

Netherlands Heart Journal Supplements

Volume 22
Supplement
April 2014
ISSN 1569-643X

Journal of the Netherlands Society of Cardiology

Abstracts

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



3 - 4 April 2014, Rai Elicium, Amsterdam

Scientific Spring Meeting of the Netherlands Society of Cardiology 2014

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*

Abstracts of the Scientific Spring Meeting of the Netherlands Society of Cardiology
4 – 5 April 2014, Rai Elicium, Amsterdam

Postersessions 4 April 2014
Session I : Congenital

AORTIC TORTUOSITY PREDICTS CARDIOVASCULAR EVENTS IN MARFAN SYNDROME

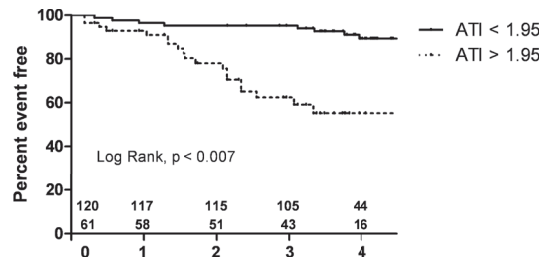
R. Franken (AMC, Amsterdam); A.W. den Hartog (AMC, Amsterdam); A. el Morabit (AMC, Amsterdam); H. Marquering (AMC, Amsterdam); J. Timmermans (UMCN Radboud, Nijmegen); A.J. Scholte (LUMC, Leiden); M.P. van den Berg (UMCG, Groningen); A.H. Zwinderman (AMC, Amsterdam); M. Groenink (AMC, Amsterdam); B.J.M. Mulder (AMC, Amsterdam)

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 losartan 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 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 ratio). Combined clinical endpoint comprised aortic dissection and elective aortic surgery.

Results: At baseline, ATI (1.9±0.2) was significantly correlated with aortic root diameter (44.3±5mm, r=0.212, p=0.013) and age (37±13, r=0.365, p<0.001). 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 higher baseline aortic tortuosity (2.0±0.2 vs. 1.9±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 in MFS (Log Rank test: p < 0.007). After three years of follow-up, losartan showed a modest trend towards lower ATI in unoperated patients (losartan: -0.015±0.1 versus no losartan: +0.023±0.1, p=0.160).

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



THE RATE OF THROMBO-EMBOLIC EVENTS IN ADULTS WITH CONGENITAL HEART DISEASE AND ATRIAL ARRHYTHMIAS

J.F. Heidendaal (AMC Amsterdam), W.H.G.J. Hoekstra (LUMC Leiden), M. Groenink (AMC, Amsterdam), S.M. Boekholdt (AMC, Amsterdam), A. Backx (AMC, Amsterdam), P.F.H.M. van Dessel (AMC, Amsterdam), J.R. de Groot (AMC, Amsterdam), B.J.M. Mulder (AMC Amsterdam), B.J. Bouma (AMC Amsterdam)

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 thrombo-embolic complications. This study aimed to assess prevalence of thrombo-embolic 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, thrombo-embolic 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 218 (11%) were known with AA (median follow-up 9 years, IQR 6-11). In 24 patients a thrombo-embolic event occurred (11%), of whom 21 had a stroke (10%), 3 a pulmonary embolism (1%) and 1 a systemic embolism (0.5%). Two patients (1%) suffered from intracranial hemorrhage. Survival free of thrombo-embolism was influenced by type of defect (log rank = 0.003; Figure 1). Highest incidence of thrombo-embolism and death was found in morbus Ebstein (25%) and patients with a univentricular heart (36%; UVH).

Conclusion: The prevalence of thrombo-embolic events in adult CHD patients with AA is 11% over a median period of 9 years. Patients with morbus Ebstein or UVH are most at risk of thrombo-embolism or fatal outcome. The results of this study underline the importance of efficient anticoagulation in AA in CHD.

Figure 1. Survival free of thrombo-embolism in CHD patients with AA. Data are displayed for univentricular heart (UVH), morbus Ebstein and remaining CHD types together. Log rank = 0.003.



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

Jouke P. Bokma (Academisch Medisch Centrum, Amsterdam); Michiel M. Winter (Academisch Medisch Centrum, Amsterdam); Thomas Oosterhof (Ziekenhuis Gelderse Vallei, Ede); Hubert W. Vliegen (Leids Universitair Medisch Centrum, Leiden); Arie P. van Dijk (Radboud Universitair medisch centrum); Mark G. Hazekamp (Academisch Medisch Centrum, Amsterdam); Dave R. Koolbergen (Academisch Medisch Centrum, Amsterdam); Barbara J.M. Mulder (Academisch Medisch Centrum, Amsterdam); Berto J. Bouma (Academisch Medisch Centrum, Amsterdam)

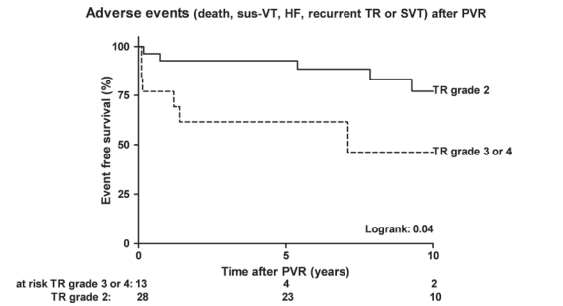
Purpose: Tetralogy of Fallot (TOF) patients may develop tricuspid regurgitation (TR) due to annulus dilation or leaflet abnormalities. Our objective was to determine outcome of patients with significant TR undergoing pulmonary valve replacement (PVR) and the effect of tricuspid valve (TV) repair.

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 II/IV 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(68%) with moderate TR (grade 2). Patients with severe pre-operative TR had higher pre-operative left ventricular volumes (p=0.04). Twelve (92%) patients with severe TR underwent concomitant 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 1.2±0.6). Adverse events occurred in 13 patients (1 death, 3 sustained VT, 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 (sus-VT >30 sec or requiring cardioversion) or heart failure (HF: Increase in NYHA class and requiring diuretics) or supraventricular tachycardia (SVT: >30 sec documented on electrocardiogram) or recurrent TR (grade 3 or higher).



NEW GENETIC APPROACHES IN PATIENTS WITH TRANSPOSITION OF THE GREAT ARTERIES

FVY Tjong (Academic Medical Center, Amsterdam); JGM Barc (Academic Medical Center, Amsterdam); AV Postma (Academic Medical Center, Amsterdam); L Beekman (Academic Medical Center, Amsterdam); M Klerk (Academic Medical Center, Amsterdam); BJM Mulder (Academic Medical Center, Amsterdam); and CR Bezzina (Academic Medical Center, Amsterdam)

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 empiric 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 (mutations present in the affected child and absent in the unaffected parents). 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 the disease.

Methods: Exome sequencing (sequencing of the coding region of the genome) was performed in 10 parent-child trios. Data from each parent-child trio was analyzed in order to identify *de novo*-mutations present in the affected child and absent in the unaffected parents. We used public exome databases to filter out common variants (minor allele frequency >1%). Variants found in this way were validated by PCR and Sanger sequencing.

Results: In 10 parent-child trios with TGA we identified six *de novo*-mutations. These six candidate genes will be screened in additional set of TGA patients (n=320) which were collected from the CONCOR database.

Conclusion: 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 I : Congenital (continued)

CARDIAC FUNCTION ONE YEAR AFTER PREGNANCY IN WOMEN WITH CONGENITAL HEART DISEASE

M.A.M. Kampman (University Medical Center Groningen, Groningen; ICIN-Netherlands Heart Institute, Utrecht); A. Balci (Isala klinieken, Zwolle); A.P.J. van Dijk (Radboud University Medical Center, Nijmegen); J.W. Roos-Hesselink (Erasmus Medical Center, Rotterdam); J.P. van Melle (University Medical Center Groningen, Groningen); M.R.M. Jongbloed (University Medical Center Leiden, Leiden); E.M.C.J. Wajon (Medical spectrum Twente, Enschede); B.J.M. Mulder (Academic Medical Center, Amsterdam); D.J. van Veldhuisen (University Medical Center Groningen, Groningen); P.G. Pieper (University Medical Center Groningen, Groningen) on behalf of the ZAHARA II investigators

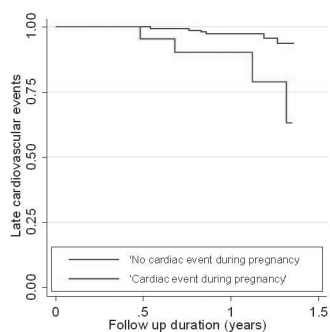
Purpose: Little is known about long term cardiovascular outcome after pregnancy in women with congenital heart disease. We, 1) observed the incidence of late cardiovascular complications and 2) compared cardiac function prior to and one year after pregnancy in women with congenital heart disease (CHD)

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 valvular 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, thrombo-embolic 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 (6.6%). Women with CVC during pregnancy were at risk for late CVC (HR 7.1, 95% CI 2.2-23.2, p=0.001, figure 1). In 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=0.022). No other significant differences 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 disease. 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

A.W. den Hartog (AMC, Amsterdam), R. Franken (AMC, Amsterdam), A.H. Zwiderman (AMC, Amsterdam), J. Timmermans (UMCN, Nijmegen), A.J. Scholte (LUMC, Leiden), M.P. van den Berg (UMCG, Groningen), V. de Waard (AMC, Amsterdam), G. Pals (VUmc, Amsterdam), B.J.M. Mulder (AMC, Amsterdam), M. Groenink (AMC, Amsterdam)

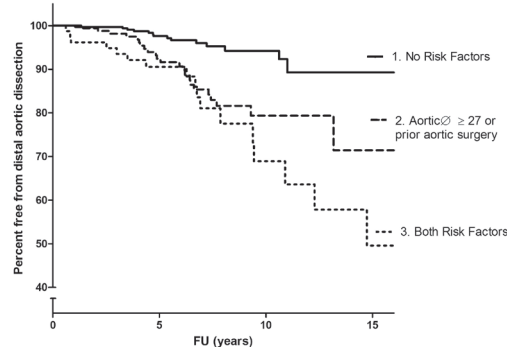
Purpose: Aortic complications beyond the ascending aorta have become a major clinical problem in patients with Marfan syndrome. The aim of our study was to identify clinical parameters associated with type B aortic dissection and to develop a risk model to predict type B aortic dissection in Marfan syndrome.

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, medicinal 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 600 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 in 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:0.3; 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 only 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.

M.A. Sluiman (AMC, Amsterdam); S. Apers (Leuven), A. Karatli (AMC, Amsterdam); M.C. Post (St. Antonius Ziekenhuis, Nieuwegein), C.H. Peels (Catharina Ziekenhuis, Eindhoven), M. Waskowsky (Isala, Zwolle), P.G. Pieper (UMCG, Groningen), B.J. Bouma (AMC, Amsterdam), P. Moons (Leuven), B.J.M. Mulder (AMC, Amsterdam)

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 severity.

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 (response rate 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-, 53% 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 (24% in 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.

Session II : Prognosis

SERIOUS UNDERESTIMATION OF THE OVERALL RISK OF CARDIOVASCULAR EVENTS IF EXTRAPOLATED FROM CARDIOVASCULAR MORTALITY: OBSERVATIONS FROM THE EPIC-NORFOLK PROSPECTIVE POPULATION STUDY

H.T. Jorstad (AMC, Amsterdam); B.E. Colkesen (AMC, Amsterdam); S.M. Boekholdt (AMC, Amsterdam); J.G.P. Tjissen (AMC, Amsterdam); R.J.G. Peters (AMC, Amsterdam)

Purpose:

Dutch guidelines recommend the use of risk charts in predicting fatal and non-fatal cardiovascular disease (CVD). These risk charts are based on the European SCORE charts that predict fatal CVD only, and use multipliers for non-fatal CVD (age 35-45 5x, 45-65 4x, 65 3x). However, these multipliers have not been validated. We therefore investigated these multipliers in a large, population-based cohort (EPIC-Norfolk).

