uation with spironolactone vs placebo was amplified in the low eGFR category (p=0.003).
Conclusion: Severe renal dysfunction was associated with higher rates of composite CV events in HFpEF. Although benefit of spironolactone was consistent across eGFR categories, AEs leading to drug discontinuation were more frequent in those with severe renal dysfunction. Thus, caution is needed with use of spironolactone to treat HFpEF in those with severe renal dysfunction where the balance of safety and efficacy may be less favourable.
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P6509
Retinal microvascular impairment in heart failure with preserved ejection fraction

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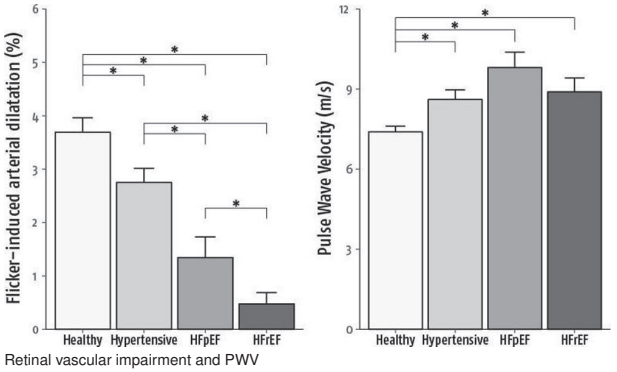
Introduction: Heart failure (HF) with preserved ejection fraction (HFpEF) accounts for half of all HF patients. In HFpEF patients, comorbidities such as hypertension, diabetes, and systemic inflammation are considered a driving force for endothelial damage. This, in turn, leads to detrimental cardiac remodeling with sustained neuroendocrine activation. The novel possibility to non-invasively estimate microvascular function is a powerful and easy to use tool.
In a prospective, observational single-center study we evaluated micro- and macrovascular function in HFpEF, HF with reduced ejection fraction (HFrEF), hypertensive (HTN) patients, and healthy controls (HC).
Methods: A total of 203 patients were enrolled: 30 HFpEF (NT-proBNP>300, LVEF>50%, HF signs and symptoms, and echocardiographic signs of diastolic dysfunction) and 38 HFrEF (LVEF<40%) patients under best medical therapy and stable disease have been prospectively included. Additionally, 58 patients with hypertension as only risk factor (patient history, treatment and/or hypertension resting recumbent) and 77 healthy controls (absence of cardiovascular risk factors and conditions) were included.
Microvascular retinal endothelial function was measured by dynamic retinal vessel analysis. It mainly reflects NO-dependent flicker-light-induced dilatation of retinal arteries (FIDart). Other vascular parameters included retinal arteriovenous ratio, pulse-wave velocity (PWV), and augmentation index. For the statistical data analyses, the generalized linear model (GLM) was applied (R 3.4.3, srvyr 0.3). To account for imbalances in potential confounders (age, sex, body mass index, blood pressure, and glucose) inverse probability weighting was used.
Results: Microvascular functional impairment spans a continuum across all groups when adjusted for potential covariates, with FIDart significantly declining from healthy > hypertensive > HFpEF > HFrEF (p<0.001). Microvascular endothelial function of retinal arteries was severely impaired in both, HFpEF (1.38±0.48%) and even more so in HFrEF (0.32±0.19%) patients, when compared to healthy controls (HC, 3.49±0.32%, p<0.001 vs. each HF groups).
Arterial stiffness (by PWV) was significantly increased in HFpEF (9.81±0.57m/s, p=0.001 vs. HC), HFrEF (8.90±0.52m/s, p=0.001 vs. HC), p=0.005), and HTN (8.61±0.36m/s, p=0.001 vs. HC) when compared to HC (7.19m/s, overall p<0.001). There was no significant difference in PWV between the HF groups (p=0.55).
Additionally, echocardiographically estimated systolic pulmonary artery pressure correlated with retinal flicker-induced venous dilatation (p=0.001, r=0.43; HFpEF vs. HFrEF p=0.25).



