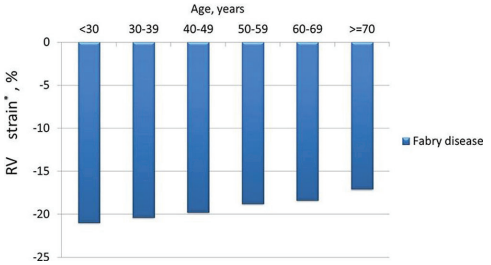
TomTec's Image-Arena™) and compared with non-FD subjects with similar baseline characteristics.
Results: A total of 240 FD and 94 Non-FD patients were enrolled. No age and gender differences were observed. (FD vs. non-FD: age 49.4±15.1 vs. 47.0±16.1 years, p=0.199; male: 47.1% vs. 52.1%, p=0.407). (Table) FD patients showed LV septal and posterior wall thickening and markedly increased LV mass compared with non-FD, although LVEF was similar. RV FAC showed no difference (38.5 vs 37.5% for FD vs Non-FD) while FD had slightly lower TAPSE. RV strain was significantly lower in FD patients. (-19.3±3.9 vs. -21.3±2.8%, p<0.001). Subgroup analysis also demonstrated a gradual decrease of RV strain with aging. (Figure)



RV strain in FD

Conclusions: Our data showed that cardiac involvement of FD is not limited to LV remodeling and that RV dysfunction was probably also involved. Speckle trackign analysis of RV may provide early detection of impaired RV function in FD patients.

2355
Treatment of cardiac manifestations in Fabry disease with the oral drug Migalastat: First 12 months results from a cohort of amenable all-comers

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Background: Fabry disease is an X-linked lysosomal storage disorder with diverse organ involvement. Cardiac symptoms manifest with myocardial hypertrophy and diffuse fibrosis, leading to progressive heart failure. Since 2001, intravenous enzyme replacement therapy has been available for specific treatment. However, due to highly varying genotypes as well as phenotypes, new drugs specifically orally available are wanted. Since May 2016, the chaperone Migalastat represents a novel form of specific therapy. Through this molecule the function of the mutated enzyme α-galactosidase A is restored. However, comprehensive results from clinical practice outside controlled trials so far have not been reported but remained anecdotal.
Objective: Cardiac and extracardial effects of this new oral therapy in patients who have amenable α-galactosidase A mutations are evaluated in a prospective monocentric register.
Methods and results: From the 290 Fabry patients treated in our center, therapy with Migalastat until then was initiated in 19 patients (mean age at start of therapy 52.7±15 years, total range 24–75 years). A follow-up visit after 3–6 months (FU 1) and another visit after 12 months (FU 2) are scheduled after initiation of Migalastat therapy. FU 1 includes a short-term diagnostic ECG, echocardiography, and examination of renal and cardiac laboratory parameters. FU 2 represents a regular annual examination, including comprehensive investigations of cardiac and extracardiac organ manifestations. In addition to clinical examinations, several specific serum biomarkers of Fabry disease such as α-galactosidase A activity and lyso-gb3 are measured before therapy and during every follow-up visit. After 3–6 months, follow-up data from 17 patients suggest beneficial effects on cardiac morphology, reducing the myocardial mass index as measured by echocardiography from 129.38±45 to 119.88±57.82 g/m^2 (p=0.02). Renal parameters remained stable. Enzyme activity was increased from 0.16±0.18 to 0.26±0.17 nmol/min/mg protein (p=0.015), Lyso-gb3 in leucocytes did not change significantly. Side effects were minor and did not cause relevant therapy discontinuation.
At the time of abstract submission, 12 months data from 6 patients were available. GFR (CKD-EPI) changed from 87.83±21.86 to 82.83±17.36 ml/min/1.73 m^2 (p=0.09), the myocardial mass, measured standardized via MRI in all patients without a cardiac device, was reduced by 6.7% (Figure 1). Enzyme activity went up from 0.13±0.20 to 0.21±0.23 nmol/min/mg protein (p=0.043, n=5), Lyso-gb3 was reduced from median 9.0 (0.7–12.8) to 6.1 (1.1–8.8) ng/ml (p=0.29, n=3).

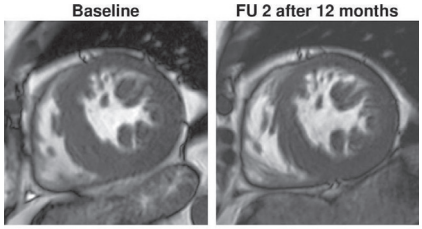

Figure 1) Cardiac progression after 1 year Migalastat therapy.