Methods:

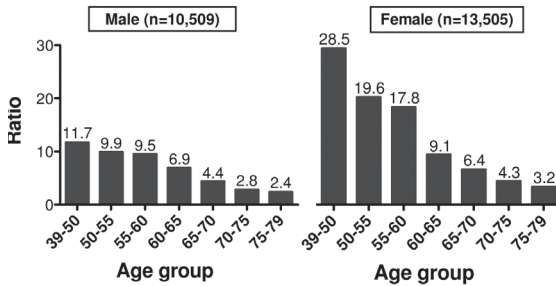
CVD mortality and total CVD (fatal plus non-fatal CVD events requiring hospitalization) were analyzed using Kaplan-Meier estimates in 24,014 men and women aged 39-79 without CVD or diabetes mellitus at baseline. CVD outcomes included death and hospitalizations for ischemic heart disease, heart failure, cerebrovascular disease, peripheral artery disease, and aortic aneurysm. The main outcome was the ratio of 10-year total CVD to 10-year CVD mortality, stratified by age and sex.

Results:

Ten-year CVD mortality was 3.9% (900 CVD deaths); the rate of total CVD events was 21.2% (4978 fatal or non-fatal CVD events). The mean overall ratio of total CVD/ CVD mortality was 5.4. This ratio decreased markedly with age: from 11.7 to 2.4 in men and from 28.5 to 3.2 in women (Figure).

Conclusion:

The relationship between 10-year total CVD and CVD mortality cannot be estimated using fixed multipliers and is dependent on age and sex. The proposed multipliers in current guidelines lead to underestimation of risk, particularly in younger age groups, and in women more than in men. These findings have important implications for individual decision-making on preventive therapy and for future guidelines.



Ratios of 10-Year Cumulative Total CVD / CVD Mortality by Sex and Age Groups. CVD = Cardiovascular disease

PREDICTORS OF OUTCOME IN ADULTS WITH CONGENITAL HEART DISEASE AFTER CARDIAC SURGERY

I.M. Blok (AMC, Amsterdam/ICIN, Utrecht); M.J. Schuuring (AMC, Amsterdam); D.R. Koelbergen (AMC, Amsterdam); M.G. Hazekamp (LUMC, Leiden); B.A. de Mol (AMC, Amsterdam); W.K. Lagrand (AMC, Amsterdam); B.J. Bouma (AMC, Amsterdam); B.J. Mulder (AMC, Amsterdam/ICIN, Utrecht)

Purpose:

Cardiac surgery is commonly performed in congenital heart disease (CHD) patients but has major impact on exercise capacity. This impact could be reduced by improving peri-operative care. We determined the clinical characteristics associated with post-operative exercise capacity.

Methods:

This prospective study is part of our clinical trial on outcome after cardiac surgery in CHD patients. In all patients clinical characteristics, laboratory tests, echocardiography and surgical data were collected. All patients underwent cardiopulmonary exercise testing (CPET) 6 weeks after surgery. We investigated the association of pre-operative characteristics with the CPET using linear regression.

Results:

In total twenty-three patients were included (mean age 42±10 years, 57% male), of whom 35% (n=8) were in NYHA class 2 or more. The mean hemoglobin (Hb) level was 8.6±0.8 mmol/L. After cardiac surgery, CPET showed a mean VO₂ max value of 24±7 ml/kg/min. Independent predictors for reduced exercise capacity were pre-operative Hb level (̄ 3.5; 95%CI 0.5 - 6.5; p=0.03) and pre-operative NYHA classification (̄ -4.7; 95%CI -8.9 - -0.5; p=0.03). (See table 1)

Conclusion:

Hemoglobin level and NYHA classification are associated with better exercise capacity after cardiac surgery in patients with CHD. These findings suggest that these patients need more intensive peri-operative care.

	Univariate analysis				Multivariate analysis		
	Mean ± SD/n	̢	95% CI	p	̢	95% CI	p
Male (%)	13 (57)	-4.7	-10.3 - 0.8	0.092			
Age	42±10	-0.2	-0.5 - -0.1	0.200			
Hemoglobin mmol/L	8.6±0.8	3.9	0.6 - 7.2	0.023	3.5	0.5 - 6.5	0.026
NYHA classification	1.39±0.58	-0.5	-0.9 - -0.7	0.026	-4.7	-8.9 - -0.5	0.030
Systolic bloodpressure (mmHg)	125±19	-0.1	-0.3 - 0.1	0.211			
Diastolic bloodpressure (mmHg)	75±8	-0.2	-0.6 - 0.2	0.235			
Ejection fraction (%)	60±8	0.1	-0.6 - 0.8	0.767			

CHARACTERISTICS OF PERSISTENT SMOKERS AND QUITTERS AFTER AN ACUTE CORONARY SYNDROME : AN ANALYSIS FROM A RANDOMISED CLINICAL TRIAL IN THE NETHERLANDS

M. Snaatse (HvA/AMC, Amsterdam); M. Minneboo (AMC, Amsterdam); W.J.M. Scholte op Reimer (HvA/AMC, Amsterdam); R.J. Peters (AMC, Amsterdam)

Purpose:

To identify the characteristics of persistent smokers after an acute coronary syndrome, compared to patients who quit smoking

Methods:

We analysed data from RESPONSE, a multicenter randomised clinical trial. Patients (18-80 years) were included within 8 weeks after an acute coronary syndrome (ACS). As part of the main study patients were randomised to a nurse-coordinated prevention program in addition to usual care (intervention) or usual care alone. The intervention has had no effect on smoking cessation. For this analysis, we omitted the group assignment. Quitters are defined as smoker at time of hospitalization and stopped in the one-year follow-up. Persistent smokers kept smoking until one-year follow-up.

Results:

Information on smoking behaviour was available in 709 (96%) patients. 156 patients quit smoking in the year after the event, whereof 128 patients immediately after the event. 168 patients were persistent smokers despite the ACS event. More persistent smokers had a positive history in CVD and a BMI>25 compared to quitters (26% vs. 13% resp. 32% vs. 24%). More quitters have a higher education profile compared to persistent smokers (33% ver. 15%). After one year quitters increase in weight; more quitters had a BMI >25 than persistent smokers, although all patients gained weight.

Conclusion:

Persistent smokers have had more previously CVD than quitters. The majority of the quitters stops immediately after their ACS. Quitters gain more weight after smoking cessation and have a higher education level. Smokers continuing smoking despite serious warnings, which means that other strategies are needed to make them stop smoking.

Table 1: Characteristics of quitters compared to smokers.

Baseline characteristics	Quitters n=156		Persistent smokers n=168	
Positive History in CVD	19	(13%)	44	(26%)
College/University Education	49	(33%)	25	(15%)
Blood Pressure > 140 mmHg	36	(24%)	33	(20%)
LDL>2.5 mmol/L	46	(31%)	66	(39%)
BMI >25 kg/m2	35	(24%)	53	(32%)
Risk profile at 1 year				
Blood Pressure > 140 mmHg	41	(28%)	43	(26%)
LDL>2.5 mmol/L	32	(22%)	62	(37%)
BMI >25 kg/m2	127	(81%)	113	(67%)

PATIENT SELECTION FOR PRIMARY PREVENTION IMPLANTABLE CARDIOVERTER DEFIBRILLATOR THERAPY USING CARDIAC MAGNETIC RESONANCE IMAGING BASED LEFT VENTRICULAR EJECTION FRACTION ASSESSMENT

A.C.J. van der Lingen (VU University Medical Center, Amsterdam); M.T. Rijnijse (VU University Medical Center, Amsterdam); R. Nijveldt (VU University Medical Center, Amsterdam); A.M. Beek (VU University Medical Center, Amsterdam); A.C. van Rossum (VU University Medical Center, Amsterdam); C.P. Allaart (VU University Medical Center, Amsterdam)

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%.

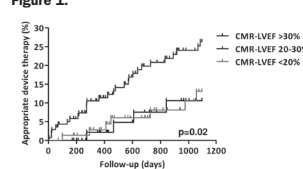
Results:

During 3 years follow-up, 16% of the total population received ADT and 8% died. Patients with LVEF<20% (n=74) had 10% ADT. However, mortality rate was higher compared with other subgroups (16%, p=0.01). In patients with LVEF>30% (n=52), event-rate was low (8% ADT and 4% mortality). Patients with LVEF 20-30% (n=139) experienced significantly more ADT (22%, p=0.02) compared with other subgroups (mortality rate 4%).

Conclusion:

Patients with CMR-LVEF of 20-30% were at highest risk for ADT, whereas patients with LVEF<20% were more likely to die. Patients with LVEF>30% had both a low ADT and mortality rate. These results suggest that CMR-LVEF assessment allows refined patient selection with highest benefit of ICD implantation in patients with CMR-LVEF 20-30%.

Figure 1:



Session II : Prognosis (continued)

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

J.T. Drost (Isala Klinieken, Zwolle); J.P.C. Grutters (Radboud Universitair Medisch centrum, Nijmegen); Y.T. van der Schouw (Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht); A.H.E.M. Maas (Radboud Universitair Medisch centrum, Nijmegen)

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 health care 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) QALY (11.7 days in good health quality). Total costs in the screening strategy were €7,748, whereas in the no screening strategy costs were €8,957, an expected saving of €1,209 (95% CI -3286; -190) per person.

Threshold analysis demonstrates that screening remains cost saving up to annual screening costs of €172 per year.

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.

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

Annelieke CMJ van Riel (AMC, Amsterdam; ICIN-NHI, Utrecht), Mark J Schuurink (AMC, Amsterdam), Anna Geke Algera (AMC, Amsterdam), Jeroen JA Rempt (AMC, Amsterdam), Arie PJ van Dijk (Radboud UMC, Nijmegen), Petronella G Pieper (UMCG, Groningen), Aeilko H Zwinderman (AMC, Amsterdam), Barbara JM Mulder (AMC, Amsterdam; ICIN-NHI, Utrecht), Berto J Bouma (AMC Amsterdam)

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:

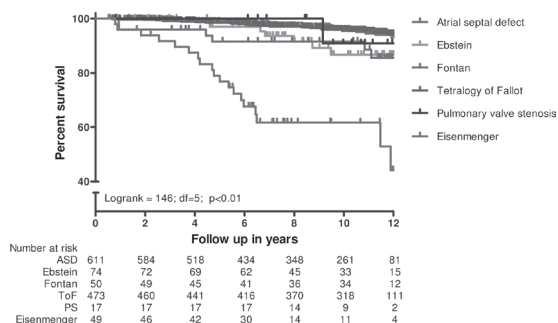
In total 1274 patients (27% of the total registered CHD population) with right-sided CHD were identified, with a mean age 32 years. Of these patients 77 died (6%, mean age 45 years), during a mean follow-up of 7.1 years. Systolic pulmonary arterial pressure (sPAP) measured by means of TTE (HR 1.02; p<0.01) and RV ejection fraction measured by CMR (HR 0.94; 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.



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

B.A. Couveiro Batista (LUMC, Leiden); P.V. Oemrawsingh (MCH, The Hague), S. Ghauharali (HagaZiekenhuis, The Hague)

Purpose:

Patients who had primary percutaneous coronary intervention (PCI) for ST-elevation 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 intra-aortic balloon pump, in-hospital coronary-artery-bypass-graft (CABG), in-hospital death and migration. MACE was defined as re-PCI, CABG, nonfatal acute-myocardial-infarction (AMI) and all-cause mortality.

Results:

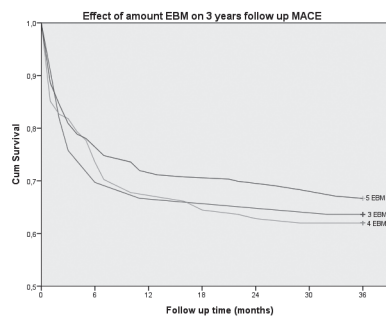
At hospital discharge, 33 patients were prescribed with 3 EBM, 121 patients with 4 EBM and 246 patients with 5 EBM. The group with 5 EBM showed a longer time to MACE at 3 years follow up (HR 1.14; 95%CI 0.64-2.01; p=0.66) compared to 3 EBM and compared to 4 EBM (HR 1.16; CI 0.81; p=0.42).

