

## SESSIE 1: Coronary heart disease & risk prediction

	7	
	Zaal 1/2	Voorzitters:
		prof. dr. Michiel Voskuil, cardioloog UMC Utrecht
		dr. Ruben Tijssen, AIOS St. Antonius Ziekenhuis
1	09.00 - 09.10	Impact of Apolipoprotein A-I Infusions on Cardiovascular Events
		After Acute Myocardial Infarction-MI by Neutrophil-Lymphocyte
		Ratio and LDL-Cholesterol Levels
		Sem A.O.F. Rikken St. Antonius Ziekenhuis, Nieuwegein; CARIM,
		Maastricht; Baim Institute for Clinical Research, Boston)
2	09.11 - 09.21	Medication Adherence After Myocardial Infarction: Patients'
		Insights from a Qualitative Interview Study
		Eline R.Harding (Diakonessenhuis, Utrecht)
3	09.22 - 09.32	Sex Differences in Cardiac Structure and Function Following
		First-Time ST-Segment Elevation Myocardial Infarction
		Kim W.L.M. Ricken (UMCG, Groningen)
4	09.33 - 09.43	A Genotype-Guided P2Y12-Inhibitor De-escalation Strategy in
		Acute Coronary Syndrome: The POPULAR-GUIDE PCI
		Qiu Ying F. van de Pol (St. Antonius Hospital, Nieuwegein)
5	09.44 - 09.54	Predicting Occlusive Myocardial Infarction Using Artificial
		Intelligence-Based Electrocardiogram Interpretation
		Dino Ahmetagic (Universitair Medisch Centrum Utrecht, Utrecht)
6	09.55 - 10.05	Colchicine in Cardiovascular Disease: Where Do We Stand Now?
		Jalina Jannink (UMC Utrecht, Utrecht)
7	10.06 - 10.16	Predictors for Change in Quality of Life in Patients with Chronic
		Coronary Syndrome Undergoing PCI
		Sanne Janssen (Zuyderland Medical Centre, Heerlen)
8	10.17 - 10.27	The ESC Guidelines for the Management of Acute Coronary
		Syndromes: Adherence in Daily Clinical Practice
		Jan-Guus W.J. Boringa (Meander Medical Center, Amersfoort)



#### Impact of Apolipoprotein A-I Infusions on Cardiovascular Events After Acute Myocardial Infarction-MI by Neutrophil-Lymphocyte Ratio and LDL-Cholesterol Levels Presenting author: S.A.O.F. Rikken

Department: Cardiology

S.A.O.F. Rikken (St. Antonius Ziekenhuis, Nieuwegein; CARIM, Maastricht; Baim Institute for Clinical Research, Boston); C.M. Gibson (Harvard, Boston); M.C. Bahit (Baim Institute for Clinical Research, Boston); D. Duffy (CSL Behring, King of Prussia); G. Chi (Beth Israel Deaconess Medical Center, Boston); S. Korjian (Baim Institute for Clinical Research, Boston); N. Mohammadnia (Radboud University Medical Center, Nijmegen); H. White (Health New Zealand Te Toka Tumai Auckland City Hospital, Auckland); ; G. Anschuetz (CSL Limited, Melbourne); B. A. Kingwell (CSL Limited, Melbourne); T. Oude Ophuis (Canisius-Wilhelmina Hospital, Nijmegen); J. C. Nicolau (Universidade de São Paulo, São Paulo); R. D. Lopes (Duke Clinical Research Institute, Durham); B. S. Lewis (Lady Davis Carmel Medical Center, Haifa); S. El Messaoudi (Radboud University Medical Center, Nijmegen); D. Vinereanu (University and Emergency Hospital, Bucharest); J.M. ten Berg (St. Antonius, Nieuwegein); S. G. Goodman (Canadian VIGOUR Centre, Edmonton); C. Bode (University of Freiburg, Freiburg); P.G. Steg (Hôpital Bichat, Paris); P. Libby (Brigham and Women's Hospital, Boston):

K.R. Bainey (University of Alberta Hospital, Edmonton); P.M. Ridker (Brigham and Women's Hospital, Boston); K. W. Mahaffey (Stanford University School of Medicine, Palo Alto); S.J. Nicholls (Victorian Heart Institute, Melbourne); R. Mehran (Zena and Michael A. Wiener Cardiovascular Institute, New York); R. A. Harrington (Weill Cornell Medicine, New York); J. H. Cornel (Noordwest Ziekenhuisgroep, Alkmaar).

#### Purpose:

The AEGIS-II trial (NCT03473223) evaluated the efficacy of CSL112, a human plasmaderived apolipoprotein A-I (apoA-I) infusion therapy, in reducing cardiovascular events following acute myocardial infarction (AMI). Given CSL112's potential anti-inflammatory effects, we conducted an exploratory post-hoc analysis to assess whether its efficacy was related to baseline neutrophil-lymphocyte ratio (NLR), a marker of systemic inflammation. and low-density lipoprotein cholesterol (LDL-C) levels.

#### Methods:

In total, 18,219 participants with AMI, multivessel coronary artery disease, and additional cardiovascular risk factors were randomized to four weekly infusions of 6 g CSL112 or placebo. The primary endpoint was a composite of cardiovascular death, myocardial infarction, or stroke (MACE). For this analysis, the risk for the primary endpoint was assessed by dichotomized baseline NLR (>median vs. ≤median) using Cox proportionalhazards models. A treatment interaction was added to the model to explore the effects of CSL112 across different NLR and dichotomized LDL-C levels (≥100 mg/dL vs. <100 mg/dL).

#### **Results:**

Among 15,966 participants, those with baseline NLR >median (3.3, N=7,983) had a significantly greater risk of MACE at 90 days (HR 1.40; 95% CI, 1.21–1.63), persisting at 180 and 365 days. In participants with both elevated NLR and LDL-C ≥100 mg/dL, CSL112 reduced MACE compared to placebo at 90 days (HR 0.63; 95% CI, 0.42-0.93), with sustained benefit at 180 and 365 days. Participants with elevated NLR and LDL-C <100 mg/dL, or lower NLR and regardless of LDL-C levels, had no significant reduction in MACE.



A significant interaction between treatment and NLR was noted at 180 days (p for interaction=0.01), and among treatment, NLR, and LDL-C at 180 days (p for interaction=0.03).

#### **Conclusion:**

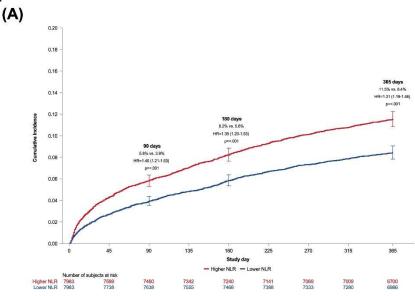
The present analysis confirms that elevated NLR serves as a predictor of MACE post-AMI and showed an associated reduction in cardiovascular events with the use of CSL112 in patients with combined elevated NLR and LDL-C  $\geq$ 100 mg/dL.

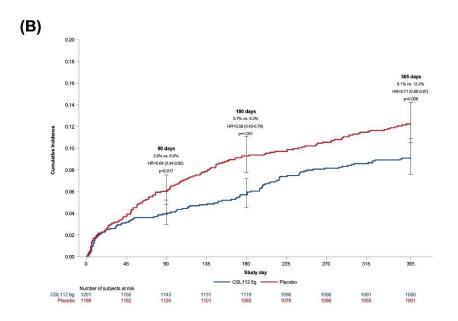
#### Keywords:

Apolipoprotein A-I, CSL112, neutrophil-lymphocyte ratio

#### Figure:

Cumulative incidence of a composite of cardiovascular death, myocardial infarction, or stroke in participants with (A) higher (>median) vs. lower ( $\leq$ median) neutrophil-lymphocyte ratio (NLR) and (B) both higher NLR and LDL-C  $\geq$ 100 mg/dL, treated with CSL112 vs. placebo over 365 days.







# Medication Adherence After Myocardial Infarction: Patients' Insights from a Qualitative Interview Study

Presenting author: E.R.Harding Department: Cardiology

<u>E.R.Harding (Diakonessenhuis, Utrecht);</u> E.R. Harding (Diakonessenhuis, Utrecht); J.H. Houtgraaf (Diakonessenhuis, Utrecht); T. Jaarsma (University Medical Center Utrecht, Utrecht & Julius Centre for Health Sciences and Primary Care, Utrecht); C.E.E. van Ofwegen-Hanekamp (Diakonessenhuis, Utrecht); M.Y. van der Ende (Diakonessenhuis, Utrecht & University Medical Center Utrecht, Utrecht)

#### **Purpose:**

Many patients fail to adhere to medication after myocardial infarction (MI), increasing their risk of recurrent cardiovascular events. This study aims to assess self-reported medication adherence after MI and to explore drivers influencing adherence.

#### Methods:

This convergent parallel mixed-methods study prospectively enrolled patients ≥18 years with MI in a medium sized teaching hospital from August 2024 until now. They completed a questionnaire two weeks and four months post-MI. Quantitative data on self-reported adherence and attitudes towards medicines was assessed by the Medication Adherence Report Scale(MARS-5, range 5-25) and the Beliefs about Medicines Questionnaire(BMQ), respectively. A MARS-5 score ≥23 indicated high adherence. Qualitative data on beliefs about medicines was explored using open-ended questions.

#### **Results:**

37 patients (mean age 67 years( $\pm$ 11), 32% female) completed the questionnaire two weeks post-MI. All patients had a MARS-5 score≥23 and 2 patients(5%) unintentionally deviated from their medication regimen once. Most patients(60%) exhibited an accepting attitude towards prescribed medicines, while the rest were ambivalent(27%), sceptical(5%) or indifferent(8%). The most important facilitator for adherence, reported by 41% of patients, is the belief that medication is essential for maintaining health. Accordingly, 73% of patients suggested that improved communication and education by healthcare providers would enhance adherence.

#### **Conclusion:**

: Shortly after MI, medication adherence seems to be high, driven by intrinsic belief in its importance for their health in which education by healthcare providers plays a major role. Currently, adherence data four months post-MI is being collected. Investigating and subsequently tackling the barriers of adherence is important for reducing cardiovascular events and healthcare costs.

#### Keywords:

Medication adherence, Myocardial infarction, Mixed-methods



# Sex Differences in Cardiac Structure and Function Following First-Time ST-Segment Elevation Myocardial Infarction

Presenting author: K.W.L.M. Ricken Department: Cardiology

<u>K.W.L.M. Ricken (UMCG, Groningen);</u> K. Panaou (UMCG, Groningen); L. Al Ali (UMCG, Groningen); I.C.C. van der Horst (Maastricht University Medical Center, Maastricht); G. Pundziute-Do Prado (UMCG, Groningen); A.A. Voors (UMCG, Groningen); E. Lipsic (UMCG, Groningen))

#### Purpose:

Sex differences in STEMI presentation and outcomes are well-documented, yet little is known about post-STEMI changes in cardiac structure and function in the era of early PCI. This study examines sex-specific differences in echocardiographic changes following first-time STEMI.

#### Methods:

We included non-diabetic first-time STEMI patients. Echocardiographic parameters were assessed during hospitalization and at 4 months. Adverse remodelling was defined as a  $\geq$ 20% increase in left ventricular end-diastolic volume (LVEDV). Functional parameters included left ventricular ejection fraction (LVEF), wall motion score index (WMSI), and left ventricle and atrial strain. Left ventricular geometry patterns were assessed at 4 months. **Results:** 

A total of 379 patients (95 women, 284 men) were included. Women had a similar age (59.9 vs. 57.8 years, p=0.138) but a higher prevalence of hypertension (42% vs. 25.6%, p=0.004), lower hemoglobin levels (8.40 vs. 9.10 mmol/L, p<0.001), and higher NT-proBNP concentrations at admission (132 vs. 67 ng/L, p<0.001) and after 24 hours (1322 vs. 784 ng/L, p<0.001). No significant difference in LV geometry patterns (eccentric or concentric) were observed between sexes at 4 months (p=0.21). Adverse LV remodelling was similar between both groups at approximately 22-23% (p=0.991). Women had smaller cardiac dimensions, lower LAVI, higher E/e' ratios, and greater LVEF at both timepoints. However, the progression of echocardiographic parameters over the 4-month period did not differ significantly between sexes.

#### Conclusion:

Despite baseline differences in patient characteristics and individual echocardiographic parameters, no sex-based disparities were found in LV geometry, adverse remodelling, or changes in cardiac structure or function between admission and 4 months.

#### Keywords:

Sex Differences, STEMI, Cardiac remodelling



#### Figure:

Graphical abstract: Comparison of men and women in (1) structural and (2) functional echocardiographic differences at baseline, and (3) sex-specific changes in these structural and functional parameters over 4 months.

Abbreviations: LVEDD, Left Ventricular End-Diastolic Diameter; LVESD, Left Ventricular End-Systolic Diameter; LAV, Left Atrial Volume; LAVI, Left Atrial Volume Index; LVEF, Left Ventricular Ejection Fraction; WMSI, Wall Motion Score Index; E/e' ratio, Ratio of Early Diastolic Transmitral Flow Velocity to Early Diastolic Mitral Annular Velocity; GLS, Global Longitudinal Strain

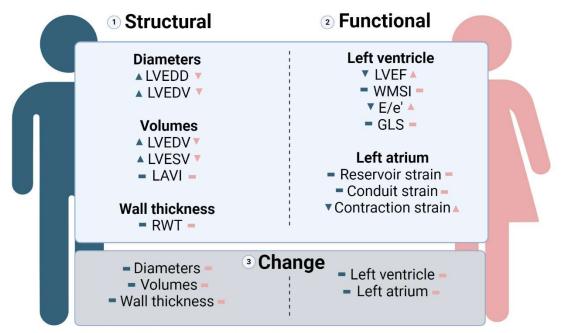


Figure legend:  $\blacktriangle$  higer compared to other sex,  $\forall$  lower compared to other sex, = no significant difference between both sexes.



Session 1: Coronary heart disease & risk prediction Abstract 4

#### A Genotype-Guided P2Y12-Inhibitor De-escalation Strategy in Acute Coronary Syndrome: The POPULAR-GUIDE PCI

Presenting author: Q.Y.F. van de Pol Department: Cardiology

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#### Purpose:

Currently, patients with acute coronary syndrome (ACS) receive standard dual antiplatelet therapy with a potent P2Y12 inhibitor and aspirin. One de-escalation strategy to balance the ischemic an bleeding risk in these patients, is switching the potent P2Y12 inhibitor to clopidogrel. However, clopidogrel activation depends on the CYP2C19 enzyme. Genetic testing for the CYP2C19 genotype, which encodes the CYP2C19 enzyme, identifies patients with decreased clopidogrel metabolism due to 1 or 2 loss of function (LOF) alleles. This enables tailored antiplatelet treatment. The objective of the study is to evaluate the safety and efficacy of routine genetic testing for guiding antiplatelet therapy in a real-world ACS population.

#### Methods:

The POPular GUIDE PCI was an initiative within the ongoing FORCE-ACS (Future Optimal Research and Care Evaluation in Patients with Acute Coronary Syndrome) Registry (NCT03823547). The POPular GUIDE PCI is an observational, multicentre, prospective implentation study including nine non-interventional and interventional cardiac centres located in the NetherlandsIn this prospective, multicenter implemenation study, patients were divded into a standard care cohort, where antiplatelet therapy was prescribed at the physician's discretion and a genotype-guided cohort. In the genotype-guided cohort, physicians were recommended to switch to clopidogrel in noncarriers of the CYP2C19 loss of function alleles during hospital admission. The primaryy endpoins were major adverse cardiac events (MACE), defined as a composite of cardiovascular death, mycardial infartion, or stroke, and major or non-major clinically relevant bleeding at one year follow-up.



#### **Results:**

A total of 9,907 patients were included in the analysis. Of these, 1,208 (12%) were included in the genotype-guided cohort, while 8,699 (88%) were assigned to the standard care cohort. MACE occurred in 107 patients (8.9%) in the genotype-guided cohort and 897 patients (10.3%) in the standard care cohort (adjHR 1.05; 95% CI 0.85-1.29; P = 0.64). Major or nonmajor clinically relevant bleeding was reported in 146 patients (12.1%) in the genotypeguided cohort compared to 1,384 patients (15.9%) in the standard care cohort (adjHR 0.79; 95% CI 0.67–0.94; P = 0.01).

#### Conclusion:

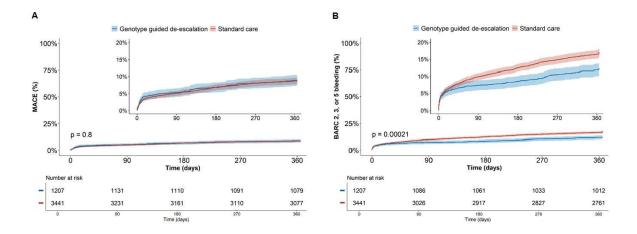
In patients with ACS requiring antiplatelet therapy, implementing a CYP2C19 genotypeguided de-escalation strategy in clinical practice significantly reduced major and non-major clinically relevant bleeding compared to standard care at 12 months, without increasing ischaemic events.

#### **Keywords:**

Acute coronary syndrome, Dual antiplatelet therapy, Genotype-guided therapy

#### Figure:

Supplementary Figure 2. Kaplan-Meier curves after propensity score matching for cumulative incidence of (A) the primary ischemic endpoint (cardiovascular mortality, myocardial infarction, or stroke), showing similar event rates between the genotype-guided cohort (blue) and standard care cohort (red), and (B) the primary bleeding endpoint (BARC 2, 3, or 5 bleeding).





# Predicting Occlusive Myocardial Infarction Using Artificial Intelligence-Based Electrocardiogram Interpretation

Presenting author: D. Ahmetagic Department: Cardiology

<u>D. Ahmetagic (Universitair Medisch Centrum Utrecht, Utrecht);</u> D. Ahmetagic (Universitair Medisch Centrum Utrecht, Utrecht); B.K.O. Arends (Universitair Medisch Centrum Utrecht, Utrecht); R.R. van der Leur (Universitair Medisch Centrum Utrecht, Utrecht); P. van der Harst (Universitair Medisch Centrum Utrecht, Utrecht); T.P. van de Hoef (Universitair Medisch Centrum Utrecht, Utrecht); R. van Es (Universitair Medisch Centrum Utrecht, Utrecht); R.

#### Purpose:

There is increasing awareness that identifying occlusive myocardial infarction (OMI) in patients without ST-elevation remains inadequate. Diagnosis is challenging due to subtle electrocardiogram (ECG) abnormalities. These can be detected reproducibly using artificial intelligence (AI). Therefore, we developed and validated an AI–based algorithm to predict OMI using ECG data.

#### Methods:

We analyzed ECGs from patients presenting with chest pain at the emergency department, cardiac care unit or catheterization laboratory of the University Medical Center Utrecht. ECGs were obtained  $\leq$  72 hours after presentation and, when performed, before coronary angiography. All patients had troponin measurements. The training set included ECGs meeting these criteria, while a separate test cohort used each patient's first ECG. There was no patient overlap between sets. We defined OMI as a culprit vessel with Thrombolysis in Myocardial Infarction (TIMI) flow 0–2. A convolutional neural network was trained to predict OMI from ECG data.

#### **Results:**

The model was trained on 13,541 ECGs from 5,118 patients and tested on 640 ECGs (median age 59 [IQR: 47–70], 55.9% male). OMI was present in 47 patients (7.3%), of whom 35% had a NSTEMI. Our algorithm achieved an area under the receiver operating characteristic curve of 0.79 (95% CI: 0.71-0.86), a sensitivity of 65% (95% CI: 52% - 78%), and a specificity of 72% (95% CI: 68% - 76%).

#### **Conclusion:**

We developed a convolutional neural network capable of predicting OMI using ECG data. With further validation, this model could assist triaging patients with chest pain in the prehospital setting.

#### Keywords:

Electrocardiogram, Occlusive myocardial infarction, Artificial intelligence



#### Colchicine in Cardiovascular Disease: Where Do We Stand Now?

Presenting author: J. Jannink Department: Vascular Medicine

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#### Purpose:

The potential role of low-dose colchicine in atherosclerotic vascular disease has been explored in multiple clinical trials. This review aims to provide an overview of the current evidence regarding the effect of colchicine in the secondary prevention of cardiovascular disease in patients with coronary artery disease or stroke.

#### Methods:

This review provides an overview of randomized trials comparing colchicine to no colchicine for the secondary prevention of atherosclerotic cardiovascular disease. A study-level metaanalysis was conducted to assess the effect of colchicine in patients with known coronary artery disease or stroke. The primary outcome was a composite of myocardial infarction, stroke and cardiovascular death. Secondary outcomes included all-cause mortality.

#### **Results:**

Nine trials, including 30,659 patients (15,255 receiving colchicine, 15,404 receiving no colchicine) with a history of coronary artery disease or stroke were included. Patients randomized to colchicine had a relative risk of 0.88 (95% confidence interval (CI) 0.81-0.95, p = 0.002; 9 trials) compared to no colchicine for the primary composite outcome. In patients with coronary disease the relative risk was 0.85 (95% CI 0.75-0.95, p = 0.097; 5 trials). In patients with a history of stroke the relative risk was 0.91 (95% Cl 0.80-1.03, p = 0.233; 2)trials). All-cause mortality did not differ between treatment groups.

#### **Conclusion:**

In patients with a history of coronary artery disease or stroke, colchicine was associated with a 12% reduction of the composite outcome of cardiovascular death, myocardial infarction or stroke when compared to placebo or no colchicine. No differences in all-cause mortality between groups was observed.

#### Keywords:

Colchicine, Inflammation, Cardiovascular disease



#### Predictors for Change in Quality of Life in Patients with Chronic Coronary Syndrome Undergoing PCI

Presenting author: S. Janssen Department: Cardiology

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#### Purpose:

In patients with chronic coronary syndrome (CCS), percutaneous coronary intervention (PCI) is performed to relieve symptoms of angina pectoris and to improve quality of life (QoL) after optimal medical therapy. This study aimed to ascertain whether the general CCS population reported improved QoL one year after PCI. In addition, it aimed to identify patient-related characteristics associated with no improvement of QoL.

#### Methods:

Data were derived from the Southeast Netherlands Heart Registry (ZON-HR), an ongoing, multicenter PCI registry. Patients with complete 36-Item Short Form Health Survey (SF36-v2) data at baseline and 1-year after PCI were included. Scores were subdivided into a physical health (PH) component and mental health (MH) component. The associations with baseline characteristics were examined using univariable binary logistic regression.

#### **Results:**

Repeated SF36-v2 data were available for 329 patients. One year after PCI, PH improved in 58.1% of patients and MH in 55.9% of patients. Patients with peripheral artery disease (PAD) had a 1.9x higher chance of no improvement of PH compared to patients without PAD (OR=1.939, 95% CI: 1.001-3.757). In addition, diabetes, male sex, a previous myocardial infarction, active smoking, and obesity showed a trend towards no PH improvement one year after PCI (Figure 1).