Retinal vascular impairment and PWV

Conclusion: Microvascular endothelial dysfunction in retinal vessels is severely impaired in HFpEF patients and arterial stiffness is increased. Hypertension shows an intermediate level of microvascular impairment. Our findings corroborate the importance of endothelial function as a mechanism and potential therapeutic target in HFpEF.
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P6510
Noninvasive evaluation of left ventricular relaxation and stiffness as diastolic function using speckle tracking echocardiography: validation study by cardiac catheterization

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Background: Left ventricular (LV) diastolic function is mainly composed of LV relaxation and LV stiffness. LV diastolic dysfunction causes elevated pulmonary capillary wedge pressure (PCWP), which leads to congestive heart failure. We reported that PCWP (ePCWP) and LV relaxation assessed by Tau (eTau) are noninvasively evaluated by speckle tracking echocardiography (STE). LV camber stiffness may be assessed with the use of two LV diastolic pressure-volume coordinates: the end-diastolic pressure and volume and the pressure and volume at the time of minimum diastolic pressure.
Purpose: We sought to noninvasively assess Tau and LV chamber stiffness using STE and validate these values by cardiac catheterization.
Methods: Echocardiography and catheterization were performed in 124 patients without valvular heart disease (age 72±8) (70 angina pectoris, 20 prior myocardial infarction, 19 hypertensive heart disease, 11 congestive heart failure and 4 paroxysmal atrial fibrillation). The ePCWP is noninvasively obtained as 10.8–12.4 x Log (left atrial active emptying function / minimum volume) mmHg. The eTau is noninvasively obtained as isovolumic relaxation time / (ln 0.9 x systolic blood pressure – ln ePCWP) ms. The estimated LV endo-diastolic pressure (e-EDP) was noninvasively calculated as 12.3–10.1 x Log (left atrial active emptying function / minimum volume) mmHg. LV camber stiffness (mmHg/ml) was calculated as LV pressure change (from minimum pressure to EDP) obtained by catheterization divided by change of LV volume during diastole which equals to stroke volume by echocardiography. Estimated chamber stiffness (e-Stiffness) was noninvasively obtained using e-EDP and 5 mmHg as minimum pressure because minimum pressure by catheterization was 5.0±2.9mmHg. Estimated LVED stress (e-Stress) was calculated as 0.334 x e-EDP x ED dimension / {ED thickness (1 + ED thickness / ED dimension)} kdynes/cm^2. The eTau, e-EDP, e-Stiffness and e-Stress were validated by catheterization.
Results: The eTau and e-EDP noninvasively estimated by STE had good correlation with Tau and EDP invasively obtained by catheterization (r=0.75 and 0.63, respectively, both p<0.001), whereas isovolumic relaxation time, e' and E/e' had a poor correlation with Tau (r=0.45, -0.27 and 0.26, all p<0.05) and E/e' had also poor correlation with EDP (r=0.24, p<0.05). The e-Stiffness and e-Stress had good correlation with stiffness and stress obtained by catheterization (r=0.69 and 0.77, p<0.001). Bland-Altman analysis revealed a good agreement between eTau and Tau and between e-Stiffness and Stiffness without fixed and proportional bias.
Conclusion: This study demonstrated that LV relaxation and stiffness may be noninvasively assessed by STE with reasonable accuracy and may have utility and value in the routine clinical practice for the diagnosis and treatment in patients with cardiac disease.

P6511
Interactive role of diastolic dysfunction and ventricular remodeling in stage a and b heart failure with preserved ejection fraction: impact on clinical practice

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Background: Patients with Heart Failure with preserved ejection fraction (HFpEF) are characterized by diastolic dysfunction (DD) and maladaptive left ventricular (LV) remodeling.
Purpose: To assess the prognostic impact of different diastolic function algorithms combined with a complex remodeling classification (CRC, including relative wall thickness, LV mass index and end-diastolic volume index) in stage A and B HFpEF.
Methods: We selected asymptomatic (stage A and B) HFpEF patients from a multicenter study, using 3 algorithms for LV diastolic function (Paulus 2007, Nagueh 2009, Nagueh 2016), together with classic and CRC. We considered a composite end-point: all-cause death, myocardial infarction, cerebrovascular events and acute pulmonary edema.
Results: We studied 1923 patients (Male 43%; age 57, 33–76 years). Nagueh 2016 identified the lowest proportion of DD (63, 3.2%) and the concordance between the 3 algorithms was low: Kappa statistic 0.22 and 0.17 considering Paulus 2007 vs Nagueh 2016 and Nagueh 2009 vs Nagueh 2016, respectively. According to CRC, 780 patients had a normal or physiologic hypertrophy, 298 concen-

tric remodeling, 85 eccentric remodeling, 294 concentric hypertrophy, 39 mixed hypertrophy, 80 dilated hypertrophy and 73 eccentric hypertrophy. After a mean follow-up of 29 months, multivariate Cox-regression (adjusted for age, gender, history of stable ischemic heart disease, classic remodeling classification) identified CRC (p=0.01), the presence of DD by Paulus 2007 (p=0.01) and Nagueh 2016 (p<0.001) as independent predictors of end-point. The coexistence of an adverse LV remodeling by CRC and DD by Nagueh 2016 was associated with the worst prognosis.
Conclusions: A concurrent structural (CRC) and functional (Nagueh 2016) analysis improves prognostic stratification in stage A and B HFpEF patients, limiting the cases of undetermined evaluation.