Conclusion:

This study shows a trend for better clinical outcome in older STEMI patients (= 65 years) who are discharged with 5 EBM after primary PCI for STEMI at 3 years follow-up when compared to 4 or 3 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.



Session III: Heart Failure

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

A. Ghanj (Isala Klinieken, Zwolle); P.P.H.M. Delnoy (Isala Klinieken, Zwolle); A. Adiyaman (Isala Klinieken, Zwolle); J.P. Ottervanger (Isala Klinieken, Zwolle); A.R. Ramdat Misier (Isala Klinieken, Zwolle); J.J. J. Smit (Isala Klinieken, Zwolle); A. Elvan (Isala Klinieken, Zwolle)

Purpose:

Septal rebound stretch (SRSsept) 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 SRSsept on response to CRT in a large population.

Methods:

A total of 138 consecutive patients with functional class II-IV heart failure who underwent CRT were studied. Echocardiography was performed at baseline and after a mean follow-up period of 22±8 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 cut-off value for SRSsept. Multivariable analyses were performed to adjust for potential confounders.

Results:

Mean age was 68±8 years (30% female). Mean baseline LV ejection fraction was 26±7%, 51% had ischemic etiology. Mean SRSsept was 4.4±3.2%, 56% of patients had SRSsept =4%. Ninety six patients (70%) were echocardiographic responders. Baseline SRSsept was significantly higher in responders compared to non-responders (5.1±3.2 vs 2.9±2.7, p<0.001). The optimal cut-off value for SRSsept was 4%. After univariate and multivariate regression analysis, baseline SRSsept >4% independently predicted the response to CRT (after adjustments OR 3.71, 95% CI 1.49-9.22, p=0.005).

Conclusions:

Baseline septal rebound stretch =4% is independently associated with response to CRT and may be helpful in identifying CRT responders.

DOES A LOW NT-PROBNP LEVEL AT ADMISSION FOR ACUTE DECOMPENSATED HEART FAILURE REPRESENT ABSENCE OF RISK FACTORS FOR MORTALITY?

M. Scheffer (AMC Amsterdam), C. Dickhoff (AMC Amsterdam), S. Stienen (AMC Amsterdam), Y.M. Pinto (AMC Amsterdam), WEM. Kok (AMC Amsterdam)

Purpose:

NT-proBNP levels at admission for ADHF are associated with short- and long-term prognosis in a concentration-dependent manner. It has been suggested that NT-proBNP might be used for the triage of patients presenting with ADHF in the Emergency Department, with high levels indicating admission and low levels possibly without need for admission. Our aim was to study the prevalence of other prognostically important risk factors in patients with different NT-proBNP levels at admission.

Methods:

Consecutive ADHF patients with an admission NT-proBNP > 1700 ng/L were asked to participate in this single-center study. Patients were divided in quartiles based on the level of NT-proBNP at admission (Group A (=4000), group B (>4001-6000), group C (6001-12999) and group D (=13000)). Next, we compared the clinical characteristics for these groups for the following independent risk factors: age = 75 years, sodium < 135 mmol/L, urea > 15 mmol/L, peripheral edema and a systolic blood pressure (SBP) = 115 mmHg. In addition, we investigated predictors for low risk in-hospital mortality (urea < 15 mmol/L and SBP > 115 mmHg).

Results:

A total number of 94 patients (50% male, age 75 (IQR 53 – 83)) was studied. Prognostically important risk factors were identified in every quartile of NT-proBNP, and no statistically significant differences between the groups with respect to these risk factors was observed. In the lower NT-proBNP group only 24% of patients demonstrated a low risk of in-hospital mortality.

Conclusion:

Prognostically important risk factors were identified in ADHF patients, which may be independent of NT-proBNP levels at admission. Future decision-making models for the triage of ADHF patients should not incorporate NT-proBNP levels alone.

Table 1

Risk factors for in-hospital mortality					
	Group 1 (NT-proBNP =4000)	Group 2 (NT-proBNP 4001-6000)	Group 3 (NT-proBNP 6001-12999)	Group 4 (NT-proBNP =13000)	p-value
Age = 75 years, n (%)	12 (52)	15 (68)	10 (44)	10 (44)	0.30
Sodium < 135 mmol/L, n (%)	5 (21)	4 (17)	7 (30)	7 (30)	0.63
Peripheral edema, n (%)	17 (77)	14 (58)	18 (86)	16 (76)	0.19
SBP = 115 mmHg, n (%)	8 (35)	5 (22)	8 (38)	6 (30)	0.64
Blood Urea Nitrogen = 15 mmol/L, n (%)	6 (43)	2 (13)	3 (19)	7 (41)	0.05
Low risk group for in-hospital mortality, n (%)	4 (24)	11 (46)	10 (56)	5 (31)	0.16

ARRHYTHMOGENIC CARDIOMYOPATHY IN A LARGE TRANSATLANTIC PATIENT COHORT

J. A. Groeneweg (University Medical Center Utrecht and ICIN-Netherlands Heart Institute, Utrecht, The Netherlands); A. Bhonsale (Johns Hopkins School of Medicine, Baltimore, Maryland); C. James (Johns Hopkins School of Medicine, Baltimore, Maryland); J.F. van der Heijden (University Medical Center Utrecht, Utrecht, The Netherlands); B. Murray (Johns Hopkins School of Medicine, Baltimore, Maryland); C. Tichnell (Johns Hopkins School of Medicine, Baltimore, Maryland); A.S. te Riele (Johns Hopkins School of Medicine, Baltimore, Maryland); A. Sawant (Johns Hopkins School of Medicine, Baltimore, Maryland); P.A. Doevendans (University Medical Center Utrecht, Utrecht, The Netherlands); J.D.H. Jongbloed (University Medical Center Groningen, Groningen, The Netherlands); H. Tandri (Johns Hopkins School of Medicine, Baltimore, Maryland); J.P. van Tintelen (University Medical Center Groningen, Groningen, The Netherlands); D.P. Judge (Johns Hopkins School of Medicine, Baltimore, Maryland); A.A.B. van Veen (University Medical Center Utrecht, Utrecht, The Netherlands); D. Dooijes (University Medical Center Utrecht, Utrecht, The Netherlands); A.A.M. Wilde (Academic Medical Center, Amsterdam, The Netherlands); R.N. Hauer (University Medical Center Utrecht and ICIN-Netherlands Heart Institute, Utrecht, The Netherlands); H. Calkins (Johns Hopkins School of Medicine, Baltimore, Maryland)

Purpose:

To study Arrhythmogenic Cardiomyopathy (AC) disease expression and genotype-phenotype correlation in a large transatlantic cohort.

Methods:

Clinical/genetic characteristics and follow-up of AC index patients fulfilling 2010 Task Force Criteria (n=395) and relatives (n=578) from US/Dutch registries were assessed (total 973 individuals, 408 families). In index patients *PKP2*, *DSP*, *JUP*, *DSG2*, *DSC2*, *TMEM43*, and *PLN* genes were screened. Familial AC was assessed in families with =2 screened individuals (n=212).

Results:

Genetic screening identified 171 (43%) *PKP2*, 11 (3%) *DSP*, 2 (0.5%) *JUP*, 17 (4%) *DSG2*, 5 (1%) *DSC2*, 1 *TMEM43*, 21 (5%) *PLN*, and 15 (4%) multiple mutations in index patients. In 39% no mutation was found. Index patients presented with sudden cardiac death (SCD, n=22)/aborted SCD (n=23) in 11%, symptoms in 333 (84%), and 17 (4%) asymptomatic. Relatives presented with SCD in 28 (5%), symptoms in 60 (10%), and 490 (85%) asymptomatic. AC was diagnosed in 179 (31%) relatives, including 21% (103/490) initially asymptomatic. Familial AC occurred in 54% (83/153) mutation positive vs. 34% (20/59) mutation negative families (p=0.008). Amongst 920 subjects presenting alive over a mean follow-up of 6 years, 30 (3%) died, 332 (36%) had sustained arrhythmias, 49 (5%) experienced heart failure, and 20 (2%) required transplantation. Index patients without mutations had enhanced sustained arrhythmia free survival compared to index patients with mutations (112 vs.189 events, p=0.002).

Conclusions:

Mutations (mostly *PKP2*) were identified in 61% of index patients. Follow-up was characterized by sustained ventricular arrhythmias, whereas heart failure/transplantation were less frequent. Genotype affects familial occurrence and sustained arrhythmia free survival.

TREATMENT OF PATIENTS WITH HER2NEU POSITIVE BREAST CANCER WITH CHEMOTHERAPY AND HER2NEU-RECEPTOR BLOCKING AGENTS: DETECTION OF CARDIOTOXICITY BY THE USE OF SERUM BIOMARKERS, 3D-ECHOCARDIOGRAPHY AND CARDIAC MRI

C. Liesting (Albert Schweitzer Hospital, Dordrecht); J.J. Brugts (Erasmus MC, Rotterdam); M.J.M. Koffard (Albert Schweitzer Hospital, Dordrecht); S. Sprangers (Albert Schweitzer Hospital, Dordrecht); M. Fouraux (Albert Schweitzer Hospital, Dordrecht); J.J.E.M. Kitzen (Albert Schweitzer Hospital, Dordrecht); H. Boersma (Erasmus MC, Rotterdam); M.D. Levin (Albert Schweitzer Hospital, Dordrecht)

Purpose:

Chemotherapy has proved to be a helpful and efficient modality of treatment in advanced malignant disease in both adjuvant and palliative settings. With the advent of monoclonal antibodies directed against tumor antigens newer strategies are explored to further improve remission and survival rates. As such, Trastuzumab has evolved as promising agent in the treatment of breast cancer over-expressing the human epidermal growth factor receptor 2 protein (HER2Neu). A well-known downside of chemotherapeutic agents has always been the increased incidence of cardiotoxicity.

Methods:

In this prospective single centre study, successive HER2Neu positive breast cancer patients starting with chemo-immunotherapy are included in the HERBAS study. Trastuzumab in combination with chemotherapy is prescribed in two different groups: early-stage and advantage-stage. Cardiac biomarkers are prospectively measured during treatment. In addition, systolic and diastolic function by 3D-echocardiography for the start and during treatment are assessed. The cardiac function and morphology will also be assessed by cardiac MRI before and after six months of treatment.

Results:

From January 2008 to December 2013 102 patients are prospectively included in the study. Overall 548 3D-echocardiographies are studied in combination with 618 cardiac biomarkers measurements. The correlations of cardiac biomarkers and outcome of 3D-echocardiographies are reported. In addition, the results of cardiac MRI before and during treatment with Her2Neu-receptor blocking agents will be presented.

Conclusions:

The predictive value of cardiac biomarkers in relation to 3D-echocardiographies and changes on MRI in breast cancer patients treated with HER2Neu-receptor blocking agents will be presented.

Session III: Heart Failure (continued)

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

J.A. Jansweijer (AMC, Amsterdam); K.Y. van Spaendonck-Zwarts (AMC, Amsterdam); J.P. van Tintelen (UMCG, Groningen); I. Christiaans (AMC, Amsterdam); M.J. van der Smagt (UMCU, Utrecht); A.M. Vermeer (AMC, Amsterdam); J.R. Gimeno (HUVA, Murcia); P. Garcia-Pavia (HUPH, Madrid); P. Charron (CHU Pitié-Salpêtrière, Paris); I. Olivetto (AOU Careggi, Firenze); A.A. Wilde (AMC, Amsterdam); Y.M. Pinto (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 arrhythmogenic right ventricular cardiomyopathy (ARVC), 4 with long QT syndrome type 1 or 2 (LQTS1 or 2), and 3 with LQTS3 or Brugada. To determine heritability (h^2), we compared correlation coefficients within monozygous twin pairs and control pairs (pathology-, age- and sex-matched sibling pairs and dizygous twin pairs) for quantitative traits ($h^2 = 2 \times (M2corr - Ccorr)$).

