



Cliff Shearman is Professor of Vascular Surgery, Southampton

## Diabetes and vascular disease in the last ten years

The last decade has seen greater awareness of the increasing scale of the problem of diabetic vascular disease and understanding of its clinical behaviour. There have been advances both in assessment and treatment but perhaps best of all is the evidence for reduction in amputation when multidisciplinary team working approaches to the condition are adopted.

Peripheral arterial disease (PAD) affecting the lower limb is a common condition. Epidemiological studies have demonstrated that it can be detected in up to 28% of the adult population. Diabetes is a strongly associated risk factor for PAD and the prevalence of diabetes in patients with PAD seems to be rapidly increasing. In the on-going REACH (Reduction of Atherothrombosis for Continued Health) Registry, 43% of participants with PAD had diabetes (Morrell et al, 2007). This seemingly high rate is reflected in other studies.

Insulin resistance is strongly linked to the development and progression of PAD and people with type 2 diabetes have 3–5 times greater chance of developing PAD than those without the condition (Uutisupa et al, 1990). Intensive blood glucose control does not appear to reduce the risk of cardiovascular death or amputation (UKPDS, 1998). However, a 1% reduction in HbA<sub>1c</sub> is associated with a 21% reduction in complications (Stratton et al, 2000). Risk factors for PAD such as hypertension, smoking and hypercholesterolaemia are extremely common in people with type 2 diabetes. Additionally, the benefits of risk factor modification – blood pressure control, lipid lowering with statins and smoking cessation – gain greater benefit for the person with diabetes than those without diabetes. Many people with diabetes-related complications and PAD have poor control that may be overlooked by the podiatrist or vascular surgeon treating the specific foot problem. This emphasises the need for a well co-ordinated multidisciplinary team.

Histological examination of atherosclerosis from people with diabetes reveals more calcification and increased presence of inflammatory cells than people without the condition. At a macrovascular level, it is commonly recognised that the disease more commonly affects the more distal parts of the circulation, particularly the calf, with relative sparing of the pedal blood vessels (Diehm et al, 2006). The microcirculation itself is often abnormal with changes in vasomotor control, thickening of the vascular endothelium and abnormalities of the platelets, which may partly explain the sudden deterioration seen in wounds that initially

appear to be healing well (Akbari and LoGerfo, 1999). The effect of this microcirculatory dysfunction tends to amplify the effects of large vessel disease (Williams et al, 2006).

People with coronary artery disease and diabetes have a worse prognosis than people without diabetes despite equivalent treatment (Donahoe et al, 2007). People with diabetes are also at considerably greater risk of lower limb amputation than people without diabetes and the detection of PAD is a strong predictor of subsequent amputation.

All of the above factors suggest that vascular disease in people with diabetes is physiologically and pathogenically different to that in people without the condition. Strategies for treatment need to recognise and take into account these differences.

### Presentation

People may present with the common symptoms of PAD – claudication, rest pain or a non-healing wound – but are more likely to present with tissue loss: foot complications are a particularly common problem (Virkkunen et al, 2004). Foot ulceration and infection are the most common complications of diabetes and 15% of people with diabetes will suffer a foot ulcer during their life. Seventy-two per cent of people with diabetes who lose their leg have a history of previous foot ulceration. In around 10%, ischaemia due to PAD will be the dominant factor at the time of presentation, but ischaemia is present to some extent in at least 60%. While the importance of detecting PAD and correcting ischaemia is well recognised, the emergency treatment of diabetic foot complications is often neglected, resulting in further tissue damage and ultimately reducing the chance of limb salvage.

The infected diabetic foot is a surgical emergency and must be treated as such. The individual should be treated by a team who are experienced with this condition and control of the diabetes established, if necessary, with an intravenous sliding scale of insulin. Infection should be combated with appropriate intravenous antibiotics and cultures obtained and removal of infected tissue and drainage of pus must be undertaken within a few hours of admission. Assessment of the underlying cause and the extent of PAD can then be undertaken when the foot has been made safe.

### Assessment

History and examination are a vital part of the assessment. Someone who can walk a mile is likely to

# ARTERIAL DISEASE PERIPHERAL

have good peripheral circulation and the presence of a palpable foot pulse makes the presence of clinically significant large vessel disease unlikely. However, it must be remembered that many of those who present with limb-threatening ischaemia have no previous vascular history.

Ankle pressures can be misleading, but are still very helpful in the majority of cases. In people with suspected PAD or in whom it is still unclear from the preliminary assessment whether arterial disease is present, an arterial duplex scan should be obtained. This is non-invasive, readily available and can also give some guidance as to the suitability of an arterial lesion for treatment. Conventional angiography has been largely replaced for diagnosis by magnetic resonance (MR) angiography or CT angiography. MR angiography has the advantage of having minimal nephrotoxic effects and both modalities are much less invasive than conventional angiography and can be performed as an outpatient examination.

