

Frailty, older people and type 2 diabetes

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Article points

1. Frailty among older people with diabetes can lead to increased risk of hypoglycaemia, and hypoglycaemia can lead to increased frailty.
2. Severe hypoglycaemic events that require assistance from someone else can increase the risk of confusion and increase the risk of falls and fractures, or premature death.
3. Completing regular medication reviews in older people with diabetes who are frail is important to reduce the risk of hypoglycaemic events.

Key words

- Cognition
- Frailty
- Older people

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It is estimated that over half of all those living with diabetes are over 65 years of age. Diabetes management becomes increasingly complex as people age, and clinicians and people with diabetes can find it difficult to balance treatment benefits and risks. With increasing age, there is an increasing risk of dementia and frailty in people with diabetes, which impact on appropriate drug regimens. In this article, the authors recommend strategies for reducing the risk of hypoglycaemia in older people who are frail and have cognitive impairment or dementia.

Type 2 diabetes is one of the most common chronic conditions in older adults, and the number of people over the age of 70 with diabetes is growing worldwide. For example, of the 2.6 million people in the UK with diabetes, at least half are over 65 years old (Diabetes UK, 2010). The prevalence of diabetes in the adult general population is 4.1%, whereas it is more than 10% among people over the age of 65 years (Diabetes UK, 2010). The prevalence approaches 25% in care home residents, who represent people who may require more care and management of comorbidities (Sinclair et al, 2001).

Frailty

Frailty is a condition characterised by reduction in physiological reserve and ability to resist physical or physiological stressors. Frailty is defined based on the presence of three or more of the following: weight loss, weakness, decreased physical activity, exhaustion and slow gait speed. People with diabetes aged 65 and over are more likely to be frail than older adults without diabetes (Abdelhafiz et al, 2015). Around 11% of people with diabetes over the age of 65 are classified as frail (Abdelhafiz et al, 2015).

The biological processes that underlie frailty are still unclear and are likely to be complex and multifactorial. However, sarcopaenia is known to be a central component of frailty, and is more common in people with diabetes than people without diabetes (Jang, 2016). The relationship between frailty and hypoglycaemia is likely to be bi-directional (Abdelhafiz et al, 2015). Hypoglycaemia can lead to

frailty, and frailty is a risk factor for hypoglycaemia in older people with diabetes.

There are various indexes and scales to classify and diagnose frailty (e.g. the Clinical Frailty Scale or CHSA 9-point Scale). The simple FRAIL scale (*Box 1*) is quick to complete and seems to be as sensitive and specific as other scales (Abdelhafiz, 2015). Some authorities recommend that it be used to screen all people over the age of 70 years for frailty.

Glycaemic targets for older people

Many guidelines on the management of type 2 diabetes do not provide specific guidance for older people; however, the International Diabetes Federation (IDF) produced a global guideline in 2013, solely for the management of people with

Box 1. The FRAIL Scale.

- F**atigue: Are you fatigued?
- R**esistance: Can you walk up a flight of stairs?
- A**mbulation: Can you walk a block?
- I**llness: Do you have more than five illnesses?
- L**oss: Have you lost 5% of your total weight in the last 6 months?

One point is given for every “yes” answer, no points are given for “no” answers. Total scores of 3–5 indicate a diagnosis of frailty, scores of 1–2 may indicate a pre-frail state, and a score of zero indicates no frailty at present.

Table 1. Metabolic targets based on functional category of older people with type 2 diabetes (International Diabetes Federation, 2013).