Results:

In DCM, we calculated a heritability of LVEF of 0.54, and of LVEDD of 0.524. In ARVC, heritability of LVEF was 0, of RVEF it was 0.858 and of LVEDD it was 0.644. In HCM, heritability of IVSd was 0. In LQTS1 and 2 heritability of QTc was 1. In LQTS3 and Brugada heritability of PQ was 0.158, of PR it was 0.256 and of QTc it was 1.

Conclusion:

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 (Erasmus Medisch Centrum, Rotterdam), M. Fouraux (Albert Schweitzer Ziekenhuis, Dordrecht), J. Bakker (Albert Schweitzer Ziekenhuis, Dordrecht), F.W.A. Verheugt (Radboudumc, Nijmegen), F.J. ten Cate (Erasmus Medisch Centrum, Rotterdam), M.A. Brouwer (Radboudumc, Nijmegen), M.J.M. Kofflard (Albert Schweitzer Ziekenhuis, Dordrecht)

Purpose:

Inadequate length-dependent activation with sarcomeric 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 94 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.

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

J.L. Bonnes, S.W. Westra, B.M. Govers, M.A. Brouwer, J.L.R.M. Smeets (Radboudumc, Nijmegen)

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 (IHD) and nonischemic heart disease (non-IHD).

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 992 days (IQR 402-1570), 25% (n=114) of patients received appropriate therapy; 16% (n=76) 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 IHD and non-IHD, two-year cumulative incidences of appropriate therapy split by age tertile are shown below. Inappropriate therapy occurred equally among the age tertiles, but was slightly more frequent in non-IHD.

Conclusion:

Whereas for non-IHD, the risk of appropriate therapy was similar across the age groups, in IHD 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.

	Age <58 yrs n=149	Age 58-68 yrs n=164	Age >68 yrs n=153	P-value
Ischemic heart disease				
Appropriate therapy	5%	32%	30%	<0.001
Appropriate shock	2%	23%	17%	0.002
Nonischemic heart disease				
Appropriate therapy	17%	18%	13%	0.824
Appropriate shock	9%	7%	11%	0.564

Session IV: Intervention

TRANSTHORACIC ECHOCARDIOGRAPHY FOR SELECTION OF GRAFT SIZE IN DAVID REIMPLANTATION TECHNIQUE

M.V. Regeer (Leids Universitair Medisch Centrum, Leiden); M.I.M. Versteegh (Leids Universitair Medisch Centrum, Leiden); R.J.M. Klautz (Leids Universitair Medisch Centrum, Leiden); M.J. Schallj (Leids Universitair Medisch Centrum, Leiden); J.J. Bax (Leids Universitair Medisch Centrum, Leiden); N. Ajmone Marsan (Leids Universitair Medisch Centrum, Leiden); V. Delgado (Leids Universitair Medisch Centrum, Leiden)

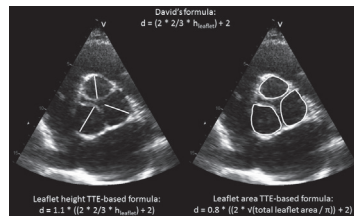
Purpose: It remains unclear whether a transthoracic echocardiography (TTE)-based formula may help in selecting the graft size during David reimplantation technique for aortic root dilation.

Methods: Forty-nine patients (47±11 years old, 84% men) who underwent David reimplantation technique 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, a respective 45%, 39% and 16% of patients 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%, 24% and 33% of patients 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 leaflet height and area TTE-based formulas 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.

Figure 1: Leaflet height and leaflet area TTE-based formulas. d: diameter, h^{leaflet}: leaflet height, TTE: Transthoracic echocardiography.



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. Nathoe (University Medical Center, Utrecht); Y. van der Graaf (University Medical Center, Utrecht); P.A. Doevendans (University Medical Center, Utrecht); Yolande Appelman (VU Universitair Medisch Centrum, Amsterdam)

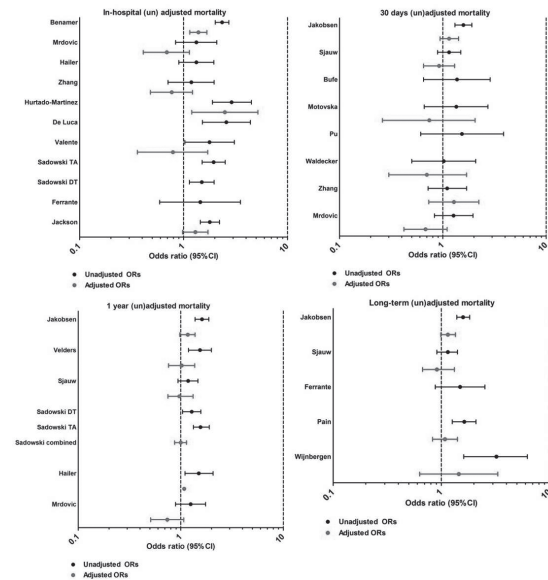
Purpose: Treatment of ST elevation myocardial infarction (STEMI) has improved enormously since the shift from thrombolysis to primary percutaneous coronary intervention (pPCI). It remains unclear whether differences in survival between women and men treated with STEMI treated with pPCI do exist. Secondly 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 21 out of 62 retrieved studies were included. At baseline, women were on average 7 years older, had more diabetes (? :24%/? :15%) and hypertension (? :58%/? :45%) and were less current smokers (? :30%/? :54%). The procedural characteristics were largely comparable except for a longer symptom-to-balloon-time (? :266 min/? : 240 min) and less use of GP IIb/IIIa inhibitors in women (? :51%/? : 57%). 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-year and long-term. All studies that published an odds or hazard ratio were included.



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

M. Liebrechts (St. Antonius Hospital, Nieuwegein); P.A. Vriesendorp (Erasmus Medical Center, Rotterdam); R.C. Steggerda (Martini Hospital, Groningen); A.F.L. Schinkel (Erasmus Medical Center, Rotterdam); R. Willems (University of Leuven, Leuven); F.J. ten Cate (Erasmus Medical Center, Rotterdam); J. van Cleemput (University of Leuven, Leuven); M. Michels (Erasmus Medical Center, Rotterdam); J.M. ten Berg (St. Antonius Hospital, Nieuwegein)

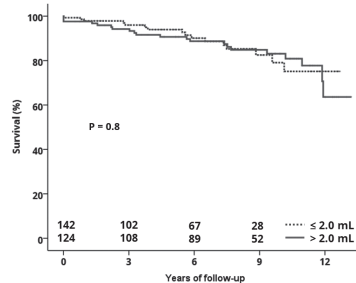
Purpose: The effect of intracoronary alcohol dosage during alcohol septal ablation (ASA) is surrounded by controversy. The aim of this study is to identify the role of alcohol dosage on mortality and adverse arrhythmic events in hypertrophic cardiomyopathy (HCM) patients treated with ASA.

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). Primary endpoints were all-cause mortality and arrhythmic events (including sudden cardiac death, resuscitated cardiac arrests, and appropriate internal converter defibrillator shocks).

Results: During 6.2 ± 3.6 years of follow-up, all-cause mortality was similar in patients who received = 2.0 ml (n=142) and > 2.0 ml (n=124) intracoronary alcohol during ASA (Figure 1). However arrhythmogenic 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: Although arrhythmic events are 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

L. Mann (LUMC, Leiden); S.F. Rodrigo (LUMC, Leiden); J. van Ramshorst (LUMC, Leiden); S.L. Beeres (LUMC, Leiden); J.J. Zwaginga (LUMC, Leiden); W.E. Fibbe (LUMC, Leiden); J.J. Bax (LUMC, Leiden); M.J. Schalij (LUMC, Leiden); D.E. Atsma (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 angina 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.

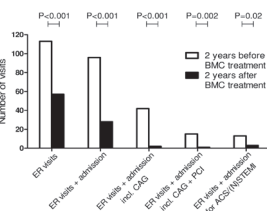
Results:

Healthcare utilization in 2 years after BMC treatment, compared to 2 years before, demonstrated a decrease of 50% in number of emergency room (ER) visits (11.3 vs. 57). Similarly, the number of ER visits with subsequent hospital admission had decreased by 71% (96 vs. 28), the number of coronary angiography 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 segments 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; CAG, coronary angiography; PCI, percutaneous coronary intervention; ACS/(N)STEMI, acute coronary syndrome/(non) ST-segment elevation myocardial infarction; BMC, bone marrow cell.

TAILORED CIRCULATORY INTERVENTION IN ADULTS WITH PULMONARY HYPERTENSION DUE TO CONGENITAL HEART DISEASE

L.E. Couperus (LUMC, Leiden); I.R. Henkens (LUMC, Leiden); H.W. Vliegen (LUMC, Leiden); M.G. Hazekamp (LUMC, Leiden); M.J. Schalij (LUMC, Leiden)

Purpose:

patients with congenital heart disease (CHD) and pulmonary hypertension (PH) often have residual shunts. Invasive intervention is aimed at optimizing pulmonary flow and ultimately prevention of RV failure. However, eligibility for such procedures is strongly dependent on the possible adaptation of pulmonary vasculature and right ventricle to circulatory changes. Guidelines are rather general and not sufficiently applicable to individual patients, who exhibit great diversity and complexity in cardiac anomalies and co-morbidity.

Methods:

We present four complex CHD-PH patients with an ambiguous indication for shunt adjustment. The first patient with a corrected Fallot's tetralogy developed right ventricular dilatation due to recanalization of a previously closed Potts anastomosis. The shunt was closed percutaneously through aortic stenting. The second patient had a congenitally corrected transposition of the great arteries and a monoventricular circulation. Severe tricuspid stenosis resulted in pulmonary venous congestion and inotropic dependence, for which an atrioseptostomy was performed. The other patients had a background of palliative surgery for pulmonary atresia and ventricular septum defect (VSD). The third patient underwent fenestrated VSD closure with peripheral pulmonary artery stenting. In the fourth patient an atrioseptostomy was performed to relieve right ventricular overload.

Results:

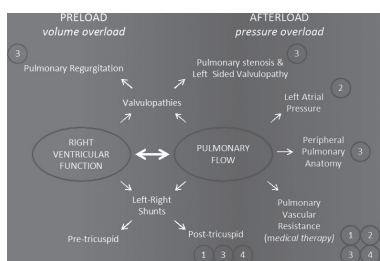
The combination of patient tailored pharmacological and invasive intervention resulted in a decline in pulmonary pressures and (temporarily) clinical improvement in all cases.

Conclusion:

our case series shows that patient tailored evaluation of disease characteristics is necessary to define appropriate treatment. Both strict registration of cases and multidisciplinary and multicentre collaboration are essential in the quest for optimal therapy.

Figure 1

Possible targets for invasive intervention to optimize pulmonary flow and prevent right ventricular failure in congenital heart disease patients with pulmonary hypertension, with categorization of patient 1-4.