With additional 11 patients reaching the second follow-up, 1-year results from 17 patients will be available until August 2018.
Conclusion: These short- and mid-term data available so far suggest positive effects of Migalastat therapy in clinical practice specifically regarding cardiac involvement when treating amenable patients with Fabry disease.
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2356
Cardiac magnetic resonance imaging in Fabry cardiomyopathy

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Introduction: Fabry disease (FD) is a rare lysosomal storage disease that affects central and peripheral nervous system, skin, heart, kidneys, etc. Heart involvement in Fabry disease is characterized by progressive left ventricular hypertrophy and myocardial fibrosis.
Objective: We used cardiac magnetic resonance imaging (CMR) with the late gadolinium enhancement (LGE) to evaluate the prevalence and features of heart involvement in patients with FD.
Material and methods: We studied 61 consecutive adult patients with FD. MRI data was acquired with 1.5 Tesla. Criteria for myocardial hypertrophy included left ventricular wall and/or interventricular septum thickening (≥12 mm) and increased left ventricular mass index (LVMI) >85 g/m^2 in males and >81 g/m^2 in females. Lyso-Gb3 level was measured in the dry blood spots with tandem mass-spectrometry in the certified laboratories.
Results: There were 38 males and 23 females aged 18 to 69 years (median of 33 years). Classic manifestations of Fabry disease were found in 54 patients (88.5%) and included neuropathic pain in 47 (75.8%), angiokeratoma in 28 (45.2%) and vortex keratopathy in 36 patients (58.1%). MRI detected myocardial hypertrophy in 26 patients (42.6%). Thirteen patients (50.0%) had symmetrical hypertrophy, and thirteen patients (50.0%) presented with asymmetrical hypertrophy. LGE cardiac imaging showed areas of fibrosis in 13 of 26 patients (50.0%) with left ventricular hypertrophy. The majority (84.6%; 11/13) of LGE-positive subjects displayed late enhancement in the basal wall. In males, heart disease occurred more frequently than in females (52.6% vs. 26.1%; p<0.05) and at younger age (median age of 41.5 vs. 54 years; p<0.05). Myocardial hypertrophy was frequently asymptomatic. Eleven of 26 patients (42.3%) presented with chest pain that was usually mild or moderate in severity, 3 patients developed atrial fibrillation (11.5%), and 1 patient (3.9%) had chronic heart failure. In our cohort, prognosis depended on kidney and cerebrovascular disease: 14 patients (29.2%) had end-stage renal disease and were treated with chronic hemodialysis or received a kidney transplant, and 8 patients (13.1%) developed stroke (one of them died). A high prevalence of end-stage renal disease in our study was due to the fact that FD in 14 of 61 patients was detected by nation-wide screening that was conducted in the Russian dialysis units. The concentration of lyso-Gb3 was significantly higher in patients with myocardial hypertrophy (29.7 vs 8.9 ng/ml; p<0.05). However, its correlation with left ventricular myocardial mass (r=0.32) and age (r=0.11) was weak or very weak.
Conclusion: Forty percent of adult patients with FD had signs of heart involvement on CMR. In males, it occurred more frequently than in females. Myocardial hypertrophy was asymptomatic in two thirds of patients and rarely leaded to heart failure. Prognosis in our cohort was related to renal and cerebrovascular outcomes.

2357
Novel electrocardiographic parameters for the detection of Fabry Disease - A comparative multi-centre study

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Introduction: Various electrocardiographic (ECG) indices have been shown to be useful for early recognition and staging of cardiac involvement in Fabry Disease (FD). However, many of them lack sufficient sensitivity and specificity.
Purpose: To detect novel ECG indices derived from digitized ECGs of patients with FD with and without cardiac involvement via comparison with ECGs from apparently healthy individuals.
Methods: Normal ECGs from 1496 apparently healthy individuals aged 18–82 years (57.4% male) were compared to those of 112 patients aged 12–86 years (38.4% male) with Fabry Disease. All ECGs were analysed centrally using the Glasgow program. Cramer V statistic was first used to pick out those parameters which were helpful in discriminating between the two groups (n=45) and a final selection was made by using two models: the FLD (Fisher Linear Discrimination) and the Logistic models yielding diagnostic performance for the detection of cardiac involvement in FD patients vs. specificity in apparently healthy individuals.
Results: The FLD model selected 11 ECG parameters and the Logistic model selected 8 parameters with 7 being shared, viz P+ Amp V2, Heart Rate, Notch/Slur

