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. ten Berg
Department: Cardiologie

S. ten Berg (Amsterdam UMC, Amsterdam); 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.
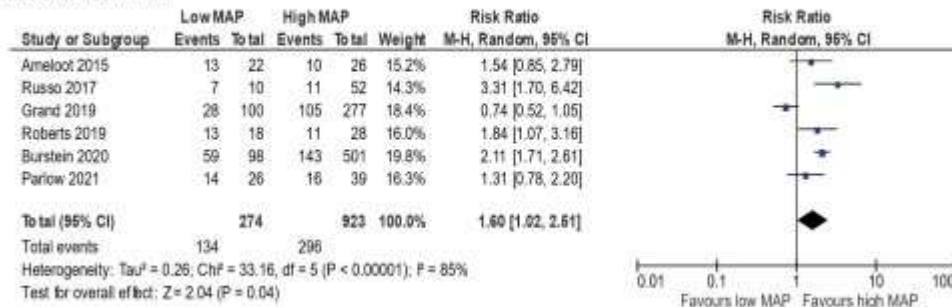
Keywords:
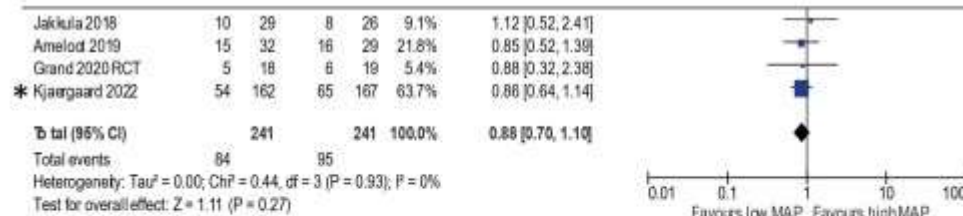Cardiogenic shock, Myocardial infarct, Mean arterial pressure

Figure:
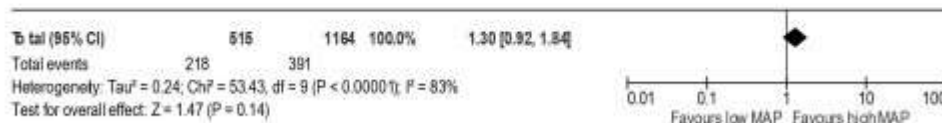
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Abstract 2

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

D.J. Noordermeer (Erasmus MC, Rotterdam); 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 Δc-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 (Δc-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

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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

