Diabetes, falls and fractures

Diabetes mellitus, falls and fractures are commonest in older age. In the United Kingdom, half of people with diabetes are aged over 65 years and a quarter over 75 years [1], and 40% of older diabetic patients report falling each year [2]. One study of frail older people in Scotland found that 86% of fractures resulted from a fall [3]. Hip fractures are 1.5 to 12 times more likely in patients with diabetes compared with non-diabetic controls, and fractures at other sites, including the humerus and spine, are also more common [4]. What are the reasons for this complex interaction between diabetes, falls and fractures, and what do we know about the pathophysiological mechanisms?

Autonomic dysfunction and postural hypotension

Orthostatic hypotension (OH) is a risk factor for falls, and interventions to decrease the severity and frequency of OH significantly reduce the incidence of falls [5]. Up to 10% of patients with diabetes have OH [6], which may be due to autonomic neuropathy, reduced baroreflex sensitivity or hypotensive medication [7]. Non-pharmacological measures include physical counter-manoeuvres [8], water drinking [9] and the avoidance of precipitating factors such as alcohol. Graded pressure stockings are beneficial, but the risks of concomitant peripheral vascular disease or neuropathy should be recognised. Common culprit drugs to be stopped (where possible) include antihypertensive agents, especially alpha blockers, anticholinergic agents, tricyclic antidepressants and major tranquilisers [5]. Where symptomatic OH or falls continue, fludrocortisone may be effective and midodrine (a peripheral alpha-adrenoceptor agonist) may be used as a second-line agent [10], but caution is required in diabetic patients as vasoconstriction may exacerbate coronary artery or peripheral vascular disease.

Postural blood pressure (BP) changes probably cause falls by impairing cerebral perfusion, but the mechanism may be more complex. In older people, BP and heart rate during walking are also dependent on gait speed and foot pressure, suggesting that gait abnormalities may independently adversely affect BP during walking [11]. The presence of OH should prompt investigation for autonomic failure, particularly if it persists after withdrawal of culprit medicines. Peripheral post-ganglionic autonomic neuropathy is seen in up to 15% patients with diabetes [6], and symptoms include temperature dysregulation, impotence and gastrointestinal disturbance. Ewing’s battery of autonomic function tests evaluate both sympathetic and parasympathetic function [12], and newer techniques such as heart rate variability [13] and Iodine-123 Metaiodobenzylguanidine (MIBG) cardiac scintigraphy [14] are promising but await adequate clinical characterisation. The identification of autonomic failure is clinically relevant, since it is associated with cardiac arrhythmia, silent myocardial ischaemia, perioperative hypotension and death [15].

Gait disorder

All patients who fall should have their gait assessed, using a simple screening tool, such as the ‘timed up and go’ test [16]. The classification of gait abnormalities due to neurological disorder [17] maps to the neurological complications of diabetes:

- Low level gait disorders comprise peripheral neuropathy, affecting motor and sensory systems with ataxia a common complication. Other complications causing low level gait abnormalities may include diabetic myopathy and statin-induced myositis.

- Middle level gait disorders are caused by ischaemic lesions in the posterior cerebral circulation or basal ganglia, influencing the spatial maps of the body and integration of sensory information.

- Higher level gait disorders involve cortical and subcortical structures causing gait apraxia, namely, equilibrium apraxia (impaired response to external stimuli), ignition apraxia (poor learned motor sequencing) or mixed gait apraxia. Gait apraxia is often linked to neurodegenerative conditions, including Alzheimer’s disease, which is also associated with type 2 diabetes [18]. For many patients, goal-directed movement is difficult and gait abnormalities result, especially when encountering a simultaneous task to perform whilst walking [19]. Unfortunately, patients with moderate to severe dementia are resistant to falls prevention strategies and there is limited evidence for interventions in gait apraxia and none specific to diabetes [20, 21]. Despite this, patients who fall, and have diabetes and dementia, may benefit from a range of targeted interventions, including medicines review and training of family and carers.

Overall, improvements can be made for diabetic patients with gait disorders as shown by a recent study of specific training to improve gait speed, balance, muscle strength and joint mobility [22]. However, although syncope is commonly associated with falls and 34% of older patients presenting with falls have carotid sinus hypersensitivity [23], there is no consistent evidence for intervention, and none specific to diabetes mellitus.
Diabetes-specific mechanisms: hypoglycaemia, diabetic polyneuropathy and retinopathy

Hypoglycaemia in general and insulin treatment in particular are risk factors for falls [24]. Metformin can cause vitamin B12 deficiency, another potential mechanism for postural instability [24]. Low HbA1c, frailty and peripheral neuropathy are associated with falls in older people with diabetes [25]. Almost a third of all patients with diabetes have neuropathy. Most have distal symmetrical or diabetic polyneuropathy (DPN), with predominantly sensory symptoms such as pain, numbness and tingling in the hands and feet [26]. Current guidance focuses on identifying vulnerable feet, screening for impaired sensation or vibration, diminished foot pulses or foot deformity and provision of foot care education, podiatry, footwear and symptomatic relief of neuropathic pain [27]. Duloxetine, amitriptyline, pregabalin and opioid analgesia are all recommended therapies [28], but they also contribute to an increased fall risks.

