Noon

1116-32 **Getting Risk Factors to Goal: Lifestyle Intervention Is Worth the Effort in Patients With Hypertension, Hyperlipidemia, and/or Hyperglycemia**

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Background: Hypertension, hyperlipidemia, and hyperglycemia are leading causes of potentially avoidable morbidity, mortality, and healthcare expenditures. National clinical guidelines promulgate therapeutic lifestyle changes (TLC) as a standard of care in the management of these cardiovascular disease risk factors. Because of the widespread availability of pharmacotherapeutic agents, however, the value of TLC per se in contemporary medical practice is often discounted by clinicians and health insurers. The aim of this study was to evaluate the precise role of TLC in helping patients achieve goal risk factor levels.
Methods: We studied the effect of TLC on the control of: blood pressure (BP) in unmedicated patients with a baseline systolic BP $\geq$ 140 mmHg (n=335) and/or diastolic BP $\geq$ 90 mmHg (n=346); LDL cholesterol in unmedicated patients with a baseline value $\geq$ 100 mg/dl (n = 1,553); and fasting blood glucose in unmedicated patients with a baseline value $\geq$ 110 mg/dl (n=249). TLC included exercise training and nutrition counseling. Interventions were based on several well established behavior change models. Patients remained unmedicated throughout the study and were evaluated at baseline and after 3 months of TLC.
Results: Systolic BP decreased from 149 $\pm$ 10 to 133 $\pm$ 15 mmHg ($p<0.05$) and 63% of patients achieved goal (i.e., <130 mmHg for patients with diabetes and/or atherosclerosis; <140 mmHg for others). Diastolic BP decreased from 95 $\pm$ 5 to 85 $\pm$ 9 mmHg ($p<0.05$) and 65% of patients achieved goal (i.e., <80 mmHg for patients with diabetes; <85 mmHg for patients with atherosclerosis; <90 mmHg for others). LDL cholesterol decreased from 143 $\pm$ 28 to 134 $\pm$ 30 mg/dl ($p<0.05$) and 27% of patients achieved goal (using ATP III criteria). Fasting glucose decreased from 144 $\pm$ 43 to 129 $\pm$ 43 mg/dl and 41% of patients achieved goal (i.e. <110 mg/dl); of patients with a baseline value compatible with diabetes (i.e., >125 mg/dl; n=141), 35% achieved a value <125 mg/dl.
Conclusion: These data show that many patients with classic cardiovascular disease risk factors can achieve goal without medications within 3 months of initiating TLC and refute the notion that intensive lifestyle intervention is not worth the effort.

Noon

1116-33A **Effect of Lipid Subfractions on Progression of Coronary Artery Disease Among Middle-Aged Women**

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Background: As part of the Stockholm Female Coronary Risk Study we studied the effects of lipid parameters on progression of CAD among a cohort of 84 women who were 65 years or younger with established CAD, not taking lipid lowering medications, and underwent serial quantitative coronary angiography (QCA) at baseline (between 1991-1994) and after 3 years.
Methods: An average of 3 months after an acute coronary syndrome the women supplied clinical and demographic data and a fasting blood sample. The association between each lipid parameter and change in mean luminal diameter in up to 10 coronary segments was estimated using multivariable mixed model analysis of variance controlling for age, index event, diabetes, hypertension, smoking, BMI, menopausal status, and hormone use.
Results: There were 568 evaluable coronary segments among the 84 women. The table shows that each of the standard lipid parameters (total cholesterol, LDL, HDL, triglycerides) and apolipoprotiens (ApoB, ApoA1, VLDL) significantly predicted progression while Lp(a) did not. The strongest and most consistent associations were found for non-HDL cholesterol and the ratio chol:HDL. Furthermore, after including either non-HDL cholesterol or chol:HDL in the model, none of the other lipid parameters significantly improved the prediction of CAD progression.
Conclusion: Non-HDL cholesterol and the ratio of chol:HDL were the best predictors of progression of CAD among this cohort of middle-aged women with established disease.

