Similar results were obtained after adjustment for MI and hypercholesterolemia.
**Conclusion:** This case-control study provides evidence that current HRT use neither increases nor decreases the risk of incident MI in postmenopausal women with diabetes.

3:00 p.m.

### 825FO-5 Prothrombotic Mutations Are Associated With Increased Cardiovascular Events in Postmenopausal Women Receiving Hormone Replacement Therapy

Francesco Dragoni, Otavio Gebara, Massimo Fini, Mauricio Wajngarten, Josè Mendes Aldrighi, Giuseppe Mercuro, Josè Antonio F. Ramires, Giuseppe M. Rosano, *San Raffaele Hospital, Roma, Italy, INCOR, Sao Paulo, Brazil.*

Recent studies have suggested that hormone replacement therapy (HRT) in postmenopausal women (PMW) may be associated with an initial increased cardiovascular risk. Recent reports suggest that the prothrombin variant 20210G to A is associated with an increased risk of events in hypertensive PMW with a previous myocardial infarction. To this end 50 PMW with documented vascular event underwent prospective evaluation of antithrombin III, protein C, free and total protein S, activated protein C resistance, fibrinogen, factor VII:C and homocysteine levels. In all the presence of antiphospholipid antibodies was investigated by kaolin clotting time (KCT), diluted Russel's viper venom time (DRVVT) and by measurement of anticardiolipin antibodies IgG and IgM (ACA-G and ACA-M). Prevalence of factor V Leiden, prothrombin variant G20210A and homozygosity for thermolabile variant C677T of the metilenetetrahydrofolate reductase (MTHFR) were evaluated and compared with those of 50 normal matched controls.
Antithrombin III and protein C were normal in all cases. One patient (2%) showed free protein S deficiency and 3 patients (6%) had activated protein C resistance. Homocysteine levels above 15 µmol/L were found in 3 patients (6%). Antiphospholipids antibodies were found in 35 patients (70%). Among women receiving HRT 87% had combined inherited and acquired prothrombotic factors (OR = 37.3, 95% CI = 8.5-564.3) while no combined prothrombotic factors were found in control PMW receiving HRT.
In conclusion vascular events in women receiving HRT are associated with a high prevalence of combined inherited and acquired prothrombotic factors. Therefore screening for prothrombotic factors may be of help in identify those women at increased risk for cardiovascular events with HRT.

3:15 p.m.

### 825FO-6 Different Effect of Hormone Replacement Therapy, DHEAS, and Tibolone on Endothelial Function in Postmenopausal Women With Increased Cardiovascular Risk

Cristiana Vitale, Otavio Gebara, Massimo Fini, Mauricio Wajngarten, Josè Mendes Aldrighi, Antonello Silvestri, Paola Rossini, Sandra Zoncu, Cristiano Sarais, Josè Antonio Ramires, Giuseppe Mercuro, Giuseppe M. Rosano, *San Raffaele Hospital, Roma, Italy, INCOR, Sao Paulo, Brazil.*

Menopause is associated with an increased cardiovascular risk and with a decrease in endothelial function Hormone replacement therapy (HRT) improves endothelial function in post-menopausal women (PMW). New alternative treatments for menopausal women have been suggested among these Tibolone (T) and di-hydroepiandrosterone sulphate (DHEAS) have been suggested to have cardioprotective effects. Although in vitro animal studies have suggested that T and DHEAS improve endothelial function, their effect in humans has never been tested. Aim of the present study was to compare the effects of HRT, DHEAS and T on endothelium-dependent flow mediated vasodilation (FMD), plasma nitrite, nitrate and endothelin-1 in 16 PMW with increased cardiovascular risk in a double-blinded double-crossover study. Women were randomized and treated for 4 weeks with either HRT, T or DHEAS. Brachial artery diameter, FMD, endothelin-1 and plasma nitrite and nitrate levels were measured at baseline and after each treatment phase.Brachial artery diameters remained unchanged after each treatment phase. HRT significantly improved FMD compared to both baseline and T and DHEAS while no effect of T or DHEAS on FMD was noted.
In conclusion HRT but not either T or DHEAS improves endothelial function and reduces plasma levels of endothelin-1 in PMW at risk of CAD.

