1020-68 **Thromboembolic Risk Stratification Based on SPAF Clinical Criteria in Patients With Paroxysmal Atrial Fibrillation and Flutter: A Prospective Transesophageal Echocardiography Study**

Nadia Benyounes, Lydia Djaouti, Charles Smadja, Catherine Albo, Franck Boccara, Ariel Cohen, *Saint Antoine University Hospital and Medical School, Paris.*

It has been reported that patients (Pts) with paroxysmal atrial fibrillation and flutter (PAT) have a lower thromboembolic (TE) risk than those with permanent atrial fibrillation (AF). However, a recent longitudinal study suggested a similar annual rate of ischemic stroke in both populations. This apparent discrepancy could be explained by differences in the frequency of transesophageal echocardiography (TEE)-detected TE risk markers.

Objective : We sought to assess TE risk markers using TEE in Pts with PAT according to the SPAF clinical criteria for risk stratification.

Methods : As part of an ongoing study based on transthoracic and TEE in atrial arrhythmia, we prospectively studied 145 Pts within 48 hours of spontaneous cardioversion of any documented PAT (AF in 120 Pts, atrial flutter or tachycardia in 25 Pts). Pts were divided into high, moderate and low clinical risk groups. The following parameters were evaluated : left atrial (LA) and LA appendage (LAA) areas, spontaneous echo contrast (SEC), LAA end diastolic emptying velocity (Vel), LAA thrombus (Thr) and thoracic aorta atheroma (TAA).

Results : The main results are summarized in the table.

	High risk (n=66)	Moderate risk (n=34)	Low risk (n=45)	p
Mean age (years)	77.9 ± 9.9	63.6 ± 7.3	54.2 ± 15.3	<0.001
LA area (cm²)	19.9 ± 5.6	19.3 ± 4	18.3 ± 5.5	0.937
LAA area (cm²)	4.9 ± 2.3	4.4 ± 1.7	4.6 ± 1.9	0.987
LAA Vel ≤25 cm/s (n,%)	13 (20.6)	10 (29.4)	13 (30)	0.460
LA SEC (n,%)	22 (35)	5 (15.1)	5 (11.6)	0.007
LAA Thr (n,%)	2 (3)	0	1 (2.2)	0.599
TAA ≥ 4mm (n,%)	15 (22.7)	5 (14.7)	2 (4.4)	0.031

There was no difference in the 3 groups with regard to LA and LAA areas, Vel and Thr. LA SEC and TAA were significantly more frequent in high risk Pts using SPAF clinical criteria.

Conclusion : These results suggest the need for a similar risk stratification and anticoagulant regimen in high-risk patients with PAT and permanent AF.

POSTER SESSION

1021 Evolving Applications of Micro Bubbles and Ultrasound

Sunday, March 17, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1021-53 **Specific Fibrin Enhancement With Targeted Echogenic Immunoliposomes**

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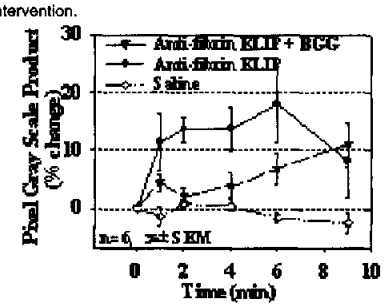
Background/Methods: Targeted echogenic immunoliposomes (ELIP) for enhancement of vasoactive and pathological components of atherosclerosis (ATH) have been developed. Non-specific intravascular ultrasound (IVUS) enhancement of fibrin by IgG ELIP has been shown. However specific binding of ELIP to fibrin, that results in IVUS enhancement has not been demonstrated. IVUS imaging occurred prior to and after IgG, anti fibrin and anti-fibrinogen conjugated ELIP injections (8mg) at 1,2,4,6,9 minutes with and without bovine gamma globulin (BGG) 1mg/ml to block non-specific binding.

