French Society of Cardiology) have set up a consensus statement on the care of the hyperglycaemic/diabetic patient during and in the immediate follow-up of acute coronary syndrome (ACS). In particular, it includes the different phases of ACS (the intensive care unit (ICU) period, the post-ICU period and the short-term follow-up period after discharge, including cardiac rehabilitation) and also embraces all of the various diagnostic and therapeutic issues with a view to optimizing the collaboration between cardiologists and diabetologists. As far as diagnostic is concerned, subjects with HbA1c greater or equal to 6.5% on admission may be considered diabetic while, in those with no known diabetes and HbA1c less than 6.5%, it is recommended that an OGTT be performed 7 to 28 days after ACS. During hospitalization in the ICU, continuous insulin treatment should be initiated in all patients when admission blood glucose levels are greater or equal to 180 mg/dL (10.0 mmol/L) and, in those with previously known diabetes, when preprandial glucose levels are greater or equal to 140 mg/dL (7.77 mmol/L) during follow-up. The recommended blood glucose target is 140–180 mg/dL (7.7–10 mmol/L) for most patients. Following the ICU period, insulin treatment is not mandatory for every patient, and other antidiabetic treatments may be considered, with the choice of optimal treatment depending on the metabolic profile of the patients. Patients should be referred to a diabetologist before discharge from hospital in cases of unknown diabetes diagnosed during ACS hospitalization, of HbA1c greater or equal to 8% at the time of admission, or newly introduced insulin therapy or severe/repeated hypoglycaemia. Referral to a diabetologist after hospital discharge is recommended if diabetes is diagnosed by the OGTT, or during cardiac rehabilitation in cases of uncontrolled diabetes (HbA1c ≥ 8%) or severe/repeated hypoglycaemia.

**ISP8: Targeting normoglycemia in dysglycaemia patients at high CV risks: what are the benefits and risks?”**

*L. Rydén, Karolinska Institutet, Stockholm, Dep Cardiology Solna, Karolinska University Hospital, Stockholm, Sweden*

Impaired fasting glucose (IFG), impaired glucose tolerance (IGT), and diabetes due arise to insufficient insulin secretion, and are risk factors for cardiovascular (CV) events. It has been argued that targeting normal fasting glucose levels with insulin may reduce CV events. This important question was studied in ORIGIN (Outcome Reduction with an Initial Glargine Intervention; ClinicalTrials.gov number, NCT00069784).

In ORIGIN people (n= 12537; mean age 63.5) with cardiovascular risk factors plus impaired fasting glucose, impaired glucose tolerance or type 2 diabetes were randomised to insulin glargine targeting a FPG <5.3 mmol/L (95 mg/dL) or standard glycaemic care for 6.2 (Inter Quartile Range 5.8, 6.7) years within a 2 x 2 factorial design. The two co-primary outcomes were CV death and non-fatal myocardial infarction or stroke, and these events plus revascularization. This important question was studied in ORIGIN (Outcome Reduction with an Initial Glargine Intervention). Am Heart J 2008; 155: 26.

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Insulin glargine had a neutral effect on CV outcomes. The lecture covered the design and outcome of the insulin part of the ORIGIN trial and put these results into perspective.

**Further information may be derived from the following publications**


**ISP9: Not all fat is bad in cardiovascular risk. Mechanistic considerations about visceral versus femoral adipose tissues.**

*M. Lafontan, Inserm/UPS UMR 1048 - I2MC- Institut des Maladies Métaboliques et Cardiovasculaires, Toulouse, France*