L.E.E.C. Zonneveld (UMCG, Groningen); 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 bumetanide (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 bumetanide 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.
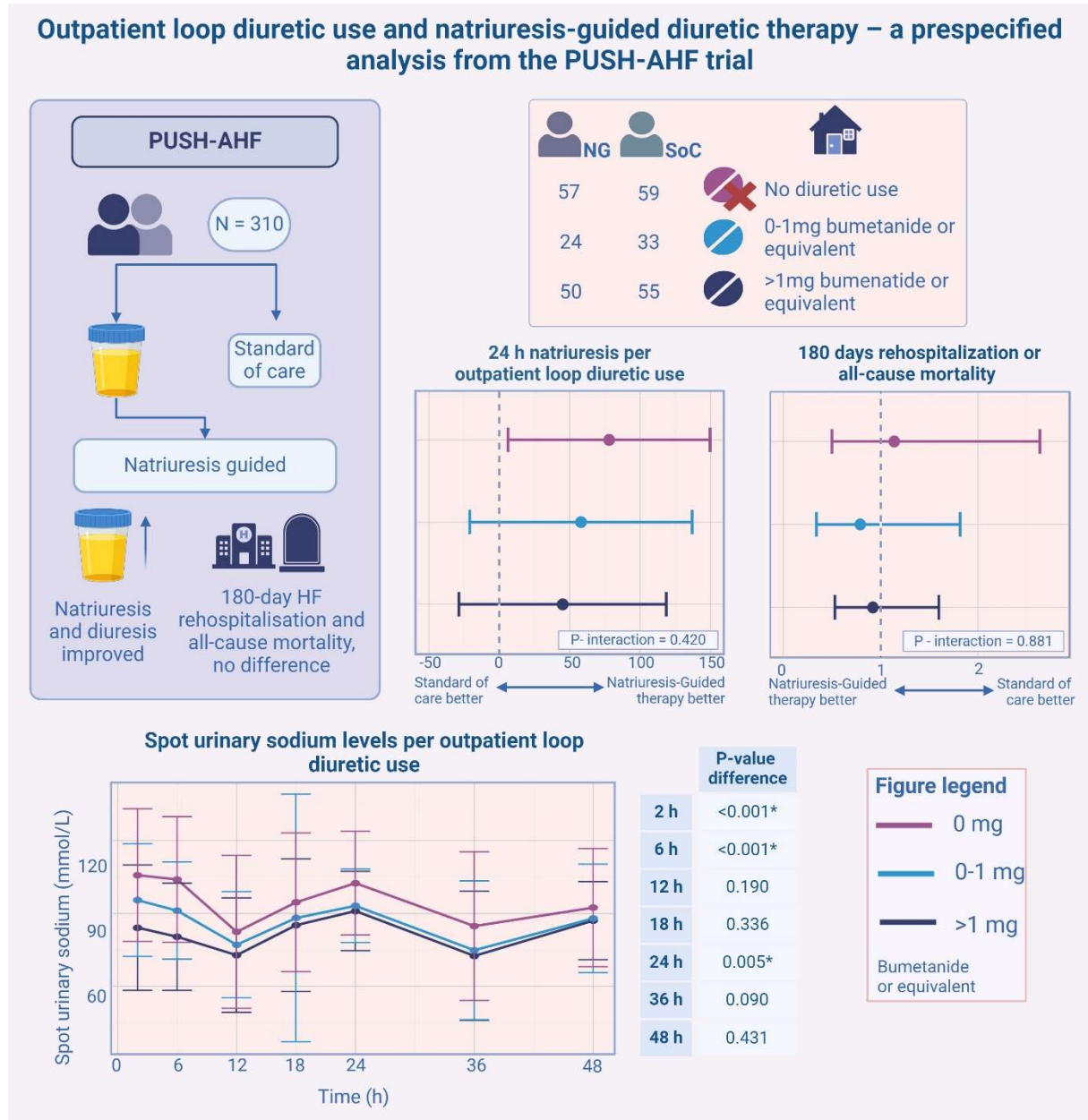
Keywords:
Loop diuretics, Acute Heart Failure, Natriuresis

Figure:

Outpatient loop diuretic use and natriuresis-guided diuretic therapy – a prespecified analysis from the PUSH-AHF trial

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Abstract 4

The Impact of Intravenous Nitroglycerin on Decongestion in a Propensity Matched Acute Heart Failure Cohort
Presenting author: M. Hoen
Department: Cardiologie

M. Hoen (Zuyderland MC, Heerlen); 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 in hypotension after 24 hours, renal dysfunction during hospitalization or occurrence 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.
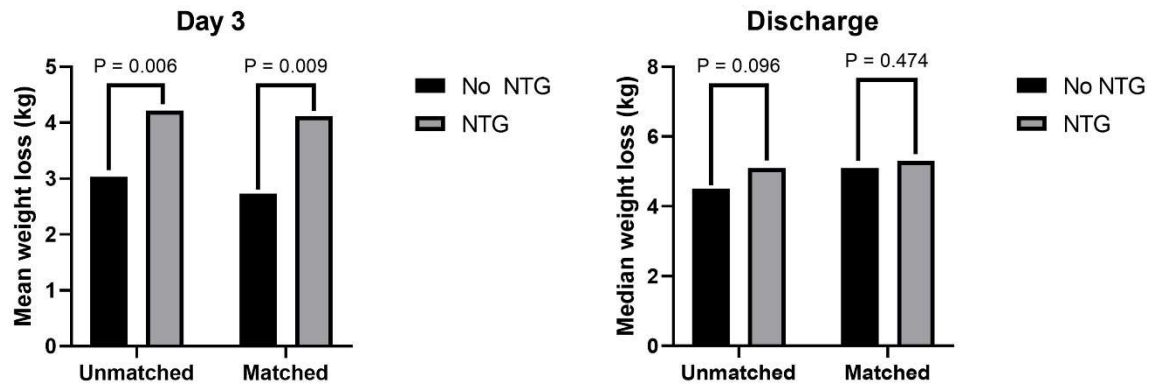
Keywords:
Nitroglycerin, Acute heart failure, Decongestion