ACUTE CHANGES IN MITRAL VALVE GEOMETRY AFTER MITRACLIP THERAPY: INSIGHTS FROM 3-DIMENSIONAL ECHOCARDIOGRAPHY

L. Al Amri (Leiden University Medical Centre, Leiden); P. Debonnaire (Leiden University Medical Centre, Leiden); F. van der Kley (Leiden University Medical Centre, Leiden); M.J. Schalij (Leiden University Medical Centre, Leiden); J.J. Bax (Leiden University Medical Centre, Leiden); N. Ajmone Marsan (Leiden University Medical Centre, Leiden); V. Delgado (Leiden University Medical Centre, Leiden)

Purpose:

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

Methods:

Three-dimensional transesophageal echocardiography performed prior to and immediately after percutaneous MV 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:

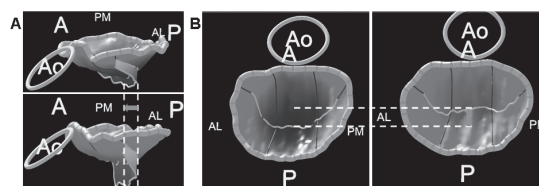
Procedural success (FMR reduction to = grade 2) was achieved in 18 (90%) patients. Overall antero-posterior and inter-commissural diameters, perimeter and area of the MV annulus did not significantly change after the procedure. Nonetheless, a post-procedural increase in anterior mitral leaflet angle (27±6° to 36±6°, p<0.001), decrease in exposed anterior leaflet length at the A2 level (27±5 mm to 25±5 mm, p=0.008) and an increase in the posterior P2 segment leaflet length (11±4 mm to 13±3 mm, p=0.04) without change in overall exposed mitral leaflet area (1451±374 mm² vs 1414±435 mm², p=0.54) indicated anterior relocation of the mitral leaflet coaptation point after MitraClip therapy. (Figure) In addition, coaptation area increased from 230±103 mm² to 303±84 mm² (p=0.004). Annular height-to-intercommissural-width ratio (18±5 % vs 17±6 %, p=0.39) and tenting volume (3.4±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 re-location of coaptation point (arrow) after (A lower panel and B right panel) versus pre (A upper panel and B left panel) percutaneous MitraClip therapy.



MITRAL REGURGITATION PRIOR TO TRANSCATHETER AORTIC VALVE REPLACEMENT IMPAIRS SURVIVAL

K. Boerlage-van Dijk (AMC, Amsterdam); E.M.A. Wiegerinck (AMC, Amsterdam); T. Takama (Saiseikai Yokohama City Eastern Hospital, Yokohama, Japan); K.T. Koch (AMC, Amsterdam); M.M. Vis (AMC, Amsterdam); B.A.J.M. De Mol (AMC, Amsterdam); J.J. Plek (AMC, Amsterdam); B.J. Bouma (AMC, Amsterdam); J. Baan Jr (AMC, Amsterdam)

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 375 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, 31% 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 (1-6 months) was not affected by baseline MR grade. Reduction of MR = 1 grade after TAVR occurred more often in patients with a ES implanted than in patients with a MC (ES: 33% vs MC: 17%, p=0.001). 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. 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

R.A. Vermond (University Medical Center Groningen, Groningen); A.H. Hobbelt (University Medical Center Groningen, Groningen); M. Rienstra (University Medical Center Groningen, Groningen); Yuri Blaauw (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 age (<60 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, old 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 (age <40 years) were compared to patients with AF onset at an age 40-60 years.

Results: Included were 446 patients, 97 (22%) < 40 years and 349 (78%) 40-60 years (Table). Mean age at AF onset was 46±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 11% 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.

	Total population (n=446)	AF onset <40 years (n=97, 22%)	AF onset 40-60 years (n=349, 78%)	P-value
Age of AF onset (years, mean±SD)	46±10	31±7	50±5	<0.001
Female sex - no.(%)	114 (26)	21 (22)	93 (27)	0.32
AF type - no.(%)				0.93
Paroxysmal	289 (65)	62 (64)	227 (65)	
Persistent	86 (19)	20 (21)	66 (19)	
Permanent	71 (16)	15 (15)	56 (16)	
Familial AF - no.(%)	119 (27)	29 (30)	90 (26)	0.42
Hypertension - no.(%)	227 (51)	29 (30)	198 (57)	<0.001
Vascular disease - no.(%)	123 (28)	20 (21)	103 (30)	0.08
Coronary artery disease - no.(%)	78 (17)	10 (10)	68 (19)	0.04
Percutaneous coronary Intervention - no.(%)	34 (8)	2 (2)	32 (9)	0.02
Diabetes mellitus - no.(%)	38 (9)	4 (4)	34 (10)	0.10
Heart failure - no.(%)	66 (15)	12 (12)	54 (15)	0.45
Body mass index >=30 kg/m ² - no.(%)	117 (26)	18 (19)	99 (28)	0.051
Excessive exercise - no.(%)	94 (21)	20 (21)	74 (21)	0.82
Number of comorbidities (mean±SD)	2.7±1.7	2.1±1.5	2.8±1.7	<0.001
Lone AF - no.(%)	19 (4)	11 (11)	8 (2)	<0.001
Left ventricular ejection fraction (%; median, range)	58 (13-76)	58(13-68)	58(15-76)	0.45
Left atrial volume index (ml/m ² ; median, range)	33 (14-97)	31 (14-97)	33 (14-84)	0.12

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

G.F.L. Kapel (LUMC, Leiden); F. Sacher (Bordeaux University Hospital, Bordeaux); AP. Wijnmaalen (LUMC, Leiden); JB. Thambo (Bordeaux University Hospital, Bordeaux); N. Derval (Bordeaux University Hospital, Bordeaux); M.J. Schalij (LUMC, Leiden); Z. Jalal (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) with documented SMVT (n=13) or considered at risk for VA underwent programmed stimulation (3 drive cycle length (CL), =3 extrastimuli, from =2 RV sites, isoproterenol) and electroanatomical substrate mapping (EAM). All identified anatomical isthmuses (AI) were evaluated for width, length and conduction velocity (CV); AI1:Tricuspid annulus (TA) and RVOT patch/scar, AI2: RV scar and pulmonary annulus (PA), AI3: PA and VSD-patch, AI4: VSD-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 (1.0 - 1.8) SMVT; VTCL 252 ms (231 - 312). The number of identified AI1, 2 and 3 was comparable for inducible and non-inducible (n=45) patients (see table). Inducible patients had significant narrower AI1 and 3, longer AI1, 2 and 3 and slower CV of AI1, 2 and 3. A critical SMVT reentry site was mapped to an AI in 24/27 patients. All AI containing reentry sites (n=28; AI1 8, AI2 2, AI3 17, AI4 1) had CV of <0.5 m/s (median CV of 0.34 m/s (0.29 - 0.39)). In contrast, 43/45 non-inducible patients had only AI with CV of =0.5m/s.

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

Table: Presence and properties of anatomical isthmuses according to patients with and without inducible sustained reentrant ventricular tachycardia (SMVT).

	SMVT non-inducible (n=45)	SMVT inducible (n=28)	p
Isthmus 1 (present)	39 (87%)	27 (96%)	0.113
Isthmus 1 width (mm)	43 ± 10	36 ± 11	0.007
Isthmus 1 length (mm)	12 ± 4	16 ± 7	0.021
Isthmus 1 CV (m/s)	1.00 (0.85 - 1.27)	0.76 (0.41 - 1.00)	0.001
Isthmus 2 (present)	11 (24%)	8 (29%)	0.615
Isthmus 2 width (mm)	30 ± 12	25 ± 11	0.344
Isthmus 2 length (mm)	13 ± 5	22 ± 7	0.011
Isthmus 2 CV (m/s)	0.89 (0.71 - 1.07)	0.47 (0.37 - 0.91)	0.033
Isthmus 3 (present)	37 (82%)	26 (93%)	0.122
Isthmus 3 width (mm)	26 ± 8	20 ± 6	0.008
Isthmus 3 length (mm)	16 ± 8	20 ± 7	0.027
Isthmus 3 CV (m/s)	0.70 (0.62 - 0.94)	0.31 (0.26 - 0.37)	<0.001
Isthmus 4 (present)	0 (0%)	4 (14%)	0.017
Isthmus 4 width (mm)		21 (14 - 23)	
Isthmus 4 length (mm)		14 (11 - 23)	
Isthmus 4 CV (m/s)		0.54 (0.20 - 1.42)	

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

N.L. Pijnenburg (VU University Medical Center, Amsterdam) M.J.B. Kemme (VU University Medical Center, Amsterdam), G.J.M. Tahapary (Medical Centrum Alkmaar, Alkmaar), C.P. Allaart (VU University Medical Center, Amsterdam)

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±8.4, 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 7.2gy*cm2 lower (37%). For further analysis, each PV pair circumference 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 (echo & CT) were found to be independent predictors for successful single round PVI. ROC curve analysis showed that minimum CF of 16g 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 16g and FTI of 400g*s.



Session V: Rhythm (continued)

FOLLOW-UP OF IDIOPATHIC VENTRICULAR FIBRILLATION (FU-IVF STUDY) – PRELIMINARY RESULTS

M. Visser (UMC Utrecht); C.E. Siegers (UMC Utrecht); P. Loh (UMC Utrecht); J.F. van der Heijden (UMC Utrecht); P.A. Doevendans (UMC Utrecht); R.J. Hassink (UMC Utrecht)

Purpose:

Idiopathic ventricular fibrillation (IVF) is the underlying cause in 5-10% of out-of-hospital cardiac arrest-patients. IVF 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 IVF-patients. Purpose of this study is to find alternative diagnoses, to determine prognosis and to improve follow-up of IVF-patients.

Methods:

This is a retrospective cross-sectional study, with 85 IVF-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, with 29/75 (39%) patients receiving appropriate shocks. Mean follow-up is 10 years, with a mortality of 12%. During follow-up 34% (29/85) of patients developed structural or electrical heart disease (e.g. arrhythmogenic cardiomyopathy, Brugada syndrome, long QT syndrome).

Conclusion:

These preliminary results show that a substantial amount of 'idiopathic' VF-patients had VF as the first symptom of underlying structural or electrical heart disease. The recurrence rate of VF is high, as is the case for mortality. These data emphasize the importance of meticulous follow-up of IVF-patients, to find diagnoses not previously known. This is important regarding right patient-treatment and family counselling.

EFFICACY AND SAFETY OF THE NEW ORAL ANTICOAGULANTS VERSUS THE VITAMIN K ANTAGONIST ACENOCOUMAROL IN "REAL WORLD" PATIENTS WITH ATRIAL FIBRILLATION.

J. Korenstra (Martini Hospital Groningen); C.A. Geluk (Martini Hospital, Groningen); J.L. Posma (Martini Hospital, Groningen); G.L. Bartels (Martini Hospital, Groningen); R.G. Tieleman (Martini Hospital, Groningen)

Purpose:

Randomized trials showed non-inferior or superior results of the new oral anticoagulants (NOACs) compared with warfarin. The aim of this study is to assess the efficacy and safety of NOACs versus acenocoumarol in patients with atrial fibrillation (AF) in daily clinical practice.

Methods:

In this retrospective study we evaluated all patients who started anticoagulation because of AF in our outpatient clinic from 2010 till 2012. In later years we preferably prescribed NOACs. Data were collected from the patient chart. Primary outcomes were stroke or systemic embolism and major bleeding, based on the definitions used in the RELY-study.

Results:

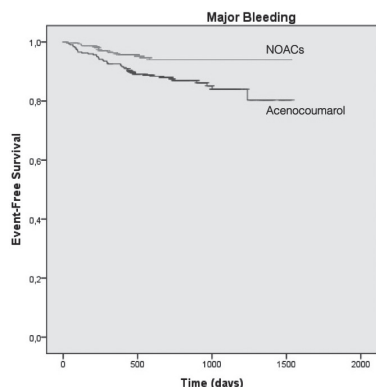
In total 326 patients started with acenocoumarol and 322 patients with a NOAC (dabigatran, rivaroxaban or apixaban). Mean follow-up duration was 2,3 ± 0,7 yr versus 1,5 ± 0,5 yr, respectively. Patients had similar baseline characteristics. The acenocoumarol patients had a mean calculated stroke risk according to the CHADS₂ score of 3,8%/yr versus 3,0%/yr in the NOAC patients. Both groups had a mean calculated bleeding risk according to the HASBLED score of 1,7%/yr. During follow-up major bleeding occurred significantly more frequent in the acenocoumarol patients compared with the NOAC patients (5,9%/yr versus 3,3%/yr, respectively, p<0.01, Figure 1). Stroke risk was 1,3%/yr in the acenocoumarol group and 0,8%/yr in de NOAC group (p=ns).

