Overtreatment of Diabetes in Older Adults

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Introduction

Several recent studies evaluating the management of diabetes in older adults have concluded that 25-52% of elderly patients are currently being overtreated, meaning they are being treated to low glycemic goals with agents that are associated with a high risk of hypoglycemia (e.g., sulfonylureas and insulin). This aggressive treatment is alarming because the effects of hypoglycemia can be detrimental in older patients, leading to a higher rate of falls and fractures and potentially increasing the risk of heart attacks, strokes, and dementia. These investigators further suggest that older patients will often not live long enough to see the microvascular and macrovascular benefits of intensive treatment. Overall, this research indicates that there is a lack of understanding among clinicians on how to appropriately manage diabetes in older patients and that clinicians need more education and guidance on treating this medical condition in this specific population. To address this, a review of research on intensive glycemic control in older patients with diabetes and a summary of guideline recommendations on the management of type 2 diabetes in older adults follows:

Clinical Research on Intensive Glycemic Control

Four key studies investigating the safety and efficacy of intensive glycated hemoglobin (HbA1c) targets in older adults have demonstrated that intensive glycemic control provides modest improvements in microvascular outcomes, no clinically meaningful improvements in macrovascular outcomes, and the potential for harmful outcomes in elderly patients. In general, this research provides the basis for the various guideline recommendations for this specific population. All four of these trials took place in the early to mid-2000s and studied older patients with type 2 diabetes.

1) Effect of intensive treatment of hyperglycaemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomized trial

The ACCORD trial investigated whether intensive glycemic therapy with a target HbA1c of <6.0% versus standard therapy with a target of 7.0%–7.9% in older adults (mean age of 62.2 years) with long standing diabetes (about 10 years) reduced cardiovascular disease morbidity, mortality, and microvascular complications. This analysis of the ACCORD trial found that intensive glycemic treatment
does not reduce the risk of microvascular outcomes, but it does delay the onset of macroalbuminuria and some measures of eye complications and neuropathy. These benefits are similar to what has been reported with intensive therapy in younger patients, but not to the same extent. This trial was terminated early (after 3.7 years) because of increases in mortality and severe hypoglycemia in the intensively treated group. The mortality rate was increased by 22% in the intensive compared with the standard treatment arm (1.41% vs 1.14% per year; HR 1.22; 95% CI 1.01-1.46). There was no clear explanation for the excess mortality in the intensive treatment arm. The researchers concluded that there are small microvascular benefits of intensive glycemic therapy in older patients, but these benefits must be weighed against the increase in mortality, weight gain, and risk of severe hypoglycemia.

2) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes (ADVANCE) 7

The ADVANCE trial evaluated whether intensive glucose control (HbA1c goal <6.5%) compared to standard glucose control (HbA1c goal <7-8%) in adults >55 years of age resulted in fewer major macrovascular events (e.g., cardiovascular events) and major microvascular events (e.g., new or worsening nephropathy or retinopathy), assessed both jointly and separately. After a five year follow-up period, the intensive regimens reduced the risk of combined major macrovascular and microvascular events by 10% vs. standard control (18.1% vs 20.0%; HR 0.90; 95% CI 0.82 to 0.98; P=0.01). When assessed separately, intensive therapy reduced the risk for major microvascular events by 14% vs. standard control (9.4% vs 10.9%; HR 0.86; 95% CI, 0.77 to 0.97, p=0.006), explained primarily by a large reduction in the incidence of nephropathy but no significant reduction in retinopathy. There was no significant difference in macrovascular events between groups. Reports of severe hypoglycemia occurred more often in the intensively controlled group (2.7% vs 1.5%; HR 1.86; 95% CI 1.42 to 2.40; p<0.001). The investigators concluded that intensive glucose control in older patients may reduce the risk of the development of and the worsening of nephropathy, but strict management of HbA1c increases the risk of hypoglycemia without other significant microvascular or macrovascular benefits.

3) Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33) 8

In the UKPDS 33 study, patients between 48 and 60 years of age with newly diagnosed type 2 diabetes were randomly assigned to an intensive therapy regimen with a sulphonylurea or insulin or a conventional regimen and followed for 10 years. Researchers found that, compared to conventional control, intensive glycemic control decreased the relative risk of microvascular complications by 25% (p=0.0099) with no significant findings for macrovascular disease. All intensive regimens increased the risk of hypoglycemia (p<0.001).
4) Long-term follow-up of intensive glycaemic control on renal outcomes in the Veterans Affairs Diabetes Trial (VADT)  

The VADT trial evaluated renal outcomes in patients (mean age 60.4 years) who received either intensive glycemic treatment or standard treatment for about 5.6 years and then were followed for another five years. The researchers found that intensive treatment significantly improved long term kidney outcomes. By the end of the study, significantly more patients who received the intensive treatment maintained an eGFR >60 ml/min/1.73 (OR 1.34; 95% CI 1.05, 1.71; p=0.02). However, severe hypoglycemia was more common in the intensive group, so the investigators cautioned that the potential benefits of the intensive therapy need to be balanced with these risks in older patients.

