

1060-132

### Combination of Aspirin and Clopidogrel Exerts Superior Antithrombotic Potency Compared to Warfarin on Mechanical Heart Valves in a Rabbit Flow Chamber

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**Background:** Lifelong oral anticoagulation (oac) is considered to be the gold standard for the prevention of thromboembolic events after implantation of artificial heart valves. In studies on the prevention of subacute coronary stent thrombosis the combination of aspirin with ADP-antagonists such as ticlopidine or clopidogrel was found to be more effective than oac. The aim of our study is to investigate the efficacy of the combination of aspirin and clopidogrel in the prevention of thrombus formation on artificial valves in an experimental animal model compared to an anticoagulation with cumarins.

**Methods:** Antithrombotic potency was investigated in a rabbit-model using a perfusion chamber regarding the formation of thrombi on leaflets of Sulzer Carbomedics mechanical heart valves.

**Studies were performed** after oral application of clopidogrel and aspirin in group I (n = 11) at best for 4 days, after minimal 5 days treatment of warfarin in group II (n = 11) and without medication in group III (n = 5). Leaflets from mechanical heart valves were placed in a flow chamber. After tracheotomy and mechanical ventilation flow chamber was filled with blood in a circuit between art. carotis and v. jugularis. We compared the weight of the leaflets before and after the experiment. Further analysis were performed by electron microscopy.

**Results:** In group III (controls) flow chamber was clotted after about 15 minutes of circulation. Comparison of weight analysis between group I and II before and after perfusion showed a superiority of clopidogrel/aspirin-treatment in preventing thrombus formation on leaflets. Mean weight difference in group I (clopidogrel/aspirin) was 11,2 mg compared to mean weight difference of 17,5 mg in group II (warfarin).

**Analysis by electron microscopy** showed less fewer thrombus formation, i.e. deposition of platelets, fibrin and erythrocytes, on leaflets exposed to blood from rabbits in group I compared to group II.

**Conclusion:** Combination of clopidogrel and aspirin exerted in an experimental animal perfusion model compared to anticoagulation with warfarin superior potency in preventing thrombus formation on artificial heart valve leaflets.

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### Role of Serial Troponin Testing for Diagnosis of Perioperative Myocardial Infarction After Cardiac Surgery

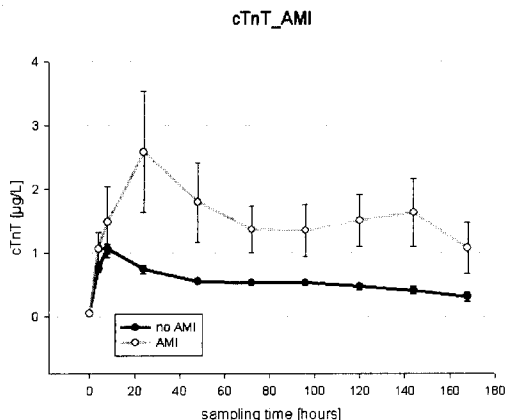
Stephanie Lehrke, Evangelos Giannitsis, Margit Müller-Bardorff, Henning Steen, Armin Opitz, Hanno Peters, Uwe KH Wiegand, Hugo A Katus, Medizinische Universität zu Lübeck, Lübeck, Germany.

**Background:** The value of serial troponin testing for diagnosis of perioperative myocardial infarction (MI) after major cardiac surgery is still unsettled.

**Methods:** We studied 204 patients undergoing major cardiac surgery, including CABG (132/204) and valve surgery (36/204). Cardiac troponin T (cTnT) was measured before crossclamping and serially at 4, 8, 24 hours and once daily thereafter for 7 days. Perioperative MI was defined as new evolving Q-waves on serial ECGs. ROC analysis was performed to obtain the optimal cTnT discriminator for perioperative MI at different time points.

