

Review

Management of Older People With Diabetes - A Focus On Mental Functions

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Abstract

The prevalence of diabetes in older people is increasing. Diabetes in old age is associated with increased risk of mental dysfunction. Cognitive dysfunction and mood disorders such as depression, anxiety and diabetes-related distress tend to coexist in older people with diabetes and appear to have bidirectional relationship acting as a risk factor and, at the same time, as a consequence of diabetes. To break the vicious circle of this complex reciprocal relationship between diabetes and mental dysfunction, early identification and treatment is important. Healthy lifestyle, appropriate glycaemic control, hypoglycaemia risk reduction and an organised and a holistic care is appropriate. Therefore, health care professionals involved in the care of older people with diabetes should be aware of this associated mental dysfunction and a collaborative care approach that includes integrated care of both physical and mental health is required.

Keywords

Diabetes; older people; cognitive dysfunction; depression; management



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1. Introduction

With increasing ageing of the population and increased life expectancy, the prevalence of diabetes in older people is likely to increase. In 2017, the global prevalence of diabetes mellitus was 8.4% of the total population and is expected to reach around 10% in 2045 [1]. Almost half of the population with diabetes are >65 years old and the highest peak (22%) occurs at the age of 75-79 years [1]. In care homes, the prevalence of diabetes is even higher and affects around one third of residents [2]. In old age, diabetes is associated with multiple comorbidities and increased prevalence of geriatric syndromes including mental disorders mainly cognitive and mood dysfunctions. Cognitive dysfunction ranges from cognitive decline, mild cognitive impairment (MCI) to dementia and mood disorders include depression, anxiety and diabetes-related distress [3-6]. Unlike other chronic conditions, diabetes care is dependent upon patient ability to perform selfcare tasks and older people with diabetes and comorbid mood disorders are likely to be lethargic, physically inactive and less compliant with self-care responsibilities resulting in long-term complications [7]. Equally important, cognitive dysfunction especially in the executive domains may interfere with diabetes self-care management and may lead to a poor glycaemic control. In addition, with the progression of dementia and the development behavioural abnormalities, diabetes management will represent a unique challenge for health care professionals [8]. Therefore, early recognition of the presence of mental disorders in older people with diabetes may lead to better outcomes. Individually tailored strategies that accommodate and adjust to the patients' cognitive abilities and mood changes to optimise their capacity for self-care will be required for older people with comorbid diabetes and mental dysfunction. This manuscript reviews the association and the impact of mental dysfunction on older people with diabetes and explores the management challenges in this group of complex patients.

2. Diabetes and Cognitive Dysfunction

In the US, dementia affects up to 16% of older people with diabetes aged ≥65 years and 24% of those aged ≥75 years [9, 10]. In France, the prevalence of cognitive impairment among older people (aged 75-79 years) with diabetes is around 29% [11]. In the UK, 56% of older people with diabetes living in care homes were found to have some form of dementia [12]. Diabetes increases the risk of vascular type dementia through persistent hyperglycaemia that increases the risk of cerebrovascular disease by inducing inflammation, endothelial dysfunction, oxidative stress and insulin resistance [13]. On the other hand, diabetes increases the risk of Alzheimer's type dementia through accelerated brain ageing due to altered amyloid metabolism, increased protein glycation and direct cerebral glucotoxicity [14]. Repeated episodes of severe hypoglycaemia, which is common in older people with diabetes, may also play a role in increasing the risk of cognitive dysfunction through direct brain cell damage [15]. It appears that diabetes increases the risk of dementia by about 2-fold. In persons with diabetes, it has been shown that the relative risk (RR) of Alzheimer's disease is 1.56 {95% confidence interval (CI) 1.41 to 1.73}, vascular dementia is 2.27 (1.94 to 2.66) and all types of dementia is 1.73 (1.65 to 1.82) compared to those without diabetes [16]. Diabetes increases the risk of MCI and the proportion of patients progressing from MCI to dementia is 1.5-3 times higher in patients with diabetes compared to those without [17, 18]. Pre-diabetes is also a risk factor for cognitive decline. In the Atherosclerosis Risk In Communities (ARIC) Study, which included 13,351 participants, aged 48-67 years at entry, diabetes in midlife was associated with a significant 19% greater decline in cognition than in those without diabetes after 20 years of follow up. Cognitive decline was significantly greater among persons with pre-diabetes {defined as HbA1c 38.8-46.4 mmol/mol (5.7-6.4%)} than those without diabetes and HbA1c 38.8 mmol/mol (<5.7%). Participants with poorly controlled {HbA1c≥ 53.0 mmol/mol (>7.0%)} or longer duration (>9 years) of diabetes had a larger decline compared to those with controlled {HbA1c<53.0 mmol/mol (7.0%)} or shorter duration (<3 years) of diabetes (p=0.071 and <0.001 respectively) [19].

