Abstracts of the Scientific Spring Congress of the Netherlands Society of Cardiology 11-12 April 2019

Postillion Convention Centre WTC Rotterdam
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 11 and 12 April 2019 in Postillion Convention Centre WTC Rotterdam.

We hope that you will enjoy reading the abstracts.

On behalf of the Chief Editorial Board,
Prof. dr. J.J. Piek
Editor in Chief Netherland Heart Journal
Session I: Arrhythmias

PHOSPHOLAMBAN (PLN) P.ARG14DEL CARDIOMYOPATHY: INSIGHT INTO AGE-RELATED PENETRANCE OF CARDIAC PHENOTYPE AND MALIGNANT VENTRICULAR ARRHYTHMIAS

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Purpose:
The founder mutation p.Arg14del in the gene encoding phospholamban (PLN) is a known cause of dilated cardiomyopathy (DCM) and arrhythmogenic cardiomyopathy (ACM). The purpose of this study is to demonstrate the age-related penetrance of cardiac phenotype and malignant VA in carriers of the PLN p.Arg14del mutation.

Methods:
Genetic analysis of PLN was performed in a clinical setting in index patients with clinical signs of DCM/ACM, or in family members of p.Arg14del carriers between 2009 and 2018. Malignant VAs were defined as sustained VA, appropriate ICD intervention or (aborted) sudden cardiac death. A cardiac phenotype was defined as malignant VA or at least one episode of clinical heart failure.

Results:
We evaluated 448 p.Arg14del carriers with a mean age of 42 +/- 17 (SD) and mean ejection fraction of 51 +/- 15% (SD) at first cardiac evaluation. Of the 448 carriers, 109 (24.3%) were probands and 339 (75.7%) were family members. 127 (28%) carriers developed a cardiac phenotype, of which 77 (61%) developed malignant VA.

Conclusion:
The prevalence of a cardiac phenotype is 50% at age 70 in carriers of the p.Arg14del mutation in PLN. Cardiac phenotypes emerge from adolescence to senior age. This suggests the need for life-long clinical cardiac follow-up starting from adolescence. Furthermore, p.Arg14del carriers are at serious risk of malignant VA during their entire lifetime, which supports the use of ICD therapy in a subset of p.Arg14del carriers.
Figures:  
Figure 1a and 1b show a Kaplan Meier curve with age as time scale, and age at cardiac phenotype and age at malignant VA respectively as event.
TOWARDS EARLY DETECTION OF A MYOCARDIAL INFARCTION THROUGH A NOVEL APPROACH OF VENTRICULAR FIBRILLATION WAVEFORM ANALYSIS

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Purpose:
To assess whether ventricular fibrillation (VF) waveform analysis may contribute to the detection of myocardial infarction (MI) during cardiac arrest, we initiated a pilot study on induced VF during ICD-implantations. If proven feasible, VF-waveform analysis could be tested as a means to early detect acute MI as underlying and treatable cause of VF in the out-of-hospital setting as well.

Methods:
VF-recordings were analysed using 12-lead electrocardiograms, during defibrillation testing after ICD-implantations (2010-2013). Four-second VF-segments prior to the shock were used to amplitude and frequency dependent VF-characteristics. These characteristics were used as input features for a support vector machine (SVM) model, to identify patients with a previous MI. Five-fold cross validation was applied for training and validation; model performances were assessed by receiver operating characteristic (ROC) analysis.

Results:
One-hundred and eighty patients were included, of which 98 (54%) had a history of MI. Figure 1 shows the ROC-curve of the machine learning model to detect a previous MI. The model had an area under the curve of 0.74 (95% CI 0.67-0.81). The positive predictive value of the model (Youden index) was 75%.

Conclusion:
This pilot study provides the first evidence that detection of a previous MI may be feasible during VF, with use of the innovative SVM-classifier. In follow-up on this study in a controlled setting, in-field studies are warranted to assess whether VF-waveform analysis may be a promising tool to detect an acute MI as well, with potential implications for in-field triage and treatment during cardiac arrest.
Figures:
Figure 1 – Receiver operating characteristic curve of the support vector machine model to identify a myocardial infarction during ventricular fibrillation.
FEASIBILITY OF PEDIATRIC PROBES IN TRANSESOPHAGEAL
ECHOCARDIOGRAPHY GUIDING OF LEFT ATRIAL APPENDAGE CLOSURE IN
ADULTS

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Purpose:
Transesophageal echocardiography is essential in the guidance of left atrial appendage closure (LAAC). Current practice often requires general anesthetics (GA) to endure a standard size probe during LAAC procedures. Smaller probes for pediatric purposes have been developed and might be useful for the guidance of LAAC in adults, eliminating the need for general anesthetics (GA) and reducing procedure times.

Methods:
In this prospective observational registry study patients were analyzed retrospectively to determine feasibility of pediatric TOE probes in adults for LAAC guidance. A standard set of LAA measurements, device compression and peri-device leakage was evaluated during procedure and by a second observer.

Results:
A total of 85 patients (56 male, mean age 72±7 years) were included. All patients underwent LAAC (76 Watchman, 9 Amplatzer Amulet), in 28 patients (33%) LAAC was combined with pulmonary vein isolation (PVI). The S8-3t micro-probe was used in 41 patients (48%) and the S7-3t mini-probe was used in 44 (52%). In 76 (38 mini-TEE, 38 micro-TEE) LAAC was successful, 7 of 9 failed procedures were due to unsuitable anatomy. Complete closure was achieved in 61/76 (29 mini-TEE, 32 micro-TEE), minimal residual flow was seen in 15/76 (8 mini-TEE, 7 micro-TEE). Device compression was comparable for mini- and micro-TEE and in accordance with recommendations. No GA was used in 93% of the patients, none of these procedures were prematurely terminated because of discomfort. No serious probe related complications were seen.

Conclusion:
The use of pediatric probes in the guidance for LAAC in adults is feasible and an attractive alternative avoiding the need for general anesthetics.
EXPLORING EPICARDIAL ADIPOSE TISSUE ACTIVITY IN ATRIAL FIBRILLATION

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Purpose:
Epicardial adipose tissue (EAT) volume has been associated with atrial fibrillation (AF), however, the underlying mechanism is unknown. EAT can directly interact with the myocardium through secretome, which can hold pro-inflammatory and pro-fibrotic factors. Therefore, we hypothesize that EAT secretome in AF patients contributes to formation of an arrhythmogenic substrate in the atrial myocardium. Our aim is to identify differentially expressed proteins and processes in EAT secretome that may be associated with the substrate of AF.

Methods:
Secretome was collected from EAT, retrieved from the left atrial appendage, from patients with persistent AF (n=3), and patients without AF (control, n=3). We performed an explorative proteomics analysis of the secretome on the platform of liquid chromatography-tandem mass spectrometry. Gene ontology (GO) analysis was conducted to interpret the biological characteristics of EAT secretome in AF.

Results:
We found 146 proteins differentially expressed in the AF secretome compared to the secretome of controls (p<0.05, fold-change>1.2). Among them, 62 proteins were increased and 84 proteins were decreased in AF. Perlecan (HSPG2) was the most significantly upregulated protein in AF (fold change 1.5, p<0.001). Myeloperoxidase (MPO) demonstrated the highest fold change, 18.1 (p<0.003). GO analysis on the 146 proteins revealed that blood coagulation in combination with fibrin clot formation was the most enriched GO process (fold enrichment 18.2, p<0.001, figure).

Conclusion:
Perlecan and MPO were upregulated in AF as were processes of blood coagulation, which may have pro-fibrotic characteristics. These findings support the hypothesis that biological activity of EAT may affect the pro-arrhythmic state of the atrial myocardium.
Figures:

Leading group term: blood coagulation, fibrin clot formation (fold enrichment 18.2). Other terms are processes closely related to the leading term, also shown by gray lines interconnecting the terms. Associations are based on similarity of protein content of the processes. Circles represent enriched group terms (p<0.00001). Red= increased proteins, blue= decreased proteins. Red/Blue= ratio between increased and decreased proteins.
WAIT-AND-SEE VERSUS ACUTE CARDIOVERSION IN RECENT-ONSET ATRIAL FIBRILLATION

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Purpose:
Acute cardioversion for patients with recent-onset atrial fibrillation (AF) is common. However, AF often terminates spontaneously. To show whether a wait-and-see approach for recent-onset symptomatic AF is non-inferior to acute cardioversion in terms of efficacy and safety.

Methods:
Multicentre prospective randomized open non-inferiority trial with blinded endpoint evaluation. Patients presenting at the emergency department with recent-onset AF were randomized to experimental wait-and-see approach or to reference care of acute cardioversion. The wait-and-see approach included prescription of rate control medication and delayed cardioversion if necessary at 48 hours. The primary endpoint is the presence of sinus rhythm at four weeks. Secondary endpoints include amongst others safety endpoints, AF recurrences and hospitalization for cardiovascular events.

Results:
437 patients were included between October 2014 and September 2018 in 15 centers in The Netherlands. Mean age was 65 years (±11 years), 40.3% were female and 43.9% had first detected AF. Palpitations was the most common symptom (n=381, 87.2%), followed by exercised induced fatigue (n=115, 26.3%), fatigue (n=114, 26.1%), dyspnea (n=100, 22.9%), chest pain (n=98, 22.4%) and (pre)syncope (n=43, 9.8%). The CHA2DS2-VASc scores 0, 1, 2 and 3 or higher occurred in 69 (15.8%), 89 (20.4%), 112 (25.6%) and 167 (38.2%), respectively. Follow up for the primary endpoint by ECG is virtually complete (99%).

Conclusion:
The results will fill an important knowledge gap on the acute treatment of AF and are therefore expected to have substantial clinical impact.
EPICARDIAL GANGLIONIC PLEXUS ABLATION DOES NOT AFFECT ATRIAL AND VENTRICULAR ECTOPIC ACTIVITY

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Purpose:
To determine the effect of GP ablation on atrial and ventricular ectopy.

Methods:
Patients from the AFACT study underwent epicardial pulmonary vein isolation (PVI) plus additional left atrial ablations when indicated. Patients were randomized to additional GP ablation or no GP ablation(control). We investigated the number of premature atrial and ventricular complexes (PAC and PVC) from 24 hour Holters at baseline, 3, 6, 9, 12 and 24 months after the procedure. All antiarrhythmic medication was discontinued after 3 months of follow-up.

Results:
In total, 1187 24-hour Holters were collected of all 240 patients of the AFACT trial, providing an 82% coverage and a median of 5 [4-6] Holters per patient. Atrial ectopy increased from baseline to 12 months (1.45[0-8.71], 3.96[1.20-24.86] PAC's/h, p<0.001), but was not associated with recurrence of AF (p=0.27). Ventricular ectopy increased from baseline to 12 months (0.56[0.083-5.38], 1.06[0.13-6.68] PVC's/h, p=0.009). GP ablation was not associated with a change in atrial or ventricular ectopic activity at any of the follow-up moments (see figure).

Conclusion:
GP ablation did not affect atrial or ventricular ectopy. However, both atrial and ventricular ectopy increased from baseline to 12 months post-procedure, potentially related to discontinuation of antiarrhythmic drugs.
Figures:

A: Median number of premature atrial complexes per hour from baseline to 24 months follow-up. B: Median number of premature ventricular complexes (PVC) per hour from baseline to 24 months follow-up.
FIRST RESULTS OF A NOVEL ULTRA-LOW CRYOABLATION SYSTEM FOR THE TREATMENT OF ATRIAL FLUTTER AND ATRIAL FIBRILLATION

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Purpose:
A novel ultra-low temperature cryoablation(ULTC) system using near critical nitrogen is designed for the treatment of atrial flutter(AFL) and atrial fibrillation(AF). ULTC reaches lower temperatures (-196 °C) and allows the use of shapeable catheters.

Methods:
In AFL patients, a cavotricuspid isthmus (CTI) lesion was created. In AF patients, antral pulmonary vein isolation (PVI) was performed. Additionally, CTI, mitral isthmus (MI) or roof and floor lines (“box”) were performed in selected patients. Acute procedural success was defined as CTI bidirectional block (BDB) in AFL patients and as PVI in AF patients.

Results:
65 patients were treated (17 AFL, 23 paroxysmal AF and 25 persistent AF). Acute success was achieved in all (17/17) AFL patients. Total ablation, procedure and fluoroscopy times were 5.4±3.4, 54±16 and 12±5 minutes respectively. A 12-month efficacy of 94% (16/17) was observed. In 48 AF patients, time to achieve PVI, total ablation and fluoroscopy times were 106±36, 12±5 and 12±7 minutes respectively. For patients with any additional lesions (16 “box”, 12 CTI and 3 MI) they were 116±33, 14±6 and 24±12 minutes respectively. PVI was achieved in 95.7% (134/140) of pulmonary veins. Two transient phrenic nerve palsies were observed and one patient had transient ST-elevation, deemed as a coronary spasm. No deaths, fistulas or tamponades were seen. Long term follow-up is ongoing, for those who reached 12 months of follow-up, 100% of paroxysmal AF patients (n=4) and 94% of persistent AF patients (n=9) showed freedom from AF.

Conclusion:
This novel cryoablation catheter system seems safe and efficient for performing CTI, PVI and additional lines. Limited long term outcomes are promising.
THORACOSCOPIC AF ABLATION IS A SUCCESSFUL TREATMENT FOR
PATIENTS WITH A GIANT LEFT ATRIUM

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F.R. Piersma, (AMC, Amsterdam), J.S.S.G. de Jong, (OLVG, Amsterdam), W.J.P. van
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Purpose:
In patients with a giant atrial volume catheter PVI is not recommended. However, surgical
PVI is being performed in patients with AF and giant LA, but with unknown efficacy. To
determine efficacy of thoracoscopic AF ablation in patients with AF a giant LA.

Methods:
Patients underwent thoracoscopic PVI (paroxysmal AF) plus additional left atrial ablations
(persistent AF). Giant LA was defined as left atrial volume index (LAVI) ≥50 ml/m2, outcome
was also assessed for LAVI ≥55 ml/m2. Prospective follow-up was performed with 24h-Holter
monitoring every three months. Primary outcome was recurrence of any atrial tachycardia
≥30 seconds.

