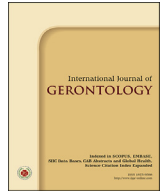




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Review Article

Blood Glucose Management of Type 2 Diabetes in the Older People[☆]Wei-Che Chen^{a,*}, Chun-Chua Lee^a, Ming-Nan Chien^a, Sung-Chen Liu^a,
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SUMMARY

With the increasing number of aged individuals in the population and the elevated prevalence of diabetes worldwide, there are more and older people with type 2 diabetes. Unfortunately, the management of diabetes in the elderly is not easy. Older people are heterogeneous. Hypoglycemia and hyperglycemia crises are more frequent and dangerous to older patients. Comorbidities, functional impairment and the available support system may influence the management of the disease. The target of glycemic control in the elderly should be based on individual conditions. Although the number of clinical trials relating to the management of type 2 diabetes in the elderly is limited, organizations have provided guidelines or statements about type 2 diabetes in the elderly. There are approved therapies or medicines for type 2 diabetes controls, but we should have more considerations for aged patients with type 2 diabetes.

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1. Introduction

By 2050, the proportion of older people in the population will increase from 15% to 25%.¹ The incidence of type 2 diabetes rises with aging. According to the Taiwan Nationwide Health Insurance database from 2000 to 2009², the diabetes prevalence rates were 21.97% for women aged 60–79 years and 23.97% for women aged 80 years and older. For men in the same age groups, the prevalence rates were 19.97% and 20.27%. The high prevalence of diabetes mellitus in the elderly challenges the medical systems.

There are some difficulties that arise from the management of type 2 diabetes in the elderly. First, it is hard to define the terms “elderly” or “older people.” The United Nations (UN) considers people 60 years of age or older to be part of the older population.³ The International Diabetes Federation (IDF) task force feels that a threshold of 70 or older ensures that people with diabetes will be more likely to exhibit those characteristics.¹ “Standards of Medical Care in Diabetes—2018” by the American Diabetes Association

(ADA) defined the aged as those > 65 years.⁴ The International Association of Gerontology and Geriatrics (IAGG) and the European Diabetes Working Party for Older People (EDWPOP) have a consensus statement for diabetes in older people, and it has limited our scope to those 70 years and older.⁵

Second, the different age thresholds can define geriatric age, but those could not match chronological and biological age in different continents. The heterogeneity of disease duration, the number and severity of complications and comorbidities, socioeconomic status, the degree of frailty and personal functions present in older people with diabetes all must be considered.⁶ The application of clinical guidelines to older patients should be based on the individual's specific conditions.¹

Many randomized controlled trials (RCTs) excluded elderly individuals to reduce the risks in performance. The IDF recognized that the evidence-based guidelines for older people with diabetes are based on deduced evidence from clinical studies in younger adults and they have limitations.¹

2. The considerations of diabetes care in the elderly

2.1. Hypoglycemia

The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial with a mean age of 63 years tried to determine the effect of

[☆] The article is the review of the documents, including current practice guidelines, consensus statements and clinical trials which were published, so the ethical approval from IRB is not necessary.

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intensive blood glucose control. However, it was terminated early due to the increased cardiovascular mortality of the intensive control arm.⁷ A severe hypoglycemic event was associated with cardiovascular death and all-cause mortality in the coming months in the Veterans Affairs Diabetes Trial.⁸

2.2. Geriatric syndrome, comorbidities and functional impairments

Geriatric syndromes are multifactorial health conditions and mean that the elderly have the accumulated effect of impairments in multiple systems and are therefore in a vulnerable situation. Diabetic complications and complicated medical conditions may contribute to cognitive decline. Type 2 diabetes was also associated with a 47% increased risk for all dementia, 39% for Alzheimer's dementia, and more than a 2-fold risk for vascular dementia among older adults in the community.⁹ More than 25% of aged patients with diabetes are victims of depression disorder.¹⁰ Depression impedes self-caring and adherence of diabetes management.¹¹ Diabetes mellitus increases the incidence of functional disability, and causes diabetic complications and complicated medical conditions. Those conditions increase the risks of diabetes management and decrease the quality of life.¹²