Conclusion:

In "real world" patients with AF, NOACs appear to be more safe and possibly more effective compared with acenocoumarol. The HASBLED score seemed to underestimate bleeding risk.

Figure 1

Kaplan Meier curves demonstrate a different event-free survival time between acenocoumarol and NOAC for major bleeding (log rank p=0.009).



PULMONARY VEIN ISOLATION WITH SECOND GENERATION CRYOBALLOON VERSUS RADIOFREQUENCY CATHETER ABLATION: A MATCHED GROUP COMPARISON

W.L. Beretty (University Medical Center Groningen, Groningen); Y. Blaauw (University Medical Center Groningen, Groningen); E.S. Tan (University Medical Center Groningen, Groningen); A.C.P. Wiesfeld (University Medical Center Groningen, Groningen); M. Rienstra (University Medical Center Groningen, Groningen); B.A. Mulder (University Medical Center Groningen, Groningen); I.C. van Gelder (University Medical Center Groningen, Groningen)

Purpose:

The second generation cryoballoon ablation (CRYO) has recently been introduced for pulmonary vein isolation (PVI) as treatment for atrial fibrillation (AF). We evaluated 6-month outcome for our first CRYO experience and compared this to radiofrequency catheter ablation (RF) treated patients.

Methods:

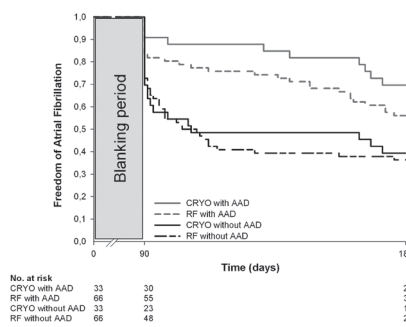
The first 33 patients who underwent CRYO ablation were retrospectively matched (1:2) with 66 patients who underwent RF. Freedom of AF was defined as no AF on Holter monitoring or electrocardiogram and no visit to emergency department for AF.

Results:

Baseline characteristics were not different between CRYO and RF. In all patients the current ablation was the first PVI. Mean age was 57±9years, and 79% were males. AF was paroxysmal in 77 (78%) and persistent in 22 (22%) patients. As compared with RF, the CRYO procedure time was shorter (147±37 vs. 200±43min, p<0.001), but fluoroscopy time longer (67±32 vs. 21±11min, P<0.001). Complications occurred in six (18%) CRYO and in four (6%) RF patients. Holter follow-up was complete in 99% of patients. Thirty-nine percent of the CRYO and 36% of the RF patients were free of AF without AAD (p=0.8). Success with AAD was observed in 70% of the CRYO group and in 56% of the RF group (p=0.3). In the CRYO group fluoroscopy time decreased with experience (76±31 vs. 56±33min, p=0.2, for respectively first vs. last 10 cases).

Conclusion:

The first experience with the cryoballoon for PVI resulted in comparable success rates as RF ablation and procedure time was significantly shorter.



POLYPHARMACY AND BLEEDING IN ATRIAL FIBRILLATION: A REAL-WORLD PROSPECTIVE COHORT STUDY ON PATIENTS USING VITAMIN-K ANTAGONISTS.

J. Jaspers Focks^{1,2}; M. Albers-Akkers²; R. Joustra¹; J. Bonnes¹; S. van Vugt¹; P. Groot-Eekhoff¹; L. Bloem-de Vries²; F. Verheugt¹; M. Brouwer¹
¹Radboud University Medical Centre, Nijmegen
²INR Trombosedienst Outpatient Anticoagulation Clinic Nijmegen, Nijmegen

Purpose:

Polypharmacy is associated with adverse clinical outcome and frailty. In view of this, physicians are often reluctant to prescribe vitamin-K antagonists (VKA) in patients with polypharmacy due to the fear of bleeding complications. However, it has never been thoroughly investigated whether polypharmacy is associated with bleeding in patients using VKA for stroke prevention in atrial fibrillation (AF).

Methods:

Patients with AF using VKA were contacted in May 2011 with questions regarding their medical history. During follow-up bleeding events were monitored. Clinically relevant bleeding comprised all bleedings of critical organs or leading to death, contact for medical aid, or dose adjustment of the VKA. Follow-up ended in August 2012. Patients were categorized in groups according to the number of concomitant drugs.

Results:

In total 2390 patients with medication data were included. The median age was 77 years (IQR 69-82) and the median CHA₂DS₂-VASc score was 4 (IQR 3-5). Patients with more drugs were older and comorbidities were more often present. During a mean follow-up of 1.2 years, overall 17% of the patients suffered from one or more bleeding events. When comparing the three groups, the proportion of patients with one or more bleeding events increased with the number of drugs taken concomitantly (Table).

Conclusions:

In this real-world cohort of AF patients using VKA, polypharmacy is associated with more bleeding events during follow-up. Moreover, polypharmacy was associated with an older age and the presence of more comorbidities. Perhaps the NOACs, with their better safety profile, could be an attractive alternative in these patients.

Number of patients with a bleeding event categorized by the number of drugs				
Patients with:	1-4 N=641	5-7 N=989	≥8 N=760	P-value
Minor bleeding	63 (9.8%)	116 (11.7%)	101 (13.3%)	0.13
Clinically relevant bleeding	34 (5.3%)	66 (6.7%)	59 (7.8%)	0.18
All bleeding	91 (14.2%)	161 (16.3%)	150 (19.7%)	0.018

Session VI: Surgery

SURGICAL TREATMENT OF ABERRANT AORTIC ORIGIN OF THE CORONARY ARTERIES

M. Kooij (Leids Universitair Medisch Centrum, Leiden); H.W. Vliegen (Leids Universitair Medisch Centrum, Leiden); M.A. de Graaf (Leids Universitair Medisch Centrum, Leiden); M.G. Hazekamp (Leids Universitair Medisch Centrum, Leiden)

Purpose:

Aberrant 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 slit-like coronary ostium. 20 had an intramural course of the proximal coronary artery. Median age at operation was 43 years. Twenty-one patients were symptomatic, 3 had myocardial infarction and 2 had been resuscitated before surgery. Diagnosis was by CT-angiography in all. Interarterial RCA repair consisted of unroofing of the coronary ostium (with/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 outpatient 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 show slight LV dysfunction. All other patients have recovered uneventfully and are asymptomatic.

Conclusions:

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

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

M. M. Mokhles (Erasmus MC, Rotterdam), S. Siregar (LUMC, Leiden), M. I. M. Versteegh (LUMC, Leiden), L. Noyez (UMCN, Nijmegen), B. van Putte (St. Antonius, Nieuwegein), A. B. A. Vonk (VUmc, Amsterdam), J. W. Roos-Hesselink (Erasmus MC, Rotterdam), A. J. J. C. Bogers (Erasmus MC, Rotterdam), J. J. M. Takkenberg (Erasmus MC, Rotterdam)*

*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=33140, 80.3%; OPCAB=6391, 15.5%) in the Netherlands between 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 critical preoperative state (5.0% vs. 4.1%, $p < 0.001$) and emergent surgery (8.4% vs. 6.2%, $p < 0.001$). Female patients were less likely to receive total arterial grafting (19.2% vs. 23.3%, $p < 0.001$) and received more often total venous grafting (5.8% vs. 4.1%, $p < 0.001$) or combination of both (74.9% vs. 72.5%, $p < 0.001$). In-hospital mortality was 1.4% (n=562) and higher in female patients (multivariate OR 1.71, 95%CI 1.33–2.12, $p < 0.001$). 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 resulted in p-values of < 0.001 for both males and females.

Conclusion:

Female patients undergoing CABG surgery present with higher logistic EuroSCORE I, receive less often total arterial grafting and have a higher risk of 30 day mortality as compared to male patients. There appears to be room for improvement of outcome in female patients by increased utilization of arterial grafts. The performance of the logistic EuroSCORE I indicates the need for the development of gender specific risk stratification models.

BENEFICIAL EFFECTS OF AORTIC VALVE REPLACEMENT ON MYOCARDIAL EFFICIENCY IN AORTIC VALVE STENOSIS PATIENTS – A PET AND CMR STUDY

A. Guclu (VUmc, Amsterdam); P. Knaepen (VUmc, Amsterdam); H.J. Harms (VUmc, Amsterdam); A.A. Lammertsma (VUmc, Amsterdam); A.C. van Rossum (VUmc, Amsterdam); J. van der Velden (VUmc, Amsterdam); T. Germans (VUmc, Amsterdam)

Purpose:

Aortic valve stenosis (AVS) is characterized by pressure overload hypertrophy of the left ventricle (LVH). The mechano-energetic effects of AVS-induced LVH leading to heart failure are unresolved. The present study was conducted to investigate myocardial external efficiency (MEE) - the ratio between external work and myocardial oxygen consumption (MVO²) - in AVS patients and to assess the effect of aortic valve replacement (AVR) on MEE. AVR-induced changes in MEE were correlated with exercise parameters.

Methods:

Ten AVS patients were included (normal coronary arteries, mean age 62±10 years, 7 male). Echocardiography was performed prior to AVR and repeated after 4 months to assess peak aortic valve gradients. Changes in LV mass (LVM) and volumes were assessed by cardiovascular magnetic resonance (CMR) imaging and external work was calculated. Additionally, [¹³C]-acetate positron emission tomography (PET) was performed to obtain MVO². Next, MEE was calculated and compared with 14 healthy controls (mean age 48±11 years, 9 male).

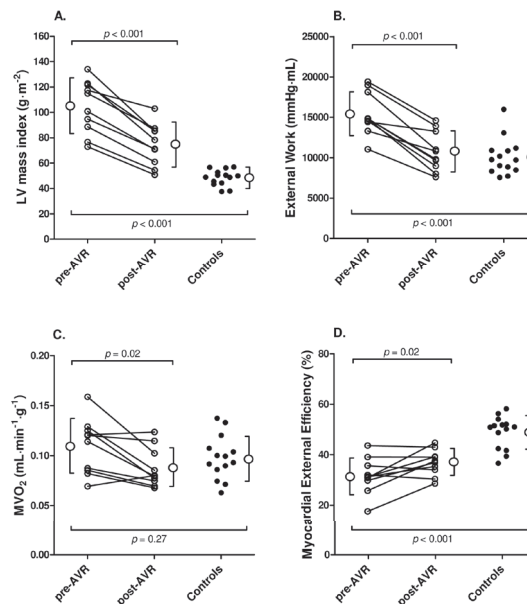
Results:

Four months after AVR, peak aortic valve gradient decreased from 88±20 to 24±12 mmHg, ($p < 0.001$), as well as LVM index from 104±21 to 75±16 g·m² ($p < 0.001$). MVO² significantly decreased from 0.11±0.03 to 0.09±0.02 mL·min⁻¹·g⁻¹, ($p = 0.02$), which was comparable to the MVO² observed in controls (0.10±0.02 mL·min⁻¹·g⁻¹). In addition, cardiac work significantly decreased from 15439±2631 to 10774±2446 mmHg·mL, ($p < 0.001$), reaching similar values as in controls (10117±2268 mmHg·mL). Consequently, AVR resulted in a significant improvement in MEE from 32±7 to 37±5 %, ($p = 0.02$), see figure 1. A significant correlation was found between absolute changes in MEE (ΔMEE) with absolute changes in exercise work (ΔWork) and absolute changes in peak VVO² (Δpeak VVO²).

Conclusion:

At 4 months follow-up, the detrimental effects of AVS are partially reversed by AVR in patients with normal coronary arteries and preserved ejection fraction, evident from regression of LV hypertrophy and improvement of MEE.

Figure 1: Scatter plots depicting LV mass index (A), external work (B), myocardial oxygen consumption (C), and myocardial external efficiency (D) values for pre-AVR, post-AVR and control patients. Data are presented as mean ± standard deviation of the mean.