#### Conclusion:

This study showed that just over half of CCS patients reported improved QoL one year after PCI. In addition, PAD was associated with the absence of improvement in the physical component of QoL. Further research should focus on identifying characteristics of CCS patients who may derive less benefit from PCI.

#### Keywords:

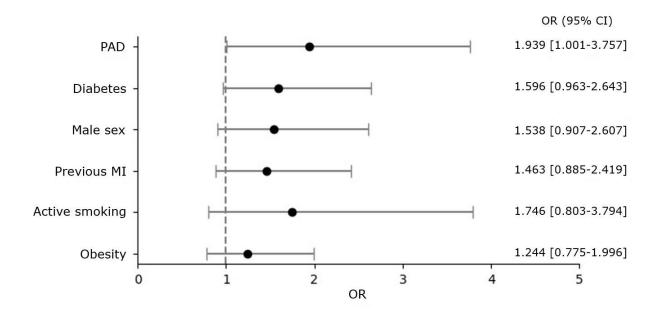
Quality of Life, Chronic Coronary Syndrome, Physical Health



#### Figure:

Figure 1: Forest plot of odds ratios of absence of improvement in physical health 1 year after PCI based on baseline characteristics.

PCI, percutaneous coronary intervention; PAD, peripheral artery disease; MI, myocardial infarction; OR, odds ratio; CI, confidence interval.





# The ESC Guidelines for the Management of Acute Coronary Syndromes: Adherence in Daily Clinical Practice

Presenting author: J.W.J. Boringa Department: Cardiology

<u>J.W.J. Boringa (Meander Medical Center, Amersfoort);</u> J. Jannink (Meander Medical Center, Amersfoort); A. Mosterd (Meander Medical Center, Amersfoort)

#### Purpose:

The guidelines aim to support cardiologists in daily practice with new knowledge. However, evidence from previous studies shows suboptimal adherence to cardiovascular prevention guidelines. This study examines to what extent cardiologists from Meander Medical Center in Amersfoort adhere to the Acute Coronary syndrome(ACS) treatment guidelines of the European Society of Cardiology(ESC) during ACS hospitalization.

#### Methods:

A prospective observational study was conducted at Meander Medical Center, Amersfoort, from September 2 2024 to October 31 2024. The study focused on ESC Class IA, IB, and IC recommendations ("indicated"). Class IIa ('should be considered') and IIb ('may be considered') recommendations were included only if relevant to the study objectives. Patients were assessed for optimal therapy across six key pillars: (I) lipid management, (II) inflammation management, (III) antithrombotic therapy, (IV) hemodynamic management (subdivided into hypertension and heart failure), (V) Type II diabetes management, and (VI) lifestyle management.

#### **Results:**

A total of 106 patients were included (mean age 66 ± 13 years, 33 (37%) women). Optimal therapy adherence across all six pillars was 24%. Adherence rates for individual pillars were as follows: lipid management; 33%, inflammation management; 22%, antithrombotic management; 100%, hypertension management; 81%, heart failure management; 67%, Type II diabetes management; 65%, and lifestyle management; 88%

#### Conclusion:

Adherence to the ESC guidelines for ACS treatment during hospitalization was suboptimal. Only 24% of patients received optimal therapy across all six therapeutic pillars. This study lends support to efforts to improve practice during ACS admission, when patients are most susceptible to interventions

#### Keywords:

Acute coronary syndrome, Guidelines, Adherence



#### Figure:

Adhe	rence to ESC guidelines in 106 consecutive			
ACS patients (no. and (%)).				
١.	Lipids, LDL target 1.4 mmol/l achieved	35 (33)		
П.	Ant-inflammatory therapy initiated	6/27 (22)		
III.	Antithrombotic			
	<ul> <li>Dual antiplatelet therapy (DAPT)</li> </ul>	106 (100)		
	<ul> <li>Eligible patients who received advice to shorten DAPT duration</li> </ul>	3 (9)		
IV.	Hemodynamic			
	<ul> <li>Hypertension (RR above 130/80 mmHG)</li> </ul>	86 (81)		
	<ul> <li>Heart Failure (initiation of guideline directed medical therapy)</li> </ul>	6/9 (67)		
V.	Diabetes Mellitus Type II optimal therapy	15/23 (65)		
VI.	Lifestyle management	88 (83)		
	<ul> <li>Flu vaccinations</li> </ul>	106 (100)		
	<ul> <li>Quit smoking conversation</li> </ul>	8/35 (23)		
Acros	s all six pillars.	25 (24)		



## SESSIE 2: Electrophysiology & devices

	Springerzaal	Voorzitters:
	_	dr. Pascal van Dessel, cardioloog MST
		dr. Tom Verstraelen, AIOS Amsterdam UMC
1	09.00 - 09.10	a Comparison of commonly Used QT Formulas in Healthy
		Subjects
		Lennaert Hoek (ICON plc, Early Development Services, Groningen,
		University of Groningen, UMC Groningen)
2	09.11 - 09.21	Smartphone Application-Based Heart Rhythm Management
		Around Cardioversion in Patients with Presumed Persistent
		Atrial Fibrillation: Feasibility Substudy of TeleConvert-AF
		Madelon D.E.A. Engels (Radboudumc, Nijmegen; MUMC+,
		Maastricht)
3	09.22 - 09.32	Re-Implantation Strategies in Cardiac Implantable Electronic
		Devices
		Leonard A. Dijkshoorn (Amsterdam UMC, Amsterdam)
4	09.33 - 09.43	Regional Implementation of a Pharmacologic Cardioversion
		Protocol: Insights in Patient Outcomes and Experience
		Jeroen A.A. van de Pol (Netherlands Heart Network, Eindhoven)
5	09.44 - 09.54	Predicting Structural Heart Disease in Cardiology Outpatients
		Using Artificial Intelligence-based Electrocardiogram
		Interpretation
		Bauke K.O. Arends (Universitu Medical Centre Utrecht, Utrecht)
6	09.55 - 10.05	PulseSelect™ Pulsed Field Ablation for Atrial Fibrillation:
		Conscious Sedation or General Anesthesia?
		Marisa van der Graaf (St. Antonius ziekenhuis, Nieuwegein)
7	10.06 - 10.16	Endocardial Findings in One- and Two-Staged Hybrid Atrial
		Fibrillation Ablation: a Dual-Center Cohort Analysis
		Luca Aerts (Maastricht Medical University Center, Maastricht)
8	10.17 - 10.27	Development of an Al Algorithm for Automated Detection of
		Cardiovascular Procedure-Related Complications
		Jippe C. Balt (St. Antoniusziekenhuis, Nieuwegein)



## Session 2: Electrophysiology & devices

Abstract 1

#### a Comparison of commonly Used QT Formulas in Healthy Subjects

Presenting author: L. Hoek Department: EDS/cardiology

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#### Purpose:

The QT interval on an ECG is influenced by heart rate, requiring correction formulas for adjusted QT (QTc) values. The European Society of Cardiology recommends Bazett's formula, while the FDA recommends Fridericia's formula for drug development. Other commonly used formulas include Framingham and Hodges. This study compared the accuracy of these four frequently used formulas in correcting the QT interval for heart rate. **Methods:** 

We retrospectively assessed ECGs from 22.063 medically assessed healthy individuals who participated in phase 1 trials between 1997 and 2023. Pearson correlation coefficient (r) between QTc and heart rate (HR) and the linear regression slope (b) were calculated for each formula and the influence of age, sex and body mass index.

#### **Results:**

The study analyzed 16,170 males and 5,893 females (mean age:  $34.9 \pm 15.3$  years) to assess QTc-heart rate (HR) correlations. The Fridericia formula showed the strongest reliability, with the lowest correlation (r = 0.018) and a nearly horizontal regression slope (b = 0.04). The Hodges (r = -0.182, b = 0.39) and Framingham (r = 0.200, b = 0.43) formulas followed. The Bazett formula performed worst (r = 0.483, b = 1.12). Fridericia remained the most accurate across subgroups except in low BMI groups and differed significantly from other formulas in both sexes (P < 0.05).

#### **Conclusion:**

The Fridericia formula is the most reliable method for correcting the QT interval for heart rate and we recommend its use in daily practice.

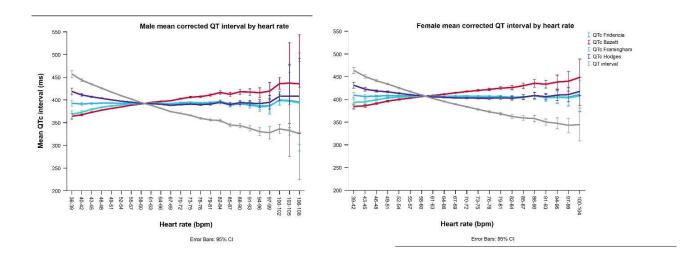
#### Keywords:

QT correction formulas, Fridericia formula, Bazett formula



#### Figure:

Comparison of measured QT intervals and all mean HR-corrected QT intervals by heart rate (n = 22,063) and per 3 beats per min including 95% CI





Session 2: Electrophysiology & devices Abstract 2

# Smartphone Application-Based Heart Rhythm Management Around Cardioversion in Patients with Presumed Persistent Atrial Fibrillation: Feasibility Substudy of TeleConvert-AF

Presenting author: M.D.E.A. Engels Department: Cardiology

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#### Purpose:

A proportion of patients with presumed persistent AF, who are scheduled for electrical cardioversion (ECV), appear to have a paroxysmal AF pattern or convert spontaneously to sinus rhythm (SR) on the ECV waiting list. This results in unnecessary visits or interventions for patients, and costs and burden for the hospitals and health insurances. TeleConvert-AF is a prospective multicentre cohort study testing the effect of smartphone application-based heart rhythm monitoring around an elective ECV on cancelling unnecessary ECV appointments in case of paroxysmal AF patterns or spontaneous conversion of AF to SR in patients with presumed persistent AF scheduled for ECV.

This substudy of the TeleConvert-AF study assesses the feasibility of the smartphone application-based heart rhythm monitoring to detect paroxysmal AF patterns and spontaneous conversion of AF to SR in patients on the waiting list of an elective ECV. **Methods:** 

Patients aged ≥18 years with presumed persistent AF on the waiting list for an elective ECV were invited to participate. Reasons for exclusion were the presence of a cardiac device or the inability to use a smartphone application. Patients were instructed to perform three heart rate and rhythm recordings daily using a photoplethysmography (PPG)-based mobile app. Recordings were performed for a minimum of two weeks prior to ECV until four weeks follow-up. Recordings were evaluated by the investigators daily, and when changes in rhythm were observed patients were referred for electrocardiogram (ECG). ECV was cancelled in case of objective spontaneous conversion or paroxysmal AF. The primary endpoint is the occurrence of a paroxysmal AF pattern or self-terminating AF to SR. The secondary endpoint is recurrence of AF after ECV.

#### **Results:**

Up to now, 824 patients were screened and 233 patients agreed to participate in this study. Overall, adherence to the instruction to perform three heart rate and rhythm recordings daily has been optimal. According to the preliminary analysis of the first 120 patients (median age of 68 years [61.25-73.75], 70% male), paroxysmal AF patterns were observed in six patients (5.0%) and 13 patients (10.8%) showed a spontaneous conversion to SR on PPG recordings by the smartphone-application, which could be confirmed by a 12 lead resting ECG. Of 92 patients (76.7%), were ECV was acutely successful and were the patients left the hospital in SR, PPG recordings by the smartphone-application detected a recurrence of either persistent or paroxysmal AF within the 4-week follow-up period in 51 patients (55.4%), which could be confirmed by ECG.



#### **Conclusion:**

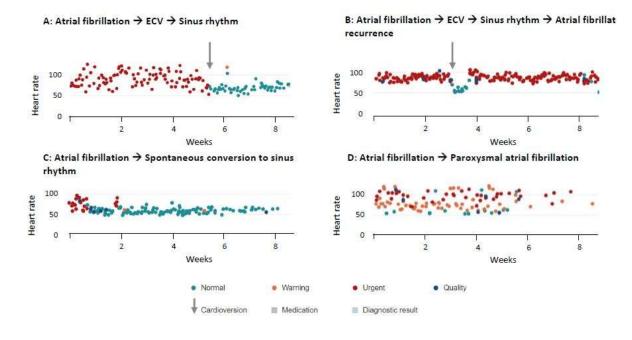
The TeleConvert-AF approach is feasible. PPG can accurately detect spontaneous conversion to SR and paroxysmal AF in patients waiting for an elective ECV. The effect of the TeleConvert-AF approach on ECV cancelation and the integration into AF treatment plans is currently investigated in the ongoing prospective TeleConvert-AF study.

#### Keywords:

Atrial Fibrillation, m-Health, Electrical cardioversion

#### Figure:

Figure 1: Representation of the four distinct patterns analysed in the Teleconvert-AF study. A) AF pre-ECV, with persistent SR after ECV; B) AF pre-ECV, with a short period of SR following ECV, followed by a recurrence of AF; C) AF at beginning of the monitoring period, with a spontaneous conversion to persistent SR; D) paroxysmal AF pattern. AF = atrial fibrillation; SR = sinus rhythm; ECV = electrical cardioversion





#### Session 2: Electrophysiology & devices Abstract 3

#### **Re-Implantation Strategies in Cardiac Implantable Electronic Devices**

Presenting author: L.A. Dijkshoorn Department: Cardiology

<u>L.A. Dijkshoorn (Amsterdam UMC, Amsterdam);</u> L.A. Dijkshoorn; K.M. Kooiman; R.A.F. de Lind van Wijngaarden (Amsterdam UMC, Amsterdam); L. Smeding (Amsterdam UMC, Amsterdam); J.A. de Veld (Amsterdam UMC, Amsterdam); A.H.G. Driessen (Amsterdam UMC, Amsterdam); R.E. Knops (Amsterdam UMC, Amsterdam); L.R.A. Olde Nordkamp (Amsterdam UMC, Amsterdam)

#### Purpose:

This study aimed to evaluate clinical success, complications and re-implantation strategy of lead extractions.

#### Methods:

A retrospective cohort study was conducted at a single center, including patients who underwent lead extraction procedures between 2015 and 2023. Outcomes included clinical successful extraction, complications, re-implantation strategy and infection recurrence. **Results:** 

Among 88 consecutive patients (median age 72yr, 84% male, 53% cardiomyopathy), a total of 40 implantable defibrillators (46%), 29 pacemaker (33%) and 19 cardiac resynchronization devices (33%) with a total of 203 leads were extracted. CIED infection was the main indication for extraction (84%). Median lead dwell time was 7 years (range 1.1–23 years). Clinical successful extraction was achieved in 78 (89%) of patients, and 4 (4.5%) experienced a major complication. Peri-procedural death was reported in 1 patient. CIED re-implantation was performed in 61%, of whom 60% transitioned to a non-transvenous device. Explanted devices were not reimplanted primarily due to a change in clinical indication. After a median follow-up of 3.8 years, 16 (18%) patients died, no infections reoccurred and none of those with non-transvenous device required transvenous implantation. **Conclusion:** 

### conclusion:

In a cohort where lead extraction was mainly performed for CIED infections, lead extraction is effective with high success rates and low peri-procedural mortality. Moreover, reimplantation with a non-transvenous systems is effective and safe.

#### Keywords:

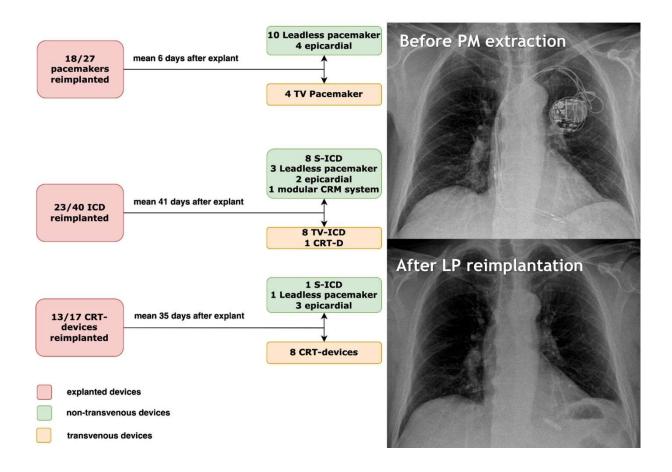
lead extraction, CIED infections, mortality



#### Figure:

Figure 1: reimplantation strategies

TV: transvenous, ICD: implantable cardioverter defibrillator, S-ICD: subcutaneous implantable cardioverter defibrillator, CRM: cardiac rhythm management, CRT: cardiac resynchronization therapy, PM: pacemaker, LP: leadless pacemaker.





Session 2: Electrophysiology & devices Abstract 4

#### Regional Implementation of a Pharmacologic Cardioversion Protocol: Insights in **Patient Outcomes and Experience**

Presenting author: J.A.A. van de Pol Department: Cardiology

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#### Purpose:

A new protocol regarding preferred pharmacologic cardioversions (PCV) and, if unsuccesfull, 24-hour delayed electric cardioversion (ECV) was implemented across four hospitals in Southeast Netherlands, working together within the Netherlands Heart Network. This study evaluates the protocol's impact on both patient outcomes and care experience.

#### Methods:

The protocol was implemented in July 2022. After a brief run-in period, data were evaluated from September 2022 to May 2023. Data were extracted from electronic patient records to assess PCV success rates and subsequent use of ECV (same or following day). A patient experience questionnaire, as developed in collaboration between an atrial fibrillation care professional network and a regional patient advisory board, was distributed by emergency cardiac care nurses following acute PCV and/or ECV to compare PCV/ECV experiences. **Results:** 

PCV was successful in 271 out of 356 patients (76%). In the 85 non-successful PCV, ECV was performed the same or following day. Of 54 eligible patient questionnaires, 28 involved ECV, 12 PCV, and 14 both. No significant differences were observed between ECV and PCV regarding overall care (9.4 vs. 9.0 out of 10, p=0.22), or variables such as information provision (p=0.58), treatment explanation (p=0.58), shared decision-making (p=0.51), feeling safe (p=0.89), safe return home (p=0.14), or experience as impactful (p=0.33). **Conclusion:** 

PCV success rates aligned with expectations from literature. Patient experiences were comparable between ECV and PCV, despite initial expectations of reduced impact and less perceived safety with PCV. Future evaluation will focus on healthcare costs to provide a comprehensive assessment of patient value.

#### **Keywords:**

Pharmacologic cardioversion, Patient experiences, Regional implementation



Session 2: Electrophysiology & devices Abstract 5

Predicting Structural Heart Disease in Cardiology Outpatients Using Artificial Intelligence-based Electrocardiogram Interpretation Presenting author: B.K.O. Arends Department: Cardiology

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#### Purpose:

The growing prevalence of structural heart disease (SHD) has increased the burden on echocardiography laboratories, further strained by a sonographer shortage. To address this, efficient diagnostic strategies are essential. Electrocardiograms (ECGs) are cost-effective, accessible, and rapid tests that could assist in SHD detection. This study aimed to develop and validate an artificial intelligence-based algorithm to predict SHD using ECG data. **Methods:** 

We analyzed ECG-echocardiogram pairs from University Medical Center Utrecht and Catharina Hospital Eindhoven, dividing data into training, validation, and testing cohorts with no patient overlap. SHD was defined as a composite endpoint of any TTE with moderate-severe biventricular dysfunction/dilatation or moderate-severe valvular disease (aortic stenosis/regurgitation, mitral/tricuspid regurgitation). We constructed a testing cohort of newly referred outpatients from both centers. An ensemble model, combining a convolutional neural network and an extreme gradient boosting algorithm, was trained to predict the composite endpoint using only ECG data.

#### **Results:**

The model was trained on 80,579 ECGs from 51,902 patients and tested on 4,052 ECGs (median age: 64 [51–73] years, 50.9% male). The composite endpoint was present in 857 patients (22.5%). In the testing cohort, the model achieved an area under the receiver operating characteristic curve of 0.80 (95% confidence interval [CI]: 0.79–0.82), sensitivity of 0.94 (95% CI: 0.92–0.95), and specificity of 0.31 (95% CI: 0.29–0.32).

#### Conclusion:

We successfully developed an ensemble model that predicts absence of SHD using ECG data alone. With further validation, this algorithm could assist in risk stratification and streamline SHD diagnostics in outpatient settings.

#### Keywords:

structural heart disease, deep learning, electrocardiogram



#### Figure:

Ensemble model performance in the outpatient test set. Abbreviations. AUPRC, area under the precision recall curve; AUROC, area under the receiving operator characteristic curve; AR, aortic regurgitation; AS, aortic stenosis; LVD, left ventricular dilatation; LVDD, left ventricular diastolic dysfunction; LVSD, left ventricular systolic dysfunction; MR, mitral regurgitation; NPV, negative predictive value; PPV, positive predictive value; RVD, right ventricular dilatation; TR, tricuspid regurgitation.

	Prevalence	AUROC	AUPRC	Sensitivity	Specificity	PPV	NPV
Composite	0.22 (0.21-0.24)	0.80 (0.79-0.82)	0.62 (0.59-0.65)	0.94 (0.92-0.95)	0.31 (0.29-0.32)	0.28 (0.26-0.30)	0.94 (0.93-0.96)
LVSD	0.07 (0.07-0.08)	0.93 (0.92-0.95)	0.66 (0.61-0.71)	0.92 (0.89-0.95)	0.79 (0.78-0.80)	0.26 (0.24-0.29)	0.99 (0.99-1.00)
LVD	0.03 (0.03-0.04)	0.93 (0.91-0.95)	0.46 (0.37-0.55)	0.88 (0.82-0.93)	0.84 (0.83-0.85)	0.16 (0.13-0.19)	1.00 (0.99-1.00)
RVSD	0.02 (0.02-0.03)	0.89 (0.86-0.92)	0.20 (0.14-0.28)	0.94 (0.89-0.98)	0.58 (0.57-0.60)	0.05 (0.04-0.06)	1.00 (1.00-1.00)
RVD	0.02 (0.02-0.03)	0.82 (0.77-0.87)	0.18 (0.11-0.26)	0.78 (0.69-0.87)	0.69 (0.67-0.70)	0.05 (0.04-0.06)	0.99 (0.99-1.00)
LVDD	0.03 (0.03-0.04)	0.81 (0.77-0.84)	0.15 (0.12-0.21)	0.94 (0.90-0.98)	0.39 (0.38-0.41)	0.05 (0.04-0.06)	0.99 (0.99-1.00)
AS	0.04 (0.03-0.04)	0.80 (0.76-0.83)	0.18 (0.13-0.24)	0.87 (0.81-0.92)	0.54 (0.52-0.56)	0.07 (0.05-0.08)	0.99 (0.99-0.99)
AR	0.02 (0.02-0.03)	0.75 (0.70-0.79)	0.10 (0.06-0.16)	0.93 (0.87-0.97)	0.37 (0.36-0.39)	0.03 (0.03-0.04)	1.00 (0.99-1.00)
MR	0.06 (0.05-0.07)	0.84 (0.82-0.87)	0.31 (0.26-0.38)	0.93 (0.90-0.96)	0.45 (0.44-0.47)	0.10 (0.09-0.11)	0.99 (0.99-0.99)
TR	0.04 (0.04-0.05)	0.86 (0.84-0.89)	0.31 (0.25-0.38)	0.93 (0.90-0.97)	0.56 (0.54-0.57)	0.09 (0.08-0.10)	0.99 (0.99-1.00)



#### Session 2: Electrophysiology & devices Abstract 6

#### PulseSelect<sup>™</sup> Pulsed Field Ablation for Atrial Fibrillation: Conscious Sedation or **General Anesthesia?**

Presenting author: M. van der Graaf Department: Cardiology

M. van der Graaf (St. Antonius ziekenhuis, Nieuwegein); B.G.S. Abeln (St. Antonius ziekenhuis, Nieuwegein); M. Liebregts (St. Antonius ziekenhuis, Nieuwegein); V.F. van Dijk (St. Antonius ziekenhuis, Nieuwegein); M.C.E.F. Wijffels (St. Antonius ziekenhuis, Nieuwegein); J.C. Balt (St. Antonius ziekenhuis, Nieuwegein); L.V.A. Boersma (St. Antonius ziekenhuis. Nieuweaein)

#### **Purpose:**

Pulmonary vein isolation (PVI) with pulsed field ablation (PFA) is typically performed under general anesthesia. However, PFA systems with an appropriate pulse profile may enable procedures under conscious sedation. In this study we assess the feasibility, efficacy and safety of performing PVI with the PulseSelect<sup>™</sup> ablation system under conscious sedation, compared to general anesthesia in patients with atrial fibrillation (AF).