Results: IGG and anti-fibrinogen and anti-fibrin ELIP without BGG non-specifically enhanced fibrin at 1min and maximally at 6 min ($p<0.01$). IgG and anti-fibrinogen ELIP were the no different from control in the presence of BGG at all times. Anti-fibrin ELIP in the presence of BGG specifically bound and enhanced fibrin at 6 min and maximally at 9 minutes vs saline ($p<0.05$).

Conclusion: In this model we have demonstrated that specific binding of ELIP is sufficient to enhance the IVUS image of fibrin. The time required for specific vs. non-specific enhancement is slightly prolonged due to competition at binding sites. These data allow for further development of ELIP for specific molecular imaging for use in staging ATH for diagnosis and intervention.



1021-54 **Effects of Various Microbubble Composition on the Interactions With Activated Leukocytes**

Hiroto Takeuchi, Koji Ohmori, Isao Kondo, Akira Oshita, Kaori Shinomiya, Kazushi Yukiiri, Yuichiro Takagi, Yang Yu, Katsufumi Mizushige, Masakazu Kohno, *Kagawa Medical University, Kagawa, Japan.*

Background: Interactions between activated neutrophils and microbubbles including adhesion and phagocytosis have been utilized to deliver microbubbles to the site of inflammation. The aim of this study was to examine the effect of various characteristics of microbubbles on this application. **Methods:** Sonicated albumin (SA: albumin shell, air), Optison® (OPT: albumin shell, octafluoropropane gas), BR1 (phospholipid shell, sulfur hexafluoride gas), and BR14 (phospholipid shell, perfluorobutane gas) (Bracco) were tested. The 4 agents were respectively incubated in RPMI 1640 medium containing serum on the cell culture slides with human neutrophils ($2x10^6$/mL) activated by phorbol-12-myristate-13-acetate at 37 degree to allow interactions on an intravital microscope. **Results:** At 3 minutes after the onset of reaction, adhesion of 1-3 microbubbles to some of the leukocytes was observed for all agents. At 15 minutes, the number of leukocytes that phagocytosed microbubbles per 50 leukocytes was 3±1 cells for SA, 12±3 cells for OPT, 12±2 cells for BR1, and 13±3 cells for BR14. At 30 minutes, no leukocytes contained microbubbles for SA, and majority of the microbubbles were digested leaving only a few leukocytes (2±1 cells) containing microbubbles for OPT. However, for BR1 and BR14, the number of leukocytes containing microbubbles remained unchanged. In addition, the size and shell structure of intracellular microbubbles remained unchanged for BR1 and BR14. **Conclusions:** This study demonstrated that the phospholipid-stabilized microbubbles are stable as compared with those with albumin shell in the cytoplasm of the leukocyte after the phagocytosis. A stable acoustical property may be better provided by these microbubbles at the site of inflammation.

1021-55 **How Well Can Real-Time Perfusion Imaging by Myocardial Contrast Echocardiography Detect Peri-Infarction Ischemia? Comparison of Adenosine Stress and Dobutamine Stress**

Chih-Hui Chin, Yan-Qiu Xing, Aldo Prado, Raeeda Gheewala, Joachim Nesser, Natesa G. Pandian, *Tufts-New England Medical Center, Boston, Massachusetts.*

Background: Peri-infarct ischemia, perfusion deficit adjacent to or around a fixed resting defect, is well detected by nuclear imaging. While real-time perfusion imaging (RTPI) using ultrasound contrast agents has been shown to detect infarction and coronary stenosis, its accuracy in the assessment of peri-infarct ischemia (where a resting perfusion defect already exists) is not known.

Methods: We employed RTPI modality (Agilent and ATL Philips) in a canine model (15 dogs) of distal coronary occlusion (CO) and proximal coronary stenosis. Using coronary flow probe recordings, physiologic significance of proximal coronary stenosis was established by confirming abolition of coronary reserve. Contrast agent, Optison was given as slow bolus injections at baseline, during prolonged distal CO, during adenosine bolus stress and during dobutamine stress. Triphenyltetrazolium chloride (TTC) staining was used to verify distal infarction. RTPI recordings at baseline, distal CO and stress protocols were randomly mixed and reviewed blindly.

