1215-27 Albumin and Phospholipid-Microbubbles Influence the Neutrophil Granulocytes: An In Vitro Experiment

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Background: Activated leucocytes can bind and subsequently phagocytose microbubbles that are used for contrast-enhanced ultrasound assessment. The purpose of this study was to investigate whether left heart contrast agents can influence the inflammatory response of human polymorphonuclear neutrophil granulocytes (PMN).

Methods: PMN isolated from peripheral blood of healthy volunteers were incubated with albumin- or phospholipid-microbubbles for 20 to 40 minutes and then stimulated with the bacterial peptide fMLP or with the calcium ionophore A23187. In other experiments activation of PMN was performed using TNF-α or the protein kinase C activator PMA before incubation with the microbubbles. The neutrophil respiratory burst activity was quantified photometrically through the superoxide-induced reduction of cytochrome C and elastase release was quantified through measuring enzymatic hydrolysis after addition of a substrate solution.

Results: Albumin- and phospholipid-microbubbles (starting at contrast agent concentrations of 5 x 10⁶ microbubbles/ml) induced an extensive oxidative response of human PMN to fMLP as well as to the calcium ionophore A23187 (maximum 213±34 % for albumin- and 161±17 % for phospholipid-microbubbles for fMLP and 232±23 % for albumin- and 169±23 % for phospholipid-microbubbles for A23187) Activation of PMN with fMLP or PMA induced also an extensive oxidative response of human PMN which was in the case of TNF-α possible at 10-fold lower contrast agent concentrations. The effect of left heart contrast agents on burst activity could be significantly impaired through preincubation of the cells with the polymerisation-inhibitor Cytochalasin B, indicating that phagocytosis of the microbubbles contributes to their effect on the burst activity. Albumin-microbubbles could also significantly amplify the release of neutrophil elastase after stimulation of PMN with fMLP or PMA.

Conclusions: Left heart contrast agents used for contrast-enhanced ultrasound assessment can activate human PMN inducing an extensive respiratory burst to secondary stimuli. The clinical relevance of this effect remains to be elucidated.

1215-28 Myocardial Capillary Damage in Myocardial Contrast Echocardiography: Influence of Ultrasound Transmit Energy

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Background: Previous animal work has demonstrated both PVCs and evidence of capillary leakage after intravenous contrast injection for MCE.

Purpose: To evaluate the frequency of PVCs and extent of capillary damage during MCE as a function of ultrasound transmit power.

Methods: 22 anesthetized rats with a tail vein catheter for contrast injection were imaged during continuous ECG recording in a 37°C water bath using 1:4 triggered fundamental ultrasound with the microbubble contrast agent Optison (Mallinckrodt). The rats were randomly assigned to four distinct transmit powers: 0dB, 3dB, 6dB, and 9dB. After 5 minutes of ultrasound exposure, the rats were euthanized and the hearts excised for examination.

Results: PVCs occurred in all 6 rats at 0dB, 5 of 6 rats at ~3dB, 1 of 6 rats at ~6dB, and none of 5 rats at ~9dB. From 0dB to ~3dB, the Evans blue area on the heart surface decreased: 111.6±21.5 mm²; 78.6±19.0 mm² and 47.4±7.1 mm² for group A, B, and C, respectively. Evans blue leakage was statistically increased (P<0.05, ANOVA test) for groups A, B, and C but not D, relative to shams.

Conclusions: Myocardial leakage induced acutely during MCE progressively diminishes after cessation of imaging to sham values after about 20 minutes. The findings have implications for the safety of diagnostic MCE and for therapeutic drug/gene delivery with this technique.

1215-30 Time- and Energy-Dependent Ischemic-Like ECG Changes During Myocardial Contrast Echocardiography in Rats

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Background: Previous studies have shown that the combined exposure of rat hearts to microbubble contrast agents and high mechanical index (MI) ultrasound (US) results in time- and energy-dependent myocardial alterations, which are mostly ischemic in origin. To test this hypothesis further, we investigated the occurrence of ischemic ECG changes during contrast echocardiography (MCE) in 11 anesthetized rats exposed to both PESDA and triggered (1Hz) US at MI of 0.2, 0.5, 1.0 and 1.6 for 3, 9, 15 or 30 min. A leads peripheral ECG was obtained just before, and immediately after MCE. ST-segment changes were measured in lead II at the J point, using the J-T interval as reference.

Results: In control animals and in those exposed to US at MI of 0.2, no ST-segment changes were noted. By contrast, significant ST-segment elevation occurred in all animals exposed to an MI ≥0.2 (P<0.05 vs. controls and MI<0.2). The amplitude of ST-segment elevation increased progressively with both the duration of US exposure and MI (graph). Conclusions: Our data show that exposure of rat hearts to high-MI US and PESDA induces ischemic-like ECG changes, whose severity is directly proportional to the energy applied and the duration of ischaemia.

1216-08 Clinical Utility of Echocardiographic Suboptimal Echocardiograms: A Multistudy Analysis

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Purpose: A 16 segment model is often used in echocardiography to evaluate myocardial function. In some echocardiographic views, an entire coronary vessel territory may be represented by a single slice. If such a segment is not visualized, single vessel disease of the subendocardial artery may be overlooked. The correct identification of wall motion abnormalities in these segments is therefore critical for the diagnosis of CAD in these vessel territories.

Methods: We analyzed data from cardiac examinations of 138 patients enrolled in two clinical studies with suramin hexanacouamide microspheres (sionovue, traccio). All patients had two or more segments poorly seen on a baseline ultrasound examination. For our analysis we used a 16 segment model and defined the following segments as critical: 4-shrinking view: apical septal, mid lateral, basal septal; 2-chamber view: apical anterior, mid inferior, basal inferior. Results: In 119 out of the 138 baseline examinations at least one critical segment was not visualized. After injection of 2 ml of SonoVue, 84 of these patients had complete visualization in all critical segments. These results were confirmed by four independent blinded reviews (2 per study, in which the number of studies with at least one critical segment not visualized decreased after SonoVue: from 64 to 29 (Reader 1 Study A), from 69 to 33 (Reader 2 Study A), from 36 to 7 (Reader 1 Study B) and from 67 to 0 patients (Reader 2 Study B). Conclusions: The inability to visualize critical segments on standard 2- and 4-chamber apical views is a frequent cause for referral to other invasive imaging modalities. By converting critical myocardial segments from non-diagnostic to diagnostic in 64 out of 112 patients (71%), a successful ultrasound examination was possible in over 70% of patients with clinically inconclusive base studies. These findings suggest that contrast echo can increase the reliability of echocardiography while potentially decreasing the cost of evaluating patients with suspected CAD.