Cardiology
Objectives: To investigate the effects of alcohol septal ablation (ASA) on microcirculatory function and myocardial energetics in patients with hypertrophic cardiomyopathy (HCM) and left ventricular outflow tract (LVOT) obstruction.

Methods: In fifteen HCM patients (age 55±9 years) who underwent ASA, echocardiography was performed prior to and 6 months after the procedure to assess LVOTG and diastolic perfusion time (DPT). Additionally, [15O]water PET was performed to obtain resting myocardial blood flow (MBF), hyperemic MBF (hMBF) and coronary vasodilator reserve (CVR). Changes in LV mass (LVM) and volumes were assessed by CMR. Myocardial oxygen consumption (MVO2) was evaluated by [11C]acetate PET in a subset of 7 patients to calculate myocardial external efficiency (MEE).

Results: After ASA, peak LVOTG decreased from 41±32 to 23±19 mmHg, p=0.04, as well as LVM (215±74 to 169±63 g, p<0.001). MBF remained unchanged (0.94±0.23 to 0.98±0.15 mL/min/g, p=0.45), whereas hMBF (2.25±0.91 to 2.80±1.18 mL/min/g, p=0.03) and CVR increased (2.55±1.23 to 3.05±1.24, p=0.05). Preoperatively, the endo-to-epicardial MBF ratio was lower during hyperemia versus rest (0.80±0.18 vs. 1.18±0.15, p<0.001). After ASA, the endo-to-epi hMBF ratio increased to 1.03±0.26 (p=0.02). Delta CVR was correlated to delta LVOTG (r= -0.82, p<0.001), delta LVM (r= -0.54, p=0.04) and delta hyperemic DPT (r=0.54, p=0.05). MEE increased from 15±6 to 20±9% (p=0.04).

Conclusions: Coronary microvascular dysfunction in obstructive HCM is at least in part reversible by relief of LVOT obstruction. After ASA, hMBF and CVR increased predominantly in the subendocardium. The improvement in CVR was closely correlated to the absolute reduction in peak LVOTG, suggesting a pronounced effect of LV loading conditions on microvascular function of the subendocardium. Furthermore, ASA has favourable effects on myocardial energetics.

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Pieter Dijkmans: No Answer.
Mark Lubberink: Yes, financial interest/arrangement ;Philips Healthcare:Investigator
Jurrien ten Berg: No Answer.
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Objectives: Diabetes is a major risk factor for cardiovascular events. Myocardial fatty acid metabolism imaging using I-123 BMIPP (BMIPP) is known as a useful modality for identifying high risk patients with ischemic heart disease. We aimed to clarify the prognostic usefulness of BMIPP-TL dual SPECT in diabetic patients.

Methods: 191 diabetic patients (68±12yrs, 123men) without any history of heart disease who underwent rest ECG-gated BMIPP-TL dual SPECT were enrolled. Summed defect score for both SPECT (BMDS, TLDS) and mismatch score (MS=TLDS-BMDS) were obtained from visual assessment with myocardial 17 segment model. Left ventricular ejection fraction and end-diastolic volume were calculated from gated TL-SPECT. Other conventional risk factors including hypertension, dyslipidemia, renal dysfunction, and hemodialysis (HD) were added to the analysis. A composite endpoint of hard event (cardiac death and myocardial infarction) and soft event (late coronary intervention>3Mo, fatal arrhythmia, and hospitalization for heart failure) were employed.

Results: The interval was 1058±511 days. During the follow up, 13 hard and 25 soft events were observed. Cox-hazard univariate analysis showed BMDS, TLDS and MS were significantly predictive for total event (p=0.001, 0.025, and 0.001, respectively). These score were no longer predictive from analysis for hard event. Multivariate analysis revealed MS or BMDS for total event (p=0.001) and hemodialysis for hard event (p=0.008) were independent prognostic indicators. Kaplan-Meier analysis revealed patients with MS≥6 had significant higher rate for total event than those without (χ² =24.1, p〈0.0001) (figure).

