Frailty and Disability in Diabetes

Sol-Ji Yoon¹, Kwang-il Kim²,³

¹Department of Internal Medicine, Kangwon National University Hospital, Chuncheon, Korea
²Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Korea
³Department of Internal Medicine, Seoul National University College of Medicine, Seoul, Korea

INTRODUCTION

Diabetes is a serious health condition for older adults that has an increasing clinical significance in aged societies. More than 25% of Korean adults over 60 years of age have diabetes mellitus, and approximately 50% of older adults have impaired fasting glucose levels. Diabetes is associated with complications including cardiovascular disease, retinopathy, renal failure, and peripheral vascular disease. The occurrence of microvascular or macrovascular diabetic complications increases significantly after 10 years of disease duration. These complications are related to functional decline, disability, and loss of quality of life. Among older adults with diabetes, geriatric syndrome, especially frailty, is emerging as a third category of complications in addition to the traditional microvascular or macrovascular diseases leading to considerable disability. Understanding the pathway from diabetes to frailty and/or disability is important for establishing early intervention and prevention strategies. This review discusses the relationship between frailty, disability, and diabetes among older adults.

FRAILTY AND DISABILITY IN OLDER DIABETIC PATIENTS

In recent years, frailty has emerged as an independent predictor associated with increased risks of adverse outcomes among older adults, irrespective of their associated comorbidities. Frailty is a state of decreased reserve and resistance to stressors resulting from cumulative declines across multiple physiologic systems with aging, which leads to vulnerability to adverse outcomes such as death, hospital admission, permanent institutionalization, falls, and additional disability. While disability is hard to reverse, frailty is a dynamic process with a wide range of interventions to reduce vulnerability. Fried et al. established a framework of the frailty phenotype in which three or more of the following criteria were present: unintentional weight loss, self-reported exhaustion, muscle weakness, slow walking speed, and low physical disability. The presence of one or two phenotype criteria describes a pre-frail state while the absence of any positive criteria describes a robust state. Another definition of frailty is the frailty index proposed by Rockwood and colleagues. In this concept, Frailty is recognized as an accumulation of deficit during aging (symptoms, diseases, condit-
Furthermore, the increased risk of sarcopenia, which is linked to frailty, is likely due to the increased risk of sarcopenia, which is linked to frailty. Hyperglycemia is associated with increased insulin resistance, chronic inflammation, oxidative stress, and mitochondrial dysfunction, all of which have deleterious effects on skeletal muscle mass and function, leading to sarcopenia. 

Because frailty might be caused by the accumulation of subclinical damage in multiple organ systems, diabetic complications may also lead to frailty. A Japanese cross-sectional study of 9,695 participants showed a significantly increased risk of frailty among individuals with a history of diabetes and lower kidney function (odds ratio = 2.76, 95% confidence interval [CI], 1.21–8.24). Among diabetic complications, autonomic neuropathy can cause orthostatic hypotension, arrhythmia, syncope, diarrhea, and bladder dysfunction. It may also result in the absence of typical hypoglycemic symptoms such as sweating, tachycardia, and tremors. It is also related to adverse events such as falls, malnutrition, and urinary incontinence and eventually leads to frailty. Frailty is also associated with adverse events such as falls, malnutrition, and urinary incontinence and eventually leads to frailty. Frailty is also associated with insulin resistance in the post-absorptive state of glucose metabolism in the presence of increased abdominal fat. A Canadian study showed lower insulin sensitivity in the frail-obese group than in the frail-lean group but observed no significant differences among the healthy, non-obese and frail-obese or frail-lean groups. Frailty is a major factor associated with an increased risk of death and disability in older adults with diabetes. Among 1,825 participants aged ≥65 years in the Toledo Study of Healthy Aging (TSHA) cohort study, individuals with diabetes died more frequently than those without diabetes (hazard ratio = 1.36; 95% CI, 1.06–1.75; p = 0.002), showing a poorer functional status at baseline. The hazard ratios for death were 1.51 (95% CI, 1.28–1.77) and 1.83 (95% CI, 1.49–2.26) for each 10-point increase in Frailty Trait Score and Frailty Index, respectively. An observational study of clinic patients with diabetes mellitus aged 50–90 years reported that participants with frailty were more likely to have new activities of daily living disability at the 6-month follow-up. Accordingly, previous evidence confirmed the close relationship between diabetes and frailty and the adverse effect of frailty on clinical outcomes among older patients with diabetes. Older adults with diabetes and frailty may experience multiple medical conditions and be trapped in vicious cycles, which lead to further functional decline. Thus, preventive approaches in older patients with frailty and diabetes are important for maintaining their healthy lifestyles.