3. Diabetes and Mood Disorders

Diabetes increases the risk of mood disorders. The prevalence of depression in persons with diabetes varies by the method of assessment. For example, rates for depressive symptoms range from 12–27%, while rates of depressive disorders, as assessed by psychiatric interview protocols, range from 8-15% in people with diabetes [7]. Structural and functional changes in the brain regions responsible for the mood occur in persons with diabetes and increase the risk of depression [20]. Hyperglycaemia reduces hippocampal neurogenesis and neuroplasticity leading to hippocampal atrophy contributing to mood symptoms [21]. Also, the burden of diabetes treatment and diabetes-related complications may lead to a sense of helplessness and hopelessness that may increase the risk of depression [22]. In the Health, Ageing, and Body Composition Study, older people (70-79 years old) with diabetes showed increased incidence of depression compared to persons without diabetes {23.5% vs 19.0%, hazard ratio (HR) 1.31, 95% CI 1.07 to 1.61 [23]. In a meta-analysis of 16 studies to examine the risk of depression associated with diabetes, both RR and HR were significant at 1.27 (95 % CI 1.17 to 1.38) and 1.23 (1.08 to 1.40) for incident depression associated with diabetes mellitus [6]. In a US study, the life time prevalence of anxiety was significantly higher (19.5%) in people with diabetes compared to those without diabetes (10.9%) [24]. A meta-analysis has shown that diabetes is associated with an increased prevalence of anxiety symptoms [25]. Anxiety and depression commonly coexist in persons with diabetes. In the Canadian community health survey, diabetes was associated with a greater likelihood of comorbid depression and anxiety {Odds ratio (OR) 1.99, 95% CI 1.22 to 3.25, p=0.006} [26]. Diabetes related-distress is a reflection of patients' worries, fears and concerns regarding the chronic and progressive burden of diabetes self-care, threats of complications and potential loss of function [27]. It is distinctive from depressive symptoms but reflects the emotional response to a demanding and complicated health-related condition. Diabetes relateddistress is linked to diabetes stressors and is viewed as part of diabetes spectrum rather than as a separate psychiatric condition [28]. It includes frustration with difficulties of self-care, family members or carers that may lead to increasing distress.

4. Diabetes-Cognition-Mood Interaction

The relationship between diabetes, cognitive dysfunction and mood disorders appears to be bidirectional. Diabetes, cognitive dysfunction and mood disorders commonly coexist and the presence of one illness increases the risk of the other. (Figure 1) It has been shown that history of cognitive dysfunction to be associated with future development of diabetes. Participants with the lowest general intelligence score (GIS) had a 2-fold greater risk for incident diabetes compared to