Patients with neuropathy have reduced walking speed, cadence and step length, particularly when walking on an irregular surface and they may have impaired peripheral sensation, reaction time and balance [29], and DPN is an independent risk factor for falls [30–32]. Ultimately, all patients with type 1 diabetes and about 60% of those with type 2 will develop retinopathy [33]. Visual loss due to diabetes (including cataracts, macular degeneration and glaucoma) may be associated with an increased risk of falls, probably due to impaired visual acuity, depth perception and contrast sensitivity [34].

Bone health

Fractures are commoner in patients with type 1 and type 2 diabetes compared with non-diabetic subjects. Type 1 diabetes is associated with more than 12 times the risk of fracture, which is mostly attributed to low Bone Mineral Density (BMD) [4]. Putative mechanisms for osteoporosis include the absence of the anabolic effect of insulin on bone, possibly via insulin-like growth factor 1 [4]. Patients with type 2 diabetes are 1.6 times more likely than people without diabetes to break a bone and 2.8 times more likely to fracture a hip. However, in type 2 diabetes, BMD is higher than non-diabetic subjects at all sites and this difference persists, after adjustment for body size, which is itself an important predictor of BMD [4, 35]. Potential mechanisms for these differences include visceral fat accumulation [36] and higher adiponectin levels [37]. There are a number of less common associations with osteoporosis: type 1 diabetes is linked to coeliac disease [38] and type 2 diabetes with hypogonadism [39]. Both these conditions significantly increase fracture risk by separate mechanisms. Poor glycaemic control is also an important consideration as accumulation of advanced glycation products potentially interferes with collagen metabolism in the bone [40]. Poor glycaemic control itself may be associated with alterations in bone turnover [41]. High blood glucose levels have been associated with a calciuric effect in patients with type 2 diabetes [42], which may contribute a further long-term link between fracture risk and poor diabetic control.

Vitamin D

There is increasing evidence that vitamin D deficiency is a cardiometabolic risk factor, promoting hypertension, impaired endothelial function, cardiovascular disease and insulin resistance [43]. Better vitamin D status has been associated with a lower incidence of type 1 diabetes in Finland [44]. However, for type 2 diabetes, there are conflicting results from vitamin D intervention studies [45, 46]. Hypothesised mechanisms for altered insulin sensitivity interacting with vitamin D include immune modulation, as vitamin D deficiency may promote increased inflammatory cytokines, which may also have a toxic effect on bone [47].

Drugs: thiazolidinediones

Finally, we are increasingly aware of the adverse effects of thiazolidinediones on bone health. The Diabetes Outcomes Progression Trial (ADOPT) study first reported the increased risk of peripheral fractures in women on rosiglitazone [48], leading to an US Food and Drug Administration (FDA) Alert in 2007 (http://www.druginjurylaw.com/rosiglitazoneHCP.pdf) and subsequent evidence suggests a class effect, with pioglitazone causing similar fractures. Although there were 1% more fractures per annum, evidence is increasing that other fracture sites (such as the spine and femur) are also affected, resulting in a doubling of fracture risk [49]. In 2009, National Institute for Health and Clinical Excellence (NICE) guidance recommended that we should ‘not commence or continue thiazolidinediones in people... at higher risk of fracture’ [50]. How should we identify high risk individuals? Bone densitometry may not help, since BMD will not predict atypical fractures of the hand and foot. Thiazolidinediones are associated with a number of other risks: cardiovascular (including myocardial infarction), fluid retention, heart failure and anaemia, so they must be used with caution in older patients.

Conclusion

Falls are common in older diabetic patients due to a number of factors: autonomic dysfunction, OH, gait disorder, peripheral neuropathy and visual impairment. Fractures are also more common, especially in type 1 diabetes, where BMD is low and in type 2 diabetes, where there are many potential factors, including treatment with thiazolidinediones. In all cases, vitamin D deficiency is common and may contribute to falls and fracture risk, although we still lack good clinical evidence for the role of vitamin D supplementation. Although falls prevention interventions may halve fracture rates, this equates to a need to treat 46 pa-
tients to prevent one fracture in the general population [51]. However, older patients with diabetes are worthy of focused intervention, since their modifiable falls and fracture risk is so much greater. Despite a disappointing lack of clinical trial evidence specific to diabetes, targeted falls prevention and bone protection in this vulnerable group is likely to yield considerable benefits.

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**References**


Human rights and healthcare: changing the culture

Despite the introduction of the Human Rights Act in 1998, there has been a relative failure to use the Act to improve care for older people. All older adults receiving health or social care should assume that they will be treated with dignity, respect, humanity and compassion. It should not be forgotten that Human Rights belong to everyone, and they cannot be taken away [1]. Unfortunately, so often, admission to a hospital or a move to a care home can lead to the loss of Human Rights, particularly for those suffering from dementia. The media have highlighted their plight. The medical profession, in particular geriatricians, is in an ideal position to provide leadership to promote a better understanding of their importance and the need to protect an individual’s rights both in hospital and in care homes [2].

The Human Rights Act makes it unlawful for any public body to act in a way, which is incompatible with the convention. Public authorities such as the NHS and local authorities have a duty to respect and protect basic human rights. These rights include:

Article 2. The right to life
Article 3. Prohibition of inhuman or degrading treatment. Inhuman and degrading treatment or care can result from inadequate care and neglect rather than a deliberate intent to do harm. This is an absolute right.