Category	Metabolic targets
1. Functionally independent New-onset diabetes, little comorbidity	<ul style="list-style-type: none"> ● HbA_{1c} target: 53–59 mmol/mol (7.0–7.5%).
2. Functionally dependent Established diabetes, impairment in performing activities of daily living.	<ul style="list-style-type: none"> ● HbA_{1c} target: 53–64 mmol/mol (7.0–8.0%). ● Drug regimens with a low hypoglycaemic risk are favoured. ● Avoid complex regimens and higher treatment burden to reduce the risk of medication errors.
Subcategory A Frailty	<ul style="list-style-type: none"> ● HbA_{1c} target: up to 70 mmol/mol (8.5%). ● Avoid or discontinue agents that might cause nausea or gastrointestinal disturbance or excess weight loss (e.g. metformin or a glucagon-like peptide-1 receptor agonist). ● Insulin may provide anabolic benefits.
Subcategory B Dementia	<ul style="list-style-type: none"> ● HbA_{1c} target: up to 70 mmol/mol (8.5%). ● Caregivers and/or family should be educated to recognize the subtle indicators of hypoglycaemia.
3. End of life Significant weight loss, short life expectancy less than one year.	<ul style="list-style-type: none"> ● The glycaemic target is to avoid symptomatic hyperglycaemia. ● Consider appropriate withdrawal of therapy, including insulin, during the terminal stage.

diabetes over the age of 70: *IDF Global Guideline for Managing Older People with Type 2 Diabetes*. The guideline recommends relaxing strict glycaemic control in the presence of comorbidities (such as functional dependency, dementia and frailty) to an HbA_{1c} up to 70 mmol/mol (8.5%; IDF, 2013). This is to reduce the risk of hypoglycaemia, which can lead to confusion and an increased risk of falls and fractures. Hypoglycaemic events can also lead to a higher risk of mortality following hospital admission, and some people may also experience permanent neurological damage. The guideline distinguishes several functional categories of older people with diabetes, and gives specific management recommendations for each category (Table 1). The NICE (2015) guideline on type 2 diabetes also recommends relaxation of glycaemic targets in the presence of frailty and dementia.

Hypoglycaemia in older people

The true prevalence of hypoglycaemia among older people is unknown. Most studies that have tried to address this question rely on the recall of hypoglycaemic episodes by participants. Accurate

recall of hypoglycaemia is notoriously difficult in any age group, and none more so than in an older population (Hope and Strain, 2013). For epidemiological purposes, “severe” hypoglycaemia is usually defined as that requiring external assistance for treatment. Episodes of severe hypoglycaemia can also be corroborated with documentary evidence from ambulance services, if the emergency services are required. The difficulties in accurate patient recall of hypoglycaemia episodes was addressed by a carefully designed prospective observational study over 9–12 months in the UK (UK Hypoglycaemia Study Group, 2007). Participants were required to return a data-collection sheet every time they experienced a severe hypoglycaemia episode.

Careful monitoring for hypoglycaemia is required during the treatment of diabetes with insulin and/or sulfonylureas, particularly in the older population. The UK Hypoglycaemia Study Group (2007) found that annual prevalence of sulfonylurea-associated severe hypoglycaemia was 7%, a prevalence similar to that observed in people with type 2 diabetes treated with insulin for <2 years. The prevalence of severe hypoglycaemia among people with type 2 diabetes

Page points

1. The International Diabetes Federation (IDF, 2013) guideline provides metabolic targets for older people based on their functional category.
2. The guideline recommends relaxing strict glycaemic control in the presence of comorbidities (such as functional dependency, dementia and frailty) to an HbA_{1c} up to 70 mmol/mol (8.5%).

Practical points

1. It is useful to check that older people with diabetes are aware of the symptoms of hypoglycaemia and know how to treat it.
2. The latest NICE (2015) guideline for type 2 diabetes recommends that drugs other than sulfonylurea can be used as monotherapy if metformin is contraindicated or not tolerated.
3. If appropriate, reducing polypharmacy should be considered among older people with diabetes.

who had received insulin treatment for >5 years was 25%, and it was 46% in those with long-standing type 1 diabetes (>15 years).

