Cardiovascular journals

Insulin resistance syndrome and its association with coronary artery disease

Jiten Vora
Consultant Physician, Royal Liverpool University Hospitals

The paper by Kendall and colleagues presents the views of a working group – 'The Partners Against Insulin Resistance Advisory Panel'. It provides an excellent overview of the syndrome and its links with coronary artery disease, incorporating the diagnosis of factors that contribute to the development of insulin resistance and its effect on the risk of coronary artery disease. The multifactorial nature of both the aetiology and the associations of insulin resistance are covered in detail.

The consequences of insulin resistance, including haemostatic and inflammatory abnormalities, altered endothelial function, abnormal free fatty acid and very-low-density lipoprotein (VLDL) metabolism, and finally impaired glucose tolerance, are also examined in detail.

Data linking these to insulin resistance is presented in a clear and precise manner. While some of the steps in the management of insulin resistance are those usually accepted as normal practice, e.g. lifestyle modification (weight management and physical activity) and intervention for hypertension and abnormal glucose tolerance, the aggressive treatment of other identified risk factors for coronary artery disease such as dyslipidaemia and thrombotic risk remain controversial.

With regard to hyperlipidaemia, in particular, the uniform approach of treatment based on biochemical parameters – rather than estimation of coronary artery risk – is presented.

Finally, evidence is presented for the management of insulin resistance syndrome with and without abnormal glucose tolerance, using insulin sensitisers.

Readers will find that the article corroborates current clinical practice, while also enabling reflection on interventions that are not currently standard clinical practice.

CORONARY ARTERY DISEASE

The challenge of insulin resistance syndrome

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 Insulin resistance is a metabolic abnormality characterised by impaired physiological response to insulin.

2 It affects more than 90% of people with type 2 diabetes and predates the development of hyperglycaemia by many years.

3 The combination of insulin resistance and several other metabolic and vascular disorders make up the insulin resistance syndrome.

4 Characteristic features of the syndrome include central obesity, hypertension, dyslipidaemia, glucose intolerance and specific abnormalities of both endothelial cell and vascular function.

5 The origins of insulin resistance are still not clear; ageing, obesity and inactivity contribute to its development but it also has a genetic component, and is very likely to be a polygenic disorder in most individuals.

6 Insulin resistance syndrome markedly increases the risk of both coronary artery disease (CAD) and type 2 diabetes, making early diagnosis and aggressive treatment crucial.

7 Diagnosis remains a challenge because of varying definitions and controversy regarding how many components presage clinical events.

8 Management involves three strategies: lifestyle interventions, e.g. weight loss and exercise, to limit insulin resistance; aggressive treatment of CAD risk factors; and treatment of abnormal glucose tolerance and diabetes.

Kendall DM, Sobel BE, Coulston AM et al, and The Partners Against Insulin Resistance Advisory Panel (2003) The insulin resistance syndrome and coronary artery disease. *Coronary Artery Disease* **14**: 335–48

CURRENT HYPERTENSION REPORTS

Management of coexistent diabetes and hypertension

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 Essential hypertension and diabetes mellitus commonly coexist, are interrelated and each exacerbates the other.

2 Very effective and specific treatments (primarily ACE inhibitors and angiotensin II [type 1] receptor antagonists) for the cardiovascular and renal complications of these disorders are now available.

3 Many large multicentre studies have provided strong clinical-based evidence that supports the use of these agents to retard the progression of cardiovascular and renal involvement and reduce their associated mortality.

4 An enlightened approach to management of the patient with diabetes and hypertension requires a clear understanding of the mechanisms inherent in the two diseases.

5 This paper examines the common pathophysiological aspects of these diseases and the evidence that provides the credibility for use of the new therapeutic interventions.

6 It is clear that a comprehensive therapeutic strategy, combining careful dietary and nutritional measures, rigid glycaemic control, aspirin, lipid therapy, and rigorous blood pressure control, is required for effective management.

Frohlich ED, Sowers JR (2003) Management of diabetic and hypertensive cardiovascular disease. *Current Hypertension Reports* **5**: 309–15

AMERICAN HEART JOURNAL

Effects of enalapril vs nisoldipine on left ventricular mass

Readability	✓ ✓
Applicability to practice	✓ ✓
WOW! factor	✓ ✓ ✓

1 This study examined the link between serial changes in electrocardiographic voltage, antihypertensive treatment and cardiovascular (CV) events.

2 Data from 468 patients with type 2 diabetes and hypertension, enrolled in the Appropriate Blood Pressure Control in Diabetes (ABCD) trial, were analysed.

