The ADA, the IDF, and the EASD have joined forces to recommend the use of the haemoglobin A1C assay for the diagnosis of diabetes. These recommendations were announced during the ADA’s 69th Conference. This is the 1st major departure in 30 years in diabetes diagnosis.

A1C values vary less than FPG values and the assay for A1C has advantages compared with the glucose assay:

⇒ A1C gives a picture of the average blood glucose level over the preceding 2 to 3 months
⇒ A1C has advantages over plasma glucose measurement, since it’s a more stable chemical moiety
⇒ The patient doesn’t need to fast, and measuring A1C is more convenient and easier for patients who will no longer be required to perform a fasting OGTT
⇒ It is correlated tightly with the risk of developing retinopathy.

A disadvantage is the cost.

The committee has determined that an A1C value of ≥ 6.5% be used for the diagnosis of diabetes. This cut-point is where risk of retinopathy starts. However, there is no hard line between diabetes and normoglycaemia, but “...an A1C of 6.5% is sufficiently sensitive and specific to identify people who have diabetes.”

Now the committee’s findings will be referred to practice groups for review of the implications and for recommendations.

Some parts of the world are not going to be able to use this, because it may be too expensive to use in the developing world. Some of these countries have severe chronic anaemia, haemolytic anaemia, and so on, where it will be necessary to fall back on traditional tests. A1C assays are inaccurate in cases of severely low haemoglobin.

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Mortality Risk Equal With Early Intervention or Drug Therapy in Diabetics With Stable Cardiovascular Disease

Results of the Bypass Angioplasty Revascularisation Investigation in Type 2 Diabetes (BARI 2D) show that mortality risk is same for patients with type 2 diabetes and stable IHD whether they are managed with optimal medical therapy, CABG, or PCI. However, CABG was associated with a reduction in risk for CV events, primarily nonfatal MI, compared with intensive medical management (IMT).

BARI 2D involved 2,368 patients with type 2 diabetes and stable IHD who were randomly assigned to early revascularisation plus IMT or IMT alone. Patients were stratified according to whether they received insulin-provision therapy — an insulin secretogogue or insulin — or insulin-sensitisation therapy.

Patients in the intervention group were assigned to either CABG or PCI, according to whichever was most appropriate. Patients assigned to CABG were higher risk. Those undergoing revascularisation were compared with those receiving IMT.

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Survival rates at 5 years were 88.3% in the revascularisation group and 87.8% in the medical therapy group ($P = 0.97$). The 5 year survival rate was 88.2% in the insulin-sensitisation group and 87.9% among patients on insulin-provision therapy ($P = 0.89$).

Major CV events (CVEs) rates were similar in all 4 patient groups. Five-year event rates were 77.2% with revascularisation and 75.9% with medical therapy ($P = 0.70$) and 77.7% with insulin sensitisation and 75.4% with those taking insulin ($P = 0.13$).

However, the event rate was significantly lower in 1 subgroup. Patients randomised to both CABG and insulin sensitisation therapy had a significantly lower rate of major CVEs [primarily nonfatal MI] than any of the other 3 treatment combination groups. Rates were 22.4% with revascularisation and 30.5% with medical therapy at 5 years among those receiving insulin sensitisation therapy ($P = 0.01$).

Severe hypoglycaemia was significantly more frequent in the group that received insulin-provision therapy (9.2%) compared with those that received insulin-sensitisation therapy (5.9%; $P = 0.003$).

The findings are not likely to change clinical practice, the BARI 2D investigators said. "From the diabetes perspective, we can be assured that insulin sensitisation drugs are not harmful and there is in fact a suggestion of benefit." The insulin-sensitising agents were associated with less weight gain and with fewer episodes of hypoglycaemia than insulin-provision therapy.

"From the cardiologist's point of view, we have identified a group of high-risk patients with extensive CVD who benefit from early revascularisation. For lower-risk patients, they can be maintained safely on medical therapy until their condition changes; These findings are consistent with the COURAGE findings."

"But nothing stays fixed for 5 years in patients with diabetes and heart disease. As they develop more angina, more episodes of ischaemia on stress testing or if the features change, physicians will have to use their clinical judgement on when to perform revascularisation." "Diabetes is not static. Things will change as beta cells die and the disease progresses."

