Current Diabetes Reports (2019) 19: 11
https://doi.org/10.1007/s11892-019-1128-3

MICROVASCULAR COMPLICATIONS—NEPHROPATHY (M AFKARIAN AND B ROSHANRAVAN, SECTION EDITORS)

Diabetes Management in Older Adults With Chronic Kidney Disease

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Published online: 15 February 2019

Abstract

Purpose of Review Older adults often live with chronic disease including diabetes and its complications. In this review, we examine the complexity and heterogeneity of older adults with diabetes and chronic kidney disease, explore the nuances in their diabetes-related monitoring, and discuss their best diabetes management.

Recent Findings Although there remains an overall lack of studies in older adults with diabetes and chronic kidney disease, recent reports have highlighted their vulnerabilities. These individuals face an increased risk of cognitive impairment and dementia, frailty, dysglycemia, polypharmacy, declining kidney function, and acute kidney injury. Their diabetes management should focus upon safer antihyperglycemic medications, close monitoring, and care individualization.

Summary Older adults with diabetes and chronic kidney disease are a complex population who requires careful diabetes management and monitoring. Research efforts might focus on improving the care and outcomes of these patients.

Keywords Diabetes · Older adults · Chronic kidney disease · Antihyperglycemic medications · Frailty · Hypoglycemia · Comorbidity

Introduction

With enhancements in medicine and improved survival, our population is aging [1]. The number of people over the age of 60 is expected to double by 2050 [1], and with the high prevalence of hypertension and obesity, not surprisingly, many of these individuals will live chronic, non-communicable disease, including diabetes and its complications [2].

Chronic kidney disease (CKD), typically defined by an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73 m^2, albuminuria, or both (for a minimum of 3 months) [3], affects 25–40% of patients with diabetes [4]. Older adults who live with both diabetes and CKD are a complex, heterogenous population that requires careful diabetes management. In this review, we illustrate their complexities, highlight their need for special monitoring, review the antihyperglycemic medications that are most efficacious and safe in this population, and provide suggestions for their best management.

This article is part of the Topical Collection on *Microvascular Complications—Nephropathy*

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The Complexity of Older Adults With Diabetes and CKD

Cognitive Impairment

Metabolism and physiological function changes as we age, and older adults frequently live with co-morbidity. This is particularly true for older adults with diabetes and CKD. In addition to living with diabetes and its complications [5], these individuals remain at increased risk of geriatric syndromes including falls, chronic pain, depression, functional, and cognitive decline [6].

The risk of dementia in diabetes and CKD is gaining increasing attention. Diabetes (type 1 or 2) is a well-recognized risk factor for the development of mild cognitive impairment (MCI) and dementia, especially vascular and Alzheimer's dementia [7]. People with type 2 diabetes develop dementia on average 2.5 years earlier than those without diabetes [8], an effect which is intensified in those who have MCI [8].

Proposed mechanisms linking diabetes with MCI or dementia, include vascular damage, abnormalities in glucose, insulin and amyloid metabolism, hypertension, and increased body mass index [7, 8]. A longer duration of diabetes (≥ 5 years) has also been associated with a 40–60% increased risk of dementia [7]. Hypoglycemia is an additional risk factor for dementia in patients with diabetes [7], and interestingly, a hemoglobin A1c (HbA1c) > 7.0% in patients with MCI has also been associated with an increased risk of conversion to dementia [9].

In older adults, CKD and end-stage kidney disease (ESKD) have also been independently linked with cognitive impairment. In addition to their underlying vascular disease [10], it is has been proposed that uremic toxins might have a direct effect on cerebral structure and function in these patients [11]. The risk of cognitive decline increases as kidney function declines [12, 13], but unfortunately, cognition does not seem to improve with dialysis [14]. CKD might also accelerate the rate of cognitive decline in patients with diabetes through processes of anemia, inflammation, or oxidative stress [15].

A synergistic relationship between diabetes and CKD on cognition in older adults has also recently been postulated. In one cross-sectional study of 1358 older adults (mean age 68.6 years), diabetes and kidney disease (eGFR < 60 ml/min/1.73 m^2) had an interactive effect on cognitive impairment as measured by the Mini-Mental State Examination (relative excess risk due to interaction of 2.74) [15]. Compared with individuals who had no diabetes or kidney disease, patients with both conditions faced a multi-adjusted odds ratio of 4.23 (95% CI, 2.10–8.49) for cognitive impairment. Mechanisms common to both diabetes and CKD, such as inflammation, peripheral vascular disease, and cardiovascular disease might explain these findings [15].