those with the highest GIS (HR 2.1, 95% CI 1.5 to 3.1, P < 0.001) [29]. The brain-derived neurotropic factor (BDNF) which is a growth factor that promotes brain functions and has antidiabetes effects, has been found to be low in persons affected by both diabetes and dementia compared to control subjects. The progressive reduction of BDNF levels correlated with the progressive decline in cognitive function and the presence of comorbid dementia and diabetes had the lowest levels of BDNF suggesting a pathogenic link between diabetes and dementia and a synergistic effect of both diseases on BDNF levels [30]. Depression also increases the risk of diabetes. In a prospective study of 4,803 community adults aged \geq 55 years, the incidence rate of diabetes was higher among depressed (19.70 per 1,000 person-years) relative to non-depressed subjects (12.36 per 1,000 person-years) independent of potential confounders including diabetes risk factors. The estimated rate of diabetes mellitus attributable to depression was 6.87%. An increased risk of diabetes mellitus was also associated with depression characteristics such as nonsevere depression, persistent depression and untreated depression [31]. Depressive symptoms have been shown to increase the risk of all types of dementia [32]. Late-life depression is associated with an increased risk of dementia and depression itself may be an early manifestation of cognitive decline [33]. On the other hand, the Survey of Health Ageing and Retirement in Europe (SHARE) study has demonstrated that lower memory performance at a given age predicted subsequent 2-year increase in depressive symptoms. For each 1-point decrement on a 10-point memory scale there was a 14.5% increased risk of depression two years later [34]. These bidirectional relations may be due to a shared common pathogenic pathway that includes insulin resistance, persistent hyperglycaemia, repeated episodes of hypoglycaemia, mitochondrial dysfunction, oxidative stress, advanced glycation end products, reduced cerebral amyloid clearance, diabetes-related complications and vascular disease [35, 36].



Figure 1 Interaction between diabetes, cognitive dysfunction and mood disorders. Diabetes and mental dysfunction appear to share common risk factors and have reciprocal relationships. AGE=Advanced glycation end products.

5. Diabetes-Cognition-Mood Consequences

The interaction between diabetes, cognitive dysfunction and mood disorders may lead to impaired self-care tasks and increased risk of hypoglycaemia and frailty, which may set a vicious circle of worsening diabetes control and eventually accelerate the path to disability [37]. Good cognitive and mood functions are required to execute self-care tasks, achieve good glycaemic control and avoid acute and long-term complications of diabetes. Cognitive dysfunction, especially impaired executive function will lead to less compliance with the prescribed regimens, erratic eating pattern and increased risk of weight loss and malnutrition. It has been shown that cognitive dysfunction is associated with significant difficulty in adherence to diet and exercise in a cohort of 1,398 persons with diabetes aged ≥60 years of age [38]. Diabetes knowledge, insulin dose adjustment, insulin injection skills, medications adherence, self-care activity and glucose monitoring were also impaired in persons with comorbid diabetes and impaired global cognition especially executive function and these impairments were exacerbated by increasing age [39]. Cognitive impairment also increases the risk of hypoglycaemia possibly due to erratic eating pattern, medication errors and weight loss. The risk of hypoglycaemia increased 3-fold in persons with comorbid diabetes and dementia compared to those with diabetes alone (HR 3.1, 95% CI 1.5 to 6.6) [40]. The risk of hypoglycaemia increases proportionally with the severity of dementia [41]. Dementia in older people with diabetes also increases the risk of frailty and both appear to share a common pathogenic pathway that includes increased oxidative stress, impaired repair and unhealthy life style [42]. The new term "cognitive frailty" has been recently introduced by an international consensus group to describe the simultaneous presence of cognitive impairment and physical frailty highlighting the link between both conditions [43]. The comorbid diabetes and depression increases the risk of physical dysfunction. In a prospective Canadian study of 1,064 older people with diabetes, mean (SD) age 59.2 (10.5) years, the risk of poor function and reduced quality of life was about three times higher (RR 2.86) for participants with four subthreshold depressive episodes compared with participants with no or minimal depression over 5 years follow up [44]. Comorbid diabetes and depression also increases the risk of mortality especially in older people. In the Nurses Health Study of 7,000 women (age range 54-79), the relative risk for all-cause and cardiovascular mortality was 1.76, 1.81 for patients with depression alone, 1.71, 2.67 for those with diabetes alone and 3.11, 5.38 for comorbid diabetes and depression [45]. In a survival analysis, mortality risk in persons ≥65 years with diabetes and depression was 78% greater than in those with diabetes alone. In contrast, for those <65 years old, the effect of depression on mortality was smaller and not statistically significant [46].

6. Management

Management of older people with comorbid diabetes and either cognitive dysfunction or mood disorders or both is complex and presents a challenge to health care professionals. Management should include regular screening for mental dysfunction, healthy lifestyle, appropriate glycaemic control, reduction of hypoglycaemia and organised holistic care to maintain autonomy, delay the progression into disability and improve quality of life. (Table 1)

Table 1 Management of older people with comorbid diabetes and mental dysfunction.

