Abstract: **P528**

**Vardenafil prevents the diastolic dysfunction**

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Introduction: Patients with diabetes mellitus exhibit cardiac dysfunction with decreased nitric monoxide production (diabetic cardiomyopathy). Elevated intracellular cyclic guanosine monophosphate (cGMP) levels contribute to an effective cardioprotection in different heart diseases. We investigated the effect of the phosphodiesterase-5A (PDE-5A) inhibitor vardenafil in left ventricular (LV) cardiomyocytes of diabetic cardiomyopathy rat model.

Materials and methods: Experiments were performed in Zucker Diabetic Fatty type male rat model (ZDF) and ZDF Lean (ZDFL) served as controls. The animals received with vehicle (ZDFLV) or 10 mg/tkg vardenafil per os (ZDFV). Permeabilized LV cardiomyocytes were used during the isometric force measurements. We registered the maximal Ca\(^{2+}\)-activated active force production (F\(_{\text{max}}\)), the Ca\(^{2+}\)-independent passive force production (F\(_{\text{passive}}\)) and the Ca\(^{2+}\)-sensitivities of cardiomyocytes (pCa50). Western immunoblotting were applied to assess the site-specific phosphorylation status of cardiac troponin-I (cTnI) and cardiac myosin binding protein C (cMyBP-C). Total phosphorylation status of titin protein was probed with ProQ Diamond phosphoprotein staining kit.

Results: We could not found significant differences between the F\(_{\text{max}}\) values between the four groups. The pCa50 and F\(_{\text{passive}}\) values were significantly higher in the ZDF rats compared to ZDFL, ZDFLV or ZDFV groups (pCa50 and F\(_{\text{passive}}\): ZDFL: 5.76±0.01 and 1.02±0.12 kN/m\(^2\) vs. ZDFLV: 5.78±0.03 and 1.03±0.14 kN/m\(^2\) vs. ZDF: 5.88±0.03 and 1.98±0.12 kN/m\(^2\) vs. ZDFV: 5.76±0.02 and 1.40±0.13 kN/m\(^2\), P<0.05, n=6-7, mean±SEM). In the ZDF rats the cTnI at Ser22/23, Ser43 and Thr143 sites were significantly lower, while vardenafil markedly increased phosphorylation of cTnI at the same sites compared to ZDF (ZDF: 0.77±0.05, 0.77±0.08 and 0.68±0.06 vs. ZDFV: 1.01±0.08, 1.35±0.18 and 1.35±0.16, respectively, P<0.05, n=4). We could not detect significant differences in the site specific phosphorylation status of cMyBP-C at Ser282 and the total phosphorylation status of titin between the ZDF and ZDFV groups.

Conclusion: Vardenafil prevented the development of diabetes mellitus-associated HFpEF.