Abstracts of the Scientific Spring Meeting of the Netherlands Society of Cardiology 2014

3 - 4 April 2014, Rai Elicium, Amsterdam
Dear reader,

We are pleased to present here the abstracts of the Scientific Spring Meeting of the Netherlands Society of Cardiology 2014 which will be held on 3 – 4 April in Rai Elicium, Amsterdam.

We hope that you will enjoy reading the abstracts.

On behalf of the Chief Editorial Board
Prof. Dr. E.E. van der Wall
AORTIC TORTUOSITY PREDICTS CARDIOVASCULAR EVENTS IN MARFAN SYNDROME

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Purpose: Patients with Marfan syndrome (MFS) have an increased risk of life-threatening aortic complications, mostly preceded by aortic dilatation. The aim of this study was to associate aortic tortuosity on clinical events and to determine whether tortuosity reduces the aortic tortuosity in adults with MFS.

Methods: In this prospective multicenter study, 233 adults with MFS underwent a gadolinium enhanced magnetic resonance imaging (MRI) of the aorta at the time of inclusion and after three years of follow-up. Patients were randomized between 100 mg losartan treatment or no additional treatment. Analysis software (3mensio) was used to measure the aortic length, geometrical length and the Aortic Tortuosity Index (ATI) (aortic length/geometric length radius). Combined clinical endpoint comprised aortic dissection and elective aortic surgery.

Results: After baseline, ATI (1.9±0.2) was significantly correlated with aortic root diameter (44.3±5mm, p<0.013) and age (37±13, p=0.005). ATI was not influenced by height or presence of scoliosis. After a mean follow-up of 49.3±8.8 months, a total of 30 events occurred. Patients with an event had a higher baseline aortic tortuosity (1.9±0.2 vs. 1.8±0.2, p=0.007) than patients without an event. Kaplan-Meier analysis demonstrated that aortic tortuosity of > 1.95 is a predictor of cardiovascular events (log Rank test: p=0.007) in patients with Marfan syndrome. After three years of follow-up, ischemia showed a modest trend towards lower ATI in unoperated patients (baseline: -0.015±0.1 vs. ATI: -0.020±0.1, p=0.060).

Conclusion: The aortic tortuosity index correlates with severity of aortic disease and predicts cardiovascular events in Marfan syndrome.

THE RATE OF THROMBOEMBOLIC EVENTS IN ADULTS WITH CONGENTIAL HEART DISEASE AND ATRIAL ARHYTHMIAS

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Background: Atrial arrhythmias (AA) occur in 15% of adult patients with congenital heart disease (CHD). They have been recognized as a major cause of morbidity, mainly due to thromboembolic complications. This study aimed to assess prevalence of thromboembolic events in CHD patients with AA.

Methods: All adult CHD patients from a tertiary referral center, registered in the Concor database, were included. AA was defined as atrial fibrillation or atrial flutter. Stroke was defined as ischemic cerebrovascular accident (CVA) or transient ischemic attack (TIA). Patient’s characteristics and frequency of AA, thromboembolic events and intracranial hemorrhage were collected. Starting point of study was defined as date of inclusion in the Concor database.

Results: Between 2002 and 2014, a total of 1976 patients with CHD were identified, of which 13% were known with AA (median follow-up 9 years, S.D.±11). In 24 patients a thromboembolic event occurred (11%), of whom 21 had a stroke (10%). A pulmonary embolism (3%) and 1 a systemic embolism (0.5%). Two patients (1%) suffered from intracranial hemorrhage. Survival free of thromboembolism was influenced by type of CHD (log Rank test: p<0.001) and 1 a systemic embolism (0.5%). Two patients (1%) suffered from thromboembolic event occurred (11%), of whom 21 had a stroke (10%), 3 a pulmonary embolism (1%). Results of this study underline the importance of efficient anticoagulation in AA in CHD.

Conclusion: Prevention of thromboembolic events in adult CHD patients with AA is 11% over a median period of 9 years. Patients with mitral stenosis or UVM are at high risk of thromboembolism or fatal outcome. The results of this study underline the importance of efficient anticoagulation in AA in CHD.

Figure 1. Survival free of thromboembolic event in CHD patients with AA. Data are displayed for univentricular heart and biventricular heart.

OUTCOME AFTER PULMONARY VALVE REPLACEMENT IN TETRALOGY OF FALLOT PATIENTS WITH TRICUSPID REGURGITATION

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Purpose: Tetralogy of Fallot (TOF) patients may develop tricuspid regurgitation (TR) due to annular dilatation or leaflet abnormalities. Our objective was to determine outcome of patients with significant TR undergoing pulmonary valve replacement (PVR) and the effect of tricuspid valve (TV) repair.

Methods: Our retrospective, multicenter cohort consisted of 157 TOF patients who had undergone PVR between 1986 and 2013. 41 TOF patients (51% male, mean age 37±10 years, follow-up 7.6±3.9 years after PVR) with at least moderate pre-operative TR (grade IV/V or higher) were included. Pre- and post-operative imaging and clinical data were collected.

Results: Thirteen (32%) patients had severe pre-operative TR (grade 3 or 4) compared to 28(58%) with moderate TR (grade 2). Patients with severe pre-operative TR had higher pre-operative left ventricular volumes (p=0.04). Twelve (32%) patients with severe TR underwent concurrent TV repair compared to 10 (36%) patients with moderate TR. Post-operative TR grade was similar in patients with severe and moderate TR (1.2±0.7 vs. 1.3±0.5). No adverse events occurred in the patients (0 death, 3 sustained V, 2 heart failure, 1 recurrent TR, 6 supraventricular tachycardia). Patients with severe pre-operative TR had an increased risk for adverse events (HR: 3.1, 95% C.I.1.02-9.46, p=0.046) despite successful TV repair:

Conclusion: In TOF patients with severe TR undergoing PVR, TV repair resulted in a pronounced decrease of TR grade. Despite successful TV repair those patients with severe pre-operative TR remained at high risk for adverse events.

Figure 1: Cumulative event free survival for 2 groups: pre-PVR TR grade 2 and TR grade 3 or 4. Composite of adverse events; death or sustained ventricular tachycardia (VF/VT≥30 sec or requiring cardioversion) or heart failure (HF, increase in NYHA class and requiring diuretics) or supraventricular tachycardia (SVT; ≥30 documented on electrocardiogram) or recurrent TR (grade 3 or higher).

EXOME SEQUENCING IDENTIFIES A NEW GENETIC APPROACH FOR TGA PATIENTS WITH TRANSPOSITION OF THE GREAT ARTERIES

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Purpose: Transposition of the great arteries (TGA) is a severe congenital heart disease (CHD) with an unknown causation. Only a few genes have been implicated in the disorder and these do not account for the majority of cases. The disease is sporadic and the TGA-empic recurrence risk for siblings is known to be very low. These observations could be compatible with the occurrence of de novo mutations in affected individuals. Our genome-wide association study (GWAS) did not identify any new causal gene.

Exome sequencing, a new genetic technology, now provides new opportunities for gene discovery in TGA by allowing the testing of this alternative inheritance model for TGA.

Methods: Exome sequencing now provides us new possibilities to identify novel genes in patients with TGA. We have identified six de novo mutations in 10 parent-child trios. Further validation in a larger cohort of TGA patients is warranted to evaluate the causality of these candidate genes.
Session 1 : Congenital (continued)

CARDIAC FUNCTION ONE YEAR AFTER PREGNANCY IN WOMEN WITH CONGENITAL HEART DISEASE
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Purpose:
Little is known about long term cardiovascular outcome after pregnancy in women with congenital heart disease. We, 1) observed the incidence of late cardiovascular complications and 2) compared cardiac function prior to and one year after pregnancy in women with congenital heart disease (CHD).

Methods:
We compared systemic ventricular ejection fraction, tricuspid annular plane systolic excursion (TAPSE), systemic ventricular end diastolic diameter (LVEDD), subpulmonary ventricular end diastolic diameter (sPVEDD), grade of valvular regurgitation or stenosis prior to and one year after pregnancy. Late cardiovascular complications (CVC) were defined as need for urgent invasive cardiovascular procedure, episodes of heart failure, arrhythmia, thromboembolic events, myocardial infarction, cardiac arrest, cardiac death, endocarditis and NYHA class deterioration occurring > 6 months after delivery.

Results:
We observed 213 pregnancies in 203 women with CHD; 12 women were again pregnant > 6 months after delivery, 18 women were lost to follow up, rendering 183 pregnancies in 173 women available for follow up. Late CVC were observed after 12 pregnancies (6%). Women with CVC during pregnancy were at risk for late CVC (HR 7.1, 95% CI 2.2-23.2; p=0.001). Women with CVC during pregnancy sPVEDD had significantly increased one year post-partum (38.5(36.0-44.0) – 44.0(38.0-55.0); p=0.001). Other significant difference were found in cardiac function or size one year after pregnancy compared to preconception values.

Conclusion:
Pregnancy does not cause permanent damage to cardiac function in women with congenital heart diseases. Women with CVC during pregnancy are prone to develop late CVC and dilatation of the subpulmonary ventricle.

Figure 1: Freedom from late cardiovascular events after pregnancy in women with cardiac events during pregnancy (red line) and women without cardiac events during pregnancy (blue line).

THE RISK OF TYPE B AORTIC DISSECTION IN MARFAN SYNDROME
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Purpose:
Aortic complications beyond the ascending aorta have become a major clinical problem in patients with Marfan syndrome. The aim of our study was to identify clinical parameters associated with type B aortic dissection and to develop a risk model to predict type B aortic dissection in Marfan syndrome.

Methods:
All adults with Marfan syndrome attending a Dutch university Marfan screening clinic were recruited. Starting point of the study was defined as the date of first available aortic images. Association of type B aortic dissection with demographics, medical treatment, FBN1 mutation, surgical history, aortic diameter, dilatation rate and distensibility was assessed.