Fat distribution is a major determinant of health. Both sex and anatomic site differences in regional fat storage have been described. Gender-related and depot-specific differences exist in the expansion of the adipose tissue (AT) mass. Visceral obesity, which is easily measured by the expansion of waist circumference, includes abdominal subcutaneous and visceral adipose tissue (vAT). Accumulation of vAT increases cardiovascular disease and type 2 diabetes risks whereas expansion of subfemoral AT exerts protection from metabolic related diseases. These epidemiological observations have raised a number of questions that will be discussed in the talk. Why do obese individuals with upper body fat distribution have more health complications compared with obese individuals with lower body fat distribution? Why does the accumulation of vAT exert stronger deleterious effects than subcutaneous AT accumulation? Is vAT expansion a causal factor or only a marker of an altered metabolic status? Some mechanistic points will be considered in the talk. Adipogenic and angiogenic differences exist between fat depts. Differences in triglyceride synthesis have also been reported. Lipoprotein lipase, glucose and fatty acid uptake differ between visceral and subcutaneous AT. Lipolytic activity of adipocytes and catecholamine-induced mobilization of triglycerides differ with fat distribution. The clear depot-specific differences in the adrenergic response of the adipocytes in vitro, related to fat cell adrenergic receptors distribution and fat cell size, have been confirmed in vivo. Using in situ microdialysis, adrenergic stimulation of abdominal lipolysis appeared to be higher than femoral lipolysis. A technique based on arteriovenous difference sampling which allows measure of fatty acid trafficking across abdominal and femoral AT has revealed a lower catecholamine-dependent lipolytic rate in femoral AT than in the abdominal AT. Once stored in femoral AT fatty acids are not readily released. Entrapment of fatty acids would prevent their ectopic deposition in liver, muscle and pancreas. Noticeable differences also exist in production of hormones, cytokines and pro-inflammatory molecules in visceral and subcutaneous AT. Finally, multiple inflammatory cells infiltrate AT and accumulate in fat deposits of the obese. They perturb adipocyte biology and could contribute to the low grade inflammation in the obese. Macrophages number is proportional to the amount of body fat and macrophages are more abundant in vAT than in subcutaneous AT. To conclude body fat distribution has a major influence on risk factors. Delineation of new properties of “good fat pads” versus “bad fat pads” and their putative targeted manipulation offer promising perspectives.

**ISP10: A model for predicting cardiovascular risk in patients with type 2 diabetes mellitus based on the ADVANCE study**

*F. Travert, Bichat Hospital and Paris 7 University, Paris, France*

We developed a new model for predicting cardiovascular risk in people with type 2 diabetes mellitus based on the ADVANCE study since we considered there is a continuing need to develop new equations to estimate reliably cardiovascular disease. We used our 4.5-year follow-up cohort of the Action in Diabetes and Vascular disease: preterax and diammicron-MR controlled evaluation (ADVANCE) to estimate coefficients for significant predictors of CVD using Cox
models. Similar Cox models were used to fit the 4-year risk of CVD in 7168 participants without previous CVD. The applicability was tested on the same sample and another dataset. A total of 473 major cardiovascular events were recorded. Age at diagnosis, known duration of diabetes, sex, pulse pressure, treated hypertension, atrial fibrillation, retinopathy, HbA1c, urinary albumin/creatinine ratio and non-HDL cholesterol at baseline were significant predictors of cardiovascular events. The model developed using these predictors displayed an acceptable discrimination (c-statistic: 0.70). The external applicability of the model was tested on an independent cohort of individuals with type 2 diabetes, where similar discrimination was demonstrated. We concluded that major cardiovascular events in real populations with type 2 diabetes can be predicted on the basis of routinely measured clinical and biological items. The model presented can be used to quantify risk in people with diabetes. The interests and limits for such a model still need to be challenged according to changing and increasing knowledge of type 2 diabetes and its complications.

**ISP11: What is behind the cardiovascular residual risk?**

*Paul Valensi, Department of Endocrinology Diabetology Nutrition, Jean Verdier hospital, Paris Nord University, CRNH-IdF, Bondy, France*

Tight control of blood glucose, lipids and blood pressure is clearly shown to be effective in the prevention of cardiovascular events in diabetic patients. As shown in the Steno-2 study a 50% reduction may be obtained in type 2 diabetic patients using a multifactorial approach targeting all these factors while all the goals were not achieved. This intensive approach which is not always easy or safe lets a substantial residual risk which requires other therapeutic approaches.

