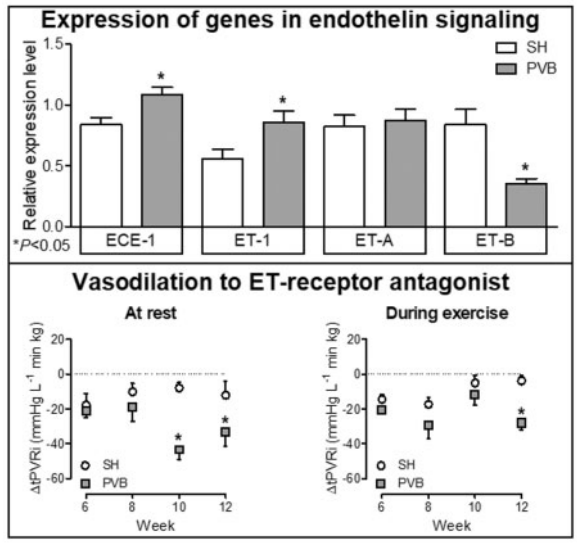
coronary artery following acute myocardial infarction. Pulmonary vascular remodeling including changes in the intima, media and adventitia, is the key structural alteration in PH. However, the role of CD271+MSCs in the pathogenesis of pulmonary hypertension (PH) are not well understood. Our objectives were to identify the role of CD271+MSCs in PB on the Patients diagnosed with PH.

Methods: We selected patients diagnosed with PH, and examined their hemodynamic parameters including pulmonary vascular resistance (PVR), mean pulmonary artery pressure (mPAP) and cardiac index (CI) by right heart catheterization. We also mesured six minutes walking (6MWT), and enforced echocardiography and blood gas analysis. Secondly, we collected blood samples and separated PB mono-nuclear cells (PBMNCs) by density gradient centrifugation. Then, we performed cell surface antigen analysis, such as CD271+CD45dim+, CD271+CD34+, CD271+CD90+, and CD271+VEGFR2+ cells in PBMNCs by flow cytometry. We compared clinical data and the frequency of CD271+MSCs in PBMNCs of patients with pulmonary hypertension. Moreover, nine patients could be followed along clinical course with drug addition in 24 months. We tried to analyze transition of the CD271+MSCs in PBMNCs and compared those change with clinical data.

Results: We selected 22 patients who matched PH criteria (group 1; n=8, group 4; n=8). The mean of WHO functional class was 2.14, and mPAP was 38.9±10.1mmHg. The average frequency of CD271+CD45dim+ in PBMNCs (0.0459±0.0376%), was higher in the patients with PH than those in patients with atrial fibrillation (n=4), angina pectoris (n=15), and healthy control (n=5) ($P<0.05$). We also found that the frequency of CD271+MSCs in PBMNCs was correlated with PVR, CI, and SPO2 ($P<0.05$). On the other hands, that wasn't correlated with 6MWT and mPAP. Interestingly, the frequency of CD271+MSCs in PBMNCs was significantly reduced along with improving PH after medical intervention in 2-24 months follow up ($P<0.05$).

Conclusion: These results suggest that CD271+MSCs in PBMNCs, derived from bone marrow to circulation, associated with the disease worsens in the case of PH. The frequency of CD271+MSCs in PBMNCs might be useful for estimation of disease severity and prognosis in PH patients.



Abstract P180 Figure. Upregulation of the ET pathway

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Transition from post- to combined pre-/post-capillary pulmonary hypertension: key role of endothelin

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Background: Pulmonary hypertension (PH) is a pathophysiological disorder that is defined by a mean pulmonary artery pressure (mPAP) of >25mmHg at rest. By far the most prevalent form (65 – 80% of all cases) is PH due to left heart disease. When left untreated, this 'passive' isolated post-capillary PH (IpcPH) can progress to active combined pre/post-capillary PH (CpcPH) characterized by chronic pulmonary vascular constriction and remodeling which can eventually result in right heart failure and death. Endothelin (ET), a potent vasoconstrictor and inducer of vascular remodeling, has been shown to be elevated in patients with PH secondary to left heart disease. However, it is currently unknown whether ET contributes to the development of pulmonary microvascular remodeling in CpcPH.

Purpose: To test the role of the vasoconstrictor endothelin in the progression from IpcPH to CpcPH.

Methods: Piglets underwent banding of the confluent of both inferior pulmonary veins (PVB n=7), or sham-operation (SH n=6). Four weeks after surgery, all animals were chronically instrumented to longitudinally assess hemodynamics for an additional 8 weeks at rest and during exercise, before and after administration of ET-A+B receptor antagonist tezosentan. Plasma was collected over time. At sacrifice, the lungs were harvested for histology and RT-qPCR, and pulmonary small arteries were isolated for wire-myograph experiments.