Results: In all but one dog, RTPI detected distal infarct as small as 9% of the left ventricle. The sensitivity, specificity and overall diagnostic accuracy of RIPI in the detection of distal infarcts were: 93%, 87%, and 90%. Sensitivity, specificity, and overall diagnostic accuracy of RTPI in the assessment of peri-infarction ischemia were: for adenosine stress, 87%, 87% and 87%; for dobutamine stress, 92%, 92% and 92%. The spatial extent of perfusion defect related to peri-infarct ischemia was similar during both adenosine and dobutamine stress ($y=0.9x+2.2$, $r=0.89$, $p<0.001$).

Conclusion: 1) Even small distal infarcts can be detected by RTPI; 2) Peri-infarct ischemia can be accurately recognized by RTPI during stress; 3) Adenosine and dobutamine stress appear equally reliable in RTPI evaluation of peri-infarct ischemia.

1021-56 **Myocardial Opacification at Intravenous Myocardial Contrast Echocardiography Depends on the Depth of Focus Point: In Vivo and In Vitro Study**

Sachiko Yagura, Kumiko Kiyoshima, Jyuri Okazaki, Hideo Hirayama, Kentaro Ohtani, Yasushi Kashiwagi, Tsutomu Toshida, Akiko Iwata, Hiroyuki Kayano, Toshihiko Asanuma, Fuminobu Ishikura, Shintaro Beppu, *Osaka University, Suita, Japan.*

Background: Myocardial opacification is not always homogeneous even in a normal heart.

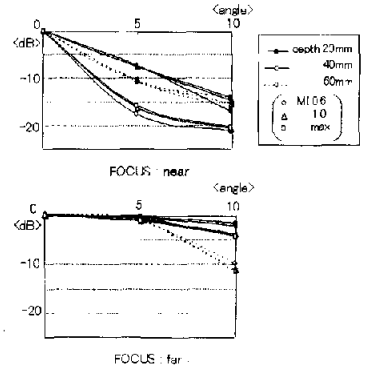
Purpose: The aim of this study is to reveal the effect of the focus point on the myocardial opacification.

Methods: In vivo, we studied baseline-subtracted peak videointensity (bs-PV) at anterior, septal and lateral walls of the short axis view by changing the position of focus at near, middle and far, during injection of Optison (0.1ml/min) in 6 open-chest dogs. In vitro, acoustic pressure at various points in a water tank was measured using a hydrophone. The hydrophone was set at 20, 40 and 60 mm from the transducer and the ultrasound beam was deviated to the 0, 5, 10 degree from the line connecting the transducer and the hydrophone. The negative peak acoustic pressure was measured at each setting by changing the focus at near, middle and far position.

Results: The opacification of the anterior wall was faint at far focus, and bs-PV was almost half of that at near focus. In vitro, when the focus was far, the acoustic pressure of the near field was still high even if the ultrasound beam did not aim the hydrophone. When the focus was near, the pressure decayed as the ultrasound beam deviated from the hydrophone.

Conclusion: When the focus point is set far, the acoustic pressure around the anterior is

steadily high even deviating away from the ultrasound beam, resulting excessive destruction of microbubbles. The focus point should be set near, when opacification of the near region is examined.



1021-57 Microvascular Behavior of Microbubbles Is Strongly Influenced by Shell Charge and Polyethyleneglycol Coat

Nicholas G. Fisher, Jonathan P. Christiansen, Alexander L. Klibanov, Howard Leong-Poi, Sanjiv Kaul, Jonathan R. Lindner, *University of Virginia, Charlottesville, Virginia.*

Background: Ultrasound imaging has demonstrated that certain experimental microbubble agents are retained within normal tissue irrespective of size. Since these microbubbles contain negatively charged lipids, we hypothesized that anionic microbubbles are retained by attachment to vascular endothelium especially when a protective polyethylene glycol (PEG) coat is absent.