Older people may not experience the typical symptoms of hypoglycaemia, and may have a reduced awareness of the initial sympathetic symptoms (i.e. tremor, shaking, sweating) associated with developing hypoglycaemia. Hence, there is less time before the later symptoms of neuroglycopenia occur, such as confusion and decreased conscious level (Matyka et al, 1997). Neurological symptoms such as slurred speech, light-headedness and unsteadiness, in addition to the neuroglycopenic symptoms, tend to be more common in older people with hypoglycaemia than in younger people (Hepburn et al, 1993). These symptoms can be misattributed by people with diabetes or by healthcare professionals to other presentations common in older age. As such, hypoglycaemia in older people may present, for example, as “off legs”, infection, acute confusion, mini-stroke, stroke, fits, or even simply “ageing”. Therefore, it is useful to check that older patients are aware of the symptoms of hypoglycaemia and know how to treat it.

Hypoglycaemia, and the associated fear of hypoglycaemia, affects mental health, quality of life and often contributes to depression; depression itself can be a symptom of hypoglycaemia (Hope and Strain, 2013). The hypoglycaemia can also affect socialisation, activities of daily living, learning and self-care capacity (Barendse et al, 2012).

Treatment considerations

Older people are at an increased risk of adverse medicine-related events due to age-related changes in pharmacokinetics (especially renal elimination) and pharmacodynamics (increased sensitivity).

NICE (2015) guidelines recommend that metformin therapy is the initial monotherapy of choice in treating type 2 diabetes. However, the British National Formulary (BNF; 2009) advises caution in the use of metformin in people with renal impairment, heart failure, hepatic impairment or in those at risk of tissue hypoxia. Sulfonylurea therapy used to be the only first-line glucose-lowering option recommended (NICE, 2009), if metformin was contraindicated, and as older people with type 2 diabetes are more likely to have renal or hepatic impairment and

heart failure, sulfonylurea therapy among older people can be a fairly common occurrence. As a result, low HbA_{1c} in older people on sulfonylurea therapies can be common. A primary care survey of nearly 4000 patients with type 2 diabetes aged 70 years or older found that of those who were on insulin or sulfonylurea therapies, nearly 30% had an HbA_{1c} of 53 mmol/mol (<7.0%), and 12% had an HbA_{1c} of 48 mmol/mol (<6.5%; Hambling et al, 2016). The latest NICE (2015) guideline for type 2 diabetes now recommends that drugs other than sulfonylurea can be used as monotherapy if metformin is contraindicated or not tolerated.

Reducing polypharmacy may be considered among older people with diabetes, if appropriate. In a study of residents with diabetes in nursing homes in Coventry, 63 residents (84%) were being prescribed four or more medications (for diabetes and cardiovascular disease). A total of 15% were on sulfonylurea monotherapy and 24% were on metformin plus sulfonylurea (Gadsby et al, 2011). Regular medication review undertaken in this group has the potential to reduce costs, minimise adverse drug reactions and increase health gain.

Cognitive impairment and dementia

Individuals with dementia have a degree of cognitive impairment that has led to significant memory problems, a degree of disorientation or a change of personality, and an inability to self-care. Physically, they may be relatively well. Dementia is a chronic condition that is becoming ever more prevalent with the ageing population, and there is growing recognition that it may develop earlier in people with diabetes than people without diabetes (Sinclair et al, 2013). There also appears to be an increased risk of dementia in people who have had episodes of severe hypoglycaemia (Hope and Strain, 2013). In addition, people with dementia or cognitive impairment who have diabetes and are treated with insulin or sulfonylurea may be more likely to develop hypoglycaemia than those without dementia. This is often due to confusion following drug regimens and taking extra doses, or being given medications regularly by carers when the individual has not eaten. The relationship between dementia and diabetes, therefore, is also likely to be bi-directional (Yaffe et al, 2013).

Box 2. Case scenario.

Betty is 84-year-old woman and has had type 2 diabetes for 25 years. She is on metformin 1 g bd, gliclazide 80 mg bd and simvastatin 40 mg once daily. She has no known diabetes complications. She has generalised osteoarthritis for which she takes up to two paracetamol 500 mg tablets four times a day. She is widowed and lives independently in a council flat. She does her own cooking and does not receive supplementary meals at home. However, she is finding it increasingly difficult to do her shopping because of unsteadiness, and she admits that she is losing her short-term memory. Her neighbour supports her by visiting for a cup of tea and chat most mornings.