Amp V2, LVH Score, Q Dur V1, QT Dispersion and Spatial QRS-T angle for the discrimination between the groups. A discriminant score (normalized between 0 and 100) by patient was then set up using the variable coefficients of the models determined from a training set of 80% of both groups. The Logistic model was ultimately selected and led to a 2x2 classification (Table 1) in a test sample of the remaining 20% of the groups giving a 99.1% sensitivity for classifying normal patients and 69.1% sensitivity for correctly classifying Fabry patients. Bootstrap simulations displayed an acceptable stability of the decision rule.
Conclusions: Novel ECG parameters identified via a two discriminant stepwise statistical approach may be useful for detection of FD patients with cardiac involvement. These data need to be confirmed in a prospective setting and through a comparison of FD patients with cardiac involvement versus non-FD-associated cardiomyopathy.
Funding Acknowledgements: Research Grant from Sanofi-Genzyme

THERE IS NO SWEET SPOT IN DIABETES

2358
Metformin regresses left ventricular hypertrophy in normotensive patients with coronary artery disease without type 2 diabetes mellitus - The MET-REMODEL trialM

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Background and aim: Left ventricular hypertrophy (LVH) is highly prevalent in patients with coronary artery disease (CAD), even in the absence of hypertension and is an independent predictor of cardiovascular mortality. Metformin has been shown to regress LV mass (LVM) in animal models of LVH. We hypothesize that metformin may regress LVH in non-diabetic and normotensive CAD patients with pre-diabetes and/or insulin resistance.
Methods: In this randomized double-blind placebo controlled trial, 68 patients (mean age 65±8 y, 25% females) with prediabetes (defined using American Diabetes Association criteria of HbA1c $\geq$39 mmol/mol and less than 48 mmol/mol) and /or insulin resistance (defined by fasting insulin resistance index $\geq$2.7) were assigned to receive either metformin (2g daily dose) or placebo for 12 months. An intention-to-treat (ITT) and per-protocol analysis was designed to determine the effect of metformin on the following study endpoints: Primary endpoint was change in left ventricular mass indexed to height1.7 (LVMI), assessed by magnetic resonance (MRI) imaging; other endpoints were changes in LVM, changes in body weight, office blood pressure (BP) and biomarkers.
Results: In the ITT analysis (n=61), metformin treatment significantly reduced: LVMI (metformin -2.7±2.3 g/m1.7 vs. placebo -1.4±2.7 g/m1.7; P=0.05), LVM (metformin -6.5±5.6g vs. placebo -3.45±6.5g; P=0.05), body weight (lowered by 3.6 kgs, p=0.002), office systolic BP (metformin -4.8±15.6 mmHg vs. placebo 4.6±15.7 mmHg; P=0.02) and reduced concentration of thiobarbituric acid reactive substances (TBARs), a biomarker for oxidative stress (p=0.04). In the on-per protocol analysis (n=56), metformin resulted in a greater reduction of LVMI (metformin -3.1±1.9 g/m1.7 vs. placebo -1.2±2.7 g/m1.7; P=0.005), LVM (metformin -7.5±4.6g vs. placebo -3.1±6.3g; P=0.005) and greater weight reduction of 4.2kgs (p=0.001).
Conclusions: Metformin treatment significantly reduced LVMI, LVM, office SBP, body weight and oxidative stress. These results reveal a novel mechanism for the cardioprotective effect of metformin and raise the possibility of using metformin in patients without type 2 diabetes with CAD.
Funding Acknowledgements: British Heart Foundation (grant number PG/14/4/30539).

2359
Association between insulin resistance and coronary plaque vulnerability in patients with acute coronary syndromes: insights from optical coherence tomography