P6512
The product of lnBNP and E/A is a novel parameter to predict left ventricular filling pressure

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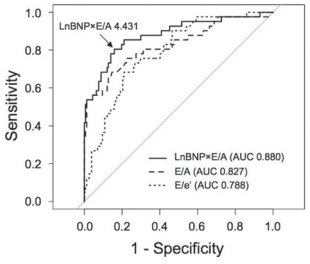
Background: Several echocardiographic parameters are currently being employed to evaluate left ventricular (LV) filling pressure. Mitral inflow early (E)/late diastolic filling velocity ratio (E/A), and E to tissue Doppler e' ratio (E/e') are widely used to estimate LV filling pressure, but not always consistent in the clinical setting especially in the patients with preserved LV ejection fraction (LVEF).
Purpose: The purpose of this study was to estimate a novel parameter by multiplying log B-type natriuretic peptide (LnBNP) and E/A (LnBNP×E/A) for the prediction of pulmonary artery wedge pressure (PAWP).
Methods: We retrospectively analyzed consequent 198 patients who underwent cardiac catheterization, echocardiography, and sampling of plasma BNP within 7 days for the diagnosis of chronic heart failure. High PAWP was determined as more than 15 mmHg of mean PAWP.
Results: The high PAWP group (n=41) showed higher age, body mass index, and levels of LnBNP than the normal PAWP group (n=157). The high PAWP group presented greater LV mass index, larger LV end-diastolic and end-systolic volume index, lower LV ejection fraction, higher E/A and E/e' ratios, and larger left atrial volume index, indicating that LV remodeling progressed in the high PAWP group. LnBNP×E/A was higher in the high PAWP group than in the normal PAWP group (12.0 [4.7–17.0] vs. 3.0 [2.0–3.9], P<0.0001). We next examined the correlation of PAWP with E/A, E/e', and LnBNP×E/A. All of those parameters were positively correlated with PAWP, but LnBNP×E/A showed the largest R value (E/A, R=0.7010; E/e', R=0.3922; LnBNP×E/A, 0.7326). In a logistic regression with age, body mass index, LV mass index, LV end-diastolic volume index, LV ejection fraction, left atrial volume index, presence of mitral regurgitation, E/e', and LnBNP×E/A in the equation, body mass index (OR = 1.39, 95% CI = 1.151–1.730) and LnBNP×E/A (OR = 1.640, 95% CI = 1.312–2.197) were significant predictors of PAWP. The values of net reclassification improvement reached statistical significance when LnBNP×E/A was added to the model; 0.7198 (95% CI 0.3846–1.0549, P<0.001). Receiver operator characteristic curve analysis for the detection of high PAWP revealed that LnBNP×E/A showed the largest area under the curve (AUC) compared to E/A (0.880 vs. 0.827, P=0.011) and E/e' (0.880 vs. 0.788, P=0.027). When the cutoff value of LnBNP×E/A was determined as 4.431, the diagnostic accuracy was sensitivity 0.805, specificity 0.841, positive predictive value 0.569, and negative predictive value 0.943 (Figure). Finally, we analyzed the patients with normal LVEF. LnBNP×E/A showed moderate correlation with PAWP (R=0.4234), and the AUC for the detection of elevated PAWP remained high (AUC 0.842) when the cutoff value was set at 4.149.

ROC curve analysis for the detection of high PAWP



Conclusion: LnBNP×E/A is a useful parameter for detecting elevated PAWP regardless of the LV ejection fraction.