Whatever the mechanism linking diabetes and CKD with dementia, its development in older adults brings major challenges, particularly in their self-management and safety [6]. A recent systematic review explored the relationship between cognitive impairment and self-care in diabetes [16] and found that those with cognitive impairment (particularly those with deficits in learning, memory, and executive function) had significant impairment in all self-care domains. They had difficulties in problem-solving, understanding their disease, and action-taking. They faced an increased risk of hospitalization, but also had lower clinic attendance, and diabetes-related screening (eye examinations, HbA1c, and low-density lipoprotein [LDL] cholesterol measurement).

Sarcopenia and Frailty

Traditional micro- and macro-vascular complications of diabetes appear to account for only half of diabetes-related disability in older adults. Sarcopenia and frailty are increasingly being considered as a third category of diabetes-related complications [17••, 18].

From the age of 30 years, there is a progressive decline in muscle mass which accelerates with time [19]. Sarcopenia, a component of the frailty construct, relates to this loss of muscle mass. Definitions of sarcopenia vary and include either gender-specific cutoffs for grip strength and appendicular lean muscle mass or loss of muscle mass with associated reduced strength and/or low physical performance [18]. Frailty is a multi-dimensional condition characterized by low physiologic reserve which leads to an increased vulnerability to physiologic and environmental stressors, when compared to others of the same age [20–22]. There is no consensus definition of frailty: it comprises both physical and psychosocial components, including reduced lean muscle mass and sarcopenia, functional impairment, cognitive impairment, mental health, and social issues [23]. Frailty is also associated with an increased risk of adverse health outcomes, such as falls, fractures, hospitalization, dependency, disability, institutionalization, and lower health-related quality of life [18, 23].

Older adults with diabetes and CKD are at increased risk of sarcopenia and frailty. In early diabetes, poor glycemic control, oxidative stress, and inflammation have been postulated to play a role in the development of sarcopenia, whereas in the later stages of diabetes, complications including peripheral neuropathy play more of a role [18]. Insulin resistance, even in patients without diabetes, has also been linked with protein energy wasting and sarcopenia in those with CKD. [24] Vitamin D deficiency is also a well-recognized risk factor for frailty and is especially apparent in patients with diabetes and CKD (those with diabetes at increased risk of low 25-hydroxyvitamin D; 1,25 dihydroxyvitamin D production can be low in CKD) [23]. Additional risk factors for frailty might include chronic disease and multimorbidity [18, 23, 25],

altered body composition including increased fat mass and reductions in muscle mass and function, malnutrition, and inflammation [26].

The prevalence of frailty has been found to increase across the CKD stages, with up to 70% of dialysis patients considered frail [6]. This effect appears independent of diabetes, cardiovascular disease, and CRP level [26]. Among patients with CKD, the frailty phenotype is associated with an increased risk of early dialysis therapy or death [26].

Dysglycemia

In addition to their risk of cognitive decline, dementia, sarcopenia, and frailty, older adults with diabetes and CKD are at risk of both hyperglycemia and hypoglycemia. Even without underlying diabetes, an eGFR< 60 ml/min/1.73m^2 has been linked with insulin resistance and reductions in insulin secretion [27]. Postulated contributing factors include vitamin D deficiency and secondary hyperparathyroidism [28, 29], reduction in GFR, acid-base homeostasis, physical activity, body composition/adiposity, and medication use [27]. If using peritoneal dialysis, patients can have higher blood sugars secondary to higher dialysate glucose [30].

The risk of hypoglycemia is also substantial in older adults with CKD, with and without diabetes. In a population-based cohort study of older adults from 2002 to 2010 (mean age 75 years), we examined the 3-year incidence of hypoglycemia across the stages of kidney disease [31]. In patients who used antihyperglycemic medications, the risk of hypoglycemia increased from 82 (95% CI, 71–94) encounters per 10,000 person-years in those with an eGFR ≥ 90 ml/min/1.73 m^2 to 785 (95% CI, 689–894) encounters per 10,000 person-years in those receiving dialysis. This graded relationship was also apparent in those who did not use antihyperglycemic medications and where kidney function was defined using a combination of eGFR and albuminuria [31].