Results:
Between 2008-2017, 357 patients underwent PVI. At baseline, giant LA was diagnosed in 72
(20.2%) patients (mean LAVI: 59.5±9.6 ml/m2), while 285 (79.8%) had a smaller left atrium
(mean LAVI: 36.3±7.8 ml/m2), p<0.001. Giant LA patients were older (mean: 61.7±6.9 vs
59.3±9.0 years, p=0.03). Sex (female: n=19, 26.4% vs n=79, 27.7%, p=0.82) was equally
distributed. They more often were diagnosed with persistent AF (n=60, 83.3%) compared to
control (n=164, 57.5%), p<0.001, but had a similar history of AF (median: 4.0[IQR: 2.0-6.0]
vs 4.0[IQR: 2.0-8.0] years, p=0.10). Freedom of any atrial tachyarrhythmia did not differ
significantly between both groups (n=43, 59.7% vs n=195, 68.4%, log rank p=0.91), figure.
This was similar for the cut-off of LAVI ≥55 ml/m2: n=24/43 (55.8%) vs n=214/314 (68.2%),
p=0.15). AF recurred in 16 (22.2%) patients with giant LA compared to 55 (19.3%) patients,
while atrial tachycardia recurred in 21 (29.2%) vs 56 (19.6%) patients, respectively, p=0.06.

Conclusion:
Thoracoscopic AF ablation is an effective therapy in patients with a giant LA and may
therefore be a feasible treatment.
Figures: Kaplan-Meier analysis of AF recurrence in patients with and without a giant left atrium.
Session II: Congenital cardiology and stroke prevention

PLASMA LEVELS OF MICROFIBRILLAR ASSOCIATED PROTEIN TYPE 4 (MFAP4) ARE PREDICTIVE FOR AORTIC DISSECTION IN PATIENTS WITH MARFAN SYNDROME

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Purpose:
Marfan syndrome (MFS) is a disorder with mutations in the fibrillin-1 gene, leading to elastic fiber degradation and increased TGF-beta signaling. The life-threatening feature of MFS is aneurysm formation with a risk of fatal aortic dissections. In a proteomics screen, we identified MFAP4, a protein involved in fibrillin-1 and elastic fiber formation, to be increased in the MFS aorta. We aim to study the role of MFAP4 in MFS aortic disease.

Methods:
MFAP4 co-localizes in the aorta with elastin and collagen fibers. In vitro experiments show that MFAP4 expression is upregulated by TGF-beta, which could explain the increased MFAP4 protein levels in the MFS aorta. In a substudy of 96 MFS patients from the COMPARE trial, MFAP4 levels correlate with aortic root diameter (r 0.30, p 0.01). Patients previously enrolled in the COMPARE trial were retrospectively analyzed. Cardiovascular events, including aortic dissection, were assessed. Plasma samples were prospectively collected at time of inclusion in the study and analyzed retrospectively on MFAP4.

Results:
In the 7 years of follow up, 5 Type B dissections occurred, all of them in patients in the upper tertile of plasma MFAP4. High plasma MFAP4 associates with poor dissection-free survival (Figure 1). Moreover, the aortic distensibility as measure for aortic stiffness and damage, was calculated throughout the aorta from available MRI images of these patients. Interestingly, in the descending thoracic aorta where type B dissections occur, the aortic distensibility is significantly lower (indicating decreased aortic elasticity) in MFS patients with high plasma MFAP4, thus associating with aortic damage.

Conclusion:
MFAP4, a protein involved in extracellular matrix assembly, is elevated in the MFS aorta. High plasma MFAP4 seems to reflect aortic damage and predicted type B aortic dissections in up to 7 years follow up.
Figures:
Figure 1.
THE PROGNOSTIC VALUE OF GROWTH DIFFERENTIATION FACTOR-15 IN ADULTS WITH PULMONARY HYPERTENSION

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Purpose:
Growth Differentiation Factor-15 (GDF-15) has been identified as prognostic marker in various cardiovascular diseases. This study investigated whether GDF-15 is associated with adverse outcomes in adults with pulmonary hypertension (PH).

Methods:
We prospectively included adults diagnosed with PH in our centre (May 2012 - October 2016). GDF-15 was measured during the diagnostic right heart catheterization. PH due to left heart disease was excluded. Survival according to tertile distribution of GDF-15 was determined using the Kaplan-Meier estimator and compared with the log-rank test for trend. Cox regression analysis was used to investigate the association between 2log transformed GDF-15 levels and the primary endpoint (death or lung transplantation) and the secondary endpoint (death, lung transplantation or heart failure). We adjusted for age and NT-proBNP in multivariable analysis.

Results:
GDF-15 was measured in 103 out of 106 patients (median age 59 years, 65% women, 51% pulmonary arterial hypertension). After a median follow-up of 23.8 [IQR 14.7-36.6] months, respectively 28 (27.2%) and 35 (34.0%) patients, reached the primary and secondary endpoint. Patients in the highest GDF-15 tertile, had the lowest survival (Figure). A significant association was found between GDF-15 and the primary endpoint (HR 1.74, 95%CI 1.34-2.25, p<0.001) and secondary endpoint (HR 1.60, 95%CI 1.27-2.01, p<0.001). The adjusted association between GDF-15 and endpoints remained significant with the primary endpoint (HR 1.43, 95%CI 1.00-2.04, p=0.049), however negated with the secondary endpoint (HR 1.29, 95%CI 0.95-1.77, p=0.108).

Conclusion:
Higher GDF-15 levels are significantly associated with an increased risk of mortality or transplantation in adults with PH, independent of age and NT-proBNP levels. GDF-15 could be a potential prognostic biomarker in PH.
Figures:
Transplant-free survival and event-free survival according to the tertile distribution of GDF-15.
RIGHT VENTRICULAR GLOBAL LONGITUDINAL STRAIN IS A POTENTIAL EARLY MARKER FOR RIGHT VENTRICULAR DYSFUNCTION IN PRECAPILLARY PULMONARY HYPERTENSION

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Purpose:
Right ventricular ejection fraction (RVEF) by cardiac magnetic resonance (CMR) is related to outcome in precapillary pulmonary hypertension-patients (pPH-patients), but this global measurement is not sensitive for early changes in right ventricular (RV) function. Strain analysis by feature tracking (FT) may be more sensitive for these early changes. The purpose of this study is to compare RV global longitudinal strain (RV-GLS) in healthy controls (HC) to pPH-patients with a preserved RVEF (pRVEF).

Methods:
pPH-patients and HC underwent CMR and echocardiography. RVEF >45% was defined as pRVEF. RV-GLS was assessed using FT-software on the 4-chamber cine image. Pearson’s R was used to calculate the correlation between RV-GLS and RVEF, the independent sample T-test to compare RV-GLS in HC to pPH-patients.

Results:
33 pPH-patients (53±15 years; 42% male), and 37 HC (age 35±11 years; 59% male) were included. Mean RVEF and RV-GLS were respectively 41.0±12% and -19.1±4.7% in pPH-patients, and 53.8±4.5% and -25.1±2.7% in HC (see table). RV-GLS strongly correlates with RVEF (Pearson’s R -0.84; P<0.001). Mean RV-GLS was lower in pPH-patients than in HC (p<0.001). In pPH-patients with pRVEF (n=14), RV-GLS was impaired compared to HC (-22.3±3.1% vs. -25.1±2.7%, p=0.002). Interestingly, in pPH-patients with pRVEF and HC matched for RVEF, RV-GLS remained lower in pPH-patients with pRVEF (-22.3±3.1% vs. -24.6±2.3%; p=0.022; see table).

Conclusion:
RV-GLS, strongly correlated with RVEF, is impaired in pPH-patients when compared to HC. More importantly, even in pPH-patients with pRVEF, RV-GLS remained significantly impaired compared to HC. This suggests that RV-GLS is an early marker of deterioration in RV function in pPH-patients.
### Figures:

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<th>P-value</th>
<th>Healthy controls matched for pRVEF (n=18)</th>
<th>pPH patients with pRVEF (n=14)</th>
<th>P-value</th>
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<td>Age - years</td>
<td>35 ± 11</td>
<td>53 ± 15</td>
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<td>35 ± 12</td>
<td>54 ± 12</td>
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<td>Male - n</td>
<td>22 (59%)</td>
<td>14 (42%)</td>
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<td>11 (61%)</td>
<td>6 (43%)</td>
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<td>TAPSE - mm</td>
<td>23.3 ± 3.4 (n=21)</td>
<td>19.7 ± 0.3 (n=33)</td>
<td>0.001</td>
<td>23.2 ± 3.3 (n=11)</td>
<td>21.3 ± 2.3 (n=14)</td>
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<td>RVSP - mmHg</td>
<td>18 ± 3 (n=23)</td>
<td>58 ± 20 (n=31)</td>
<td>&lt;0.001</td>
<td>18 ± 3 (n=12)</td>
<td>48 ± 21 (n=13)</td>
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<td>RVEF - %</td>
<td>53.8 ± 4.5</td>
<td>41.0 ± 12</td>
<td>&lt;0.001</td>
<td>51.5 ± 4.7</td>
<td>51.0 ± 6.9</td>
<td>0.780</td>
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<tr>
<td>RV GLS - %</td>
<td>-25.1 ± 2.7</td>
<td>-19.1 ± 4.7</td>
<td>&lt;0.001</td>
<td>-24.6 ± 2.3</td>
<td>-22.3 ± 3.1</td>
<td>0.022</td>
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pPH, precapillary pulmonary hypertension; pRVEF, preserved right ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion; RVSP, right ventricular systolic pressure; RV, right ventricular; RVEF, right ventricular ejection fraction; RV GLS, right ventricular global longitudinal strain. Continuous variables are expressed as mean ± standard deviation.
MEDICATION PATTERNS TO PREDICT MORTALITY IN ADULT CONGENITAL HEART DISEASE

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Purpose:
Adults with congenital heart disease (ACHD) often require pharmacotherapy. We assessed whether subgroups of ACHD with distinct medication patterns have different outcome.

Methods:
ACHD-patients of the CONCOR-registry were identified in the national Dispensed Drug Register (2006-2014). We performed unsupervised cluster analysis, phenomapping, of data on all drugs at baseline (13 categories classified following the Anatomical-Therapeutic-Chemical classification) and analyzed differences in mortality.

Results:
Data of 14,138 ACHD-patients (age 35[24-48] years, 49% male, 34% moderate and 9% severe defects) were included. Phenomapping identified three subgroups with distinct medication patterns. A “cardiovascular” cluster (n=8317), with high use of cardiovascular drugs (51%), was the oldest and had most patients with severe (10%) and left-sided lesions (e.g. bicuspid aortic valve; 11%). A “low medication use” cluster (n=3501) contained young, mainly female patients (70%), mostly with mild defects (60%). Many used anti-infectives (59%) and drugs for the genito-urinary tract (53%), but there was relative low use of other drugs. A third “comorbidity” cluster (n=2320) had many extra-cardiac drugs, with the highest proportion of patients with genetic syndromes (7%), and polypharmacy (≥5 drugs) (36%). 8-year cumulative survival was 92% in the “cardiovascular” group. It was better for the “low medication use” group (98%, HR=0.50[95%CI 0.37-0.78]). Despite the distinct medication pattern, survival was not different for the “comorbidity” group compared to the “cardiovascular” group after correction for age, sex, and defect severity (95%, HR=0.89[95%CI 0.71-1.11]).

Conclusion:
We identified three subgroups of ACHD, with “cardiovascular”, “low medication use”, and “comorbidity” medication patterns. Most patients had a “cardiovascular” pattern. Patients in the “comorbidity” group more often had extra-cardiac medication and polypharmacy, possibly indicating higher morbidity, but mortality risk was high both in patients with the “cardiovascular” and “comorbidity” pattern.
Figures:
Figure: Kaplan-Meier survival curve of the three phenogroups with distinct medication patterns.
THE PROGNOSTIC VALUE OF MYOCARDIAL DEFORMATION IN PATIENTS WITH CONGENITAL AORTIC STENOSIS

R.W. van Grootel (Erasmus MC, Rotterdam); R.W.J. van Grootel (Erasmus MC, Rotterdam); A.T. van den Hoven (Erasmus MC, Rotterdam); D. Bowen (Erasmus MC, Rotterdam); T. Ris (Erasmus MC, Rotterdam); J.W. Roos-Hesselink (Erasmus MC, Rotterdam); A.E. van den Bosch (Erasmus MC, Rotterdam)

Purpose:
Congenital aortic stenosis (AoS) is associated with significant mortality and morbidity but predictors for clinical outcome are scarce. Strain analysis provides a robust and reproducible method for early detection of left ventricular (LV) dysfunction, which might be of prognostic value. Therefore we aimed to assess the prognostic value of LV global longitudinal strain (GLS) and global longitudinal early diastolic strain rate (GLSre) with regard to cardiovascular events.

Methods:
This prospective study, included clinically stable patients with congenital AoS between 2011-2013. LV GLS and GLSre was performed in the apical 4, 3 and 2-chamber views using Tomtec software. The endpoint was a composite of death, heart failure, hospitalization, arrhythmia, thrombo-embolic events and re-intervention.

Results:
In total 138 patients were included (33[26-43]years, 86(62%) male), NYHA class I: 134(97%). Mean LV GLS was -15.3 ± 3.2%, GLSre 0.66 ± 0.18 s-1. Both correlated with NT-proBNP, LV volumes and ejection fraction (strongest LV GLS with LV EF: r -0.539, p<0.001, strongest LV GLSre with age: r -0.376 p<0.001). During median follow-up of 5.9[5.5-6.2]years, the endpoint occurred in 53(38%) patients: 4 patients died, 9 developed heart failure, 22 arrhythmias, 8 thrombo-embolic events and 35 re-interventions. Both LV GLS (standardized HR (sHR 0.62(95%CI 0.47-0.81) and GLSre(sHR 0.62(95%CI 0.47-0.83) were associated with the endpoint. Additional multivariable analysis showed that both GLS and GLSre were associated independent of left atrial volume, NT-proBNP and prior re-interventions.