P6513
Cardiac and renal fibrosis and insulin administration in a rat model of diabetic cardiomyopathy

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Background: Diabetic cardiomyopathy results in diastolic dysfunction due to protein modification and metabolic disorder separate from hypertension and coronary artery disease. Cardiac and renal fibrosis can develop with diabetes mellitus (DM). While the anti-fibrotic effects of glucagon-like peptide 1 agonists and sodium glucose co-transporter 2 have been investigated, the cardiorenal properties of insulin treatment are unknown.
Purpose: The objective is to characterize the amount of cardiac and renal fibrosis associated with insulin administration in a rat model of diabetic cardiomyopathy.
Methods: 41 male Wistar rats were divided into controls, untreated DM, and insulin-treated DM groups. Streptozotocin (STZ) was administered to induce DM. Two months later, 11.5 u/kg/day of insulin or saline as a sham control were delivered by Alzet pumps, implanted subcutaneously over the course of 1 month. Echocardiography was used to assess cardiac structure and function. Neurohormonal markers were determined by radioimmunoassay. The animal was sacrifice and cardiac and renal tissue harvested. Trichrome and picrosirius red staining were used to determine fibrosis.
Results: Diabetes was confirmed in the untreated DM group (435±20 mg/dL). Glucose levels were not different between the treated DM and control groups (108±15 vs 110±3 mg/dL, p=0.86). Heart weight to body weight was increased in the treated DM vs control group (3.09±0.10 vs 2.64±0.06 mg/g, p<0.01). LV diameter in diastole is greater for the treated DM vs control group (7.95±0.19 vs 6.2±0.2 mm, p<0.01). Furthermore, by trichrome staining, LV interstitial, kidney medulla, and pancreas fibrosis were greater in the treated DM vs control group (3.53±0.36 vs 0.32±0.07% p<0.01; 3.74±0.30 vs 1.36±0.43% p<0.01; 2.55±0.33 vs 1.27±0.74 p=0.04, respectively). There was greater 24 hour urine protein excretion in the treated DM vs control group (1.87±0.22 vs 0.78±0.1, p<0.01. Plasma cGMP was lower in the treated DM vs control group (2.3±0.24 vs 4.9±0.9, p=0.03).
Conclusions: While there was no difference in glucose levels between the insulin-treated DM and control groups, there was greater fibrosis in the group with insulin-treated DM. The findings suggest DM even with insulin treatment leads to the entity of diabetic cardiomyopathy, manifested by a reduction in plasma cGMP levels and increased cardiorenal fibrosis. Further research is needed to determine which antiglycemic agent in DM may result in rescue of cardiac and renal fibrosis.

P6514
Tau as a predictor of cardiac events in cardiomyopathy with systolic and/or diastolic dysfunction

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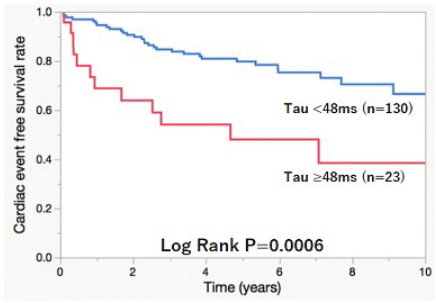
Background and purpose: Cardiomyopathy with systolic and/or diastolic dysfunction is responsible for morbidity and mortality, and is a major cause of heart failure hospitalization. Various studies have demonstrated that diastolic functional damage may precede abnormalities in systolic ventricular performance. So it is important to estimate the diastolic function regardless of systolic function. Though the time constant of left ventricular pressure decay (Tau) is a standard examination to evaluate relaxation function of left ventricular, little is known about the association between Tau and the long-term clinical outcome in cardiomyopathy.
Methods: Between March 1998 and October 2017, we enrolled consecutive 280 cardiomyopathy patients (53.9±12.7 years) with NYHA I to III, including 153 patients with dilated cardiomyopathy (DCM) and 127 patients with hypertrophic cardiomyopathy (HCM). DCM was defined as <50% left ventricular ejection fraction (LV-EF) and LV end-diastolic dimension ≥55 mm. HCM was defined as ≥15mm Left ventricular maximum wall thickness and ≥50% LV-EF. All patients underwent laboratory measurements, echocardiography and cardiac catheterization analysis. A pigtail catheter with micromanometer was advanced into LV cavity for recording intracardiac pressure curve and Tau. We divided all patients into two groups (Tau<48 group and Tau≥48ms group) and investigated the correlation of these groups and the rates of cardiac events (sudden cardiac death, ventricular tachycardia, or admission because of worsening HF).
Results: In DCM patients, the mean LV-EF was 33.0% and the plasma brain natriuretic peptide (BNP) level was 207.3 pg/mL at baseline. BNP (182 vs 353

Figure A: DCM patients (n=153)



Cardiac events

		Tau<48.0 (n = 130)	Tau≥48.0 (n = 23)
sudden cardiac death	n (%)	3 (2.3)	2 (8.6)
ventricular tachycardia	n (%)	4 (3.0)	2 (8.6)
admission due to worsening heart failure	n (%)	23 (17.6)	8 (34.7)

Kaplan-Meier survival curve