Macrovascular disease in type 2 diabetes

Type 2 diabetes is associated with a 2 - 4-fold increased risk of cardiovascular disease (CVD), and over half the excess mortality in subjects with type 2 diabetes is due to this complication.1 The development of macrovascular disease in type 2 diabetes is partly related to chronic hyperglycaemia, but also to other associated atherogenic factors, including dyslipidaemia, oxidative stress, endothelial damage, hypercoagulability and activation of inflammatory pathways.2 This complex interaction between metabolic factors, coagulation, inflammatory and other mediators in the development of macrovascular disease is demonstrated in the proportionately smaller effect of glycaemic control on macrovascular disease as opposed to microvascular disease. For example, in the United Kingdom Prospective Diabetes Study (UKPDS), microvascular disease increased almost 10-fold over a range of HbA1c from < 6.0% to > 10%, while macrovascular disease increased only 2-fold over the same range of glycaemia.3 Furthermore, clinical assessment of cardiovascular disease is confounded both by the high prevalence of silent myocardial ischaemia, estimated to occur in 10 - 15% of subjects with diabetes as opposed to 1 - 4% in non-diabetic persons3 and the poor performance of the traditional screening test for myocardial ischaemia — stress electrocardiography (ECG). Stress ECG testing is reported to have a sensitivity of 47% and specificity of 81%.4 The poor performance of the stress ECG, the high prevalence of silent ischaemia and the importance of accurate diagnosis and management of CVD has led to a number of newer diagnostic modalities which include stress echocardiography, stress isotope scanning and, more recently, electron beam computed tomographic (EBCT) determination of coronary calcification. The presence of coronary artery calcium is a marker of atherosclerosis and its detection with EBCT has a sensitivity of 95 - 99% for obstructive coronary artery disease, but lower specificity of 23 - 57%.5

What of the situation in South Africa, particularly in the black population? Few studies have addressed the epidemiology, pathogenesis and clinical manifestations of macrovascular disease in the black population of South Africa, although a number of studies have commenced or are in the planning stages. It is clearly inappropriate to extrapolate from conclusions in other communities and ethnic groups and, furthermore, fundamental ethnic variations may exist to alter susceptibility to various complications. A study comparing coronary artery calcification (detected with digital subtraction fluoroscopy) in black and white Americans with no symptoms, but with risk factors for coronary artery disease, showed that despite less coronary artery calcium, black participants (including 27% with diabetes) had a higher risk of coronary heart disease events than the white participants over 70 months of follow-up.6

The article by Professor Paul Rheeder and colleagues (p. 79) takes a step toward addressing the large hiatus in knowledge of macrovascular disease in the black population of South Africa with type 2 diabetes.7 Rheeder and co-workers (including medical students) focus on the clinical assessment of peripheral vascular disease in black women in a primary health care facility and argue that simple palpation of peripheral pulses by competent clinical examination, augmented with relatively inexpensive arterial Doppler measurements, is crucial to the evaluation of this particular macrovascular complication in this setting. Against the backdrop of increasingly expensive technology-driven methods of assessment of other vascular regions, this is refreshing and sound advice that will require dedicated translation into widespread practice at all levels of diabetes care. In most parts of South Africa, however, the recommendation for the relatively inexpensive ankle-brachial pressure measurement in all persons with type 2 diabetes aged over 40 years (among the other recommendations by an expert consensus committee) is not likely to be implemented owing to shortages of trained staff and equipment, but represents a challenge that may be achievable with enough will and support. Interestingly, plain radiographs revealed intimal or media calcification in only 8 of 81 subjects, which indicates that vascular calcification in this population may not occur to the same degree or carry the same significance as in other populations. The ongoing evolution of South African society, linked with increasing westernisation of much of the population, suggests that macrovascular disease may increase in the next decade and provides a cogent argument to dispense with anecdotal impressions of the extent and clinical manifestations of macrovascular disease in black South Africans and instead generate robust scientific data in this regard.

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Fortunately newer DXA systems that incorporate IVA (Hologic scanners) or LVA (Lunar scanners) overcome all these disadvantages. The technique uses a DXA system on a digital X-ray imaging device, but with the advantages of parallel beam geometry.

**Advantages of IVA or LVA**

1. Evaluation for spine fractures can be done without referral for X-ray. This can be done simultaneously with the DXA.
2. There is much less radiation exposure.
3. A single image of upper dorsal and lower lumbar spine can be obtained.
4. Images are digital and can be stored on computer for display and analysis at any time for comparison.

**Limitations of IVA/LVA**

1. There is lower resolution than with standard X-ray.
2. The field of view is narrower and one may miss other abnormalities such as aneurysms and tumours.
3. The higher dorsal vertebrae are not clearly visualised, but 97% of vertebral bodies are analysable up to T7.
4. Patients with high body mass index have a poorer clarity.

Use of IVA or LVA shows an overall sensitivity of 68% when compared with reading of a spine X-ray by a radiologist. Of the 32 missed, 12% were unanalysable on IVA, 20% were classified as normal on IVA, and the majority of missed fractures were graded as mild. IVA or LVA will therefore capture 4 out of 5 and the majority of missed fractures were graded as sable on IVA, 20% were classified as normal on IVA, 6. IVA or a lateral X-ray assessment is an integral component of follow-up for osteoporosis. Several methods exist for measuring treatment efficacy, including: (i) presence or absence of clinical fractures; (ii) measurement of height; (iii) comparative BMD, and (iv) turnover markers. Based on current National Osteoporosis Foundation of South Africa (NOFSA) guidelines, an incident fracture while on adequate therapy is an indication to review treatment.

**Conclusion**

NOFSA is of the opinion that assessment of the lateral spine either by lateral X-ray of the dorsal and lumbar spine or by IVA/LVA should be a routine part of fracture risk assessment in a substantial portion of patients, particularly older patients in whom vertebral fractures are common and in whom BMD, particularly at the spine, becomes increasingly inaccurate and difficult to evaluate.

To limit costs such assessments are best done at the point of service, reducing the need for referral for X-rays and increased cost due to a second appointment for review of X-rays.

Upgrading of DXA machines to offer IVA or LVA involves considerable cost. An appropriate payment for IVA or LVA would therefore be just. The long-term cost savings and long-term benefit to patients are obvious.

**Who should have IVA/LVA?**

1. Patients with a low BMD.
2. Subjects with BMD-independent risk factors for the development of osteoporosis (e.g. family history, previous history of fracture, propensity to falls, high bone turnover, etc.).
3. Elderly patients.
4. Patients on chronic (> 6 months) glucocorticoid therapy.
5. Patients with clinically significant height loss.
6. IVA or a lateral X-ray assessment is an integral component of follow-up for osteoporosis. Several patients on chronic glucocorticoid therapy or with low BMD should have IVA/LVA.

**References from the editorial on p. 71:**