Results:
Between 1998 and 2013, 54 type B aortic dissections occurred in 60 Marfan patients (36±14 years, 52% male). Mean diameter of the proximal descending aorta before type B aortic dissection was 31±7 mm. Independent variables associated with type B aortic dissection were (A) prior prophylactic aortic surgery (HR=2.1; 95%CI:1.2-3.8; p=0.010), and (B) proximal descending aorta >27mm (HR=2.2; 95%CI:1.1-4.3; p=0.020). In the risk model, the 10 years occurrence of type B aortic dissection was (A) 0.4%, (B) 5.2%, (C) 11.9%. The low, moderate, and high risk patients was 6%, 19%, and 34%, respectively. Angiotensin-II receptor blocker therapy was associated with less type B aortic dissections (HR=0.9; 95%CI:0.1-0.9; p=0.030).

Conclusion:
Marfan patients with prior prophylactic aortic surgery are at substantial risk for type B aortic dissection when the descending aorta is slightly dilated. Angiotensin-II receptor blocker therapy seems to be protective in the prevention of type B aortic dissections.

Figure: Percentage freedom of type B aortic dissection in the 3 different patient groups

LIFE INSURANCE PROBLEMS FOR PATIENTS WITH CONGENITAL HEART DISEASE
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Purpose:
While congenital heart disease (CHD) has become a chronic disease, most patients experience problems applying for insurance or mortgage. Data on these applications are very limited in CHD. We studied insurance and mortgage applications in CHD patients.

Methods:
Patients were randomly selected from CONCOR, the Dutch national database of adults with CHD, and were sent a questionnaire on problems concerning health, life or disability insurances, pension and mortgage. All data were analysed per different CHD (congenital heart disease) groups.

Results:
In January 2013, 406 patients (median age 39 (IQR 29-48), 52% male) were randomly selected from CONCOR (n=14.187). Of these, 202 patients (50% female) responded (> 6 months after exclusion 53%) returned the questionnaire. Forty percent had mild, 50% had moderate and 10% had severe CHD. The application rates were similar for the different severity groups (82% health, 33% disability and 50 life insurance and 55% for a mortgage). Problems (refusal, delay in acceptance and especially paying a higher premium) were seen in 8% of patients who applied for health, 33% for life, and 20% for disability insurance and in 27% of patients applying for a mortgage. For life insurance, problems were most frequent and increased with CHD severity (4% mild to 74% in severe CHD). When comparing with data from literature on patients with other chronic diseases, application rates were higher among CHD patients (versus respectively 68%, 29 and 39%), whereas more problems were seen.

Conclusion:
Adults with CHD who apply for any insurance but especially life insurances experience a substantial amount of problems including higher refusal rates and higher premiums. Insurance companies should be better informed on improved prognosis when taking CHD into account for an application.
Patient Selection for Primary Prevention Implantable Cardioverter Defibrillator Therapy Using Cardiac Magnetic Resonance Imaging Based Left Ventricular Ejection Fraction Assessment

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Purpose:
The primary eligibility criterion (LVEF=35%) for primary prevention ICD therapy is based on clinical trials using 2D-echocardiography. However, cardiac magnetic resonance imaging (CMR) is considered the gold standard for LVEF assessment with higher accuracy and reproducibility. CMR-LVEF assessment may result in refined patient selection but data on the follow-up of CMR-selected ICD patients is lacking. The aim of this study was to evaluate benefit from ICD implantation using CMR-LVEF assessment.

Methods:
265 patients referred for primary prevention ICD implantation with CMR-LVEF<35% were retrospectively included (71% male, age 66±10 years, 56% ischemic cardiomyopathy). Patients were selected who underwent CMR-LVEF assessment within 6 months prior to implantation. The occurrence of appropriate device therapy (ADT) and all-cause mortality were evaluated during 3 years follow-up for the total population and in subgroups with LVEF<20%, LVEF 20-30%, and LVEF>30%.

Results:
During 3 years follow-up, 16% of the total population received ADT and 8% died. Patients with LVEF<20% were at highest risk for ADT, whereas patients with LVEF>30% had both a low ADT and mortality rate. Patients with LVEF>30% were at highest risk for ADT, whereas patients with LVEF>30% had both a low ADT and mortality rate.

Conclusion:
Patients with CMRLVEF of 20-30% were at highest risk for ADT, whereas patients with CMRLVEF>30% were more likely to die. Patients with CMRLVEF>30% had both a low ADT and mortality rate.

Figure 1:

Table 1: Characteristics of quitters compared to smokers.

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Quitters (n=156)</th>
<th>Persistent smokers (n=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive history in CVD</td>
<td>19 (12%)</td>
<td>44 (20%)</td>
</tr>
<tr>
<td>Diabetes on medication</td>
<td>35 (22%)</td>
<td>44 (22%)</td>
</tr>
<tr>
<td>Blood Pressure &gt; 140 mmHg</td>
<td>35 (22%)</td>
<td>33 (22%)</td>
</tr>
<tr>
<td>BMI &gt; 25 kg/m²</td>
<td>25 (16%)</td>
<td>53 (22%)</td>
</tr>
<tr>
<td>Risk profile at 5 year</td>
<td>44 (28%)</td>
<td>24 (12%)</td>
</tr>
</tbody>
</table>

Table 2: Prediction of clinical outcome in 265 patients after cardiac surgery.

<table>
<thead>
<tr>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (%)</td>
<td>n=141</td>
</tr>
<tr>
<td>Blood Pressure &gt; 140 mmHg</td>
<td>42 (30%)</td>
</tr>
<tr>
<td>BMI &gt; 25 kg/m²</td>
<td>39 (28%)</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.3 (0.4-2.7)</td>
</tr>
<tr>
<td>Presence of diabetes</td>
<td>31 (22%)</td>
</tr>
<tr>
<td>NYHA Class IV</td>
<td>28 (20%)</td>
</tr>
<tr>
<td>LVEF&lt;20%</td>
<td>25 (18%)</td>
</tr>
<tr>
<td>Event rate during year</td>
<td>8% (20%)</td>
</tr>
</tbody>
</table>

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Session II: Prognosis (continued)

COST-EFFECTIVENESS ANALYSIS OF A YEARLY HYPERTENSION SCREENING IN WOMEN WITH A HISTORY OF PRE-ECLAMPSIA

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Purpose: Women with a history of preeclampsia (PE) are at increased risk for future hypertension and cardiovascular disease (CVD). Until now, it is not clear whether preventive measures are needed in these high-risk women. In the present study we evaluated the cost-effectiveness of a simple hypertension screening strategy in women post PE.

Methods: A decision-analytic Markov model was constructed to evaluate healthcare costs and effects of screening for hypertension in women post PE, compared with no screening, based on available literature. Screening consisted of a postpartum yearly blood pressure measurement during a timeframe of 20 years. Cardiovascular events and CVD mortality were defined as health states. Outcomes were measured in absolute costs, events, life-years and quality-adjusted life-years (QALYs).

Results: Over a 20 year time horizon events occurred in 0.072 percent of the population after screening, and in 0.085 percent of the population without screening. QALYs increased from 16.36 (no screening strategy) to 16.40 (screening strategy), an increment of 0.0320 (95% CI 0.0124; 0.0582). The incremental cost-effectiveness ratio was €4172 per QALY gained.

Conclusion: Yearly hypertension screening in women with a history of PE may save costs, for at least similar quality of life and survival due to prevented CVD compared with standard care.

INFLUENCE OF DISCHARGE MEDICATION ON OUTCOME IN ELDERLY PATIENTS (= 65 YEARS) WITH ST-SEGMENT ELEVATION MI AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION AT 1, 2 AND 3 YEARS FOLLOW UP.

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Purpose: Patients who had primary percutaneous coronary intervention (PCI) for STElevation myocardial infarction (STEMI), current guidelines recommend prescription of 5 types of medication for optimal secondary prevention: dual-antiplatelet therapy, statins, beta-blockers and ACE-inhibitors. Although the risk of subsequent clinical events, including death, is higher in patients older than 65 years, these patients are less likely to receive optimal evidence-based medication (5 EBM) at discharge. This study compared survival and major adverse-cardiac-events (MACE) of patients = 65 years with optimal EBM (5 EBM) with 3 and 4 EBM during 3 years follow-up.

Methods: Retrospective data of 400 patients = 65 years presenting between 2006-2010 were included from the The Hague-Delft Heart center database. Exclusion criteria were cardiogenic shock, needing an intravenous balloon pump, in-hospital coronary artery bypass graft (CABG), in-hospital death and migration. MACE was defined as re-PCI, CABG, non-fatal acute myocardial infarction (AMI) and all-cause mortality.

Results: At hospital discharge, 33 patients who prescribed with 3 EBM, 121 patients with 4 EBM and 246 patients with 5 EBM. The group with 5 EBM showed a longer time to MACE at 3 years follow up (HR 1.14; 95%CI 0.64-2.01; p=0.66) compared to 3 EBM and compared to 4 EBM (HR 1.14; CI 0.81; p=0.42).

Conclusion: This study shows a trend for better clinical outcome in older STEMl patients (= 65 years) who are discharged with 5 EBM after primary PCI for STEMI at 3 years follow-up compared to 3 or 4 EBM. The current data support a strict adherence to the guidelines in the elderly, despite possible side effects or medication compliance issues.

Figure 1. Influence of amount EBM on 3 years follow-up MACE.

Kaplan-Meier analysis demonstrated that patients in the 5 EBM group had a longer time to MACE compared to the 3 or 4 EBM groups in the 3 years follow-up period. The differences were non-significant.

CLINICAL PREDICTORS OF MORTALITY IN ADULTS WITH RIGHT-SIDED CONGENITAL HEART DISEASE

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Purpose: Patients with right-sided congenital heart disease (CHD) experience increased risk of mortality and morbidity in adulthood, due to longstanding pressure and volume overload of the right ventricle (RV). This study was designed to identify risk factors for all-cause mortality in patients with right-sided CHD.

Methods: Adults with right-sided CHD, followed between 2002 and 2012 in three congenital heart centers were identified. Right-sided CHD included atrial septal defect, Ebstein’s anomaly, Fontan circulation, Tetralogy of Fallot, pulmonary stenosis and Eisenmenger syndrome. Clinical characteristics, electrocardiography, echocardiography (TTE), cardiovascular magnetic resonance imaging (CMR) and outcome data were analysed. Cox proportional hazards analysis was used to assess the most valuable predictors of mortality.