2.3. Hyperglycemia crisis

Hyperglycemic hyperosmolar state (HHS) and diabetic ketoacidosis (DKA) are considered hyperglycemic crises. Age is the risk factor of mortality.¹³ New diabetes cases in older individuals and older people with diabetes who are unaware of their disease or unable to take fluids are at risk for HHS.¹⁴

2.4. Polypharmacy

Polypharmacy is defined as the use of multiple medications. With the progression of diabetes, patients may need more medications and polypharmacy may present. Polypharmacy is also a factor in diabetes-related comorbidity. However, polypharmacy increases the risk of drug adverse effects, drug-drug interactions, drug-disease interactions and interference of medical adherence.^{15,16} Polypharmacy may mean that aged patients have more risk of falling.¹⁷

2.5. Support system

Due to possible frailty, cognitive decline, comorbidity and functional impairment, a support system is more important for older adults with diabetes than for younger adults.^{12,18}

2.6. The target of treatment

A multicenter, prospective RCT¹⁹ included 1173 older people in Japan (mean age was 72) with type 2 diabetes and followed them for 3 years. There was a small but significant difference in HbA1c between the intensive and conservative groups (7.9% vs 8.1%, $P < 0.05$) in the first year and not a significant difference in the next 2 years. There was no significant difference in fatal and non-fatal events. A retrospective cohort study with 71,092 patients with type 2 diabetes and who were ≥ 60 years of age in Northern California found that an A1C level $< 8\%$ in older people could reduce the complications and mortality, but an A1C level $< 6\%$ was related to mortality risk.²⁰ A U-shape relationship was found between A1C and mortality in the elderly with type 2 diabetes.

For most patients, the HbA1c target is suggested as below 7%^{1,21–23} or 6.5%²⁴ in current practice guidelines. Patient-centered management within those guidelines is suggested,^{22,23,25} with those options having a balance between the benefits of diabetes control and the risks of hypoglycemia.

The glycemic goals of the guides from those major organizations are from 7.0% to 8.5% (Table 1).

3. Options of medication

3.1. Metformin

In the guidelines or consensus statements of IAGG & EDWPOP, ADA & AGS and IDF, Metformin can be considered as the first-line medication. The outcome trials of metformin for older patients with diabetes are lacking, but a cohort study suggests that metformin reduces mortality and prevents frailty in older patients with diabetes.²⁸

Metformin has some limitations. Gastrointestinal upset is the most common adverse event in clinical practice. Fatal lactic acidosis is the major adverse event with the most concerns. Metformin is contraindicated in the condition of renal-function impairment, dehydration or chronic diseases with tissue hypoxia, etc. Other

Table 1

The glycemic targets from the clinical guides or consensus reports from the major organizations.

Organizations	Years	Glycemic goal of HbA1c for the elderly with diabetes
IAGG & EDWPOP ⁵	2012	7%–7.5%
ADA & AGS ¹⁵	2012	Healthy: $< 7.5\%$ Complex/intermediate: $< 8.0\%$ Very complex/poor health: $< 8.5\%$
IDF ¹	2013	Functionally independent: 7.0%–7.5% Functionally dependent: 7.0%–8.0% Frail: Up to 8.5% Dementia: Up to 8.5%
CDA ^{22,26}	2013	End of life: Avoid symptomatic hyperglycemia HbA1C target $\leq 8.5\%$ for patients with limited life expectancy, functional dependency, a history of severe hypoglycemia, advanced comorbidities, or a failure to target with treatment intensification The same glycemic targets apply to the healthy elderly as to younger people with diabetes.
JDS ²⁷	2013	1% higher for frail elderly patients than that for other age groups
ADA, "Older Adults: Standards of Medical Care in Diabetes-2018" ⁴	2018	Healthy status, HbA1c $< 7.5\%$ Complex/intermediate health, HbA1c $< 8\%$ Very complex/poor health, HbA1c $< 8.5\%$

CDA, Canadian Diabetes Association; JDS, Japan Diabetes Society.

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