Figure:

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

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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

D.C.H. Ceelen (University of Groningen, Groningen); 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.
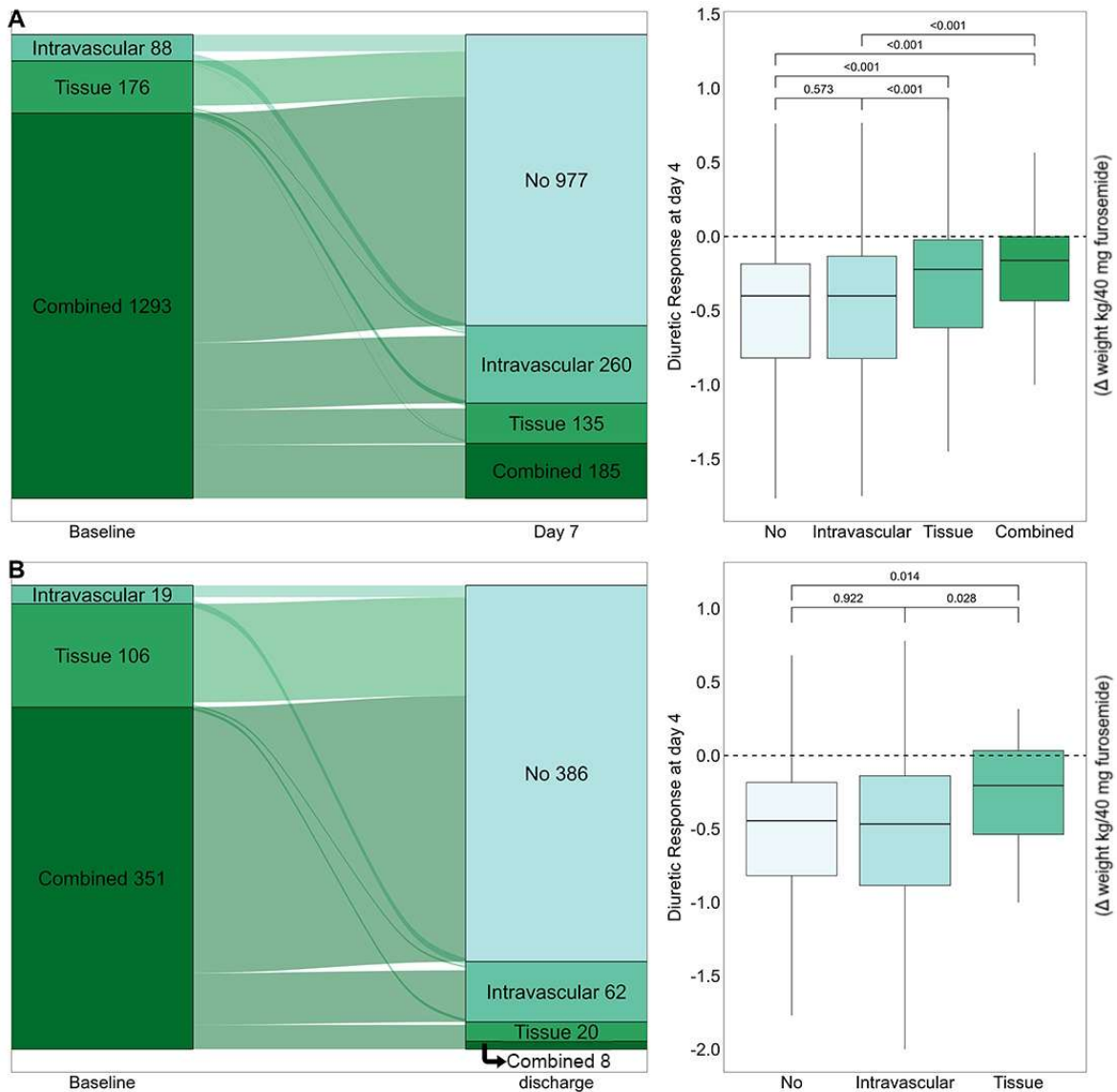
Keywords:
Heart Failure, Congestion, Diuretic