The reasons for hypoglycemia in older adults with diabetes and CKD can be manifold. Many antihyperglycemic medications are cleared by the kidneys, putting patients with CKD at increased risk of drug-induced hypoglycemia [32, 33]. Muscle wasting and dysfunction might also contribute to reduced insulin clearance [27]. Patients with CKD and diabetes also have more medical comorbidities (including autonomic neuropathy) which might increase their susceptibility to hypoglycemia [34, 35]. Additionally, they often have longer-standing diabetes which is a known risk factor for hypoglycemia [35]. Dementia, MCI, poor meal planning, and insulin product mix-ups have also been implicated [36–38]. In patients with CKD without diabetes, hypoglycemia might be related to malnutrition with lower glycogen stores [39] and reduced renal gluconeogenesis [40, 41].

Compounding their hypoglycemia risk is that older adults with diabetes often experience impaired awareness of hypoglycemia. In a study of patients with type 2 diabetes, those age ≥ 65 years had a different awareness and response to hypoglycemia than younger individuals (age 39–64 years). They also had a less pronounced increase in autonomic and neuroglycopenic symptoms at the end of hypoglycemic plateaus [42]. The study did not specifically evaluate if these effects were independent of beta blocker use.

Over recent years, hospitalizations for hypoglycemia have surpassed the number for hyperglycemia, especially in those ≥ 75 years. In a study of US Medicare beneficiaries from 1999 to 2011, hospitalization rates for hypoglycemia were nearly twofold higher in those ≥ 75 years compared with those 65–74 years [38]. Hypoglycemia can have significant consequences for patients including cardiac disturbances, neurological complications, impaired quality of life, and even death [43]. Prevention is thus key in the older adult population.

Polypharmacy

With their many medical conditions, older adults with CKD and diabetes are at increased risk of polypharmacy. In a study of 685 nursing home residents, 53.3% reported using five to nine medications (defined as polypharmacy), and 16.4% had evidence of excessive polypharmacy (ten or more medications). An eGFR < 60 ml/min/1.73 m^2 was associated with polypharmacy in multivariable analysis [44]. Unfortunately, polypharmacy has been linked with adverse drug reactions [45], especially in those with CKD.

Heterogeneity

It is important to emphasize that older adults with diabetes are a heterogenous population. Although many live with functional impairment, comorbidities, polypharmacy, and have frequent hypoglycemia, others do not. Older adults can have new-onset type 2 diabetes after their diagnosis of CKD, if their kidney disease is due to non-diabetic glomerular syndromes (which are more common in older adults) [46]. Older adults with type 1 diabetes also now survive into older age [47]. Thus, age does not always equate with patient complexity.

Special Monitoring

Increased attention has been paid to the need for special diabetes-related monitoring in older adults with diabetes (i.e., monitoring of kidney function and glycemic control).

Impact of Aging on Measures of Kidney Function

The measurement of kidney function (filtration and secretion) can be challenging in older adults. GFR is typically used to provide a measure of functioning

nephrons, and in clinical practice, it is estimated using the clearance of the endogenous marker, creatinine [48]. Formulae including the Cockcroft–Gault, [49] the Modification of Diet in Renal Disease, [50] and the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) [51] are validated creatinine-based formulae to estimate kidney function. These estimating equations were, however, not specifically developed in older adults [52].

Additionally, there are limitations to using creatinine to estimate GFR in older patients. Creatinine production is dependent upon muscle mass, and in older adults, the production of creatinine can be heterogeneous [52]. Patients can also have variable creatinine secretion (e.g., those with nephrotic syndrome) [53]. Thus, despite having a normal creatinine, older adults can have "concealed renal failure" with a declining GFR [54].

Recently, new eGFR formulas have been proposed which use cystatin C and creatinine as endogenous markers. Although more validation studies are needed, these equations (e.g., Berlin Initiative Study 2 Equation) seem to yield smaller biases in renal function measurement than creatinine-based formulae [52]. Such equations are, however, not routinely available.

Although the best measures of kidney function in older patients remain controversial, all equations seem to provide similar estimates when GFR is < 30 ml/min/1.73 m^2, which is a frequent cutoff to guide drug dosing [55]. It might be reasonable then to use any equation to guide antihyperglycemic medication dosing [56]. If there is need to accurately quantify kidney function (e.g., in cases where highly toxic drugs or kidney transplantation are being considered), one might perform a nuclear measurement of GFR (i.e., renal scan). Although 24 urine creatinine collections can also be considered in these situations [57], there remains the possibility of inaccurate collections especially in older adults.