Conclusion:
Left ventricular GLS and GLSre are reduced in adult patients with congenital AoS. Both markers are associated with adverse cardiac events and have clear clinical relevance.
Figures:
CORRECT DOSING OF NOAC IN A RECENT REAL-WORLD COHORT: IS UNDER OR OVERUSE STILL AN IMPORTANT PROBLEM?

M.A. Schotborgh (Spaarne Gasthuis, Haarlem); M.A. Schotborgh (Spaarne Gasthuis, Haarlem); R. Tukkie (Spaarne Gasthuis, Haarlem)

Purpose:
There is limited real life data on non-vitamin K antagonist oral anticoagulants (NOACs) dosing.
Studies have shown that 12.5 to 34% of patients receiving NOACs were incorrectly dosed.\(^1\) One of those studies even showed a trend for higher risk of adverse events in these patients.\(^1\) In theory, recent ESC guidelines\(^3,4\) and education programs should lead to less incorrect prescriptions. We investigated whether patients still received an inadequate dose of NOACs and explored the reasons.

Methods:
We performed a retrospective cohort study of daily clinical practice. Data of all patients seen at our hospital in the month October 2018 that received prescription for a NOAC for atrial fibrillation were collected, including parameters used for dose adjustments of NOACs.

Results:
251 patients were included. Data are presented in the table. Reasons for incorrect higher dosing were not accounting for kidney dysfunction, bodyweight or drug-drug interaction. Reasons for incorrect reduced dosing were not accounting for concurrent use of anti-platelet therapy, improved kidney function and not complying to package label criteria.

Conclusion:
Compared to the literature our data show less incorrect dosing of NOACs. However, there were still patients receiving an inadequate dose. Guidelines and the package label should be carefully considered in specific subgroups of patients. In this real world cohort at our institution only a small proportion of patients received an incorrect NOAC dose, but still there is room for improvement.

Figures:
Table, results

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<th>Normal dose n (% of total)</th>
<th>Reduced dose n (% of total)</th>
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<td>Correct</td>
<td>153 (61.0)</td>
<td>82 (32.7)</td>
<td>235 (93.6)</td>
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<tr>
<td>Incorrect</td>
<td>5 (2.0)</td>
<td>11 (4.3)</td>
<td>16 (6.4)</td>
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THE DIAGNOSTIC AND THERAPEUTIC YIELD OF TRANSTHORACIC ECHOCARDIOGRAPHY IN 474 PATIENTS WITH ISCHEMIC STROKE OR TIA OF UNDETERMINED CAUSE

G.H. van der Maten (Medisch Spectrum Twente, Enschede); J.M.B. Reimer (UMCU, Utrecht); M.F.L. Meijs (Medisch Spectrum Twente, Enschede); C. von Birgelen (Medisch Spectrum Twente, Enschede); M. Brusse-Keizer (Medisch Spectrum Twente, Enschede); M.H. den Hertog (Isala, Zwolle)

Purpose:
The evaluation of ischemic stroke and TIA of undetermined cause often includes transthoracic echocardiography (TTE). Since there is ongoing controversy regarding the indication for echocardiography in this setting, our aim was to assess the diagnostic and therapeutic yield of TTE in patients with recent ischemic stroke or TIA of undetermined cause.

Methods:
We retrospectively evaluated all patients with ischemic stroke or TIA of undetermined cause after standard diagnostic work-up, who were treated between January 2014 and December 2017, and had undergone TTE for evaluating a possible cardioembolic source. A major cardioembolic source was defined as an echocardiographic finding probably related to stroke or TIA warranting change of therapy. A minor cardioembolic source was defined as a possible cause of stroke or TIA, however not warranting different therapy.

Results:
Four hundred seventy-four of 667 patients with ischemic stroke or TIA of undetermined cause underwent TTE. Mean age was 65.6±13.8 years, 260 (54.9%) were male and 383 (80.8%) had ischemic stroke. In 30 patients, TTE showed a potential cardioembolic source corresponding with a diagnostic yield of 6.3%. In 10 patients a major cardioembolic source was found, corresponding with a therapeutic yield of 2.1%. Eight of these 10 patients had cardiac complaints or ECG abnormalities.

Conclusion:
The therapeutic yield of routine TTE in patients with ischemic stroke or TIA of undetermined cause is low. Our current multi-center registry aims to develop a prediction model for selecting patients based on certain criteria, in order to improve the (cost-)effectiveness of TTE in these patients.
RISK OF THROMBOEMBOLISM IN PATIENTS WITH MILD CONGENITAL HEART DISEASE AND ATRIAL ARRHYTHMIAS

T.C. Hankel (Academic Medical Center, Amsterdam); T.C. Hankel (Academic Medical Center, Amsterdam); O.I. Woudstra (Academic Medical Center, Amsterdam); H. Yang (Academic Medical Center, Amsterdam); T.C. Konings (VU University Medical Center); A.P.J. van Dijk (Radboud University Medical Center Nijmegen, Nijmegen); M.C. Post (St. Antonius Hospital, Nieuwegein); F.J. Meijboom (University Medical Center Utrecht, Utrecht); B.J.M. Mulder (Academic Medical Center, Amsterdam); B.J. Bouma (Academic Medical Center, Amsterdam)

Purpose:
Current guidelines on oral anticoagulation (OAC) in adults with congenital heart disease (CHD) and atrial arrhythmias (AA) consist of heterogeneous and divergent recommendations. Data on the risk of thromboembolism (TE), especially in case of mild CHD and AA, are missing. Therefore, we aimed to evaluate the incidence of TE in patient with mild CHD and AA.

Methods:
Consecutive adults with mild CHD and recurrent or sustained non-valvular AA from 5 tertiary centers were identified using a national ACHD registry. After two years of prospective follow-up, thromboembolism, major bleeding and death were assessed.

Results:
In total, 97 adults with mild CHD (mean age 61±14 years, 51% male) with various defects (including 61% with an atrial septal defect, 11% ventricular septal defect and 10% bicuspid aortic valve) and AA were included. The patients were treated with OAC (68%), antiplatelet therapy (10%) or no antithrombotic therapy (22%). The CHA2DS2-VASc score was higher than 2 was in 68% (n=45), 30% (n=3) and 30% (n=3) respectively. After a median of two years follow-up, 2 thromboembolisms, 1 major bleeding and 2 deaths occurred in patients treated with OAC. All patients with events had a CHA2DS2-VASc score >2. No events occurred in the patients with antiplatelet therapy or no antithrombotic therapy. The five year follow-up will be available soon.

Conclusion:
After two years follow-up, 2 thromboembolisms occurred in patients with mild CHD and a CHA2DS2-VASc score >2. No thromboembolic events occurred in patients with CHA2DS2-VASc score <2 treated without OAC. For patients with mild CHD, it seems appropriate to start antithrombotic therapy based on the CHA2DS2-VASc score similar to the general population.
THE IMPACT OF LEADLESS PACEMAKER THERAPY ON CARDIAC AND ATRIOVENTRICULAR VALVE FUNCTION THROUGH 12 MONTHS’ FOLLOW-UP

N.E.G. Beurskens (Amsterdam UMC, locatie AMC, Amsterdam); N.E.G. Beurskens (Amsterdam UMC, locatie AMC, Amsterdam); F.V.Y. Tjong (Amsterdam UMC, locatie AMC, Amsterdam); R.H.A. de Bruin-Bon (Amsterdam UMC, locatie AMC, Amsterdam); K.J. Dasselaar (Amsterdam UMC, locatie AMC, Amsterdam); W.J. Kuijt, MD* (Amsterdam UMC, locatie AMC, Amsterdam); A.A.M. Wilde (Amsterdam UMC, locatie AMC, Amsterdam); R.E. Knops (Amsterdam UMC, locatie AMC, Amsterdam)

Purpose:
Endocardial pacemaker leads and right ventricular (RV) pacing are well-known causes of tricuspid valve (TV), mitral valve (MV) and cardiac dysfunction. Lead-related adverse consequences can potentially be mitigated by LP therapy by eliminating the presence of a transvalvular lead. This study assessed the impact of leadless pacemaker (LP) placement on cardiac and valvular structure and function.

Methods:
Echocardiographic studies before and 12 ± 1 months after LP implantation were performed between January 2013 and May 2018 at our center.

Results:
A total of 53 patients were included, of whom 28 were implanted with a Nanostim and 25 with a Micra LP device. TV regurgitation (TR) was graded as being more severe in 23 (43%) of patients at 12 ± 1 months compared to baseline (p<0.001). Compared with an apical position, an RV septal position of the LP was associated with increased TV incompetence (odds ratio 5.20, 95% confidence interval 1.22-22.2, p= 0.03). An increase in MV regurgitation (MR) was observed in 38% of patients (p=0.006). LP implantation resulted in a reduction of RV function, according to a lower tricuspid annular plane systolic excursion (18.6 ± 6.81 versus 16.2 ± 6.52 mm, p=0.003) and RV tricuspid lateral annular systolic velocity (11.8 ± 3.04 versus 10.9 ± 2.49 cm/s, p=0.02), and a higher RV Tei index (0.40 ± 0.10 versus 0.50 ± 0.16, p=0.04). LP implantation was further associated with a reduction of left ventricular (LV) ejection fraction (53.5 ± 8.55 versus 50.2 ± 8.55%, p=0.03) and elevated LV Tei index (0.48 ± 0.12 versus 0.69 ± 0.27, p=0.003).

Conclusion:
LP therapy is unexpectedly associated with an increase in TV dysfunction through 12 months’ follow-up, most likely due to the mechanical impact of the intracardiac device on the TV or its subvalvular apparatus. Furthermore, LP therapy seems to adversely impact MV and biventricular function.
OPEN CHEST EXTRACORPOREAL CIRCULATION SUPPORTED 3D MULTI-ELECTRODE VT SUBSTRATE ABLATION AFTER FAILED PERCUTANEOUS ENDOCARDIAL AND EPICARDIAL ABLATIONS, A CASE SERIES

D.M.Haanschoten (Isala, Zwolle); D.M. Haanschoten, MD (Isala, Zwolle); A. Adiyaman, MD PhD (Isala, Zwolle); J.J.J. Smit, MD, PhD (Isala, Zwolle); P.P.H.D Delnoy, MD, PhD (Isala, Zwolle); A. Elvan, MD PhD (Isala, Zwolle)

Purpose:
We assessed the feasibility of open chest extracorporeal circulation supported 3D multi-electrode mapping and targeted VT substrate ablation in patients with previously failed percutaneous endocardial and epicardial VT ablations.

Methods:
In patients with previously failed percutaneous endocardial and epicardial VT ablations, open chest extracorporeal circulation (ECC) supported epicardial mapping and ablation was performed. In a hybrid EP lab setting, open chest detailed 3D electroanatomic maps were acquired during SR and VT using a multi-electrode mapping catheter (HD Grid, Abbott or Pentaray, Biosense Webster). Irrigated radiofrequency current ablations of all inducible VTs were performed with a contact force ablation catheter.

Results:
In 5 patients with structural heart disease (3 with previous CABG and old myocardial infarction and 2 with nonischemic cardiomyopathy) and recurrent VT/VF, pericardial access was not possible after ≥1 failed percutaneous endocardial and epicardial ablations. In these patients, open chest ECC supported epicardial multi-electrode mapping and ablation was performed. In all patients VTs were inducible prior to ablation. Number of inducible VT morphologies varied between 2-5. Mapping during SR was performed using a multi-electrode catheter (HD Grid, Abbott or Pentaray, Biosense Webster) to localize the area of interest. Mapping during VT was performed to localize the critical parts of the VT substrate. Overall, acute success was achieved in all 5 patients, with complete VT abolition in 4 (80%) and partial abolition in 1 (20%). In 1 patient, damage to the venous graft occurred after sternotomy and this patient with a severely reduced LVEF (16%) remained VT free, however died 1 month after the ablation due to sepsis and multi-organ failure. The remaining patients were free from VT/VF.

Conclusion:
In patients with previously failed percutaneous endocardial and epicardial VT ablations, open chest ECC supported multi-electrode epicardial mapping revealed a VT substrate in all patients, and targeted epicardial ablation abolished VT substrate in these patients.
INCREASED DONOR AGE LEADS TO A HIGHER NEED FOR PERMANENT PACING AFTER ORTHOTOPIC HEART TRANSPLANTATION

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Purpose:
Extreme shortage in donors in the Netherlands has led to increasingly aging donors in heart transplantations (HT). The aim of the study was to evaluate the relationship between donor age and the need for a permanent pacemaker (PPM) implantation after HT.

Methods:
All HTs in our center between 1984 and August 2018 were retrospectively analysed. Retransplantation within 30 days (n=2) and patients who died within 30 days post-HT (n=53) were excluded. 664 HTs were included. Based on the donor age the HTs were divided into three groups: Group I (<35 years, n=361), Group II (35–50 years, n=207) and Group III (>50 years, n=96). Primary outcome was the implantation of a PPM post-HT, either early (≤90 days) or late (>90 days).

Results:
Before 2000 (the moment of immunosuppressive regime switch from cyclosporine- to tacrolimus-based therapy), the average donor age was 26 [IQR 20-35] and after 2000 42 [IQR 25-51] (P<0.001). The median follow-up was 9 years [IQR 4-14]. PPM rates are shown in the table. Median time for early PPM was 37 days [IQR 29-42] and 7.6 years [IQR 3.4-13.4] for late PPM. Indications for PPM implantation were sinus node dysfunction in 52.1% and atrioventricular block in 47.9%. Mean ischemic times were not statistically different between Group I, II and III (178 ± 47, 181 ± 46 and 184 ± 46, respectively, P=0.37).