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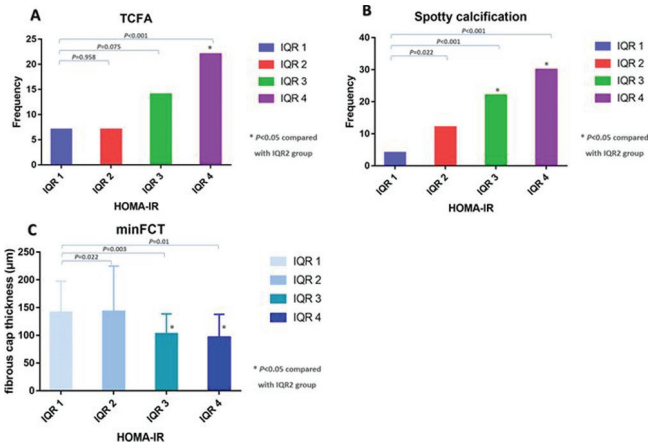
Background: Insulin resistance plays an important role in atherosclerosis progression and therefore increases the risk of adverse cardiovascular events. However, the pathophysiological basis for the association between insulin resistance and adverse cardiac events is not well understood.
Objective: The aim of the present study was to investigate the correlation between insulin resistance and OCT-identified culprit plaque characteristics in acute coronary syndrome (ACS) patients.
Methods: Patients with acute coronary syndrome who underwent selective coronary intervention were prospectively enrolled. OCT imaging was performed at culprit lesions. IR was assessed using the homeostasis model assessment of insulin resistance (HOMA-IR). Subjects were divided into four interquartile ranges according to HOMA-IR values.
Results: A total of 159 culprit lesions were identified in 145 patients. The prevalence rates of thin-capped fibroatheroma (TCFA) were significantly different among the four groups (17.5% [IQR1 group] vs 17.9% [IQR2 group] vs 35.0% [IQR3 group] vs 55.0% [IQR4 group]; P=0.001). Minimal fibrous cap thickness was inversely correlated with HOMA-IR level (141.35±56.28μm [IQR1 group] vs 142.82±82.17μm [IQR2 group] vs 102.14±36.52μm [IQR3 group] vs 96.00±41.82 [IQR4 group]; P<0.001). Spotty calcification prevalence was also significantly different among the 4 groups (5.9% [IQR1 group] vs 17.6% [IQR2 group] vs 32.4% [IQR3 group] vs 44.1% [IQR4 group]; P<0.001). Compared with the bottom quartile, subjects with elevated HOMA-IR values had higher prevalence of macrophages infiltration (P<0.001) and microvessels (P=0.023).
On multivariate analysis, Ln HOMA-IR (OR 6.022; 95% CI: 3.007–12.060; P<0.001) was an independent predictor for the presence of spotty calcification.

Logistic regression analysis for predicting the presence of spotty calcification

Variables	Odds ratio	95% confidence interval	P value
Hypertension	0.634	0.290–1.387	0.254
CRP	0.987	0.935–1.041	0.625
Hyperlipidemia	2.404	1.043–5.541	0.040
Ln HOMA-IR	6.022	3.007–12.060	<0.001



Correlation of OCT findigns and HOMA-IR

Conclusion: Increased insulin resistance estimated by HOMA-IR was significantly associated with higher prevalence rates of TCFA, spotty calcification, macrophages and microvessels in ACS. Contrarily, minimal fibrous cap thickness was inversely correlated with HOMA-IR level.

2360
Impact of statin treatment on the prevalence of lesion vulnerability and instability features in patients with diabetes mellitus - Insights from the COMBINE (FFR-OCT) Study

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Background: Statin treatment reduces adverse cardiovascular events either in primary or in secondary prevention. Nevertheless, there is a paucity of data presenting the impact of statins on plaque morphology as assessed by optical coherence tomography (OCT).
Purpose: The aim of this study was to assess plaque morphology by OCT in non-ischemic [fractional flow reserve (FFR) negative (>0.80)] lesions in diabetic patients with or without statin pre-treatment.
Methods: We performed the OCT analysis of the first 200 patients enrolled in the COMBINE trial (NCT02989740); a multi-center, prospective, natural history study which combines OCT morphologic and FFR hemodynamic assessment of non-culprit lesions to better predict adverse event outcomes in diabetic patients. OCT was used to study plaque morphology and identify vulnerable plaque features.
Results: Forty-three out of 200 diabetic patients had no statin pre-treatment. The presence of acute coronary syndrome (ACS) was 27.0% and did not differ between the two subgroups (p=0.533). Patients without statin pre-treatment were characterized by lower rate of diagnosed hypercholesterolemia (34.9% vs. 65.0%; p<0.001), male gender (46.5% vs. 66.2%; p=0.018), active smokers (7.0% vs. 23.6%; p=0.013) and previous ACS (18.6% vs. 37.6%; p=0.020), however, the insulin treatment was more frequent (48.8% vs. 33.1%; p=0.044), respectively. We analysed 235 lesions in 200 patients; see results in Table 1.
Conclusions: Diabetic patients without statin pre-treatment show a higher prevalence of plaque vulnerability and instability features like a greater lipid arc, thinner fibrotic cap and more ruptured plaques with a trend of more frequent thin-cap fi-