Much of this research has helped inform guideline recommendations on the management of diabetes, including the appropriateness of strict or more relaxed glycemic targets in older patients. A summary of guideline recommendations follows:

**Appropriate HbA1c Targets: Guideline Recommendations**

*American Diabetes Association (ADA): Standards of Medical Care in Diabetes:*  

The ADA guidelines, updated for 2019, recommend that a reasonable HbA1c goal for most adults is <7%. However, the guidelines note that providers should be vigilant in preventing hypoglycemia and should not aggressively attempt to achieve near-normal HbA1c levels in patients in whom such targets cannot be safely and reasonably achieved. Because of the increased risk for hypoglycemia in older adults, the ADA states that medications with a low risk of hypoglycemia are preferred in this population. Above all, an older patient’s HbA1c goal should be individualized and numerous factors, including physician judgement and patient preferences, should be considered. Additionally, glycemic goals should be periodically adjusted for older patients due to their changing functional and cognitive status. Providers may reasonably suggest more stringent HbA1c goals (such as <7.5%) for selected individuals who are healthy and have few coexisting chronic illnesses if this can be achieved without significant hypoglycemia or other adverse effects of treatment. A stringent HbA1c goal is appropriate for patients with a short duration of diabetes, diabetes treated with only lifestyle or metformin only, long life expectancy, and no significant cardiovascular disease, intact cognitive function and functional status. Providers may suggest less stringent goals (<8%–8.5%) for patients with a history of severe hypoglycemia, limited life expectancy, advanced microvascular or macrovascular complications, extensive comorbid conditions, cognitive impairment, functional dependence, or long-standing diabetes in whom the goal is difficult to achieve despite diabetes self-management education, appropriate glucose monitoring, and effective doses of multiple glucose-lowering agents including insulin. At a minimum, glycemic goals for all patients should avoid symptoms and complications of hyperglycemia.
American Association of Clinical Endocrinologists/American College of Endocrinology (AACE/ACE) Guidelines:

The AACE/ACE guidelines state that, when possible, an HbA1c <6.5% should be achieved for most patients. While these guidelines are not as detailed with regard to diabetes management in older adults specifically, they also recommend individualized therapy and balancing age, comorbidities, and hypoglycemia risk when determining fasting blood glucose and HbA1c goals. Even in older adults, these guidelines support an HbA1c goal of <6.5% if this can be achieved without hypoglycemia or other undesirable consequences. HbA1c goals of 6.5% up to 8.0% may be appropriate for some patients who cannot achieve lower targets without adverse outcomes. Similar to the ADA guidelines, AACE/ACE notes that this goal would be most appropriate for older patients who are at increased risk for hypoglycemia, have a limited life expectancy, advanced renal disease, established macrovascular complications, extensive comorbid conditions, or long-standing diabetes and have not been able to attain a strict HbA1c goal. For patients with less stringent HbA1c goals, it is most important to ensure the patient remains free of polydipsia, polyuria, polyphagia, and other hyperglycemia-associated symptoms.

The Society for Post-Acute and Long-Term Care Medicine (AMDA) Clinical Practice Guideline on Diabetes Management in the Post-Acute and Long-Term Care Setting:

The AMDA guidelines provide similar recommendations with respect to HbA1c goals in older adults. An HbA1c goal of <7.5% is considered reasonable for healthy older adults with a long remaining life expectancy. Given an intermediate life expectancy, hypoglycemia/fall risk, and high treatment burden, AMDA recommends that complex older adults with multiple coexisting chronic illnesses, mild to moderate cognitive impairment, or multiple impairments in activities of daily living should be treated to an HbA1c goal of <8%. In older adults with very complex health issues, moderate to severe cognitive impairment, and/or significant dependencies in activities of daily living, AMDA recommends a more relaxed HbA1c goal of <8.5%. Similar to the ADA and AACE/ACE guidelines, AMDA notes that these categories may not fit each specific patient and thus treatment should be individualized per provider and patient preferences.

Conclusion

In general, clinical practice guidelines suggest moving away from a one size fits all approach when managing diabetes, and this is especially true when treating older patients. While some research demonstrates the microvascular benefits of strict HbA1c goals, older patients may be at an increased risk for hypoglycemia with more intensive glycemic control and may not live long enough to experience the benefits of such a regimen. Therefore, more relaxed, patient-specific goals should be considered. Despite these recommendations in the guidelines, recent evidence suggests that overtreatment of diabetes in older adults remains an issue, with up to 25-52% of older patients potentially being treated to goals or with medications that may do more harm than good. Given this evidence, clinicians should review glycemic targets for older patients on a case-by-case basis and determine if de-escalation of therapy makes sense.
Reference:


