Table 1

^{99m}Tc-PYP scan	n (%)	Age, years mean ± SD	Gender M/F	LVEF, % mean ± SD	AF +/–
Positive	9 (26)	82±13	5/4	50±12	5/4
Negative	26 (74)	81±10	11/15	51±17	10/16

Conclusions: Prevalence of positive 99mTc-PYP scan is relatively high (26%) in patients with non-ischemic and non-valvular heart failure over sixty years of age. Since several TTR-modifying drugs are under development, screening of cardiac ATTR by technetium-labeled bone scintigraphy should be more encouraged.

P582 | BENCH
Effects of the soluble guanylate cyclase stimulator riociguat in pressure-overload induced heart failure in mice

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Background: The NO-independent soluble guanylate cyclase (sGC) stimulator Riociguat is a promising drug with beneficial effects in patients suffering from severe heart failure (HF) and pulmonary hypertension. Animal studies, analysing the relevance and therapeutic potential of this sGC-stimulator in chronic HF are still rare.
Methods: Pressure overload was induced by transverse aortic constriction (TAC) in 7 weeks old male C57Bl6/N mice. Animals with sham surgery served as controls. Three weeks after TAC when cardiac hypertrophy has developed either Riociguat (RIO; 3 mg/kg) or placebo were administered by gavage daily for 5 more weeks (n=12 per group). Sham animals were also treated with RIO or placebo in the same drug regime (n=12 per group). The heart function in all groups was evaluated weekly by small animal echocardiography. Eight weeks after TAC proteomes of the left ventricles (LV) of sham and TAC mice were analysed by mass spectrometry and significantly altered proteins were categorised using Ingenuity Pathway Analysis (IPA).
Results: In TAC mice heart function decreased over time after surgery, whereas in sham mice no changes occurred. After administration of RIO, the TAC mice (TAC/RIO) exhibited an increase in left ventricular ejection fraction (LVEF; 48.4±5 vs. 33.4±5.5%; $p \leq 0.001$) compared to the TAC placebo group (TAC/P). After 3 weeks of drug administration, the heart function of the TAC/RIO group recovered and achieved the left ventricular systolic function similar to sham placebo mice, whereas the TAC/P group showed a further decrease (TAC/RIO vs. TAC/P: LVEF 56.3±7.9 vs. 30.6±4%; $p \leq 0.001$). The heart function in the TAC/RIO group remained stable until the end of the study. The left ventricular mass (LVM) increased in both TAC groups to the same extent until the 6th week after surgery. In week 7 and 8 after surgery, LVM of TAC/RIO decreased whereas LVM in TAC/P showed a further increase (127.2±17.3 vs. 159±21 mg, 129.8±18.5 vs. 156.4±24.9 mg; $p \leq 0.001$). In line with the reduced LVM in week 8, Sirius red staining of the myocardial tissue sections revealed a lower extend of fibrous material in TAC/RIO than in TAC/P. The proteome analysis showed that alterations of proteins assigned to the category "cardiovascular diseases" due to TAC were partially reverted upon drug treatment in TAC/RIO. Also the HF marker Myosin-7, which was more than tenfold higher in TAC/P compared to the sham group, was much less abundant in TAC/RIO.
Conclusion: In this study, we could demonstrate a beneficial effect of sGC stimulation in pressure overload induced HF. The stimulation of sGC not only improved the heart function, but also reduced the hypertrophic response to TAC.

P583 | BENCH
DPP-4 inhibition ameliorates the progression of heart failure after pressure overload through modulation of collagen type 3