Conclusions: In diabetic patients, fatty acid metabolism or perfusion mismatch obtained from BMIPP-TL dual SPECT is a useful prognostic tool for adverse cardiac event.
Impaired myocardial energetics precede coronary microvascular dysfunction and ventricular hypertrophy in carriers of the hypertrophic cardiomyopathy MYBPC3 mutation

OBJECTIVES: Hypertrophic cardiomyopathy (HCM) is a genetic cardiac disease characterized by an abnormal contractile apparatus, with subsequent increased energetic cost to force production. Insights into the causative factors of impaired energy metabolism and its relation to the onset of ventricular hypertrophy and microvascular dysfunction are of clinical importance. Therefore, the aim was to investigate myocardial energetics in asymptomatic HCM mutation carriers.

METHODS: Sixteen subjects with a MYBPC3 mutation underwent [11C]acetate positron emission tomography (PET) to obtain myocardial oxygen consumption (MVO2). By use of cardiovascular magnetic resonance (CMR) imaging, LV volumes and mass were defined to calculate myocardial external efficiency (MEE), i.e. the ratio between external work and MVO2 per gram of myocardial tissue. Resting myocardial blood flow (MBF) and hyperemic MBF (hMBF) were assessed by [15O]water PET. Eleven healthy family relatives, all non-carriers, underwent similar scanning protocols to serve as a control group.

RESULTS: MVO2 was comparable between the carriers and controls (0.16±0.05 vs. 0.15±0.04 mL/min/g, p=0.42), as was LVM (93±25 vs. 99±21 g, p=0.85). External work, however, was markedly reduced in the carriers (7398±1384 vs. 9196±2515 mmHg*mL, p=0.07). Hence, MEE was significantly decreased in the carriers compared to controls (26±10 vs. 36±8%, p=0.02). MBF and hMBF were comparable between the carriers and controls (1.22±0.34 vs. 1.18±0.31 mL/min/g, p=0.73 and 4.02±0.93 vs. 4.04±0.91 mL/min/g, p=0.94, respectively).

CONCLUSIONS: Asymptomatic HCM mutation carriers already show reduced myocardial work generation in relation to oxygen consumption, in the absence of hypertrophy and flow abnormalities. Hence, impaired myocardial energetics precede the occurrence of microvascular dysfunction and ventricular hypertrophy, and may constitute a primary component of the pathological cascades in HCM.
Objectives: The development of a near-infrared fluorescence (NIRF) fibrin-targeted sensor could enable highly sensitive in vivo optical imaging of thrombosis syndromes. Here we synthesize and validate a new fibrin-targeted peptide that enables multimodal NIRF imaging of murine deep vein thrombosis (DVT).

Methods: We synthesized a fibrin-targeted peptide conjugated to an NIR fluorochrome Cy7 (Cy7-YDEChyPCYGLCYIQ, ex/em 743/767nm). The NIRF agent is based on a fibrin peptide (EP-2104R) that has completed phase 2 clinical MRI trials. In vitro binding of the NIRF peptide to human plasma clots was assessed by fluorescence reflectance imaging (FRI) system (ex/em 740/790). Next, the fibrin-targeted NIRF agent was injected in vivo in a murine DVT model (topical ferric chloride applied to the femoral or jugular vein). Intravital fluorescence microscopy (IVFM) of femoral vessels was performed in mice with acute (2 hours old, n = 5) and sub-acute (72 hours old, n = 3) thrombi. Noninvasive fluorescence molecular tomography (FMT)-computed tomography (CT) was next performed in mice with sub-acute jugular vein DVT (n=2), followed by ex vivo imaging.

Results: In vitro clot-binding analyses showed a significantly higher NIRF clot target-to-background ratio (TBR) of fibrin-targeted peptide than free Cy7, and its binding was significantly blocked with a 100-fold excess of competitor peptide, indicating that the engineered NIRF peptide is fibrin specific. IVFM of femoral DVT also demonstrated a high TBR both in acute (mean TBR = 2.9 ± 0.3) and sub-acute (mean TBR = 3.9 ± 0.5) thrombi. Noninvasive FMT-CT demonstrated strong focal signal in the left jugular DVT compared with right sham-operated jugular vein.

Conclusions: The synthesized NIRF fibrin-targeted peptide avidly binds human clots and enables sensitive, fast multimodal optical imaging detection of acute and sub-acute DVT in vivo.

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