COMMON PROBLEMS AMONG DIABETIC PATIENTS WITH FRAILTY OR DISABILITY

Hypoglycemia
Older adults with frailty have an increased risk of hypoglycemia as most of these individuals have problems with loss of appetite and weight loss. Recurrent hypoglycemia is common in older patients with diabetes but is less likely to be recognized and, thus, is under-reported by patients and healthcare professionals. The lack of recognition is mainly due to the predominance of neurological symptoms (dizziness or visual disturbance) rather than autonomic symptoms (palpitation, sweating, anxiety, and nausea) associated with hypoglycemia among older adults as the autonomic symptoms are decreased and counter-regulatory responses to hypoglycemia are reduced in older people. Severe hypoglycemia often leads to hospitalization in older adults, which could lead to the deterioration of a patient’s general condition and, eventually, frailty and disability. Repeated hypoglycemia is likely to result in frailty, disability, and poor health outcomes.

Falls
Falls are a common problem in older adults with frailty. A Japanese study showed that lower walking speed, one of the manifestations of frailty, was associated with falls in patients with type 2 diabetes. The risk factors for falls among patients with diabetes include polypharmacy, muscle weakness, previous stroke, motor and sensory neuropathy, poor glycemic control, hypoglycemia, insulin use,
Sarcopenia
Patients who have diabetes mellitus, particularly when associated with renal failure, show an accelerated loss of muscle function. Sarcopenia is an age-related decline in muscle function and mass. Sarcopenia is associated with increased disability and mortality and most likely forms the basis of frailty in patients with type 2 diabetes.

PREVENTION AND MANAGEMENT OF FRAILTY AMONG DIABETIC PATIENTS

Diabetes management may require assessments in the medical, psychological, functional, and social domains. In addition to the classic cardiovascular and microvascular disease, older adults with diabetes and frailty should be assessed for a group of conditions termed geriatric syndrome, which includes cognitive dysfunction, functional impairment, falls/fractures, polypharmacy, depression, vision and hearing impairment, urinary incontinence, and nutritional problems. This comprehensive medical evaluation may provide a framework to determine targets and therapeutic approaches and to identify individuals with significantly impaired functional status such as visual and lower-extremity complications or cognitive impairment, which may impact their ability to self-manage their diabetes.

Diabetes management strategies for robust older adults with diabetes are similar to those for younger adults. However, older adults with frailty should be provided individualized risk-minimization care plans according to the functional status and life expectancy. The American Geriatric Society suggests a glycosylated hemoglobin (HbA1c) target of 7.5%–8.0% for older adults. However, glycemic control targets may vary depending on the patient’s frailty status. An HbA1c target of 7.0%–7.5% is suitable for functionally independent older adults with a reasonable life expectancy, while a target of 8%–9% is appropriate for older adults with frailty and those with dementia and a life expectancy of fewer than 10 years.

Sulfonylurea or insulin, which can increase the incidence of hypoglycemia, should be used with care in dependent patients with frailty and cognitive impairment. Glimepiride has a long half-life and can result in severe and prolonged hypoglycemia. If sulfonylureas are used, short-acting agents such as glipizide or gliclazide are preferred.

Metformin can be a first-line choice of treatment in older patients with diabetes and frailty. Patients with frailty should be monitored carefully for weight loss and gastrointestinal side effects. Thiazolidinedione should be used with care in patients with congestive heart failure and those at risk for falls or fractures. Dipeptidyl peptidase 4 (DPP-4) inhibitors are effective and reasonably safe in older adults. Because glucagon-like peptide 1-receptor agonists may be associated with gastrointestinal side effects and weight loss, they may not be desirable in underweight individuals with frailty. As only injectable forms are available, they should also be considered only when caregiver support is available. While sodium-glucose cotransporter 2 inhibitors appear to be well-tolerated by older adults, long-term data are scarce. In addition, sodium-glucose transport protein 2 (SGLT2) inhibitors act as osmotic diuretics and are associated with weight loss as well as reduced blood pressure. Accordingly, these agents should be used with caution in older patients treated with antihypertensive agents, especially diuretics.

Diabetes nutritional therapy may have a protective effect against the development of frailty. Many older people lack adequate nutritional intake particularly that of protein, while also requiring increased dietary protein intake to compensate for age-related anabolic resistance. Older adults are recommended to consume 1.0–1.2 g protein per kg of body weight per day to maintain and regain lean body mass and function. Optimal nutrition with adequate protein intake combined with exercise programs, including aerobic and resistance training, could reduce the risks of sarcopenia and frailty. Treatment of diabetic autonomic neuropathy in older adults is complex because of their poor tolerability to many pharmacologic treatment options. It is essential to search for the secondary causes and decrease the intake of medications that may contribute to the patient’s symptoms. Lifestyle interventions such as diet alteration may help to reduce the need for pharmacologic treatments and their associated risks of adverse effects.
CONCLUSION

Diabetes is frequently accompanied by frailty and they share pathways leading to disability, morbidity, and mortality in older adults. Early recognition of frailty in older diabetic patients allows comprehensive multi-component interventions including physical exercise, nutritional support, and medication adjustment. Moreover, better strategies can be established for diabetes management, including setting glycemic goals, selecting anti-diabetic agents, and implementing other preventative interventions. Identification of the common mechanisms and the development of new therapeutic interventions are needed to meet the increasing demand for the management of older diabetic patients due to population aging.

CONFLICT OF INTEREST DISCLOSURES

The researchers claim no conflicts of interest.

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