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**Conclusion:** Our pilot study shows a superior correlation between RAV and RAP measured by right heart catheterization compared with IVC size and respiratory variation. We are currently conducting a study on a larger cohort of patients in order to validate these results.

**P5944 | BEDSIDE**

**Detection of clinically stable myocardial ischaemic segments confirmed by invasive fractional flow reserve using resting 2D speckle tracking echocardiographic multi-layer strain: 13 months follow up**

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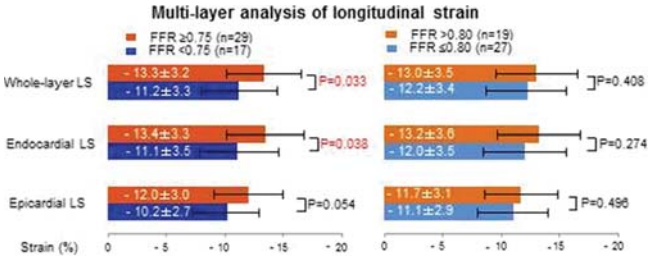
**Background:** Endocardial layer of left ventricular (LV) wall is more vulnerable to ischemia than epicardial layer. Multi-layer speckle tracking transthoracic echocardiography (TTE) yields quantitative strain measurements of LV endocardial and epicardial layers contributing to early detection of ischemic myocardium without drug or exercise loading.
**Purpose:** To detect LV myocardial stable ischemic segments using non-invasive multi-layer TTE and confirm actual prognosis.
**Methods:** This was a retrospective analysis of 39 stable patients (32 males; 65.8±11.9 yr) with 46 coronary arteries with ≥50% stenosis confirmed by invasive coronary angiography undergoing invasive fractional flow reserve (FFR) measurement and TTE (Vivid E9) within 36 days without clinical incident. On TTE, regional longitudinal strain (LS) in whole, endocardial, and epicardial layer supplied by stenotic coronary vessels was calculated. Patients were followed for a median of 13 months. Adverse events included death, myocardial infarction (MI) and urgent revascularization.
**Results:** Of 46 vessels, FFR was <0.75, ≥0.75, ≤0.80 and >0.80 in 17, 29, 27 and 19 vessels, respectively. Whole- layer and endocardial LS were significantly greater in LV segments with FFR<0.75 than when FFR≥0.75 (both P<0.05). No significant differences of epicardial LS between LV segments with FFR<0.75 and ≥0.75 and of all LS between LV segments with FFR≤0.80 or FFR>0.80 were observed. Endocardial LS showed a slightly negative correlation with FFR (R=–0.299, P=0.044). Adverse events occurred in one patient (MI) whose FFR was 0.56.




**Conclusion:** In stable subjects with coronary arteries with ≥50% stenosis, regional whole-layer and endocardial, but not epicardial LS distinguished LV segments with FFR<0.75 from those with ≥0.75 using 2D TTE.

## ION CHANNEL AND CARDIOMYOPATHY: THE NEGLECTED LINK

**P5945 | BENCH**

**A missense mutation in the transcription factor TBX20 gene causes long QT syndrome**

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**Introduction:** We describe a heterozygous missense mutation in the gene encoding the T-box transcription factor TBX20 found in a proband diagnosed with long QT syndrome. The proband is a 45 aged male who has been asymptomatic so far. Clinical evaluation of the family led to the identification of two sisters who died suddenly and two other diagnosed with long QT syndrome who wear implantable defibrillators. His mother was successfully resuscitated from sudden death and recently died from leukaemia. Next Generation Sequencing of samples from the proband and affected relatives revealed a missense mutation located in the transactivation domain of TBX20 (p.R311C), that was confirmed by Sanger. Screening for mutations in all described long QT syndrome genes was negative.
**Purpose:** This work aimed to determine the functional consequences of this mutation and the mechanism by which it can lead to QT interval prolongation.
**Methods:** WT and mutated TBX20 tagged with GFP were expressed in HL-1 cells and endogenous currents were recorded at room temperature using the whole-cell patch-clamp.
**Results:** Expression of WT or p.R311C TBX20 in HL-1 cells did not significantly modified peak or late sodium current (INa) compared to that recorded in control conditions (–45.9±17.0 pA/pF and –2.1±0.5 pA/pF, respectively). Identical results were obtained when L-type calcium (ICa,L) and inward rectifier (IK1) currents were analyzed. Next, we determined putative effects of the mutation on the IKr measured as the dofetilide-sensitive current. Expression of WT TBX20 significantly increased IKr tail current density (from 2.5±0.3 to 3.6±0.3 pA/pF at +60 mV, P<0.05). Interestingly, p.R311C TBX20 markedly reduced tail current density to 2.0±0.2 pA/pF (P<0.05). However, neither WT nor p.R311C TBX20 modified the density of the dofetilide-insensitive current (IKs). A mathematical model of human ventricular action potential demonstrated that p.R311C TBX20 prolonged action potential duration (APD) measured at 50 and 90% of repolarization by 26.7 and 28.3%, respectively. Analysis of the promoter sequence of the ion channels responsible for IKr (KCNH2) revealed a conserved TBX20 binding motif near the transcription start site. Luciferase reporter assays demonstrated that WT TBX20 significantly increased KCNH2 promoter activity, whereas p.R311C TBX20 mutation completely abrogated this effect.
**Conclusions:** The present results demonstrate that a missense mutation in TBX20 lead to APD lengthening by means of a reduction in IKr density and allow the identification of TBX20 as a novel gene associated with long QT syndrome.