Results: In total 1274 patients (27% of the total registered CHD population) with right-sided CHD were identified, with a mean age 32 years. Of these patients 77 died (6%, mean age 45 years), during a mean follow-up of 7.1 years. Systolic pulmonary arterial pressure (sPAP) measured by means of TTE (HR 1.02, p=0.01) and RV ejection fraction measured by CMR (HR 0.41, p=0.03), corrected for diagnosis, were the strongest predictors for mortality. Patients with a sPAP >40 mmHg and RV ejection fraction <40% were most likely to suffer from all-cause mortality.

Conclusion: Systolic pulmonary arterial pressure and right ventricular ejection fraction are predictive of all-cause mortality in adults with right-sided CHD. These findings may improve risk stratification and design of future therapeutic trials.

Figure 1. Kaplan-Meier analysis

Kaplan-Meier curves per type of defect. ASD – atrial septal defect; ToF – Tetralogy of Fallot; PS – Pulmonary stenosis.
Abstracts

Session III: Heart Failure

SEPTAL REBOUND STRETCH AS PREDICTOR OF ECHOCARDIOGRAPHIC RESPONSE TO CARDIAC RESynchronizAtion THERAPY

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Purpose: Septal rebound stretch (SRSept) reflects an inefficient deformation of the septum during systole and is a potential new tool to predict response to Cardiac Resynchronization Therapy (CRT). However, there are only limited data on the potential predictive value. In this study we assessed the predictive value of SRSept on response to CRT in a large population.

Methods: A total of 136 consecutive patients with functional class III/IV heart failure who underwent CRT were studied. Echocardiography was performed at baseline and after a mean follow-up period of 26.6 months. Echocardiographic response to CRT was defined as a reduction in LV end-systolic volume =15%. Receiver operating characteristic curve analysis was performed to define the optimal cutoff value for SRSept. Multivariable analyses were performed to adjust for potential confounders.

Results: Mean age was 68±8 years (30% female). Mean baseline LV ejection fraction was 38±9%. Most patients had ischemic etiology. Mean SRSept was 4±3±3%, 56% of patients had SRSept >4%. Ninety six patients (70%) were echocardiographic responders. Baseline SRSept was significantly higher in responders compared to non-responders (5±1±3 vs. 2±9±2, p<0.001). The optimal cut-off value for SRSept was 4%. After univariate and multivariable regression analysis, baseline SRSept >4% independently predicted the response to CRT after adjustments OR 1.9±1.3 vs 2.9±2.7, p<0.001). The optimal cut-off value for SRSept was 4%. Differences in outcome were also observed for left ventricular ejection fraction, left ventricular mass index, and age. The area under the ROC was 0.78. A cutoff value of 4% septal rebound stretch had a sensitivity of 0.77 and a specificity of 0.67 to predict response to CRT.
Abstracts

Session III: Heart Failure (continued)

**THE INCIDENCE OF ICD THERAPY: AGE-DEPENDENT DIFFERENCES BETWEEN ISCHEMIC AND NONISCHEMIC HEART DISEASE**

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**Purpose:** Controversy exists on the impact of age on the occurrence of appropriate and inappropriate ICD therapies. Given the higher risk of death from other causes, it has been suggested that older patients may receive less ICD therapy. We investigated the impact of age on the incidence of ICD therapy in patients with ischemic (HD) and nonischemic heart disease (non-HD).

**Methods:** Cohort study of 466 ICD-patients with follow-up at the Radboud University Medical Centre (2005-2012). ICD interrogation was routinely performed; in case of ICD therapy (ATP or shock) appropriateness was assessed. Percentages of ICD therapies were compared by age tertiles.

**Results:** During a median follow-up of 962 days (IQR 402-1570), 25% (n=114) of patients received appropriate therapy. 16% (n=74) received a shock and 17% (n=79) ATP. Eleven percent (n=52) received inappropriate therapy, 7% (n=33): a shock and 7% (n=33) ATP. For HD and non-HD, two-year cumulative incidences of appropriate therapy split by age tertiles are shown below. Inappropriate therapy occurred equally among the age tertiles, but was slightly more frequent in non-HD.

**Conclusion:** Whereas for non-HD, the risk of inappropriate therapy was similar across the age groups, in HD the risk was markedly higher in older patients. These data support the use of ICD therapy across the age groups, although a firm relation with increased survival has yet to be established.

<table>
<thead>
<tr>
<th>Age &lt;58 yrs</th>
<th>Age 58-68 yrs</th>
<th>Age &gt;68 yrs</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td>Ischemic heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appropriate therapy</td>
<td>5%</td>
<td>3%</td>
<td>3%</td>
</tr>
<tr>
<td>Appropriate shock</td>
<td>7%</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Nonischemic heart disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Appropriate therapy</td>
<td>13%</td>
<td>13%</td>
<td>12%</td>
</tr>
<tr>
<td>Appropriate shock</td>
<td>7%</td>
<td>7%</td>
<td>7%</td>
</tr>
</tbody>
</table>

**IS CLINICAL SEVERITY OF TRAITS IN INHERITED HEART DISEASE FULLY DETERMINED BY GENETIC BACKGROUND?**

J.A. Wijmenga (AMC, Amsterdam); I.Y. van Spaandonk-Zwaa (AMC, Amsterdam); J.P. van der Heijden (UMCG, Groningen); I. Christiaans (AMC, Amsterdam); M.J.van der Smagt (UNMC, Utah); A.M. Verweij (AMC, Amsterdam); J.R. Gimo (RINA, Mumbai); P. Garcia-Pavia (HUPH, Madrid); P. Charron (CHU Pitié-Salpêtrière, Paris); I. Oliveto (ADG, Genf); A.A. Wilde (AMC, Amsterdam); I.M. Prins (AMC, Amsterdam)

**Purpose:** Discrete gene mutations can cause cardiomyopathies and ion channel disease. The clinical expression of such diseases varies greatly. It is often proposed that this is attributable to variation in genetic background and modifier genes. To study this we collected monozygous twins with an inherited cardiomyopathy or ion channel disease.

**Methods:** We collected 34 monozygous twin-pairs: 7 with dilated cardiomyopathy (DCM), 11 with hypertrophic cardiomyopathy (HCM), 5 with amyloidoma, 4 with arrhythmogenic right ventricular cardiomyopathy (ARVC), 4 with long QT syndrome type 1 or 2 (LQT1 or 2), and 3 with LQT3 or Brugada. To determine heritability (H2), we compared correlation coefficients within monozygous twin pairs and control pairs (pathology-, age- and sex-matched sibling pairs and dingozygous twin pairs) for quantitative traits (H2 = 2x(MZcorr – DZcorr)).

**Results:** These data strongly suggest that part of the clinical variability in patients with an inherited heart disease cannot be explained by genomic variation. Certain traits like QTc are more likely to be under tight genomic control than other traits like IVSd. This can guide the search for genetic modifiers and helps to explain often debated phenotypic variability.

**STRESS-INDUCED TROPONIN RISE IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY: ASSOCIATIONS WITH SARCOMERE MUTATION AND MRI CHARACTERISTICS**

D.H.F. Gommans (Radboudumc, Nijmegen); G.E. Cramer (Radboudumc, Nijmegen); M. Michels (Praxis Medisch Centrum, Rotterdam); M. Foucau (Albert Schweitzer Ziekenhuis, Dordrecht); J. Bakker (Albert Schweitzer Ziekenhuis, Dordrecht); F.W.A. Verheugt (Radboudumc, Nijmegen); F.J. ten Cate (Praxis Medisch Centrum, Rotterdam); M.A. Brouwer (Radboudumc, Nijmegen); M.J.M. Kofflard (Albert Schweitzer Ziekenhuis, Dordrecht)

**Purpose:** Inadequate length-dependent activation with sarcomere dysfunction and microvascular dysfunction are just two different proposed mechanisms of disease in hypertrophic cardiomyopathy (HCM). Both these mechanisms may result in ischemia followed by myocardial injury, especially during exercise. We investigated whether exercise can elicit cardiac troponin release from the hypertrophied heart, and if so which factors are associated with the stress-induced release.

**Methods:** In 44 genotyped HCM patients a bicycle exercise stress test was performed. Before and 6 hours after the exercise test troponin T was measured using a highly-sensitive troponin assay. A troponin rise was defined as a >20% rise in concentration. Prior to the exercise test cardiac MRI was performed to assess the presence of myocardial edema and fibrosis.

**Results:** Troponin rise occurred in 32 patients. There were no differences between sarcomere mutation negative and positive patients with regard to the incidence of troponin rise. Also, the duration of exercise and LV mass did not differ between patients with or without a rise in troponin concentration. Patients with a troponin rise were more likely to have imaging evidence of edema and fibrosis.

**Conclusion:** We conclude that a troponin rise was present in a third of our patients. Interestingly, stress-induced troponin rise was associated with the presence of edema and fibrosis on MRI, whereas sarcomere mutation status and LV mass, both potentially related to ischemia, were not.