3 Patients were randomised to enalapril (ACE inhibitor) or nisoldipine (calcium-channel blocker) treatment, and to intensive or moderate treatment goals.

4 An electrocardiographic index for increased left ventricular (LV) mass, the adjusted Cornell voltage, was measured serially by treatment group. Cox proportional analysis was used to define the association between voltage changes and cardiovascular (CV) events.

5 During 5 years follow-up, decline in voltage was significantly greater in patients treated with enalapril than in those receiving nisoldipine ($P = 0.002$).

6 There were no significant voltage differences between patients treated intensively and those treated moderately.

7 Treatment assignment (enalapril vs nisoldipine) was the strongest predictor of CV events, but coronary disease at baseline, duration of diabetes and change in voltage were also independent predictors of CV events.

8 The greater reduction in LV mass with enalapril, as reflected by a greater decline in voltage, may partly explain the finding, in the ABCD trial, of a lower risk of MI with enalapril.

Havranek EP, Esler A, Estacio RO et al (2003) Differential effects of antihypertensive agents on electrocardiographic voltage: results from the Appropriate Blood Pressure Control in Diabetes (ABCD) trial. *American Heart Journal* **145**: 993–98

CURRENT OPINIONS IN CARDIOLOGY

Current treatment of dyslipidaemia

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 Type 2 diabetes and the closely related metabolic syndrome have reached epidemic proportions and are associated with significant risk of cardiovascular (CV) disease.

2 Aggressive management of all risk factors, particularly atherogenic dyslipidaemia, is important, not only to prevent CV disease but also to reduce morbidity and mortality.

3 Dyslipidaemia is characterised by raised triglyceride-rich lipoproteins, low HDL cholesterol, small, dense, LDL particles, increased postprandial lipaemia, and abnormal apoA1 and apoB metabolism, all of which accelerate atherosclerosis.

4 Combinations of lipid-modifying agents – statins, fenofibrate, niacin, ezetimibe and adjunctive therapy – are more effective in helping patients achieve therapeutic goals.

Cottrell DA, Marshall BJ, Falko JM (2003) Therapeutic approaches to dyslipidaemia in diabetes mellitus and metabolic syndrome. *Current Opinions in Cardiology* **18**: 301-08

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Albuminuria linked with LV function

Readability	✓ ✓
Applicability to practice	✓ ✓
WOW! factor	✓ ✓ ✓

1 Albuminuria is a strong predictor of cardiovascular disease (CVD) in diabetes, but the mechanism is unclear.

2 This study compared left ventricular (LV) systolic and diastolic function in three groups of American Indians with diabetes: group I ($n = 685$) no albuminuria (< 30 mg albumin/g creatinine); group II ($n = 519$) microalbuminuria (30–60 mg/g); group III ($n = 372$) macroalbuminuria (> 30 mg/g).

3 LV systolic function decreased stepwise from group I to group III. Results were similar for diastolic LV filling.

4 Albuminuria remained independently associated with abnormal systolic and diastolic function after adjusting for age, gender, blood pressure, duration of diabetes and other covariates.

5 The independent association of albuminuria with worse LV function may partly explain the link between albuminuria and increased CV events.

Liu JE, Robbins DC, Palmieri V et al (2003) Association of albuminuria with systolic and diastolic left ventricular function in type 2 diabetes: The Strong Heart Study. *Journal of the American College of Cardiology* **41**: 2022–028

STROKE

Prolongation of QTc interval predicts future strokes

Readability	✓ ✓
Applicability to practice	✓ ✓
WOW! factor	✓ ✓

1 This long-term prospective study assessed the predictors of stroke in diabetes, with particular emphasis on abnormalities of QT interval.

2 A total of 417 patients with type 2 diabetes were followed up for a median of 57 months (range 2–84 months), during which time 40 incident strokes occurred.

3 QTc interval prolongation($\geq 470\ ms^{1/2}$) was an independent predictor of stroke, increasing the risk of stroke approximately threefold after adjustment for other potential risk factors.

4 Other independent predictive factors for stroke were: older age; previous cerebrovascular disease; increased 24 h proteinuria, serum triglycerides and left ventricular mass; and decreased HDL cholesterol.

5 Intervention studies are needed to assess whether QTc can be modified.

Cardoso CRL, Salles GF, Deccache W (2003) QTc interval prolongation is a predictor of future strokes in patients with type 2 diabetes mellitus. *Stroke* **34**: 2187–94

'The greater reduction in LV mass with enalapril, as reflected by greater decline in voltage, may partly explain the finding, in the ABCD trial, of a lower risk of MI with enalapril.'

'The independent association of albuminuria with worse LV function may partly explain the link between albuminuria and increased cardiovascular events.'