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**1001-0**

**Effect of Free Fatty Acid Inhibition on Left Ventricular Function in Diabetic Patients With Coronary Artery Disease**

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In diabetic patients with coronary artery disease free fatty acid blockade with trimetazidine improves myocardial glucose utilization. Aim of the present study was to evaluate whether the metabolic effect of Trimetazidine on left ventricular function in diabetic patients with coronary artery disease. We evaluated the effect of chronic administration of Trimetazidine on left ventricular dimensions and systolic function in 32 patients y (24 males and 8 females, mean (SE) age = 67±6 years) with NIDDM and ischemic cardiomyopathy. Patients were randomized to receive on top of standard therapy either Trimetazidine (20 mg, tids) or Placebo (tids) and were evaluated at baseline and after 6 months. Demographic data were comparable between the two groups with respect to sex, age, distribution of CAD, and glicated haemoglobin levels. In the Placebo group, baseline LV systolic function was 52±1.5 mm in the Trimetazidine group, respectively (NS). Compared to baseline, LVEF increased by 5.4±0.5% (p=0.05) in the TMZ group while unchanged in the Placebo group (p=0.01). LVEF improved in diabetics with ischemic heart disease TMZ added to standard medical therapy has beneficial effect on LV volumes and on LVEF compared to placebo. This effect may be related to the effect of TMZ upon cardiac glucose utilization.

**Noon**

**1001-10**

**Testosterone Replacement Confers a Favorable Cytokine Profile in Men With Low Serum Testosterone and Coronary Disease**

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Background Men with atherosclerotic coronary disease have lower serum testosterone (T) levels than men with normal angiograms. T has immune-modulating properties and replacement therapy inhibits atherogenesis in castrated, male, cholesterol-fed animals. In vitro evidence suggests that T suppresses pro-inflammatory cytokines such as tumour necrosis factor (TNF-α) and potentiates the expression of anti-inflammatory cytokines such as interleukin (IL)-10, these effects may mediate the atheroprotective effect observed in animals. The effect of T replacement therapy on inflammation in men with coronary disease is explored for the first time in this study.

Methods This was a randomised placebo controlled crossover study of 1 month T replacement (Sustanon 100) versus placebo in 20 men (age 61 ±9 years) with symptomatic arterial disease (total T < 1.7 nmol/L and angiographic proven coronary disease ≥ 20% stenosis of ≥ 1 epicardial coronary artery). Serum cytokines (TNF-α, IL-1β, and IL-6), cholesterol profiles (total cholesterol, low density Lipoprotein, high density lipoprotein, triglycerides) and hormones (total T and bioavailable T) were measured at baseline and after treatment from the T and placebo phase. All results are displayed as mean ± SD. Delta analysis was used to test significance.

Results Compared to placebo, T reduced both TNF-α (41 ± 1.9 vs 2.5 ± 0.9 pg/ml, p=0.007) and IL-1β (10 ± 0.3 vs 0.2 ± 0.6 pg/ml, p=0.04). An increase in IL-10 approached significance (0.2 ± 0.2 vs 0.87 ± 3.2 pg/ml, p=0.08). There was a trend in reduction in total cholesterol with T (0.26 ± 0.5 vs 0.005 ± 0.5 mmol/L, p=0.1).

Conclusions Testosterone replacement in this cohort shifts the cytokine balance to a state of reduced inflammation, this may have positive effects on atherosclerotic plaque biology. Since the prevalence of hypogonadism in men with coronary disease is high (23%) and the risk of vascular complications and mortality is in part determined by inflammation. Testosterone may offer prognostic benefit to a large proportion of men with overt coronary disease.

**Noon**

**1001-11**

**Lower Doses of Hormone Replacement Therapy Did Not Increase hsC-Reactive Protein or F1+2 Levels but Improved Flow-Mediated Dilation in Postmenopausal Women: A Randomized, Double-Blind, Crossover Study**

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Objective: The effects of hormone replacement therapy (HRT) can affect many aspects relevant to cardiovascular disease including vasomotor function, inflammation, and hemostasis. Recent studies have demonstrated that current doses of HRT exert a mixture of both protective and adverse effects. In the current study, we compared the effects of lower doses of HRT (L-HRT) and conventional doses of HRT (C-HRT) on a variety of relevant cardiovascular parameters.

