.

Results:
Clinical diagnoses in these 188 patients (mean age 61.0±18.3 years, BP 136±18/83±10 mmHg, 55% female) are shown in the Table. Upon active standing, 102 patients (54.3%) met the BP-criteria for IOH (mean -45.4±13.8/-28.1±11.4mmHg within 15 sec after standing). Of those, 18 had sustained orthostatic hypotension, 48 did not report symptoms of hypoperfusion, and in 15 patients history/additional tests revealed an alternative diagnosis. Two patients did not meet the BP-criteria, but history also strongly indicated IOH. Thus, 23 patients (12.2%) were diagnosed with IOH, of whom 52% used antihypertensive drugs (mostly beta-blockers). The squatting-to-standing test (n=127) did not increase the number of patients diagnosed with IOH.

Conclusion:
IOH is highly prevalent in patients with unexplained syncope. Therefore, beat-to-beat-BP-measurement should be considered in the analysis of unexplained syncope.
Figure 1: Diagnosis in 188 consecutive outpatients with previously unexplained syncope after evaluation in a multidisciplinary syncope unit in a tertiary health care centre.
RISK OF MISCLASSIFICATION WITH A NON-FASTING LIPID PROFILE IN SECONDARY CARDIOVASCULAR PREVENTION

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Purpose:
Routinely fasting is not necessary for measuring the lipid profile according to the latest European consensus. However, LDL-C concentrations tend to be lower in the non-fasting state with risk of misclassification. The extent of misclassification in secondary cardiovascular prevention with a non-fasting lipid profile was studied.

Methods:
Patients on stable lipid lowering therapy for secondary cardiovascular prevention measured a fasting and non-fasting lipid profile. Cut-off values for LDL-C, non-HDL-C and apolipoprotein B were set at <1.8 mmol/l, <2.6 mmol/l and <0.8 g/l, respectively. Study outcomes were net misclassification with non-fasting LDL-C (using the Friedewald formula), direct LDL-C, non-HDL-C and apolipoprotein B, with non-inferiority defined as a net misclassification <10%.

Results:
329 patients completed the study. Non-fasting measurements resulted in lower LDL-C (-0.2±0.4 mmol/l, p<0.001), direct LDL-C (-0.1±0.2 mmol/l, p=0.001), non-HDL-C (-0.1±0.4 mmol/l, p=0.004) and apolipoprotein B (-0.02±0.10 g/l, p=0.004), whereas triglycerides were higher (0.35±0.62 mmol/l, p<0.001). 36.0% of the patients reached an LDL-C target of <1.8 mmol/l in the fasting state with a significant net misclassification of 10.7% (95% CI 6.4–15.0%) in the non-fasting state. In the non-fasting state net misclassification with direct LDL-C was 5.7% (95% CI 2.1–9.2%), 4.0% (95% CI 1.0–7.4%) with non-HDL-C and 4.1% (95% CI 1.1–9.1%) with apolipoprotein B.

Conclusion:
Use of non-fasting LDL-C as treatment target in secondary cardiovascular prevention results in significant misclassification with subsequent risk of undertreatment. In contrast, non-fasting direct LDL-C, non-HDL-C and apolipoprotein B are reliable parameters as treatment target in secondary cardiovascular prevention with negligible risk of misclassification.
5 YEAR FOLLOW-UP OF PATIENTS SEEN FOR THE FIRST TIME AT A DUTCH FAST LANE OUT-PATIENT CARDIOLOGY CLINIC (FLOCC)

T. Lenderink (Zuyderland, Heerlen); E. Balkestein (Adelante, Hoensbroek)

**Purpose:**
To investigate reasons for referral, diagnostic procedures, diagnosis and long term survival of patients referred for the first time to a fast lane out-patient cardiology clinic.

**Methods:**
Patients were seen twice on the same day part. The first visit comprised of medical history taking, physical examination by the cardiologist and obtaining an ECG. After additional diagnostic testing for which were available laboratory tests, exercise testing, echocardiography and chest X ray, a second visit followed at which results and further follow up were discussed.