**DISCRETE GENOMIC VARIATION IS PARTLY RESPONSIBLE FOR INHERITED HEART DISEASE VARIABILITY:**

M.J. van Ommen; M.A. Bijlsma; B.W. Ferreira; S.W. Westra; G. van Kranen; M. Brouwer (Radboudumc, Nijmegen); A.M. Vermeer (AMC, Amsterdam); J.R. Gimeno (HUVA, Murcia); I. Christiaans (AMC, Amsterdam); M.J. van der Smagt (UNMC, Utah); A.M. Verweij (AMC, Amsterdam); J.R. Gimo (RINA, Mumbai); P. Garcia-Pavia (HUPH, Madrid); P. Charron (CHU Pitié-Salpêtrière, Paris); I. Oliveto (ADG, Genf); A.A. Wilde (AMC, Amsterdam); I.M. Prins (AMC, Amsterdam)

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**Stress-induced troponin rise in patients with hypertrophic cardiomyopathy: associations with sarcomere mutation and MRI characteristics.**

D.H.F. Gommans (Radboudumc, Nijmegen); G.E. Cramer (Radboudumc, Nijmegen); M. Michels (Praxis Medisch Centrum, Rotterdam); M. Foucau (Albert Schweitzer Ziekenhuis, Dordrecht); J. Bakker (Albert Schweitzer Ziekenhuis, Dordrecht); F.W.A. Verheugt (Radboudumc, Nijmegen); F.J. ten Cate (Praxis Medisch Centrum, Rotterdam); M.A. Brouwer (Radboudumc, Nijmegen); M.J.M. Kofflard (Albert Schweitzer Ziekenhuis, Dordrecht)

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**Conclusion:** We conclude that a troponin rise was present in a third of our patients. Interestingly, stress-induced troponin rise was associated with the presence of edema and fibrosis on MRI, whereas sarcomere mutation status and LV mass, both potentially related to ischemia, were not.
Session IV: Intervention

TRANSTHORACIC ECHOCARDIOGRAPHY FOR SELECTION OF GRAFT SIZE IN DAVID REIMPLANTATION TECHNIQUE

M.V. Raggi (Leids Universitair Medisch Centrum, Leiden); M.M.M. Venselaar (Leids Universitair Medisch Centrum, Leiden); H.J.M. Klaauw (Leids Universitair Medisch Centrum, Leiden); A.M. Schalij (Leids Universitair Medisch Centrum, Leiden); J.J. Bax (Leids Universitair Medisch Centrum, Leiden); N. Almair Mansan (Leids Universitair Medisch Centrum, Leiden); V. Degeijs (Leids Universitair Medisch Centrum, Leiden)

Purpose:
It remains unclear whether a transthoracic echocardiography (TTE)-based formula may help in selecting the graft size during David reimplantation technique for aortic root dilation.

Methods:
Forty-nine patients (47±11 years old, 84% men) who underwent David reimplantation techniques were evaluated. Leaflet height and leaflet area TTE-based formulas were developed to select the graft size (Figure 1). The implanted graft size was based on the David’s formula, measuring the leaflet height with surgical callipers. The agreement between these formulas and the eventually implanted graft size was evaluated. In addition, the incidence of >2+ residual aortic regurgitation (AR) for each formula was evaluated.

Results:
The incidence of >2+ residual AR was 76%. Based on TTE-derived formula including the leaflet height, it was as high as 45%. In 30% and 16% of patients the received the same, a larger or smaller graft than based on David’s formula. Based on TTE-derived formula including the leaflet area, a respective 43%. In 24% and 33% of patients the received the same, a larger or smaller graft. The incidence of >2+ residual AR in patients who underwent isolated David’s procedure and received the same or smaller graft size than recommended by the formula was 83% and 94%, respectively.

Conclusion:
In patients undergoing David reimplantation technique, graft sizing can be performed with TTE. Leaflet height TTE-based formula recommended more frequently an undersized graft than leaflet area.

GENDER DIFFERENCES IN BASELINE CHARACTERISTICS, PROCEDURAL FEATURES AND OUTCOME IN STEMI PATIENTS TREATED WITH PRIMARY PCI: A SYSTEMATIC REVIEW OF PROGNOSTIC STUDIES

M.G. van der Meer (University Medical Center, Utrecht); H.M. Nathoo (University Medical Center, Utrecht); J. van der Gaaf (University Medical Center, Utrecht); P.A. Ossewaarde (University Medical Center, Utrecht); R. Willems (University Medical Center, Utrecht); N. Vullers (University Medical Center, Utrecht)

Purpose:
Treatment of ST elevation myocardial infarction (STEMI) has improved enormously since the shift from thrombolytic to primary percutaneous coronary intervention (pPCI). It remains unclear whether differences in survival between women and men treated with STEMI treated with pPCI do exist. Secondly, it is unknown whether potential differences can be explained by gender or by differences in baseline- or procedural characteristics. Therefore we systematically reviewed the available evidence.

Methods:
On 10-05-2013 PubMed, Embase and Cochrane were searched for studies comprising original data on STEMI patients treated with pPCI. A separate gender analysis including more than 100 women was a requirement. Data on baseline profile, procedural characteristics and outcome were extracted and pooled whenever possible.

Results:
In total 25 out of 62 retrieved studies were included. At baseline, women were on average 7 years older, had more diabetes (7.2%/7.1%) and hypertension (7.5%/7.4%) and were less current smokers (7.3%/7.4%). The procedural characteristics were largely comparable except for a longer symptom-to-balloon time (1.26±0.40 mm) and less use of GP IIb/IIIa inhibitors in women (7.5%/7.3%). The outcome was characterized by a higher short- and long-term crude mortality in women. Although we were not able to pool adjusted mortality rates due to heterogeneity of the separate studies, in practically all studies the difference in mortality disappeared after adjustment for baseline and procedural characteristics.

Conclusion:
A higher mortality is indeed present in women with STEMI and can be explained by their unfavourable risk profile and a longer symptom-to-balloon time.

Figure 1: Unadjusted and adjusted mortality of women and men at four points in time: in-hospital, 30 days, 1 and 5 years. All studies that published an odds or hazard ratio were included.

AMOUNT OF ALCOHOL HAS NO EFFECT ON MORTALITY AFTER ALCOHOL SEPTAL ABLATION

M. Liebrigt (St. Antonius Hospital, Nieuwegein); P.A. Wiersinga (Eramus Medical Center, Rotterdam); R.C. Steggerda (Martini Hospital, Groningen); A.F.L. Schinkel (Eramus Medical Center, Rotterdam); W. Willems (University of Leuven, Leuven); F.J. ten Bogaard (Eramus Medical Center, Rotterdam); J. van Daeleput (University of Leuven, Leuven); M. Michel (Eramus Medical Center, Rotterdam); J.M. ten Bogaard (St. Antonius Hospital, Nieuwegein)

Purpose:
The effect of intracoronary alcohol dosage during alcohol septal ablation (ASA) is surrounded by controversy. The aim of this study is to identify the role of alcohol dosage on mortality and adverse arrhythmic events in hypertrophic cardiomyopathy (HCM) patients treated with ASA.

Methods:
In this multi-center study 321 consecutive HCM patients underwent ASA between 1999 and November 2012. In 55 patients (17%) the dosage could not be retrieved, and these were excluded from further analysis. Median dose of alcohol was 2.0 ml (range 0.6-8). The effect of intracoronary alcohol dosage during ASA, survival are more frequent in patients who received higher alcohol dosage (9 events, 6.3%, p = 0.05), especially in the first 30 days post-procedure (10/25 events). However arrhythmic events were slightly increased after the use of high alcohol dosage (16 events, 13.6%) compared with lower alcohol (9 events, 6.3%, p = 0.05), especially in the first 30 days post-procedure (10/25 events).

Conclusion:
Alcohol dosage was more frequent in patients who received high amounts of alcohol during ASA, survival was similar in both groups.

Figure 1: Kaplan-Meier survival in 266 patients after alcohol septal ablation.
Session IV: Intervention (continued)

CELL THERAPY FOR REFRACTORY ANGINA PECTORIS REDUCES HOSPITAL ADMISSIONS, ER VISITS AND (N)STEMI

1. Maaro (LUMC, Leiden); S.F. Rodrigo (LUMC, Leiden); I. van Rens (UMC Utrecht, Utrecht); B.J. Bredenoord (UMC Utrecht, Utrecht); J.J. Zwaginga (LUMC, Leiden); W.E. Ribbe (LUMC, Leiden); J.J. Bos (LUMC, Leiden); M.J. Schaaf (LUMC, Leiden); D.E. Boomsma (LUMC, Leiden)

Purpose:
Cell therapy is a novel treatment option for no-option patients with refractory angina and severe coronary artery disease. Previous clinical studies demonstrated that intramyocardial bone marrow cell (BMC) injection improves myocardial perfusion and reduces symptoms. However, the effect on angina-related healthcare utilization, and thereby healthcare costs, is currently unknown. The current study evaluates the effect of intramyocardial BMC injection on healthcare utilization in patients with refractory angina and chronic myocardial ischemia.

Methods:
A total of 100 patients (64±9 years; 88% men) with severe angina pectoris despite optimal medical therapy received intramyocardial BMC injections in the setting of a pilot study, a randomized trial, or a prospective registry, successively. Healthcare utilization in the 2 years before and 2 years after BMC treatment is compared.

Results:
Healthcare utilization in 2 years before BMC treatment, compared to 2 years after, demonstrated a decrease of 50% in number of emergency room (ER) visits (113 vs. 57). Similarly, the number of ER visits with subsequent hospital admission had decreased by 71% (96 vs. 28). The number of coronary angiographies performed during these admission had decreased by 95% (42 vs. 2), and the number of performed percutaneous coronary interventions had decreased by 93% (15 vs. 1). The occurrence of (non) ST elevation myocardial infarction was reduced from 13 to 3 after BMC injection (77% reduction).

Conclusion:
The current findings indicate that BMC therapy substantially reduces angina-related healthcare utilization and improves clinical outcome.

Figure 1: Total number of ER visits and hospital admissions in 100 patients 2 years before intramyocardial BMC injection and 2 years after BMC injection.

ER, emergency room; BMC, bone marrow cell

ACUTE CHANGES IN MITRAL VALVE GEOMETRY AFTER MITRACLIP THERAPY: INSIGHTS FROM 3D MILLISECOND ECOCARDIOGRAPHY

1. L.J. Aarn (Leiden University Medical Centre, Leiden); P. Dobsonann (Leiden University Medical Centre, Leiden); F. van der Kleij (Leiden University Medical Centre, Leiden); M.J. Schryver (Leiden University Medical Centre, Leiden); L.J. Bos (Leiden University Medical Centre, Leiden); N. Amroge Marisian (Leiden University Medical Centre, Leiden); Y. Deloia (Leiden University Medical Centre, Leiden)

Purpose:
To evaluate the acute effects of percutaneous edge-to-edge mitral valve (MMV) repair on MV geometry in patients with functional mitral regurgitation (FMR).