**Results:** A total of 13/204 patients suffered a perioperative MI. In these patients, cTnT levels at all time-points beyond 8 hours and peak cTnT levels were higher compared to patients without perioperative MI (figure). ROC analysis yielded an optimal discriminator above 1.26 µg/L at 24 hours (AUC 0.69, sens 54%, spec 87%). In addition, time to peak was higher in patients with perioperative MI (43.4 vs 26.4h, p=0.03).

**Conclusions:** Serial cTnT testing may be useful in identifying patients with a perioperative myocardial infarction following major cardiac surgery.



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### The Utility of the ACC/AHA Guidelines for Screening Angiography in Patients Undergoing Surgical Repair for Mitral Regurgitation

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**Background:** As routine screening angiography is performed for the majority of patients undergoing mitral repair at our institution, we evaluated the utility of the 1998 ACC/AHA guidelines on a review of 400 patients who underwent surgery for mitral regurgitation from 1987 to 1999.

**Methods:** Coronary angiography was performed and disease defined as lumen narrowing of  $\geq 50\%$ . Risk factors for coronary disease were: age (males  $> 35$  or females  $> 51$  years), family history, smoking, diabetes, and hypercholesterolemia. Evaluated ACC/AHA indications were: history of angina / MI and presence of  $\geq 1$  risk factor. Etiology was determined by histopathology of operative valve specimens. Sensitivity (Sn), specificity (Sp) and likelihood ratio positive (LR+) for coronary disease on angiography were calculated for each risk.

**Results:** Of 400 patients, angiographic details were unavailable in 12 (3%), and 29 (7.5%) had no angiography due to emergent status (24 with and 5 without defined indications). Angiography was performed in 359 (92.5%) patients with a mean age of 65 ( $\pm 10$ ) years consisting of 234 (65.2%) males. The etiologies for mitral disease were degenerative (82.7%), rheumatic (7.0%), ischemic (5.6%) and endocarditis (4.7%).

Prevalence of coronary disease and proportion of concomitant bypass surgery was 28.1% and 22.3% respectively.

Proportion of patients fulfilling either indication for angiography was 99.4%, Sn 1.00, Sp 0.01, LR+ 1.01, with age criterion alone in 98.1%, Sn 1.00, Sp 0.03, LR+ 1.03. Angina was present in 30.9%, Sn 0.59, Sp 0.80, LR+ 3.01.

Of 248 patients without angina or MI, indications were: hypertension in 24.6%, Sn 0.26, Sp 0.87, LR+ 1.98; hypercholesterolemia in 43.1%, Sn 0.20, Sp 0.89, LR+ 1.85; smoking in 26.6%, Sn 0.24, Sp 0.86, LR+ 1.77; diabetes in 5.6%, Sn 0.21, Sp 0.84, LR+ 1.30 and family history in 9.6%, Sn 0.17, Sp 0.83, LR+ 1.01.

**Conclusions:** ACC / AHA guidelines have excellent Sn, but very low Sp. Similar result is achieved with age as the sole criterion for angiography. Angina was the best predictor of coronary disease. Almost all patients qualify for angiography, but only a minority had concomitant bypass surgery. More stringent criteria may improve the cost effectiveness of the guidelines.

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### Elevated Serum Interleukin-6 Has Prognostic Significance for Postoperative Outcome in Patients Undergoing Cardiothoracic Surgery