**P5946 | BENCH**

**VEGF-B induces a unique electrophysiological phenotype in mouse heart**

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**Background:** Cardiac effects of vascular growth factors (VEGFs) have mainly been studied in the context of angiogenic gene therapy to enhance perfusion of the heart. However, the role of VEGFs in the heart seems not to be restricted only to angiogenesis. Recently, VEGF-B has been implicated in myocardial metabolism and is involved in and modulates heart's response to pathological stress. However, the effects of VEGF-B on myocardial function are not known.
**Purpose:** The purpose of this study was to assess the effects of VEGF-B on the contractile and electrophysiological properties of the mouse heart.
**Methods:** Echocardiographic and ECG monitoring of cardiac-specific VEGF-B overexpressing mice (TG) and their litter mate controls (WT) were done with Vevo2100 small animal ultrasound. The effect of beta-adrenoceptor agonist, dobutamin, on ECG was studied by i.p. injections. Conventional whole-cell voltage- and current-clamp was used for currents and action potential recordings (Axopatch 200B). Gene expressions were measured with qPCR and Western blot.
**Results:** In vivo contractile function or the morphology of TG hearts did not differ from WT hearts. However, ECG measurements showed a decrease in the R and S amplitudes as well as in PQ time and an increase in the QRS time in TG mice compared to the WT mice. Isolated TG cardiomyocytes had increased duration (APD90; 55.8%, p=0.005) and rise time (47.1%, p=0.00001) of the action potentials. These were accompanied by a decrease in the density of the sodium current (20.8% at –40mV, p=0.0005) and in the transient outward K+-current (57% at 50mV, p=0.0004), while ultra-rapid (34.8%, p=0.04 at 50mV) and steady state K+-currents (149%, p=0.01, at 50 mV) were both increased. In line with this, expressions of ion-channel subunits were changed; SCN5A, a gene of voltage-gated sodium channel (type V, alpha) was downregulated by 32.2% (p=0.02), Kcnip2 gene (Kv channel-interacting protein 2) downregulated by 42% (p=0.03) and Kcna5 gene (potassium voltage-gated channel) was upregulated by 36% (p=0.03). These electrophysiological changes predisposed TG animals to catecholamine-induced arrhythmias; upon dobutamine injection 60% TG vs. 10% WT mice developed severe arrhythmias.
**Conclusion:** Cardiac VEGF-B overexpression results in remodelling of cardiomyocyte ion currents, resulting in changes of the action potential waveform and unique ECG changes resembling those seen in long-QT-syndromes. Altogether, cardiac overexpression of VEGF-B induces a unique electrophysiological phenotype predisposing animals to arrhythmias.

**P5947 | BENCH**

**Heart failure is associated with distinct remodelling of atrial repolarising K2P K+ channels in patients with atrial fibrillation**

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Introduction - The prevalence of atrial fibrillation (AF) increases with advanced stages of heart failure (HF). Molecular effects of ventricular dysfunction on atrial arrhythmogenesis remain to be elucidated. We hypothesized that repolarising two-pore-domain (K2P) K+ channels are differentially regulated and contribute to proarrhythmic substrate in AF patients with concomitant HF.
**Purpose:** The purpose of this study was to assess K2P channel remodelling in patients with AF complicated by varying HF stages.
**Methods:** Right atrial tissue was acquired from a cohort of 135 patients with

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