Conclusion:
The need for an early PPM is statistically higher in HTs with a donor age >50 years. However, the long-term survival was non-inferior in patients with a PPM.
<table>
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<th>Group 3</th>
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<tr>
<td></td>
<td>n (%)</td>
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<tr>
<td><strong>Total</strong></td>
<td>664</td>
<td>361</td>
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<td>19 (9)</td>
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<td>&lt; 0.001</td>
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<td>57 (59)</td>
<td>29 (8)</td>
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INTERMEDIATE OUTCOMES IN CRT FOLLOW-UP; ASSOCIATIONS TO LONG TERM OUTCOME

A.M.W. van Stipdonk (MUMC+, Maastricht); M. Ghossein (MUMC+, Maastricht); M. Kloosterman (UMCG, Groningen); I.A.H. ter Horst (UMCU, Utrecht), F.W. Prinzen (UM, Maastricht); M. Meine (UMCU, Utrecht); K. Vernooy (MUMC, Maastricht), A.H. Maass (UMCG, Groningen).

Purpose:
Cardiac resynchronization therapy (CRT) reverses cardiac remodelling, reduces heart failure complaints and HF hospitalizations, and reduces mortality in the long term. However it is not known how intermediate endpoints are associated with long term mortality in CRT patients. The objective of this study was to evaluate the individual associations of intermediate endpoints with long term outcome in CRT patients.

Methods:
874 patients from a multicentre retrospective CRT database were included in this study. Intermediate endpoints were improvement in NYHA functional class and echocardiographic LVESV reduction at 6 months post-implantation, and HF hospitalization within the first year post-implantation. Long term outcome was the combined event of LVAD implantation, cardiac transplantation or all-cause mortality.

Results:
NYHA class improvement and echocardiographic response at 6 months post implant are associated (p=0.001) Both NYHA class improvement (p<0.001) and LVESV reduction (p<0.001) are significantly associated to the occurrence of both HF hospitalization. NYHA class improvement (p<0.001, HR 1.94), LVESV reduction (p=0.017, HR 1.36) and HF hospitalization (p<0.001, HR 5.0) is also significantly associated to the occurrence of long term events. However, intermediate endpoints occurring during follow-up are not independently associated to long term outcome in CRT patients.

Conclusion:
Intermediate outcomes in CRT patients are all associated, and events during follow-up therefore identify those patients at increased risk of poor long term outcome. Though as intermediate term outcomes and long term prognosis have no association independent from baseline characteristics, these results put emphasis on the importance of patient selection, as well as strenuous follow-up in CRT.
Figures:
Figure 1. HF functional class improvement, echocardiographic response, and HF hospitalizations in association with long-term clinical outcomes.
MYOCARDIAL DAMAGE AS A RESULT OF IMPLANTATION AND DEFIBRILLATION TESTING IN TRANSVENOUS AND SUBCUTANEOUS IMPLANTABLE CARDIOVERTER-DEFIBRILLATORS

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Purpose:
Myocardial damage of implantation and defibrillation testing (DFT) of subcutaneous implantable defibrillators (S-ICD) versus transvenous implantable defibrillators (TV-ICD) has not been evaluated in humans. Previous studies in TV-ICD patients have showed myocardial damage, but it has not been reported if this is the result of DFT or active fixation of the ICD lead.

Methods:
In this four-arm study, enrolling 20 patients in each arm, we examined high sensitivity troponin I (hs-TnI) level changes after TV-ICD implantation with DFT (arm A), TV-ICD implantation without DFT (arm B), TV-ICD generator replacement with DFT (arm C) and S-ICD implantation with DFT (arm D). Change in hs-TnI was calculated between hs-TnI at baseline and 6-8 hours after DFT or end of the procedure.

Results:
Patients in arm A, in which a lead was actively fixated during implant, had a mean rise in hs-TnI of 0.025 ug/l (figure). In arm B the rise was 0.018 ug/l, in arm C 0.009 ug/l and in arm D 0.001 ug/l. Arm A had a significant rise in hs-TnI compared to both arm C and arm D (p = 0.029 and p = 0.001 respectively). Arm B, which enrolled patients implanted with an TV-ICD without DFT also had a significant rise of hs-TnI compared with arm D (p = 0.029). There was no significant difference between arm A and B (p = 0.41) or arm C and D (p = 0.165)figure).

Conclusion:
Elevation in cardiac enzymes after ICD implantation seems to be the result of myocardial damage due to active lead fixation during implant and not the effect of DFT. DFT in S-ICD implantation, and in TV-ICD replacement did not result in significant myocardial damage.
Figures:
Arm A: Transvenous ICD (TV-ICD) implantation with DFT. Arm B: Transvenous ICD implantation without DFT. Arm C: TV-ICD generator replacement and DFT. Arm D: Subcutaneous ICD implantation with DFT. DFT = Defibrillation Test. Hs-TnT = high sensitive troponin
USEFULNESS OF A STANDARD 12-LEAD ELECTROCARDIOGRAM TO PREDICT THE ELIGIBILITY FOR A SUBCUTANEOUS DEFIBRILLATOR

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Purpose:
Currently, the eligibility for a subcutaneous implantable defibrillator (S-ICD) system relies on a pre-implant vector screening based on the automated screening tool (AST). We aimed to investigate 12-lead ECG characteristics associated with eligibility for an S-ICD in a heterogeneous population at risk for sudden cardiac death (SCD). The goal is to determine patient eligibility for S-ICD using the standard 12-lead ECG, thereby avoiding additional AST screening.

Methods:
We prospectively evaluated the eligibility for an S-ICD in 254 consecutive patients at risk for SCD. We identified 12-lead ECG parameters which were independently associated with AST passing (≥1 vector) using multivariable logistical regression analysis in our derivation cohort. The final model was tested in a separate validation cohort.

Results:
The overall passing rate was 92% in our derivation cohort. Independent 12-lead ECG characteristics associated with AST passing were QRS≤130 ms, absence of QRS/T discordance in lead II and R/T-ratio ≥3.5 in lead II. Eighty-three of 254 patients (33%) fulfilled these three criteria and had a passing rate of 100%. Of the validation cohort, 37 of 60 patients (62%) fulfilled all three criteria and also had a passing rate of 100%. The interobserver agreement for applying the ECG model was 90% (Cohen’s Kappa= 0.80).

Conclusion:
Using the standard 12-lead ECG, we developed a simple screening model with a high specificity for S-ICD eligibility. Our results suggest that patients who fulfill the three ECG criteria do not need additional AST-screening. Therefore, we propose a simple flowchart to determine eligibility for an S-ICD that can be easily implemented in daily clinical practice (Figure).
Figures:
Proposed screening model for S-ICD screening

A patient is a S-ICD candidate when met all the following criteria:
- No pacing indication
- No CRT indication
- No history of monomorphic VT
- Patients preference for S-ICD

A patient will pass the 12-lead ECG screening when met all the following criteria:
- QRS duration ≤130 ms
- Absence of QRS/T-wave discordance in lead II
- R/T-ratio ≥3.5 in lead II
LEADLESS PACING. GOING FOR THE JUGULAR. RUNNING HEAD: THE JUGULAR APPROACH

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Purpose:
Leadless pacing is generally performed from a femoral approach. However, the femoral route is not always available. Until now, data regarding implantation using a jugular approach other than a single case report is lacking.

Methods:
Case records of all patients who underwent internal jugular venous (IJV) leadless pacemaker implantation (Micra, Medtronic) at our center were analysed retrospectively.

Results:
19 patients underwent IJV leadless pacemaker implantation, 9 female, mean age 77.5 ±9.6 yrs; permanent AF in all patients with normal left ventricular ejection fraction. Implant indication was AV conduction disturbance in 10, pre AV node ablation in 7 and replacement of a conventional VVI pacemaker in 2 (infection in 1 and lead malfunction in the other). The device was positioned at the superior septum in 7 patients, apicoseptal in 7 patients and midseptal in 5 patients. In 12 patients, a sufficient device position was obtained at the first attempt, in 3 at the 2nd, in 1 at the 3rd, in 1 at the 4th and in 2 at 6th attempt. The mean pacing threshold was 0.56± 0.39V at 0.24 ms pulse width, sensed amplitude was 9.1±3.2mV , mean fluoroscopy duration 3.1±1.6 min. There were no vascular or other complications. At follow-up electrical parameters remained stable in 18 of 19 patients.

Conclusion:
Although experience is minimal, we suggest that the IJV approach is safe and may be considered in patients where the femoral approach is contraindicated.
THE EXPERIENCES OF WOMEN WITH A SUBCUTANEOUS IMPLANTABLE CARDIOVERTER DEFIBRILLATOR

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Purpose:
The subcutaneous implantable cardioverter defibrillator (S-ICD) is positioned in close proximity of the left mamma. This may result in issues particularly for female patients, such as limitations in clothing, breastfeeding or self-perception. Female patients are however underrepresented in most large S-ICD studies, thus underexposing these gender-specific issues which may impact their daily life substantially.

Objective: To assess the issues female S-ICD patients are experiencing and provide practical ‘tips and tricks’ to reduce their discomfort.

Methods:
All female patients implanted with an S-ICD in a large tertiary center between February 2009 and November 2018 received a single questionnaire with questions on physical, esthetical and situational issues.

Results:
Patients were categorized in three age groups, 18-39 years (n=30), 40-55 years (n=36) and >55 years (n=21). All patients (100%) in the youngest age group experienced substantial discomfort while wearing a bra, specifically with the linings and the sideband (figure A and B). Women preferred a more cranial position of the S-ICD generator with the lower sideband supporting the device (figure C). A position of the S-ICD generator posterior from the lining of the left cup also reduced discomfort. While no-one reported problems with childbirth, a minority did report problems with breast engorgement. Sexuality and self-perception was not altered after S-ICD implant in this group.

Conclusion:
Female S-ICD patients experience gender-specific issues with a substantial impact on their daily life. Implanters should use bra position during pre-implant marking to reduce daily discomfort and provide adequate counseling.
Figures:
Figure A and B: this position of the S-ICD caused substantial discomfort in women while wearing a bra. Figure C: this position of the S-ICD is preferred by women.
Session IV: Coronary disease

A CARDIOVASCULAR MAGNETIC RESONANCE OR COMPUTED TOMOGRAPHY ANGIOGRAPHY FIRST GUIDED STRATEGY VERSUS ROUTINE CLINICAL CARE IN HIGH-SENSITIVE TROPOIN-POSITIVE SUSPECTED NON-ST-ELEVATION MYOCARDIAL INFARCTION (CARMENTA). A RANDOMIZED CONTROLLED TRIAL.

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Purpose:
Patients with suspected non-ST-elevation-myocardial-infarction (MI) and elevated high-sensitivity cardiac-troponins (hs-cTn) often routinely undergo invasive coronary angiography (ICA) but many do not have obstructive coronary artery disease (CAD). The primary hypothesis is whether a cardiovascular magnetic resonance (CMR) or computed tomography angiography (CTA) first versus a routine invasive strategy reduces the proportion of ICA with no detrimental effect on clinical outcome.

Methods:
In this randomized controlled trial (NCT01559467), 207 patients (64 years on average, 62% male) with acute chest pain, elevated hs-cTnT levels (>14ng/L) and inconclusive electrocardiogram were randomized to a routine invasive, CMR first or CTA first strategy. Follow-up ICA was recommended when initial CMR or CTA suggested myocardial ischemia, infarction or obstructive CAD (>70% stenosis). Primary efficacy and safety endpoints were referral to ICA during hospitalization and one-year outcomes (major adverse cardiac events and complications), respectively.

Results:
The CMR and CTA first strategies reduced ICA compared to routine clinical care (87% [p=0.001], 66% [p<0.001], and 100%, respectively). Clinical outcome was similar in all strategies (Figure). Obstructive CAD after ICA was found in 61% in the routine clinical care, in 69% in the CMR (p=0.308 vs. routine) and in 85% in the CTA first (p=0.006 vs. routine) strategy. In the non-CMR and non-CTA arms, follow-up CMR and CTA were performed in 67% and 13% of patients and led to a new diagnosis in 33% and 3%, respectively, p<0.001.

Conclusion:
A novel strategy of implementing CMR or CTA first in the diagnostic process in suspected non–ST-elevation-MI is a safe gatekeeper for ICA.
Figures:
Kaplan-Meier estimates of adverse cardiac events during 1-year follow-up. Panel A shows the cumulative event rate and hazard ratios (HR) between strategies of major adverse cardiac events (MACE, i.e. a composite of all-cause mortality, recurrent myocardia

Panel A.
Composite endpoint: major adverse cardiac events (MACE)

Overall Log Rank: p=0.733
HR (CMR vs routine clinical care) = 1.01 (95% CI 0.33-3.12)
HR (CTA vs routine clinical care) = 0.64 (95% CI 0.18-2.27)
HR (CMR vs CTA) = 1.58 (95% CI 0.45-5.61)

Panel B.
Composite endpoint: MACE and other adverse events including complications

Overall Log Rank: p=0.537
HR (CMR vs routine clinical care) = 0.78 (95% CI 0.37-1.61)
HR (CTA vs routine clinical care) = 0.66 (95% CI 0.31-1.42)
HR (CMR vs CTA) = 1.19 (95% CI 0.53-2.66)
PRE-HOSPITAL VERSUS HOSPITAL ACQUIRED HEART SCORE FOR RISK CLASSIFICATION OF SUSPECTED NSTE-ACS

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Purpose:
Although there is increasing evidence that in patients with suspected NSTE-ACS the pre-hospital acquired HEART score has strong predictive value, hospital and pre-hospital acquired HEART-scores have never been compared directly.

Methods:
In 699 patients with suspected NSTE-ACS, the HEART-score was independently prospectively assessed in the pre-hospital setting by ambulance paramedics and in the hospital by physicians. The hospital assessed HEART-score was considered the gold standard. Low-risk (HEART-score ≤ 3) was considered a negative test. Endpoint was occurrence of MACE within 45 days.