Methods and Results: This randomized, double-blind, crossover study included fifty-seven women who received micronized progesterone 100 mg with either conjugated equine estrogen 0.625 mg (C-HRT) or 0.3 mg (L-HRT) daily for 2 months. L-HRT showed comparable effects to C-HRT on HDL cholesterol and triglyceride levels, but not on LDL cholesterol levels. C-HRT and L-HRT significantly improved the percent flow-mediated dilator response to hyperemia from baseline values (both p<0.001) by a similar degree

(p=0.719). C-HRT significantly increased high sensitivity CRP (hsCRP) levels from baseline values (p<0.001), however, L-HRT did not significantly change hsCRP (p=0.874). C-HRT increased L-Antithrombin III from baseline values (p=0.042) and L-HRT reduced plasma PAI-1 antigen levels from baseline values (p=0.002 and p=0.038, respectively) to a similar degree (p=0.18). **=P<0.05;***=P<0.01;****=P<0.001 vs. Base-line. Data= means±SEM or median (25%-75%).

**Noon**

**1001-12**

**Prevention of Flight-Related Thrombosis With Low-Molecular Weight Heparin**

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The LONFLIT studies established that in high-risk subjects after long (> 10 hours) flights, the incidence of deep vein thrombosis (DVT) is on average 3.6%. This study had evaluated prevention in high-risk subjects with low-molecular weight heparin (LMWH). Of 776 subjects contacted for the study, 458 were included and randomized, into three groups: 1) control group (no prophylaxis); 2) aspirin treatment group (0.4 g of oral, soluble aspirin; one dose daily for 3 days, starting 12 hours before the beginning of the flight); 3) LMWH group (4000 UI; dose of enoxaparine, between 2 and 3 hours before flights). Subjects with potential problems due to prophylaxis with aspirin or LMWH were excluded. A total of 422 subjects completed the study (dropouts were due to low compliance or travel ). RESULTS. Age, sex and risk distribution were comparable in the groups. Mean age was 52 (range, 27-78; SD, 12; 63% males). Of the 142 controls (8.6%) had thrombotic event (51% DVT, 49% PE). Of the 372 aspirin patients (21.6% had thrombotic event (47% DVT, 53% PE). Of the 208 LMWH patients (28%) had thrombotic event (19% DVT, 19% PE). In the aspirin group (139 subjects) there were 6 events (4.3%) with 4 DVTs. DVT was asymptomatic in 68% of subjects and 93% of DVTs were observed in subjects sitting in non-aisle seats. Mild gastrointestinal symptoms were reported in 11% of patients taking aspirin. In conclusion one fixed dose of LMWH is an important option to consider in high-risk subjects during long-haul flights.

**Noon**

**1001-13**

**Gender Bias Against Women: Men Receive Prophylaxis More Often to Prevent Deep Venous Thrombosis**

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We investigated gender differences in the prevention of acute deep vein thrombosis (DVT). We used the database of the DVT FREE, a prospective 183-center US registry of 5,451 consecutive patients (46.9% men, 53.1% women) with ultrasound-confirmed DVT. Detailed information about DVT prophylaxis and medical comorbidities prior to the onset of the acute DVT was available for 4,652 patients. Men more often than women (33.9% vs. 29.1%; OR 1.23, 95% CI 1.08-1.38; p = 0.001) received mechanical or pharmacological prophylaxis 30 days prior to the onset of acute DVT. Multivariate adjustment for baseline characteristics and DVT risk factors did not change this finding (Figure). Men were 20% more likely to receive prophylaxis (adjusted OR 1.20, 95% CI 1.03-1.41; p = 0.021). Among 2,454 patients hospitalized at the time of DVT diagnosis, 53.5% of women and 46.5% of men had not received prophylaxis or treatment prior to the acute DVT (p = 0.042). When DVT prophylaxis was administered, the type of prophylaxis (66.9% vs. 66.3% pharmacological prophylaxis, 23.8% vs. 23.2% pneumatic compression devices, 16.7% vs. 16.4% vascular compression stockings) was similar between men and women. Outdated and disturbing and provocative finding was identification of gender bias against women: failure to administer DVT prophylaxis to high-risk women more than men who subsequently developed acute DVT within 30 days. Future efforts should focus on improved implementation of DVT prophylaxis guidelines among patients at high risk, especially women.
A New Approach to Anticoagulation Therapy: The Fiscal and Quality Impact of Computerized Decision Support and Point of Care Testing