Methods: Lipid microbubbles of similar size with either a net neutral or anionic charge were prepared, with or without PEG-40 stearate. The microvascular behavior of the microbubbles was assessed by intravital microscopy of the cremaster muscle in 9 mice. Twenty optical fields (0.2 mm^3 tissue per OF) were observed at 2 and 10 min following intravenous injection of $4x10^7$ fluorescently-labeled bubbles. Pulmonary and myocardial retention of microbubbles was assessed by low-MI myocardial contrast echocardiography in 6 dogs following bolus intravenous injections of microbubbles.

Results: Neutral microbubbles with or without PEG were rarely retained within the cremasteric microcirculation. Anionic microbubbles (zeta potential -75 mV) without PEG adhered to the endothelial surface of capillaries for several seconds to >10 min. The mean number retained decreased with time (4.3±0.3 versus 2.0±0.9 mm^{-3} at 2 and 10 min, p<0.01). The presence of surface PEG significantly (p<0.01) reduced anionic microbubble retention (1.4±0.1 mm^{-3} and 0.9 ±0.1 mm^{-3} at 2 and 10 min). Myocardial retention of anionic microbubbles without PEG was confirmed by persistent myocardial opacification 10 min after injection. Pulmonary capillary retention was greater for anionic microbubbles without PEG compared to neutral microbubbles with PEG, as determined by the percent signal loss from the RV to LV cavity, (66±14 versus 35±16 %, signal loss p<0.01).

Conclusions: The surface charge and presence of PEG influence the microvascular behaviour of lipid microbubbles. Anionic microbubbles without PEG are retained in capillaries thereby increasing their pulmonary retention. However, capillary retention may be advantageous for delayed myocardial imaging.

1021-58 Skin Perfusion Assessed by Contrast Ultrasound Predicts Tissue Survival In a Free Flap Model

Jonathan P. Christiansen, Howard Leong-Poi, Lester R. Amiss, David B. Drake, Sanjiv Kaul, Jonathan R. Lindner, *University of Virginia, Charlottesville, Virginia.*

Background. Successful autologous skin flap grafting, widely used to correct traumatic and other wound defects, depends on adequate perfusion in the transposed tissue. Post-operative venous occlusion is a common cause of flap failure in patients. Currently a reliable, non-invasive means for assessing perfusion in soft tissue flaps that can accurately predict survival is not available . We hypothesized that contrast ultrasound could assess skin perfusion and would predict long-term flap survival following post-operative venous occlusion.

Methods. Autologous abdominal skin flaps, with a left epigastric vascular pedicle, were created in 10 rats. Venous occlusion (5 hrs) was performed on Day 2. Perfusion in the flap and adjacent normal skin was assessed using real-time pulse inversion imaging (MI = 0.1) during intravenous infusion of Optison, prior to occlusion and 24 hr after reflow. Quantitative measurements of capillary blood volume (CBV) in the flap were expressed as a ratio to that in the normal skin. Flap perfusion was also qualitatively assessed by a blinded observer and scored as normal, reduced, or absent. Flap survival was assessed on Day 7.

Results. Following surgery perfusion assessment was possible in all flaps and hyperemia was seen prior to venous occlusion (CBV ratio 1.5±0.26). At Day 7, 4 flaps survived and 6 were necrotic. Proximal flap perfusion 24hrs after venous occlusion was significantly greater in flaps that survived vs those that became necrotic (CBV ratio 0.8±0.09 vs 0.2±0.1, p=0.0001). Qualitative assessment of the presence of perfusion (either normal or reduced) by the blinded observer correlated well with quantitative data, and predicted flap outcome in all cases.

Conclusions. Skin perfusion may be assessed quantitatively and qualitatively by contrast ultrasound. Perfusion 24hrs following a secondary ischemic insult in a free flap accurately predicts subsequent tissue survival. These findings have important implications for the bedside assessment of skin flap viability and for determining treatment strategies.

POSTER SESSION

1022 Advances in Prognostic Assessment With Nuclear Imaging

Sunday, March 17, 2002, 9:00 a.m.-11:00 a.m.
Georgia World Congress Center, Hall G
Presentation Hour: 10:00 a.m.-11:00 a.m.