Methods:
Three-dimensional transesophageal echocardiography performed prior to and immediately after percutaneous MMV repair using the MitraClip device was studied in 20 consecutive patients (age 72±10 years). By using dedicated mitral modeling software, acute procedural effects on mitral annular and leaflet geometry were evaluated.

Results:
Procedural success (FMR reduction to = grade 2) was achieved in 18 (90%) patients. Overall anterior-posterior and inter-commissural diameters, perimeter and area of the MV annulus did not significantly change after the procedure. Nonetheless, a post-procedural increase in anterior leaflet angle (27±5º to 38±10º, p<0.005), decrease in exposed anterior leaflet length at the A2 level (27±5 mm to 20±5 mm, p=0.008) and an increase in the posterior P2 segment leaflet length (11±4 mm to 13±1 mm, p=0.04) without change in overall exposed mitral leaflet area (1451±374 mm² vs 1414±45 mm², p=0.54) indicated anterior relocation of the mitral leaflet coaptation point after MitraClip therapy. (Figures) In addition, coaptation area increased from 230±123 mm² to 302±64 mm² (p=0.004). Annular height-to-intercommisural width ratio (1885± 1976 µm vs. 1736± 2085 µm, p=0.39) and tenting volume (1.4±1.6 ml vs. 3.5±2.5 ml, p=0.88) remained unchanged after MitraClip therapy, suggesting no increase in leaflet stress.

Conclusion:
Percutaneous MitraClip therapy favourably affects mitral valve geometry in FMR patients mainly by increasing coaptation area and relocating the coaptation point anteriorly.

Figure: Acute effect of MitraClip therapy on 3-dimensional mitral valve geometry.

INCREASE IN COAPTATION AREA AND ANTERIOR RELOCATION OF COAPTATION POINT (ARROW) AFTER (A) TOWER PANEL AND (B) TOWER PANEL OF TAVR

MIRAL REGURGITATION PRIOR TO TRANSCATHETER AORRIC VALVE REPLACEMENT

K. Kojima (Jichi Medical School, Tochigi, Japan); F. Hori (Jichi Medical School, Tochigi, Japan); K. Murayama (Jichi Medical School, Tochigi, Japan); K. Kojima (Jichi Medical School, Tochigi, Japan); F. Hori (Jichi Medical School, Tochigi, Japan)

Purpose:
Current data about the impact of mitral regurgitation (MR) in patients who undergo transcatheter aortic valve replacement (TAVR) are conflicting. The aim of this study was to assess the influence of MR on outcome in patients treated by TAVR.

Methods:
We included 975 consecutive patients who underwent TAVR by transfemoral transapical or transaortic approach with a Medtronic CoreValve (MC) or Edwards Sapien (ES) bioprosthesis. MR grade was determined pre-and post TAVR.

Results:
From the 173 patients (46%) with MR grade = 2 at baseline, 33% improved to MR grade = 1 after TAVR. From the 202 patients with pre-procedural MR grade = 1, 19% worsened to MR grade = 2 after TAVR. Two-year survival is impaired in patients with a MR grade = 2 at baseline (log-rank p=0.008). NYHA functional class at follow-up TAVR was not affected by baseline MR grade. Reduction of MR = 1 grade after TAVR occurred more often in patients with an ES bioprosthesis than in patients with a MC (ES: 33% vs MC: 17%, p=0.01). Paravalvular aortic regurgitation (PAR) grade = 2 after TAVR was associated with worsening of MR = 1 grade (p=0.02).

Conclusion:
Almost half of the patients who undergo TAVR have MR grade = 2 prior to the procedure. This reduces two-year survival after TAVR, but has no effect on functional status. Valve implantation of an ES bioprosthesis is associated with a favourable effect on MR, whereas PAR after TAVR is associated with worsening of MR grade.
Session V: Rhythm

CLINICAL PROFILE OF YOUNG ONSET ATRIAL FIBRILLATION

P.A. Vermond (University Medical Center Groningen, Groningen); A.H. Holdbee (University Medical Center Groningen, Groningen); M. Rienstra (University Medical Center Groningen, Groningen); Turu Blauw (University Medical Center Groningen, Groningen); I.C. van Gelder (University Medical Center Groningen, Groningen)

Purpose:
Atrial fibrillation (AF) is mostly observed in elderly in the presence of underlying disease. However AF more and more starts at younger ages (<40 years, "young onset AF"), even at an age <40 years. Data on this group of patients is sparse.

Methods:
This is a single-center observational prospective study performed in a tertiary referral center. Consecutive patients who had developed AF < 60 years were included. Detailed information on underlying disease, age and new risk factors for AF and family history was collected. Familial AF was defined as AF occurring in at least one first-degree family member before the age of 60 years. Patients with very young onset of AF (< 40 years) were compared to patients with AF onset at an age ≥ 40 years.

Results:
Included were 446 patients, 97 (22%) < 40 years and 349 (78%) 40-60 years (Table). Mean age of AF onset was 48±10 years, 26% were women. The majority had paroxysmal AF. Familial AF was present in 27%. Underlying heart disease and obesity was often observed albeit less frequently in patients with AF starting < 40 years. Lone AF occurred in 13% at an age < 40 years, and in 2% at an age 40-60 years.

Conclusion:
Young onset AF is associated with a high prevalence of comorbidities, including hypertension, vascular disease and obesity, even in patients with AF onset ≥ 40 years. Lone AF is rare.

<table>
<thead>
<tr>
<th>Total population (n=446)</th>
<th>AF onset &lt;40 years (n=97, 22%)</th>
<th>AF onset ≥40 years (n=349, 78%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of AF onset (years, mean±SD)</td>
<td>48±10</td>
<td>36±7</td>
<td>36±5</td>
</tr>
<tr>
<td>Female sex – no. (%)</td>
<td>31 (32)</td>
<td>21 (22)</td>
<td>93 (27)</td>
</tr>
<tr>
<td>AF type – (%)(n=442)</td>
<td></td>
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<tr>
<td>Paroxysmal</td>
<td>288 (65)</td>
<td>62 (64)</td>
<td>227 (65)</td>
</tr>
<tr>
<td>Persistent</td>
<td>60 (13)</td>
<td>20 (21)</td>
<td>40 (12)</td>
</tr>
<tr>
<td>Familial AF – no. (%)</td>
<td>119 (27)</td>
<td>29 (30)</td>
<td>90 (26)</td>
</tr>
<tr>
<td>Underlying heart disease – no. (%)</td>
<td>323 (73)</td>
<td>20 (21)</td>
<td>303 (87)</td>
</tr>
<tr>
<td>Obesity – no. (%)</td>
<td>193 (43)</td>
<td>10 (10)</td>
<td>183 (53)</td>
</tr>
<tr>
<td>Diabetes mellitus – no. (%)</td>
<td>38 (9)</td>
<td>4 (4)</td>
<td>34 (10)</td>
</tr>
<tr>
<td>Heart failure – no. (%)</td>
<td>68 (15)</td>
<td>12 (13)</td>
<td>56 (16)</td>
</tr>
<tr>
<td>Body mass index ≥30 kg/m² – no. (%)</td>
<td>117 (26)</td>
<td>18 (19)</td>
<td>99 (29)</td>
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<td>Creatinine &gt;1.5 mg/dl – no. (%)</td>
<td>39 (9)</td>
<td>7 (7)</td>
<td>32 (9)</td>
</tr>
<tr>
<td>Number of comorbidities (mean±SD)</td>
<td>3.2±1.7</td>
<td>1.8±1.5</td>
<td>3.6±1.7</td>
</tr>
<tr>
<td>Lone AF – no. (%)</td>
<td>10 (11)</td>
<td>11 (11)</td>
<td>8 (2)</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (% median, range)</td>
<td>57 (13-81)</td>
<td>59 (13-83)</td>
<td>56 (13-75)</td>
</tr>
<tr>
<td>Left atrial volume index (ml/m² median, range)</td>
<td>33 (14-97)</td>
<td>35 (14-97)</td>
<td>33 (14-84)</td>
</tr>
</tbody>
</table>

SLOW CONDUCTING ANATOMICAL ISTHMUSES ARE THE SUBSTRATE FOR VENTRICULAR TACHYCARDIA IN REPAIRED TETRALOGY OF FALLOT

G.E. Kager (LUMC, Leiden); F. Sacher (Bordeaux University Hospital, Bordeaux); AF. van Wijhe (LUMC, Leiden); JB. Thambor (Bordeaux University Hospital, Bordeaux); N. Derbal (Bordeaux University Hospital, Bordeaux); M. Schäfl (LUMC, Leiden); Z. Jalek (Bordeaux University Hospital, Bordeaux); K. Zeppenfeld (LUMC, Leiden)

Purpose:
The majority of ventricular arrhythmias (VA) in repaired Tetralogy of Fallot (rTOF) are sustained reentrant ventricular tachycardia (SMVT) related to four anatomical isthmuses. Specific anatomical isthmuses characteristics may be related to SMVT.

Methods:
Seventy-three consecutive rTOF patients (40±16 years, 63% male) were studied before VA ablation. 3D thoracic and right atrial (RA) electroanatomical maps were acquired and from RV and RA sites, entrainment and electroanatomical substrate mapping were performed. All identified anatomical isthmuses (AI) were evaluated for width, length and conduction velocity (CV). All thoracic and RA (PV patch, scar, RV, RV scar and pulmonary annulus (PA), AIS, PV and RA patch, AIV, VAIS patch and TA). The relation between VT reentry circuit sites and AI was determined by pace and/or entrainment mapping.

Results:
Twenty-eight patients (13±28 prior documented SMVT) were inducible for a median of 1.0 (0.0 – 1.5) SMVT; VTCL 252 ms (231 – 312). The number of identified A1, 2 and 3 was comparable for inducible and non-inducible (n=45) patients (see Table). Inducible patients had significant narrower A1, 2, 3, longer A1, 2 and 3 and lower CV of A1, 2 and 3. A critical SMVT reentry site was mapped to an A1 in 24/27 patients. All A1 containing reentry circuits (n=26; A1, A2, A3, 173, A1 and RVO patch) without inducible and non-inducible patients had only AI with CV of >0.5 m/s.

Conclusion:
Slow conducting anatomical isthmuses with CV<0.5 m/s are the dominant substrate for SMVT in rTOF.

<table>
<thead>
<tr>
<th>Table: Presence and properties of anatomical isthmuses according to patients with and without inducible ventricular tachycardia (SMVT)</th>
</tr>
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<tbody>
<tr>
<td>StepInducible SMVT non-inducible SMVT β (p-value)</td>
</tr>
<tr>
<td>Isthmus 1 (present)</td>
</tr>
<tr>
<td>Isthmus 1 width (mm)</td>
</tr>
<tr>
<td>Isthmus 1 length (mm)</td>
</tr>
<tr>
<td>Isthmus 1 CV (m/s)</td>
</tr>
<tr>
<td>Isthmus 2 (present)</td>
</tr>
<tr>
<td>Isthmus 2 width (mm)</td>
</tr>
<tr>
<td>Isthmus 2 length (mm)</td>
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<tr>
<td>Isthmus 2 CV (m/s)</td>
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<tr>
<td>Isthmus 3 (present)</td>
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<tr>
<td>Isthmus 3 width (mm)</td>
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<tr>
<td>Isthmus 3 length (mm)</td>
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<tr>
<td>Isthmus 3 CV (m/s)</td>
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<tr>
<td>Isthmus 4 (present)</td>
</tr>
<tr>
<td>Isthmus 4 width (mm)</td>
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<tr>
<td>Isthmus 4 length (mm)</td>
</tr>
<tr>
<td>Isthmus 4 CV (m/s)</td>
</tr>
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</table>

CONTACT FORCE AS A PREDICTOR OF ‘SINGLE ROUND ISOLATION’ IN PULMONARY VEIN ISOLATION

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Purpose:
Not achieving pulmonary vein isolation (PVI) after the first round of ablation (single round PVI) may result in localized edema with non-durable lesions and may lead to longer procedure times. Catheter-tissue contact plays a pivotal role in achieving optimal lesions. The SmartTouch™ CF-sensing catheter enables measurement of catheter tip contact force (CF), but optimal CF values have yet to be determined. We investigated optimal CF and force-time integral (FTI) for achieving single round PVI with the SmartTouch™ catheter.

Methods and Results:
106 patients (age 60.4±16.4, 71(67%) male) underwent primary PVI with the SmartTouch™ catheter. Single round isolation of both PV pairs was achieved in 24.5% of the patients. On average, procedures with single round isolation lasted 39 min shorter (37%), and radiation burden was 7.2%±2.0% lower (37%). For further analysis, each PV pair circulation was divided into six regions. Direct isolation was achieved in 80% of all PV regions. Both mean and minimum CF and FTI were significantly higher in PV regions where direct isolation was achieved. Smaller LA volumes (r<0.1) and CT were found to be independent predictors for successful single round PVI. ROC curve analysis showed that minimum CF of 18g and minimum FTI of 400g*s had a specificity of 0.95 for excluding persistent conduction per PV region after single round.

Conclusion:
Single round PVI is achieved more often with higher CF and FTI, and results in a shorter procedure time and lower radiation burden. We propose pursuing a minimum CF of 18g and FTI of 400g*s.

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FOLLOW-UP OF IDIOPATHIC VENTRICULAR FIBRILLATION (FLUVF STUDY) – PRELIMINARY RESULTS
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Purpose:
Idiopathic ventricular fibrillation (VF) is the underlying cause in 5-10% of out-of-hospital cardiac arrest patients. RF is defined as VF of unknown origin: no structural nor electrical heart disease is present upon first presentation. Little is known about long-term outcome and clinical characteristics during follow-up of RF patients. Purpose of this study is to find alternative diagnoses, to determine prognosis and to improve follow-up of RF patients.

Methods:
This is a retrospective cross-sectional study, with 85 RF-Patients diagnosed since 1985. The follow-up is still work in progress. Since 1985 new diagnoses were described (e.g. Brugada syndrome) and diagnostics changed (e.g., DNA analysis). In our cohort additional investigations were performed to find alternative diagnoses and clinical follow-up data were collected.

Preliminary results:
50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years. In 22% (19/85) a previous history of syncope was reported and 75 patients received an ICD, 50 males and 35 females are included, with a mean age at event of 41.6 years.
**Session VI: Surgery**

**SURGICAL TREATMENT OF ABDOMINAL AORTIC ORIGIN OF THE CORONARY ARTERIES**

M. Kool (Leids Universitair Medisch Centrum, Leiden); H. M. Wegien (Leids Universitair Medisch Centrum, Leiden); N.A. de Graaf (Leids Universitair Medisch Centrum, Leiden); M.G. Hazekamp (Leids Universitair Medisch Centrum, Leiden).

**Purpose:**

Abdominal aortic origin of the coronary arteries can be life threatening and may be treated surgically. Consensus exists that all interarterial LCA should be surgically repaired. For interarterial RCA the discussion is open. The purpose of this study was to analyze our surgical experience.

**Methods:**

From 2001 until 2014, 25 patients were operated for interarterial RCA (21) or interarterial LCA (4). All patients had a stilt-like coronary ostium, 20 had an intramural course of the proximal coronary artery. Median age at operation was 43 years. Twenty-nine patients were symptomatic, 3 had myocardial infarction and 2 had been revascularized before surgery. Diagnosis was by CT-angiography in all. Intermural RCA repair consisted of unroofing of the coronary ostium (with or without reimplantation into the original sinus) in 20 patients and CABG on the RCA in 1. Surgery for interarterial LCA was ostium reconstruction in 3 patients and reimplantation in 1. Follow-up was by analysis of independent records, direct patient contact, echocardiography and electrocardiography.

**Results:**

Median follow-up was 3 years. One patient was lost in follow-up. No mortality occurred. Three patients had ischemia with ventricular fibrillation shortly after surgery and were successfully resuscitated. Two underwent immediate re-operation. Two of these patients suffered a LV dysfunction. All other patients have recovered uneventfully and are asymptomatic.

**Conclusions:**

Surgery for abrupt aortic origin of the coronary arteries is safe with some risk of postoperative cardiogenic shock, especially after interarterial LCA reconstruction. We strongly believe that stilt-like ostium and intramural coronary course are absolute indications for surgical repair.

**GENDER DIFFERENCES AND EARLY OUTCOME AFTER CORONARY ARTERY BYPASS GRAFT SURGERY: A NATIONWIDE STUDY**

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*On behalf of the data registry committee of the Netherlands Association for Cardio-Thoracic Surgery.*

**Purpose:**

To compare women with men with respect to baseline characteristics and short-term outcome in a contemporary cohort of patients that underwent CABG surgery.

**Methods:**

All patients (n=41269), 78% males (n=32154) that underwent CABG surgery (conventional or minimally invasive) from January 2007 and December 2011 were included in this study. Differences in patient and procedural characteristics, and in-hospital outcome were compared between male and female patients.

**Results:**

Female patients were older (mean age 69 vs. 66 years, p<0.001), had higher logistic EuroSCORE I (median, 6.7 vs. 4.2, p<0.001), presented more often with clinical symptoms (5.9% vs. 4.1%, p<0.001) and emergent surgery (6.4% vs. 6.2%, p=0.01). Female patients were less likely to receive total arterial grafting (19.2% vs. 25.1%, p<0.001) and received more often total venous grafting (6.8% vs. 4.1%, p<0.001) or combination of both (74.9% vs. 72.5%, p=0.001). In-hospital mortality was 1% (n=582) and higher in female patients multivariate OR 1.71, 95%CI 1.38–2.12, p<0.001. In males, the AUC for the logistic EuroSCORE I was 0.86 (95%CI 0.85–0.88) versus 0.82 (95%CI 0.79–0.85) in females. The calibration of this model was the only independent predictor of delirium. Further study is warranted to determine whether multidimensional geriatric assessment has the potential to improve risk stratification models.

**Conclusions:**

After TAVI using the left subclavian artery, post-operative delirium occurred in almost one-third of patients. Delirium was defined according to the Diagnostic and Statistical Manual for Mental Disorders. Clinical follow-up was assessed at discharge, 30 days and 1 year. Baseline and clinical characteristics were analyzed in search for potential independent mediators of delirium.

**Incidences, Clinical Consequences and Risk Factors of Delirium after Transcatheter Aortic Valve Implantation (TAVI) in BAVS Patients – A Pilot and Multi-Center Study**

K. van der Wulp; (VUmc, Amsterdam); M. van der Wulp; (VUmc, Amsterdam); C. Kievit (Radboud UMC, Nijmegen); Menko Jan de Boer (Radboud UMC, Nijmegen); Peter C. Kruyt (Radboud UMC, Nijmegen).

**Purpose:**

To study the incidence, clinical consequences and risk factors of delirium in patients undergoing Transcatheter Aortic Valve Implantation (TAVI) through the left subclavian artery.

**Methods:**

We studied 125 consecutive patients who underwent TAVI between 2009 and 2012 using the left subclavian artery as primary access site. Delirium was defined according to the Diagnostic and Statistical Manual for Mental Disorders. Clinical follow-up was assessed at discharge, 30 days and 1 year. Baseline and clinical characteristics were analyzed in search for potential independent mediators of delirium.

**Results:**

Post procedural delirium was observed in 39 (31%) patients. Delirium was associated with prolonged hospital stay (median 12 vs. 9 days) and lower 30-day and 1-year survival (58 ± 8% vs. 79 ± 5%; p=0.01). Using standard peripertative clinical screening, age was the only independent predictor of delirium.