Healthy life style

- Maintain physical activity
- Tai chi mind and body exercise
- Achieving ideal body weight
- High fibres low glycaemic diet

Glycaemic control

- Overall glycaemic control may improve cognitive function
- Stability of blood glucose and less variability of HbA1c may have a positive effect on cognition
- Glycaemic control may improve depressive symptoms

Reducing hypoglycaemia

- Medications with less hypoglycaemic potential should be firstly chosen
- Simplification of complicated insulin regimens
- Deintensification of medication as patient's function declines
- High calorific nutritional supplements in malnourished patients

Care delivery

- Flexible care that is sensitive to patient's changing mental function
- Shared protocols between primary and secondary care
- Staff training for various aspects of care for comorbid diabetes and mental dysfunction
- Integrated physical and mental health care

6.1 Screening

Screening for cognitive dysfunction or mood disorders should be part of annual review or earlier if non-adherence to self-care tasks occurs. Adherence to self-care tasks and compliance with diabetes regimens diminishes as cognitive dysfunction or mood disorders develops. Clinicians should be aware that dementia may be associated with language impairment, disorientation and personality changes, which may mimic the symptoms of hypoglycaemia [47]. Recurrent unexplained hypoglycaemia, new difficulties in handling insulin injections, forgetfulness of insulin doses or erratic eating pattern should trigger screening for mental dysfunction. (Table 2) Short screening tools are summarised in Table 3 [48-51].

Table 2 Triggers for early screening for mental dysfunction.

- Erratic eating pattern or missing meals
- Unexplained or recurrent hypoglycaemia
- Increased forgetfulness of recognising or self-treating of hypoglycaemia
- Non-compliance with medications, diet or self-care
- Reduced skills of handling insulin injections
- Reduced skills of adjusting insulin dosages
- Significant weight loss or weight gain
- Increased social isolation and reluctance to seek medical care
- Self-reporting symptoms of depressed mood, anxiety or distress
- Unexplained fatigue and lack of energy

Table 3 Short screening tools for mental dysfunction [48-51].

A. Cognitive dysfunction

Mini-Cog

Ask the patients to repeat three items such as key, lemon and balloon then provide a clock face and ask them to:

- Draw the numbers of the clock face
- Draw the hands of the clock to show time as ten to three
- Recall the three items

*Score: One mark for each task performed and for each item remembered, a score \leq 3/5 defines cognitive impairment

B. Mood disorders

Short screening tools can be used for rapid screening of mood disorders then detailed tests for those who score positive

Depression (PHQ-2)²⁶

Ask the patients whether they have:

- Little interest in doing things?
- Been feeling down, depressed or hopeless?

*Score: Any positive answer triggers assessment using the detailed (PHQ-9)

Anxiety (GAD-2) 82

Ask the patients whether, over last 2 weeks, they are:

- Feeling nervous, anxious or on edge?
- Not being able to stop or control worrying?

*Score: Give 0 for not at all, 1 for several days, 2 for >half the days, 3 for nearly every day, a score of \geq 3/6 defines anxiety

Distress (PAID-1)⁸³

• Whether patient is worrying about the future and the possibility of serious complications?

*Score: A positive answer suggests underlying diabetes- related emotional distress

6.2 Healthy Lifestyle

The Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) study has demonstrated a beneficial effect of exercise and nutrition on cognitive