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Background: Dipeptidyl peptidase-4 (DPP-4) inhibitors are oral hypoglycemic agents. Many basic researches reported that DPP-4 inhibitors have protective effects on various organs including pancreas, liver, kidney, brain and heart. There are several papers that demonstrate the cardioprotective effects of DPP-4 inhibitors in pressure overload-induced heart failure, but its effects on cardiac fibrosis are not well known.
Purpose: The purpose of this study is to elucidate the role of DPP-4 on cardiac fibrosis in pressure overload-induced heart failure by using in vivo experiment.
Methods: Wild-type C57BL/6 mice (Control) and DPP-4 knockout mice (DPP-4KO) were subjected to transverse aortic constriction (TAC). Wild-type mice were then treated with vehicle or DPP-4 inhibitor (DPP-4i, MK-0626, 3mg/kg/day). Left ventricular function and hypertrophy were assessed by echocardiography at 0, 2, and 4 weeks after TAC. The cell surface area of cardiomyocyte, myocardial fibrosis and quality of collagen fibers were assessed at 2 and 4 weeks after TAC. The structure of myocardium and collagen content were assessed at 4 weeks after TAC by transmission electron microscope.
Results: Fractional shortening was significantly higher in DPP-4i group and DPP-4KO group compared with Control group (Control, 36.4±1.6%, DPP-4i, 40.4±1.5%, DPP-4KO, 42.4±0.3%, $p<0.05$) at 4 weeks after TAC. The degree of cardiac hypertrophy was not different between three groups at 2 and 4 weeks after TAC. The degree of myocardial fibrosis was significantly lower in DPP-4i group and DPP-4KO group compared with Control group (Control, 5.0±0.7%, DPP-4i, 2.4±0.3%, DPP-4KO, 2.3±0.3%, $p<0.05$) at 4 weeks after TAC by using Masson trichrome staining. We analyzed the quality of collagen fibers by using Picrosirius red staining. The degree of collagen type III in myocardium was decreased in DPP-4KO group compared with Control group (Control, 1.1±0.2%, DPP-4KO, 0.4±0.1%, $p<0.05$) at 2 weeks after TAC. In transmission electron microscope findings, there were no significant differences in structure of cardiomyocytes between Control group and DPP-4KO group. Although there was no significant difference in structure of collagen fibers between Control group and DPP-4KO group, the density of collagen fibrils was coarse in DPP-4KO group compared with Control group at 4 weeks after TAC.
Conclusions: DPP-4 inhibition ameliorates the progression of heart failure after pressure overload-induced heart failure through inhibition of collagen type III.

P584 | BEDSIDE
Anticholinergic bronchodilator improves both pulmonary and cardiac functions in patients with heart failure with reduced ejection fraction complicated with chronic obstructive pulmonary disease

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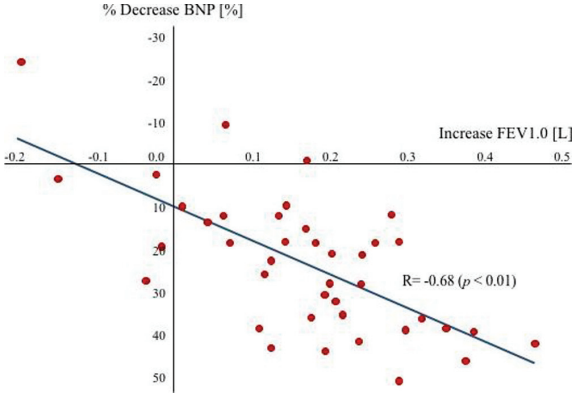
Background: Unrecognized heart failure with reduced ejection fraction (HFrEF) is common in elderly patients with stable chronic obstructive pulmonary disease (COPD), and a combination of these two diseases are prevalent in the elderly population.
Purpose: We investigated whether tiotropium, anticholinergic bronchodilator therapy improves the severity of not only COPD but also heart failure in patients with HFrEF and COPD.
Methods: Following a two-week baseline period, 40 participants receiving standard therapy for heart failure were randomly divided into groups A or B and enrolled in the crossover design study. Group A inhaled tiotropium 5mcg/day for 28 days and then had observational period for 28 days. Group B had observational period for 28 days and then inhaled tiotropium 5mcg/day for 28 days. We measured spirogram, the distance of 6-minute walk (6MWD), biomarkers of heart failure and echocardiographic parameters at Day 1, Day 29 and Day 56.
Results: With tiotropium, St George's Respiratory Questionnaire (SGRQ) score improved from 44.7±7.4 to 37.3±9.3 ($p<0.001$) in Group A and from 47.9±9.7 to 36.8±8.3 ($p<0.001$) in Group B. FEV1.0 increased from 1.56±0.11 to 1.74±0.16 L ($p<0.001$) in Group A and from 1.60±0.12 to 1.75±0.18 L ($p<0.001$) in Group B. 6MWD increased from 405±57 to 424±46 m ($p<0.05$) in Group A and from 399±74 to 422±58 m ($p<0.05$) in Group B. Both in Groups A and B, left ventricular ejection fraction increased with tiotropium from 36.3±2.4% to 41.8±5.9% ($p<0.01$) and from 35.7±3.8% to 41.6±3.8% ($p<0.01$). Tiotropium decreased plasma BNP levels from 374±94 to 263±92 pg/ml ($p<0.001$) in Group A and from 358±110 to 246±101 pg/ml ($p<0.001$) in Group B. There was a significant correlation between the percent decrease of the plasma BNP level and the absolute change of FEV1.0.



Relationship between BNP and FEV1.0

Conclusion: Anticholinergic bronchodilator therapy improved not only pulmonary function, but also the severity of heart failure in patients with HFrEF complicated with COPD.