INCIDENCE, CLINICAL CONSEQUENCES AND RISK FACTORS OF DELIRIUM AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION (TAVI)

K. van der Wulp (Jeroen Bosch Ziekenhuis, 's Hertogenbosch), Yvonne Schoon (Radboud UMC, Nijmegen), Michel W.A. Verkroost (Radboud UMC, Nijmegen), Helmut R. Gehlmann (Radboud UMC, Nijmegen), M.H. van Wely (Radboud UMC, Nijmegen), Luc J.B.M.L. Noyez (Radboud UMC, Nijmegen), Henry A. van Swieten (Radboud UMC, Nijmegen), Harry Suryapranata (Radboud UMC, Nijmegen), Menko Jan de Boer (Radboud UMC, Nijmegen), Peter C. Kievit (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 perioperative clinical screening, age was the only independent predictor of delirium.

Conclusion:

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); H.M. Nathoe (University Medical Centre, Utrecht); J.M. Dieleman (University Medical Centre, Utrecht); M.J. ten Berg (University Medical Centre, Utrecht); J. Kluin (University Medical Centre, Utrecht); D. van Dijk (University Medical Centre, Utrecht)

Purpose:

Postoperative new-onset atrial fibrillation (PNAF) is the most common 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 consequent 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 Dexamethasone for Cardiac Surgery-PNAF trial (DECS-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.

Results:

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 ($P=0.01$). 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.
Surgery analysed versus the control group, i.e. CABG.
† valve surgery included aortic and/or mitral valve surgery.

Characteristic/Variable	Odds ratio	95% Confidence Interval	P-value
Age	1.051	1.034-1.068	<0.001
CABG plus Valve, #	2.946	1.781-4.873	<0.001
Single Valve, #, †	3.086	2.032-4.687	<0.001
Multiple Valve, #, †	1.886	0.487-7.309	0.359
WBC, preoperatively	1.043	0.963-1.130	0.302
WBC, Day 1	1.026	0.976-1.078	0.311
WBC, Day 2	1.034	0.992-1.078	0.110
WBC, Day 3	1.030	0.960-1.106	0.412
WBC, Day 4	1.085	1.013-1.161	0.020

A DOUBLE BARRELED MYXOMA

M. Kuindersma (Slingeland Ziekenhuis, Doetinchem), E.O.F. van Gorselen (Slingeland Ziekenhuis, Doetinchem), F.Z. Ramjankhan (Universitair Medisch Centrum, Utrecht), W.F. Terstra (Slingeland Ziekenhuis, Doetinchem)

Case-presentation:

A 28-years old female patient was presented to our emergency department/ward with neurological deficits caused by multiple cerebral infarctions in both cerebral hemispheres. Besides neurological deficits, a tumour pel was found. ECG showed sinus rhythm and laboratory findings were normal.

Medical imaging:

Additional transthoracic cardiac ultrasound revealed two large masses in both atria, adherent to tricuspid and mitral valve (fig 1). With a clinical diagnosis of biatrial myxoma, patient was referred for thoracic surgery.

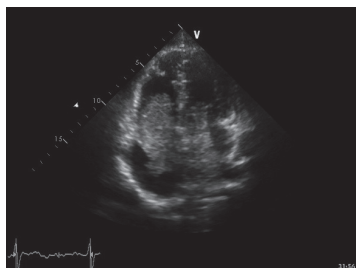
Treatment:

A resection of both masses was performed, leaving behind a large intra-atrial septal defect. The procedure was combined with a Goretex patch to reconstruct the intra-atrial septal defect. Pathology report confirmed the diagnosis of biatrial 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 congenital multipotent mesenchyme, and can arise in any of the cardiac chambers with 75-80% in the left atrium. Bi-atrial 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 bi-atrial myxoma. Treatment consists out of surgical resection, often combined with intra-atrial septal defect reconstruction.

[apical 4 chamber view with giant biatrial myxoma]



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

B. Maesen (Maastricht University Medical Center, Maastricht); C. Afonso (Oxford University, Oxford); S. Zeemering (Maastricht University Medical Center, Maastricht); R. Burton (Oxford University, Oxford); J. Eckstein (University Hospital Basel, Basel); A. van Hunnik (Maastricht University Medical Center, Maastricht); D. Stuckey (Imperial College, London); D. Tyler (Oxford University, Oxford); J.G. Maessen (Maastricht University Medical Center, Maastricht); V. Grau (Oxford University, Oxford); S. Verheule (Maastricht University Medical Center, Maastricht); P. Kohl (Imperial College, London); U. Schotten (Maastricht University Medical Center, Maastricht)

Purpose:

Progression of atrial fibrillation (AF) is caused by electrical and structural remodeling. Fibrosis and altered connexin expression are known alterations in atrial tissue structure contributing to the development of an AF substrate. 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 (AFCL) and number of fibrillation waves per second (waves/s) were quantified. Mapped tissue regions were excised and reconstructed by high-resolution MRI (voxel size [78x78x78] μm^3), allowing myocardial fat quantification within the atrial wall using a Fatty Infiltration Score (FIS, quantification of proportion fat per electrode grid).

Results:

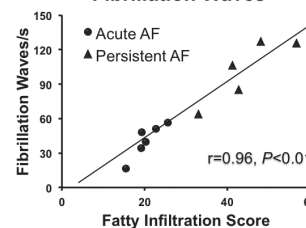
AFCL(ms) was shorter in persAF than in aAF (103 ± 20 vs. 127 ± 15 , $P<0.05$) and waves/s were higher in persAF than in aAF (102 ± 27 vs. 41 ± 14 , $P<0.01$).

The degree of fatty infiltration was much higher in persAF than aAF (FIS= 44.3 ± 8.7 vs. FIS= 20.4 ± 3.5 , $P<0.01$). Waves/s correlated well with fatty infiltration across (bivariate $r=0.96$, $P<0.01$; see Figure) & corrected for the 2 groups (partial $r=0.87$, $P<0.01$). AFCL correlated inversely with fatty infiltration ($r=-0.81$, $P<0.01$).

Conclusion:

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

Correlation between Fatty Infiltration and Number of Fibrillation Waves



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

F.R. Halfwerk (Thorax Centrum Twente, Enschede); F. Damanik (University of Twente); J. Rouwkema (University of Twente, Enschede); L. Moroni (University of Twente, Enschede); R. Siddappa (EMCM, Nijmegen); J.G. Grandjean (Thorax Centrum Twente, Enschede)

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 tissue was characterised by histological, and biomechanical analysis, *in vitro* biocompatibility, and Scanning Electron Microscopy (SEM). Human Umbilical Vein Endothelial Cells (HUVECs) were cultured on both the fibrous, and serous parietal pericardium.

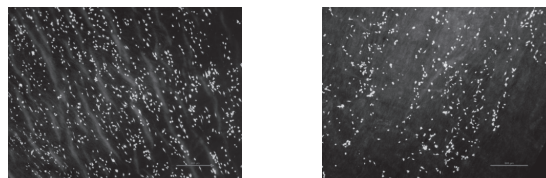
Results:

Preliminary results indicate tissue histo-architecture preservation, and maintenance of mechanical integrity. *In vitro* results showed a recellularisation of HUVECs in the pericardium, with a preference for the serous pericardium. SEM imaging identified only a minimally disorganised extracellular matrix structure.

Conclusion:

Pericardium, decellularised with supercritical carbon dioxide, is a novel biomaterial without intensive treatment of chemicals, and is able to function as a graft for recellularisation. These findings have to be confirmed in further research, with also identifying the best origin of pericardium, followed by *in vivo* experiments. Ultimately, using decellularised supercritical carbon dioxide pericardium in cardio-thoracic surgery can, among other things, improve the long-term outcomes in open heart surgery.

Figure 1. Non-fluorescent Calcein AM is converted into fluorescent Calcein (green) in living cells, showing a preferred orientation in line with pre-existing collagen fibres (red). Left image: serous pericardium, right: fibrous pericardium. Scale bar is 100 μm .



Session VII: Experimental/ACS

IMPAIRED FUNCTION OF THE SINO-ATRIAL NODE IN A VEGF OVER-EXPRESSION MODEL

E.E. Calkoen (LUMC, Leiden), R. Vicente-Steijn(LUMC, Leiden), N.D. Hahurij (LUMC, Leiden), C. van Munsteren (LUMC, Leiden), A.C. Gittenberger-de Groot(LUMC, Leiden), N.A. Blom(LUMC, Leiden), M.C. de Ruiter (LUMC, Leiden), A.A. Roest (LUMC, Leiden), M.R.M. Jongbloed (LUMC, Leiden)

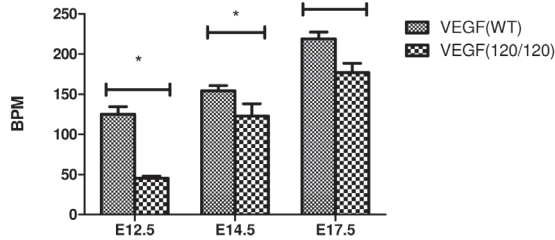
Purpose: Mutations in Vascular Endothelial Growth Factor-A (VEGF) are associated with congenital heart defects. VEGF120/120 mice over express VEGF. In the current study we aimed to assess the effect of VEGF over-expression on the sino-atrial node (SAN).

Methods: Heart rate (HR) was assessed in VEGF120/120 and wildtype (WT) embryos with high frequency ultrasound in sedated (Isoflurane 1.5%) VEGF+/120 pregnant mice under stable vital parameters at embryonic day (E)12.5, 14.5 and 17.5 and by optical mapping at E12.5. The morphology was studied using antibodies for troponinI, Nkx2.5, HCN4, Cx40, Cx43, NCAM and TH. SAN volume measurements were performed and quantitative PCR was used to assess HCN1, HCN4, TBX3, TBX5, Cx40, Cx43 expression in the SAN.

Results: The blindly measured mean heart rate during fetal echocardiography was significantly lower in VEGF120/120 embryos compared to WT controls (figure1). 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 autonomic innervation were observed. Preliminary qPCR data show differences in levels of pacemaker genes in the SAN of VEGF 120/120 mutant embryos compared to WT.

Conclusion: Over-expression of VEGF results in an abnormal function of the SAN, possibly due to the effect of the VEGF/notch pathway on pacemaker genes.

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.



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

P.F. Teunissen (VUmc, Amsterdam), G.A. de Waard (VUmc, Amsterdam), M.R. Hollander (VUmc, Amsterdam), L.F. Robbers (VUmc, Amsterdam), I. Danad (VUmc, Amsterdam), M.W. Heymans (VUmc, Amsterdam), R.P. Amier (VUmc, Amsterdam), P.S. Biesbroek (VUmc, Amsterdam), A.A. Lammertsma (VUmc, Amsterdam), C.P. Allaart (VUmc, Amsterdam), J.S. Lemkes (VUmc, Amsterdam), Y.E. Appelman (VUmc, Amsterdam), K.M. Marques (VUmc, Amsterdam), J.G. Bronzwaer (VUmc, Amsterdam), A.J. Horrevoets (VUmc, Amsterdam), A.C. van Rossum (VUmc, Amsterdam), A.M. Beek (VUmc, Amsterdam), P. Knaapen (VUmc, Amsterdam), N. van Royen (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 these patients myocardial perfusion does 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 (MVI) at cardiovascular magnetic resonance (CMR) and to reduced myocardial perfusion at positron 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, MVI was defined as a subendocardial recess of myocardium with low signal intensity within the gadolinium-enhanced area. To discriminate between normal and 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 MVI and 27 did not. The mean HMR in the culprit artery was 3.00±1.41. HMR in the culprit artery in patients with MVI was significantly higher than in patients without MVI (MVI: 3.64 ± 1.57 vs. no MVI: 2.53 ± 1.03, p=0.02). Multivariable analysis showed that HMR was predictive for MVI. High HMR also correlated to decreased myocardial blood flow (MBF) on PET (CFR<2.0: 3.66±1.42 vs. CFR=2.0: 2.52±0.94; p=0.02).