function in older people with diabetes [52]. Structured aerobic or resistance training for a period of 12 weeks has been shown to promote several aspects of cognitive functions including improved attention and concentration in subjects with diabetes [53]. In the Look AHEAD (Action for Health in Diabetes) study of 5,145 participants with type 2 diabetes, mean (SD) age 58.7 (6.8) years equally randomised to intensive life style intervention (ILI) or usual care, ILI significantly reduced the incidence of depressive symptoms (HR 0.85, 95% CI 0.75 to 0.97, P=0.02) and preserved better function in the intervention group (P < 0.01) although it did not improve cognitive function [54, 55]. A recent meta-analysis to evaluate the efficacy of exercise or physical activity on cognition in adults with type 2 diabetes, did not demonstrate clear results and concluded that large-scale randomised trials are still required [56]. Tai chi, which involves a series of slowly, performed dance like postures may have a potential beneficial effects in improving general wellbeing and reducing depressive symptoms [57]. A Mediterranean diet rich in olive oil and fibres such as vegetables, fruits, beans and nuts combined with activity and stress management can improve several markers of wellness and ageing including cognitive function and reduce the risk of dementia [58]. Low glycaemic load breakfast has been shown to improve cognitive function in obese women with glucose intolerance [59]. Food and drinks rich in flavonoids may also reduce the risk of cognitive dysfunction with the lowest risk of incident cognitive disorders at a daily consumption level of 1-2 cups of coffee [60].

6.3 Glycaemic Control

Significant longitudinal associations between HbA1c levels and long-term cognitive decline have been recently reported in the English Longitudinal Study of Ageing [61]. This suggests that glycaemic control may improve cognitive function and reduce incident dementia. However, tight glycaemic control as demonstrated in the Action to Control Cardiovascular Risk in Diabetes Follow Up-Memory in Diabetes study (ACCORD-MIND) was not associated with better cognitive function [62]. This negative effect may be due to the fact that the ACCORD-MIND study was of relatively short duration (only 3.3 years), or tight glycaemic control achieved has led to recurrent episodes of hypoglycaemia which may cause frequent damage to the brain cells negating any beneficial effect of tightly controlled glycaemia on cognitive function. Other studies have shown a beneficial effect of long term and stable glycaemic control on cognitive function [63, 64]. Not only overall glycaemic control, but also daily fluctuations in blood glucose levels appear to be associated with increased risk of cognitive dysfunction. Instability of HbA1c or variability of blood glucose levels are associated with worse cognitive performance, increased mortality and grey matter atrophy in older people with diabetes suggesting that a stable glycaemic level in the middle range is associated with lower risks [65]. Glucose peaks over time of 21 years also appear to be associated with increased risk of dementia suggesting that targeting theses peaks, and not only the average glycaemia, may have a long-term positive effect on cognition [66]. Therefore, future studies are still needed to further investigate whether glycaemic control and stability of daily blood glucose levels would result in a reduction in the incidence of dementia. Poor glycaemic control is associated with increased prevalence of depressive symptoms [67]. Although, there is little literature on the effect of glycaemic control on depression, it has been recently reported that better glycaemic control may have a positive effect on depressive symptoms [68].

6.4 Reducing Hypoglycaemia

With increasing age, the neurological rather than the autonomic manifestations of hypoglycaemia predominate and may be confused with symptoms of dementia [47]. The risk of hypoglycaemia increases with deterioration of mental function therefore, anti-diabetic medications need to be regularly reviewed or adjusted as the patient' mental function progressively declines. For example, it has been shown that older people with comorbid diabetes and dementia are unnecessarily intensively treated with anti-diabetic medications that have high hypoglycaemic potential such as insulin and sulfonylureas [69]. Medications with less hypoglycaemic potential should be firstly chosen in these patients. Relaxing HbA1c targets in this group of patients may not be enough to reduce the risk of hypoglycaemia as continuous glucose monitoring has shown that asymptomatic hypoglycaemia is common regardless of HbA1c levels [70]. Monitoring of blood glucose has value in patients treated with insulin but not in those taking oral therapy [71]. However, it may be required in patients on oral therapy who suffer from mental dysfunction and have an erratic eating pattern. If insulin is used, once daily insulin analogues have less potential of hypoglycaemia. Short acting insulin analogues administered only after meal consumption in patients with irregular eating pattern may be a safe option to avoid hypoglycaemia if a meal is missed. Simplification of complicated insulin regimens to a once daily injection has been successful [72]. Deintensification or complete withdrawal of anti-diabetic therapy in patients with comorbid type 2 diabetes and dementia who have significant weight loss, tight glycaemic control (HbA1c <6.0%) and recurrent hypoglycaemia has been achieved in some of them without deterioration of their glycaemic control [73, 74]. Therefore, glycaemic control should be regularly monitored and anti-diabetic medications adjusted to avoid hypoglycaemia targets should be dynamic and suit patients changing mental functions and balance the benefits of glycaemic control with the increasing risks of hypoglycaemia as patients' functional level progressively declines. Older people with diabetes and mental dysfunction may have reduced nutritional intake, weight loss and increased risk of hypoglycaemia. Diminished hepatic glycogen storage due to anorexia predisposes patients to more severe episodes of hypoglycaemia. Therefore, besides reviewing the hypoglycaemic therapy, the addition of nutritional supplements with high calorie drinks may be useful to help reduce hypoglycaemia and replenish glycogen stores.

