

performed using CP-H associated with ESR, dihydroethidium (DHE) oxidative fluorescence and immunohistochemistry (gp91phox and p22phox).

**Results:** During the pre-ischemic period, an aged-related decrease in myocardial functional parameters (coronary flow, left ventricular developed pressure, heart rate) was observed. After ischemia, we noted a partial functional recovery which was higher in Y hearts compared with A and O hearts (respectively  $17.0 \pm 2.2$ ,  $5.0 \pm 2.8$ ,  $5.4 \pm 2.6$  % of the preischemic values). Our results showed a large release of oxidized CP-H (CP\*) during the first minutes of reperfusion which was increased with age (1,296 $\pm$ 164 AU in Y hearts, 2,052 $\pm$ 188 AU in A hearts, 2,425 $\pm$ 405 AU in O hearts). The activity and expression of the vascular NADPH oxidase increased with age according to the ESR approach (14 $\pm$ 1 AU in Y group, 20 $\pm$ 3 AU in A group, 33 $\pm$ 4 AU in O group), fluorescence microscopy (DHE) and immunohistochemistry for gp91phox (0.7 $\pm$ 0.1 AU in Y group, 1.5 $\pm$ 0.1 AU in A group, 2.1 $\pm$ 0.1 AU in O group) and p22 phox; NADPH oxidase involved in these changes being localized in endothelial cells.

**Conclusion:** Our study suggests that myocardial function and adaptation to ischemia-reperfusion decrease during aging and is related to an higher level of oxidative stress. Endothelial NADPH oxidase appears to be an important contributor to the age-related cardiovascular deterioration.

1002-82

### Impact of Body Mass Index on Outcomes After Primary Angioplasty in Acute Myocardial Infarction: The Obesity Paradox

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**Background** The significance of body mass index (BMI) in pts with acute myocardial infarction (AMI) undergoing primary percutaneous coronary intervention (PCI) is unknown. **Methods and Results.** In the CADILLAC trial, 2035 pts undergoing primary PCI for AMI were divided into 3 groups based on BMI: non-obese (<25), mildly obese ( $\geq 25$  to <30) and very obese ( $\geq 30$  kg/m<sup>2</sup>). Non-obese pts were older, more frequently female, and had higher rate of intervention on LAD, while very obese pts had higher prevalence of diabetes and hyperlipidemia. Target vessel reference diameter was smaller in non-obese (median 2.89 mm) compared to mildly obese (3.01 mm, P<0.0001) and very obese pts (3.05mm, P<0.0001), while number of diseased vessels and ejection fraction did not differ among the groups. The rates of 1-year mortality and of disabling stroke were highest in non-obese pts (Table). However, by multivariate analysis, non-obese pts were not at increased risk of mortality compared with mildly obese (HR=0.68, 95% CI 0.35, 1.32) and severely obese pts (HR=0.55, 95% CI 0.22, 1.34). Rather, predictors of 1-year mortality included age (P=0.0002), LAD infarct vessel (P=0.002), and reduced ejection fraction (P<0.0001). **Conclusions.** Compared to obese pts, the 1-year prognosis of pts with low-normal BMI is significantly worse after primary PCI for AMI. This apparent "obesity paradox" may be explained by the fact that non-obese pts presenting with AMI are older and more frequently have anterior infarction than their obese counterparts.

Endpoint, %	Body mass index (kg/m <sup>2</sup> )			P-value*
	<25.0 N=552	$\geq 25.0$ to <30.0 N=915	$\geq 30.0$ N=568	
Death	7.5	3.6	1.8	<0.0001
Any MI	1.9	2.4	2.7	0.68
Ischemic TVR	11.4	13.8	14.5	0.27
Disabling stroke	1.4	0.1	0.4	0.006
Any MACE	18.9	17.1	17.0	0.65

\*By analysis of variance. TVR=target vessel revascularization. MACE=major adverse cardiac events

1002-83

### Prognostic Indications of a Novel Biological Marker of Cardiac Ischemia in Patients Presenting With Chest Pain in an Emergency Setting

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**Background:** Ischemia Modified Albumin (IMA)<sup>TM</sup> measured by the Albumin Cobalt Binding (ACB<sup>®</sup>) test (Ischemia Technologies, Denver, CO, USA) is a new quantitative biomarker which measures cobalt binding capacity of albumin modified as a result of myocardial ischemia. This study was conducted to investigate IMA in patients presenting with chest pain and assess its relationship to cardiac outcome at 6 weeks.

**Methods:** 95 patients (60  $\pm$  17 yrs, 56 males) with chest pain at presentation were studied. Serum samples were collected and traditional cardiac necrosis markers (total CK activity, CKMB, Troponin I (cTnI), Myoglobin) as well as IMA (measured on the KoneLab 20) were determined. Serum for IMA was separated and stored at -20°C prior to analysis. Cut-off values for CK, CKMB, cTnI, Myoglobin and ACB were 180 U/L, 10 U/L, 0.25  $\mu$ g/L, 110  $\mu$ g/L and 85 U/mL, respectively.