All patients in BARI 2D received intensive risk factor modification with weight loss, dietary intervention, lipid-lowering therapy, and other interventions. That's why the event rates were so low, and they were low in all of the groups. "We don't think of it as a lack of benefit. It's not the procedure, it's the risks. This reinforces the importance of diet and exercise in maintaining quality of life and from keeping patients from having to undergo revascularisation in the first place."


Sugar-sweetened beverages may promote weight gain through a lowered satiety response compared with solid food with similar caloric content. In addition, these drinks can disturb energy homeostasis. In a study by Ludwig et al of 548 children with an average age of 11.7 years, each additional daily serving of a sugar-sweetened beverage increased body mass index by a mean of 0.24 kg/m². The results, which were published in the February 17, 2001, issue of The Lancet, also demonstrated that this incremental increase in beverage consumption increased the risk for obesity by 60%.

In the other study reported in Arch Pediatr Adolesc Med. 2009;163:328–335, both lower consumption of sugar-sweetened beverages and higher physical activity improved metabolic and anthropometric outcomes. The combination of these 2 variables was synergistic in improving insulin resistance and concentrations of high-density lipoprotein cholesterol and triglycerides. However, there was no effect modification of both variables for blood pressure or anthropometric outcomes.
Analyses From ACCORD, ADVANCE Shed New Light on Intensive Glucose Control in Type 2 Diabetes

Updated information from two major trials shed new light on the role of intensive glucose control in patients with type 2 diabetes. Investigators from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial reported that low blood glucose levels do not explain the excess deaths seen in the intensive control group.

“We have been investigating a number of different candidates for such a cause. The leading candidates are hypoglycaemia, which can be harmful for high-risk individuals; change of weight, which would change the metabolic situation of these people; different drugs or combinations of drugs; and rapid changes or low levels of glucose.”

ACCORD Analysis
The ACCORD study, conducted at 77 sites in North America, incorporated three strategies for intensive or standard control of blood sugars, blood pressure, or lipids in 10,251 adults. The BP and lipid portions of the trial are scheduled to end on June 30, 2009. For diabetes treatment, physicians could choose from any of the approved drug classes.

The goal of the trial was for the intensive treatment group to reach a HbA1c <6% and for the standard treatment group to reach a level between 7.0% and 7.9%, but findings showed a 20% increased mortality risk in the intensive treatment group (N. Engl. J. Med. 2008; 358:2545-9). Analyses of the interim results could find no specific reason for the increased risk of death from intensive glycaemic control.

The excess mortality risk in the intensively treated group occurred among those who failed to reach HbA1c levels close to 6%, and under 7%. This was a paradox, because the intensive treatment was aimed at lowering HbA1c yet increased the risk of death. “We don’t know why this is, what it was about the participants themselves, or about the way they were treated. Other analyses are under way to identify this. But we think this has important clinical implications: that people who easily achieve HbA1c < 7% do not necessarily have an increase of CV risk by doing so. But the ones who struggle to improve their glucose control appear to be at risk.”

Findings related to hypoglycaemia were presented, which was defined as a blood glucose <50 mg/dL or symptoms consistent with hypoglycaemia and recovery with glucagon or an oral carbohydrate. Among the 451 deaths that occurred in both groups combined, 7% had at least one severe hypoglycaemic event that required medical assistance.

Women, African Americans, those with diabetes complications such as kidney disease, those who were older, and those with a lower education level had a higher risk of hypoglycaemia. In addition, those who had poor glycaemic control were at greater risk of severe hypoglycaemia during the study. Also those with the greatest drop in HbA1c between baseline and the 4-month visit were found to be at lower risk.

Within both the intensive and standard hypoglycaemia arms, having a hypoglycaemic episode was associated with an increased risk of death. This risk was greater among standard-arm participants. It did not reach statistical significance among intensive-arm participants. However, among those who had experienced severe hypoglycaemia, the risk of death was greater among standard-arm participants. Thus, at this point, it is not believed that severe hypoglycaemia – as it was measured in ACCORD – is responsible for the increased risk of death seen among intensive arm participants.

