Frailty and hypoglycaemia in older people with type 2 diabetes: Therapeutic implications

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Older people with diabetes are a heterogeneous population who experience varying degrees of functional level ranging from a fit individual living independently in the community to a fully dependent person residing in a care home. Diabetes management strategies are often based on evidence from studies of younger people, which may be inappropriate or underestimate the risk of hypoglycaemia in older age. Therefore, therapeutic interventions must be individualised and functional status should be considered as a key modulator for goal setting rather than HbA_{1c} level.

What is frailty?

Frailty is regarded as a wasting disease, with weight loss, due to under nutrition, sitting at the heart of its criteria. Poor oral health among older people with diabetes, such as bad dentition, dry mouth, altered taste sensation, reduced palatability and appetite change are all associated with a suboptimal nutritional state contributing, in combination with multiple comorbidities, to malnutrition and the progression towards frailty (Rizvi, 2009). Sarcopenia or muscle mass loss is another component of frailty and is accelerated by the presence of diabetes.

The weight loss associated with frailty may increase insulin sensitivity and improve glucose tolerance due to the loss of visceral fat. Therefore, with the emergence of frailty, the dynamics of insulin and glucose may shift in a direction that improves insulin sensitivity and reduces hyperglycaemia. Chronic diseases associated with protein energy malnutrition, muscle wasting and frailty have been shown to be associated with spontaneous resolution of hyperglycaemia and normalisation of HbA_{1c} levels, a condition termed "burnt out diabetes" (Kovesdy et al, 2010). Therefore, the emergence of frailty may change the natural history of type 2 diabetes from a progressive to a regressive course, increasing the risk of hypoglycaemia if glucose-lowering medication is not reviewed.

Frailty and hypoglycaemia

Frailty and hypoglycaemia have a bidirectional relationship. Recurrent undetected hypoglycaemic events due to impaired autonomic response are common in older people with diabetes and may lead to cognitive impairment, physical dysfunction and frailty. In turn, frailty is associated with increased risk of hypoglycaemia mainly due to significant weight loss, even among individuals who are not taking hypoglycaemic medications. The increase in mortality observed in the ACCORD and ADVANCE studies was not directly explained by the high rate of hypoglycaemia but were due to the vulnerability of the populations who suffered from such events (Bonds et al, 2010; Zoungas et al, 2010). Hypoglycaemia in old age, therefore, appears to be a marker of vulnerability and frailty rather than a direct cause of adverse events. Studies that showed an increased risk of mortality in people with low HbA_{1c} have revealed evidence of inflammation, such as elevated ferritin levels and evidence of malnutrition (e.g. low cholesterol and low serum albumin), in these population, which suggests poor general health and underlying frailty (Abdelhafiz et al, 2014). Therefore, it is appropriate to consider low HbA_{1c} in certain older people, especially those with recurrent hypoglycaemia, as a biochemical marker of frailty and a surrogate marker of "burnt out diabetes", rather than a direct cause of adverse outcomes.

Therapeutic implications of frailty

The management of older people with diabetes should be individualised taking into consideration individuals' functional level and the presence or absence of frailty. General health of the individual should be measured by the overall functional state,

Table 1. Metabolic targets based on functional category of older people with type 2 diabetes.

Category	Metabolic targets
Functionally independent New-onset diabetes, little comorbidity	**Tight** ● Similar to younger-age glycaemic target. ● HbA_{1c} target: 53 mmol/mol (7.0%).
Functionally dependent Established diabetes, impairment in performing activities of daily living	**Relaxed** ● Emphasis on patient safety, diminished self-care ability and there is a focus on maintaining self-autonomy. ● HbA_{1c} target: 58–64 mmol/mol (7.5–8.0%).

Frail
Significant weight loss, short life expectancy less than one year
	Symptomatic
	● Emphasis on patient comfort.
	● Short-term targets of daily blood glucose (>4 mmol/L but <15 mmol/L) are more relevant than long-term HbA_{1c} due to the limited life expectancy.
	● If appropriate, HbA_{1c} target: 64–75 mmol/mol (8.0–9.0%).
	● Consider medications withdrawal if:
	  ● Significant weight loss.
	  ● Recurrent hypoglycaemia.
	  ● Low HbA_{1c}.
	  ● Dementia with erratic eating pattern leading to hypoglycaemia.

which ultimately determines life expectancy, rather than by individual diseases or chronological age. Treatment targets should aim at maintaining the highest degree of self-autonomy and quality of life, and there are three broad functional categories that can be used to set goals (*Table 1*). Targets for frail older people should focus on short-term, day-to-day blood glucose control to avoid symptomatic hyper- or hypoglycaemia, which may lead to recurrent hospitalisation and poor quality of life. Keeping blood glucose in a "comfort zone" of 4–15 mmol/L may ensure "comfort care" – avoiding extreme blood glucose levels to occur to maintain mental function and general well-being. Being frail with significant weight loss and malnutrition may lead to a vicious circle of increased risk of hypoglycaemia and worsening frailty. Therefore, these high-risk individuals with significant weight loss and frailty should be recognised by healthcare professionals and have their hypoglycaemic medications reviewed, either to reduce dosage or consider withdrawal. Possible indicators for successful withdrawal of hypoglycaemic medications include the presence of multiple comorbidities and frailty phenotypes such as significant weight loss, reduced physical activity, slow gait speed, muscle weakness and exhaustion. The development of dementia can also increase the risk of hypoglycaemia due to erratic eating pattern.

Conclusion

Healthcare professionals who care for older people with type 2 diabetes should be vigilant in identifying those who are frail. Recurrent hypoglycaemic episodes and significant weight loss in frail older people should not be overlooked as these factors are associated with adverse outcomes. Glycaemic targets based on the overall functional state in older age are more practical than following the targets for younger population. Therefore, it is sensible that hypoglycaemic medication is reduced or even stopped in frail older people if clinically indicated. ■

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"Glycaemic targets based on the overall functional state in older age are more practical than following the standard glycaemic targets for younger population."