Original Articles

Challenges in investigating Peripheral Vascular Disease in patients with Diabetes and Cardiovascular Diseases

S Vara, A Palmer, D Robbins, A Thapar, C Kyriakides & S Dindyal

Given the increasing prevalence of diabetes, with cardiovascular disease representing the principle cause of death and morbidity amongst diabetics,[1] it is imperative that early investigation and then intervention is achieved. Diabetic patients are at increased risk of peripheral arterial disease (PAD), with an earlier onset and a more severe and diffuse manifestation often being seen. The key factors in diabetic arteriopathy include vascular smooth vessel dysfunction, inflammation, hypercoagulability and endothelial dysfunction. Moreover, the presence of PAD is a marker of generalised atherosclerosis and is a strong indicator of increased morbidity and mortality due to cardiovascular ischaemic events, with the risk of atherothrombotic events increasing in the presence of concomitant diabetes.[2]

Ankle Brachial Pressure Index (ABPI)

When considering the management of diabetic foot infections, consideration must be taken to evaluate and consider the presence of an ischaemic component, for which healing can be improved by the correction of even a moderate degree of ischemia.[3, 4] Diabetic patients have an increased likelihood of atherosclerotic disease affecting infrageniculate arteries, often with sparing of the foot arteries, thus allowing arterial reconstruction to the distal vessels.[4] However, the non-invasive vascular tests used to evaluate the extent of the ischemia have several significant limitations, in the presence of diabetes. The presence of medial artery calcinosis, common amongst diabetics and those with chronic renal failure, can result in incompressible arteries which produce spuriously elevated segmental systolic pressures and Ankle Brachial Pressure Indices (ABPI).[4] Vessel incompressibility should be suspected when the ABPI exceeds 1.30, thus warranting the use of photoplethysmography or pulse-volume recordings to record toe-pressure measurements and abnormal monophasic waveforms.[5]

Duplex ultrasound

Arterial calcinosis can also limit the utility of duplex ultrasound through alteration of pressure waveforms and the calcified lesions impairing vessel wall visualisation.[6,7] Despite the sensitivity and specificity being arguably less than that of Computed Tomography Angiogram (CTA) or Magnetic Resonance Imaging (MRI) approaches, its wide availability and lack of any contrast agents makes its use favourable in diabetic nephropathy patients in particular.[8] Furthermore, insonation in the region of open ulcers or excessive scarring may also not be possible.[9] In some obese patients, there may be reduced accuracy of the test in proximal aorto-iliac arterial segments.[10, 7]

Cross-sectional imaging

Arteriography using CTA or MRI approaches are generally needed for revascularisation procedures, however the use of iodinated contrast agents can be a point of concern in diabetics with renal disease. Furthermore, adverse effects of MRI imaging contrast in patients with renal dysfunction, namely systemic fibrosis with gadolinium-based contrast agents, mean that MRI angiography is often not used in diabetics.[8] Patients with end-stage renal disease, who are often diabetic, often require complex treatment due to a greater involvement of the distal and pedal vessels, superimposed heavy calcifications, and the presence of widespread disease.[11] Moreover, the presence of metal implants in patients' bodies during MRI scanning can cause excessive magnetic field interactions, limiting their use.[12] However, Time-of-flight (TOF) MRA can be performed using either a 2D or 3D acquisition mode, without the need for administration of gadolinium. Although it allows peripheral vasculature to be evaluated without using ionising radiation exposure and contrast agents, the lengthier scan times when compared to other methods sometimes makes its use less favourable.[13]

For diabetic foot, radiographs are the preferred initial imaging modality, allowing an insight into foot architecture, weight-bearing and cortical destruction.[14] However, radiographic changes of charcot neuropathic osteoarthropathy (CN) have a low sensitivity and often have a delayed

Sarina Vara

Annika Palmer

Daniel Robbins

Ankur Thapar

Constantinos Kyriakides

Shiva Dindyal

presentation.[15] In the diagnosis of osteomyelitis, the sensitivity of plain films is dependent on the chronicity of the infection and the extent of the bone loss, with at least 30-50% bone loss needed to show visible changes on the radiograph.[16] In contrast, MRI can detect subtle changes in the early stages of active CN,[14] meaning that those patients unable to undergo MRI may require isotope bone scans and CT imaging to monitor inflammatory and infective changes.

Restenosis following angioplasty and outcomes in diabetics

The hyperglycaemia, dyslipidaemia and insulin resistance that characterise diabetes influence the progression of vascular inflammation and endothelial cell dysfunction.[17] The vascular abnormalities that cause atherosclerosis in diabetics are often present prior to diagnosis, and increase in severity the longer the disease progression and the worsening blood glucose control.[18] By contributing to increased plaque burden and instability, these worsen the complexity of vascular disease.[19] Restenosis amongst diabetics can be attributed to the inflammatory state and oxidative stress that is worsened by poor glycaemic control.[20]

Summary

Ultimately, several factors contribute to the complexity of the treatment and outcome of patients with coexistent diabetes and peripheral vascular disease. These include comorbidities, neuropathy, foot deformity and the presence of infection.[21] The presence of poor glycaemic control has been associated with an increased risk of adverse outcomes following vascular surgery or endovascular intervention.[22]

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