The explanation for the increased mortality among those in the intensive control arm remains unclear and requires further research. Evaluations of other factors such as the impact of weight changes, patient compliance, and diabetes medications are currently underway.

Findings From VADT Analysis
Analysis of data from the Veterans Affairs Diabetes Trial found that the risk of CVEs, including death, was reduced by 40% among adults who initiated intensive glucose control in the first 15 years after a diagnosis of type 2 diabetes, but this effect was not seen in among adults who initiated intensive glucose control 16-20 years after diagnosis.

Moreover, initiation of intensive control 20 yrs+ after diagnosis increased the risk of CVEs, including death. The study enrolled 1,791 patients from 20 VA medical centres nationwide. Mean age at study entry was 60 yrs. 97% were men, 62% were non-Hispanic whites, 16% were African American, 16% were Hispanic, and 5% from other races. The trial ended in May 2008 (N. Engl. J. Med. 2009; 360:129-39).

More than one-third (40%) had prior CVEs, 80% had hypertension, and >50% had lipid abnormalities. Most were obese and their average HbA1c level was 9.5%. Patients were allocated to an intensive or standard glucose lowering therapy, with most patients receiving two to three oral anti-diabetes agents plus insulin.

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Patients in both treatment groups were treated with maximum lipid, blood pressure, diet, and lifestyle control, which included education and counselling on exercise, diet, and smoking.

The main factor that decreased mortality risk was the patient's level of HDL cholesterol. An 80% decrease in the risk of CVEs, including mortality, was observed for every 10-mg increase in HDL-cholesterol level above each patient's baseline, a 50% decrease in risk of a first primary CVE for every 10-mg increase in HDL, and a 55% decrease in risk of all-cause mortality for every 10-mg increase in HDL.

The benefit was as high as a reduction of 90% in some deaths with an improvement in HDL. Both intensive and standard treatment groups had strong benefits from the HDL.

Severe hypoglycaemia was another factor found to increase the risks of adverse events and death. In both groups combined, patients who had experienced hypoglycaemia severe enough to cause changes in consciousness had an 88% increase in primary CVEs and a threefold increase in cardiovascular death.

Multiple hypoglycaemic events strongly increased the risk of death. That increase in risk was more in the standard group than in the intensive group. On the other hand, three times as many events occurred in the intensive group as with the standard group. This data is still being broken down into smaller segments to see how this worked out.

The findings underscore the notion that type 2 diabetes “is an extremely heterogeneous disease.” This may be a clue to breaking down diabetes into manageable subgroups. In the short term, it is strongly recommended that severe hypoglycaemia be avoided whenever possible. Thus, a key message from the trial is to treat diabetes “early, and treat carefully”, adjust HbA1c goals to the individual patient, and encourage patients to report all episodes of hypoglycaemia.

A new study has shed light on the lipid factors that drive CV risk in statin-treated patients with type 2 diabetes. Researchers from centres in Austria and Liechtenstein, monitored over a 5.6-year period 449 statin-treated patients with angiographically proven stable coronary artery disease; about one-third of the patients had type 2 diabetes. During the follow-up, 156 of the patients (37.4%) had a vascular event.

Overall, the factors that significantly predicted vascular events were low HDL cholesterol (standardised adjusted hazard ratio 0.73), low apolipoprotein A1 (hazard ratio 0.77), a small LDL particle diameter (hazard ratio 0.76) and high triglycerides (hazard ratio 1.20). Total cholesterol, LDL cholesterol and apolipoprotein B did not significantly predict vascular events.

An analysis by diabetes status showed that the patients with type 2 diabetes had a significantly higher risk of vascular events than non-diabetic patients. As in the overall population, low HDL cholesterol, low apolipoprotein A1, a small LDL particle diameter and high triglycerides predicted vascular risk, while total cholesterol, LDL cholesterol and apolipoprotein B did not.

Based on these findings, interventions addressing the high triglyceride/low HDL pattern of diabetic dyslipidaemia could be promising options to further reduce cardiovascular risk in statin-treated coronary patients with diabetes.

Source: European Association for the Study of Diabetes’ 44th annual scientific meeting, Rome, Italy, 7-11 September 2008.