Her neighbour takes her to her diabetes annual review. Her weight is 53 kg (BMI 23 kg/m²) and her blood pressure is 130/80 mmHg. She has no microalbuminuria and her estimated glomerular filtration rate is 60 mL/min/1.73 m². Her total cholesterol is 4 mmol/L and her HbA_{1c} is 48 mmol/mol (6.5%). Betty says that she manages to look after herself with the help of her neighbour.

Her practice diabetes nurse and GP are delighted with all her results, which show that the diabetes and all risk factors for

complications are very well controlled. She is advised to continue with all her medications and come again for review in 12 months.

Three months later

Betty is found by her neighbour on the floor when she calls in for her morning visit. She appears to have fallen out of bed. An emergency ambulance is called and a glucose reading of 2 mmol/L recorded, which is agreed to be the likely cause of the fall. She is given intravenous glucose and taken into hospital, where her gliclazide was stopped.

Following discharge to primary care, Betty receives a FRAIL score of 4, and is categorised as functionally dependent following the International Diabetes Federation (2013) guidelines.

Actions

- Healthcare staff were delighted with her results. Do you think her results were “good” in the context of her overall health?
- Would you have diagnosed her frailty and increased risk of hypoglycaemia at her diabetes annual review?
- Should her gliclazide have been stopped at her annual review?

Screening for cognitive impairment in primary care using a simple, quick test, such as the Mini Cog test, has been shown to be a practical and appropriate cognitive screen for older people with diabetes. The Mini Cog test can be easily integrated into the annual diabetes review of older people to help identify those who may benefit from extra assistance with their management.

Practical action points

- Stop sulfonylurea therapy in an older person with a low HbA_{1c} (<53 mmol/mol [7.0%]) and review with a further HbA_{1c} test in 3–6 months. If additional glucose-lowering therapy is felt to be necessary, consider using an agent with a low propensity to cause hypoglycaemia, such as a dipeptidyl-peptidase-4 inhibitor at appropriate dose for renal function.

- Review agreed glycaemic control targets and see if in the presence of comorbidities a higher HbA_{1c} target should be used in line with IDF (2013) guidelines.
- Exempt the older person from the Quality and Outcomes Framework glycaemic target clinical indicator (in England, Wales and Northern Ireland).
- Consider screening for frailty (e.g. FRAIL Scale) and cognitive impairment (e.g. Mini Cog) at the diabetes annual review for all people aged 70 years and over.
- Consider the case scenario in *Box 2*. Is this a familiar scenario? What would you do?

Conclusion

Hypoglycaemia (both mild and severe) is a significant problem in older people with type 2 diabetes on

Quick guide

- **Mild cognitive impairment:** Cognitive impairment is when a person has trouble remembering, learning new things, concentrating, or making decisions that affect their everyday life. Cognitive impairment ranges from mild to severe.
- **Dementia:** A chronic or persistent disorder of the mental processes caused by brain disease or injury and marked by memory disorders, personality changes, and impaired reasoning.
- **Tests for cognition in primary care:** e.g. Mini Cog, Mini Mental State

“It is good practice to review all frail, older people and those with dementia who have type 2 diabetes to consider whether they may be over-treated and to stop sulfonylurea therapy if hypoglycaemia is felt to be a significant risk.”

sulfonylurea or insulin therapy. It increases risks of falls, fractures, hospitalisation and death, but as hypoglycaemia in older people can be difficult to recognise, it needs a high index of suspicion. Many with HbA_{1c} levels indicative of “good” control may be at significant risk. It is good practice to review all frail, older people and those with dementia who have type 2 diabetes to consider whether they may be over-treated and to stop sulfonylurea therapy if hypoglycaemia is felt to be a significant risk. ■

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