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Inflammatory cytokines become elevated during cardiothoracic surgery procedures. Many studies have sought to characterize the differences in cytokine expression based on technical approaches, e.g. pump vs. off-pump CABG surgery. We undertook a prospective study to investigate the relationship between the inflammatory cytokines, IL-6, sIL-2R, sTNF-R (p55), and sTNF-R (p75), and clinical outcomes as prognostic predictors of post-operative management and outcome in patients (n=65) who had cardiothoracic operations. Three sequential blood samples were collected: (1) prior to induction of anesthesia, (2) completion of surgery, and (3) 24-hours after the induction of anesthesia. Pre-determined clinical outcome measures included ICU length of stay (ICULOS), total length of stay (TOTLOS), post-operative ventilation duration (VentTime), duration of vasopressor (PressorTime) and inotropic (InotropeTime) requirements, and complication rate. The pre-operative cytokine levels did not correlate with the outcome data, however IL-6 levels from time points 2 and 3 were found to have independently demonstrated statistically significant prognostic value in regard to the pre-determined outcome measures, ICULOS (p<0.01), TOTLOS (p<0.02), VentTime (p<0.01), PressorTime (p<0.01), and InotropeTime (p<0.01). sIL-2R, sTNF-R (p55), and sTNF-R (p75) had less influential prognostic significance. Operative Bypass time independently showed prognostic value for ICULOS (p<0.01), TOTLOS (p<0.01), and PressorTime (p<0.01). Elevated levels of cytokines cause Systemic Inflammatory Response Syndrome (SIRS) in patients undergoing cardiothoracic procedures, which manifest as increased ICULOS, TOTLOS, ventilatory support, inotropic and vasopressor requirements. Of the operative variables, bypass time had the greatest prognostic value. IL-6 appears to play a major role in mediating post-operative outcome and may facilitate decision-making for critically ill cardiothoracic patients.

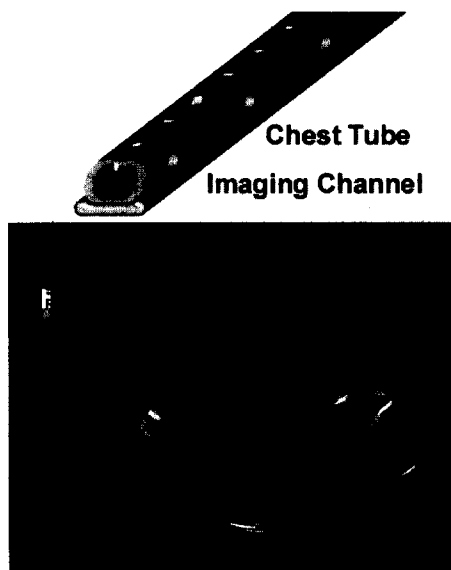
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### Use of Substernal Echocardiography in Patients on Ventricular Assist Devices: Initial Experience

John D. Blizzard, H. Storm Floten, Mathew Slater, Robert Lowe, David J. Sahn, Anthony J. Furnary, Oregon Health & Science University, Portland, Oregon.

**Background:** Echocardiography is sometimes difficult in postop patients who may have dressings, poor windows and are difficult to reposition. Transesophageal echo carries the disadvantages of patient stress, respiratory compromise or the need to further sedate conscious patients. We have previously reported a dual lumen chest tube drain device with a sealed substernal echocardiography (SEE) lumen 36 Fr (SEE-IT® Medtronics Corporation) that allows insertion of a 10.2mm non-sterile miniplane TEE probe into a substernal position where it can be positioned and rotated for cardiac imaging intra- and postoperatively. **Methods:** At OHSU, 5 patients were studied serially for periods of up to 5 days with intermittent echo imaging performed by surgeons on their rounds used

to aid decision making regarding management, ventricular assist settings/termination of assist. All patients were heart failure patients who had undergone LVAD, BiVAD insertion  $\pm$  concomitant procedures including multiple bypass, grafting, and/or atrioventricular valve repair. The SEE tube placed on the anterior RV surface provided optimal windows for imaging of RV and LV function as well as color Doppler visualization of valvular regurgitation. **Results:** All patients tolerated SEE with no alteration of vital signs, and there were no complications despite multiple TEE probe introductions; quantitative and qualitative observations precluded the need for other imaging procedures and assisted VAD management.



## POSTER SESSION

## 1085 Prosthetic Valves and Aortic Regurgitation

Monday, March 18, 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.

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## Evaluation of the Newly Designed Aortic Root Prosthesis and the Role of Leaflet Repair in the Valve Sparing Operation

**Mano J. Thubrikar,** Kenton J. Zehr, Francis Robicsek, Eric Skipper, Geoffrey Gong, Brett L. Fowler, *Heineman Medical Research Laboratory, Carolinas Medical Center, Charlotte, North Carolina, Mayo Clinic, Rochester, Minnesota.*

**Introduction:** A newly designed aortic root prosthesis with compliant sinuses was evaluated and the role of leaflet repair was studied in the valve sparing operation.