**Conclusions:**

After TAVI using the left subclavian artery, post-operative delirium occurred in almost one-third of patients with an adverse impact on clinical outcome. Using standard clinical screening, age was the only independent predictor of delirium. Further study is warranted to determine whether multidimensional geriatric assessment has the potential to improve risk stratification and clinical outcome in this setting.
Session VI: Surgery (continued)

WHITE BLOOD CELL COUNT AND NEW-ONSET ATRIAL FIBRILLATION AFTER CARDIAC SURGERY

K.A. Jacob (University Medical Centre, Utrecht); M.M. Naters (University Medical Centre, Utrecht); S.M. Diekman (University Medical Centre, Utrecht); M.J. ten Berge (University Medical Centre, Utrecht); J. Alvin (University Medical Centre, Utrecht); D. van Dijk (University Medical Centre, Utrecht)

Purpose:
Postoperative new-onset atrial fibrillation (PNAF) is the commonest complication following cardiac surgery. The inflammatory response, as a potential underlying mechanism, has been extensively studied by various inflammatory markers and white blood cell count (WBC) is the only present consequential inflammatory marker predicting PNAF. This study aimed to determine the association between pre- and postoperative WBC and PNAF.

Methods:
Patients, aged 18 years or older, undergoing elective cardiac surgery with a sinus rhythm preoperatively were recruited from the Desamidea database for Cardiac Surgery- PNAF trial (ECCS-PNAF) for this observational, post-hoc cohort study. WBC was prospectively routinely measured preoperatively and once during each of the first four postoperative days. Development of PNAF was evaluated in all patients with continuous Holter monitoring for the first 5 days postoperatively.

657 patients were included in this trial and 277 developed PNAF. 572 patients were included in the primary analysis. Independent t-tests comparing postoperative WBC in both groups revealed that WBC was significantly higher in the PNAF group on day 2 (P=0.03) and day 4 (P=0.02), and Multivariate analysis showed that preoperative and postoperative WBC, day 1-3 were not associated with PNAF. A High WBC on postoperative day 4 was related to the development of PNAF (Table 1). Additionally, older age, CABG plus valve surgery and single valve surgery were correlated with the occurrence of PNAF.

Conclusion:
Preoperative and postoperative WBC were not associated with the development of PNAF.

Table 1. Multiple Regression Analysis of the Risk of PNAF, using multiple patient characteristics, and white blood cell count (WBC) at the 5 timepoints.

<table>
<thead>
<tr>
<th>Characteristic/Variable</th>
<th>ODDS ratio</th>
<th>95% Confidence Interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.064</td>
<td>1.039-1.098</td>
<td>0.005</td>
</tr>
<tr>
<td>CABG plus Valve, #</td>
<td>2.846</td>
<td>1.786-4.873</td>
<td>0.0005</td>
</tr>
<tr>
<td>Single Valve, #, ¶</td>
<td>1.566</td>
<td>0.992-2.516</td>
<td>0.058</td>
</tr>
<tr>
<td>Multiple Valve, #, ¶</td>
<td>1.486</td>
<td>0.497-4.709</td>
<td>0.219</td>
</tr>
<tr>
<td>WBC, preoperatively</td>
<td>1.043</td>
<td>0.963-1.136</td>
<td>0.020</td>
</tr>
<tr>
<td>WBC, Day 1</td>
<td>1.046</td>
<td>0.989-1.009</td>
<td>0.028</td>
</tr>
<tr>
<td>WBC, Day 2</td>
<td>1.034</td>
<td>0.992-1.078</td>
<td>0.010</td>
</tr>
<tr>
<td>WBC, Day 3</td>
<td>1.030</td>
<td>0.990-1.065</td>
<td>0.042</td>
</tr>
<tr>
<td>WBC, Day 4</td>
<td>1.025</td>
<td>0.991-1.061</td>
<td>0.044</td>
</tr>
</tbody>
</table>

A DOUBLE BARRELED MYXOMA

M. Kuizingen (Slingeland Ziekenhuis, Doetinchem); E.O.F. van Goresen (Slingeland Ziekenhuis, Doetinchem); F.Z. Rangarajan (Universitair Medisch Centrum, Utrecht); W.F. Terpstra (Slingeland Ziekenhuis, Doetinchem)

Case-presentation:
A 28-years old female patient was presented to our emergency department/ward with atrial fibrillation and post-infarct atrial flutter. The patient had a past medical history of hypertension and type-2 diabetes mellitus. The patient had undergone a coronary artery bypass grafting surgery 1 year ago, subsequent to a non-Q wave myocardial infarction. The patient had been well after the surgery, and was referred for the current episode of atrial fibrillation.

A resection of both masses was performed, leaving behind a large intra-atrial septal defect. Pathology report confirmed the diagnosis of bialtrial myxoma. After surgical treatment, patient had complete cardiac and neurological recovery.

Conclusion:
Atrial myxoma is the most common benign tumour of the heart. These tumours arise from the endocardial or intramural epicardial mesenchyme, and can arise in any of the cardiac chambers. Bialtrial myxoma is a very rare condition, and has seldom been described in literature. In this particular case a pre-existing patent foramen ovale is possibly the cause of bialtrial myxoma. Treatment consists out of surgical resection, often combined with intra-atrial septal defect reconstruction.

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[Image of a chamber view with giant bialtrial myxoma]

DEGREE OF FATTY INFILTRATION CONTRIBUTES TO THE COMPLEXITY OF THE SUBSTRATE FOR ATRIAL FIBRILLATION IN GOAT LEFT ATRIA

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Purpose:
Progression of atrial fibrillation (AF) is caused by electrical and structural remodelling. Fibrosis and altered connexin expression are known alterations in atrial tissue structure contributing to the development of AF substrates. To date, the effect of fatty infiltration on AF conduction has not been studied. We hypothesize that the degree of fatty infiltration is an important determinant of AF progression and AF complexity in goat left atria (LA).

Methods:
LA epicardial high-density contact mapping (256 electrodes) was performed in goats with acutely induced (aAF, n=6) and persistent AF (persAF, n=5). After analysis of unipolar AF electrograms, AF cycle length (AFL) and number of fibrillation waves per second (waves/s) were quantified. Map reconstruction was performed and reconstitution of high-resolution MRI (vesicle size [78x78x78] μm3, allowing myocardial fat quantification within the atrial wall using a Fatty Infiltration Score (FIS, quantification of proportion fat per electrode grid).

Results:
FIS (mm3) was shorter in persAF than in aAF (103±20 vs. 127±15, P=0.05) and waves/s were higher in persAF than in aAF (103±20 vs. 127±15, P=0.05). The degree of fatty infiltration was much higher in persAF than in aAF (FIS=44.3±8.7 vs. FIS=20.4±3.5, P<0.01). Waves/s correlated well with fatty infiltration across (visves=−0.96, P<0.01; see Figure 1) & corrected for the 2 groups (partial r=−0.87, P<0.01). AFL correlation inversely with fatty infiltration (r=−0.81, P<0.01).

Conclusion:
Persistance of AF is associated with a fatty infiltration in goat left atria. Fatty infiltration seems to be an important determinant of AF complexity that deserves further targeted investigation.

[Image of a wavefront map showing the propagation of atrial fibrillation]

STATE OF THE HEART: THE POTENTIAL OF DECELLULARISED PERICARDIUM BY SUPERCRITICAL CARBON DIOXIDE PROCESSING FOR CARDIOTHORACIC SURGERY

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Purpose:
Several biomaterials, such as pericardium, are used as a temporary graft for heart tissue recovery, reconstruction of heart valves, and aortic wall, and pericardial closure. However, these materials induce a pro-inflammatory response, tend to calcify, and show formation of scar tissue. Thus, our aim is to develop a biomaterial that withstands these disadvantages, and has full remodelling properties.

Methods:
Porcine, and bovine pericardium was decellularised by supercritical carbon dioxide. The formation of scar tissue. Thus, our aim is to develop a biomaterial that withstands these disadvantages, and has full remodelling properties.

Results:
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Conclusion:
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[Image of a histological section showing the three-dimensional structure of the pericardial tissue]
Abstracts

Session VII: Experimental/ACS

DOPPLER-DERIVED HYPEREMIC MICROVASCULAR RESISTANCE PREDICTS THE OCCURRENCE OF MICROVASCULAR INJURY AND MICROVASCULAR PERFUSION DEFICITS AFTER ANGIOGRAPHICALLY SUCCESSFUL PRIMARY PERCUTANEOUS CORONARY INTERVENTION

P.F. Trounson (VUMC, Amsterdam), G.A. de Waard (VUMC, Amsterdam), M.R. Holander (VUMC, Amsterdam), L.F. Robbers (VUMC, Amsterdam), J. Danan (VUMC, Amsterdam), M.W. de Weert (VUMC, Amsterdam), P.F. Anwar (VUMC, Amsterdam), P.S. Biesbroek (VUMC, Amsterdam), A.A. Lammertse (VUMC, Amsterdam), C.P. Allaart (VUMC, Amsterdam), M.P. Aliaat (VUMC, Amsterdam), A.W. de Vries (VUMC, Amsterdam), A.M. Beek (VUMC, Amsterdam), R. Knapen (VUMC, Amsterdam), N. van Rogen (VUMC, Amsterdam)

Purpose: Primary percutaneous coronary intervention (PCI) leads to optimal angiographic restoration of flow in more than 90% of ST elevated myocardial infarction (STEMI) patients. However, in a large proportion of patients myocardial perfusion is not recover adequately despite good angiographic results. This study aimed to investigate whether intracoronary Doppler flow and pressure measurements are related to the occurrence of microvascular injury (MI) at cardiac magnetic resonance imaging (CMR) to evaluate the relation between peak myocardial perfusion at positive emission tomography (PET) as measured in the days following a myocardial infarction.

Methods: 52 STEMI patients were included and treated with primary PCI. Directly following successful revascularization, intracoronary Doppler flow and pressure measurements were obtained in the culprit artery and in an unobstructed reference coronary artery. Pressure flow derived hyperemic microvascular resistance (HMR) was defined as the ratio between distal pressure and flow velocity. CMR cine and LGE imaging and H215O PET imaging were performed 4-6 days after successful PCI. Using CMR, MI was defined as a subendocardial recess of myocardium with low signal intensity within the gadolinium-enhanced myocardium. Abnormal myocardial blood flow on PET imaging, the coronary flow reserve (CFR) was used. CFR was defined as the ratio between peak myocardial blood flow (MBF) after induction of hyperemia by adenosine administration and MBF under basal conditions.