**Results:**
In the first quarter of 2007 a total of 419 patients were seen as true first referrals at the FLOCC. 360 were referred by general practitioners, 55 by other specialists and 5 were self-referral. The three largest referral groups were: chest complaints (44%); palpitations (19%) and dyspnoea (12%). Discharge from follow up occurred on the same day in 39%, another 38% after additional investigations (mostly 24-hour ECG). Five patients were admitted the same day. During 5 years of follow-up thirty-five patients died: 15 of cardiac, 18 of non-cardiac and 2 of unknown causes. One out of five, initially discharged, patients were referred again: 50% with the same and 50% for another reason.

**Conclusion:**
This study supports the creation of extramural cardiology clinics ‘1.5 lijnszorg’, as 80% of ‘first time cardiology’ patients seen at the FLOCC were discharged after investigations easily available for the GP. Additional time and cost reduction can be achieved by Holter analysis previous to the first visit in case of palpitations.

**Table 1:** Reason for referral to FLOCC

<table>
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<tr>
<th>Reason for Referral</th>
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<th>Female (225)</th>
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</tr>
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<tbody>
<tr>
<td></td>
<td>(% of gender group)</td>
<td></td>
<td>(% of gender group)</td>
<td></td>
</tr>
<tr>
<td>Chest pain</td>
<td>95 (49%)</td>
<td>56</td>
<td>90 (40%)</td>
<td>58</td>
</tr>
<tr>
<td>Palpitations</td>
<td>23 (12%)</td>
<td>54</td>
<td>58 (26%)</td>
<td>49</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>22 (11%)</td>
<td>62</td>
<td>28 (12%)</td>
<td>68</td>
</tr>
<tr>
<td>Sudden Loss of Consciousness</td>
<td>14 (7%)</td>
<td>58</td>
<td>11 (5%)</td>
<td>52</td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>16 (8%)</td>
<td>58</td>
<td>7 (3%)</td>
<td>68</td>
</tr>
<tr>
<td>Screening for cardiac disease</td>
<td>12 (6%)</td>
<td>49</td>
<td>8 (4%)</td>
<td>54</td>
</tr>
<tr>
<td>Murmur</td>
<td>5 (3%)</td>
<td>63</td>
<td>11 (5%)</td>
<td>65</td>
</tr>
<tr>
<td>Pre-Operative Screening</td>
<td>5 (3%)</td>
<td>66</td>
<td>9 (4%)</td>
<td>61</td>
</tr>
<tr>
<td>Cardiac origin of emboli</td>
<td>2 (1%)</td>
<td>64</td>
<td>3 (1%)</td>
<td>49</td>
</tr>
</tbody>
</table>
EDUCATIONAL INTERVENTION TO REDUCE OUTPATIENT INAPPROPRIATE ECHOCARDIOGRAMS

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Purpose:
In order to optimize the use of limited resources in healthcare, criteria for appropriate use of multiple diagnostic examinations have been developed. Among these are the appropriate use criteria (AUC) for transthoracic echocardiography (TTE), which have been shown to reduce the amount of unnecessary TTE’s. Reducing the number of unnecessary TTE’s will have impact on healthcare by reduction of costs, optimized distribution of resources and a decrease in waiting periods which, in some hospitals, are as long as 6 months. Transthoracic echocardiography (TTE) is the cornerstone of cardiac imaging due to its non-invasive, easy access and bedside imaging properties which gives the clinician a tremendous amount of information. This, however, has a flipside. The number of TTE requisitions rapidly increased in the last decade[1]. This increase cannot be explained by a rise in disease prevalence.

Methods:
We conducted a prospective observational cohort study in 3 different hospitals (2 academic and one large community hospital). In these 3 hospitals both cardiologists and cardiology residents were invited for an educational intervention on the AUC for TTE. At each centre, before and after the educational intervention, a random sample of 200 TTE orders from the outpatient clinic was evaluated for appropriateness according to the AUC guidelines 2011. The proportions of inappropriate TTE orders before and after the intervention were compared.

Results:
Before the intervention, the proportion of inappropriate TTEs was 18% compared to 8% after the intervention (p<.05). Three clinical scenarios accounted for two-thirds (66%) of all inappropriate TTE orders. The most common inappropriate indications (without a change in clinical status) were: 1) premature routine surveillance of mild/moderate valvular heart disease; 2) premature routine surveillance of prosthetic heart valves (mechanical / biological valves) and 3) premature routine surveillance of aortic dimensions.