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

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Abstract 6

Frailty in Elderly Heart Failure Patients, How Applicable is the VMS Frailty Score?
Presenting author: M. Niesing-Lut
Department: Cardiologie

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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

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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.
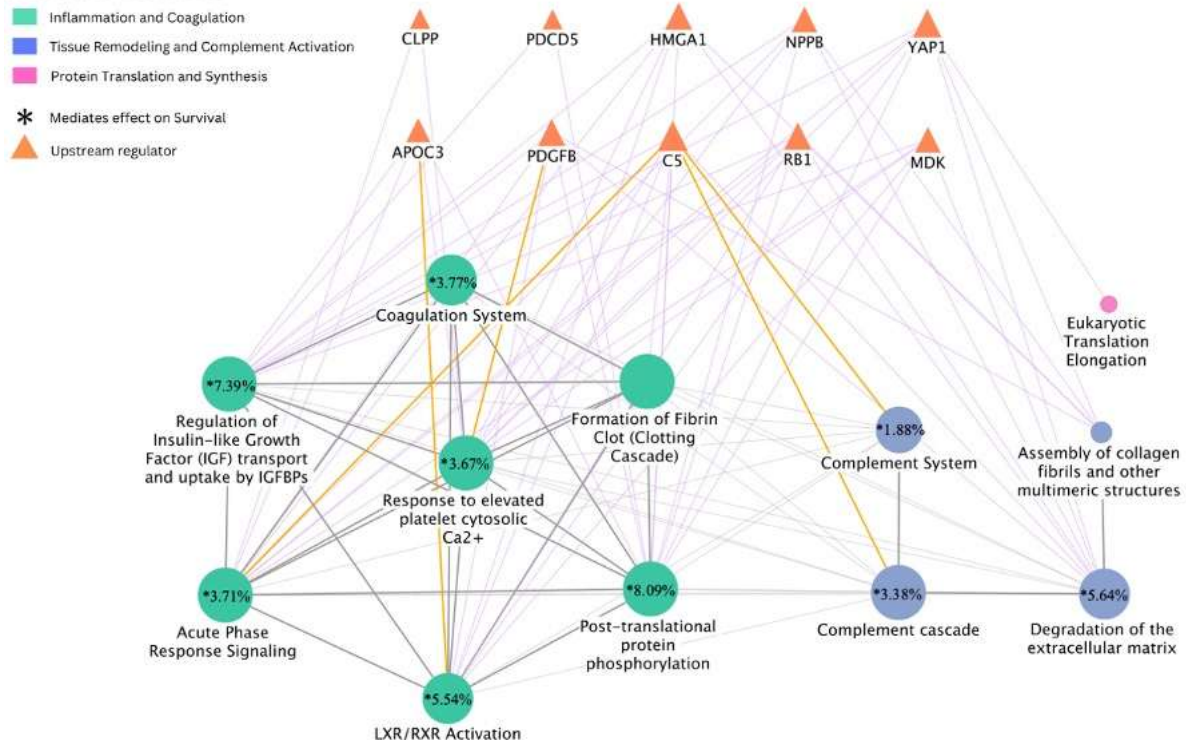
Session 5: (Acute) Heart failure
Abstract 8

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