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Background: Improved use of anticoagulation therapy has been identified as a priority for the National Stroke Medicare Quality Improvement Project. Specialized anticoagulation clinics have been shown to improve quality of care, but are limited by expense and degree of expertise required. To address these issues, we evaluated a new approach to anticoagulation therapy, utilizing Point of Care (POC) testing in combination with computerized decision support (CDS).

Methods: As part of a National Institutes of Health supported study, two clinic systems were compared with respect to approaches used for anticoagulation and clinical results achieved. One system (patient control group, n=51) used a traditional approach consisting of centralized laboratory testing, paper based record keeping and telephone contact. Another system (patient test group, n=139) utilized an experimental approach combining POC testing and CDS with centralized decision support. The systems were compared with respect to approaches used for anticoagulation and clinical results achieved. Only one year of data was collected for each group.

Results: Over a one-year period, test and control groups were compared with respect to the endpoints listed. For the test group, INR compliance was 62%, compared to 38% for the control group (p<0.01). Documentation of INR goal and indication for therapy were 86% for the test group and 51% for controls (p<0.01). The test group generated new revenue of $320.56 per patient per year, with labor related costs reduced by 74%. In the controls, 13 complications occurred, costing $336,347.44. The test group experienced 4 complications, with costs totaling $225.00, over Holter monitoring was conducted at 2, 3 and 6 months. Time-related prevalence of AF was determined by nonlinear mixed-model data analysis with temporal decomposition to accommodate different risk factors in different time frames, a novel technique. There were no complications related to the pulmonary vein isolation using the bipolar clamp.

Conclusions: From our preliminary experience intraoperative bipolar radiofrequency ablation of AF seems to be rapid, safe and effective. Early postoperative AF is common, but does not seem to predict long-term cure.

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Bipolar Radiofrequency Isolation of the Pulmonary Veins for Treatment of Atrial Fibrillation

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Objectives: To determine safety and time-related clinical effectiveness of bipolar radiofrequency isolation of the pulmonary veins in patients with symptomatic atrial fibrillation (AF) undergoing open heart surgery.

Methods and Results: From November 2001 to April 2003, 134 patients underwent surgical ablation of AF using a bipolar clamp (AtriCure®). Mean age was 68 years and 54% were men. Median preoperative duration of AF was 24 months. AF was paroxysmal in 24%, persistent in 25% and permanent in 51%. Mean left atrial diameter was 5.4±0.96 cm. Patients were followed with Holter monitoring for a median of 5 days post OP. All patients had bilateral pulmonary vein isolation and excision or exclusion of the left atrial appendage and 44% had right atrial lesions. Mean ablation time was 16 minutes. Moreover, Holter monitoring was conducted at 2, 3 and 6 months. Time-related prevalence of AF was determined by nonlinear mixed-model data analysis with temporal decomposition to accommodate different risk factors in different time frames, a novel technique. There were no complications related to the pulmonary vein isolation using the bipolar clamp.

Long term Prevalence of AF decreased to 15% by 3 months after surgery (figure 1). Conclusions: From our preliminary experience intraoperative bipolar radiofrequency ablation of AF seems to be rapid, safe and effective. Early postoperative AF is common, but does not seem to predict long-term cure.