Results: 25 patients developed MI and 27 did not. The mean HMR in the culprit artery was 3.0±0.4 in patients with myocardial infarction was significantly higher than in patients without MI (MI: 3.6 ± 1.51 vs. no MI: 2.53 ± 1.03, p=0.02). Multivariable analysis showed that HMR was predictive for MI. HMR was also correlated to decreased myocardial blood flow (MBF) on PET (CFR<2.0: 3.6±0.12 vs. CFR>2.0: 2.5±0.34, p=0.02).

Conclusion: Elevated Doppler flow-derived HMR correlates to CMR-defined MI as well as decreased myocardial blood flow measured by PET.

TRACING AN ISL-1+ MYOCARDIAL BRIDGE BETWEEN THE SINUS VENOSUS MYOCARDIUM AND AV CANAL: A POSSIBLE CONTRIBUTION TO THE AV NODE


Purpose: The most common form of supraventricular tachycardia in adults is atrioventricular nodal re-entry tachycardia, which is caused by the presence of anatomy and electrophysiologically distinct pathways within the AV node. A possible explanation for the presence of distinct cell types within the AV node could be a different embryological origin of these cell populations. We used in vivo physical lineage tracing in chicken embryos to trace the fate of cells from the sinus venosus myocardium to the cardiac conduction system (CCS).

Methods: The Isl-1+/+sinus venosus myocardium was labelled by injecting a solution of fluorescent dyes (DiO/5-TAMRA, Invitrogen) after 2.5 days of development using a micropipet (NM300 Nalini). Embryos were hatched and analyzed after 24 and 48 hours of reinnovation.

Conclusion: After labeling of the sinus venosus myocardium, cells could be traced to an Isl-1+/Isl1-5/Tntr51+ bridge of tissue between the sinus venosus and AV canal myocardium, which was the so-called the SV-AVC bridge. This bridge showed expression of HCM4, indicating a role in CCS development. In murine embryos the SV-AVC could also be identified and Isl-1+, Isl1-, and HCM4 co-localized in this tissue.

We describe an Isl1+/+Sinus/HCN4+ myocardial bridge, which connects the sinus venosus myocardium to the myocardium of the AV canal. Physical lineage tracing experiments showed that the myocardium of the sinus venosus contributes to the SV-AVC bridge. We hypothesize a cellular contribution from the sinus venosus myocardium to the AV node, which could explain the presence of different cell types in this region.

INTERIM FEATURES OF THE SINUS NODE DURING EARLY DEVELOPMENT


Purpose: Mutations in Vascular Endothelial Growth Factor-A (VEGF) are associated with congenital heart defects. VEGF120/120 mice over express VEGF. In the current study we aimed to assess the effect of VEGF over-expression on the sino-atrial node (SAN).

Results: The atrial heart rate (HR) was assessed in VEGF120/120 and wildtype (WT) embryos with high frequency ultrasound in isolated (isoflurane 1.5%) VEGF120/120 pregnant mice under stable vital parameters at embryonic day (E)12.5, 14.5 and 17.5 and by optical mapping of E12.5. The morphology was studied using antibodies for tropoelin, Nestin, HCN4, Cx40, Cx43, NCAM and HCM. SAN volume measurements were performed and quantitative PCR was used to assess HCN, HCM4, TBX3, TBX5, Cx40, Cx43 expression in the SAN.

Conclusion: The blindly measured mean heart rate during fetal echocardiography was significantly lower in VEGF120/120 embryos compared to WT controls (fig1). Optical mapping confirmed a lower heart rate. Consistent with these data, morphometric analysis revealed a significant smaller SAN volume at E12.5 and E17.5 in mutants. The SAN of mutant embryos had an aberrant shape, with abnormal vasculature. No changes in automatic interaction were observed. Preliminary qPCR data show differences in levels of pacemaker genes in the SAN of VEGF 120/120 mutant embryos compared to WT.

Figure 1: Lower heart rate in beats per minute (BPM) in VEGF120/120 embryos compared to wild type controls at embryonic day (E) 12.5, 14.5 and 17.5.

RADIUS VERSUS FEMORAL ACCESS FOR CORONARY ANGIOGRAPHY AND INTERVENTION IN PATIENTS WITH ACUTE CORONARY SYNDROMES: RESULTS OF THE ZWOLLE MYOCARDIAL INFARCTION STUDY GROUP

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Purpose: Radial access is associated with lower risk of complications compared to femoral access. The purpose of this study was to assess the efficacy and safety of radial versus femoral access in patients (pts) with acute coronary syndromes (ACS) who underwent coronary angiography and/or PCI.

Methods: Of the 3384 ACS pts, 56.1% were diagnosed with STEMI and 43.9% with a NSTEMI on admission. Coronary angiography was performed in 2950/3384 (86.9%) and in 671/2950 (23%) by radial access. PCI was performed in 2181/2950 (74%) of the pts. No differences in baseline or angiographic characteristics were present between radial vs femoral access patients except for diagnosis of ST-STEMI 54.6% vs 60.0%, p=0.011, MIPE use: 1.1% vs 6.7%, p=0.001, and Killip class>2: 8.6% vs 12.9%, p=0.012. The primary endpoint occurred less often in the radial group as compared to the femoral group (1.5% vs 3.6%, p=0.008). The subgroup of pts with a moderate, high or very high CRUSADE bleeding score (1.8% vs 8.3%, p=0.014) had a smaller primary endpoint (HR 0.39; 95% CI, 0.18–0.99, p=0.050), as well as for 30-day mortality (HR 0.24; 95% CI, 0.077–0.790, p=0.018).

Conclusion: Radial access in ACS patients significantly reduced 30 day non CABG-related major and minor bleeding and 30-day mortality compared with femoral access, with similar PCI success. Radial access remained an independent predictor for 30-day non CABG-related bleeding and all cause mortality. The beneficial effect of radial access was highest in patients at high risk of bleeding.

Figure 1: 30-day event curve of net adverse clinical events.
Session VII: Experimental/ACS (continued)

IN VITRO SONOTHROMBOLYSIS IN WHOLE BLOOD FOR MYOCARDIAL NO-REFLOW

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Purpose:
Acute myocardial infarction can be treated with percutaneous coronary intervention. Adequate microvascular perfusion is often not restored due to microvascular obstruction (MVO), partly caused by microvascular microthrombi. This nega tively influences clinical outcomes. We tested the hypothesis that ultrasound (US) mediated microbubble (MB) destruction can achieve microvascular distal lysis in our in vitro MVO model.

Methods:
The model comprised of a phantom vessel containing an intraluminal mesh with 40 µm pores to simulate a cross section of the microcirculation. Bovine blood microthrombi (1)

in vitro

MVO

Acute myocardial infarction can be treated with percutaneous coronary intervention. Adequate microvascular perfusion is often not restored due to microvascular obstruction (MVO), partly caused by microvascular microthrombi. This negatively influences clinical outcomes. We tested the hypothesis that ultrasound (US) mediated microbubble (MB) destruction can achieve microvascular distal lysis in our in vitro MVO model.

Results:
After 20 minutes of treatment, the pressure drop with 3000 cycles/pulse length (58 ± 14 %) was higher than with 500 cycles (p=0.037). US therapy with 5000 cycles provided higher initial pressure change (46 ± 17 %) compared to low dose tPA (15 ± 10 %) (p=0.007). tPA was however needed to provide complete sonothrombolysis; 20 minute 5000 cycle US + tPA combination therapy achieved better lysis (88 ± 8 %) compared to 5000 cycle (p=0.004) reaching the same effect as with PBS perfusates (92 ± 8 %) (p=0.678). (Fig.1)

Conclusions:
High acoustic pressure sonothrombolysis with MB can achieve reperfusion in whole blood, but with less efficacy than in PBS, suggesting that differences in fluid dynamics affect bubble dynamics. Adding tPA resolved this issue, showing that low dose tPA with PBS perfusates (92 ± 8 %) (p=0.678). (Fig.1)

Figure Lytic effect (mean±SD) improved significantly between treatment with 5000 cycles and 500 cycles + tPA (p=0.004, ANOVA). At 10 minutes of therapy, a statistically significant difference was observed in favor of treatment with 5000 cycles compared to tPA alone (p=0.006, ANOVA). n=3 for all samples.

Reference:
Abstracts

Session VII: Experimental/ACS (continued)

VALIDATION OF FLUOROSCOPY ASSISTED SCORING OF MYOCARDIAL HYPOPERFUSION (FLASH) AS A NOVEL, ANGIOGRAPHIC METHOD TO ASSESS CORONARY BLOOD FLOW IN PATIENTS AFTER PRIMARY PCI

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Purpose:
Coronary blood flow in the setting of acute myocardial infarction can be assessed angiographically using TIMI flow grade, TIMI frame count and myocardial blush grade. Invasive methods like intracoronary Doppler flow velocity or thermodilution can also be used but come with increased risk and costs. We recently developed a novel algorithm to assess coronary blood flow angiographically: Fluoroscopy Assisted Scoring of Myocardial Hypoperfusion (FLASH). In this present study, we validate this algorithm by comparing it to intracoronary blood flow measurements.

Methods:
Intracoronary Doppler flow velocity measurements were obtained directly following primary PCI in 30 STEMI patients. Coronary angiographic flow was calculated by multiplying the contrast passage time by vessel length and cross-sectional area measured using Quantitative Coronary Angiography. Intracoronary measured blood flow was calculated by multiplying Doppler average peak flow velocity, measured just distally to the stent, with the cross-sectional area of the expanded stent.

Results:
There was a good correlation between coronary angiographic flow and intracoronary measured flow (Pearson’s R=0.64, p<0.001). No significant correlation was found between TIMI frame count and intracoronary measured flow (Pearson’s R=-0.35, p=0.10).

Conclusion:
Coronary blood flow measurements determined by FLASH algorithm were significantly correlated with intracoronary blood flow measurements by Doppler velocity wire.

Figure 1
Correlation between FLASH flow and Intracoronary measured flow.