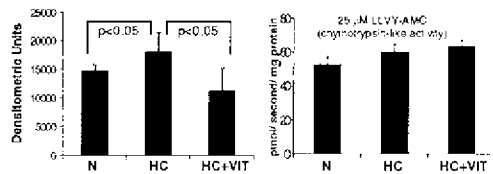


P1645 The coronary ubiquitin proteasome system is functionally active in the early stage of atherogenesis

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Background: The ubiquitin proteasome system (UPS) is involved in the removal of damaged proteins and the activation of transcription factors like nuclear factor kappa B. Recent reports, however, questioned the functional activity of the UPS under conditions of increased oxidative stress, including the early stage of atherosclerosis.

Methods and Results: For a study period of 12 weeks, female domestic pigs were placed on a normal chow diet (N) or on a hypercholesterolemic diet without (HC) or with daily vitamin C (1000 mg) and E (100 IU/kg) supplementation (HC+VIT) (n=5 per group). Compared with N, plasma concentration of total cholesterol was higher in both HC and HC+VIT (84 ± 4 vs. 413 ± 213 and 450 ± 104 mg/dL, respectively, $p < 0.05$ for N vs. HC and HC+VIT). Serum LDL-malondialdehyde concentration was higher in HC than in N and HC+VIT (8.7 ± 0.5 vs. 7.2 ± 0.9 and 6.3 ± 0.6 nmol/mg protein, $p < 0.05$). Tissue activities of radical scavenger enzymes were lower in HC than in N and HC+VIT (catalase: 12.5 ± 2.5 vs. 20.5 ± 2.9 and 21.0 ± 2.2 IU/mg protein, $p < 0.05$; MnSOD: 2.0 ± 0.2 vs. 2.5 ± 0.1 and 2.4 ± 0.1 IU/mg protein, $p < 0.05$). As demonstrated by immunoblotting, the level of ubiquitination in the coronary arterial wall 42.3% and 49% higher in HC than in N and HC+VIT, which was not attributable to an impairment in 20S proteasome proteolytic activity (figure). As seen by double-immunostaining, ubiquitin conjugates accumulated predominantly in the cytoplasm of media smooth muscle cells.



Conclusions: These results demonstrate that the UPS is functionally active in experimental early atherogenesis in association with an increase in oxidative stress. This study supports a role for UPS in the pathophysiology of atherosclerosis.

P1646 Improved haemodynamics with a novel chest compression device

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Introduction: The purpose of this clinical study was to determine if a novel chest compression device (AutoPulse?, Revivant Corp.) would exhibit increased circulation when compared to manual chest compression during cardiopulmonary resuscitation (CPR).

Methods: A total of 31 sequential patients with in-hospital sudden cardiac arrest were screened and 16 successfully enrolled (68 ± 6 years, female). All patients had received prior treatment for cardiac disease and most had other co-morbid illness. Patients were included following 10 minutes of failed ACLS protocol. Fluid-filled catheters were advanced into the thoracic aorta and the right atrium. Placement was confirmed by pressure waveforms and chest radiograph. The coronary perfusion pressure (CPP) was measured as the difference between the aortic and right atrial pressure during the chest compression's decompressed state. Following 10 minutes of failed ACLS and catheter placement, patients received alternating manual and AutoPulse? chest compressions for 90 seconds each. Chest compressions were administered without ventilation pause at 100 beats/min manual and 60 beats/min AutoPulse?. All patients received endotracheal intubation and ventilated by bag-valve at 12 breaths/minute between compressions. Epinephrine (1 mg IV bolus) was given at the request of the attending physician at 4 to 5 minute intervals.

Results: AutoPulse? chest compressions increased peak aortic pressure from 122 ± 11 mm Hg to 150 ± 8 mm Hg (mean \pm SEM, $p < 0.05$) as well as peak right atrial pressure from 85 ± 9 mm Hg to 126 ± 8 mm Hg ($p < 0.002$). Furthermore, AutoPulse? chest compressions increased CPP from 15 ± 3 mm Hg to 20 ± 3 mm Hg ($p < 0.02$). For the average patient, this increase in CPP with the AutoPulse? was 62%. Manual chest compressions were of consistent high quality (47 ± 3 kg), and in all cases meeting or exceeding AHA guidelines for depth of compression.

Conclusion: Previous research has shown that increased CPP was correlated to increased coronary blood flow and increased survival from sudden cardiac arrest. The AutoPulse? demonstrated increased circulation over manual chest compressions during CPR as measured by CPP and indicated increased coronary and systemic blood flow.

