ABSTRACTS
NVVC Voorjaarscongres 2025
Donderdag 10 april
09.00 – 10.30 uur

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** *Paula 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)*

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Abstract 1

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

Presenting author: E. Pet
Department: Experimental Cardiology

E. Pet (UMCG, Groningen); 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 µM) 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% ±4.3% ($p<0.001$) increase in tissue dilatation, an 8.9%±4% ($p<0.001$) decrease in systolic force generation, and a 22.1%±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

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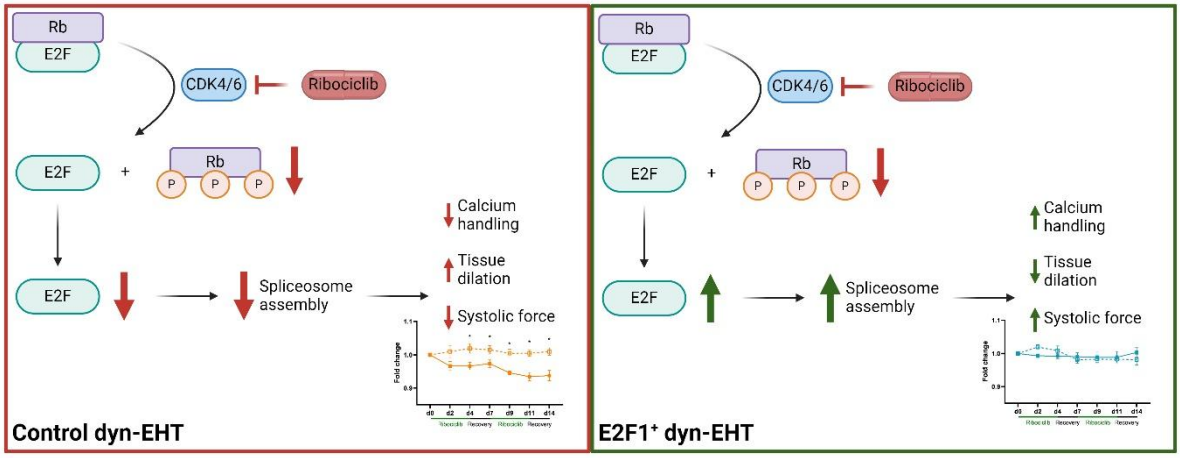
Figure:



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Abstract 2

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

B.J. van Essen (UMCG, Groningen); 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

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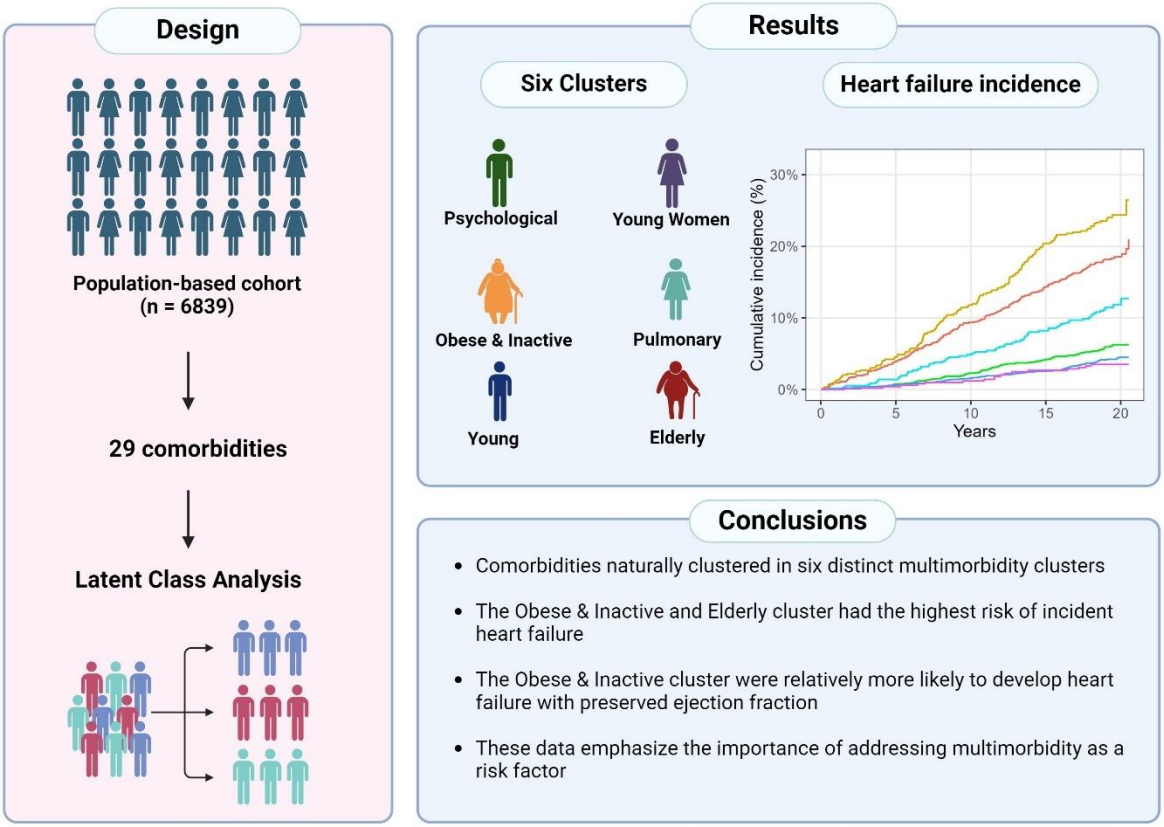
Figure:



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Session 6: Cardiomyopathy & genetics
Abstract 3

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

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

G.H.D. Voordes (UMCG, Groningen); 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

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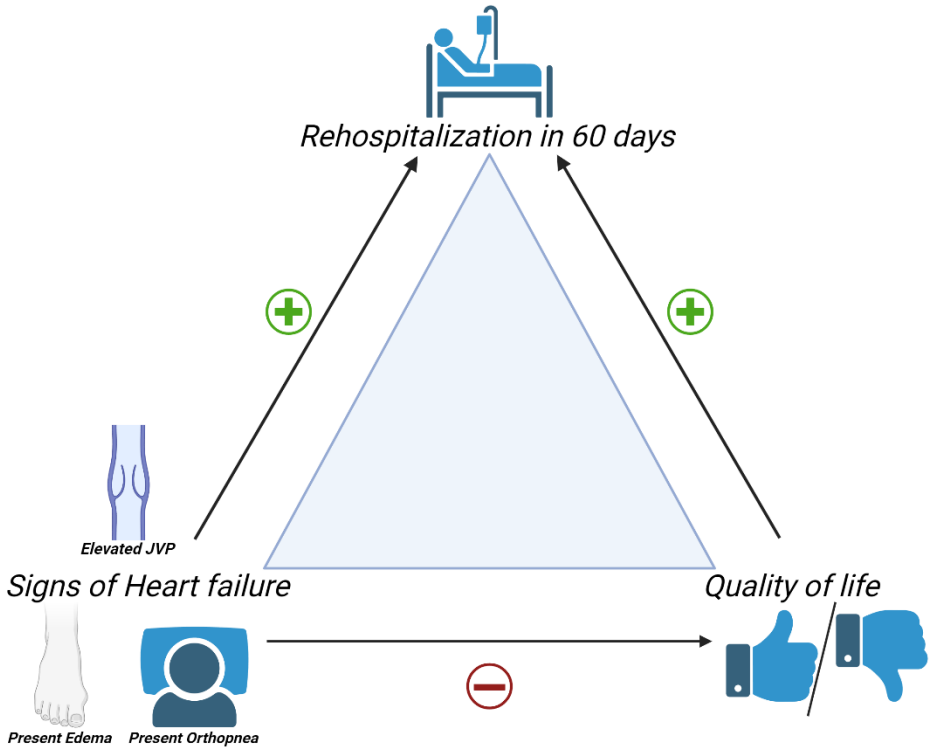

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Abstract 4

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); 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.