Results:
In 516 (74%) patients pre-hospital and hospital risk classification was similar, in 50 (7%) pre-hospital risk classification was false negative (45 days mortality 0%) and in 133 (19%) false positive (45 days mortality 1.5%). False negative risk classifications were caused by differences in history (100%), risk factor assessment (66%), and troponin (18%), and more common in older patients. Occurrence of MACE was comparable in pre-hospital and hospital low-risk patients (2.9 versus 2.7%, p=0.9). Incidence of MACE was 0% in the true negative group, 26% in the true positive group, 10% in the false negative group and 5% in the false positive group. Predictive value of both pre-hospital and hospital acquired HEART-scores were high, although AUC of hospital acquired HEART-score was higher (0.84 vs 0.74, p<0.01).

Conclusion:
In approximately 25% of patients there is disagreement among hospital and pre-hospital acquired HEART-score, mainly by risk overestimation in the pre-hospital group. Since disagreement is mainly due to different scoring of history and risk factors, additional training may improve pre-hospital scoring.
LONG-TERM OUTCOMES POST PCI OR CABG IN ELDERLY PATIENTS WITH MULTIVESSEL DISEASE AND/OR LEFT MAIN DISEASE

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Purpose:
This study aims to compare coronary artery bypass grafting (CABG) with percutaneous coronary intervention (PCI) in elderly patients with multivessel disease (MVD) and/or left main (LM) disease, considering completeness of revascularisation and severity of coronary artery disease (CAD).

Methods:
All patients aged ≥ 75 years with MVD or LM disease who underwent revascularisation between 2012-2016 were included. Angiography was assessed on severity of CAD. Based on the revascularised vessels, completeness of revascularisation was determined. Primary endpoint was three year mortality. Secondary endpoint was a composite of recurrent angina, cardiac rehospitalisation and repeat revascularisation at three year.

Results:
A total of 597 patients were included. Mean follow-up was 1467 days. At baseline, patients in the PCI-group were older, more often had a medical history of CABG and more frequently underwent an urgent procedure compared to patients in the CABG-group. Three year mortality was significantly lower in patients who underwent CABG compared to PCI (13.9 vs. 23.1%, p=0.006). However, after adjustment, this difference was not significant anymore (HR 1.47 [95%CI 0.97-2.24], p=0.07). The secondary endpoint occurred more often in patients who underwent PCI versus CABG (31.7 vs. 46.4%, p=0.001), this difference remained significant after correction (HR 1.57 [1.18-2.08], p=0.002). Neither completeness of revascularization nor severity of CAD was a predictor for the primary or secondary endpoint.

Conclusion:
We identified no significant difference in survival between PCI or CABG in elderly patients with MVD and/or LM disease. However, patients undergoing CABG have a lower risk of recurrent angina, cardiac rehospitalisation and repeat revascularisation compared to PCI.
Figures:
Kaplan Meier curve three years mortality PCI vs. CABG
DIAGNOSTIC VALUE OF THE ELECTROCARDIOGRAM IN THE ASSESSMENT OF PRIOR MYOCARDIAL INFARCTION

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Purpose:
The gold standard in the assessment of prior MI is cardiac magnetic resonance imaging (CMR) with late gadolinium enhancement (LGE). In daily practice, the electrocardiogram (ECG) plays a major role in the evaluation of MI. However, the predictive value of the ECG remains unknown. This study evaluates the diagnostic value of the ECG in the assessment of prior MI.

Methods:
Of all 1097 performed CMR with LGE between January 2014 and December 2017, 974 patients were included in this retrospective study. Data collection was conducted by examination of electronic patient files. Twelve-lead ECGs were blinded and analyzed by two cardiologists. Disagreement of interpretation was solved by judgement of a third cardiologist. Outcomes of CMR with LGE were used as gold standard.

Results:
The sensitivity of the ECG in the detection of MI was 38,0% with a 95% confidence interval (CI) of 31,6-44,8%. The specificity was 86,9% (95% CI 84,4-89,1%). The positive- and negative predictive value were respectively 43,6% (95% CI 36,4-50,9%) and 84,0% (95% CI 81,4-86,5%). In 170 ECG’s (17,5%), the two cardiologists disagreed on the presence or absence of MI. Inter rater variability was moderate (kappa 0,52, 95% CI 0,45-0,58, p<0,001).

Conclusion:
The ECG has a low diagnostic value in the detection of prior MI. However, if the ECG shows no signs of prior MI, the absence of MI is likely. This study confirms that decisions concerning prior MI should not solely be based on an ECG.

Figures:
Overview of results of ECG and CMR with LGE in the assessment of MI

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Purpose:
Percutaneous coronary intervention (PCI) of chronic total occlusions (CTO) are high risk procedures with low success rates compared to standard PCI. Recently the 'hybrid approach' method has been developed to increase success rate. In 2015 we set up a program to systematically treat CTO’s by this hybrid approach. This included appointment of 3 dedicated CTO operators, schooling by proctor and investment in new, high-end materials. This retrospective, observational registry aims to report achieved results in a single, off site PCI-centre.

Methods:
We reviewed all CTO procedures between January 2012 and December 2017. All procedures performed by one of three dedicated operators after December 2014 were assigned to the hybrid group, all procedures done before this time or performed by a non-CTO operator were assigned to the non-hybrid group. Procedural techniques, difficulty of lesion, J-CTO scores, outcomes and complications were analysed.

Results:
A total of 505 procedures were included in the study. 80.7% were male. Mean age was 66 ± 10 years. The average J-CTO score was 1.9 ± 1.1, which was significantly higher in the hybrid group (2.1 ± 1.2 vs. 1.6 ± 1.1; p <0.000). Overall procedural success rate was 75.4% with a significantly higher success rate in the hybrid group (81.2% vs. 68.2%; p <0.001). Combining both groups, overall success rate increased over the years (2012 - 2017 respectively 65.2%, 60.0%, 71.7%, 78.2%, 81.3% and 82.5%). Complication rate was higher in the hybrid group, 13 (4.6%) in the hybrid group vs. 1 (0.4%) in the non-hybrid group (p=0.026).

Conclusion:
By introducing a systematic CTO program, including use of the hybrid approach, we observed higher success rates of PCI CTO, despite an increase of complexity of the lesions (higher J-CTO). There was a significant increase in MACE, however MACE occurrence rates are in accordance with current literature.
Figures:

Figure 1. Attempts and successful attempt by year

- **Attempts**
- **Success**
- **Percentage success**
CONTEMPORARY BIODEGRADABLE POLYMER-COATED VERSUS DURABLE POLYMER-COATED DRUG-ELUTING STENTS IN ALL-COMER PATIENTS OF THE RANDOMIZED BIO-RESORT (TWENTE III) TRIAL AT 3-YEARS

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Purpose:
To assess the 3-year outcome of patients treated with two contemporary biodegradable polymer-coated very thin strut drug-eluting stents (DES) versus a durable polymer-coated thin strut DES. Biodegradable polymer-coated DES ultimately leave only bare-metal stents in the coronary arteries, which has the theoretical advantage that the absence of polymer may lower the risk of ischemic complications after several years.

Methods:
The BIO-RESORT (TWENTE III) randomized clinical trial, is a multi-center investigator-initiated patient-and-assessor blinded study that enrolled 3,514 all-comer patients who required stenting. Non-inferiority was established at 1-year between either biodegradable polymer DES (Synergy everolimus-eluting stent and Orsiro sirolimus-eluting stent) versus the durable polymer DES (Resolute Integrity zotarolimus-eluting stent). The main clinical endpoint is target vessel failure (TVF), a composite of safety (cardiac death or target vessel myocardial infarction) and efficacy (target vessel revascularization).

Results:
Follow-up data at 3-years was available in 96.6% of all trial participants. At 3-year follow-up, the main clinical endpoint TVF occurred in 8.7% (199/2,341) of the patients treated with biodegradable polymer DES and 10.0% (115/1,173) of the patients treated with durable polymer DES (plog-rank=0.19). The rate of definite-or-probable stent thrombosis was low and similar in both, biodegradable and durable polymer DES, and there was no difference in other clinical endpoints.

Conclusion:
Contemporary DES, assessed in BIO-RESORT, showed favorable 3-year safety and efficacy outcomes that were similar in biodegradable polymer-coated versus durable polymer-coated DES.
Figures:
Cumulative incidence of target vessel failure (a composite of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization) at 3-years follow-up. Abbreviations: DES = drug-eluting stent; BP-DES = bio

**Target vessel failure at 3-years**

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$p = 0.19$, HR 0.86 (0.68–1.08)
THE DIAGNOSTIC ROLE OF CARDIAC MAGNETIC RESONANCE IMAGING AS INITIAL TEST IN SUSPECTED NON-ST ELEVATION MYOCARDIAL INFARCTION

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Purpose:
A cardiac magnetic resonance imaging (CMR)-directed strategy improves the diagnostic yield of invasive coronary angiography (ICA) in stable coronary artery disease (CAD).
Evidence on the diagnostic accuracy of CMR to detect obstructive CAD in non-ST elevation myocardial infarction (NSTEMI) is limited.

Methods:
This study is a sub-analysis of a randomized controlled trial that investigated whether a non-invasive imaging first strategy safely reduced the number of ICA compared to routine clinical care in suspected NSTEMI (acute chest pain, inconclusive electrocardiogram, high-sensitivity cardiac troponin-T (hs-cTnT) levels >14ng/L). All patients underwent CMR prior to ICA (1 day, range 0-6 days). A stepwise approach was used to assess the diagnostic accuracy of CMR to detect obstructive CAD (stenosis ≥70%). Regional abnormalities in ≥2 adjacent segments on cine, T2-weighted and delayed enhancement imaging suggestive of underlying CAD were evaluated first and when normal or non-diagnostic, on adenosine-stress perfusion imaging as a second step (Figure).

Results:
Of 51 patients included (63±10 years, 51% male), 34 (67%) had obstructive and 17 (33%) had non-obstructive CAD. The sensitivity, specificity and overall accuracy of step one and two were 71%, 71% and 71% vs. 80%, 92% and 86%, respectively. When both steps were combined, sensitivity, specificity and overall accuracy were 94%, 65% and 84%, respectively. In the 17 patients with non-obstructive CAD, CMR still showed an MI in 5 (29%) and stress cardiomyopathy in one.

Conclusion:
CMR, particularly stress perfusion imaging, accurately detects obstructive CAD in hs-cTnT-positive suspected NSTEMI. Non-obstructive CAD is common with almost one-third having an MI by CMR.
Figures:
CAD = coronary artery disease; CI = confidence interval; CMR = cardiac magnetic resonance imaging; CTA = computed tomography angiography; DE = delayed enhancement; ICA = invasive coronary angiography; NSTEMI = non-ST elevation myocardial infarction

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<th>Procedure</th>
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<th>Specificity (%) (95% CI)</th>
<th>Overall accuracy (%) (95% CI)</th>
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<td>Stress perfusion imaging (step 2)</td>
<td>80 (44 - 97)</td>
<td>92 (62 - 99)</td>
<td>86 (65 - 97)</td>
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<td>Combination of step 1 and 2</td>
<td>94 (80 - 99)</td>
<td>65 (38 - 86)</td>
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RELATIONSHIPS BETWEEN EXTENT OF ISCHEMIC BURDEN AND CHANGES IN ABSOLUTE MYOCARDIAL PERFUSION AFTER CHRONIC TOTAL OCCLUSION PERCUTANEOUS CORONARY INTERVENTION

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Purpose:
The present study explored the relationships between baseline ischemic burden findings and subsequent changes in absolute myocardial perfusion after chronic coronary total occlusion (CTO) percutaneous coronary intervention (PCI).

Methods:
Consecutive patients underwent serial [15O]H2O positron emission tomography prior and after successful CTO PCI. Change in perfusion defect size (in myocardial segments), quantitative (hyperemic) myocardial blood flow (MBF) and coronary flow reserve (CFR) in the CTO area were compared between patients with a limited (0-1 segment), moderate (2-3 segments) and large perfusion defect (≥4 segments) at baseline.

Results:
193 patients were included, with 15, 61 and 117 patients having a limited, moderate and large perfusion defect at baseline. Hyperemic MBF and CFR were lower in a large perfusion defect compared to smaller defects (all comparisons p<0.01). The median decrease in defect size was 1 [0-1] vs 2 [1-3] vs 4 [2-5] in patients with a limited, moderate and large defect (all comparisons p<0.01), whereas hyperemic MBF and CFR improved significantly regardless of baseline defect size (between groups p=0.45 and p=0.55, respectively). Furthermore, when all 193 patients were divided in a lowest, median and highest tertile based on hyperemic MBF and CFR at baseline, changes in hyperemic MBF and CFR after CTO PCI were comparable between patients in different tertiles (between groups p=0.75 and p=0.79, respectively)

Conclusion:
Patients with a CTO and a larger perfusion defect have more severe hyperemic MBF and CFR levels. Major reductions in ischemic burden can be achieved by CTO PCI, with more defect size reduction in patients with a larger perfusion defect, whereas hyperemic MBF and CFR improve significantly and irrespective of baseline values.
Session V: Invasive Cardiology

EARLY OUTCOMES AFTER PERCUTANEOUS CLOSURE OF ACCESS SITE IN TAVR USING THE NOVEL VASCULAR CLOSURE DEVICE PLUG-BASED-MANTATM

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Purpose:
A new collagen-based MANTA TM vascular closure device (VCD), was developed for closing large-bore arteriotomies after transfemoral transcatheter aortic valve replacement (TAVI). We evaluated safety and feasibility in terms of vascular complications, bleedings and 30 days outcomes of the collagen-based VCD, MANTA TM VCD compared with the suture-based VCD, Prostar® XL in a cohort of patients undergoing transfemoral TAVI.

Methods:
Retrospective comparative study of consecutive patients who underwent transfemoral TAVI and percutaneous closure in a tertiary hospital between January 2015-April 2018. A total of 366 patients were included. MANTA TM VCD was used in 168 patients and Prostar® XL VCD in 198 patients.