#### Methods:

Single center registry of AF patients undergoing an ablation with the PulseSelect™ (Medtronic, Minneapolis, USA) PFA system, between January 29th and December 31th, 2024 at the St. Antonius Hospital. Conscious sedation (CS) was used if no anesthesiology team was available to provide general anesthesia (GA). Endpoints included acute isolation of ablation targets, procedural characteristics and freedom from adverse events within 30 days. **Results:** 

The analysis included 174 patients (67.2% male, mean age 62.8±9.3 years), with 62.1% having paroxysmal AF. GA was used in 132 (75.9%) vs. CS in 42 patients (24.1%). There were no differences in baseline characteristics between the groups. Median skin-to-skin procedural time was comparable between groups: GA 39.0 min [IQR 34.0;46.0] vs. CS 42.0 min [IQR 37.5; 46.0], P= N.S and acute procedural efficacy was 100% in both groups. One patient in the GA group experienced a major bleeding complication. Intravenous lidocaine was administered in a subset of patients who experienced coughing during the procedure, with overall positive effects.

#### **Conclusion:**

Conscious sedation offers an efficient and safe alternative for PulseSelect™ PFA procedures, eliminating risks of general anesthesia and reducing personnel required for airway management.

#### **Keywords:**

Atrial fibrillation, Pulsed field ablation, Conscious sedation



#### Figure:

Data is presented as counts (percentages) for categorical data, means ± standard deviations for normally distributed continuous data and median [interquartile range] non-normally distributed continuous data. Abbreviations: LVEF: Left Ventricular Ejection Fraction; LAVI: Left Atrial Volume index.

#### TABLE 1

	Conscious sedation (n = 42)	General anesthesia (n = 132)	p-value	
Age, years	60.6 ± 9.6	63.4 ± 9.1	0.102	
Female sex	12 (28.6)	45 ( 34.1)	0.635	
LVEF >50%	34 (82.9)	99 ( 76.7)	0.536	
Enlargement left atrium (LAVI > 35ml/m <sup>2</sup> )	14 (40.0)	43 ( 35.5)	0.777	
CHA2DS2-VA score				
0	20 (47.6)	46 ( 35.1)		
1	10 (23.8)	36 ( 27.5)		
2+	12 (28.6)	49 ( 37.4)		
Total number of applications	32.0 [32.0, 33.0]	33.0 [32.0, 36.0]	0.001	
Procedure time (min)	42.0 [37.5, 46.0]	39.0 [34.0, 46.0]	0.108	
Fluoroscopy duration (min)	11.5 [10.0, 12.2]	12.0 [10.0, 15.0]	0.090	
Acute procedural success	42 (100.0)	132 (100.0)	1.000	



#### Session 2: Electrophysiology & devices Abstract 7

# Endocardial Findings in One- and Two-Staged Hybrid Atrial Fibrillation Ablation: a Dual-Center Cohort Analysis

Presenting author: L. Aerts Department: Cardiothoracic surgery

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#### Purpose:

Hybrid AF ablation combines thoracoscopic epicardial ablation with a transvenous endocardial approach. Electrophysiological findings during the endocardial part of hybrid ablation have not been reported in detail.

#### Methods:

This retrospective study included patients with symptomatic paroxysmal, persistent and longstanding-persistent AF who underwent 1-or-2-staged hybrid ablation. Here we discuss endocardial validation, touch up, and additional endocardial ablations. Secondly, findings during redo catheter ablation were described.

#### **Results:**

In the one-stage group there were more LSPAF patients (39.3% vs 10.3%, p=0.032), less prior catheter ablations (39.3% vs 79.3%, p=0.039) and a longer AF duration (117 vs 33 months, p=0.009), compared to two-staged patients. Endocardial validation confirmed entrance and exit block in the box lesion in 91.2% of one-stage and 86.2% of two-staged patients. Touch-up lesions and additional endocardial ablations during the hybrid procedure are described in table 1. Freedom from ATA at 12, 24, and 36 months was 71.4%, 66.3%, and 44.2% in the one-stage, and 82.8%, 59.1%, and 59.1% in the two-staged group. Complication rates were low.

Redo catheter ablations were performed in 5 one-stage patients with a mean interval of 15.4 months post-procedure, and in 1 two-staged patient after 8 months. During these redo ablations, isolation of pulmonary veins and box lesions was persistent. However, redo ablation did not result in freedom from ATA during follow up.

#### **Conclusion:**

The endocardial component of hybrid ablation confirms lesion completeness, with comparable outcomes between one- and two-staged approaches. Redo procedures after hybrid ablation did not result in freedom from ATA.

#### Keywords:

Hybrid AF ablation, Endocardial validation, Electrophysiological mapping



#### Figure:

Table 1. Procedural findings

Variable	Overall cohort	One Stage	Two Staged	p-value
	(n=57)	(n=28)	(n=29)	
SVC isolation (%)	55 (96.5%)	27 (96.4%)	28 (96.6%)	1.000
Additional epicardial lines				
lsthmus line (%)	2 (3.5%)	2 (7.1%)	0	0.237
LAA management (%)	56 (98.2%)	27 (96.4%)	29 (100%)	0.491
Touch -up				
Re-isolation roof line	2 (3.5%)		2 (6.9%)	
Re-isolation floor line	4 (7.0%)	1 (3.6%)	3 (10.3%)	
Re-isolation LPVs	1 (1.8%)	1 (3.6%)		
Re-isolation RPVs	1 (1.8%)	1 (3.6%)		
Additional endocardial lines				
CTI (%)	28 (93.0%)	28 (100%)	25 (86.2%)	0.112
Mitraal isthmus line (%)	11 (19.3%)	9 (32.1)	2 (6.9%)	0.021
Extra ablation LA (%)	3 (5.3%)	0	3 (10.3%)	0.237
Extra ablation RA (%)	3 (5.3%)	0	3 (10.3%)	0.237
RAA (%)	2 (3.5%)	0	2 (6.9%)	0.491
Intercaval line (%)	1 (1.8%)	1 (3.6%)	0	0.491
SVC (%)	2 (3.5%)	2 (7.1%)	0	0.237
CTI: cavotricuspid isthmus line, EC	V: electrical cardio	version, LA: left	atrium, LAA: lef	t atrial
appendage, LSPV: left superior pulmonary vein, SD: standard deviation, SR: sinus rhythm,				
SVC: superior vena cava, RA: right	atrium, RAA: right	atrial appendag	e, RPVs: right p	ulmonary
veins.				



Session 2: Electrophysiology & devices Abstract 8

#### **Development of an Al Algorithm for Automated Detection of Cardiovascular Procedure-Related Complications** Presenting author: J.C. Balt Department: Cardiologie

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#### Purpose:

In the present study, we describe the development of a fully automated, artificial intelligence (AI) driven complication registration, independent of health care worker input, after percutaneous coronary intervention (PCI), pulmonary vein isolation (PVI) and trans catheter aortic valve implantation (TAVI). This algorithm was designed to identify the most important complications (stroke, tamponade and vascular complications) in Epic, an electronic patient record system (EPRS) that is used worldwide.

#### Methods:

We created an AI model designed to identify complications in EPIC healthcare files following cardiac procedures at the St. Antonius Hospital in the Netherlands. After consent from the medical ethical committee, we collected anonymized data from EPIC healthcare files, conducting all analyses on a compute cluster situated within St. Antonius Hospital. The database consisted of 6564 cardiac procedures (PVI, PTCA and TAVI) performed at our hospital from 2017 to 2022. Diverse data sources were used, such as the registered diagnosis, procedure-logs, medication, laboratory measurements, clinical notes, and discharge letters. To ensure consistency, we adhered to data standardization using the OMOP Common Data Model and ZIB, a Dutch information standard mandatory for all hospitals. Standardization simplifies the integration of the AI model in current and future hospital settings.

Our model underwent training and testing using data from all patients undergoing PCI, PVI, or TAVI at our hospital from 2017 to 2022. The dataset was divided into a training and test set (n=2999) and a prospective validation set (n=3565). We developed models for specific complications—bleeding, tamponade, CVA, and phrenic paralysis—defined by the Dutch Heart Registration (NHR; see Table 1). For bleeding, the definition was expanded to include clinically relevant incidents, such as a bleeding that prolonged hospital stay, requiring surgical intervention or blood transfusion. The primary objective of the model was to achieve 100% sensitivity to avoid missing any complication, accepting a lower specificity and – consequently- false positives.

#### Approach

We employed a systematic ten-step approach, outlined in Figure 1. Steps 1-4 involved splitting the training dataset into groups with and without complications. Clinical presentations and patterns of each complication were discussed in workshops with healthcare professionals. These patterns were translated into data statements, forming the basis for a weak labeled dataset (see below for definition). Both structured data (medication,



lab measures, data from procedure-logs) and unstructured data (notes, discharge letters) were considered, flagging a patient if any statement was true within an admission. Manual reviews of selected files generated a strong dataset (see below), serving as the gold standard for fine-tuning and validating our models. A random sample of non-selected files did not yield additional complication cases.

In Step 5, Machine learning was employed to identify additional signals in the training set. Step 6 involved assessing whether the explained patterns aligned with the patient context, removing correlational signals from the model. For example the administration of fluoroscopic contrast was found as an additional signal by the model for CVA. It was removed because correlated with the making of a CT scan to diagnose a CVA. Step 7 integrated the three models into one, combining the identified criteria from Step 2 using structured and unstructured data, together with the additional signals found with machine learning. Different models

were applied for each complication, employing random forest (see below) and boosting classifiers (see below) for structured data and transformer embedding's for unstructured data. For fine-tuning we utilized the optuna framework (see below) for high sensitivity. Transparent and trustworthy results were ensured by incorporating explainable AI techniques, including small decision trees and exploration of synonyms for common associated words with each complication.

Step 8 tested the performance of the combined models on the validation dataset. In Step 9 and 10, manual checks were conducted on all files labeled as complications together with a random sample of files without a complication. We are reporting specificity, sensitivity, and precision for each model on both the training and validation datasets.

#### **Results:**

6564 patients who underwent PVI, PCI or TAVI procedures at our hospital between 2017 and 2022. The dataset was split into a training and test set (n=2999) and a prospective validation set (n=3565). Baseline characteristics are shown in table 1.

Sensitivity, specificity, positive predictive value and F-score for the automated detection of complications stroke, tamponade, bleeding and phrenic nerve palsy after PVI, PTCA and TAVI are shown in Table 2 and table 3. A sensitivity between 94.4% and 100% was achieved, while specificity ranged from 99.4% to 100%. This resulted in positive predictive values ranging from 47.5% to 81%, with F-scores varying between 0.64 and 0.87. Due to insufficient data, a meaningful AI-model for phrenic nerve palsy could not be created. This model used selected criteria only, containing structured data (such as medication, lab measures, procedures) and unstructured data (such as notes, discharge letters).

#### **Conclusion:**

We now have an AI driven tool that can automatically identify virtually all complications from the patient health care files, with very high sensitivity. This is achieved without the burden of prospective registration for the healthcare provider and without the intervention of data managers. This provides crucial input in the PDCA cycle, thereby aiding in patient safety and health care quality.

#### Keywords:

Artificial intelligence, complication registration,



## **SESSIE 3: Imaging & diagnostics**

	Zaal 10	Voorzitters:
		dr. Miranda Bijvoet, cardioloog Maastricht UMC+
		dr. Rosemarijn Jansen, cardioloog i.o. St. Antonius Ziekenhuis
1	09.00 - 09.10	Three-Dimensional CT for pre-Procedural Planning of PCI for
		Ostial RCA Lesions: a Randomized Controlled Pilot Trial
		Deborah M.F. van den Buijs (Medical Center Leeuwarden)
2	09.11 - 09.21	Large Language Models Are Accurate and Efficient in Automatic
		Annotation of Free-Text Coronary Computed Tomography
		Angiography Reports
		Gaby Liao (Leiden University Medical Center, Leiden)
3	09.22 - 09.32	Exploring Iron Deficiency in Engineered Heart Tissues: A New
		Approach to Understanding Cardiac Health
		Sam Majoor (UMCG, Groningen)
4	09.33 - 09.43	LGE-Based Simulations to Improve ICD Therapy Prediction in
		Post-Infarct Patients
		Janneke C. Burger (Amsterdam UMC, Amsterdam)
5	09.44 - 09.54	Comparative Analysis of CT and CMR-derived Ventricular
		Models using ADAS 3D and inHEART for VT Substrate
		Assessment
		Damian Laan (Amsterdam UMC, Amsterdam)
6	09.55 - 10.05	Left Atrial Atrain has Prognostic Value in Dilated
		Cardiomyopathy Patients with Recovered Ejection Fraction
L	40.00 40.40	Max F.G.H.M. Venner (CARIM, Maastricht)
7	10.06 - 10.16	Optimizing Heart Rate with Metoprolol for Coronary CT
		Angiography: a Dose-Response Analysis and
		Recommendations from a Large Cohort
	40.47 40.07	Victor A. Verpalen (Amsterdam UMC, Amsterdam)
8	10.17 - 10.27	Individuals with Type 2 Diabetes Have Increased Coronary
		Plaque Burden and Plaque Progression During 10-Year Serial
		Coronary CT Angiography Follow-up
		Emilie L. Gaillard (Amsterdam UMC, Amsterdam)



Session 3: Imaging & diagnostics Abstract 1

#### Three-Dimensional CT for pre-Procedural Planning of PCI for Ostial RCA Lesions: a **Randomized Controlled Pilot Trial**

Presenting author: D.M.F. van den Buijs Department: Cardiology

D.M.F. van den Buijs (Medical Center Leeuwarden, Leeuwarden); E.M. Poels (Ziekenhuis Oost-Limburg, Genk); E. Willems (Ziekenhuis Oost-Limburg, Genk); D. Cottens (Ziekenhuis Oost-Limburg, Genk); K. Dotremont; K. de Leener; E. Meekers (Ziekenhuis Oost-Limburg, Genk); B. Ferdinande (Ziekenhuis Oost-Limburg, Genk); M. Vrolix (Ziekenhuis Oost-Limburg, Genk); J. Dens (Ziekenhuis Oost-Limburg, Genk); K. Ameloot (Ziekenhuis Oost-Limburg, Genk)

#### Purpose:

Geographical stent-ostium mismatch is an important predictor of target lesion failure after percutaneous coronary intervention (PCI) of an aorto-ostial right coronary artery (RCA) lesion. Optimal visualization of the aorto-ostial plane is crucial for precise stent implantation at the level of the ostium. To investigate whether pre-procedural 3-dimensional coronary CT (3DCT) with determination of the optimal viewing angle would allow for more precise stent implantation and reduce time, procedural contrast and radiation dose.

#### Methods:

In this single-center, prospective, open label, core-lab blinded trial, a total of 30 patients with an aorto-ostial RCA lesion were randomly assigned to either PCI with a pre-procedural 3DCT or angiography guided PCI. The optimal working view angle was determined by 3DCT in the intervention group and by operators' discretion in the control group. Primary endpoint was the percentage of patients without geographical mismatch as determined by IVUS.

#### **Results:**

3DCT determined C-arm angles were heterogenous but in general more extreme LAO projections were used (p<0.0001). While stent implantation was in the optimal position in all patients randomized to the intervention group, geographical mismatch was present in n=5 (33%) patients randomized to the control group (p=0.06). Mean amount of procedural contrast (p < 0.0001), mean radiation (p = 0.03) and median procedure time (p = 0.03) were significantly lower in the intervention group. The 3DCT scan was able to predict calcium arc (p<0.0001) and minimum luminal area by IVUS (p=0.003).

#### **Conclusion:**

Pre-procedural 3DCT planning for PCI of aorto-ostial RCA lesions allows for optimal stent positioning while reducing procedure time, contrast and radiation use.

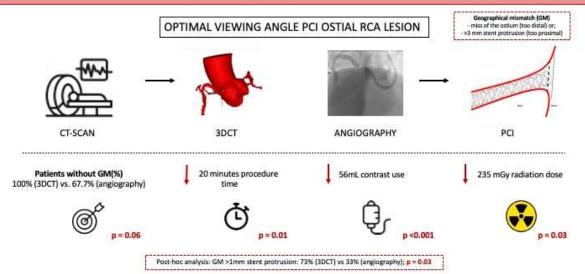
#### **Keywords:**

Ostial right coronary artery stenosis, percutaneous coronary intervention, 3-dimensional CT



Figure:

Three-dimensional computer tomography for pre-procedural planning of percutaneous coronary intervention for ostial right coronary artery lesions: a randomized controlled pilot trial





Session 3: Imaging & diagnostics Abstract 2

#### Large Language Models Are Accurate and Efficient in Automatic Annotation of Free-Text Coronary Computed Tomography Angiography Reports Presenting author: G. Liao Department: Cardiology

<u>G. Liao (Leiden University Medical Center, Leiden);</u> G. Liao (Leiden University Medical Center, Leiden); E.A.S. Polomski (Leiden University Medical Center, Leiden); A.A.M. al Jaff (Leiden University Medical Center, Leiden); M.L. Antoni (Leiden University Medical Center, Leiden); M.M. Van Buchem (Leiden University Medical Center, Leiden); J.W. Jukema (Leiden University Medical Center, Leiden); J.C. Heemelaar (Leiden University Medical Center, Leiden) Center, Leiden)

#### Purpose:

Manual adjudication of free-text coronary computed tomography angiography (CCTA) reports for research is a time-consuming and resource-intensive process, which is not scalable to large sample sizes (e.g. hospital database wide analysis). Large Language Models (LLM) may be a promising tool due to excellent language understanding capabilities. However, no evidence is available on the performance metrics of LLMs with Dutch medical jargon. Therefore, the aim of this study is to validate an open-source LLM in transforming free-text reports to a discrete, actionable dataset of CCTA.

#### Methods:

A total of 970 CCTA reports were manually adjudicated in a prior study on late effects of cancer treatment to extract parameters (scan quality, coronary dominance and significant coronary stenosis), and were used as the golden standard. We developed an automated LLM-pipeline (LLaMa 3.1) that iterates through each report to extract the same variables. 100 reports were randomly selected for prompt engineering, and another 100 for validation. The outcomes of interest were: precision, recall, F1-score and processing time. **Results:** 

# The LLM-pipeline exhibited a high accuracy in adjudicating free-text CCTA reports compared to the gold standard (precision=0.90, recall=0.93, F1-score=0.91), while simultaneously reducing the processing time by tenfold compared to manual annotation (median 38 sec vs 388 sec for 10 reports). The most common discrepancy was ambiguous phrasing (N=11). **Conclusion:**

Our study highlights the potential of open-source LLM-pipelines to automatically acquire discrete data from free-text CCTA reports with high accuracy. Future perspectives will emphasize external validation of LLMs within other Dutch hospitals and data extraction of other cardiac investigations.

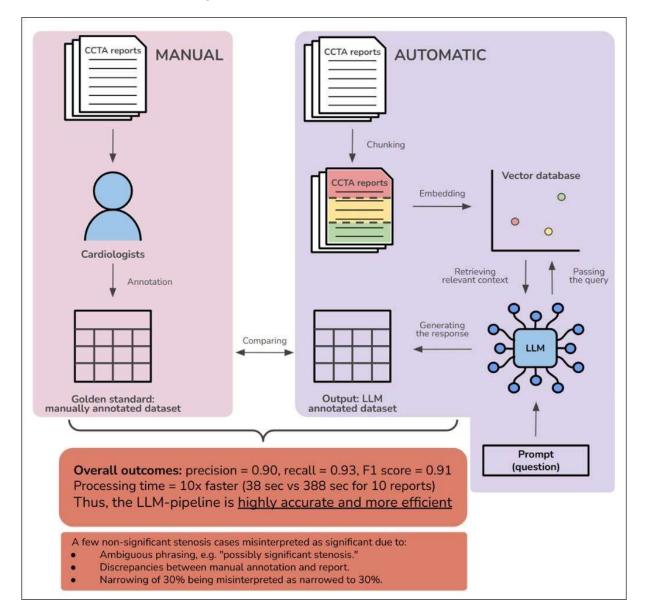
#### Keywords:

Coronary Computed Tomography Angiography, Large Language Models, Implementation Science



#### Figure:

Figure 1. Schematic representation of the LLM-pipeline to extract data from Dutch CCTA reports. CCTA reports are initially segmented in chunks, which are transformed in vector embeddings to form a vector database. Subsequently, the LLM retrieves relevant context from the vector database to generate a response for the prompt.





Session 3: Imaging & diagnostics Abstract 3

## **Exploring Iron Deficiency in Engineered Heart Tissues: A New Approach to Understanding Cardiac Health** Presenting author: S. Majoor

Department: Experimental Cardiology

<u>S. Majoor (UMCG, Groningen);</u> N. Grote Beverborg (UMCG, Groningen); N. Bömer (UMCG, Groningen); P. van der Meer (UMCG, Groningen)

#### Purpose:

Background: Addressing the knowledge gap in the early molecular mechanisms of heart failure (HF) pathogenesis is crucial. Notably, approximately 50% of HF patients are affected by iron deficiency (ID), a condition that impairs critical physiological processes such as erythropoiesis, oxygen storage, and mitochondrial respiration. Hence, ID leads to a progression of HF symptoms and worsens the prognosis. This study aims to understand the functional and pathophysiological consequences of ID on the human myocardium using human Pluripotent Stem Cell (hPSC)-derived 3D Dynamically Cultured Engineered Heart Tissues (Dyn-EHT).