Multivariable Adjusted Mean Lumen Diameter Progression (um)

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P-trend
Total Chol	109	61	135	258	**0.01**
LDL	81	35	171	164	**0.02**
HDL	246	107	177	61	**0.002**
Triglycerides	80	126	135	237	**0.005**
ApoB	75	91	142	258	**0.004**
ApoA1	238	53	184	73	**0.04**
VLDL	60	103	154	223	**0.002**
Lp(a)	169	100	91	136	**0.48**
Chol:HDL	47	80	190	211	**0.0002**
ApoB:ApoA1	30	148	21	287	**0.004**
Non-HDL-C	20	140	133	287	**<0.0001**

Noon

1116-33 **Renal Transplant Function as a Risk Factor for Cardiovascular Events and for All Cause Mortality in a Renal Transplant Population: Experience From the ALERT Trial**

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Background: ALERT was a randomized, placebo-controlled, study of the effects of Fluvastatin on cardiovascular and renal endpoints in transplant recipients with a stable renal function followed for 5-6 years. The design and major outcomes have been published (Lancet, June 14, 2003). In this population the role of conventional cardiac risk factor has not been fully established. **Methods:** A univariate risk factor analysis was performed in the placebo group to assess the influence of creatinine as a risk factor for cardiovascular and non cardiovascular endpoints. **Results:** A total of 2102 patients (total cholesterol 155-348 mg/dl) were recruited, of whom 1052 received placebo. The mean age was 50 years (30-75) , 66% male, 85% first transplant recipients and 22 % live donor recipients. The average serum creatinine at inclusion was 147 umol/l (range 70- 300).The relative risk for a 10 unit increase in creatinine and the frequency of events in the 1st quartile (<111 umol/L) compared with the 4th Q (>167 umol/L) are presented :

End point	Relative Risk	95% CI	P value	1st Q (<111 µmol /L)	4th Q (>167 µmol/L)
MACE	1.05	1.02-1.08	0.0007	11.5%	16.0%
Cardiac Death	1.03	1.05-1.13	<0.0001	4.2%	8.0%
Non fatal MI	1.01	0.96-1.06	0.6426	6.5 %	6.3 %
Stroke	1.03	0.97-1.08	0.3550	5.8%	5.5%
All Cause Mortality	1.01	1.01-1.01	<0.0001	11.2%	22.7%
Non-CV Mortality	1.01	1.00-1.01	0.0005	5.4%	10.1%

*MACE (Major Adverse Cardiac Event: cardiac death, MI, revascularization procedure)
Conclusion: In renal transplant recipients with stable function, serum creatinine is a risk factor for MACE, cardiac death, cardiac death, non-cardiovascular mortality and all cause mortality but not for stroke or non-fatal myocardial infarction. These findings are borne out in multivariate analyses adjusting for other cardiovascular risk factors.

Noon

1116-34 **Inhibition of 3-Hydroxy-3-Methylglutaryl Coenzyme a Reductase Attenuates Expression of Inducible Nitric Oxide Synthase in Cardiac Myocytes: A Possible Link With Direct Myocardial Protection During Ischemia-Reperfusion**

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Cytokine-induced nitric oxide (NO) is implicated in myocardial apoptosis. Since statins reduce myocardial apoptosis, we examined the effects of simvastatin (S) on inducible NO synthase (iNOS) expression in cardiac myocytes, which may explain cardioprotection observed in *in vivo* models. H9c2 cardiac myocytes were treated with S $\pm$ mevalonate (10^{-4} mol/L), geranyl-geranyl-pyrophosphate or farnesyl-pyrophosphate (10^{-4} mol/L) for 30 min, then stimulated for 0 - 48 h with interleukin (IL)-1α 20 ng/mL or tumor necrosis factor (TNF)-α 20 ng/mL. Untreated H9c2 cells exhibited little iNOS which was markedly increased by cytokines, as demonstrated by immunoblotting and nitrite assay. In the absence of any cytotoxicity S concentration-dependently inhibited IL-1α/TNF-α-induced expression of iNOS protein and mRNA (measured by reverse-transcrition polymerase chain reaction), as well as nitrite production, an effect starting at 10^{-7} mol/L for IL-1α/TNF-α stimulation of iNOS activity and protein expression, and at 10^{-8} mol/L for IL-1α/TNF-α stimulation of iNOS mRNA expression, effects all reverted by mevalonate and geranyl-geranyl pyrophosphate, but not by farnesyl-pyrophosphate. In the Table: *p<.05 vs