P1647 Platelet function is associated with the amount of neointimal hyperplasia after stent implantation in porcine coronary arteries

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Purpose: The purpose of this study was investigate the correlation between platelet function and neointimal hyperplasia after stent implantation in porcine coronary arteries.

Methods: 34 stents (diameter of 3.1 ± 0.2 mm and length of 14.8 ± 1.7 mm) (EuroCOR GmbH, Bonn, Germany) were implanted (8 atm pressure, 30 seconds inflation time) in 26 pigs either into the left anterior or circumflex coronary artery under general anaesthesia and after administration of 200 IU of heparin per kg bodyweight. For prevention of acute and subacute stent thrombosis, the pigs received 250 mg aspirine and 250 mg ticlopidine daily (500 mg ticlopidine as a loading dose 1 day before the intervention). After 4 week follow-up, diagnostic coronary angiography was repeated and intravascular ultrasound (IVUS) was performed. IVUS results were evaluated off-line using a computer-assisted 3D-analysis system (EchoPlaque 2, Indec Systems). Arterial blood samples were drawn before and 1 hour after the intervention, and the counts of white blood cells and platelets were measured. According to literature data, the function of platelets was derived from platelet size (mean platelet volume, MPV; platelet large cell ratio, P-LCR; platelet distribution width, PDW). Larger platelets were regarded more reactive than smaller ones.

Results: At follow-up, maximal neointimal thickness and neointimal volume as assessed by IVUS were 0.2 ± 0.1 mm and 19.8 ± 14.1 mm³, respectively. White blood cell count was not associated with the amount of neointima (pre intervention $16,800 \pm 5,100$, post $17,600 \pm 4,500$ cells/ml, $p = \text{non-significant}$, n.s.; normal range 7,000-20,000 cells/ml). Platelet count pre intervention was $459,000 \pm 122,000$, post intervention $409,000 \pm 133,000$ cells/ml ($p = \text{n.s.}$; normal range: 325,000-715,000 cells/ml). Higher MPV, P-LCR and PDW measured before intervention were significantly correlated with a larger amount of neointima as expressed by maximal neointimal thickness (MPV: $r = 0.43$, $p < 0.05$; P-LCR: $r = 0.56$, $p < 0.01$; PDW: $r = 0.46$, $p < 0.01$) and mean neointimal area (MPV: $r = 0.36$, $p < 0.05$; P-LCR: $r = 0.51$, $p < 0.01$; PDW: $r = 0.44$, $p < 0.05$).

Conclusion: Higher activity of circulating platelets is significantly associated with an increased amount of neointimal hyperplasia in the porcine model of coronary in-stent-restenosis.

P1648 Flow-dependent vasodilatation in the normo- and hypertensive rats under conditions of nitric oxide synthase inhibition

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Objective: To investigate a possible role of nitric oxide (NO) in the maintenance of arterial distensibility, conductivity, and intravascular pressure stability in normotensive Wistar-Kyoto (WKY) compared to spontaneously hypertensive rats (SHR).

Methods: Blood perfusion of hindquarter vascular bed, prior to and 15 min after a subsequent administration of nitric oxide synthase inhibitor L-NAME (10 mg/kg, iv), was performed on anesthetized and mechanically ventilated WKY (n=10) and SHR (n=11) male rats. The perfusion schedule was set at a step-wise flow rate mode, from 1.5 to 12 ml/min, to achieve perfusion pressure (PP) values 30 to 250 mm Hg.

Results: Thereafter, the following parameters were mathematically derived from "flow-pressure" dependencies: hydraulic resistance (HR), vascular distensibility (VD), and index of intravascular pressure stability (IPS) which is inversely related to the difference between maximal and minimal PP. The "flow-pressure" dependencies were plotted both before and after L-NAME injection. The blockade of NO synthesis increased systemic blood pressure both in WKY and SHR on 31 and 36%, respectively. It was associated with the increase in HR of the hindquarter vessels and concomitant decrease in IPS. After L-NAME administration, VD became significantly less in WKY (-0.16 ± 0.05 vs. 0.52 ± 0.06 , $p < 0.01$) while in SHR it became higher (0.68 ± 0.15 vs. 0.2 ± 0.07 , $p < 0.05$).

Conclusions: The results obtained support the key role of NO in the maintenance of conductivity and intravascular pressure stability both in WKY and SHR. The major determinant of VD in this model, flow-dependent vasodilatation in normotensive (WKY) rats involves NO release as a primary mechanism in contrast to SHR in which VD seems to be regulated by another factors.