#### Methods:

Methods: By using hPSC-derived cardiomyocytes, and hPSC-derived cardiac fibroblasts in combination with applied pre-load, the human heart composition was mimicked in Dyn-EHTs as close as currently possible. Dyn-EHTs were iron depleted by treatment with the iron chelator deferoxamine (DFO), DFO was used in various concentrations for four days. Videos of the Dyn-EHTs were made daily to asses functional parameters such as contractile force, pacing frequency, and systolic/ diastolic stress. Iron deficiency was assessed by measuring transferrin receptor (TfRC) mRNA expression.

#### **Results:**

Results: A total of 66 tissues were engineered (at least N=6/dose). After four days of DFO treatment, a dose dependent increase in TfRC mRNA expression was measured Functional parameters of the Dyn-EHTs will be quantified in the upcoming months using analyses of the taken videos.

#### Conclusion:

Conclusions: Administration of DFO results in a dose dependent iron deficiency in Dyn-EHTs. The Dyn-EHT model forms our foundation of further in vitro research into iron deficiency. Aiding in the further understand the pathophysiology of ID in the heart.

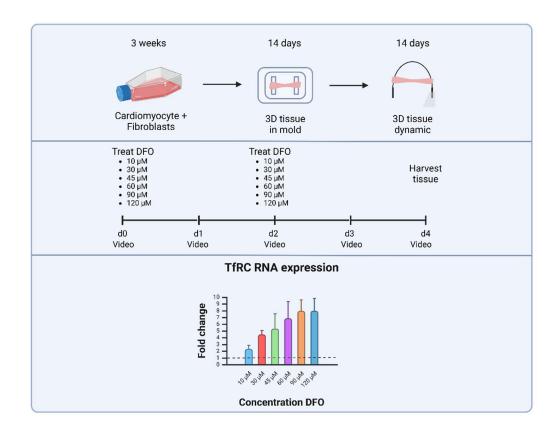
#### Keywords:

Heart Failure, Iron Deficiency, Engineered Heart Tissue



#### Figure:

Figure description: Graphical abstract; panel one schematically represents the Dyn-EHT formation process. Panel two depicts the DFO treatment scheme following the Dyn-EHT maturation. The last panel shows the dose response of TfRC RNA expression to increasing doses of DFO. Dyn-EHT: dynamically cultured Engineered heart tissues, DFO: Deferoxamine, TfRC: Transferrin receptor.





# Session 3: Imaging & diagnostics

Abstract 4

### LGE-Based Simulations to Improve ICD Therapy Prediction in Post-Infarct Patients

Presenting author: J. C. Burger Department: Cardiology

<u>J.C. Burger (Amsterdam University Medical Center, Amsterdam);</u> J.C. Burger (Amsterdam University Medical Center, Amsterdam); L.H.G.A. Hopman (Amsterdam University Medical Center, Amsterdam); F. Campos; A.C. van der Lingen (Amsterdam University Medical Center, Amsterdam); C.P. Allaart (Amsterdam University Medical Center, Amsterdam); P.G. Postema (Amsterdam University Medical Center, Amsterdam); M.J.B. Kemme (Amsterdam University Medical Center, Amsterdam); M.J.W. Götte (Amsterdam University Medical Center, Amsterdam); M.J. Bishop (Amsterdam University Medical Center, Amsterdam); V. van Halm (Amsterdam University Medical Center, Amsterdam); P. Bhagirath (Amsterdam University Medical Center, Amsterdam)

#### Purpose:

Late gadolinium enhancement (LGE)-based modelling techniques have recently emerged to identify key predictors of implantable cardioverter defibrillator (ICD) therapy using patient-specific models, addressing limitations of structural risk stratification methods. The Virtual Induction and Treatment of Arrhythmias (VITA) framework detects critical ventricular tachycardia (VT) isthmuses, proving a tool for arrhythmogenic risk stratification. This study aims to evaluate the relationship between LGE-derived simulation metrics and appropriate ICD therapy.

#### Methods:

Ischemic cardiomyopathy (ICM) patients who underwent LGE imaging prior to ICD implantation were retrospectively identified. LGE images were post-processed using a commercially available semi-automatic segmentation platform. Subsequent mesh model generation was performed through customized scripts. The meshes were used as input for Reaction-Eikonal modelling to obtain simulation metrics.

#### **Results:**

Out of 90 ICM patients, 31 (34.4%) received appropriate ICD therapy. VITA metrics showed a significantly larger number of VTs (97.7 $\pm$ 82.1 vs. 35.1 $\pm$ 43.3, p<0.001), unique VTs (6.3 $\pm$ 4.5 vs. 2.4 $\pm$ 2.6, p<0.001), mean round-trip time (RTT) (183.0 $\pm$ 83.9 vs. 102.1 $\pm$ 90.7, p<0.001) and max RTT (241.3 $\pm$ 125.1 vs. 118.9 $\pm$ 112.3, p<0.001), in patients with an event. Regression analyses including simulation metrics indicated a significant association between VITA metrics and an event; total VTs (HR 1.01; CI 1.00-1.01, p=0.006), unique VTs (HR 1.01; 1.00-1.01, p=0.01) and max RTT (HR 1.01; 1.00-1.01, p=0.01) and max RTT (HR 1.01; 1.00-1.01, p=0.03).

#### Conclusion:

LGE-derived quantitative simulation metrics exhibited predictive capability for ICD therapy, highlighting its potential role in improving risk stratification in ICM patients. These findings warrant further investigations into arrhythmia simulations in clinical settings to improve patient outcomes.

#### Keywords:

Implantable Cardioverter Defibrillator, Ventricular Arrhythmia, Computational Modelling



**Figure:** VITA simulation pipeline and outcome differences in patients with and without an event.

E-CMR segmentation	Scar model	Computational mesh	VITA simulations
			Round-trip time (RT)
	ř	Key results	Ļ
	WITH appropriate therapy		t WITHOUT appropriate ICD therapy
	WITH appropriate		
ICE	WITH appropriate • therapy	ICM patien	ICD therapy
ICE Total VTs	WITH appropriate 9 therapy 97	ICM patien	ICD therapy 35



Session 3: Imaging & diagnostics Abstract 5

## Comparative Analysis of CT and CMR-derived Ventricular Models using ADAS 3D and inHEART for VT Substrate Assessment Presenting author: D. Laan

Department: Cardiology

<u>D. Laan (Amsterdam University Medical Center, Amsterdam);</u> D. Laan (Amsterdam University Medical Center, Amsterdam); L.H.G.A. Hopman (Amsterdam University Medical Center, Amsterdam); M. Götte (Amsterdam University Medical Center, Amsterdam); C.P. Allaart (Amsterdam University Medical Center, Amsterdam); M.J.B. Kemme (Amsterdam University Medical Center, Amsterdam); P.G. Postema (Amsterdam University Medical Center, Amsterdam); P. Bhagirath (Amsterdam University Medical Center, Amsterdam)

#### Purpose:

Advances in post-processing software for cardiac magnetic resonance imaging (CMR) and cardiac computed tomography (CCT) have enhanced procedural guidance for catheter ablation. However, a direct comparison between ADAS 3D LV (ADAS LV Medical, Spain) and inHEART (IHU LIRYC and Inria, France) remains unexplored. This study compares CCT- and CMR-derived ventricular substrate models in ischemic and non-ischemic VT patients using ADAS 3D and inHEART to assess inter-platform differences.

#### Methods: Patients who underv

Patients who underwent both CCT and CMR prior to VT ablation were retrospectively identified. ADAS 3D was used to generate three-dimensional, patient-specific substrate models, while inHEART processed LGE-CMR images and published them via its online platform. A custom scoring system evaluated scar mass, transmurality, wall thickness, scar core, and conduction corridor visualization.

#### **Results:**

Sixteen patients (8 ischemic, 8 non-ischemic) were analyzed. ADAS 3D provided better conduction corridor visualization (Figure 1). No significant differences were found in borderzone measurements (ischemic: Z = -1.52, p = 0.128; non-ischemic: Z = -0.73, p = 0.46). Scar core analysis yielded comparable results (ischemic: Z = -0.51, p = 0.61; non-ischemic: Z = -0.63, p = 0.53). ADAS 3D achieved higher average scores, trending toward significance.

#### Conclusion:

ADAS 3D and inHEART exhibit distinct strengths in pre-VT ablation imaging. inHEART offers remote processing with minimal user input, while ADAS 3D requires on-site processing and expertise but provides more detailed visualization. Platform choice should consider clinician experience, equipment availability, and visualization needs. Future research should assess the impact of these differences on procedural outcomes.

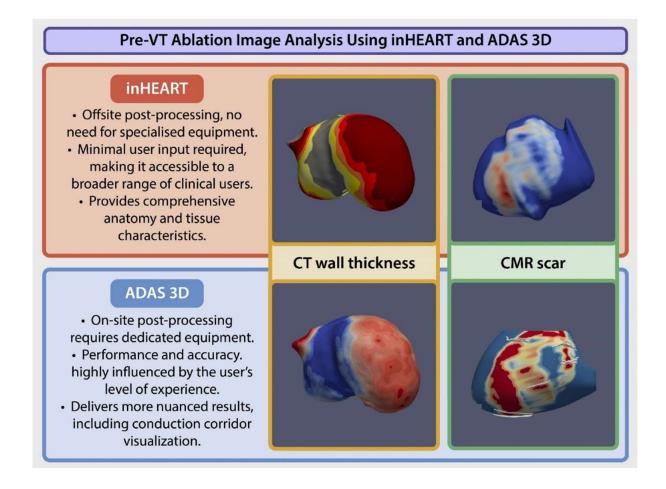
#### Keywords:

ventricular tachycardia, late-gadolinium enhancement, substrate



#### Figure:

Figure 1. Pre-VT ablation image analysis using inHEART and ADAS 3D





Session 3: Imaging & diagnostics Abstract 6

#### Left Atrial Atrain has Prognostic Value in Dilated Cardiomyopathy Patients with **Recovered Ejection Fraction**

Presenting author: M.F.G.H.M. Venner Department: Cardiology

M.F.G.H.M. Venner (CARIM, Maastricht); M.F.G.H.M. Venner (CARIM, Maastricht); J.A.J. Verdonschot (CARIM, Maastricht); C. Knackstedt (CARIM, Maastricht); M.A. Sikking (CARIM, Maastricht); M.T.H.M. Henkens (CARIM, Maastricht); M.R. Hazebroek (Zuyderland Ziekenhuis, Heerlen); A.G. Raafs (CARIM, Maastricht); S.R.B. Heymans (CARIM, Maastricht)

#### Purpose:

In dilated cardiomyopathy (DCM), structural recovery does not equal recovery of cardiac function when based on conventional parameters such as left ventricular ejection fraction (LVEF). The role of left atrial (LA) function (strain) to predict prognosis in DCM patients with recovered EF, remains unknown. This study evaluates the prognostic value of echocardiographic LA strain in DCM patients with recovered election fraction. Methods:

DCM patients with recovered EF ( $\geq$ 50% and  $\geq$ 5 EF point increase from baseline). Primary endpoint was the combination of mortality, heart failure (HF) hospitalization, or lifethreatening arrhythmias. Harrel's C-indexes and likelihood-ratio-test were performed to determine the value of LA strain in a multivariable survival model using the primary endpoint.

#### **Results:**

A total of 201 DCM patients were included (age 58 [47-63] years, 60% male). Thirty-nine patients (19%) reached the primary endpoint (follow-up 7 years). Based on univariable analysis, LA conduit strain was a stronger predictor of outcome compared to reservoir and booster strain. LA conduit strain (HR:3.14, 95%-confidence interval [CI]:1.01-9.77, p=0.048), age (HR:1.10, 95%-CI:1.05-1.16, p<0.001), NYHA class>2 (HR:3.97, 95%-CI:1.49-10.57, p=0.005) and LVMI (HR:1.03, 95%-CI:1.01-1.05, p=0.002) remained associated in the multivariable model. Adding LA conduit strain to other independent predictors (NYHA class, age, and LVMI) significantly improved the calibration and accuracy of the prediction model (p=0.03).

#### **Conclusion:**

Echocardiographic LA conduit strain is an independent and incremental predictor of adverse outcome in DCM patients with recovered LVEF, outperforming LV GLS. LA conduit strain should be measured in DCM patients with recovered ejection fraction to improve risk stratification.

#### Keywords:

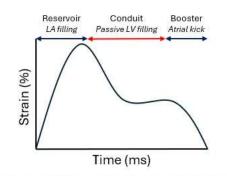
Dilated cardiomyopathy, speckle tracking strain, left atrial phasic function

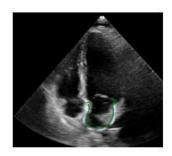


#### Figure:

Using speckle tracking echocardiography the LA conduit strain can be measured, which reflects the passive LV filling during diastole. In a multivariable adjusted model, LA conduit strain is an independent and incremental predictor of outcome (combination of all-cause mortality, heart failure hospitalization and life-threatening arrhythmias) on top of known predictors.

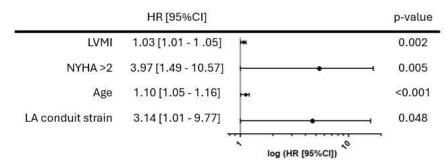
#### Echocardiographic speckle tracking left atrial (LA) strain in dilated cardiomyopathy





#### Multivariable adjusted analysis

Outcome: mortality, heart failure hospitalization and life-threatening arrhythmias





Session 3: Imaging & diagnostics Abstract 7

**Optimizing Heart Rate with Metoprolol for Coronary CT Angiography: a Dose-Response Analysis and Recommendations from a Large Cohort** Presenting author: V.A. Verpalen Department: Cardiology

V.A. Verpalen (Amsterdam UMC, Amsterdam); V.A. Verpalen (Amsterdam UMC,

Amsterdam); W.R. van de Vijver (Amsterdam UMC, Amsterdam); O.G. Silveirinha (Amsterdam UMC, Amsterdam); C.F. Coerkamp (Amsterdam UMC, Amsterdam); B.E.P.M. Claessen (Amsterdam UMC, Amsterdam); G.A. Somsen (Cardiology Centers of the Netherlands (CCN), Amsterdam); K.J. Franssen (Amsterdam UMC, Amsterdam); I.I. Tulevski (Cardiology Centers of the Netherlands (CCN), Amsterdam); M.M. Winter (Amsterdam UMC, Amsterdam); J.P.S. Henriques (Amsterdam UMC, Amsterdam); R.A.P. Takx (Amsterdam UMC, Amsterdam); R.N. Planken (Mayo Clinic, Rochester)

#### Purpose:

A low heart rate (HR) during coronary computed tomography angiography (CCTA) optimizes image quality. This study aimed to investigate the dose-response effect of oral metoprolol succinate and tartrate on HR in patients prepared for CCTA and to assess the association between patient characteristics and failure to achieve the target HR <60 beats per minute (bpm).

#### Methods:

This retrospective study included 4569 consecutive patients scheduled for CCTA between 2022-2023. Patients were categorized according to the adopted metoprolol preparation strategy (group 1-4). HR was measured at the outpatient visit (T1), CCTA intake (T2), prescan (T3) and during CCTA (T4).

#### **Results:**

In total, 67% of the patients achieved the target HR <60 bpm at T4. The 3830 patients prepared with succinate (groups 2 and 4) had a mean dose-response of -6.2±10.4 bpm from T1-T2, only 41% achieved the target HR at T2, and 33% (1266/3830) received additional tartrate at T2 (group 4). Those patients prepared with succinate and tartrate demonstrated a reduced dose-response effect of tartrate from T2-T4 compared with patients receiving tartrate only (-11.8±7.9 versus -15.4±7.9 bpm). Female sex, a higher BMI, diabetes, and higher baseline HRs were independently associated with failure to achieve the target HR. **Conclusion:** 

This study demonstrates the dose-response effect of metoprolol on HR before CCTA, highlighting underdosing of both succinate and tartrate, without safety concerns. Tartrate was more effective, particularly in patients without prior succinate preparation. Doses of 100 mg are recommended for most patients with an HR >65 bpm, guided by patient characteristics.

#### Keywords:

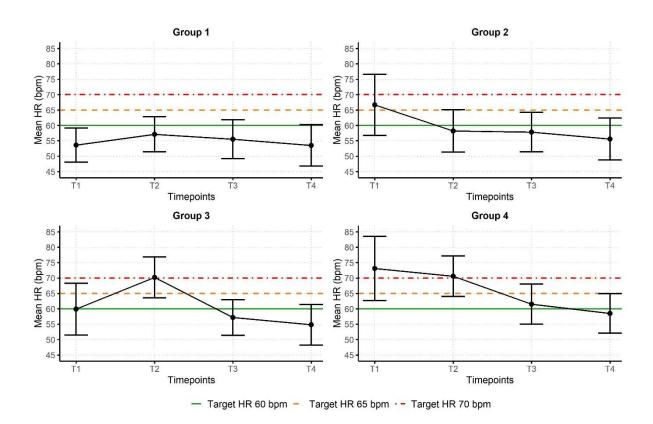
Coronary computed tomography angiography, Heart rate, Beta-blockers



#### Figure:

T1, outpatient visit; T2, CCTA intake 60 minutes before scan; T3, pre-scan; T4, during CCTA.

Group 1 = Patients not prepared with metoprolol before CCTA; Group 2 = Patients prepared with metoprolol succinate days before CCTA, no metoprolol tartrate 60 minutes before CCTA; Group 3 = Patients prepared with metoprolol tartrate 60 minutes before CCTA, no metoprolol succinate days before CCTA; Group 4 = Patients prepared with metoprolol succinate days before CCTA; Group 4 = Patients prepared with metoprolol succinate days before CCTA AND metoprolol tartrate 60 minutes before CCTA





Session 3: Imaging & diagnostics Abstract 8

Individuals with Type 2 Diabetes Have Increased Coronary Plaque Burden and Plaque Progression During 10-Year Serial Coronary CT Angiography Follow-up Presenting author:

Department: cardiologie en vasculaire geneeskunde

<u>E.L. Gaillard (Amsterdam UMC, Amsterdam);</u> E.L. Gaillard (Amsterdam UMC, Amsterdam); N.S. Nurmohamed (Amsterdam UMC, Amsterdam); M.J. Bom (Amsterdam UMC, Amsterdam); S. Ibrahim (Amsterdam UMC, Amsterdam); R.N. Planken (Amsterdam UMC, Amsterdam); S.M. Boekholdt (Amsterdam UMC, Amsterdam); A.D. Choi (Amsterdam UMC, Amsterdam); E.S.G. Stroes (Amsterdam UMC, Amsterdam); Paul Knaapen (Amsterdam UMC, Amsterdam)

#### Purpose:

Individuals diagnosed with type 2 diabetes mellitus (T2DM) are at high risk for coronary artery disease, however, data on long-term progression of coronary artery plaque burden is lacking. This study investigated atherosclerotic plaque characteristics and long-term coronary plaque progression in patients with and without T2DM.

#### Methods:

Per-protocol, patients from a coronary CT angiography (CCTA) cohort were invited for repeat CCTA imaging, regardless of symptoms. A total of 299 patients underwent follow-up imaging with a median scan interval of 10.2 [IQR 8.7-11.2] years. Patients who underwent coronary artery bypass grafting and vessels revascularized by percutaneous coronary intervention were excluded. Scans were analyzed using atherosclerosis imaging-quantitative CCTA analysis (AI-QCT; Cleerly Inc.). The associations between diabetic status, baseline and follow-up plaque burden and characteristics were evaluated using multivariable regression adjusted for clinical risk factors, statin use, baseline plaque volumes and scanner settings. **Results:** 

In total, 267 patients were included, 44 (16.5%) had T2DM at baseline. The mean age was  $57\pm7$  years, 43% were women. At baseline, patients with T2DM had a median percent atheroma volume (PAV) of 5.1 (1.7, 10.9), patients without T2DM had a median PAV of 2.2 (0.5, 5.8). Adjusted for clinical risk factors, patients with T2DM had higher plaque burden at both baseline and follow-up (Figure 1). After adjustment for clinical risk factors and baseline plaque volumes, individuals with T2DM had a higher rate of plaque progression. The difference in PAV caused by T2DM was similar to the effect of a 16-year age difference. After 10 years of follow-up, patients with T2DM had a higher prevalence of both high-risk plaque (OR 3.07; p<0.001) and low-density plaque (OR 2.97; p<0.001).

#### Conclusion:

Patients with T2DM had a more than twofold higher coronary plaque burden, an increased rate of plaque progression during 10-year follow-up, and had an increased prevalence of high-risk and low-density plaque.

#### Keywords:

imaging, coronary artery disease, diabetes mellitus



#### Figure:

Shown are beta coefficients for Type 2 Diabetes Mellitus compared to no Diabetes Mellitus from linear regression models. Adjusted models account for sex, age and clinical risk factors, which include body mass index, systolic blood pressure, LDL cholesterol, lipoprotein(a), triglycerides, hypertension, hypercholesterolemia, smoking, family history of coronary artery disease and statin use.

Outcome variable		β (95% CI)	p-value	
Baseline imaging	1			
Percent atheroma volume		3.39 (1.32 to 5.46)	0.001	
		2.41 (0.36 to 4.46)	0.022	
Percent non-calcified plaque volume	-	1.83 (0.70 to 2.96)	0.002	
		1.29 (0.18 to 2.39)	0.023	
Percent calcified plaque volume		1.56 (0.45 to 2.66)	0.006	
		1.14 (0.04 to 2.24)	0.044	
Follow-up imaging (10 years)				
Percent atheroma volume		5.49 (2.53 to 8.45)	0.000	
	· · · · · · · · · · · · · · · · · · ·	4.72 (1.83 to 7.61)	0.002	
Percent non-calcified plaque volume		2.57 (1.22 to 3.93)	0.000	
		2.36 (1.02 to 3.70)	0.001	
Percent calcified plaque volume		2.57 (1.22 to 3.93)	0.000	
	-	2.36 (1.02 to 3.70)	0.001	
Change (delta)				
Percent atheroma volume		4.41 (2.81 to 6.01)	0.000	
		3.78 (2.18 to 5.38)	0.000	
		2.97 (1.51 to 4.42)	0.000	
Percent non-calcified plaque volume	184	1.68 (0.91 to 2.45)	0.000	
	-	1.56 (0.74 to 2.38)	0.000	Linear regression model
	-	1.45 (0.63 to 2.27)	0.001	
Percent calcified plague volume		2.73 (1.58 to 3.89)	0.000	Unadjusted
	-	2.22 (1.05 to 3.38)	0.000	Adjusted for clinical risk factors
	-	1.78 (0.70 to 2.87)	0.001	Adjusted for clinical risk factors and baseline plaque w

#### Figure 1. Associations between Type 2 Diabetes Mellitus and Coronary Plaque Burden and Progression

Shown are beta coefficients for Type 2 Diabetes Mellitus compared to no Diabetes Mellitus from linear regression models. Adjusted models account for sex, age, and clinical risk factors, which include body mass index, systolic blood pressure, LDL cholesterol, lipoprotein(a), triglycerides, hypertension, hypercholesterolemia, smoking, family history of coronary artery disease, and statin use. Changes were calculated as the difference between follow-up and baseline values.