High triglycerides with low HDL-cholesterol levels are often neglected while they may increase the cardiovascular risk as shown in the ACCORD LIPID study. Targeting these lipid alterations once the LDL-cholesterol goal is achieved should attenuate the residual risk.

Ankle brachial index, intima-media thickness, artery stiffness or BNP may be considered as useful markers which bring a predictive value additional to the usual risk estimate.

Some diabetic complications including silent coronary artery disease and cardiac autonomic neuropathy are significant predictors of major cardiac events. Their predictive value is additional to routine risk factors. These complications may therefore partly account for the residual risk. For instance silent myocardial ischemia and silent coronary disease remain associated with an increased risk in patients fairly controlled for the usual risk factors. The detection of such cardiovascular disorders may help to estimate more accurately the risk in particular in patients considered at intermediary risk. This should encourage to assess diabetic patients for these disorders but to do so once the predefined individual goals for blood glucose, LDL-cholesterol and blood pressure are achieved, and may lead to intensify the treatments and to apply specific additional tailored therapeutic approaches. However the cost-effectiveness of this strategy needs to be evaluated.

**ISP12: Role of postprandial hyperglycemia and glycemic variability**

*A. Ceriello, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain*

Large randomized studies have established that early intensive glycemic control reduces the risk of diabetic complications, both micro and macrovascular. However, epidemiological and prospective data support a long-term influence of early metabolic control on clinical outcomes. This phenomenon has recently been defined as “Metabolic Memory.” Furthermore, evidences suggest that both “Postprandial Hyperglycemia” and “Glucose Variability” may also be independent risk factors for cardiovascular complications in diabetes. Studies suggest that all these different situations of hyperglycemia share a common pathogenetic mechanism, increased oxidative stress, producing endothelial dysfunction. The therapeutic challenge deriving from these evidences is a need not only for an early tight glycemic control, but also for maintaining glycaemia always in a strict normal narrow range.

**ISP13: Advanced glycation endproducts in food and medicine**

*C. G. Schalkwijk, Maastricht University Medical Centre, Maastricht, the Netherlands*

Dietary factors can modulate inflammation and endothelial function which are closely associated with the development of vascular complications. Therefore, medical nutrition therapy plays an important role in the management of vascular complications. Among other factors, advanced glycation endproducts (AGEs) in food are potential risk factors for inflammation and vascular complications, especially in patients with impaired renal function. Maillard products are formed during processing of food, and become incorporated in body components after intestinal absorption. It has now become apparent from animal models that dietary AGEs represent a significant source of circulating and tissue AGEs. Although only a minor part of ingested AGEs are absorbed and deposited in tissues, they may manifest pathological effects similar to their endogenous counterparts. Experiments performed in animal models have indicated a significant role for dietary AGEs in inducing insulin resistance atherosclerosis and impaired wound healing. In a group of diabetic subjects, dietary AGE was associated with increased levels of serum AGEs in parallel with impaired flow mediated dilation and increased serum markers of inflammation as well as markers of endothelial dysfunction. However, since high-AGE containing diets were produced by cooking, these data doesn’t directly implicate that AGEs are doing the damage. The biological effects may be due to other components as induced by cooking. Taken together, these data are suggestive, but not conclusive, for a role for dietary AGEs in inducing inflammation, insulin resistance and vascular dysfunction.

Notwithstanding these comments, the above mentioned important studies indicate a relationship between dietary AGEs and postprandial levels of AGEs. Whether the uptake of AGEs from the diet has biological consequences for inflammatory activity, vascular function and insulin resistance deserves further investigation.

**ISP14: Exercise, sympa-tho-vagal balance and postprandial glucose profile**

*D. Chapelot, Université Paris 13, Sorbonne Paris Cité, Bobigny, France*

There is now a general agreement for considering that postprandial hyperglycemia (PPHG) is a major and independent risk factor of cardiovascular diseases and should be a specific target of type 2 diabetes (T2D) therapy. The benefit of exercise on insulin-sensitivity, not only after training but also after a single session, has revieved a convincing experimental support. However, its effect on PPHG is still debated. Moreover, an apparently paradoxical impaired glucose

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