Conclusion: Elevated Doppler-flow-derived HMR correlates to CMR-defined MVI 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?

T.P. Kelder (LUMC, Leiden); R. Vicente-Steijn (LUMC, Leiden); M.C. de Ruiter (LUMC, Leiden); M.J. Schalij (LUMC, Leiden); R.E. Poelmann (LUMC, Leiden); A.C. Gittenberger-de Groot (LUMC, Leiden); M.R.M. Jongbloed (LUMC, Leiden)

Purpose: The most common form of supraventricular tachycardia in adults is atrioventricular nodal re-entry tachycardia, which is caused by the presence of anatomically 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 ovo* 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+/cTnI+ sinus venosus myocardium was labelled by injecting a solution of fluorescent dyes (Dil/5-TAMRA, Invitrogen) after 2.5 days of development using a microinjector (IM-300 Narishige). Embryos were harvested and analyzed after 24 and 48 hours of reincubation.

Results: After labelling of the sinus venosus myocardium, cells could be traced to an Isl-1+/cTnI+ bridge of tissue between the sinus venosus and AV canal myocardium, which was termed the SV-AVC bridge. This bridge showed expression of HCN4, indicating a role in CCS development. In murine embryos the SV-AVC could also be identified and Isl-1, cTnI and HCN4 co-localized in this tissue.

Conclusion: We describe an Isl-1+/cTnI+/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.

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

R.S. Hermanides, S. Kilic, J.P. Ottervanger, J.H. Dambrink, A.T.M. Gosselink, E. Kolkman, V. Roelvink, E. Kedhi, A.W.J. van 't Hof, (Isala, Zwolle)

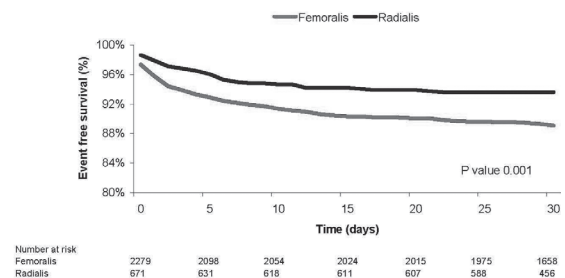
Purpose: Trials have suggested that radial access for percutaneous coronary intervention (PCI) reduces vascular complications and bleeding compared with femoral access. Aim of this study was to assess the efficacy and safety of radial access versus femoral access in patients (pts) with acute coronary syndromes (ACS) who underwent coronary angiography with possible intervention.

Methods: This is a single-centre, large, prospective observational registration of all STEMI and NSTEMI pts who underwent coronary angiography and/or (primary) PCI in the period January 2010 – December 2012. Primary endpoint was 30-day non CABG-related major and minor bleeding. All safety- and clinical parameters, including bleeding were performed by 2 independent investigators.

Results: 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 (89%) and in 671/2950 (23%) pts 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 STEMI: 54.6% vs 60.0%, p=0.011, IABP 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), especially in the subgroup of pts with a moderate, high or very high CRUSADE bleeding score (1.8% vs 8.3%, p=0.014, p value for interaction 0.195). 30-day mortality was significantly lower in the radial group as compared to the femoral group (1.7% vs 4.8%, p<0.014). After multivariate correction, radial access remained an independent predictor for the primary endpoint (HR 0.397; 95% CI, 0.158 – 0.999, p=0.050, as well as for 30-day mortality (HR 0.247; 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 SONOTROMBOLYSIS IN WHOLE BLOOD FOR MYOCARDIAL NO-REFLOW

S.T. Roos (VUmc, Amsterdam) (ICIN, Utrecht); F.T. Yu (Center for Ultrasound Molecular Imaging and Therapeutics, Pittsburgh); X. Chen (Center for Ultrasound Molecular Imaging and Therapeutics, Pittsburgh); O. Kamp (VUmc, Amsterdam) (ICIN, Utrecht); J.J. Pacella (Center for Ultrasound Molecular Imaging and Therapeutics, Pittsburgh); F.S. Villanueva (Center for Ultrasound Molecular Imaging and Therapeutics, Pittsburgh)

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 thrombi. This negatively influences clinical outcomes. We tested the hypothesis that ultrasound (US) mediated microbubble (MB) destruction can achieve microvascular clot lysis in our *in vitro* MVO model.⁽¹⁾

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 were injected into the blood filled system, increasing upstream pressure, measured with an upstream fluid filled transducer. Partially degassed bovine whole blood and lipid MBs (2x10⁶ MB/ml) were infused at 0.75ml/min. US was delivered at 1 MHz with a variable pulse length and peak-to-peak pressure of 1.5MPa. US was applied for 20 minutes during continuous pressure monitoring, in pulses every 3 seconds to allow MB replenishment between pulses. Control experiments utilized no MB, no US or saline as the perfusate. Experimental manipulations included the addition of tPA to the blood perfusate during US and MB delivery.

Results:

After 20 minutes of treatment, the pressure drop with 3000 cycles pulse length (58 ± 14 %) was higher than with 1000 cycles (34 ± 22 %) (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 (60 ± 15 %) (p=0.004) reaching the same effect as with PBS perfusate (92 ± 6 %) (p=0.678). (Fig1).

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 US and MB may be needed to achieve optimal reperfusion.

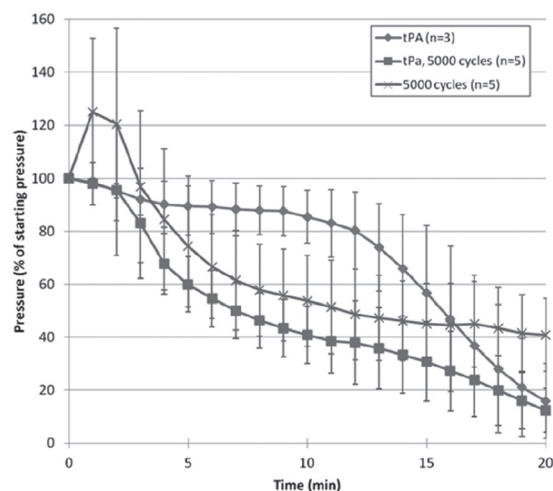


Figure Lytic effect (mean±SD) improved significantly between treatment with 5000 cycles and 5000 cycles + tPA (p<0.001, ANOVA). At 10 minutes of therapy, a statistically significant difference was observed in favor of treatment with tPA + 5000 cycles compared to tPA alone (p=0.006, ANOVA). n=3 for all samples.

Reference:

1. Leeman JE, Kim JS, Yu FT, Chen X, Kim K, Wang J, Chen X, Villanueva FS, Pacella JJ. Effect of acoustic conditions on microbubble-mediated microvascular sonothrombolysis. *Ultrasound Med Biol* 2012;**38**(9):1589-1598.

FFR AND IFR HAVE AN EQUIVALENT DIAGNOSTIC ACCURACY WHEN COMPARED TO MYOCARDIAL BLOOD FLOW QUANTIFIED BY [15O]H2O PET PERFUSION IMAGING

Guus de Waard VUMC Amsterdam (presenting author); Ibrahim Danad VUMC Amsterdam; Ricardo Petracco Imperial College London; Paul Teunissen VUMC Amsterdam; Alexander Nap VUMC Amsterdam; Maarten van Leeuwen VUMC Amsterdam; Pieter Rajmakers VUMC Amsterdam; Adriaan Lammertsma VUMC Amsterdam; Justin Davies Imperial College London; Koen Marques VUMC Amsterdam; Paul Knaapen VUMC Amsterdam; Niels van Royen VUMC Amsterdam

Purpose:

Revascularization of intermediate coronary artery stenosis guided by the fractional flow reserve (FFR) improves clinical outcomes and is recommended by clinical guidelines. Recently, it has been proposed that physiological lesion assessment during resting conditions might render an equivalent diagnostic accuracy. This study evaluated the performance of the established FFR, and baseline instantaneous wave-free ratio (iFR) in comparison to the non-invasive established reference standard for quantification of myocardial perfusion; [¹⁵O]H₂O positron emission tomography (PET) imaging.

Methods:

This study included 49 intermediate coronary stenoses (=40% diameter) in patients with suspected coronary artery disease who were scheduled for coronary angiography. [¹⁵O]H₂O PET perfusion imaging and intracoronary pressure measurements were obtained both under basal and during hyperemic conditions (induced by adenosine administration). FFR and iFR were computed and the diagnostic performance of each pressure index was compared to hyperemic myocardial blood flow (MBF) quantified by PET perfusion imaging. Cut-off values were predefined: 2.3 mL·min⁻¹·g⁻¹ for PET MBF, 0.80 for FFR and 0.90 for iFR.

Results:

Median stenosis diameter was 62% [IQR 50 - 75%]. Classification agreement with PET was 76% for FFR and 76% for iFR. Diagnostic agreement as expressed by area under the receiver operator curve was similar for both physiological indices: 0.85 for FFR and 0.86 for iFR (p=0.71).

Conclusion:

FFR and iFR have an equivalent diagnostic accuracy for the assessment of intermediate stenoses when compared to [¹⁵O]H₂O PET perfusion imaging.

PARASYMPATHOMIMETIC STIMULATION PROVOKES VAGALLY MEDIATED PREMATURE VENTRICULAR CONTRACTIONS DURING ELECTROPHYSIOLOGIC STUDY AND ABLATION

W. Kassenberg (University Medical Center, Utrecht); J. van der Heijden (University Medical Center, Utrecht); R. Hassink (University Medical Center, Utrecht); P. Doevendans (University Medical Center, Utrecht); P. Loh (University Medical Center, Utrecht)

Purpose:

During electrophysiologic study (EPS) and radiofrequency (RF) ablation of mainly vagally mediated, symptomatic premature ventricular contractions (PVC), ectopy may be absent due to stress induced sympathetic stimulation or sedative drugs. We hypothesized that pharmacological stimulation of the parasympathetic nervous system may provoke PVC's.

Methods and results:

We included three female patients with frequent symptomatic PVC's with left bundle branch block morphology and vertical axis, compatible with right ventricular outflow tract (RVOT) origin. Previous RF ablation attempts failed because PVC's were absent and could not be provoked by sympathetic stimulation (isoprenaline), atropine, adenosine, esmolol or sedation. Procedures were conducted under general anaesthesia (n=2) and Propofol sedation (n=1). A parasympathomimetic drug (Neostigmine, 1 mg) was administered intravenously (iv). After 7-15 minutes clinical PVC's appeared and enabled successful ablation in all 3 patients.

Earliest activation during mapping was found postero-lateral, septal and anterior in the RVOT in the three patients respectively. Early signals were found up to 40ms before QRS.

Post ablation provocation with Neostigmine was done in two patients. No PVC's were induced. One patient received the maximum dose pre ablation. All procedures were free of complications.

Follow up of 3, 4 and 21 months in 3 patients respectively showed no recurrence of clinical ectopic contractions on 24 hours Holter monitoring.

Conclusion:

In electrophysiological study and ablation procedures where mainly vagally mediated PVC's are non-inducible due to sympathetic stimulation (stress) and/or sedative drugs, stimulation of the parasympathetic nervous system with Neostigmine provokes ventricular ectopy and enables activation mapping and ablation.

Figure Surface ECG recording lead III during EPS: administration of 1mg Neostigmine and induction of frequent clinical PVC's



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

M.J.P. van Hout (VU university medical center, Amsterdam); G. de Waard(VU university medical center, Amsterdam); P.S. Blesbroek(VU university medical center, Amsterdam); S. Roos(VU university medical center, Amsterdam); P. Teunissen(VU university medical center, Amsterdam); K. Marques(VU university medical center, Amsterdam); P. Knaapen(VU university medical center, Amsterdam); N. van Royen(VU university medical center, Amsterdam)

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 the present study, we validate this algorithm by comparing it to intracoronary 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.