Arterial disease will often be present, but the decision as to which individual needs revascularisation can be difficult and often remains a clinical one. Transcutaneous oxygen tension measurement on the foot may help, but often still leaves a group in whom it remains unclear if the wound will heal.

Any reduction in blood supply will have an adverse effect on wound healing. If intervention looks relatively low risk, for example an angioplasty of the iliac artery, then it would seem reasonable to proceed to early revascularisation if the patient is fit. If revascularisation is high risk, such as a pedal bypass in an unfit patient, then it may be prudent to optimise the wound healing environment first (eradicate infection, treat any comorbidity and reduce oedema with elevation of the limb) and proceed to revascularisation only if the wound fails to respond.

## Treatment

In all cases, identification and correction of associated risk factors must not be neglected. Still less than 50% of people with PAD get adequate attention to this aspect of their care (Morrell et al, 2007). There is probably nothing that can be done to improve their long-term outcome more than this.

Revascularisation can be achieved in two ways, endovascular techniques (angioplasty) or bypass surgery (sometimes involving endarterectomy). The evolution of angioplasty with low profile catheters, stents and recently drug-eluting stents has expanded the role of this treatment. Sub-intimal angioplasty – the creation of a false passage in the wall of the diseased artery – seems to be technically much more applicable in many individuals with distal diabetic vascular disease, thus expanding the role of endovascular interventions (Davies et al, 2007). Although initial technical success is high, the long-term patency is poor. The seems to be particularly evident in people with diabetes where the re-stenoses rate is higher (Baumgartner, 2007). Interestingly, this seems to have little adverse effect on limb salvage, possibly because tissue healing has been established while the angioplasty has remained open.

The role of surgical bypass has had champions for many years, but the surgery is challenging and time

consuming. A large meta-analysis of results from 32 centres demonstrates that excellent results can be achieved. In total, 2320 grafts were undertaken for limb salvage; 86% were in people with diabetes, 62% were pedal bypasses and 10% were secondary procedures. In this series limb salvage at 5 years was 78%. Due to the presence of other conditions such as ischaemic heart disease and renal impairment, the mortality rate for surgery in people with diabetes is higher, but the graft patency is the same as those without diabetes (Virkkunen et al, 2004).

The bypass versus angioplasty in severe limb ischaemia trial (BASIL) compared angioplasty versus surgery in people with severe limb ischaemia, 24% of whom had diabetes (Adam et al, 2005). In this study, there was no difference in amputation-free survival between the two treatment groups (55%), although initial technical failure rate for angioplasty was over 20%. It seems logical on this basis to attempt endovascular treatment initially and undertake surgery if this does not succeed. One caveat to this approach is that it is apparent that in some technically successful angioplasties the foot wound does not heal, presumably due to more distal disease and in these cases limb salvage rates are lower (Bakken et al, 2007). Some form of assessment after angioplasty is essential, either clinical improvement in the wound or an increase in  $TcPO_2$ .

## Conclusion

The proportion of people with PAD who have diabetes is currently increasing and is likely to continue to do so. Those with diabetes and vascular disease have a markedly increased CV risk and it is important that anyone treating this group ensures that their risk factors are checked and modified appropriately.

Diabetic vascular disease is distinct from non-diabetic disease in many ways and this influences how it should be treated. In particular the presentation of these individuals is more often as an emergency with infection of a foot ulcer. Treatment needs to be rapid and carried out by multidisciplinary teams experienced in the management of this problem so that subsequent investigation and, when appropriate, treatment of the vascular disease can be undertaken. ■

Adam DJ et al (2005) *Lancet* **366**: 1925–34

Akbari CM, LoGerfo FW (1999) *Journal of Vascular Surgery* **30**: 373–84

Bakken AM et al (2007) *Journal of Vascular Surgery* **46**: 946–58

Baumgartner I (2007) In Greenhalgh RM (ed) *More Vascular and Endovascular Challenges*. BIBA Publishing, London

Davies N et al (2007) In Earnshaw JJ, Murie JA (eds). *The evidence for vascular surgery*. Second Edition. TFM Publishing Ltd, Shrewsbury

Diehm N et al (2006) *European Journal of Vascular and Endovascular Surgery* **31**: 59–63

Donahoe SM et al (2007) *JAMA* **298**: 765–75

Morrell J et al (2007) *British Journal of Cardiology* **14**: supplement 3

Uutisupa MU et al (1990) *Circulation* **82**: 27–36

UKPDS Group (1998) UKPDS 33. *Lancet* **352**: 837–53

Schaper W, Buschmann I (1999) *American Heart Journal* **99**: 2224–6

Stratton IM et al (2000) *BMJ* **321**: 405–12

Virkkunen J et al (2004) *Journal of Vascular Surgery* **40**: 761–7

Williams DT et al (2006) *Journal of Vascular Surgery* **44**: 770–5