**Effect of HRT, Tibolone or DHEAS on Endothelial Function**

| | Baseline | HRT | T | DHEAS |
|---|---|---|---|---|
| Brachial artery (mm) | 4.06±0.3 | 4.0.7±0.3 | 4.07±0.2 | 4.06±0.3 |
| FMD (%) | 7.3±0.8 | 11.94±0.8** | 6.9±0.5 | 6.4±0.9 |
| Nitrite+nitrate (Nox) | 40.6±11.7 | 48.4±7.8 | 39.9±8.2 | 34.7±11.8 |
| Endothelin-1 (pg/ml) | 3.1±0.8 | 2.7±0.7* | 3.1±1.7 | 3.4±0.7 |

*=p<0.05; **=p<0.01

POSTER SESSION

## 1128 Endothelium, Lipids, and Vascular Function

Monday, March 18, 2002, 3:00 p.m.-5:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

### 1128-85 Effect of the Angiotensinogen M235T Polymorphism on Human Coronary Vascular Endothelial Function

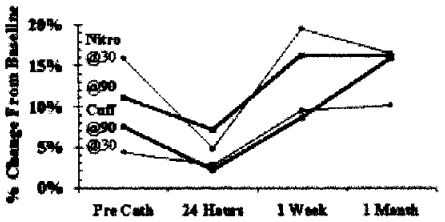
Julian Halcox, Suresh Narayanan, Abhiram Prasad, Colleen Satorius, William H. Schenke, Neal Epstein, Arshed A. Quyyumi, *NHLBI, Bethesda, Maryland.*

**Introduction:** A missense substitution in exon 2 of the angiotensinogen gene (T704-C) encoding threonine instead of methionine at position 235 (M235T) may influence the risk of vascular disease. We hypothesized that this polymorphism is associated with coronary vascular endothelial dysfunction.
**Methods:** Angiotensinogen M235T genotyping was performed in 118 Caucasian patients with mild coronary atherosclerosis (<50% stenosis) or angiographically smooth coronary arteries undergoing cardiac catheterization. Changes in coronary vascular resistance (δCVR) and epicardial artery diameter (δD) were measured as indices of microvascular and epicardial coronary vasodilator capacity during administration of intra-coronary acetylcholine (ACH, 15µg/min), and sodium nitroprusside (SNP, 20µg/min), to test endothelium-dependent and -independent coronary vascular function, respectively.
**Results:** 235T allele frequency was 0.40. Coronary microvascular dilation with ACH was reduced in TT compared to MT+TT patients (δCVR: -36±9% vs -49±6%, p=0.04), whereas responses to SNP were similar in both groups (δCVR: -48±7% vs -54±2%, p=0.35]). In the epicardial coronary circulation, a net vasoconstrictor response with ACH was observed in TT individuals, compared with a net vasodilator response in MM+MT subjects (-5.2±2.3% vs +2.2±1.0%, p=0.003). Epicardial responses to SNP were similar in TT and MM+TT genotype groups (+23±5% vs +21±2%, p=0.73). This impaired microvascular and epicardial coronary endothelial function observed in TT patients was independent of conventional risk factors (age, gender, smoking, hyperlipidemia, diabetes, hypertension) for endothelial dysfunction by multivariate analysis (δCVR: p=0.04 and δD: p=0.03).
**Conclusions:** Individuals homozygous for the angiotensinogen 235T allele have impaired endothelium-dependent coronary artery vasodilation compared with MM+MT subjects. This finding provides mechanistic insight into the increased association between the 235T allele and hypertension, atherosclerosis, and myocardial infarction observed in several epidemiologic studies.

### 1128-86 Endothelial Dysfunction Following Radial Artery Cannulization

Michael G. Del Core, Christopher Price, Lance LaMadrid, Kay Ryshon, Syed M. Mohiuddin, *Creighton University, Omaha, Nebraska.*

Background: There is an increasing tendency to use arterial conduits, including the radial artery (RA), for coronary artery bypass surgery. At the same time, invasive cardiologists are increasingly using the RA as a conduit for cardiac catheterization. The purpose of this study was to assess endothelial function following RA cannulization. Methods: 20 patients scheduled to undergo diagnostic catheterization via the radial approach underwent non-invasive evaluation of endothelial function. RA diameter was measured at baseline, then at 30 and 90 seconds following reactive hyperemia (endothelial dependent), and following administration of Nitroglycerin (endothelial independent). These measurements were obtained prior to catheterization, within 24 hours, at one week, and at one month following catheterization. Results: Reduced endothelial function in the RA was evident 24 hours after catheterization regardless of the dilation technique. Endothelial function measured at 1 week and 1 month in the radial artery was significantly improved over 24 hour values for nitro at 30 seconds (p=0.023 and p=0.016, respectively), and cuff at 90 seconds (p=0.045 and p=0.026, respectively). Nonsignificant improvements in endothelial function were evident at the remaining interventions between 1 week and 1 month.




Conclusion: RA catheterization results in endothelial dysfunction following catheterization and may have implications for its use as an arterial conduit in coronary artery bypass surgery.

### 1128-87 Effect of Xanthine Oxidase Inhibition on Endothelial Function in Smokers

Sasidhar Guthikonda, Christine Sinkey, Therese Barenz, William G. Haynes, *University of Iowa, Iowa City, Iowa.*

***Background:*** Cigarette smoking causes endothelial dysfunction, possibly due to oxidant stress. One proposed mechanism has been generation of oxidant species by the enzyme xanthine oxidase (XO). We tested the hypothesis that XO impairs endothelial function in