mortality (covariate-adjusted for sex, age and systolic BP) hazard ratio (HR) 0.97[0.49–1.93].

However, among patients with diabetic nephropathy, 61(41%) patients with the highest (third tertile) vs. 29(20%) the lowest (first tertile) PlGF level died during follow-up (log rank, $p = 0.006$). In a Cox regression analysis, the highest vs. lowest PlGF tertile was predictive of all-cause and cardiovascular mortality HR 1.88[1.12–3.17] ($p = 0.018$) and HR 2.93[1.45–5.89] ($p = 0.003$), respectively (adjusted for sex, age, smoking, systolic BP, HbA1c, cholesterol, GFR, logUAE, antihypertensive treatment and previous CVD). In contrast, higher levels of PlGF did not predict development of ESRD or rate of decline in GFR after adjustment for conventional risk factors ($p = 0.49$ and $p = 0.56$, respectively). Evaluating PlGF as a continuous variable introduced only minor changes in the statistical output.

**Conclusion:** In type 1 diabetic patients with diabetic nephropathy higher levels of PlGF predict all-cause and cardiovascular mortality, but not deterioration of kidney function.

## PP.6.255 EFFECTS OF ILOPROST ON ENDOTHELIAL CELL DYSFUNCTION IN PULMONARY ARTERIAL HYPERTENSION ASSOCIATED TO SYSTEMIC SCLERODERMA

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**Background:** Pulmonary arterial hypertension (PAH), is a complication of systemic scleroderma(SSc) characterized by increased pressure in the pulmonary circulation and associated dysfunction of the pulmonary vascular endothelial cells (EC). In recent years novel drugs including iloprost, have been shown to improve pulmonary haemodynamics.

**Objectives:** To investigate the effects of iloprost on EC dysfunction evaluating the circulating levels of soluble markers of EC activity in patients with SSc after six months of treatment.

**Methods:** 28 patients (21 women and 7 men, aged $36.44 \pm 1{,}63$ yrs, duration of disease was $7.50 \pm 2.08$ years) with SSc and 18 healthy subjects as controls have been studied. Every patient received intravenous Iloprost at the dose of 2ng/kg/min on 10 consecutive days over a period of 8 hours/day. Maintenance infusion was received on one day for 8 hours every 3 or 4 weeks according to the clinical presentation. At baseline, systolic pulmonary pressure (sPAP) evaluated by Doppler-echocardiogram was $68.5 \pm 17.1$ mmHg, exercise capacity measured by 6-min walking test was $355.2 \pm 108.5$ meters. Blood samples were collected to determine the circulating levels of the following soluble markers of EC activity: selectins (ES, LS, PS), thrombomodulin (TM), nitric oxide (NO).

**Results:** At baseline the circulating levels of all soluble markers of EC activity were significantly higher in patients when compared to controls ($p < 0.01$). After six months of observation the level of ES, PS, NO decreased, TM remained unchanged and LS increased. Walking distance in 6 minutes increased in 17 patients (60.7%), sPAP decreased in 23 patients (82.1%), As expected, an inverse correlation between the changes of sPAP and 6-min-walk test before and after iloprost therapy was found. Moreover a positive correlation between variations of PS and of sPAP was observed.

**Conclusion:** Our data confirm a severe EC dysfunction in patients with sclerodermic PAH, demonstrated by elevated circulating levels of soluble markers of EC activity. After three months of treatment, iloprost was able to improve exercise capacity and pulmonary haemodinamics and to reduce EC dysfunction.

## PP.6.256 PREDICTORS FOR ENDOTHELIAL DYSFUNCTION IMPROVEMENT IN HYPERTENSIVE PATIENTS

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**Objective:** To evaluate the predictors for endothelial dysfunction improvement after 6 months of treatment in patients with uncomplicated hypertension.

**Method:** 170 subjects with mild to moderate hypertension (HTN), without previous treatment and with endothelial dysfunction (ED) evaluated by impaired flow-mediated vasodilation (FMD) < 10% at baseline (noninvasive estimated at the brachial artery level) were included. The demographic, hemodynamic and humoral characteristics were recorded. All the patients received pharmacological treatment. A secondary evaluation was performed after 6 months of therapy.