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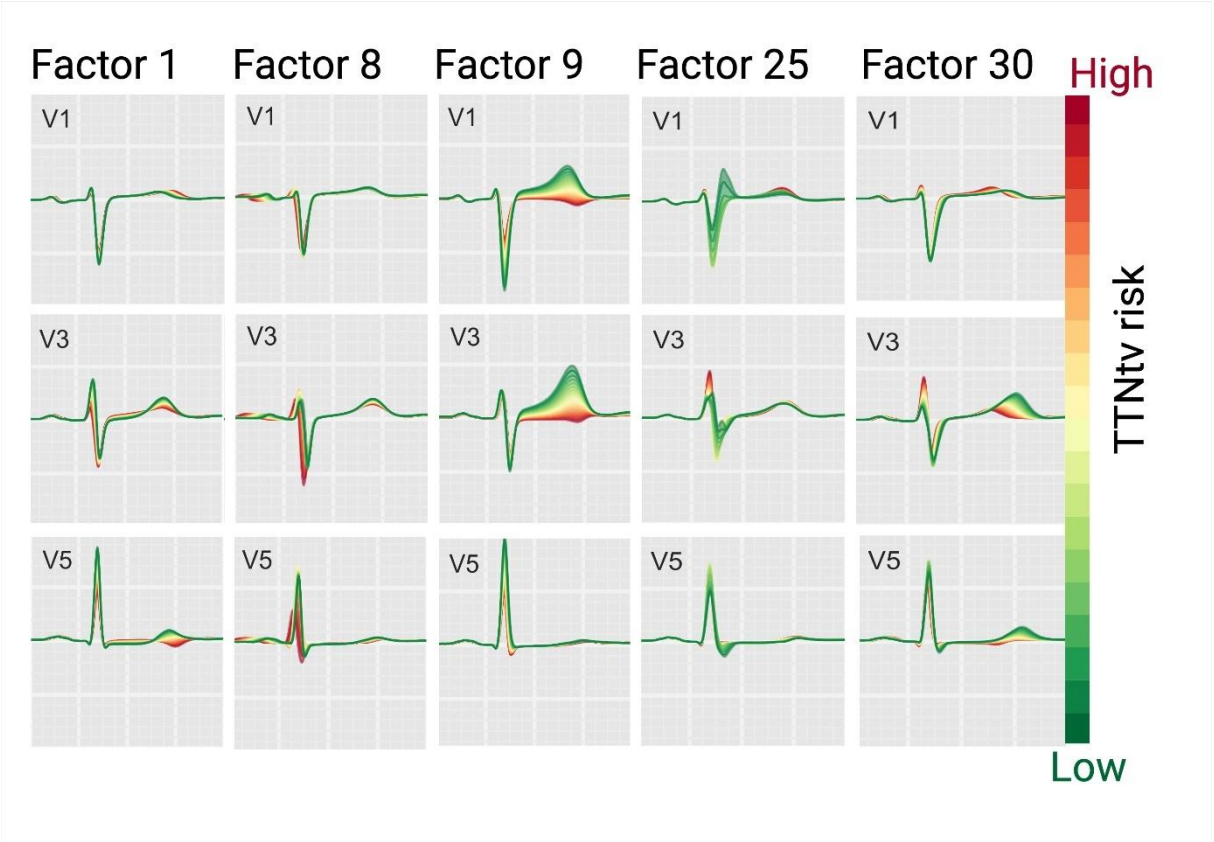
Keywords:
Dilated cardiomyopathy, Titin truncating variants, Electrocardiogram

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.



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Abstract 5

A dynamic Risk Prediction Model for Heart Failure in Phospholamban p.(Arg14del)-Positive Individuals: a Step Towards Patient Selection for Future Genetic Therapies

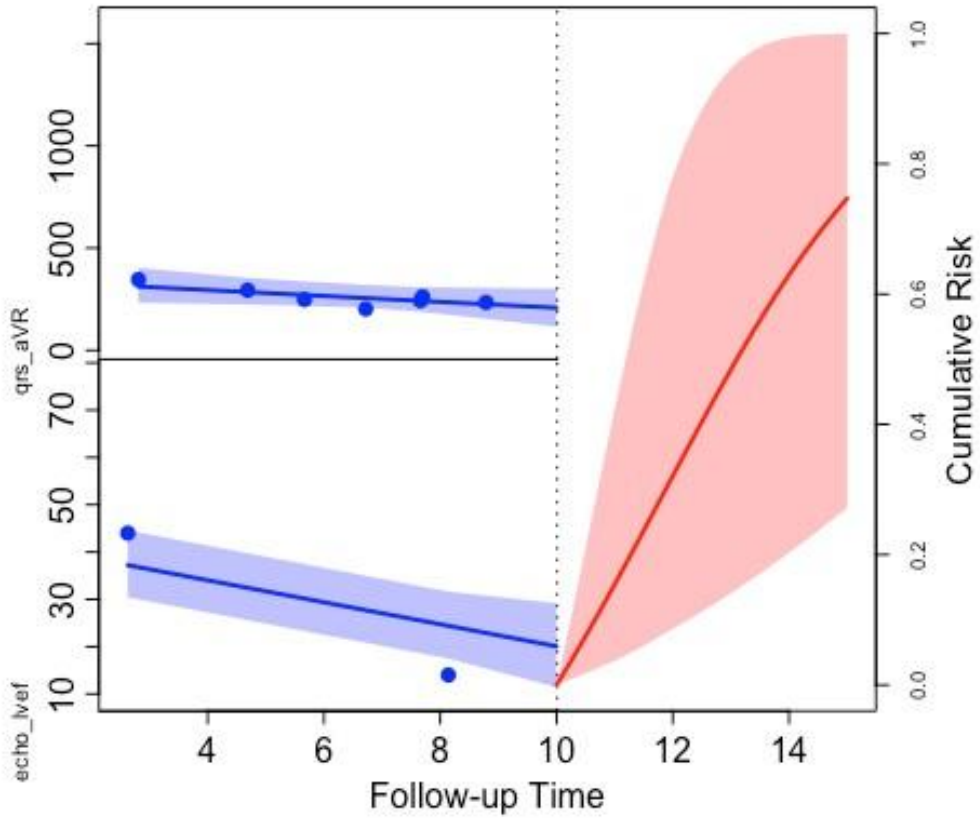
Presenting author: M.Y.C. van der Heide
Department: Cardiology