6.5 Care Delivery

A holistic multidisciplinary and collaborative care that integrates physical and mental health for older people with diabetes is ideal.

<u>Care Plans.</u> Care plans should reflect patients' stage of mental function. Patients should maintain their self-autonomy as possible but this should be adequately balanced with their safety. Therefore, periodic assessments is required to determine which self-care tasks patients can independently but safely perform and which tasks will need some or full assistance. Patients usually maintain their independence in performing some tasks even if they are dependent on carers in other areas. Carers themselves should be regularly assessed for their competence to care, as they are usually patients' spouses with changing cognitive and physical abilities. Educational programmes should also be suitable for patients and carers 'cognitive abilities. Care plans should be flexible and sensitive to the changing mental function and needs of these patients. Nutritional

guidelines should not be too restrictive but tailored to be healthy and to reflect personal preferences. Individuals are free to exercise personal choices with respect to food selection. Diabetes treatment is then adjusted accordingly.

<u>Care Setting.</u> Older people with comorbid diabetes and mental dysfunction are less likely to have their diabetes regularly monitored and they had an increased risk of diabetes complications that led to hospitalisations especially for life-threatening and preventable events [75]. Sharing care protocols between the primary and the secondary care may ensure adequate communications between the two settings, improve diabetes monitoring and may help reduce unnecessary visits to emergency department and hospital admissions. Also a partnership between patients, their carers and health care professionals is necessary. Health care system should be able to recognise the impact of mental dysfunction diagnosis on the management of diabetes, to organise services that allow long enough time for the clinical consultation for individualised care and develop good collaboration across specialities and organisations to improve quality of care of this complex group of patients [76].

<u>Care Training.</u> Increasing awareness of the links between diabetes and mental dysfunction may help in delivering adequate care [77]. Clinicians involved in the diabetes management will need to develop skills in the recognition and care for mental dysfunction when it develops. They need to acquire skills in early and timely screening. They also need to understand the relevant impact of mental dysfunction on diabetes management such as erratic eating patterns. On the other hand, clinicians involved in the mental dysfunction management for older people with comorbid diabetes need to be aware of the care-needs of these complex group of patients such as dietary requirements and blood glucose monitoring. They also need to be able to recognise and treat hypoglycaemic episodes. Formal training in the overall clinical aspects of diabetes and liaising with diabetes care team in issues relevant to reducing the risks of hypoglycaemia, hyperglycaemic crisis, falls, medications review and a focus on maintaining quality of life is required [78].

7. Conclusions

The global prevalence of comorbid diabetes and mental dysfunction is increasing. Cognitive dysfunction especially in the executive domains and depression will interfere with diabetes self-care. With the progression of mental dysfunction and the development of behavioural abnormalities, diabetes management will represent a unique challenge for health care professionals. Therefore, staff caring for these patients will need adequate training in the management of their complex needs. Care plans should be individualised according to patients' functional level and targets are gradually relaxed as the patient' function continue to deteriorate.

8. Key Points

- The prevalence of diabetes in older people is increasing due to ageing of the population.
- Diabetes in old age is associated with increased risk of mental dysfunction.
- There is a reciprocal relationship between diabetes, cognitive dysfunction and mood disorders.
- Mental dysfunction will have a negative impact on diabetes self-care.
- Integrated collaborative care that incorporates physical and mental health care professionals is required.

Author Contributions

Ahmed H Abdelhafiz was the sole author.

Competing Interests

The author has declared that no competing interests exist.

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