that subjects in the CAD + MI group, who had the lowest level of TC and LDL-C, achieved more effective statin treatment.

In conclusion, our study shows that CAD preceded with primary MI influences plasma OPG levels in late middle aged subjects only and does not determine OPG levels in young elderly subjects. However, the presence of CAD was defined according to participants' declaration and was not confirmed in coronary angiography examination and subject recruitment was performed in a consecutive manner; thus some methodological bias in the assessment of population risk factors is possible. Information on the time elapsed from MI has not been collected; thus the relationship between OPG levels and extent of disease has not been examined.

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The interventricular septum in pulmonary hypertension does not show features of right ventricular failure ☆

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To the Editor:

Chronic pressure overload in patients with pulmonary hypertension (PH) results in hypertrophy, dilatation, metabolic alterations [1–3] and disturbed oxygen and calcium handling of the right ventricular (RV) free wall, leading to RV failure [4,5]. Being structurally and functionally related to the left ventricle (LV), the interventricular septum (IVS) might adapt differently to high RV pressures compared with the RV free wall.

The IVS plays a major role in the maintenance of RV function [6–8]. In PH, its function is impaired and associated with poor prognosis [9,10]. A comparison of remodeling processes of the IVS and the RV free wall may contribute to better understand the development of RV dysfunction in PH. Moreover if IVS remodeling does not reflect global processes of right heart remodeling, this would imply that IVS biopsies which have been advocated for the clinical management of PH patients because of a higher complication risk of RV wall biopsies [11] might have limited potential.

The aim of the current study was to assess whether the IVS shows similar changes in morphology and glucose metabolism as the RV free wall in PH patients in vivo. In addition, we studied whether cellular alterations of the IVS were comparable to the RV free wall in a monocrotaline PH rat model.

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Seventeen prevalent patients with a clinical stable condition of idiopathic pulmonary arterial hypertension (IPAH) were included. They underwent right heart catheterization and exercise testing [12]. The IVS, RV and LV free wall mass and myocardial glucose uptake rate (MRglu) were studied using magnetic resonance imaging (MRI) and [^{18}F]-2-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) respectively as described previously [12–15]. A priori, the study was approved by the local Medical Ethics Committee and each patient gave written informed consent (approval number: 2007/259). In addition, seventeen age and gender matched control subjects without history of cardiopulmonary diseases underwent MRI.

A male Wistar rat PH model was used to assess cardiac cellular changes [16]. The study was approved by the local Animal Ethics Committee (approval number: FYS11-03). Severe PH was induced in eight rats with subcutaneous injection of 60 mg/kg monocrotaline. Eight animals were used as healthy controls. After three weeks follow-up, in vivo cardiac function was measured using echocardiography before the rats were sacrificed. Cardiomyocyte cross sectional area (CSA), capillary density, fibrosis and leukocyte infiltration were measured [16–19].

Cardiac segments were compared by two-way repeated measurements analysis of variance with Bonferroni post-hoc testing. Differences between groups were assessed using unpaired t-tests. SPSS 20.0 (SPSS Inc., Chicago) was used for statistical analysis. Data are presented as mean ± SD, unless stated otherwise. A p-value <0.05 was considered significant.

Table 1 shows the characteristics and MRI-parameters of IPAH patients and controls. Fig. 1 demonstrates a higher RV free wall mass ($p < 0.001$) but comparable IVS mass ($p > 0.05$) in IPAH compared to controls. PET in IPAH patients showed that MRglu in the IVS was higher than in the RV (0.34 ± 0.09 vs. 0.25 ± 0.08 μmol/g/min, $p < 0.01$) and comparable to the LV (0.33 ± 0.09 μmol/g/min, $p = 0.38$).

Table 1
Clinical characteristics and MRI measurements of patients with idiopathic pulmonary arterial hypertension (IPAH) and control subjects.

Variable	IPAH patients (n = 17)	Control subjects (n = 17)	p value
Age, years	46 ± 13	46 ± 16	0.89
Female/male, n	16/1	16/1	1.00
BSA, g/m^2	1.83 ± 0.19	1.79 ± 0.15	0.53
NYHA class, II/III, n	9/8		
NT-proBNP, ng/L	1383 ± 1790		
6MWT, distance, m	453 ± 140		
Hemodynamics			
mPAP, mm Hg	52 ± 15		
RAP, mm Hg	8 ± 7		
PVR, dyne · s · cm^{-5}	693 ± 369		
PAWP, mm Hg	10 ± 4		
CI, L/min/m^2	3.1 ± 1.2		
SvO_2, %	65 ± 8		
MRI parameters			
RV free wall mass, g/m^2	56 ± 12	18 ± 3	<0.001
RVEDV, ml/m^2	82 ± 15	65 ± 14	<0.01
RVEF, %	39 ± 15	61 ± 8	<0.001
SV, ml/m^2	33 ± 11	44 ± 10	0.001
LVEDV, ml/m^2	52 ± 16	67 ± 15	<0.01
LVEF, %	64 ± 9	66 ± 6	0.41
LV free wall mass, g/m^2	41 ± 10	41 ± 9	0.81
IVS mass, g/m^2	17 ± 4	14 ± 2	0.05