Conclusion:
We have demonstrated that the proportion of inappropriately requested TTEs is significantly lower after an educational intervention. In addition, we observed that two-thirds of all inappropriate TTE orders are related to only three scenarios. Potentially, additional education targeting these scenarios may further reduce the number of requests for inappropriate TTEs.
THE RELATIONSHIP BETWEEN LIFELONG EXERCISE VOLUME AND CORONARY ATHEROSCLEROSIS

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Purpose:
Higher levels of physical activity are associated with a lower risk of cardiovascular events. Nevertheless, there is debate on the dose-response curve of exercise and cardiovascular outcomes and whether high volumes of exercise may accelerate coronary atherosclerosis. We aimed to determine the relationship between lifelong exercise volumes and atherosclerotic coronary artery disease.

Methods:
Lifelong exercise history was recorded in male athletes who underwent a sports medical examination and a non-contrast and contrast-enhanced computed tomography scan to assess coronary artery calcification (CAC) and plaque characteristics. Exercise volumes were multiplied by metabolic equivalent of task (MET) scores to calculate MET-min/week. Participants were classified according to <1000 MET-min/week, 1000-2000 MET-min/week or >2000 MET-min/week.

Results:
284 men (55±7 years) were included. CAC was present in 150/284 (53%) participants with a median CAC score of 35.8 [9.3-145.8]. Athletes with a lifelong exercise volume >2000 MET-min/week (n=75) more frequently had CAC (68%, OR=3.2 (95%CI: 1.6-6.6)) and plaque (77%, OR=3.3 (95%CI: 1.6-7.1)) compared to <1000 MET-min/week (n=88, 43% and 56% respectively). Among participants with plaques, the most active group had fewer mixed plaques (48% versus 69%, OR=.35 (95%CI: .15–.85) and more often had only calcified plaques (38% versus 16%, OR=3.57 (95%CI: 1.28–9.97)) compared to the least active group. There was no difference in location of CAC or plaque.

Conclusion:
High lifelong exercise volumes are associated with a higher prevalence of CAC and atherosclerotic plaques. Nevertheless, plaque characteristics are more benign in athletes performing >2000 MET-min/week, with fewer mixed plaques and more often only calcified plaques.
USE OF OPTIMAL MEDICAL THERAPY IN ACUTE CORONARY SYNDROME PATIENTS WITH A PREVIOUS HISTORY OF CARDIOVASCULAR DISEASE

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Purpose:
Data on optimal medical therapy (OMT) use in patients with previous cardiovascular disease (CVD) in a real-world setting is sparse. We studied the use OMT in acute coronary syndrome (ACS) patients and previous CVD in a real-world setting and the relation between the use of OMT and in-hospital and 30-day mortality.

Methods:
In a single-centre registry of patients with ACS admitted between 2006-2014, we analysed differences between patients with previous CVD and those without. In patients with previous CVD, we compared patients with or without OMT before admission. OMT was defined as the use of aspirin, statin, beta-blocker and ACE-inhibitor or ATII blocker. Main outcomes were in-hospital and 30-day death. We used a multivariate regression analysis to adjust for the non-randomised nature of the comparison.

Results:
There were 1690 patients with previous CVD and 6903 without CVD. Information on OMT was available for 95% of patients with previous CVD. OMT use before admission was higher in the CVD group (30.5% vs. 2.8%, p<0.001). Patients with OMT before admission were younger (69.9 (SD 10.9) vs. 72.0 (SD 11.3) years, p<0.001) and had higher rates of cardiovascular risk factors. Patients with OMT before admission had lower rates of in-hospital (3.3% vs. 5.9%, p<0.05) and 30-day mortality (4.1% vs. 7.7%, p<0.01). After adjustment, not using OMT at discharge was associated with 30-day mortality (OR 28.33 (95% Confidential Interval 6.69-119.93), p<0.001).

Conclusion:
This study showed that only 30% of ACS patients with previous CVD used OMT at the moment of the acute (second) event. OMT use before admission and at discharge was independently associated with lower in-hospital and 30-day death rates.