### SESSIE 4: Cardiac surgery & valvular heart disease

	Zaal 11	Voorzitters:
		dr. Berto Bouma, cardioloog, Amsterdam UMC
		dr. Laura Kerkmeijer, AIOS Meander MC
1	09.00 - 09.10	Outcome After Endoscopic Coronary Artery Bypass Grafting
		Compared to Conventional Bypass Surgery
		Ferdi Akca (Catharina Hospital, Eindhoven)
2	09.11 - 09.21	VARC-HBR Criteria Validation in Anticoagulated TAVI Patients
		Christiaan.C. Overduin (St. Antonius Ziekenhuis, Nieuwegein)
3	09.22 - 09.32	Validation of the Dutch and Danish Version of the Toronto Aortic
		Stenosis Quality of Life Questionnaire in Patients Undergoing
		TAVI: a Pre-Specified POPular PAUSE TAVI Substudy.
		Puck J.A. van Nuland (St. Antonius Hospital, Nieuwegein)
4	09.33 - 09.43	Clinical Characteristics and Outcomes of Mitral Regurgitation
		Patients Stratified by Atrial and Ventricular Dysfunction in the
		SMILE Registry
		Myrthe J.M. Welman (Maastricht UMC+, CARIM, Maastricht University)
5	09.44 - 09.54	Epicardial Fat Increases over Time after Heart and Lung
		Transplantation
		Britt C.J. van Dijk (Erasmus MC, Rotterdam)
6	09.55 - 10.05	Less Symptom Improvement in Patients Undergoing TAVI with
		Concomitant COPD, Atrial Fibrillation and Heart Failure
		Kees H. van Bergeijk (UMCG, Groningen)
7	10.06 - 10.16	1-Year Survival of Frail Patients Similar to the Overall Group after
		Transcatheter Edge-to-Edge Repair for Mitral Regurgitation
		Abby E. Geerlings (Amsterdam UMC, Amsterdam)
8	10.17 - 10.27	Safety of Left Atrial Appendage Amputation During Cardiothoracic
		Surgery
		Marc M. Terpstra (Amsterdam UMC, Amsterdam)



# Outcome After Endoscopic Coronary Artery Bypass Grafting Compared to Conventional Bypass Surgery

Presenting author: F. Akca Department: Cardiothoracic Surgery

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#### Purpose:

This study compared the perioperative outcomes after endoscopic-assisted minimally invasive coronary artery bypass grafting (Endo-CAB) with conventional sternotomy approaches in both single and multivessel coronary artery disease (CAD), performed at the Catharina Hospital in Eindhoven.

#### Methods:

We included patients between 2022 and 2025 undergoing off-pump Endo-CAB (total n=505) and compared outcomes with conventional sternotomy surgery using propensity score matching (PSM). After PSM 136 Endo-CAB's were compared to 130 sternotomy procedures for single vessel disease (1:1 ratio); and 73 total arterial Endo-CAB's were compared to 137 sternotomy procedures for multivessel disease (1:2 ratio). We used 'textbook outcome' as a patient-orientated outcome measure, defined as the absence of 30-day mortality, re-exploration for bleeding, postoperative ischaemia, cardiac tamponade, cerebrovascular events, wound infection, new onset arrhythmias, pneumonia, placement of chest drains and prolonged hospital stay (>7 days).

#### Results:

Endo-CAB demonstrated significantly higher rates of textbook outcome in both single-vessel (81.9% vs. 59.6%, p<0.001) and multivessel CAD (78.1% vs. 59.1%, p=0.009) compared to sternotomy. Patients undergoing Endo-CAB had shorter hospital stay (single-vessel: 3.0 vs. 5.0 days, p<0.001; multivessel: 4.0 vs. 6.0 days, p<0.001) and reduced blood loss (single-vessel: 225 vs. 450 mL, p<0.001; multivessel: 360 vs. 490 mL, p<0.001).

#### **Conclusion:**

Minimally invasive single-vessel and multivessel Endo-CAB provided superior perioperative outcomes compared to conventional sternotomy bypass surgery. These findings support the broader adoption of minimally invasive techniques in coronary revascularization.

#### Keywords:

Minimally invasive bypass grafting, Endo-CAB, CABG

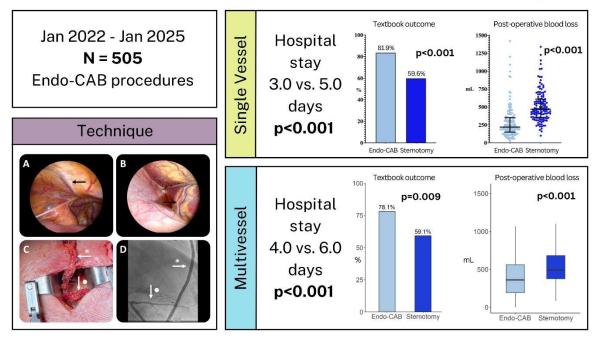


Figure:

### Outcome After Endoscopic Coronary Artery Bypass Grafting Compared to Conventional Bypass Surgery



Ferdi Akca, De Qing Görtzen, Fleur Sampon, Koen Teeuwen, Pim Tonino & Joost Ter Woorst





#### VARC-HBR Criteria Validation in Anticoagulated TAVI Patients

Presenting author: D.C. Overduin Department: Caridology

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#### Purpose:

Bleeding remains frequent after transcatheter aortic valve implantation (TAVI). Recently, the Valve Academic Research Consortium High Bleeding Risk (VARC-HBR) criteria were introduced to identify patients at (very) high risk of bleeding. This study aimed to evaluate the validity of the VARC-HBR criteria for predicting bleeding risk in TAVI patients and compare its performance with other existing criteria.

#### Methods:

Data were obtained from the POPular PAUSE TAVI trial, a randomized clinical trial which evaluated the safety and efficacy of continuation versus interruption of oral anticoagulation during TAVI. Major and minor bleeding risk criteria were identified at baseline, and bleeding events were captured up to 30 days after TAVI. Patients were classified into three groups: with  $\leq 1$  minor criterion (moderate risk), with 1 major or 2 minor criteria (high risk), and with  $\geq 2$  major or  $\geq 3$  minor criteria (very high risk).

#### **Results:**

A total of 856 patients were included: 332 (39%) were classified at moderate bleeding risk, 337 (39%) at high bleeding risk, and 187 (22%) at very high bleeding risk. Major bleeding occurred in 4.2% of moderate-risk patients, 9.5% in the high-risk group, and 15.0% in the very high-risk group (p<0.001). Receiver operating characteristics analysis showed a moderate discriminative performance (area under the curve = 0.64, 95% CI: 0.58–0.70). Despite higher-than-expected event rates, the VARC-HBR criteria demonstrated good calibration with observed outcomes.



#### **Conclusion:**

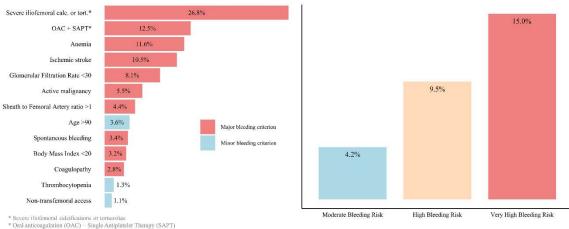
The VARC-HBR criteria effectively identified distinct subgroups with stepwise increase in major bleeding post-TAVI. However, its predictive performance for individual risk was moderate.

#### Keywords:

Oral anticoagulation, Bleeding Risk, TAVI

#### Figure:

Prevalence of VARC-HBR criteria and incidence of major bleeding stratified into three risk groups as defined by the VARC-HBR criteria.





#### Validation of the Dutch and Danish Version of the Toronto Aortic Stenosis Quality of Life Questionnaire in Patients Undergoing TAVI: a Pre-Specified POPular PAUSE TAVI Substudy.

Presenting author: P.J.A. van Nuland Department: Cardiology

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#### Purpose:

The Toronto Aortic Stenosis Quality of Life Questionnaire (TASQ) was recently developed to assess health-related quality of life in patients with aortic stenosis. This study aimed to validate the Dutch and Danish versions of the TASQ among patients undergoing transcatheter aortic valve implantation (TAVI).

#### Methods:

This pre-specified POPular PAUSE TAVI substudy was designed as a prospective observational validation study with repeated cross-sectional quality of life measurements. Dutch and Danish translations of the TASQ were obtained before the start of patient enrollment. The Kansas City Cardiomyopathy Questionnaire (KCCQ) was used as reference standard. Questionnaires were completed before TAVI, and at 30 and 90 days follow-up. **Results:** 

A total of 811 patients were included, 92.0% were Dutch or Belgian and 8.0% were Danish. The response rate was 91.2% before TAVI, 89.6% at 30 days, and 86.8% at 90 days followup. The TASQ total score improved significantly from baseline to 30 days (68.7 ±19.1 vs. 83.5 ±18.9; p<0.001) and stabilized at 90 days (83.9 ±19.4; p=0.20), in line with changes observed in the KCCQ summary scores (Figure 1). Internal consistency for the TASQ score was excellent, with Cronbach's  $\alpha$  being respectively 0.91, 0.93 and 0.94 over time. The TASQ total score demonstrated high correlation with the KCCQ overall summary score (0.82), indicating good construct validity. Floor and ceiling effects were minimal.

#### Conclusion:

The Dutch and Danish versions of the TASQ are reliable, valid, and responsive for measurement of health-related quality of life in patients with severe aortic stenosis undergoing TAVI.

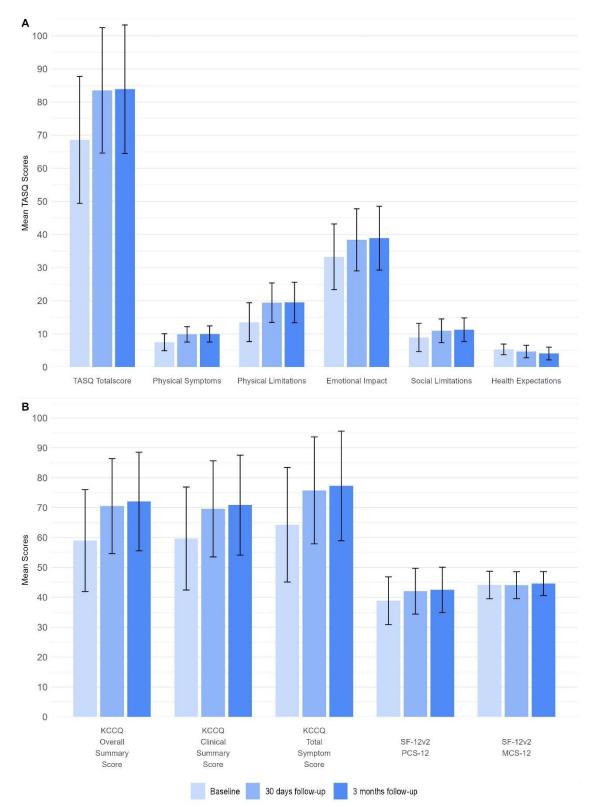
#### Keywords:

Aortic Stenosis, Transcatheter aortic valve implantation (TAVI), Toronto Aortic Stenosis Quality of Life Questionnaire (TASQ)



Figure:

Figure 1. A) TASQ scores during follow-up. B) KCCQ and SF-12v2 scores during follow-up.





#### **Clinical Characteristics and Outcomes of Mitral Regurgitation Patients Stratified by Atrial and Ventricular Dysfunction in the SMILE Registry** Presenting author: M.J.M. Welman Department: Cardiology

M.J.M. Welman (Maastricht University Medical Centre+, Maastricht; Cardiovascular

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#### Purpose:

Mitral regurgitation (MR) is often asymptomatic, leading to delayed diagnosis and treatment. The Significant Insufficiency Limburg Evaluation (SMILE) registry, which collects data from all hospitals in Limburg, the Netherlands, was established to evaluate disease progression and identify predictors of successful treatment. This study provides an overview of the clinical characteristics of MR patients classified by atrial and/or ventricular dysfunction, aiming to raise clinical awareness and support personalized treatment strategies.

#### Methods:

The SMILE registry includes all patients with moderate-to-severe MR. In a recent interim analysis, patients were classified into four groups: isolated MR (n=35), atrial-dysfunctional MR (n=159), ventricular-dysfunctional MR (n=25), and atrial-ventricular-dysfunctional MR (n=25). The classification was based on left atrial volume index (>42 ml/m<sup>3</sup>), left ventricular end-diastolic diameter (>53 female mm, >59 mm male), and left ventricular ejection fraction (<45%). Key demographics, echocardiographic parameters, and quality of life outcomes were analyzed.

#### **Results:**

No significant differences in physical and mental quality of life were observed across groups. Male patients were most prevalent in the atrial-ventricular-dysfunctional group (68.0%). Primary MR was most common in isolated MR (80%) and least in atrial-ventricular-dysfunctional MR (12.0%). Among patients with one year of follow-up, the atrial-ventricular-dysfunctional group had the highest rate of heart failure hospitalizations (22.2%). This group also had the highest percentage of cases referred to heart team discussion, although mitral valve interventions were more frequent in atrial-dysfunctional MR.

#### **Conclusion:**

The SMILE registry highlights diverse MR manifestations. Despite hemodynamic differences, quality of life remains similar across groups. Further follow-up will clarify long-term outcomes and refine patient-specific treatment strategies.



#### Keywords:

Mitral Regurgitation, Atrial and Ventricular Dysfunction, SMILE Registry

#### Figure:

Table 1: Clinical Characteristics and Outcomes of Mitral Regurgitation Patients Stratified by Atrial and/or Ventricular Dysfunction. Data is represented as median [p25–p75] or n (%). ERO: Effective Regurgitant Orifice; MI: Mitral Insufficiency; MVP: Mitral Valve Repair; NYHA: New York Heart Association Functional Class; PISA: Proximal Isovelocity Surface Area; sPAP: Systolic Pulmonary Artery Pressure; TEER: Transcatheter Edge-to-Edge Repair; TI: Tricuspid Insufficiency.

	Isolated MI	Atrial dysfunction	Ventricular Dysfunction	Atrial- ventricular dysfunction	
Baseline	n=35	<i>n</i> =159	n=25	n=25	
Age	71.0 [64.0,78.5]	76 [69.0, 81.0]	73.0 [64.0,80.0]	75.0 [68.0, 78.0]	
Male	19 (54.3)	95 (59.7)	15 (60.0)	17 (68.0)	
NYHA					
t	24 (68.6)	82 (51.6)	9 (36.0)	9 (36.0)	
Ш	7 (20.0)	59 (37.1)	13 (52.0)	13 (52.0)	
III	3 (8.5)	17 (10.7)	3 (12.0)	3 (12.0)	
IV	1 (2.9)	1 (0.6)	0 (0.0)	0 (0.0)	
Atrial fibrillation	4 (11.4)	53 (33.3)	8 (32.0)	5 (20.0)	
Pacemaker rhythm	2 (5.7)	9 (5.7)	3 (12.0)	2 (8.0)	
Heart rate	79.0 [70.0, 88.0]	72.0 [63.0, 84.0]	73.0 [64.0, 87.0]	67.5 [58.0, 77.5]	
Aetiology					
Primary	28 (80)	99 (62.3)	9 (36.0)	3 (12.0)	
Secondary	2 (5.7)	46 (28.9)	14 (56.0)	21 (84.0)	
Unknown	5 (14.3)	14 (8.8)	2 (8.0)	1 (4.0)	
MI grade					
П	16 (45.7)	50 (31.4)	9 (36.0)	9 (36.0)	
III	14 (40.0)	55 (34.6)	8 (32.0)	10 (40.0)	
IV	5 (14.3)	54 (34.0)	8 (32.0)	6 (24.0)	
ERO	0.24 [0.14, 0.41]	0.26 [0.18, 0.40]	0.22 [0.19, 0.32]	0.22 [0.15, 0.30]	
Regurgitation	15.0 [11.0, 19.5]	37.20 [24.0, 48.0]	34.15 [31.0, 39.3]	29.8 [27.7, 37.9]	
volume	rsid Proticestations (contractions)			47 62 574501 89 1426 5446 51	
e/a ratio	1.1 [0.8, 1.3]	1.3 [1.1, 1.9]	1.2 [0.8, 1.5]	1.4 [1.1, 2.2]	
E wave	89.1 [72.7, 108.0]	102.2 [78.1, 127.3]	92.1 [76.4, 104.0]	93.4 [72.1, 119.0]	
Vena contracta	5.0 [4.0, 6.0]	6.0 [5.0, 7.2]	5.4 [3.9, 6.2]	6.2 [6.0, 8.2]	
Pisa radius	6.4 [5.0, 8.8]	8.10 [6.8, 11.8]	8.0 [6.5, 9.0]	7.5 [6.2, 9.6]	
sPAP	28.0 [25.0, 38.30]	32.6 [26.1, 40.0]	32.7 [25.4, 39.0]	35.0 [28.0, 40.0]	
TI					
None	10 (28.6)	43 (27.0)	5 (20.0)	4 (16.0)	
Trace	7 (20.0)	22 (13.8)	5 (20.0)	6 (24.0)	
Mild	14 (40.0)	56 (35.2)	10 (40.0)	9 (36.0)	
Moderate	2 (5.7)	27 (17.0)	3 (12.0)	5 (20.0)	
Severe	2 (5.7)	11 (7.0)	2 (8.0)	1 (4.0)	
Follow-up 1 year	<i>n</i> =12	n=38	<i>n</i> =9	<i>n=</i> 9	
Heart failure	0 (0.0)	0 (0.0)	0 (0.0)	2 (22.2)	
admission					
Mortality	0 (0.0)	2 (5.3)	1 (11.1)	0 (0.0)	
Heart team	1 (8.3)	9 (23.7)	2 (22.2)	5 (55.6)	
discussion					
TEER	0 (0.0)	1 (2.6) 0 (0.0) 1 (		1 (11.1)	
MVP	0 (0.0)	7 (18.4)	0 (0.0)	0 (0.0)	
Carillon	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)	



#### Epicardial Fat Increases over Time after Heart and Lung Transplantation

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#### Purpose:

Epicardial fat (EF) has gained attention as indicator of cardiovascular disease. Posttransplantation immunosuppression is known to increase cardiometabolic risk factors, such as obesity, diabetes and hypertension. It remains unknown whether it also effects the EF amount. We performed a pilot study to measure EF over a one-year period.

#### Methods:

We included heart (HT) or lung (LT) transplantation patients with CT-scans post-transplant and one year later. Anonymized, randomized scans were assessed for the EF-degree by two independent observers at three pre-defined spots, using a quantitative scale (1[minimal EF present]-4[maximum EF present] per spot; total EF 3-12). EF-differences were calculated. Data on body mass index (BMI), steroid usage and rejection was extracted from the patient database.

#### **Results:**

We included 19 HT patients and 137 LT patients, shown in Table 1.

At transplantation, HT patients were younger than LT patients (54[IQR39-61] vs. 60[IQR53-64], p=0.012) and less often female (16% vs. 45%, p=0.023). Rejection episodes and steroid usage in the first year post-transplant did not differ between the groups.

EF increased in HT patients from 4[IQR3-4] to 4[IQR4-5] (p=0.021) and in LT patients from 5[IQR4-6] to 6[5-7] (p<0.001). BMI remained stable in HT patients, but increased in LT patients from 24[IQR21-27] to 25[IQR22-28] (p<0.001).

Higher BMI at follow-up is associated with an EF-increase (OR1.14, 95%CI1.00–1.30, p=0.047).

#### **Conclusion:**

This pilot shows the EF-degree increased among thoracic transplant patients over one year, associated with BMI. Targeting EF might be a potential strategy to reduce cardiovascular risks in transplant patients. This will be studied in the DAPARHT-study.

#### Keywords:

Heart transplantation, Metabolic syndrome, Cardiometabolic risk



#### Figure:

Table 1: baseline characteristics

[]=IQR, ()=95%CI, BMI = body mass index, CT = computed tomography, EF = epicardial fat, HT = heart transplantation, kg = kilogram, LT = lung transplantation, m = meter, mg = milligram, n = number, p = p-value, Tx = transplantation,

	HT (n=19)			LT (n=137)			р
Age at Tx years	54[39-61]			60 [53-64]			0.012
Female n, %	3 (16)			62 (45)			0.023
Patients with rejection episodes in first year <i>n, %</i>	6 (32)			62 (45)			0.33
Steroid usage in first year <i>n, %</i>	19 (100)			137 (100)			-
СТ	Baseline	Follow-up	р	Baseline	Follow-up	р	
Days post-Tx	35 [15-50]	411 (374-448)	-	19 [14-32]	388 [345-437]	-	1
Total EF score on CT	4 [3-4]	4 [4-5]	0.021	5 [4-6]	6 [5-7]	<0.001	1
BMI, kg/m <sup>2</sup>	24 (22-26)	24 (22-26)	0.56	24 [21-27]	25 [22-28]	<0.001	1



# Less Symptom Improvement in Patients Undergoing TAVI with Concomitant COPD, Atrial Fibrillation and Heart Failure

Presenting author: K.H. van Bergeijk Department: Cardiology

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#### Purpose:

Comorbidities like a history of chronic obstructive pulmonary disease (COPD), atrial fibrillation (AF) and heart failure (HF) can cause similar symptoms as aortic stenosis (AS). However, how they influence symptom improvement and long-term outcomes after transcatheter aortic valve implantation (TAVI) is unclear.

#### Methods:

A history of COPD, AF and HF were collected in three TAVI cohorts (Groningen, Netherlands, Brescia, Italy and Bern, Switzerland). Symptom improvement was defined as ≥1 improvement of New York Heart Association (NYHA) functional class at 12 months (6 months or 30 days if not available), compared with baseline. Adverse events were defined as cardiovascular mortality, stroke or heart failure hospitalisation at 1 and 5-year follow-up (VARC-3).

#### **Results:**

The pooled analysis included 5173 patients (mean age of 81.5 years and 51% female). Patients with COPD, AF or HF were accepted for TAVI at significantly lower mean aortic valve pressure gradients and low-flow, low-gradient AS and higher NYHA class. After adjusting for sex, NYHA class, age, other comorbidities, flow-type and cardiac damage stage before TAVI, a history of COPD (Odds Ratio (OR) 1.75 (95% Confidence interval (CI) 1.11, 2.76), p=0.017) and a history of HF (OR: 1.65 (95% 1.05, 2.60), p=0.031) were associated with lack of symptom improvement, while AF was not (OR: 1.12 (0.71, 1.740, p=0.629). Patients with COPD, AF or HF had higher risks of adverse events and lower survival at long-term follow-up.

#### Conclusion:

Patients with symptomatic AS and concomitant comorbidities of COPD, AF and HF, undergo TAVI at a lower severity of AS, and have a higher symptomatic burden and higher cardiac damage stage before TAVI. They have a greater risk of residual symptoms, and a higher risk of long-term adverse events.