**Methods:** In vitro, 8 aortic root prostheses were sewn to 8 normal (human) aortic valves and studied in a left heart simulator. In 7 patients, with annuloaortic ectasia and mild to severe AI, the aortic root was reconstructed with the prosthesis and the valve was spared while on cardio-pulmonary bypass. The sinus height (Hs), and the valve diameter at the sinotubular junction (STJ-D) were measured from patients' TEE. Also, after the aorta and the sinuses were excised during surgery, the valve size at the sinotubular junction was measured while moving the commissures centrally till adequate leaflet coaptation was achieved, and then compared with the "normal" valve size in an adult of similar height and weight.

**Results:** In vitro, all of the valves spared, using the newly designed aortic root prosthesis, showed the normal dynamics with no AI. In contrast, in three patients the leaflet free-edge had to be shortened to reduce the AI. None of the patients' valves showed complete competence. Four patients had trace AI and 3 had mild AI. In the normal intact valve the ratio Hs/STJ-D was 0.8 - 1, in the dilated aortic root it was 0.5 - 0.7, and after the valve sparing it was restored to 0.8 - 1. In the patients, the valve size after the aortic root excision was 3 - 6 mm larger than that in a similar size adult, indicating that the leaflets were stretched.

**Conclusions:** In the valve sparing operation, one may encounter both the dilated aortic root and stretched leaflets. Replacing only the aortic root with a prosthesis will reduce AI, but for complete valvular competence shortening of the leaflet free edge may be required. The newly designed aortic root prosthesis appears to function well in this procedure.

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## Lipids in Patients With Aortic Valve Replacement: Impact of Preoperative Cholesterol and Triglyceride Levels on the Degeneration of Pericardial Valve Prostheses

**Georg Nollert,** Jessica Miksch, Bruno Reichart, *Department of Cardiac Surgery, University of Munich, Munich, Germany.*

**Background:** Recent studies demonstrated the influence of cholesterol on the progression of aortic stenosis. We hypothesized that high lipid levels may also stimulate the degeneration of pericardial heart valves and lead to reoperation due to structural valve failure especially in younger patients with high degeneration rates.

**Methods:** In 1984 and 1985 246 patients received pericardial aortic heart valves (61% male, age  $56 \pm 11$  years) and had preoperative lipid investigations at our institution. These patients received a Hancock Extracorporeal valve (HE; n=177) or a Carpentier Edwards pericardial valve (CEP; n=4) in aortic or mitral (HE n= 63; CEP n= 30) position. Double valve replacement was performed in 29 patients.

**Results:** Operative, 1, 5, 10, and 15 years actuarial survival was 90%, 84%, 66%, 48%, and 41% respectively. Freedom from reoperation at 5, 10, and 15 years was 75%, 25%, and 11%. Patients younger than 60 years who had to be reoperated within 10 years had higher preoperative cholesterol ( $235 \pm 59$ mg/dl vs.  $194 \pm 39$ mg/dl;  $p=0.05$ ) and triglyceride levels ( $143 \pm 61$ mg/dl vs.  $95 \pm 32$ mg/dl;  $p=0.035$ ) than those reoperated after 10 years. In order to calculate the influence of preoperative lipid levels on the degeneration rate patients were split into quartiles. Patients below 60 years of the lowest and highest cholesterol quartiles were free of reoperation in 83% vs. 65%, 40% vs. 0%, and 11% vs. 0% ( $p=0.008$ ) at 5, 10, and 15 years. The figures for the lower and higher triglyceride halves were 76% vs. 71%, 36% vs. 8%, and 11% vs. 0% ( $p=0.015$ ). The differences were similar for young patients after solitary aortic valve replacement (cholesterol  $p=0.0019$ ; triglyceride  $p=0.08$ ). However, in this subgroup older patients with low cholesterol levels had more reoperations than those with high levels ( $p=0.045$ ). Survival was independent from cholesterol levels, but high triglyceride values ( $>170$  mg/dl) were related to worse outcome ( $p=0.004$ ).