Results:
Vascular access site closure with the MANTA TM VCD was successful in 98.8% and in 98.5% with the Prostar® XL in the treated patients. VARC-2 defined major vascular complication and major bleeding was similar in both cohorts (MANTA TM vs Prostar® XL): 0.6% vs 1.0% (P=0.661) and 0.6% vs 1.5% (P=0.102) respectively. Minor vascular complications and minor bleeding, however, were significantly more frequent (10.7 vs 18.8%, P=0.003), and (13.7 vs 19.7%, P=0.080) respectively) in the Prostar® XL cohort. Thirty-days all-cause mortality was 2.7%, without significant difference between the groups.

Conclusion:
The MANTA TM device is a safe and feasible option for vascular access closure in patients undergoing transfemoral TAVI.
IMPACT OF SEVERE LESION CALCIFICATION ON CLINICAL OUTCOME OF PATIENTS TREATED WITH CONTEMPORARY DRUG-ELUTING STENTS IN THE RANDOMIZED BIO-RESORT TRIAL

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Purpose:
The outcome of patients with severe target lesion calcification, treated with contemporary biodegradable polymer and durable polymer-coated drug-eluting stents (DES), is greatly unknown. We assessed the impact of severe target lesion calcification on 2-year clinical outcome of patients treated by percutaneous coronary intervention (PCI) with contemporary DES.

Methods:
BIO-RESORT is a large-scale randomized clinical trial that included 3,514 all-comer patients requiring PCI, who were categorized into patients with versus without severe target lesion calcification. The main clinical endpoint target vessel failure (TVF) is a composite of cardiac death, target vessel-related myocardial infarction (MI) or clinically indicated target vessel revascularization (TVR).

Results:
Patients with severely calcified lesions (n=783, 22.3%) were older (67.0±10.0 vs. 63.1±10.8 years, p<0.001), and had more diabetes (20.7% vs. 16.9%, p=0.02), hypertension (51.7% vs. 44.6%, p<0.001) and hypercholesterolemia (42.9% vs. 36.6%, p=0.001) than patients without severe lesion calcification (n=2,731, 77.7%). At 2-year follow-up (available in 98.8%), TVF occurred in 9.8% vs. 6.5% (p=0.001) of patients with versus without severely calcified target lesions. That significant difference was driven by a difference in target vessel MI (4.6% vs. 2.3%, p<0.001). Between patient groups, there was no difference in TVR (4.6% vs. 3.8%, p=0.36) and definite-or-probable stent thrombosis (0.9% vs. 0.7%, p=0.64). Landmark analysis showed that the difference in TVF resulted from a difference during the first 48 hours (4.5% vs. 1.5%, p<0.001).

Conclusion:
Stenting of severely calcified coronary lesions with contemporary DES is associated with an increased adverse event risk, in particular during the first 48 hours after PCI.
Figures:
Cumulative incidence of target vessel failure (a composite of cardiac death, target vessel-related myocardial infarction, or clinically indicated target vessel revascularization) at 2-years, with landmark at 48 hours.
URGENCY AND APICAL ACCESS SIGNIFICANTLY INCREASE ONE-YEAR TRANSCATHETER VALVE IMPLANTATION MORTALITY

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Purpose:
For the treatment of symptomatic aortic valve stenosis, trans-catheter aortic valve replacements (TAVI) are not only well established in elderly, high-risk and in-operable patient populations, but their indication range is rapidly expanding. For example, there is extensive research going on to introduce TAVI in younger patients and for urgent indications. Our aim was to compare all-cause mortality between urgent and planned TAVI procedures and to assess the impact of apical procedures on TAVI survival.

Methods:
Retrospective analysis of a single centre TAVI database was performed. Patients undergoing transapical or transfemoral TAVI between 01.01.2014 and 31.12.2017 and providing consent to participate in anonymous scientific research were included. Any device implantation during an unplanned hospitalisation was treated as urgent. All-cause mortality was determined based on health insurance status. Groups were formed based on access site and urgency (trans-femoral [TF], trans-apical [TA], urgent trans-femoral [UTF] and urgent trans-apical [UTA]). Continuous variables were compared with One-way ANOVA or Kruskal-Wallis tests, while categorical variables were compared with Chi-square test. Survival analysis was performed with Kaplan-Meier curves and Cox regression analysis. Variables are shown with interquartile range or standard deviation, depending on their distribution.

Results:
Altogether 518 patients (346 TF, 123 TA, 32 UTF, 17 UTA) were included in the analysis. Apical and urgent patients had significantly higher mortality rates then their respective counterparts and TF survival was better than TA survival (TF: 6.9%, TA: 15.4%, UTF: 25.8%, UTA: 51.2%; overall p<0.001, TF vs TA p=0.04, TF vs UTF p<0.001, TA vs UTA p=0.008). Further group comparisons revealed that elective femoral procedures required the shortest hospitalisations (7 vs 10 vs 23 vs 18 in days; TF, TA, UTF, UTA respectively; p<0.001) and more patients undergoing urgent procedures had a left ventricular ejection fractions <40% (7% vs. 10% vs 29% vs 29%, TA, TF, UTF, UTA respectively; p=0.015), worse renal function (96 [77-116] vs 94 [81-120] vs 102 [79-146] vs 117 [95-154] in umol/l; p<0.05 and p<0.05 for TF vs UTF and higher procedural risk expressed by Euroscore II (TF 2.86 [1.77-4.32] vs. TA 3.62 [2.28-6.44] vs. UTF 5.5 [4.09-9.58] vs. UTA 4.84 [3.325-16-14], p<0.0001). Other available parameters (height, weight, BMI, Diabetes, Chronic lung disease, prior valve surgery and prior CVE) were comparable among study groups, although men tended to undergo more apical procedures. Cox-regression analysis using significantly different variables as covariates revealed that for the whole population only access site (p=0.003; HR:2.202) and urgency (p<0.001, HR: 3.22) had an independent effect on mortality. To get a grasp of the overall clinical condition of urgent patients, admission-to-procedure time (T1), thus stabilization was calculated. Sub-group analysis with access site and T1 as covariates showed that only T1 had marked effect on mortality (p=0.49, HR: 1.040/day).

Conclusion:
Access site and urgency both determine 1-year mortality and the more time is needed to stabilize urgent patients, the smaller their chance for survival becomes.
Figures:
Figure 1. Kaplan-Meier curves showing 1-year survival after femoral, apical and urgent procedures.
PREOPERATIVE FRAILTY PARAMETERS AS PREDICTORS FOR OUTCOMES AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Purpose:
Guidelines suggest to use frailty characteristics in the work-up for a transcatheter aortic valve implantation (TAVI). There are many frailty-screening tools with different components. The prognostic value of the individual parameters in frailty is yet unclear. The objective of this systematic review and meta-analysis was to find and pool predictors for one-year mortality after TAVI.

Methods:
We followed a two-step approach. First, we searched OVID-MEDLINE for RCTs on TAVI to identify frailty parameters used in these studies. Second, we searched OVID-MEDLINE and OVID-EMBASE from inception to April 12, 2018 to find publications on frailty parameters and predictors for outcomes after TAVI. Articles were included for pooled analysis if the studied frailty parameters were dichotomized with clear cut-off values based on common standards or clinical practice and reported adjusted hazard ratios (HR) of one-year mortality after TAVI.

Results:
We calculated pooled effect estimates of 49 studies based on dichotomized frailty-scores (HR: 2.16, 95%CI: 1.57-3.00), chronic lung disease (HR: 1.57, 95%CI: 1.45-1.70), eGFR < 30 ml/min (HR: 1.95, 95%CI: 1.68-2.29), BMI<20 kg/m2 (HR: 1.49, 95%CI: 1.09-2.03), hypoalbuminemia (HR: 1.77, 95%CI: 1.38-2.25), anemia (HR: 2.08, 95%CI: 0.93-4.66), low gait speed (HR: 13.33, 95%CI: 1.75-101.49) and KATZ-ADL score 1 or more deficits (HR: 5.16, 95%CI: 0.77-34.47).

Conclusion:
We identified multiple frailty parameters used in TAVI research in this meta-analysis which were predictive for one year mortality. Chronic lung disease, chronic kidney disease, underweight, hypoalbuminemia, a low frailty score, anemia, low gait speed and an ADL deficiency were associated with worse one-year outcomes.
**Figures:**
Hazard ratios for 1-year mortality summarizing all comorbidity/frailty categories

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<th>Random Effects Model (Hazard Ratio)</th>
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<th>95% CI</th>
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<td>[1.45; 1.70]</td>
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<td>eGFR &lt; 30 ml/min</td>
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<td>1.95</td>
<td>[1.68; 2.29]</td>
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<td>BMI &lt; 20 kg/m²</td>
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<td>1.49</td>
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<td>[1.38; 2.25]</td>
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<td>Low frailty score</td>
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<td>Anemia</td>
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<td>ADL deficiency</td>
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<td>5.16</td>
<td>[0.77; 34.47]</td>
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</table>
A COMPARISON BETWEEN THE DIAGNOSTIC PERFORMANCE OF QUANTITATIVE FLOW RATIO AND NON-INVASIVE IMAGING MODALITIES FOR DIAGNOSING MYOCARDIAL ISCHEMIA. A PACIFIC-TRIAL INTERIM ANALYSIS

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Purpose:
To compare the diagnostic performance of Quantitative Flow Ratio (QFR) with coronary computed tomography angiography (CCTA), single-photon emission tomography (SPECT), and positron emission tomography (PET) for diagnosing myocardial ischemia defined by fractional flow reserve (FFR).

Methods:
For this interim analysis QFR computation was retrospectively attempted in 109 patients (327 vessels) of the 208 patients included in the PACIFIC-trial. Patients underwent 256-slice CCTA, Tetrofosmin SPECT, and [15O]H2O PET prior to ICA in conjunction with FFR measurements of all major coronary arteries. ICA images were acquired without the use of a dedicated QFR acquisition protocol. QFR was calculated using a fixed empiric hyperemic flow velocity (fQFR) as well as using a patient specific flow velocity based on contrast passage through the coronary (cQFR). All analysis were performed on a per vessel level.

Results:
A total of 41 vessels were excluded due to the presence of a subtotal/total occlusion through which wire passage was not possible. Fixed QFR computation succeeded in 152 (53%) vessels while cQFR analysis was successful in 140 (49%) vessels. Both fQFR and cQFR had a good correlation with FFR (R=0.774, p<0.001 and R=0.790, p<0.001), with minimal average bias, and good intra class correlation coefficient (0.889, p<0.001 and 0.880 p<0.001). Fixed QFR as well as cQFR had a numerically higher diagnostic accuracy (90%, and 88%) in comparison with CCTA (72%), SPECT (81%), and PET (79%). In total 133 vessels with matched FFR, cQFR, fQFR, CCTA, SPECT, and PET results were available for the comparative analysis on diagnostic performance. The diagnostic performance of fQFR and cQFR was comparable (c-statistics: 0.923 vs. 0.928, p=0.451) and superior to non-invasive imaging modalities (CCTA: 0.784, p=0.004, p=0.003; SPECT: 0.659, p<0.001, p<0.001, PET: 0.817, p=0.008, p=0.006). Coronary CTA and PET performed alike (c-statistic: 0.784 vs. 0.817, p=0.568) and outperformed SPECT (0.659, p=0.023, p=0.002).

Conclusion:
Fixed QFR and cQFR correlate well with FFR resulting in a high diagnostic performance on a per vessel level. In the present retrospective analysis, QFR outperformed CCTA, SPECT, and PET on a per vessel basis with the important footnote that fQFR and cQFR could only be computed in 53%, and 49% of the vessels.
Figures:
Comparative c-statistic analysis of 133 vessels with matched FFR, cQFR, fQFR, CCTA, SPECT, and PET results.
INTRAMYOCARDIAL INJECTIONS GUIDED BY ACTIVE MRI-TRACKING FOR REGENERATIVE THERAPY

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Purpose:
Regenerative therapy for the treatment of heart failure is a promising prospect that could provide major benefit to millions of patients. It also poses a unique set of challenges with regards to not only the underlying biology of specific cell types, but also in terms of delivery and retention of therapies in the myocardium.
Late-gadolinium enhancement on cardiac MRI is considered the gold standard for assessment of myocardial infarction. However, MRI is rarely used to guide intramyocardial therapy. MRI has important advantages over the currently used delivery methods in terms of accuracy, reproducibility, independency of patent coronary arteries, and exposure to ionizing radiation. Within the MIGRATE consortium we collaborated to develop an actively-tracked steerable MRI compatible injection catheter compatible with a new, MRI visible biomaterial. Here, we report on the feasibility of MR-guided delivery of biological therapies to the heart in four healthy pigs.

Methods:
The injection catheter was adapted from an existing electrophysiology ablation catheter created by Imricor. It has active tracking capabilities with integrated receiver coils and a deflectable tip for accurate steering. The catheter was used in a 1.5T MRI equipped with the Philips iSuite iMRI platform. A supramolecular hydrogel, developed by the TU/e, was used for the injections. For this experiment the hydrogel was crosslinked with dotarem for MRI-visibility. For active tracking a 3D-roadmap scan was acquired prior to the intervention. A 3D-shell of the endocardium was created in ITK-SNAP. During active tracking the interventional software platform displays the catheter location on the proper scan planes and renders a model of the cathetertip inside the 3D-shell. Passive visualization was performed using 2D balanced TFE sequences with a framerate of 2-5Hz.

Results:
After induction of anesthesia the pigs were transferred to the MR-room. The catheter was introduced via the femoral artery. Under active tracking we could successfully pass the catheter retrogradely towards the left ventricle and through the aortic valve. Handling of the catheter under active tracking was intuitive and allowed us to inject at desired locations. Ex-vivo MRI-scanning of the excised heart confirmed successful injections at several of the expected locations. However, not all injections could be identified. This could be caused by unsuccessful injections (potentially due to the novel nature of the technique) or by incomplete retention of the hydrogel.