Results: PVB swine gradually developed PH with increased mPAP (40±7 vs 18±4mmHg) and pulmonary vascular resistance (tPVRi: 250±62 vs 105±15mmHg·L−1·min·kg both $p<0.01$).
RT-qPCR showed increased expression of endothelin converting enzyme (ECE-1) and endothelin (ET-1), unchanged expression of the ET-A, and downregulation of the ET-B receptor which is also the clearance receptor. This resulted in increased ET plasma levels from week 10 onward (8.0±1.0 vs 4.0±0.9pg/ml $p<0.05$), and a more pronounced vasodilation to in vivo administration of tezosentan at week 10 at rest (ΔtPVRi: -33±9 vs -12±8mmHg·L−1·min·kg $P<0.05$), and at week 12 at rest and during exercise. Isolated vessel experiments showed decreased vasodilation to substance P (endothelial dysfunction) in PVB lower lobes vs SH lower lobes (50±5 vs 70±12%) and increased vasoconstriction to KCl in PVB swine (13.4±0.7 vs 7.9±0.7mN both $p<0.05$), consistent with increased muscularization seen with histology. Moreover, maximal vasoconstriction to ET was increased (17.5±0.7 vs 9.9±0.7mN) whereas ET sensitivity was decreased (LogEC50: -7.5±0.2 vs 8.3±0.2M).

Conclusions: PVB swine gradually developed pulmonary hypertension with structural and functional vascular remodeling. From week 10 onward, ET-activity was increased, initiating pre-capillary aspects to the originally isolated post-capillary PH. Early inhibition of the ET pathway could be an interesting pharmacotherapeutic approach to stop progression of post-capillary PH.

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Association between adrenomedullin polymorphism and high blood pressure in a population of Lithuanian children and adolescents

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Introduction: High blood pressure (HBP) affects almost a half of the adult population worldwide and is one of the major risk factors of cardiovascular disease. The prevalence of overweight and obesity is increasing in economically developed countries and this tendency is related not only in adults but also in children and adolescents. In addition to environmental factors, a series of genome-wide association studies have identified nearly 30 new loci linked with resting BP and hypertension risk. However still unclear how these genetic variation influences blood pressure. In this study, we selected adrenomedullin (ADM) that is a vasodilator peptide which plays a critical role in blood pressure homeostasis and has a wide range of biological functions. Its role in blood pressure regulation has been examined in numerous different studies by showing that ADM could be a promising biomarker for cardiovascular disease in the future.

Purpose: The aim of this study was to evaluate the association of ADM gene polymorphism and HBP among Lithuanian children and adolescents aged 12-15 years.

Methods: This was a cross-sectional study of a randomly selected sample of 675 12-15-year-old adolescents who participated in the survey "The Prevalence and Risk Factors of HBP in 12-15-Year-Old Lithuanian Children and Adolescents (from November 2010 to April 2012)". All participants underwent anthropometric measurements. According to "The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents", normal BP was defined as SBP and DBP less than the 90th percentile, and HBP was defined as SBP and DBP ≥90th percentile for sex, age, and height. The participants with HBP were screened on two separate occasions. Single-nucleotide polymorphism (SNP) of ADM gene (rs7129220) was evaluated using real-time PCR. Adjusted odds ratios (aORs) with 95 % confidence intervals (CI) for the associations were estimated using multivariate logistic regression models.

Results: The prevalence of high blood pressure (BP ≥90th percentile) was 36.9%. Boys were more likely to have HBP than girls (OR =2.03; 95% CI 1.48–2.79, $P < 0.001$). Overweight/obesity and high WC (≥75th percentile) were associated with HBP (OR = 3.88; 95% CI 2.53–5.96, $P < 0.001$ and OR = 5.80; 95% CI 3.51–9.56, $P < 0.001$). In the multivariate analysis – after adjustment for sex, BMI and WC, carries of ADM AG genotype (vs. carriers of ADM GG genotype), ADM AG+AA genotype (vs. carriers of ADM GG genotype) had higher odds of having HBP in codominant (aOR = 1.55; 95% CI 1.02–2.37, P = 0.041, and in dominant (aOR = 1.65; 95% CI 1.09–2.49, P = 0.017) inheritance models. Significant association was also observed in additive model (aOR = 1.67; 95% CI 1.14–2.43, P = 0.008). The lowest Akaike information criterion was for additive model.

Conclusion: Our data indicate that ADM gene polymorphism was significantly associated with higher odds of HBP in Lithuanian adolescents aged 12–15 years.