M.Y.C. van der Heide (AUMC, Amsterdam); 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.



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Abstract 6

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

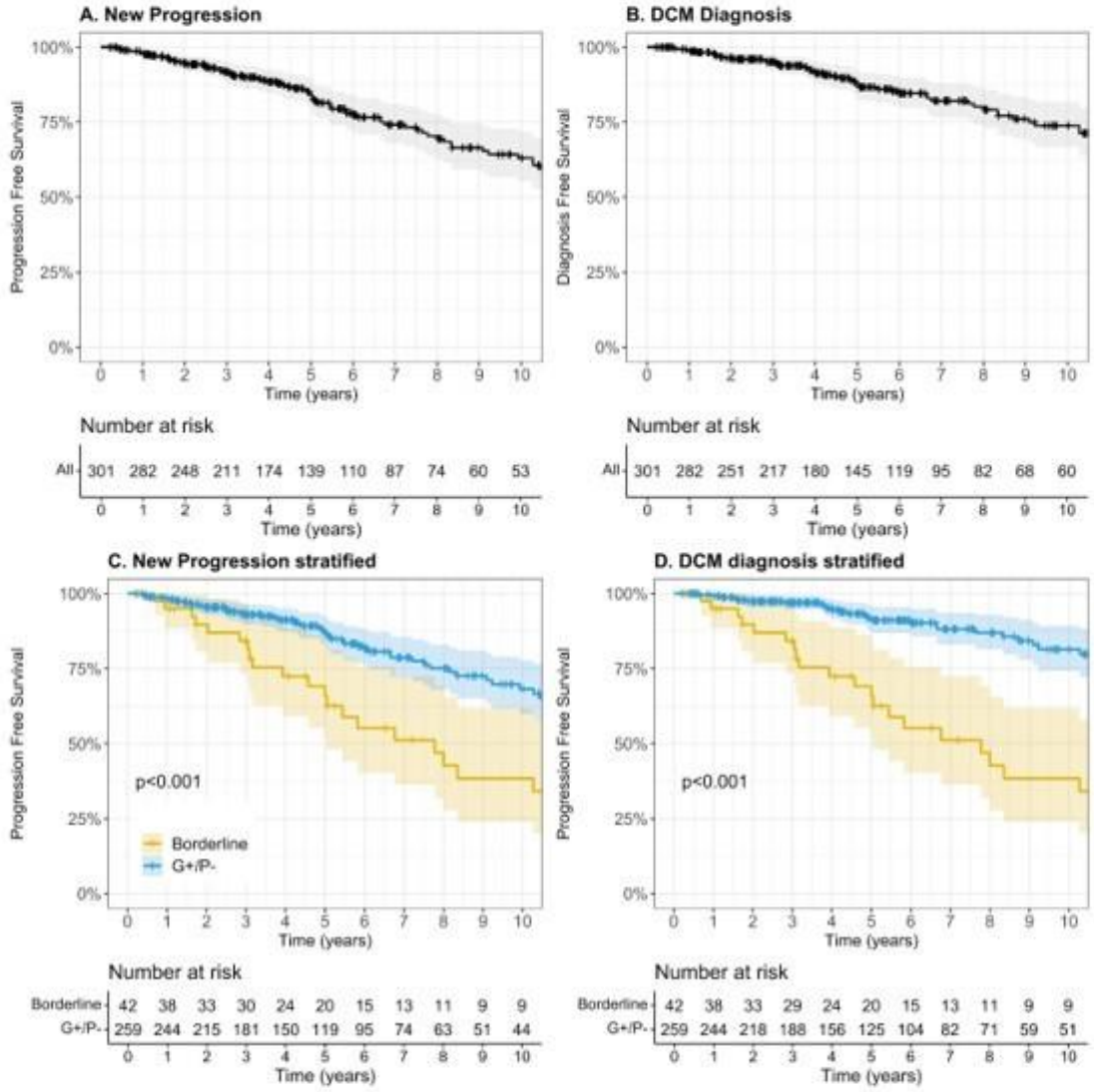
N.J. Beelen (CARIM, Maastricht); S.A. Muller (Utrecht UMC, Utrecht); *N.J. Beelen (CARIM, Maastricht); S.A. Muller (Utrecht UMC, Utrecht); A. Paldino (Azienda Sanitaria Univeritaria Giuliano Isontina, Trieste); C.R. Vissing (Copenhagen University Hospital Rigshospitalet, Copenhagen); R. Johnson (Victor 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 ≥30 years, male sex and borderline DCM, three distinct profiles were established: (1) relatives with borderline DCM, (2) females ≥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.