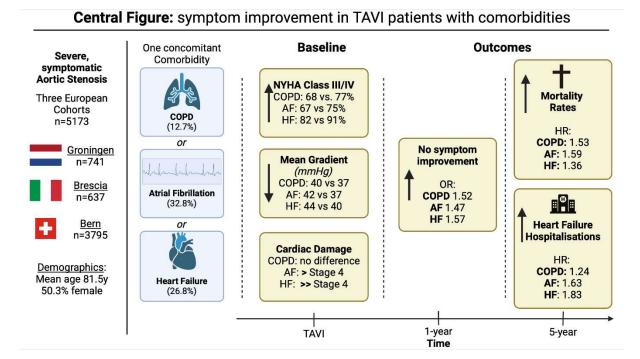


#### Keywords:

TAVI, Symptoms, Comorbidities

#### Figure:

Central Figure, showing main results of this retrospective, cohort study.





#### 1-Year Survival of Frail Patients Similar to the Overall Group after Transcatheter Edgeto-Edge Repair for Mitral Regurgitation

Presenting author: A.E. Geerlings Department: Cardiology

<u>A.E. Geerlings (Amsterdam UMC, Amsterdam);</u> D. Robbers-Visser (Amsterdam UMC, Amsterdam); S.M. Boekholdt (Amsterdam UMC, Amsterdam); M.M. Vis (Amsterdam UMC, Amsterdam); M. A.M. Beijk (Amsterdam UMC, Amsterdam); J.S. Lemkes (Amsterdam UMC, Amsterdam); R.J. de Winter (Amsterdam UMC, Amsterdam); J. Baan (Amsterdam UMC, Amsterdam); B.J. Bouma (Amsterdam UMC, Amsterdam)

#### Purpose:

Mitral valve transcatheter edge-to-edge repair (M-TEER) is a well-accepted treatment in patients with severe mitral regurgitation (MR) considered high-risk for conventional surgery. In general the outcome is excellent, but it is unknown whether this is also valid for patients with low body-mass index (BMI), advanced age, or poor left ventricular ejection fraction (LVEF).

#### Methods:

This retrospective single-center cohort study included all consecutive patients who underwent an M-TEER procedure at the Amsterdam UMC. Patients were classified into three frail groups: (1) BMI < 20 kg/m<sup>2</sup> (2) Age > 85, and (3) LVEF< 30%. The primary endpoint was defined as all-cause mortality 12 months after M-TEER. Kaplan-Meier curves were used to analyse survival.

#### **Results:**

We included a total of 178 patients, 90 (51%) male, mean age 75.7 years, 110 (61%) had secondary MR. A total of 12 (6.7%) had an BMI <20, 27 (15.2%) were >85 years old, 50 (28%) had a LVEF <30%. Overall survival at 12 months was 83% patients (148), for those with the BMI<20 group 75% (9), 84% (42) with a LVEF<30% and 81% (22) with age>85 years, all not significant (Figure 1).

#### Conclusion:

Our results show that 12-months survival of extreme frail patients undergoing M-TEER does not significantly differ from the overall M-TEER population. Therefore, M-TEER can still be considered in extreme frail patients.

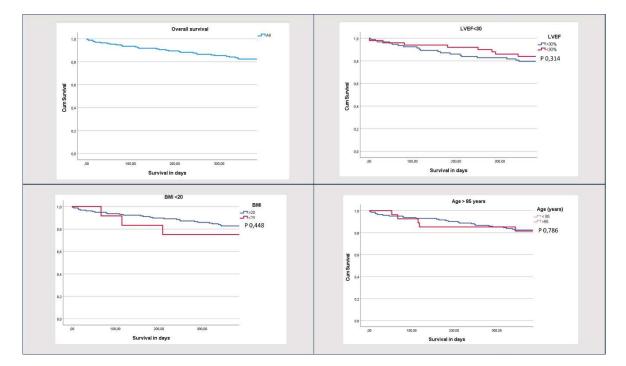
#### Keywords:

M-TEER, Valvular disease, Mitral valce



#### Figure:

1-year survival of frail patient groups





#### Safety of Left Atrial Appendage Amputation During Cardiothoracic Surgery

Presenting author: Marc M. Terpstra Department: Cardiologie

<u>M.M. Terpstra (Amsterdam UMC, Amsterdam);</u> M.M. Terpstra (Amsterdam UMC, Amsterdam); M.H. van der Ree (Amsterdam UMC, Amsterdam); N.W.E. van den berg (Amsterdam UMC, Amsterdam); W.J.P van Boven (Amstedam UMC, Amsterdam); A.H.G. Driessen (Amsterdam UMC, Amsterdam); J.R. de Groot (Amsterdam UMC, Amsterdam)

#### Purpose:

Patients with atrial fibrillation (AF) are at risk for ischemic strokes, often originating from the left atrial appendage (LAA). Preventive LAA amputation (LAAA) during cardiac surgery has been shown to reduce ischemic stroke risk, both in patients with and without AF. However, the short-term safety and functional implication of LAAA in non-AF patients remain poorly understood. Besides possible surgical complications, there are suggestions that LAAA could lead to postoperative AF or influence neurohumoral changes resulting in fluid overload. Purpose: To evaluate the safety of LAAA in patients without a history of AF undergoing routine cardiac surgery.

#### Methods:

Patients underwent elective cardiac surgery between May 5 2015 and April 18 2018 in two high volume centers. Main inclusion criteria were a CHA2DS2-VASc≥ 2 and no history of AF. Patients without a history of AF, that participated in the PREDICT-AF study (NCT03130985) underwent concomitant LAAA and were compared with patients undergoing cardiothoracic surgery who were approached for participation in PREDICT-AF, but declined and did not undergo LAAA. Informed consent for the retrospective use of data was obtained through an opt-out procedure in these patients. The primary outcome of this analysis was the number of patients with any serious adverse event within 30 days postoperatively. Secondary outcomes were AF within 30 days postoperatively, death, rethoracotomy, time on extra corporal circulation (ECC) and heart failure related symptoms assessed through congestion on x-chest and weight trends. Adverse events were independently adjudicated by a cardiothoracic surgeon using pre-specified definitions

#### **Results:**

One hundred and fifty patients in PREDICT-AF underwent LAAA. Two hundred and eightyfour eligible patients declined participation in PREDICT-AF and formed the control group. Patients in the LAAA group were more frequently male (87.3% vs 72.5%; p=0.001), were taller (176.0cm  $\pm$  8.2 vs 172.6cm  $\pm$  9.9; p<0.001) and weighed more (86.1kg [IQR 80.0 -92.2] vs 81.6kg [IQR 71.9 - 91.1]; p=0.001) compared to controls. There were no significant differences in occurrences of serious adverse events (8% vs 12%; p=0.265), deaths (1.3% vs 1.8%; p=1) or rethoracotomies (3.3% vs 1.8%; p=0.483) between the LAAA and control group. Also, there was no difference in the incidence of postoperative AF (57, 38% vs 90, 31.7%; p=0.225), ECC time (104.5 minutes [IQR 81.0 - 129.0] vs 98.0 [IQR 80.0 - 124.5] p=0.371) or the presence of chest x-ray congestion (26.0% vs 27.8%; p=0.771) between the groups (Figure 1A). The spline plot of Perioperative weight change relative to baseline over time , reveals no notable differences between the two groups (Figure 1B). **Conclusion:** 

#### LAAA during routing cardiothoracic surgery is not associated with more surgical



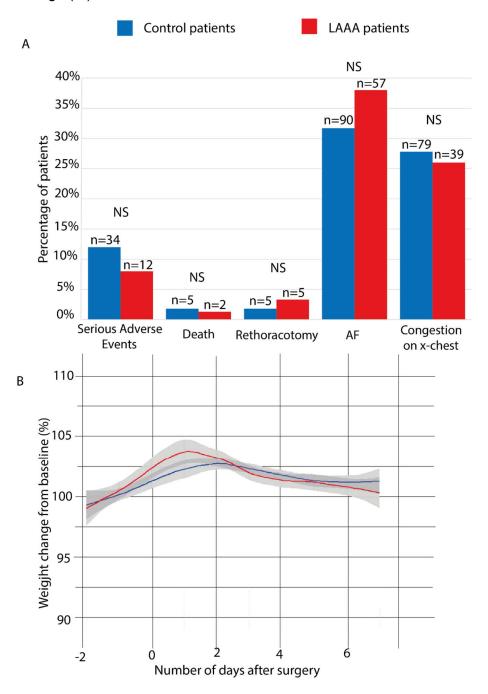
complications, postoperative atrial arrhythmias or heart failure related symptoms. Given the generally high AF risk in patients undergoing cardiothoracic surgery, a strategy to preemptively resect the LAA may be feasible and safe.

#### Keywords:

Left atrial appendage amputation, Postoperative safety, Cardiac surgery

#### Figure:

A. Percentage of patients with serious adverse events, death, a rethoracotomy or AF in 30 days after surgery and congestion on postoperative chest x-ray. B. Perioperative weight change (%) relative to baseline over time.





# SESSIE 5: (Acute) Heart failure

	Theaterzaal	Voorzitters:
		dr. Olivier Manintveld, cardioloog Erasmus MC
		dr. Joëlle Elias, AIOS UMC Utrecht
1	09.00 - 09.10	Mean Arterial Pressure Levels in Cardiogenic Shock from Acute
		Myocardial Infarction: A Meta-Analysis
		Sanne ten Berg (Amsterdam UMC, Amsterdam)
2	09.11 - 09.21	Red Blood Cell Distribution Width: a Novel Predictive Marker for
		New-Onset Heart Failure in the General Population
		Danielle J. Noordermeer (Erasmus MC, Rotterdam)
3	09.22 - 09.32	Loop diuretic Use Before an Acute Heart Failure Hospitalization
		Drives Natriuretic Response but Not the Efficacy of Natriuresis-
		Guided Diuretic Therapy
		Lara E.E.C. Zonneveld (UMCG, Groningen)
4	09.33 - 09.43	The Impact of Intravenous Nitroglycerin on Decongestion in a
		Propensity Matched Acute Heart Failure Cohort
		Mick Hoen (Zuyderland MC, Heerlen)
5	09.44 - 09.54	Clinical Profiles and Prognostic Impact of Residual Intravascular
		and Tissue Congestion in Acute Heart Failure
		Daan C.H. Ceelen (University of Groningen, Groningen)
6	09.55 - 10.05	Frailty in Elderly Heart Failure Patients, How Applicable is the VMS
		Frailty Score?
		Marlies Niesing-Lut (Alrijne Ziekenhuis, Leiderdorp)
7	10.06 - 10.16	Pathophysiological Pathways Related to Elevated Soluble ST2
		Concentrations and Survival in Patients with Heart Failure
		Thijmen S.A. Bergwerff (University of Groningen, UMC Groningen)
8	10.17 - 10.27	Individual Natriuretic and Diuretic Response in Acute Heart
		Failure: Insights from the PUSH-AHF Pharmacological Substudy
		Iris E. Beldhuis (UMCG, Groningen)



Session 5: (Acute) Heart failure Abstract 1

#### Mean Arterial Pressure Levels in Cardiogenic Shock from Acute Myocardial Infarction: A Meta-Analysis Presenting author: S. ton Borg

Presenting author: S. ten Berg Department: Cardiologie

<u>S. ten Berg (Amsterdam UMC, Amsterdam);</u> M. Bogerd (Amsterdam UMC, Amsterdam); E.J. Peters (Amsterdam UMC, Amsterdam); K. Ameloot (Ziekenhuis Oost Limburg, Genk); J. Grand (Copenhagen University Hospital Rigshospitalet, Copenhagen); J.J. Russo (University of Ottaway Heart insitiute, Ottawa); J.C. Jentzer (Mayo Clinic, Rochester); P. Di Santo University of Ottaway Heart insitiute, Ottawa); R. Mathew University of Ottaway Heart insitiute, Ottawa); B. Hibbert (Mayo Clinic, Rochester); J. Kjaergaard (Copenhagen University Hospital Rigshospitalet, Copenhagen); M.A.S. Meyer (Copenhagen University Hospital Rigshospitalet, Copenhagen); M.B. Skrifvars (Helsinki University Hospital, Helsinki); B.W. Roberts (Cooper University Health Care, Camden); A. Malekzadeh (Amsterdam UMC, Amsterdam); W.K. Lagrand (Amsterdam UMC, Amsterdam); A.E. Engström (Amsterdam UMC, Amsterdam); L.C. Otterspoor, A.P.J. Vlaar (Amsterdam UMC, Amsterdam); J.P.S. Henriques (Amsterdam UMC, Amsterdam)

#### Purpose:

Optimal mean arterial pressure (MAP) targets for improving outcomes in patients with acute myocardial infarction (AMI) related cardiogenic shock (CS) and out-of-hospital cardiac arrest (OHCA) remain unclear. This comprehensive systematic review and meta-analysis aimed to evaluate the effects of different MAP levels on short-term mortality in AMICS patients, including those with AMI-OHCA.

#### Methods:

We conducted a systematic search of MEDLINE (OVID), EMBASE (OVID), CINAHL (Ebsco) and Cochrane CENTRAL databases. Eligible studies reported outcomes for AMICS patients for at least two groups of different MAP levels. Both randomized clinical trials (RCTs) and observational studies were eligible. Authors were proactively contacted for supplementary AMI data. Random-effects models were used to pool data.

#### **Results:**

Of 7,728 screened studies, 57 were assessed for eligibility, and 11 were included in the final analysis (4 RCTs and 7 observational studies). This meta-analysis included 3,846 all-CS patients, of whom 1,679 AMICS. In the AMICS patients, observational data indicated higher mortality in the low-MAP group, but both combined RCT and observational data (42.3% vs. 33.6%, RR 1.30, 95% CI 0.92-1.84) and RCTs alone (34.9% vs. 39.4%, RR 0.88, 95% CI 0.70-1.10) showed no significant difference between low- and high-MAP groups. **Conclusion:** 

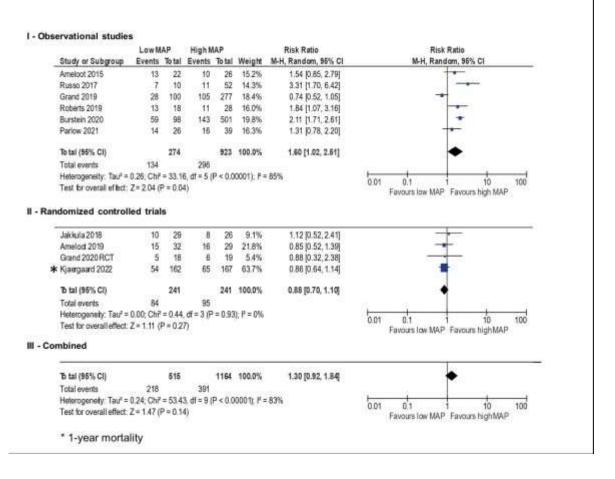
Our meta-analysis showed no significant difference in mortality between high- and low-MAP levels in AMICS patients, including AMI-OHCA. Although observational data indicated an association between the low-MAP group and increased short-term mortality, this was not observed in RCTs or when combining observational and RCT data. Future research should prioritize identifying optimal, potentially lower, blood pressure targets.

#### Keywords:

Cardiogenic shock, Myocardial infarct, Mean arterial pressure



#### Figure:





Session 5: (Acute) Heart failure Abstract 2

# Red Blood Cell Distribution Width: a Novel Predictive Marker for New-Onset Heart Failure in the General Population

Presenting author: D.J. Noordermeer Department: Cardiometabolic Epidemiology

<u>D.J. Noordermeer (Erasmus MC, Rotterdam);</u> D.J. Noordermeer (Erasmus MC, Rotterdam); M. Kavousi (Erasmus MC, Rotterdam); A.E. van den Bosch (Erasmus MC, Rotterdam)

#### Purpose:

Red blood cell distribution width (RDW), a routine component of complete blood counts, is inexpensive and widely available, making it a promising screening tool for heart failure (HF). This study evaluates RDW's predictive value for new-onset HF in the general population and compares its performance with that of NT-proBNP.

#### Methods:

This study included 5,814 individuals (57% women) without prior HF from a prospective population-based cohort with available RDW data. For NT-proBNP, a separate cohort of 3,393 participants was used. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated. The fully adjusted model incorporated the easily accessible Pooled Cohort Equations (PCE) variables, including systolic blood pressure, total and high-density lipoprotein (HDL) cholesterol, diabetes, smoking, and antihypertensive medication use. The added predictive value of RDW and NT-proBNP beyond the PCE model was quantified using the  $\Delta$ c-statistic.

#### **Results:**

Over a median follow-up of 7 years, 433 new HF events occurred, corresponding to an incidence rate of 10.4 per 1,000 person-years. In the fully adjusted model, each 1% increase in RDW was associated with a 1.26-fold higher HF risk (HR 1.26, 95% CI, 1.18–1.36; P < 0.001). Individuals in the highest RDW quartile had an HR of 2.07 (95%, 1.58-2.72) for HF. Adding RDW to the PCE model significantly improved predictive performance ( $\Delta$ c-statistic = 0.014), comparable to NT-proBNP.

#### Conclusion:

Elevated RDW is a strong predictor of new-onset HF. Its widespread availability, low costs and robust predictive power, suggest a promising role for RDW as a biomarker for HF risk stratification.

#### Keywords:

Heart failure, RDW, Risk prediction



Session 5: (Acute) Heart failure Abstract 3

Loop diuretic Use Before an Acute Heart Failure Hospitalization Drives Natriuretic Response but Not the Efficacy of Natriuresis-Guided Diuretic Therapy Presenting author: L.E.E.C. Zonneveld Department: Cardiologie

<u>L.E.E.C. Zonneveld (UMCG, Groningen);</u> L.E.E.C. Zonneveld (UMCG, Groningen); K. Damman (UMCG, Groningen); I.E. Beldhuis (UMCG, Groningen); P. van der Meer (UMCG, Groningen); A.A. Voors (UMCG, Groningen); J.M. ter Maaten (UMCG, Groningen)

#### Purpose:

Diuretic resistance in acute heart failure (AHF) is common, especially in patients on loop diuretics before admission. It is unclear whether natriuresis-guided therapy differs based on prior diuretic use or helps overcome resistance. In this study the effects of natriuresis guided therapy is compared between patients with and without outpatient loop diuretic use. **Methods:** 

In this pre-specified sub-analysis of the PUSH-AHF trial, with the dual primary outcome of 24 h natriuresis and the combined outcome of heart failure hospitalization or all-cause mortality at 180 days, the association between outpatient loop diuretic use, outcomes and the effect of natriuresis-guided therapy as compared with standard of care was evaluated.

#### **Results:**

Out of 310 randomized patients, 133 (43%) patients did not use loop diuretic therapy prior to admission, 65 (21%) used 0-1 mg burnetanide (or equivalent) and 112 (36%) used >1 mg. Outpatient loop diuretic use did not significantly modify the treatment effect of natriuresis-guided therapy on natriuresis at 24 h (p-interaction = 0.420) and the combined endpoint of HF rehospitalization or all-cause mortality at 180 days (p-interaction = 0.881). Patients with outpatient loop diuretic use generally had lower spot urinary sodium during the first 48 h compared to patients with no outpatient loop diuretic use. The group with >1mg outpatient burnetanide use had the lowest spot urinary sodium and required more frequent intensification per protocol in the beginning of the treatment, despite starting with higher dosages as standardized per protocol.

#### Conclusion:

Acute heart failure patients with loop diuretic use prior to admission showed reduced natriuresis and diuresis, especially at higher doses and regardless of standardized starting dosage. The effect of natriuresis guided diuretic therapy on decongestion was however maintained over the entire spectrum of outpatient pre-admission loop diuretic use.

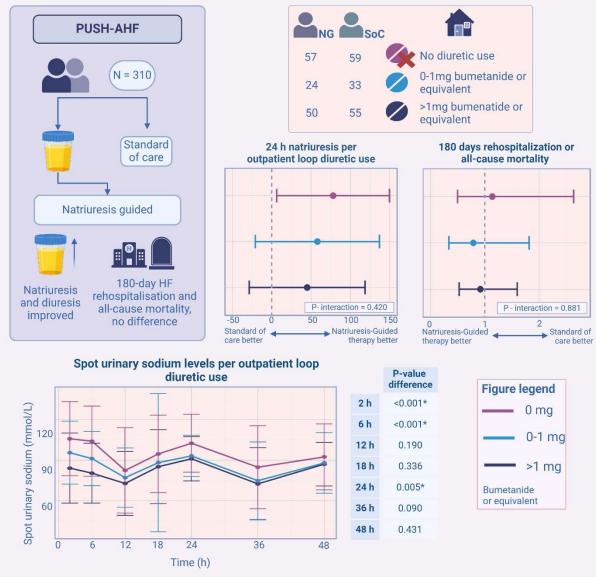
#### **Keywords:**

Loop diuretics, Acute Heart Failure, Natriuresis



Figure:







Session 5: (Acute) Heart failure Abstract 4

# The Impact of Intravenous Nitroglycerin on Decongestion in a Propensity Matched Acute Heart Failure Cohort

Presenting author: M. Hoen Department: Cardiologie

<u>M. Hoen (Zuyderland MC, Heerlen);</u> M. Hoen (Zuyderland MC, Heerlen); Mattia Pagnoni (Lausanne University Hospital, Lausanne); Paolo Meani (MUMC+, Maastricht); Sandra Sanders–Van Wijk (Zuyderland MC, Heerlen); Hans-Peter Brunner-La Rocca (MUMC+, Maastricht)

#### Purpose:

Acute heart failure (AHF) is prevalent and yields a high rate of re-hospitalization and mortality, along with increasing health care costs. IV nitroglycerin (NTG) might help with decongestion and symptom relief due to reducing venous return, lowering afterload and increasing stroke volume, but data in real-world cohorts are scarce.

#### Methods:

This was a retrospective cohort study; subjects were included between January of 2011 and March of 2017. Subjects (> 18 years), hospitalized with a primary diagnosis of AHF were eligible for this study.

Propensity score matching was used to create two comparable groups. Afterwards, univariable regression was used to assess the relationship between NTG use and weight loss, length of treatment and hospitalization and safety endpoints.

#### Results:

Of the 372 subjects included in this study, data of 192 subjects were used after propensity matching (mean age 77 years, 50% male). Delta weight loss from baseline to day 3 of hospitalization was significantly increased in the NTG group in both unmatched (standardized-B = 0.184, P = 0.006) and matched subjects (standardized-B = 0.239, P = 0.009), figure 1. There was no significant difference in duration of IV diuretic treatment or total hospitalization. There was no significant difference of hypokalemia. The NTG group showed higher in-hospital mortality, but this difference was non-significant (standardized-B = 7.472, P = 0.062).

#### Conclusion:

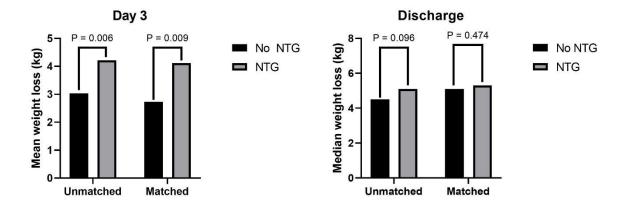
The use of IV nitroglycerin may promote short term weight loss in AHF, while showing no other significant differences. In-hospital mortality was non-significantly increased in the subjects receiving NTG.