**Results:** Both systolic and diastolic BP were significantly decreased ($p < 0{,}001$) when compared with the beginning of the study. Parameters of vascular function were improved in all patients after 6 months: FMD increased from $5{,}20 \pm 0{,}92\%$ to $9{,}88 \pm 3{,}06\%$ ($p < 0{,}001$), and FMD/NTG ratio (NTG = endothelium independent-vasodilation) from $0{,}30 \pm 0{,}05$ to $0{,}57 \pm 0{,}18$ ($p < 0{,}001$). Improvement of ED (defined by FMD > 10%) after treatment was obtained in 60% patients -significantly higher than in the rest of 40% patients with persistent ED (FMD < 10%)($p < 0{,}009$). Based on Spearman correlation coefficient in a bivariate analysis (SPSS15), we founded conversely proportionally associations between endothelial dysfunction and the following variables: a high body mass index ($rs2 = 0{,}025$; $p < 0{,}037$), a longer duration of HTN ($rs2 = 0{,}022$; $p < 0{,}05$), a higher brachial artery diameter at baseline ($rs2 = 0{,}023$; $p < 0{,}045$) and after 6 mo ($rs2 = 0{,}029$; $p < 0{,}025$). The following variables were directly correlated with ED: low values of FMD at baseline ($rs2 = 0{,}027$; $p < 0{,}032$), FMD at 6 mo ($rs2 = 0{,}855$; $p < 0{,}0001$), FMD/NTG ratio at baseline ($rs2 = 0{,}229$; $p < 0{,}003$) and after 6 mo ($rs2 = 0{,}849$; $p < 0{,}0001$), monotherapy as antihypertensive treatment ($rs2 = 0{,}085$; $p < 0{,}001$). By multivariate analysis (logistic regression) the following variables were negative predictors: BMI, duration of HTN, brachial artery diameter at baseline and after 6 mo. The positive predictors were: FMD at baseline, FMD/NTG ratio at baseline, double antihypertensive therapy.

**Conclusions:** This study demonstrates that, in order to improve the endothelial dysfunction in hypertensives, patients must be treated as soon as possible, even in uncomplicated mild or moderate HTN, rather with combination of antihypertensive agents than in monotherapy.

## PP.6.257 RESISTANCE AND MUSCULAR ARTERY ENDOTHELIAL FUNCTION IN SUBJECTS WITH UNTREATED ESSENTIAL HYPERTENSION

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Previous studies have yielded conflicting results relating to endothelium-dependent vasomotor function in essential hypertension. One, as yet unresolved question, is whether endothelial function depends upon pulse pressure or mean blood pressure and whether it differs in muscular arteries and resistance vessels in which pulse pressure is attenuated. We examined endothelial function in forearm resistance and muscular arteries. Eighteen subjects (6 women, mean age ± SD $44 \pm 12$ years) with uncomplicated, untreated essential hypertension (blood pressure $155 \pm 13/97 \pm 7$ mmHg) and 18 normotensive controls (6 women, aged $41 \pm 9$ years, blood pressure $124 \pm 8/72 \pm 7$ mmHg) were studied. The study was approved by the local research ethics committee and all subjects gave written informed consent. Resistance vessel endothelial function was examined by measuring the forearm blood flow response to brachial artery infusion of acetylcholine (7.5 and 15 μg/min, each dose for 5 min) and salbutamol (endothelium-dependent β 2-adrenergic agonist, 0.07, 0.24 and 0.84 μg/min, each dose for 5 min) in the presence and absence of the nitric oxide synthase inhibitor NG-monomethyl-L-arginine (L-NMMA). Endothelial function of muscular arteries was assessed by the pulse wave response (change in augmentation index, δAIx) to systemic administration of salbutamol (5 μg/min for 20 min). Forearm blood flow responses to acetylcholine and salbutamol were similar in hypertensive and control subjects but pulse wave responses to salbutamol were attenuated in hypertensive compared to control subjects (δAIx $0.2 \pm 0.04$ vs $4.1 \pm 0.1$ %, $P < 0.05$). These results are consistent with previous findings of preserved endothelium-dependent vasodilation in the microvasculature of subjects with essential hypertension but suggest that endothelial dysfunction is present in muscular arteries which influence pressure wave reflection and which are exposed to the pulsatile component of blood pressure.

## PP.6.258 ARTERIAL STRUCTURAL CHANGES AND ENDOTHELIAL FUNCTION IN PATIENTS WITH CORONARY ARTERY DISEASE, ESSENTIAL HYPERTENSION AND THEIR CONJUNCTION

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**Ojective:** To estimate structural changes and endothelial function of arteries in pts with Coronary Artery Disease (CAD), Essential Hypertension (EH) and their conjunction.

**Material and Methods:** The study involved 3 groups of pts (n = 120): 1st gr - 34 pts with CAD (angina pectoris, coronary artery stenoses more than 70%, ischaemia by ECG stress-test; mean age 57 yrs, 76% males, 54%smokers);