6MWT = six-minute walking test, BSA = body surface area, CI = cardiac index, NYHA = New York Heart Association, mPAP = mean pulmonary artery pressure, NT-proBNP = N-terminal pro-brain natriuretic peptide, PAWP = pulmonary arterial wedge pressure, PVR = pulmonary vascular resistance, RAP = right atrial pressure, SvO_2 = mixed venous oxygen saturation. IVS = interventricular septum, LV = left ventricular, LVEDV = left ventricular end-diastolic volume, LVEF = left ventricular ejection fraction, RV = right ventricular, RVEDV = right ventricular end-diastolic volume, RVEF = right ventricular ejection fraction, SV = stroke volume. Data are presented as mean ± SD.

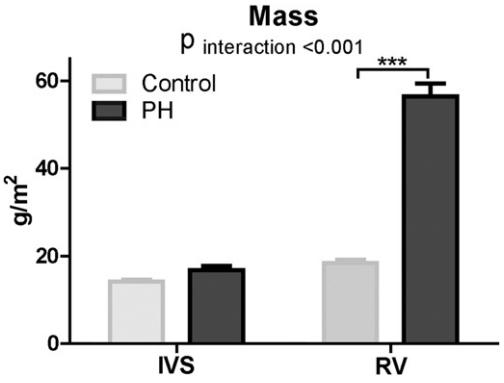

Fig. 1. Interventricular septum (IVS) and right ventricular (RV) free wall mass measured by cardiac magnetic resonance imaging (MRI).Control subjects (gray) and patients with idiopathic pulmonary arterial hypertension (IPAH) (black). RV free wall mass index was significantly increased in IPAH compared to controls. In contrast, IVS mass was similar in both groups. Data are presented as mean ± SEM. ***$p < 0.001$.

Table 2 shows echocardiography results of the PH rats. Although RV free wall thickness was increased in PH compared with controls ($p < 0.001$), IVS wall thickness was not ($p = 0.24$) ($p_{interaction} < 0.001$). Fig. 2 demonstrates a higher cardiomyocyte CSA in the RV free wall of PH rats than of controls ($p < 0.001$). In PH but not in controls, we found larger cardiomyocytes on the right side of the IVS similar to RV free wall and smaller cardiomyocytes on the left side of the IVS, comparable to the LV free wall (Fig. 3).

Although the number of capillaries was similar in both groups, the capillary density in PH was decreased in the RV free wall due to increased CSA but preserved in the IVS ($p_{interaction} < 0.001$). The amount of fibrosis was increased in both the RV free wall and IVS of PH rats compared with controls but the magnitude of increase was smaller in the IVS ($p_{interaction} < 0.001$). Leukocyte infiltration was present in the RV free wall but absent in the IVS of PH rats. We did not observe regional heterogeneity in the IVS with respect to capillary density, fibrosis and leukocyte infiltration (not shown).

In the transition from RV adaptation towards failure in PH, several RV free wall changes have been reported: hypertrophy, metabolic changes, altered cardiomyocyte contractile properties, disturbed calcium and oxygen handling, fibrosis and inflammation [4,5]. The absence of such changes in the IVS in the present study indicates a different biological response to pressure overload than the RV free

Table 2
Rat echocardiographic parameters.

Variable	PH rats	Control rats	p value
eRVSP, mm Hg	81.4 ± 5.5	24.4 ± 5.1	<0.001
PVR index, mm Hg/ml/min/mg	13.46 ± 3.37	0.76 ± 0.20	<0.001
SV, ml	0.07 ± 0.01	0.21 ± 0.04	<0.001
Heart rate, bpm	264 ± 28	432 ± 22	<0.001
CI, ml/min/g	0.08 ± 0.02	0.34 ± 0.07	<0.001
TAPSE, mm	1.4 ± 0.4	3.1 ± 0.3	<0.001
RVWT, mm	1.3 ± 0.1	1.1 ± 0.1	<0.001
IVSWT, mm	1.5 ± 0.1	1.6 ± 0.1	0.24
LVWT, mm	1.7 ± 0.1	1.7 ± 0.1	0.74
RVEDD, mm	7.2 ± 0.4	3.5 ± 0.7	<0.001
LVEDD, mm	5.2 ± 0.6	8.4 ± 0.7	<0.001
RVWT/RVEDD	0.18 ± 0.01	0.32 ± 0.08	<0.001
LVWT/LVEDD	0.34 ± 0.06	0.20 ± 0.02	<0.001

eRVSP = estimated right ventricular systolic pressure, PH = pulmonary hypertension, PVR = pulmonary vascular resistance, TAPSE = tricuspid annular plane systolic excursion, RVWT = right ventricular wall thickness, IVSWT = interventricular septum wall thickness, LVWT = left ventricular wall thickness, RVEDD = right ventricular end diastolic diameter, LVEDD = left ventricular end diastolic diameter. Data are presented as mean ± SD.