#### Keywords:

Nitroglycerin, Acute heart failure, Decongestion



**Figure:** Figure 1: Weight loss from baseline to day 3 and discharge





Session 5: (Acute) Heart failure Abstract 5

# Clinical Profiles and Prognostic Impact of Residual Intravascular and Tissue Congestion in Acute Heart Failure

Presenting author: D.C.H. Ceelen Department: Cardiology

<u>D.C.H. Ceelen (University of Groningen, Groningen);</u> D.C.H. Ceelen (University of Groningen, Groningen); J.M. ter Maaten (University of Groningen, Groningen); G.H.D. Voordes (University of Groningen, Groningen); G. Cotter (Momentum Research, North Carolina); B.A. Davison (Momentum Research, North Carolina); G. Filippatos (Attikon University Hospital, Athens); P.S. Pang (Indiana University School of Medicine, Indianapolis); C. Gimpelewicz (Novartis Pharma, Basel); J.R. Teerlink (San Francisco Veterans Affairs Medical Center, San Francisco); A.A. Voors (University of Groningen, Groningen)

# Purpose:

Residual congestion is often observed in patients discharged from an acute heart failure hospitalisation (AHF). Residual congestion is associated with an increased risk of early mortality and rehospitalisation. Two distinct phenotypes of congestion (i.e. intravascular and tissue congestion) have been proposed. This study aims to identify clinical characteristics of residual congestion phenotypes and evaluate their relationship with clinical outcomes, including comparisons to decongested patients.

#### Methods:

Congested patients from two large AHF trials, PROTECT (Rolofylline; derivation) and RELAX-AHF2 (Serelaxin; validation), were classified based on clinical signs at day 7/discharge into intravascular (jugular venous pressure), tissue (pulmonary rales/peripheral oedema), or a combined congestion phenotype. Cox regression assessed 180-day mortality after adjusting for risk factors.

# Results:

We included 1557 patients with predominantly combined (i.e. tissue and intravascular) congestion at admission, with a median age of 72 and ejection fraction of 30%. By day 7, 580 (37%) patients had residual congestion. In these patients, intravascular congestion (n=260; 45%) was the most common phenotype, followed by combined (n=185; 32%) and tissue (n=135; 23%) phenotypes. During hospitalisation, patients with residual intravascular congestion showed a stronger diuretic response, received lower intravenous loop diuretic doses, and had shorter hospital stays compared to other residual congestion phenotypes. Compared to patients without residual congestion, those with residual intravascular and tissue congestion had increased risks of 180-day mortality (HR 1.69, 95%CI 1.15-2.49, p=0.007, and HR 2.07, 95%CI 1.25-3.41, p=0.005, respectively). In the RELAX-AHF2 substudy (n=476), where follow-up congestion measurements were available, similar results were observed.

# **Conclusion:**

At discharge from an AHF hospital admission, over one-third of patients had residual congestion. Patients with residual intravascular congestion had shown a better diuretic response and shorter hospital stay than those with residual tissue/combined congestion. However, 180-day mortality was similar in patients with residual tissue and intravascular congestion, while both had a higher mortality than patients without residual congestion.

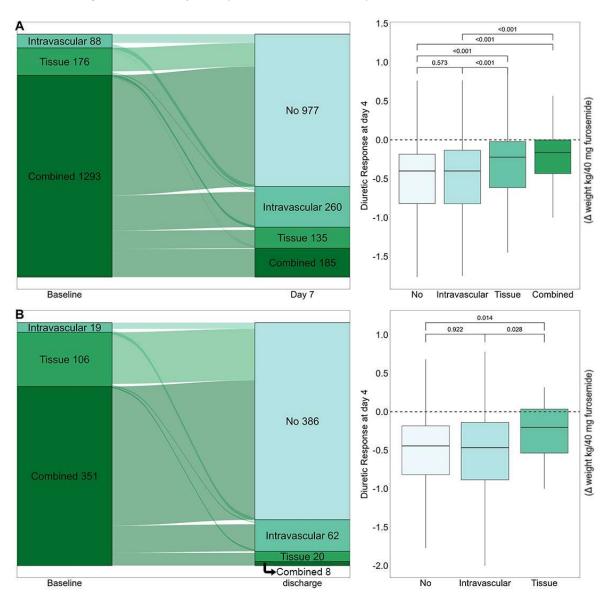


# Keywords:

Heart Failure, Congestion, Diuretic

# Figure:

Abstract Figure 1 - Temporal changes in congestion phenotypes and diuretic response per residual congestion phenotype. A) PROTECT cohort B) RELAX-AHF2 cohort.





Session 5: (Acute) Heart failure Abstract 6

Frailty in Elderly Heart Failure Patients, How Applicable is the VMS Frailty Score?

Presenting author: M. Niesing-Lut Department: Cardiologie

<u>M. Niesing-Lut (Alrijne Ziekenhuis, Leiderdorp);</u> M. Niesing-Lut (Alrijne ziekenhuis, Leiderdorp); J. van der Laken (Alrijne ziekenhuis, Leiderdorp); C.M.H.B. Lucas (Alrijne Ziekenhuis, Leiderdorp)

# Purpose:

Frailty is common in heart failure patients, especially the elderly, impacting care planning. Many hospitals use the VMS frailty score, but its applicability for heart failure patients remains unclear. We compared the VMS score in 43 patients with clinical frailty assessments by two experienced VS heart failure specialists.

# Methods:

Forty-three patients were assessed for frailty using the VMS score and clinical judgment by VS heart failure based on four frailty domains: physical, psychological, social, and functional. Patient characteristics were recorded.

# **Results:**

The cohort consisted of elderly heart failure patients (71–93 years, mean 81), with 25 males, HFrEF 46%, HFpEF 21%, and HFmrEF 33%. The VMS score identified 20 frail patients, while clinical assessment found 15. Discrepancies were observed in 11 cases: 8 were frail per VMS but not clinically, while 3 were frail by clinical judgment but not by VMS. In patients aged 80+, VMS classified 8 more as frail than clinical assessment.

# Conclusion:

The VMS frailty scale, widely used for elderly patients, yields different results in heart failure patients compared to clinical judgment. More patients were classified as frail by VMS, suggesting it captures different characteristics. This highlights the need for a heart failure-specific frailty score. Our next step is assessing patients using the HFA frailty score, with results to be presented in the future.

# Keywords:

Heart failure, Elderly, Frailty



Session 5: (Acute) Heart failure Abstract 7

Pathophysiological Pathways Related to Elevated Soluble ST2 Concentrations and **Survival in Patients with Heart Failure** Presenting author: T.S.A. Bergwerff Department: Cardiology

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#### Purpose:

In patients with heart failure (HF), elevated plasma concentrations of soluble ST2 (sST2) are strongly and consistently associated with poor clinical outcomes. However, the mechanisms linking sST2 to survival in HF patients remain unclear. We studied pathophysiological pathways related to plasma sST2 concentrations using a proteomics approach. Methods:

This study included a subset of the BIOSTAT-CHF cohort. Plasma sST2 was measured using Luminex-assay. In 467 patient plasma samples, 7253 proteins were identified using the Somalogics-assay. Kaplan-Meier and Cox-regression analyses were performed to evaluate survival. We performed linear regression for protein expression, pathway analysis using Ingenuity Pathway Analysis (IPA) and network clustering. The relationship between sST2, pathways, and survival was evaluated using causal mediation models.

#### **Results:**

Patients with high sST2 had higher NYHA-class, more signs and symptoms of HF, and higher NTproBNP concentrations. Patients with elevated sST2 had an increased 2-year mortality risk (HR=1.67, p<0.001). We found 1116 upregulated and 1250 downregulated proteins associated with ST2-concentration (FDR-adjusted p<0.05). IPA identified 12 significant pathways. The strongest upregulated pathways included extracellular matrix (ECM) degradation, translation elongation, and collagen fibrils assembly, which are critical for tissue structure. Conversely, the strongest downregulated pathways involved regulation of



insulin-like growth factor transport and uptake by IGFBPs, complement cascade, and protein phosphorylation, suggesting a change in metabolic processes and immune responses. There were 9 pathways, including ECM degradation and protein phosphorylation, found to be significant individual mediators (see figure).

#### Conclusion:

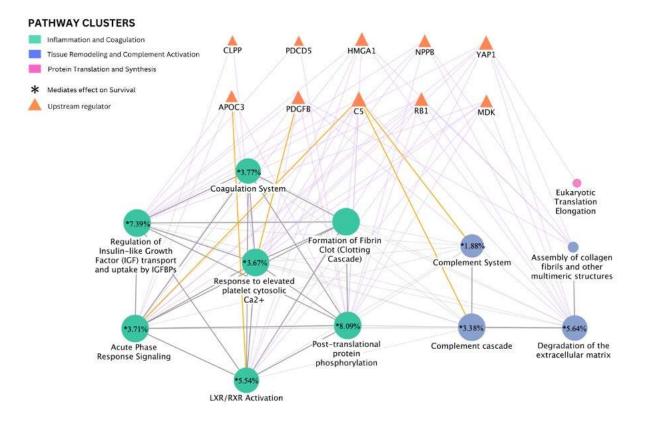
Elevated sST2 concentration correlates with upregulated pathways related to tissue structure, partially mediating the association between sST2 plasma concentration and survival.

#### Keywords:

Heart Failure, Proteomics, Biomarker

#### Figure:

Figure 1: This figure illustrates the outcomes of the pathway analysis, network clustering, and mediation analysis. Pathways identified as significant mediators of the relationship between sST2 and survival are indicated with an asterisk (\*). Percentages within the pathway nodes indicate the proportion of the total effect mediated by each pathway. Connections between pathways are represented by grey lines, indicating sharing of proteins. Upstream regulators are depicted as orange triangles, with orange lines signifying their direct presence in pathways. Purple lines indicate indirect involvement, where the regulator influences a protein within the pathway. Pathway clusters are colour-coded based on their functional categories.





Session 5: (Acute) Heart failure Abstract 8

# Individual Natriuretic and Diuretic Response in Acute Heart Failure: Insights from the **PUSH-AHF Pharmacological Substudy** Presenting author: I.E. Beldhuis

Department: Cardiology

I.E. Beldhuis (University Medical Center Groningen, Groningen); I. E. Beldhuis (University Medical Center Groningen, Groningen); J.M. ter Maaten (University Medical Center Groningen, Groningen); P van der Meer (University Medical Center Groningen, Groningen); J. E. Coster (University Medical Center Groningen, Groningen); L. Baumhove (University Medical Center Groningen, Groningen); J. A. Krikken (University Medical Center Groningen, Groningen); W. Nieuwland (University Medical Center Groningen, Groningen); D. J. van Veldhuisen (University Medical Center Groningen, Groningen); A. A. Voors (University Medical Center Groningen, Groningen); K. Damman (University Medical Center Groningen, Groningen)

# **Purpose:**

Guidelines recommend tailoring loop diuretic therapy in acute heart failure (AHF) based on the natriuretic response two hours post-dosing. However, detailed analyses of pharmacological responses in contemporary AHF patients are limited.

#### Methods:

We included a subset of 17 patients with AHF enrolled in the PUSH-AHF trial. Plasma bumetanide, sodium, creatinine, chloride, and urea levels were assessed at baseline, 2 and 6 hours after intravenous loop diuretic administration. Urinary volume, sodium, potassium. creatinine, chloride and urea were assessed at baseline and every 30 minutes for 6 hours. Urinary excretion trajectories and plasma concentrations over time were evaluated.

# **Results:**

The median age was 81 [IQR 73-85] years, 24% was female and baseline eGFR was 39 [IQR 32-44mL/min/1.73m2]. The median administered bumetanide intravenous bolus dose was 4 [IQR 2-5] mg. Median bumetanide plasma levels increased from 28ug/L to 204ug/L at 2 hours and decreasing thereafter to 44ug/L at 6 hours. Peak urine output was reached within 1 hour. Median urinary sodium increased from 61mmol/L at baseline, to a maximum of 104 mmol/L at 1.5 hours, and decreasing to 75mmol/L after 6 hours. There were marked inter-individual differences in the trajectories of natriuresis. Higher 2-hour urinary sodium was independently associated with greater 6-hour diuretic response.

#### Conclusion:

In contemporary AHF patients following a dose of loop diuretic, peak diuretic response based on urine volume is achieved within 1 hour, whereas peak urinary sodium is reached after 1.5 hours. These findings support the use of a 2-hour urinary sodium assessment to evaluate diuretic response.

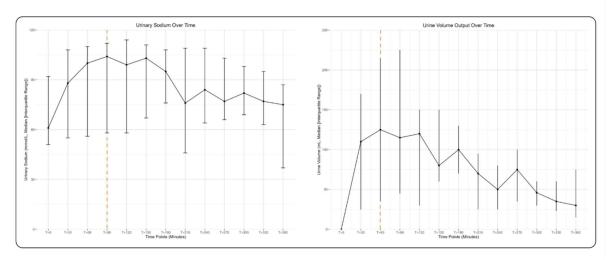
#### **Keywords:**

acute heart failure, urinary excretion trajectories, intravenous loop diuretic administration



# Figure:

Figure 1. Trajectories in urinary sodium and urine output





# **SESSIE 6: Cardiomyopathy & genetics**

	Zaal 12	Voorzitters:
		dr. Moniek Cox, cardioloog UMC Groningen
		dr. Jurrien Kuneman, AIOS Haaglanden MC
1	09.00 - 09.10	CDK4/6 Inhibitor Ribociclib Induces Cardiotoxicity Through
		Impaired E2F1-Regulated Spliceosome Assembly
		Eva Pet (UMCG, Groningen)
2	09.11 - 09.21	Obesity and Inactivity Cluster the Strongest Risk Factor for the
		Development of Heart Failure in a Population-Based Study
		Bart J. van Essen (UMCG, Groningen)
3	09.22 - 09.32	Signs of Congestion, Quality of Life and Short Term
		Rehospitalization in Patients with Heart Failure
		Geert H.D. Voordes (UMCG, Groningen)
4	09.33 - 09.43	Enhanced Detection of Titin Truncating Variant-Specific ECG
		Features in Dilated Cardiomyopathy Using a Deep Neural
		Network Analysis
		Astrid B.M. Heymans (Cardiovascular Research Institute Maastricht)
5	09.44 - 09.54	A dynamic Risk Prediction Model for Heart Failure in
		Phospholamban p.(Arg14del)-Positive Individuals: a Step
		Towards Patient Selection for Future Genetic Therapies
		Myrthe Y.C. van der Heide (AUMC, Amsterdam)
6	09.55 - 10.05	Optimizing Screening Intervals for At-risk Relatives of Dilated
		Cardiomyopathy Carrying a TTN Truncating Variant: a Multi-State
		Model Approach
		Nina Beelen (CARIM, Maastricht)
7	10.06 - 10.16	Recent Advancements in the Diagnosis and Treatment of
		Transthyretin Amyloid Cardiomyopathy Patients Lead to
		Changing Patients Characteristics and Improved Outcome
		Paulo Rijs Alonso (Erasmus MC, Rotterdam)
8	10.17 - 10.27	Real-World Experience Using Mavacamten in Patients with
		Obstructive Hypertrophic Cardiomyopathy
		Anna van Hoogdalem (Erasmus MC, Rotterdam)



# CDK4/6 Inhibitor Ribociclib Induces Cardiotoxicity Through Impaired E2F1-Regulated Spliceosome Assembly

Presenting author: E. Pet Department: Experimental Cardiology

<u>E. Pet (UMCG, Groningen);</u> E. Pet (UMCG, Groningen); I. Braga Dias (UMCG, Groningen); A. N. Linders (UMCG, Groningen); R. L. Jagersma (UMCG, Groningen); F.E. Deiman (UMCG, Groningen); J. Zhu (UMCG, Groningen); A. Feinberg (Carnegie Mellon University, Pittsburgh), N. Bomer, P. van der Meer (UMCG, Groningen)

# Purpose:

Ribociclib, a novel chemotherapeutic agent for metastatic breast cancer, functions as a cyclin-dependent kinase 4/6 (CDK4/6) inhibitor, involving the CDK4/6-Rb-E2F1 pathway. Ribociclib use associates with development of heart failure, yet the causality of cardiac effects remains to be explored. This study aims to investigate ribociclib's cardiotoxic effects in dynamic human engineered heart tissues (dyn-EHTs), focusing on the CDK4/6-Rb-E2F1 axis.

#### Methods:

Dyn-EHTs were generated using iPSC-CMs and treated with repeated ribociclib dosing (7  $\mu$ M) to mimic clinical drug administration. To determine the role of downstream E2F1 in this dysfunction, an E2F1-overexpressing iPSC line was made with which contractility assays were performed and dyn-EHTs were generated. To explore underlying mechanisms of E2F1 involvement, RNA-sequencing was performed on E2F1-overexpressing dyn-EHT (n=4) and scrambled (SCR) dyn-EHT (n=4).

#### **Results:**

Upon treatment with ribociclib, dyn-EHTs exhibited a 17.0%  $\pm$ 4.3% (p<0.001) increase in tissue dilatation, an 8.9%  $\pm$ 4% (p<0.001) decrease in systolic force generation, and a 22.1%  $\pm$ 5.7% (p<0.001) increase in systolic stress, indicating significant cardiac dysfunction. Overexpression of E2F1 in iPSCs resulted in a threefold increase in E2F1 protein expression and successfully mitigated the ribociclib-induced tissue dilatation(p=0.007), decreased systolic force generation (p=0.005), and increased systolic stress(p=0.004) of SCR tissues. RNA sequencing revealed impairment of spliceosome assembly as an underlying pathway in the control dyn-EHT that is attenuated in the E2F1 overexpressed tissues.

# **Conclusion:**

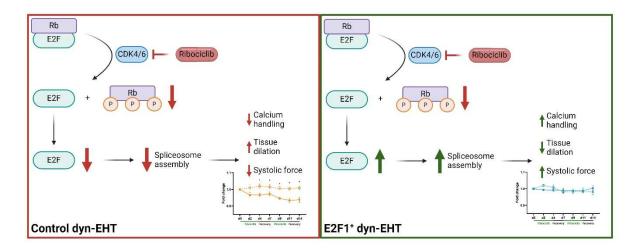
Ribociclib induces significant cardiotoxic effects in dyn-EHTs and iPSC-CMs through the CDK4/6-Rb-E2F1 pathway and could be caused by impaired spliceosome assembly. The prevention of these effects by E2F1 overexpression highlights this pathway's involvement in ribociclib's cardiotoxic profile.

#### Keywords:

Cardiotoxicity, CDK4/6 Inhibitor, CardioOncology



Figure:





# Obesity and Inactivity Cluster the Strongest Risk Factor for the Development of Heart Failure in a Population-Based Study

Presenting author: B.J. van Essen Department: Cardiology

<u>B.J. van Essen (UMCG, Groningen);</u> B.J. van Essen\*; N.A. En Dan\*; G.N. Tharsana (UMCG, Groningen); P. Kaur (UMCG, Groningen); J.E. Emmens (UMCG, Groningen); W. Ouwerkerk (Amsterdam UMC); R.T. Gansevoort (UMCG, Groningen); S.J.L. Bakker (UMC, Groningen); R.A. de Boer (Erasmus MC), K. Damman (UMCG, Groningen); D.J. van Veldhuisen (UMCG, Groningen); A.A. Voors (UMCG, Groningen); J. Tromp (UMCG, Groningen)

#### Purpose:

Background: Comorbidities are associated with an increased risk of incident heart failure (HF). However, comorbidities usually cluster together and data on the association between multimorbidity clusters and incident HF with preserved and reduced ejection fraction are lacking. Therefore, this study investigated the association between multimorbidity clusters and incident HF.

#### Methods:

Methods: We identified multimorbidity patterns in 6839 participants from the prospective observational Prevention of Renal and Vascular End-stage Disease (PREVEND) cohort study using latent class analysis and investigated their association with new-onset HF. **Results:** 

Results: The participants' mean age at baseline was 53.8 years, and 50% were women. We identified six multimorbidity clusters: 1) young [N = 2118, youngest age and lowest number of chronic conditions], 2) elderly [N = 1198, oldest age, high prevalence of chronic kidney disease and hypercholesterolemia], 3) pulmonary disease [N = 578, high prevalence of respiratory problems], 4) young women [N = 527, 72.3% women, high prevalence of myalgic encephalomyelitis, anxiety and stress], 5) psychological [N = 1815, high prevalence of depression] and 6) obese/physical inactivity [N = 603, high prevalence of obesity, hypertension, myocardial infarction and stroke]. During 110,621 person-years of follow-up 622 participants developed heart failure of which 390 HF with reduced ejection fraction (HFrEF) and 220 with preserved ejection fraction (HFpEF). After adjusting for potential confounders, the elderly (adjusted hazard ratio (aHR) 2.46, 95% confidence interval (CI) 1.89-3.20), pulmonary disease (aHR 2.10, 95% CI 1.51-2.92), and obese/physical inactivity (aHR 3.80, 95% CI 2.86-5.06) clusters had a higher risk of HF compared with the young cluster, which had the lowest risk. Among all clusters, patients were more likely to develop HFrEF compared to HFpEF. However, the obese/physical inactivity cluster was relatively more likely to develop HFpEF than HFrEF.

#### Conclusion:

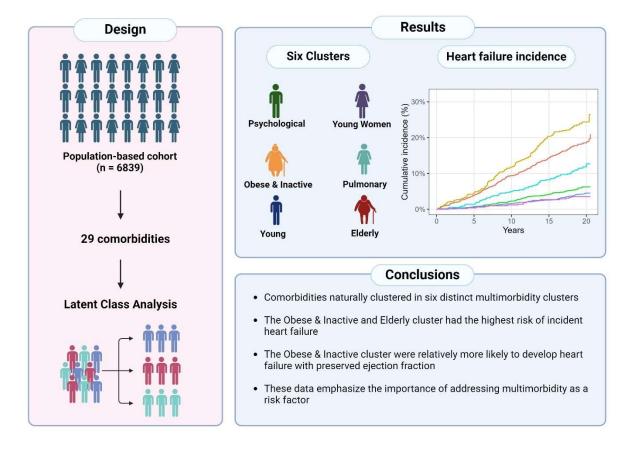
Conclusions: Comorbidities naturally clustered in six distinct multimorbidity clusters, each impacting participants' HF risk differently. These data emphasize the importance of addressing multimorbidity as a risk factor for HF.

#### Keywords:

Heart failure, Multimorbidity, Clusters



# Figure:





# Signs of Congestion, Quality of Life and Short Term Rehospitalization in Patients with Heart Failure

Presenting author: G.H.D. Voordes Department: Cardiology

<u>G.H.D. Voordes (UMCG, Groningen);</u> G.H.D. Voordes (UMCG, Groningen) A.A. Voors (UMCG, Groningen); H. Qin (UMCG, Groningen); J.M. ter Maaten (UMCG, Groningen); K. Damman (UMC, Groningen)

# Purpose:

Aims: Signs of congestion are a treatment target in patients with heart failure (HF), as they affect patients' wellbeing and congestion scores are associated with the risk of early readmission. However, which individual sign of congestion has the strongest association with quality of life (QoL) and HF-rehospitalization remains uncertain.