**Results:** Time from chest pain onset to presentation was less than 1 hour in 8 patients (8.5%), 1-2 hours in 15 patients (16%), 2-3 hours in 26 patients (27%), 3-6 hours in 13 patients (13.8%), 6-12 hours in 25 patients (26.5%), and >12 hours in 7 patients (7.2%). Myoglobin was elevated in 17 patients (17.8 %), total CK in 24 patients (25.3 %) and cTnI in 14 patients (14.7%) consistent with a high risk population arriving late with respect to pain onset. IMA (100  $\pm$  10 U/mL) was elevated in 84 patients (88%). There was no correlation between IMA and any necrosis marker. When considering adverse cardiac events

at 6 weeks (ischemic ECG changes, cTnI increase, MI, revascularisation and death due to cardiac complication), presentation IMA sensitivity was 97.5% (95% CI: 86.8-99.6%), specificity was 17.9% (95% CI: 8.9-30.4%) and NPV was 90.9% (95% CI: 74-100%). IMA was significantly lower in 57 patients with no complications (95  $\pm$  11 U/mL) versus 12 patients with follow-up complications (103  $\pm$  7 U/mL), p < 0.05.

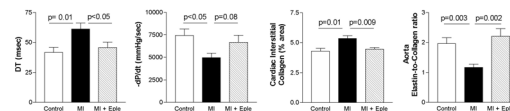
**Conclusions:** Our results show that IMA is a highly sensitive marker for coronary syndromes even in patients with normal cardiac necrosis marker values, however, it is non-specific. Negative predictive value is high for safe rule-out. IMA could be a useful tool for predicting future cardiac complications in patients with chest pain in the emergency setting.

1002-84

### Eplerenone Normalizes Diastolic Relaxation and Extracellular Matrix Accumulation in Aged Rats With Myocardial Infarction

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**Background:** The incidence and severity of CVdiseases increase rapidly with age. Aldosterone blockers have shown benefits in patients with LV dysfunction after MI and in HF. However, efficacy of these agents in experimental models of MI in aged animals has not been explored. **Methods:** 16-month old rats were divided into controls (sham, n= 9), MI (coronary artery ligation, n= 9) and MI with eplerenone in diet (MI + Eple, 120 mg/kg/d, n= 9). Treatment started 18 days after surgery, until sacrifice 3 months later. LV function and dimensions were investigated by echocardiography and hemodynamics. Cardiac fibrosis and the elastin-to-collagen ratio in thoracic aorta were evaluated by histology. **Results:** Untreated MI rats had systolic impairment (LVEF: 58  $\pm$  8 vs. 73  $\pm$  2 % in controls, p< 0.05) and clear evidence of diastolic dysfunction (increase of E wave deceleration time DT, and decrease of E wave velocity from 73  $\pm$  3 to 63  $\pm$  5 cm/s (p< 0.05), increase of isovolumic relaxation time from 22  $\pm$  2 to 28  $\pm$  3 ms). LV relaxation was depressed in MI rats (-dP/dt: -33%). Cardiac interstitial fibrosis increased by 23%, while aorta elastin-to-collagen ratio decreased by 40% (Figure). Eplerenone normalized echocardiographic and hemodynamic parameters of diastolic relaxation, cardiac interstitial fibrosis and elastin-to-collagen ratio in aorta (Figure). **Conclusion:** Eplerenone was well tolerated by aged rats. Aldosterone blockade normalized diastolic relaxation after MI, and blunted cardiac and aortic collagen accumulation.



1002-97

### Effects of Preinfarction Angina Pectoris on Left Ventricular Function in Diabetic Patients With a First ST-Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention

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**INTRODUCTION:** In patients with acute myocardial infarction undergoing primary percutaneous coronary intervention (PCI) the presence of preinfarction angina (PA), clinical sign of the phenomenon known as "ischemic preconditioning", has been shown to exert in the ischemic myocardium a protective effect on left ventricular function. Whether the same occurs in diabetic patients (DP) remains unknown.

**METHODS:** We studied 183 nondiabetic patients (NDP) (mean age 67 years, 29% female) and 153 DP (age 69 years, 39% female), hospitalized in our Coronary Care Unit for a first ST-segment elevation acute myocardial infarction and treated with successful PCI on the culprit lesion (TIMI 3 flow restored). 2D-echocardiographic left ventricular ejection function (LVEF) on admission was compared with LVEF at hospital discharge. Time from angina pectoris to balloon (TAB), ST-segment resolution  $\geq 50\%$ , T-wave inversion after PCI, CK-MB peak and in-hospital events were compared in both groups.

**RESULTS:** In the study population, PA was found in 137 subjects (mean age 67 years, 35% female, 62 DP). When PA was present, creatine kinase peak was sensibly lower in NDP (986 vs 1659 U/L p=0.025) with earlier ST-segment resolution (9.5 vs 18.3 hours p=0.009) and T-wave inversion (90 minutes after PCI: 62.0% vs 37.3% p=0.007), while no differences were instead observed in diabetic ones (all p=ns). Furthermore, in DP an inverse correlation was evidenced between LVEF after PCI and TAB (R=-0.47 p=0.019) but not in NDP with PA (R=-0.23 p=ns). At discharge, LVEF improvement was superior in NDP (+13.6% vs +8.9% p=ns) especially when PA was present (+21.6% vs 8.1% p=0.041), while in DP with PA no differences were evidenced (+8.5% vs +9.3% p=ns). Similarly, PA was associated to reduced incidence of left ventricular expansion (4.0% vs 14.9% p=0.049) and cardiac failure (12.0% vs 26.9% p=0.035) only in NDP.

**CONCLUSIONS:** Our results suggest that in diabetic patients with acute myocardial infarction treated with percutaneous coronary intervention, PA do not induce protective effects in the ischemic myocardium, probably due to loss of myocyte preconditioning which reduces tolerance to ischemia and worsens left ventricular function.