Metabolic Syndrome Interventions

The metabolic syndrome represents a cluster of risk factors (ie, obesity, hypertension, elevated triglycerides, low HDL-cholesterol, and insulin resistance) which lead to an increased risk of heart disease, stroke, and type 2 diabetes. The effects of lifestyle and pharmacologic interventions were discussed during this special session held in collaboration with the World Metabolic Syndrome Project.

According to Jean-Pierre Després, PhD, Quebec Heart Institute, Canada, intra-abdominal or visceral fat, more than overall weight, plays a significant role in the development of the metabolic syndrome [Després J-P and Lemieux I. *Nature* 2006]. He reported on the results of a program developed to assess the effect of lifestyle modification in the clinical management of viscerally obese men. Patients (n=185) saw a dietician and an exercise physiologist once per month. After 1 year, there was a significant reduction vs baseline in both subcutaneous (19%) and visceral fat (29%) (both p<0.0001) accompanied by an overall reduction of 7 kg in body weight and an 8.6 cm decrease in waist circumference. Significant improvements were also seen in all of the risk factors associated with the metabolic syndrome (Table 1).

Table 1. Changes in Risk Factor Levels After 1 Year of Diet and Exercise.

Risk Factor	Change	p value
Triglyceride level (mmol/L)	-21%	p<0.001
HDL-C level (mmol/L)	+14%	p<0.001
Glucose (mmol/L)		
Fasting	-2%	p<0.005
2-hour plasma	-14%	p<0.0001
Insulin (pmol/L)		
Fasting	-34%	p<0.001
Oral glucose tolerance	-46%	p<0.0001
Blood Pressure (mm/Hg)		
Systolic	-3.7	p<0.001
Diastolic	-5.6	p<0.001
Heart Rate (beat/min)	-5.6	p<0.001

Particularly important was the finding that changes in visceral fat could not be predicted by changes in body weight.

According to Dr. Després, "We need to go beyond body weight, beyond healthy weight, beyond BMI. We need to increase energy expenditure, which will in turn reduce visceral adipose tissue and lower the risk for cardiovascular disease and diabetes."

Philip Barter, MD, The Heart Research Institute, Sydney, Australia, discussed pharmacologic interventions in the management of the risk factors associated with the metabolic syndrome.

Numerous studies have proven that statins reduce cardiovascular events (Figure 1).

Highlights from the
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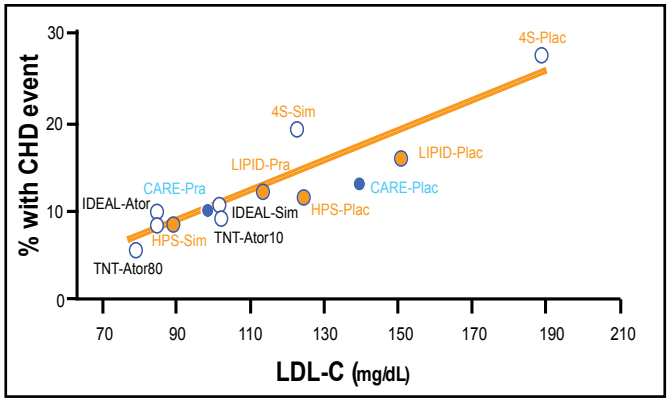
Figure 1. Statin Trials: LDL-C Levels vs Events.



Deedwania and colleagues have shown, however, that intensive lowering of LDL-C produced even greater benefit in patients with both coronary heart disease and the metabolic syndrome. Their analysis comprised data from 5,584 patients randomly assigned to receive either atorvastatin 10 mg (n=2,820) or 80 mg per day (n=2,764). Although at a median follow-up of 4.9 years, irrespective of treatment assignment, significantly more patients with metabolic syndrome (11.3%) had a major cardiovascular event than those without metabolic syndrome (8.0%; p<0·0001); the increased risk was significantly reduced by intensive therapy, as shown by significantly fewer events in patients receiving atorvastatin 80 mg (262, 9.5%) vs those receiving the lower dose (367, 13%) (HR 0·71; 95% CI 0·61, 0·84; p<0·0001) [Deedwania P et al. *Lancet* 2006].

Several studies that assessed the efficacy of fibrates in the treatment of patients with the metabolic syndrome such as the Helsinki Heart Study [Tenkanen L et al. *Circulation* 1995; Manninen V et al. *Circulation* 1992], the VA-HIT Study [Rubins HB et al. *Arch Int Med* 2002], and the BIP study [BIP Study Group. *Circulation* 2000], have shown that the benefits of fibrates were greatest in people with risk factors for the metabolic syndrome such as increased body weight, particularly if associated with low LDL-C, elevated plasma triglycerides, and elevated fasting plasma insulin levels.

According to Dr. Barter, although, theoretically there may be advantages to using statins and fibrates in combination, and studies are underway, this has not been proven. Furthermore, combination of high-dose statins and fibrate (in particular gemfibrozil) has been shown to increase the risk of rhabdomyolysis. Other pharmacologic approaches such as the cannabinoid-1 receptor blockers (rimonabant) are also being investigated but their efficacy in reducing cardiovascular events has not yet been demonstrated.

STEMI: From Trials to Clinical Practice

Alexandros Skarlos, MD, Klinikum Ludwigshafen, Germany, presented a registry analysis demonstrating that STEMI patients admitted to hospitals with a cath lab are treated with significantly higher rates of reperfusion and guideline-recommended adjunctive therapies and that this treatment is associated with a lower 1-year mortality.

The results are based on an analysis of data from the ACOS registry for 8,303 STEMI patients of whom 6,351 (76.5%) were initially admitted to a hospital with a cath lab and 1,952 (23.5%) to a hospital without such a facility.

During the first 24 hours, reperfusion therapy was significantly more common in hospitals equipped with a cath lab (75.6%) vs those without (54%; p<0.0001). A comparison of other treatments and in-hospital and 1-year mortality rates are shown in Table 1.

Table 1. Treatment and Mortality Differences.

	Hospitals with cath lab	Hospitals without cath lab	p-value
Reperfusion Procedures <24h			
Primary PCI	51.8%	9.2%	<0.001
Lysis	23.8%	44.7%	<0.001
Door-to-balloon time	75 min	148 min	<0.0001
Adjunctive therapy <48h			
Aspirin	91.5%	89.7%	<0.05
Clopidogrel	60.2%	18.9%	<0.0001
GP IIb/IIIa	46.7%	8.9%	<0.0001
β-Blockers	80.0%	75.8%	<0.0001
ACE-inhibitors	65.6%	57.1%	<0.0001
Mortality			
In-hospital	8.8%	11.5%	<0.001
1-year	13.7%	19.9%	<0.0001

Most therapy guidelines are based on clinical trial results. However, many patients seen in clinical practice are not represented in clinical trials. Oliver Koeth, MD, Klinikum Ludwigshafen, Germany, presented results of a registry designed to assess whether the patients typically excluded from clinical trials would benefit from guideline adherence.

Data for 36,247 STEMI patients from the MITRA (Maximal Individual Therapy of Acute Myocardial Infarction) PLUS registry were analyzed. Patients were assigned to two groups: those who failed to meet the typical inclusion criteria for most clinical trials (n=16,621) and those who met the criteria (n=19,626). Excluded patients were further assigned to subgroups based on common clinical trial exclusion criteria: age ≥75 years (n=9,360), pre-