# Methods:

Methods and Results: We included 1551 HF-patients hospitalized for worsening heart failure. QoL was assessed using the Kansas City Cardiomyopathy Questionnaire-23 (KCCQ-23) on the same day as physical examination. We performed linear- and Cox-regression to find associations of signs of HF to QoL and 60-day HF rehospitalization. All analyses were externally validated in a similar independent cohort.

#### Results:

Patients with worse QoL were older, more often female and had more comorbidities and signs of HF. In multivariable regression analyses, peripheral edema and orthopnea (st.Beta - 0.210, p<0.001 and st.Beta -0.206, p<0.001, respectively) had the strongest association with worse QoL. Elevated Jugular Venous Pressure (JVP) was the only multivariable adjusted congestive sign associated with higher risk of 60-day HF-rehospitalization (HR 1.64 [1.03-2.60], p=0.038). QoL was significantly associated with 60-day HF rehospitalization (HR 1.09 [1.04–1.14]), per 5 units KCCQ-decrease; p<0.001). The presence or absence of signs of congestion did not modify the association between QoL and 60-day HF rehospitalization. **Conclusion:** 

# Conclusion:

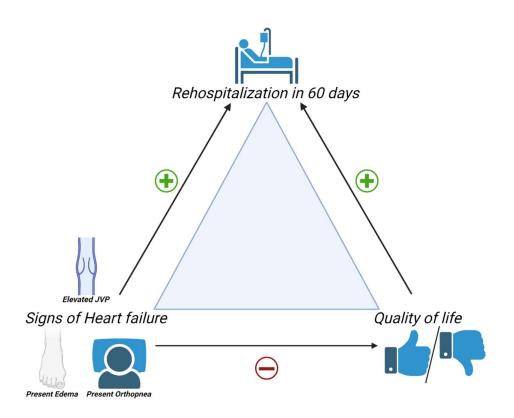
Peripheral edema and orthopnea showed the strongest association with QoL in patients admitted for HF. JVP had the strongest association with the risk of 60-day rehospitalization. Clinically, it is important to distinguish between individual signs due to the discrepancy of their impact on outcome.

#### Keywords:

Heart Failure, Signs and symptoms, Quality of Life



Figure:





Enhanced Detection of Titin Truncating Variant-Specific ECG Features in Dilated Cardiomyopathy Using a Deep Neural Network Analysis Presenting author: A.B.M. Heymans Department: Cardiology

A.B.M. Heymans (Cardiovascular Research Institute Maastricht, Maastricht); A.B.M.

Heymans (Cardiovascular Research Institute Maastricht, Maastricht); R.R. van de Leur (University Medical Center Utrecht, Utrecht); P. Wang (Maastricht University Medical Center, Maastricht); M.F.G.H.M. Venner (Cardiovascular Research Institute Maastricht, Maastricht); N.J. Beelen (Cardiovascular Research Institute Maastricht, Maastricht); S.A. Muller (University Medical Center Utrecht, Utrecht); I.M.E. Faassen (Cardiovascular Research Institute Maastricht, Maastricht); A.S.J.M. te Riele (University Medical Center Utrecht, Utrecht); R. van Es (University Medical Center Utrecht, Utrecht, Utrecht); E. González-López (Puerta de Hierro University Hospital, Madrid); P. Garcia-Pavia (Puerta de Hierro University Hospital, Madrid); S.R.B. Heymans (Maastricht University Medical Center, Maastricht); J.A.J. Verdonschot (Cardiovascular Research Institute Maastricht, Maastricht)

#### Purpose:

Titin truncating variants (TTNtv) are the leading genetic cause of dilated cardiomyopathy (DCM), found in familial (20-25%) and acquired (8-15%) DCM. Although recommended, routine genetic testing is not always feasible in every center. This study aimed to identify ECG parameters predictive of an underlying TTNtv in patients with DCM, comparing conventional ECG analysis with an ECG-based Deep Neural Network (DNN) algorithm, to facilitate timely genetic diagnosis.

#### Methods:

This retrospective multinational study compared baseline ECGs from 99 DCM patients with (likely) pathogenic TTNtv to 318 gene-elusive DCM patients. Conventional ECG parameters (e.g., QRS duration) were extracted, the DNN compressed ECGs into 21 numerical interpretable factors. Predictive performance of both models was compared, adjusted for age, sex, and left ventricular ejection fraction (LVEF).

#### **Results:**

TTNtv patients were younger (50.5 vs 56.9 years, p<0.001), predominantly male (69.7% vs 54.7%, p=0.008), and had lower LVEF (28.0% vs 35.0%, p<0.001). Conventional ECG analysis identified shorter QRS duration (p<0.001), prolonged PR interval (p<0.001), more lateral inverted T-waves (p=0.034), and lower QRS voltage (p=0.092) as TTNtv characteristics. The DNN visualized the influence of its factors on ECG morphology predicting TTNtv (e.g., factor 8 prolonged PR interval, factor 1 inferolateral and factor 9 anterior T-wave flattening and inversion). Both conventional and DNN models performed well (c-statistic: conventional 0.84, DNN 0.87, p=0.136), but the latter demonstrated superior reclassification (integrated discrimination improvement: 0.05, p=0.026), and model fit (likelihood-ratio test p<0.001).

#### **Conclusion:**

Conventional ECG and DNN reveal TTNtv-specific features, with the DNN showing superior performance, emphasizing its potential in diagnostics.



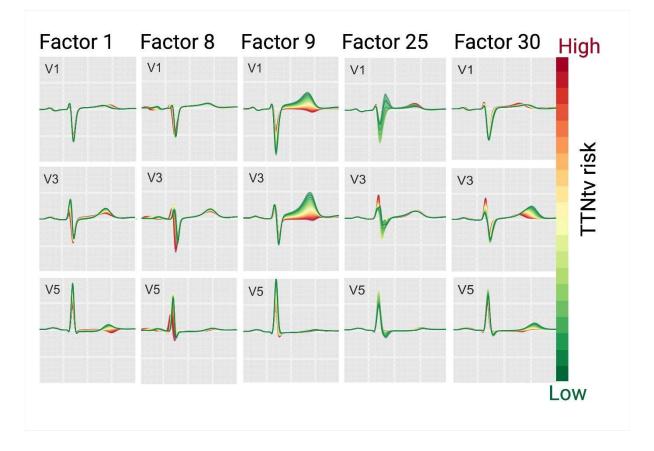
# Keywords:

Dilated cardiomyopathy, Titin truncating variants, Electrocardiogram

# Figure:

Figure 1. ECG reconstruction by the Deep Neural Network, illustrating the impact of TTNtv presence on ECG morphology.

The network's decoder reconstructs 12-lead ECGs using the 21 numerical, interpretable factors. This figure demonstrates for five factors in three leads that a high TTNtv presence risk (red) is linked to lateral ST deviation and T-wave inversion (Factor 1), prolonged PR interval (Factor 8), anterior T-wave flattening/inversion (Factor 9), and a shortened QTc interval (Factor 30). In contrast, Factor 25 indicates that a low TTNtv risk (green) is associated with a right bundle branch delay pattern.





A dynamic Risk Prediction Model for Heart Failure in Phospholamban p.(Arg14del)-Positive Individuals: a Step Towards Patient Selection for Future Genetic Therapies Presenting author: M.Y.C. van der Heide Department: Cardiology

<u>M.Y.C. van der Heide (AUMC, Amsterdam);</u> M.Y.C. van der Heide (AUMC, Amsterdam); T.E. Verstraelen (AUMC, Amsterdam); R. de Brouwer (UMCG, Groningen); E. van Drie (UMCU, Utrecht); A.C. Houweling (AUMC, Amsterdam); C. Dickhoff (Dijklander ziekenhuis, Hoorn); T. Germans (NWZ, Alkmaar); A.S.J.M. te Riele (UMCU, Utrecht); K.Y. van Spaendonck-Zwarts (UMCG, Groningen); M.G.P.J. Cox (UMCG, Groningen); J.P. van Tintelen (UMCU, Utrecht); J.A. Kors (Erasmus MC, Rotterdam); P.G. Postema (AUMC, Amsterdam); A.H. Zwinderman (AUMC, Amsterdam); A.A.M. Wilde (AUMC, Amsterdam)

#### Purpose:

Future genetic therapies are emerging rapidly and could be lifesaving for patients with an inherited cardiomyopathies. For phospholamban (PLN) p.(Arg14del)-positive individuals, accurate risk prediction is crucial to identify those who will benefit most, as this variant exhibits reduced penetrance and a highly variable expression. The purpose of this study is to identify PLN p.(Arg14del)-positive individuals at risk of heart failure using a dynamic heart failure risk model.

#### Methods:

A total of 330 PLN p.(Arg14del)-positive individuals without prior heart failure or myocardial infarction was included. A joint model was created, combining two linear mixed-effect models and a Cox regression model. The first mixed-effect model analyzed the QRS amplitude (lead aVR; mV) derived from 12-lead ECG, adjusted for sex; penalized regression identified lead aVR as best predictor. The second mixed-effect model included left ventricular ejection fraction (LVEF, %) from echocardiography. Both longitudinal trends and age at first clinical evaluation were incorporated into the Cox model.

#### **Results:**

Over a median follow-up of 7.1 years (IQR 3.6-11.6) after first clinical evaluation, 35 individuals reached a composite heart failure endpoint, including heart failure hospitalization, left- or biventricular assist device implantation, heart transplantation or heart failure-related death. The prediction model developed performed well, with three-year AUC ranging from 0.83 to 0.93 during a ten year follow-up.

#### Conclusion:

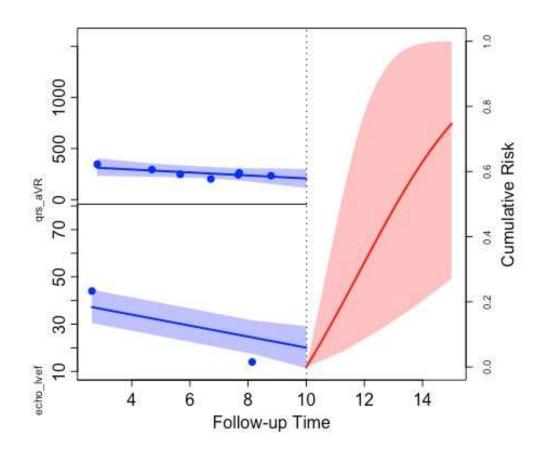
This study presents a dynamic model incorporating longitudinal ECG and echocardiographic data to predict heart failure risk in PLN p.(Arg14del)-positive individuals, offering a foundation for optimizing patient selection for future genetic therapies.

#### Keywords:

Phospholamban p.(Arg14del) cardiomyopathy, Heart failure, Genetic therapy



**Figure:** Figure 1. Example individual trajectory and risk prediction.





Optimizing Screening Intervals for At-risk Relatives of Dilated Cardiomyopathy Carrying a TTN Truncating Variant: a Multi-State Model Approach Presenting author: N.J. Beelen Department: Cardiology

N.J. Beelen (CARIM, Maastricht); S.A. Muller (Utrecht UMC, Utrecht); N.J. Beelen (CARIM, Maastricht); S.A. Muller (Utrecht UMC, Utrecht); A. Paldino (Azienda Sanitaria Univeritaria Giuliano Isontina, Trieste); C.R. Vissing (Copenhagen University Hospital Rigshospitalet, Copenhagen); R. Johnson (Victor Chang Cardiac Research Institute, Australia); D. Kramarenko (Amsterdam UMC. Amsterdam): M. Dal Ferro (Azienda Sanitaria Univeritaria Giuliano Isontina, Trieste); M. Merlo (Azienda Sanitaria Univeritaria Giuliano Isontina, Trieste); S.L.V.M. Stroeks (CARIM, Maastricht); S.R.B. Heymans (CARIM, Maastricht); A.S. Amin (Amsterdam UMC, Amsterdam); D. Fatkin (Victor Chang Cardiac Research Institute, Australia); P. Garcia-Pavia (Hospital Universitario Puerta de Hierro Majadahonda, Madrid); A.S.J.M. te Riele (Utrecht UMC, Utrecht); J.A.J Verdonschot (CARIM, Maastricht)

#### Purpose:

Cardiomyopathy guidelines recommend screening of at-risk relatives for dilated cardiomyopathy (DCM) every 1-3 years, straining clinical resources. Truncating variants in TTN (TTNtv) are the most prevalent etiology, however the diagnostic yield of screening is low. Risk-based stratification could optimize screening intervals and management. This study examined the clinical predictors of DCM development in TTNtv relatives.

#### Methods:

Relatives carrying a (likely) pathogenic TTNtv from seven international centers underwent cardiac and genetic screening. We defined three stages of DCM development: (1) phenotype negative (no abnormalities), (2) borderline DCM (left ventricular (LV) dilatation >2SD OR LV ejection fraction (EF)<50%), and (3) DCM (LV dilatation >2SD AND LVEF<50%). DCM predictors were determined using follow-up data.

#### **Results:**

Among 413 relatives, 301 relatives had follow-up (median of 5.7 years); 24.6% developed borderline DCM, and 17.3% developed definite DCM (Figure 1). Based on the identified risk factors, age  $\geq$  30 years, male sex and borderline DCM, three distinct profiles were established: (1) relatives with borderline DCM, (2) females  $\geq$  30 years and males, and (3) female relatives <30 years. A screening algorithm was developed, recommending intervals of 1, 3 and 5 years, optimizing the balance between safety and effectiveness.

# **Conclusion:**

Unaffected relatives with a TTNtv can be stratified into three risk profiles based on age, sex and echocardiographic measures, with a recommended cardiac screening interval of 1, 3 and 5 years respectively. Genotype specific risk prediction for relatives will allow us to optimize clinical resources.

#### Keywords:

Cardiogenetics, Family screening, Titine



# Figure:

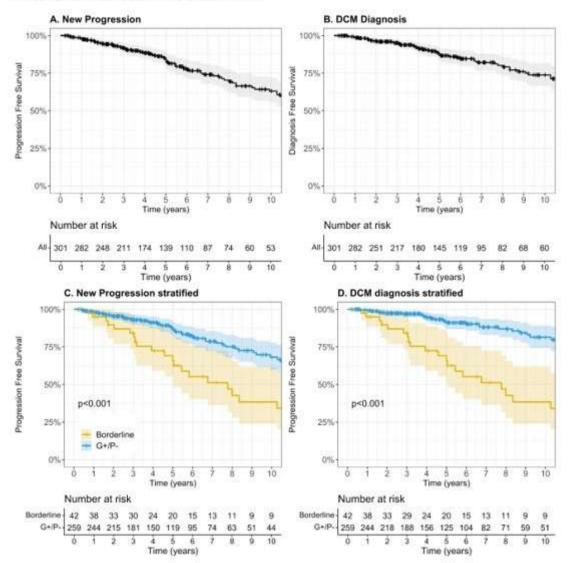


Figure 1. Survival from primary endpoints

Survival of (A) any progression to new DCM criteria in the overall cohort; (B) progression to DCM diagnosis in the overall cohort; (C) any progression to new DCM criteria stratified by baseline clinical phenotype; (D) progression to DCM diagnosis stratified by baseline clinical phenotype. Black, yellow, and blue lines depict the overall cohort, family members with borderline DCM, genotype positive/phenotype negative family members, respectively. Shaded areas visualize the 95% CI. Abbreviations as in text.



# Recent Advancements in the Diagnosis and Treatment of Transthyretin Amyloid Cardiomyopathy Patients Lead to Changing Patients Characteristics and Improved Outcome

Presenting author: Department: Cardiologie

<u>P. Rijs Alonso (Erasmus MC, Rotterdam);</u> P. Rijs Alonso (Erasmus MC, Rotterdam); P.P.M. Zwetsloot (Erasmus MC, Rotterdam); S.A.C. Schoonvelde (Erasmus MC, Rotterdam); R. Wiersema (Erasmus MC, Rotterdam); I. Van Kuijk (Erasmus MC, Rotterdam); A.F.L. Schinkel (Erasmus MC, Rotterdam); A.J. Koppelaar (Erasmus MC, Rotterdam); M.A. Van Slegtenhorst (Erasmus MC, Rotterdam); W.P. Te Rijdt (Erasmus MC, Rotterdam); K.H. Lam (Erasmus MC, Rotterdam); R. Wester (Erasmus MC, Rotterdam); R.A. De Boer (Erasmus MC, Rotterdam); A. Hirsch (Erasmus MC, Rotterdam); M. Michels (Erasmus MC, Rotterdam)

#### Purpose:

Transthyretin amyloidosis (ATTR) is increasingly being recognized as an important cause of cardiomyopathy (CM) and heart failure. Advancements in non-invasive diagnostic techniques and treatment have improved disease recognition and prognosis. The purpose of this study was to evaluate the impact of these advancements on diagnosis and outcome to improve clinical care.

#### Methods:

This retrospective, observational study included 125 ATTR-CM adult patients referred to the Erasmus Medical Centre from 2014-2024. Demographics, clinical characteristics and disease-specific factors at diagnosis at our tertiary referral centre were analysed. Two time periods were defined to evaluate trends over time, <2021 and ≥2021, coinciding with the implementation of tafamidis, a selective TTR stabilizer, in the Netherlands.

#### **Results:**

Comparing <2021 to ≥2021, the number of ATTR-CM referrals has increased (18% vs 82%; p<0.001). The average age at diagnosis has increased (74±9.5 vs 78±6.3 years; p<0.001) and more frequently, diagnosed patients were male (64% vs 86%; p<0.001). Betablocker and loop diuretic-usage was unchanged, while use of SGLT2 inhibitors increased (10% vs 39%; p=0.01) and use of mineralocorticoid receptor antagonist decreased at baseline (81% vs 53%; p=0.01).

#### Conclusion:

In recent years, the number of ATTR-CM referrals has increased significantly, with changing patient characteristics and improved survival. The results of this study underscore the advancements in the field of ATTR-CM.

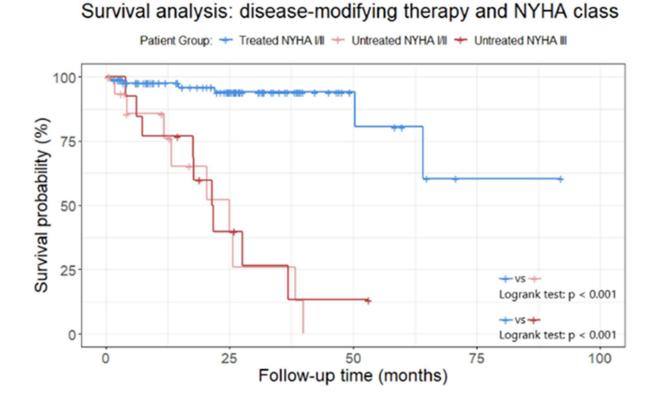
#### Keywords:

Cardiac amyloidosis, Transthyretin,



# Figure:

Figure 1 shows the survival probability of ATTR-CM patients treated and not treated with disease modifying therapy (tafamidis/patisiran) grouped by New York Heart Association (NYHA) class. N = 89 for treated NYHA I/II, n = 17 for untreated NYHA I/II and n = 9 for untreated NYHA III.





# **Real-World Experience Using Mavacamten in Patients with Obstructive Hypertrophic** Cardiomyopathy

Presenting author: A. van Hoogdalem Department: Cardiologie

A. van Hoogdalem (Erasmus MC); P.P Zwetsloot (Erasmus MC); S. Schoonvelde (Erasmus MC); D. Bowen (Erasmus MC); B. Raposo Loff Barreto (Erasmus MC); A. Schinkel (Erasmus MC); A. Koppelaar (Erasmus MC); R. de Boer (Erasmus MC); A. Hirsch (Erasmus MC); M.Michels (Erasmus MC);

# Purpose:

Hypertrophic cardiomyopathy (HCM) is the most common inherited heart disease, with heterogeneous clinical manifestations. In selected patients, obstruction of the LV out-flow tract (LVOT) causes exertional symptoms (e.g. obstructive HCM (oHCM)). Mavacamten, a cardiac myosin modulator has recently been introduced as an effective oHCM therapy. This study presents real-world experience of mavacamten as a treatment for oHCM.

#### Methods:

In this prospective observational cohort study, patients at Erasmus Medical Center who provided informed consent, were recorded for at least 12 weeks follow-up and were prescribed mavacamten for oHCM between January 2024 and November 2024 were included. Baseline characteristics, serial echocardiography, clinical outcomes including NYHA class, biomarkers, left ventricular ejection fraction (LVEF) and LVOT gradients, adverse events (LVEF<50%, atrial fibrillation(AF)) and side effects were recorded.

#### **Results:**

45 patients were included (Table 1). LVOT gradients decreased after 12 weeks of treatment (resting gradients from 60±40 to 22±19 mmHg (p<0.001) and Valsalva-induced gradients from 98±33 to 49±33 mmHg (p<0.001)). LVEF remained within physiological ranges (LVEF=63±6% vs 61±6%, p=0.096). A reduction in NYHA class (mean NYHA=2.4±0.5 vs NYHA=1.8±0.7, p<0.001) and in biomarkers (median NT-proBNP=64 (IQR=159) vs 27.5 (IQR=66) pmol/L, p=0.017; median hsTnT=13.5 (IQR=7.8) vs 11.5 (IQR=6.5) ng/L, p=0.001) were observed. Few participants developed adverse events (LVEF <50% (n=1) and AF (n=5)), causing discontinuation in one patient. After 12 weeks, further significant reductions in gradients, NYHA class and biomarkers were observed.

#### **Conclusion:**

Mavacamten is an effective and safe treatment for oHCM in a real-world clinical setting. Future research should focus on identifying the risk of adverse events or non-response.

#### **Keywords:**

Obstructive Hypertrophic Cardiomyopathy, Mavacamten, Real-world evidence



# Figure:

Table 1. Baseline characteristics         Baseline characteristics (n=45)			
Age (SD)	61 (12.5)		
Sex (female, %)	21 (47%)		
Weight (kg) (SD)	84 (19.5)		
BMI (kg/m²) (SD)	28 (4.9)		
Septal reduction therapy	4 (9%)		
ICD	10 (22%)		
HCM Genotype	15/20/10		
(positive/negative/unknown)			
CYP2C19-genotype	0/5/36/0/4		
(slow/intermediate/normal/fast/ultrafast) Mean LVEF (%) (SD)	63 (5.7)		
Mean LVOT rest (mmHg) (SD)	60.5 (40.5)		
Mean LVOT Valsalva (mmHg) (SD)	98.3 (32.7)		
Mean LVWT (mm) (SD)	18 (3.6)		
Median NT-proBNP (pmol/L) (IQR)	64 (158.5)		
Median hsTnt (ng/L) (IQR)	13.5 (7.75)		
NYHA class 3	16 (36%)		
% on BB	64		
% on CCB	27		
% on BB or CCB	87		

*ICD* = *Implantable cardioverter-defibrillator, LVEF* = *left ventricular ejection fraction, LVWT* = *left ventricular wall thickness, NYHA* = *New York Heart Association, BB* = *betablocker, CCB* = *calcium channel blocker*