1022-59 Prognostic Value of Stress Myocardial Perfusion SPECT In Patients With Markedly Reduced Left Ventricular Function

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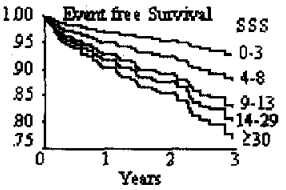
Background: The role of stress myocardial perfusion in predicting cardiac events in patients with markedly reduced left ventricular (LV) function is controversial.
Methods: We identified 599 patients who underwent rest Tl-201/stress Tc-99m sestamibi gated SPECT (treadmill exercise or adenosine), and had LV ejection fraction (EF)<35% by gated SPECT. Patients were followed up for 2.1+/-0.7 yrs. Follow-up time was censored at the occurrence of cardiac death, myocardial infarction (MI) or revascularization. Perfusion images were scored using a 20-segment model and a 0-4 scale, and summed stress (SSS) and rest (SRS) scores were derived.
Results: During follow-up 58 cardiac deaths and 14 non-fatal MIs occurred. Multivariate Cox regression demonstrated that SSS was a significant predictor of cardiac events, after adjusting for clinical and EF data (p=0.02), whereas SRS was insignificant (p=0.1). Adjusted 3-year survival rates without MI were 93% for SSS 0-3, 88% for 4-8, 84% for 9-13, 80% for 14-29, and 77% for SSS>/=30 (Figure). The number of segments with reversible perfusion defect and the number of those with non-reversible defect were both independent predictors of cardiac events (p=0.02 and 0.01, respectively).
Conclusion: The overall amount of perfusion abnormality at stress and the extent of stress induced ischemia are independent predictors of outcome in patients with EF<35%. Thus, stress myocardial perfusion provides significant prognostic information in patients with markedly reduced EF.



1022-60 Comparison of Post-Stress 99mTc-Sestamibi Lung Uptake and Transient Ventricular Dilation in Severe Ischemia

Claudio Marcassa, Michele Galli, Riccardo Campini, Paolo Calza, Pantaleo Giannuzzi, *Salvatore Maugeri Foundation, IRCCS, Veruno, Italy.*

Background. Transient ischemic dilation (TID) and high lung/heart ratio (L/H) in thallium-201 scintigraphy are related to the severity of ischemia. How accurate are these parameters in stress sestamibi SPECT is still controversial.
Methods. The TID index and L/H were calculated in 360 consecutive pts (63±9 years; 53% male) with known or suspected CAD (22% with old MI), undergoing dual-day stress (187 pts exercise and 173 dipyridamole) - rest sestamibi Gated-SPECT imaging. L/H was calculated from a summed anterior projection on post-stress images, acquired 40-45 min after the injection; the perfusion defect size was calculated from polar maps of tracer distribution by comparison with our normal data-base (mean - 2SD). A (stress - rest) tracer uptake defect >5% defined the presence of stress-induced ischemia. Post-stress and rest LV EF was automatically calculated using the QGS method; a TID index was also calculated. Severe ischemia was defined as the presence of either a reversible defect>15% of LV surface or a decrease in LVEF from rest to stress >5%, or both.
Results. Severe ischemia was documented in 48 pts (13%; 25 with a reversible defect>15%, 14 with a LVEF decrease >5% and 9 with both) . L/H was 0.36±0.06 and 0.29±0.05 in pts with or withouth severe ischemia, respectively (p<0.0001). TID index was 1.08±0.22 and 1.37±0.45, respectively, in pts with or without severe ischemia (p<0.001).
By ROC analysis, L/H better correlated with the occurrence of severe ischemia (area-under-curve 0.81 [CI 0.76-0.92]; sensitivity 79%, specificity 89%) than TID index (area-under-curve 0.72 [CI 0.61-0.81], sensitivity 59%, specificity 83%; p<0.05). The best cut-off values of L/H and TID index for the detection of severe ischemia were 0.32 and 1.19, respectively.
Conclusions. Elevated (>0.32) L/H on post-stress sestamibi SPECT seems to yield an accuracy in the detection of patients with severe ischemia better than that provided by TID. Differences between lung tracer kinetic and in LV volumes recovery after stress could explain these results.