Conclusion:
iMRI-guidance of intramyocardial injections is feasible. The combination of active and passive tracking allows intuitive catheter handling as well as real-time confirmation of injection success. Adoption of interventional MRI for application of therapy could potentially be an important step forward to boost effectiveness of regenerative therapies.
SEX-RELATED DIFFERENCES IN CALCIFICATION IN AORTIC VALVE STENOSIS: APPLICATION OF A NON-INVASIVE IMAGING STRATEGY USING 18F-NAF PET/CT

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Purpose:
Aortic valve calcification (AVC) is a key factor in development and progression of aortic valve stenosis (AS). Females tend to have less AVC for similar AS hemodynamic severity when compared to males. Recently, a dominant role for valvular fibrosis in females was suggested by histology. Therefore, the aim of this study was to assess sex differences in calcification activity in development and progression of AS using a clinically available combined 18F-sodiumfluoride (18F-NaF) PET/CT.

Methods:
One hundred and forty six patients (29 female, 117 male) with mild to severe aortic valve stenosis underwent combined 18F-NaF PET and contrast-enhanced CT scanning. 18F-NaF quantification was performed using the most diseased segment approach with maximum and mean target-to-background both calculated.

Results:
In the population as a whole 25% (n=37) had mild, 56% (n=81) moderate and 16% (n=23) severe AS. Ranges of TBRmax and TBRmean measurements in the total population and in female and male subgroups are presented in Figure 1. TBRmean showed no significant differences between males and females. However, male sex was associated with higher TBRmax in both univariable regression and multivariable regression, adjusted for stenosis severity and cardiovascular risk factors.

Conclusion:
Males show a higher calcification burden, and maximum activity in regions with developing calcification as reflected by TBRmax is higher than values seen in females. These findings merit further investigation in longitudinal studies investigating progression of AS and clinical relevance of calcification activity differences.
Figures:
Figure 1: Calcification activity in aortic valve stenosis in males and females. A: TBRmax. B: TBRmean
CHARACTERISTICS, TREATMENT AND OUTCOME IN TRANSIENT ST-ELEVATION MYOCARDIAL INFARCTION VERSUS ST-ELEVATION MYOCARDIAL INFARCTION

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Purpose:
An estimated 4-24% of patients presenting with ST-elevation MI (STEMI) subsequently show resolution of ST-elevation and symptoms before revascularisation. The mechanisms of spontaneous reperfusion in STEMI are unclear. Given the more favourable outcome of transient STEMI (TSTEMI) it is important to get insights in differential aspects of patients with either persistent or transient coronary occlusion.

Methods:
We included 251 patients from two cohorts with either TSTEMI (n=141) or STEMI (n=110). Demographics, clinical, angiographic and laboratory data were documented. Cardiac magnetic resonance imaging (MRI) was performed at 2-8 days and clinical follow-up at one year.

Results:
TSTEMI patients had slightly more cardiovascular risk factors compared to STEMI patients with more frequently previous percutaneous coronary intervention (PCI) (5.7 versus 3.6%, p<0.001) and higher cholesterol values (total cholesterol respectively 5.3±1.1 versus 4.7±1.1 mmol/L, p<0.001). Furthermore, at admission TSTEMI patients had higher levels of thrombocytes compared to STEMI (262±69 versus 234±70∙10⁹/L, p=0.02). In 40% of STEMI patients a high thrombus burden was found, while 41% of TSTEMI patients had no angiographic evidence of thrombus at all (p<0.001). In TSTEMI patients median MRI-derived infarct size was 1.4% (IQR, 0.0-3.7%) compared to 8.8% (IQR, 3.9-17.1; p<0.001) in STEMI patients. Furthermore, microvascular obstruction (MVO) was more frequently present in patients with STEMI than with TSTEMI (34.6 versus 4.2%, p<0.001, respectively). Mortality at 1-year follow-up was low in both groups (TSTEMI 2.2% versus STEMI 2.8%, p=0.76).

Conclusion:
Transient STEMI is an acute coronary syndrome distinct from STEMI, resulting in less myocardial injury compared to STEMI.
Session VI: General Cardiology

MOBILE HEALTH IN ADULT PATIENTS WITH CONGENITAL HEART DISEASE: SEEK AND YOU SHALL FIND

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Purpose:
Adult patients with congenital heart disease (ACHD) have an increased risk of cardiac arrhythmias and hypertension. However, diagnosis of these entities can be challenging in clinical practice. We aimed to determine whether mobile health (mHealth) telemonitoring could be used as a diagnostic tool for cardiac arrhythmias and hypertension in these patients.

Methods:
We performed a prospective registry of symptomatic ACHD patients in two medical centers in the Netherlands. Symptoms were defined as palpitations (with or without documented arrhythmias) in the last three years. All patients were enrolled in an mHealth telemonitoring program, evaluating heart rhythm and blood pressure using a mobile device and smartphone.

Results:
In total, 97 symptomatic patients with ACHD were enrolled, mean age 44.8 years and 31% male. Median follow-up was 9.0 months. Sixty patients were known with cardiac arrhythmias, in 9 of whom recurrent arrhythmias were registered. During follow-up, of the 37 patients with palpitations with no diagnosis at baseline, 34 regularly performed a single lead EKG and in four patients a new diagnosis was established. In two patients atrial fibrillation was diagnosed, one patient registered a supraventricular tachycardia during palpitations, one patient was diagnosed with sinus node dysfunction. Blood pressure measurements were available in 89 patients of whom three were diagnosed with previously unknown hypertension. In seven patients antihypertensive treatment was adjusted as a result of mHealth blood pressure monitoring.

Conclusion:
mHealth telemonitoring may be used as an easy diagnostic tool in ACHD patients. It may detect new arrhythmias and follow blood pressure in daily life accurately, which may facilitate swift therapeutic adaptations.
INFECTIVE ENDOCARDITIS IN THE NETHERLANDS: CURRENT EPIDEMIOLOGICAL PROFILE AND IN-HOSPITAL MORTALITY, DATA FROM THE EURO-ENDO REGISTRY

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Purpose: Infective endocarditis (IE) is a serious infectious disease with a high in-hospital and long term mortality. Progress in prevention, diagnostic approach and management of IE have been made in the recent decades. However, morbidity and mortality of IE remain high. Few studies on IE profile have been performed in the Netherlands. The aim of this study was to assess current in-hospital mortality and to present a contemporary overview of baseline characteristics of IE in the Netherlands.

Methods: This is a prospective observational cohort study of patients with IE We used data of the EURO-ENDO registry. Seven hospitals in the Netherlands have participated and included patients with IE between April 2016 and April 2018.

Results: A total of 139 patients were included. In-hospital mortality was 14.4% (20 patients). Nearly thirty percent presented with prosthetic valve endocarditis (PVE), 7.2% with cardiac device related infective endocarditis and 3.6% with aortic root prosthesis. Furthermore, we observed early use of imaging for diagnosis and an increase in urgent surgery (50.4%). Embolic events were associated with higher in-hospital mortality. Age and S. aureus IE were independent risk factors for in-hospital mortality.

Conclusion: We observed a decrease in in-hospital mortality in the Netherlands compared to earlier publications. This might be attributable to the increase of urgent surgery and early diagnosis and multidisciplinary management of IE. Further data on one-year mortality of IE in the Netherlands is expected in the summer of 2019.
**Figures:**

Values expressed as N (percentage) and median (interquartile range)

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>N=139 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>95 (68.3%)</td>
</tr>
<tr>
<td>Mean age</td>
<td>63.9 (57.0 – 75.0)</td>
</tr>
<tr>
<td>Previous endocarditis</td>
<td>9 (6.5%)</td>
</tr>
<tr>
<td>Congenital heart disease</td>
<td>14 (10.1%)</td>
</tr>
<tr>
<td>Previous valve surgery</td>
<td>47 (33.8%)</td>
</tr>
<tr>
<td>Prosthetic valve at admission</td>
<td>46 (33.1%)</td>
</tr>
<tr>
<td>Device therapy at admission</td>
<td>17 (12.2%)</td>
</tr>
<tr>
<td>Positive culture</td>
<td>127 (91.4%)</td>
</tr>
<tr>
<td>Positive culture, major criterium</td>
<td>106 (76.3%)</td>
</tr>
<tr>
<td>Positive culture, minor criterium</td>
<td>21 (15.1%)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>31 (22.3%)</td>
</tr>
<tr>
<td>Streptococci</td>
<td>59 (42.4%)</td>
</tr>
<tr>
<td>Enterococci</td>
<td>16 (11.5%)</td>
</tr>
<tr>
<td>Other</td>
<td>24 (17.3%)</td>
</tr>
<tr>
<td>Native valve endocarditis (NVE)</td>
<td>85 (61.2%)</td>
</tr>
<tr>
<td>Prosthetic valve endocarditis (PVE)</td>
<td>41 (29.5%)</td>
</tr>
<tr>
<td>Cardiac device related IE (CDRIE)</td>
<td>10 (7.2%)</td>
</tr>
<tr>
<td>Aortic root/ ascending aorta prosthesis IE</td>
<td>5 (3.6%)</td>
</tr>
<tr>
<td>Aortic valve IE</td>
<td>87 (62.6%)</td>
</tr>
<tr>
<td>Mitral valve IE</td>
<td>41 (29.5%)</td>
</tr>
<tr>
<td>Pulmonary valve IE</td>
<td>6 (4.3%)</td>
</tr>
<tr>
<td>Tricuspid valve IE</td>
<td>3 (2.2%)</td>
</tr>
<tr>
<td>Surgery</td>
<td>70 (50.4%)</td>
</tr>
<tr>
<td>Definite IE</td>
<td>116 (83.5%)</td>
</tr>
<tr>
<td>Possible IE</td>
<td>23 (16.5%)</td>
</tr>
</tbody>
</table>

**Mortality and adverse events under treatment**

<table>
<thead>
<tr>
<th>Event</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thirty day mortality</td>
<td>11 (7.9%)</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>20 (14.4%)</td>
</tr>
<tr>
<td>Embolic events</td>
<td>23 (16.5%)</td>
</tr>
<tr>
<td>Congestive heart failure or cardiogenic shock</td>
<td>21 (15.1%)</td>
</tr>
</tbody>
</table>
Purpose:
In recent years, studies have debated the impact of gender on the presentation and clinical course of HCM, with research showing that at time of myectomy, women are older, have worse diastolic function and more advanced cardiac remodeling. The clinical impact of these differences is unknown.

Methods:
We included 221 HCM patients (57% men) who underwent septal myectomy and are followed in our center. Time to treatment was calculated in relation to symptom onset. Pre- and post-operative clinical and echocardiographic data were collected. Gender differences were assessed at baseline and in survival analyses for the composite endpoint of all-cause mortality, cardiac transplantation, re-intervention and aborted sudden cardiac death.

Results:
Women were older at time of myectomy (49 vs. 54 years, p<0.01), but time until treatment was similar (5.0 [1.7 – 9.1] vs. 5.2 [2.4-14.0] years; p>0.05). Mean wall thickness and left-atrial diameter were the same for men and women, but were higher in women when correcting for body surface area (absolute: 20 vs. 20 mm, 48 vs 46 mm, p>0.05; corrected: 9.8 vs. 11.5 mm/m², 23.4 vs. 26.5 mm/m², p<0.01). Symptoms improved in 95% of men and 89% of women and the mean gradient reduction was 75% and 74% (p>0.05 for both). After 6.1 [2.9 – 10.1] years, 24% of women and 23% of men had reached the composite endpoint (p>0.05).

Conclusion:
Although women present later in life and seem to have more advanced disease at time of myectomy, time to treatment is similar and survival after myectomy is excellent for both men and women.
Figures:
Kaplan-Meier survival curves for men and women.

![Survival Curves](image)

- **Survival (%)**
- **Time (years)**
- **Women**: 96, 55, 31, 19, 14
- **Men**: 125, 84, 33, 14, 11

*p = 0.30*
MEDICAL TREATMENT OF OCTOGENARIANS WITH CHRONIC HEART FAILURE: DATA FROM CHECK-HF

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

Purpose:
Elderly heart failure (HF) patients are underrepresented in clinical trials, though comprise a substantial number of patients in real-world practice. Particularly, data in octogenarians on actual use of HF therapies are scarce. The purpose of this study was to evaluate practice-based medical treatment of chronic HF patients aged>80 years, from a large registry at HF outpatient clinics.

Methods:
We analyzed 3,490 octogenarians with chronic HF at 34 Dutch outpatient clinics in the period between 2013 and 2016. The mean age was 84.7±3.6 years, 49% were females. The study patients were divided into HF with preserved ejection fraction (HFpEF) (LVEF≥50% (n=911(26.1%) and HF with reduced ejection fraction (HFrEF, LVEF <50% (n=2,579(73.9%)), according to the 2012 ESC HF Guidelines.

Results:
Most HFrEF patients aged >80 years received a beta-blocker and RAS-blocker, 77.0% and 71.6% respectively. An MRA was prescribed in 51.4% of patients and diuretics in 90.4%. All three of the HF medication (beta-blocker, RAS-inhibitor and MRA) were given in 28.7% of octogenarians with HFrEF. In total 65 patients (2.5%) received ivabradine. At least 50% of target doses of beta-blockers, RAS-inhibitor and MRA were prescribed in 36.9%, 40.4% and 50.1% of the total group of octogenarians with HFrEF, respectively. In HFpEF, beta-blocker, RAS-inhibitor and MRA were used by 74.3%, 62.0% and 44.6% of patients, respectively.