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Abstract 7

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

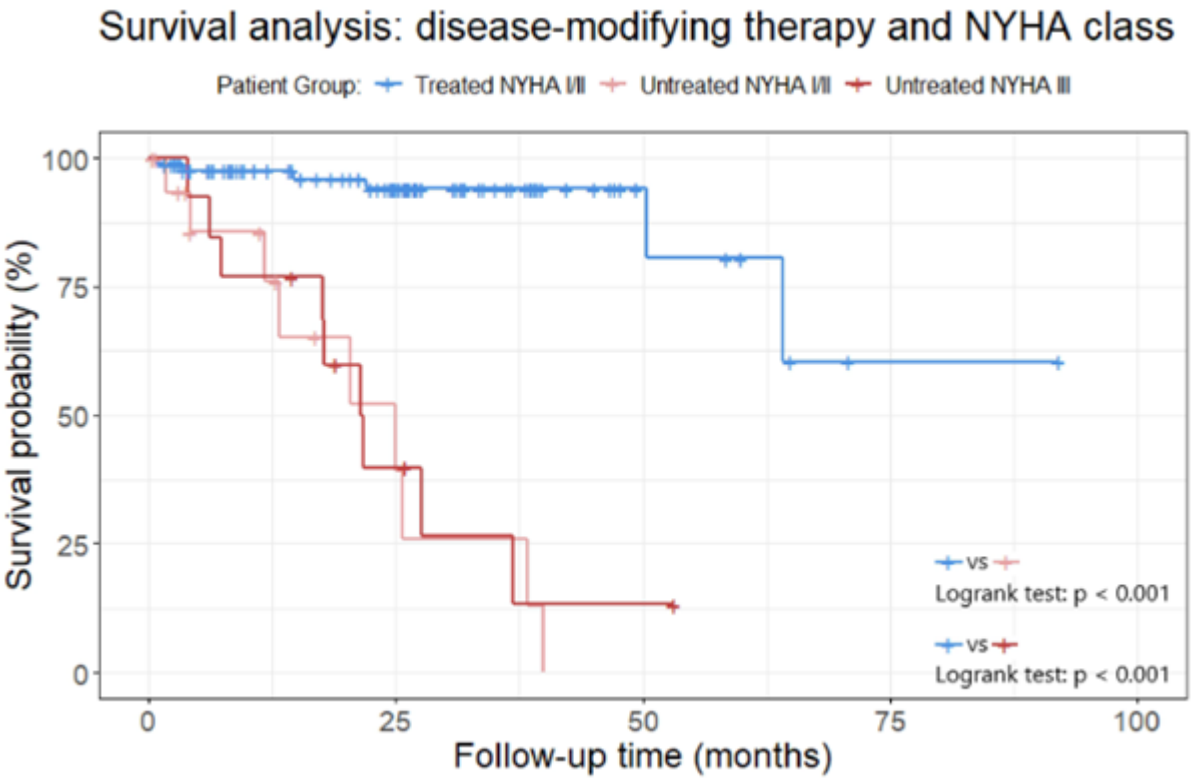
Presenting author:
Department: Cardiologie

P. Rijs Alonso (Erasmus MC, Rotterdam); 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.



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Abstract 8

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/m^2) (SD)	28 (4.9)
Septal reduction therapy	4 (9%)
ICD	10 (22%)
HCM Genotype (positive/negative/unknown)	15/20/10
CYP2C19-genotype (slow/intermediate/normal/fast/ultrafast)	0/5/36/0/4
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