**Conclusions:** Preoperative cholesterol and triglyceride levels are predictors of structural valve failure of pericardial valves. Lowering of triglyceride and cholesterol levels may be a new concept to reduce degeneration of pericardial valves in patients younger than 60 years.

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## Outcomes 15 Years After Valve Replacement With a Mechanical Versus Bioprosthetic Valve in Patients Between 60 and 70 Years of Age

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**Background:** The choice between mechanical prosthesis (MP) and bioprosthesis (BP) between 60 and 70 years of age remains controversial. **Methods:** In order to document this choice a cooperative and retrospective study analyses the outcome of 441 patients operated on in 1985. **Results:** The valvulopathy was aortic, mitral and mitroaortic in respectively 244, 134 and 63 patients. MP and BP were implanted respectively 228 (52%) and 204 (46%) patients; 9 mitroaortic (2%) had both a BP and a MP. The operative mortality (27 cases) was 6.1% lower for aortic patients (3.5%) than for mitral (7%) and bivalvular (13%) patients. On follow-up 244 patients (55%) died. The 15 years actuarial survival rates are not different for mitral disease between BP (31%) and MP (25%) (ns). It is better for aortic MP (47%) than for BP (26%) ( $p<0.001$ ). The valve related mortality is higher for mitral valve (MP 28%, BP 25%) than for aortic (MP 17%, BP 16%). The non cardiac mortality is higher than the valve related mortality in every group except for mitral BP. Primary valve failure occurs for 8% of aortic BP versus 30% of mitral BP. Valve related complications concern 22% of aortic BP, 26% of aortic MP, 32% of mitral MP and 59% of mitral BP. Among the monovalvular diseases, 15 years actuarial survival rates is respectively 47% for women and 34% for men. **Conclusion:** These results contra indicate the use of mitral BP before 70 years. For aortic diseases the rate of primary valve failure is actually low at 15 years after surgery. Nevertheless in the cohort, half of the women and a third of men have reached or have turned eighty. So it seems more advisable to prefer MP to BP before seventy to avoid late re-operations.

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## Elevated B-Type Natriuretic Peptide in Patients With Asymptomatic Aortic Regurgitation and Normal Left Ventricular Systolic Function

**Micah J. Eimer,** Deborah Ekery, Vera Rigolin, Maryl Johnson, Mihai Gheorghiad, Robert Bonow, William G. Cotts, *Northwestern University Medical School, Chicago, Illinois.*

**Background:** Chronic aortic regurgitation (AR) imposes a progressive hemodynamic burden upon the left ventricle (LV). Management is based on symptoms and LV size and function. To determine if B-Type natriuretic peptide (BNP), a hormone secreted by ventricular myocytes under strain, may play a role in decision making for patients with AR, we measured BNP levels in patients with chronic asymptomatic AR and normal LV systolic function.

**Methods:** Ten asymptomatic male patients with isolated AR, age  $31-70$ y ( $48.5 \pm 14.7$ ), underwent echocardiography and measurement of serum BNP levels. Standard echocardiographic parameters were recorded and AR was quantified by the ratio of jet height (JH) to LV outflow tract (LVOT) in the parasternal long axis view. Four males age 29-54 ( $40.25 \pm 11.7$ ) with normal echocardiograms served as controls.

**Results:** There was no significant difference in age or ejection fraction between patients and controls. The mean BNP level was nearly fourfold higher in patients with AR compared to controls ( $23.7 \pm 23.1$  vs  $6.1 \pm 4.2$ pg/ml  $p=.04$ ). Using linear regression analysis, significant ( $p<.05$ ) univariate predictors of BNP in patients with AR include: LV mass index ( $r=.75$ ), LV end diastolic volume ( $r=.68$ ), LV end systolic volume ( $r=.59$ ), LV end