Conclusion:
The majority of octogenarians received guidelines-recommended HF medication. However, target doses of beta-blockers and RAS-inhibitor were prescribed in the minority. Although, it is unclear whether very elderly patients benefit to a similar extent from HF medication compared to younger patients.
CARDIAC RESYNCHRONIZATION THERAPY WITH A SINGLE LEFT VENTRICULAR SEPTAL PACING ELECTRODE: ACUTE HEMODYNAMIC AND ELECTROPHYSIOLOGICAL EFFECTS

F.C.W.M. Salden (Maastricht University, Maastricht); F.C.W.M. Salden (Maastricht University, Maastricht); J.G. Luermans (Maastricht UMC+, Maastricht); S.W. Westra (Radboudumc, Nijmegen); R. Cornelussen (Medtronic, Maastricht); S. Ghosh (Medtronic, Mounds View); F.W. Prinzen (Maastricht University, Maastricht); K. Vernooy (Maastricht UMC+, Maastricht & Radboudumc, Nijmegen)

Purpose:
Cardiac resynchronization therapy (CRT) is usually performed with a right (RV) and left ventricular (LV) lead. In a previous patient study, pacing the interventricular septum permanently on the LV endocardial side (LV septum) proved feasible in patients with sinus node dysfunction. The purpose of this study was to investigate the effects of LV septal pacing as compared to conventional biventricular (BiV) pacing with respect to acute hemodynamic and electrophysiological effects in CRT indicated heart failure patients.

Methods:
Temporary LV septal pacing (transarterial approach) and pacing in the conventional BiV mode using the implanted leads was performed in 26 patients (QRS duration 163 ± 17 ms, 23 left bundle branch block patients) undergoing CRT implantation. Acute hemodynamic response (relative to baseline AAI pacing) was assessed by LVdP/dtmax. Multi-electrode body-surface mapping, what has been used previously to characterize electrical dyssynchrony in CRT patients, was evaluated using the standard deviation of activation times (SDAT) (figure, right panel).

Results:
LV septal pacing resulted in a significant LV dP/dtmax increase, that was comparable to conventional BiV pacing (figure, left panel). Combined RV and LV septal pacing did not provide an additional increase. LV septal pacing resulted in a significantly larger reduction in SDAT than RV plus LV septal pacing and conventional BiV pacing (figure, middle panel).

Conclusion:
LV septal pacing results in acute hemodynamic improvement and electrical resynchronization that is at least as good as conventional BiV pacing. These results suggest that LV septal pacing with a single ventricular lead may serve as an alternative to conventional BiV pacing for cardiac resynchronization.
Figures:

- **Δ LVdP/dt max**
  - LV septum: *P < 0.05 compared to baseline
  - RV + LV septum: **P < 0.01 compared to baseline
  - BIV conventional

- **Δ SDAT**
  - LV septum: *
  - RV + LV septum: **
  - BIV conventional: *

- **Isochronal maps**
  - Baseline: Anterior 42 ms, Posterior 17 ms
  - LV septum (apical): Anterior 28 ms
  - BIV conventional

*Note: The color bar indicates the range of SDAT values from 0 to 110 ms.*
DIFFERENCES IN HEART FAILURE THERAPY BETWEEN DUTCH HEART FAILURE CLINICS: AN ANALYSIS OF THE CHECK-HF REGISTRY

J.F. Veenis (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); J.J. Brugts (Erasmus MC, Rotterdam); for the CHECK-HF investigators

Purpose:
Heart failure (HF) is associated with poor prognosis, high morbidity and mortality. The prognosis can be optimized by guideline adherence, which also can be used as a benchmark of quality of care. The purpose of this study was to evaluate differences in HF-treatment use between Dutch HF-clinics.

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), and focus on the differences in prescription rates between the participating clinics in patients with heart failure with reduced ejection fraction (HFrEF).

Results:
A total of 8,360 HFrEF patients were included with a mean age of 72.3±11.8 years (ranging between 69.1±11.9 and 76.6±10.0 between the clinics), 63.9% were men (ranging between 54.3% and 78.1%), 27.3% were in NYHA III/IV (ranging between 8.8% and 62.1%) and the average eGFR was 59.6±24.6mL/min (ranging between 45.7±23.5 and 97.1±16.5).
The prescription rates ranges from 58.9% to 97.4% for beta-blocker (p<0.01), 61.9% to 97.1% for RAS-inhibitors (p<0.01), 29.9% to 86.8% for MRA (p<0.01), 0.0% to 31.3% for ivabradine (p<0.01) and 64.9% to 100.0% for diuretics (p<0.01), as shown in Figure 1. Also, the percentage of patients who received the target dose differed significantly, 5.9% to 29.1% for beta-blocker (p<0.01), 18.4% to 56.1% for RAS-inhibitor (p<0.01) and 13.2% to 60.6% for MRA (p<0.01).

Conclusion:
The prescription rates and prescribed dosages of HF-medication differ significantly between HF clinics in the Netherlands.
Figures:
Figure 1. Prescription rates and prescribed dosages per participating clinic
EARLY SIGNS OF CARDIAC DYSFUNCTION IN OBESITY PATIENTS, RESULTS OF THE CARDIOBESE STUDY

S.M. Snelder (Franciscus Gasthuis, Rotterdam); L.E. de Groot - de Laat (Maasstad Ziekenhuis, Rotterdam); L.U. Biter (Franciscus Gasthuis, Rotterdam); M. Castro Cabezas (Franciscus Gasthuis, Rotterdam); N. Pouw (Franciscus Gasthuis, Rotterdam); E. Birnie (Franciscus Gasthuis, Rotterdam); B. Boxma - de Klerk (Franciscus Gasthuis, Rotterdam); R.A. Klaassen (Maasstad ziekenhuis, Rotterdam); F. Zijlstra (Erasmus MC, Rotterdam); B.M. van Dalen (Franciscus Gasthuis, Rotterdam)

Purpose:
Obesity is becoming a global epidemic. Current knowledge on early signs of cardiac dysfunction in obesity patients is insufficient. The onset of heart failure in obesity patients cannot be fully explained by the presence of traditional cardiovascular risk factors. Our aim is to detect early signs of cardiac dysfunction in obesity patients without known cardiovascular disease.

Methods:
The CARDIOBESE-study is a cross-sectional multicentre study of 100 obesity patients scheduled for bariatric surgery (body mass index (BMI) ≥35 kg/m²) without known cardiovascular disease, and 50 age-matched and gender-matched non-obese controls (BMI ≤30 kg/m²). Echocardiography, blood and urine biomarkers and Holter monitoring were used to identify parameters that are able to show cardiac dysfunction at a very early stage in obesity patients.

Results:
Obesity patients had impaired left ventricular ejection fraction, global longitudinal strain (GLS) and diastolic function parameters as compared to the non-obese controls (Table). CRP and heart rate were increased, whereas heart rate variability (Standard deviation of NN intervals, SDNN) was decreased. Obesity patients were subdivided in patients with abnormal (<17%, n=56) or normal GLS (n=36). Comparison between these patients revealed no differences regarding BMI, prevalence of comorbidities or CRP value. Nevertheless, patients with abnormal GLS had a higher waist circumference and lower SDNN.

Conclusion:
There is a high prevalence of subclinical cardiac dysfunction in obesity patients, which appears to be related to abdominal fat and decreased heart rate variability (as a measure of autonomic nervous system dysfunction), and not to BMI, traditional cardiovascular risk factors or CRP.
# Figures:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Non-Obese controls (n=50)</th>
<th>Obesity patients (n=100)</th>
<th>p-value</th>
<th>Obesity patients with normal GLS (n=36)</th>
<th>Obesity patients with impaired GLS (n=56)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>49.2 ± 9.5</td>
<td>47.9 ± 7.6</td>
<td>0.36</td>
<td>47.0 ± 7.1</td>
<td>48.3 ± 7.0</td>
<td>0.08</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.0 ± 3.2</td>
<td>24.9 ± 4.1</td>
<td>&lt;0.001</td>
<td>42.7 ± 4.2</td>
<td>42.7 ± 4.1</td>
<td>0.98</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>81.1 ± 10.4</td>
<td>133.1 ± 12.3</td>
<td>&lt;0.001</td>
<td>128.2 ± 11.5</td>
<td>135.2 ± 10.5</td>
<td>0.006</td>
</tr>
<tr>
<td>Diabetes Mellitus (%)</td>
<td>0</td>
<td>22 (22%)</td>
<td>&lt;0.001</td>
<td>7 (10.4%)</td>
<td>12 (21.4%)</td>
<td>0.81</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>4 (8%)</td>
<td>32 (32%)</td>
<td>&lt;0.001</td>
<td>11 (30.6%)</td>
<td>18 (32.1%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Global longitudinal strain (%)</td>
<td>-20.1 ± 1.6</td>
<td>-16.3 ± 2.9</td>
<td>&lt;0.001</td>
<td>-19.1 ± 1.3</td>
<td>-14.5 ± 2.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>65.3 ± 5.4</td>
<td>56.6 ± 7.2</td>
<td>&lt;0.001</td>
<td>61.5 ± 5.8</td>
<td>53.6 ± 6.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral inflow E-wave (cm/s)</td>
<td>73.2 ± 12.7</td>
<td>68.9 ± 13.9</td>
<td>0.07</td>
<td>74.3 ± 15.5</td>
<td>65.5 ± 12.1</td>
<td>0.003</td>
</tr>
<tr>
<td>Mitral inflow A-wave (cm/s)</td>
<td>63.7 ± 12.5</td>
<td>69.9 ± 13.8</td>
<td>0.01</td>
<td>70.7 ± 12.2</td>
<td>70.1 ± 13.4</td>
<td>0.85</td>
</tr>
<tr>
<td>E/A Ratio</td>
<td>1.19 ± 0.26</td>
<td>1.01 ± 0.3</td>
<td>&lt;0.001</td>
<td>1.08 ± 0.2</td>
<td>0.96 ± 0.27</td>
<td>0.048</td>
</tr>
<tr>
<td>Septal e’ velocity (cm/s)</td>
<td>10.3 ± 9.8</td>
<td>8.1 ± 1.8</td>
<td>0.03</td>
<td>8.2 ± 1.0</td>
<td>7.8 ± 1.7</td>
<td>0.24</td>
</tr>
<tr>
<td>Lateral e” velocity (cm/s)</td>
<td>13.3 ± 6.3</td>
<td>10.6 ± 3.1</td>
<td>0.001</td>
<td>11.7 ± 3.7</td>
<td>9.8 ± 2.6</td>
<td>0.007</td>
</tr>
<tr>
<td>E/e’</td>
<td>8.5 ± 2.1</td>
<td>8.9 ± 2.5</td>
<td>0.32</td>
<td>9.5 ± 2.4</td>
<td>8.7 ± 2.5</td>
<td>0.136</td>
</tr>
<tr>
<td>LA volume index (ml/m²)</td>
<td>25.8 ± 6.1</td>
<td>25.9 ± 7.7</td>
<td>0.91</td>
<td>26.5 ± 7.1</td>
<td>25.2 ± 7.1</td>
<td>0.39</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>1.9 ± 2.9</td>
<td>8.8 ± 8.8</td>
<td>&lt;0.001</td>
<td>8.5 ± 7.3</td>
<td>9.3 ± 10.1</td>
<td>0.67</td>
</tr>
<tr>
<td>BNP (pmol/L)</td>
<td>6.9 ± 7.1</td>
<td>7.3 ± 9.6</td>
<td>0.79</td>
<td>9.1 ± 9.7</td>
<td>6.6 ± 9.9</td>
<td>0.23</td>
</tr>
<tr>
<td>Average heart rate (bpm)</td>
<td>72.3 ± 9.6</td>
<td>82.8 ± 10.2</td>
<td>&lt;0.001</td>
<td>81.2 ± 10.0</td>
<td>83.6 ± 10.4</td>
<td>0.28</td>
</tr>
<tr>
<td>SDNN</td>
<td>162.2 ± 35.4</td>
<td>159.4 ± 46.0</td>
<td>&lt;0.001</td>
<td>150.4 ± 46.3</td>
<td>158.0 ± 41.2</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**BMI** = Body Mass Index, LV ejection fraction = Left Ventricular ejection fraction, LA = Left atrium, CRP = C-reactive protein, BNP = Brain natriuretic peptide; SDNN = Standard deviation of NN intervals.
ADDED VALUE OF COMPUTED TOMOGRAPHY FRACTIONAL FLOW RESERVE (FFRCT) IN THE DIAGNOSIS OF CORONARY ARTERY DISEASE (CAD)

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Purpose:
Multiple non-invasive tests are performed as part of the standard protocol to diagnose CAD, but all are limited to either anatomical or functional assessments. FFRCT is a new non-invasive test that combines anatomical and functional characteristics based on the principles of invasive FFR. This study aims to evaluate the added value of FFRCT beyond the currently used tests.

Methods:
Patients having the clinical suspicion of angina pectoris between 2010 and 2011 were included in this cross-sectional study. All underwent exercise stress electrocardiography (X-ECG), SPECT, CT coronary angiography (CCTA) and FFRCT as part of the Horoscope study. Invasive coronary angiography (ICA) and FFR were used as reference standard. Missing values were multiple imputed and five combined models mimicking the clinical workflow were fitted. The area under the receiver operating characteristic (AUROC) curve and Akaike Information Criteria (AIC) were used for comparison.

Results:
89 (44%) of the 202 patients included in the analysis had a FFR of ≤0.80, while positive tests were found for X-ECG, SPECT, CCTA and FFRCT in 41%, 47%, 53% and 50% of the cases. The model including pre-test-likelihood and X-ECG had an AUROC of 0.78 (AIC:236), which significantly increases to 0.89 by adding SPECT (AIC:170), to 0.87 by adding CCTA (AIC:191), to 0.92 when adding FFRCT (AIC:155) and to 0.94 when adding CCTA and SPECT (AIC:140).

Conclusion:
This study shows adding FFRCT leads to an increased AUROC and a decreased AIC compared to the basic model. It therefore improves the diagnostic work-up beyond SPECT or CCTA alone in the diagnosis of CAD.
**Figures:**

ROC-curves for all diagnostic models and its AIC and AUC. FFRCT has an improved AUC compared to the basic model and the models including SPECT or CCTA alone, while its AIC is decreased. The model including both SPECT and CCTA has the highest AUC and the I

<table>
<thead>
<tr>
<th>Model</th>
<th>Model 2</th>
<th>Model 3</th>
<th>Model 4</th>
<th>Model 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic model</td>
<td>+ SPECT</td>
<td>+ CCTA</td>
<td>+ CCTA + FFRCT</td>
<td>+ SPECT + CCTA</td>
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