Trajectory of Kidney Function Among Older Adults

Due to fibrosis, tubular atrophy, obliterated arterioles, vascular resistance, and defective autoregulation, GFR and tubular secretion decline naturally with time in older individuals [58]. In a study of 4380 patients (mean age 72 years), 6% had an annual decline of eGFR > 3 ml/min per 1.73 m^2 when using creatinine-based equations, and 25% had an annual decline of eGFR > 3 ml/min/1.73 m^2 when cystatin C–based equations were used [59]. It is also known that older adults with diabetes and CKD face an increased risk of acute kidney injury (AKI) [2], which might be due to comorbid disease such as prostatic hypertrophy or congestive heart failure [2] or the use of nephrotoxic medications [2, 58].

Glycemic Control

In addition to monitoring their kidney function, special attention needs to be paid to glycemic monitoring in older adults with CKD. Where HbA1c is suggested for monitoring in most healthy individuals, this test is affected by reduced red cell survival, use of erythropoietin, hemoglobin modifications, and mechanical destruction of blood cells [60, 61]. These conditions are often present in CKD, and the correlation between HbA1c and fasting glucose weakens with lower kidney function [61].

The use of glycated albumin and fructosamine as alternative measures of glycemic control in patients with CKD has been suggested, but these measures may be equally flawed [62]. Their usefulness depends upon normal serum albumin levels, which are rarely observed in patients with CKD as they often have altered plasma protein turnover. Moreover, glycated albumin and fructosamine are affected by many physiological conditions and may fail to serve as stable markers [63].

In the absence of consistent and sufficient data to show superiority of their use over HbA1c as markers for glycemic control, it would be reasonable to continue using HbA1c or capillary blood glucose to monitor glycemic control in this population.

Challenges in Diabetes Management

Antihyperglycemic Agents

A cornerstone of diabetes management is the administration of antihyperglycemic drugs. Over the last several years, the armamentarium of drugs available to treat patients with diabetes has grown. Unfortunately, however, therapeutic choices can be limited in older adults, especially in those with CKD.

Metformin

Due to its low cost, neutral effect on weight, low risk of hypoglycemia, and effectiveness in lowering blood glucose, metformin is currently the recommended first-line therapy for the management of diabetes [64]. However, in older adults, particularly in those with CKD, metformin has been reported to increase the risk of lactic acidosis and gastrointestinal (GI) side effects [65]. In those with CKD, it is suggested that metformin can be used without dose reduction to an eGFR > 45 mL/min/1.73 m^2 but that a reduction to 1000 mg daily be used in patients with eGFR 30–44 mL/min/1.73 m^2 [65]. Although recommendations vary, metformin is not advised in those with a serum creatinine ≥ 1.5 mg/dL in men or ≥ 1.4 mg/dL in women, when eGFR is < 30 mL/min, or in those over the age of 80 with reduced kidney function [65].

Sulfonylureas

Sulfonylureas are effective agents for lowering blood glucose and are often used in combination with other glucose-lowering agents, including metformin. Hypoglycemia can, however, occur with these drugs, and this effect appears most pronounced in older adults with CKD due to reduced renal clearance of these agents and their metabolites [66]. Chlorpropamide and glyburide/glibenclamide should be avoided in the elderly because of their high hypoglycemia risk [67]. Glipizide, gliclazide, and glimepiride are safer options because their clearance and half-life are not heavily affected by renal function [68]. It is currently suggested that these agents still be used with caution in those with eGFR < 60 mL/min/1.73 m^2 [69, 70].

TZDs

Thiazolidinediones do not cause hypoglycemia as monotherapy and have durable effects on glycemic control. However, they are associated with weight gain, fluid retention, edema, congestive heart failure, and bladder cancer [65], and in older women in particular, an increased risk of fragility fracture has been described [71, 72]. As such, these agents should not be used in patients with New York Heart Association (NYHA) class III or IV heart failure or in older adults with osteoporosis. Bone density should be monitored when these agents are prescribed in patients with osteopenia. Rosiglitazone and pioglitazone are both metabolized by the liver; therefore, dose adjustment is not needed in patients with CKD [63]. Nonetheless, the risk of fluid retention makes the use of these drugs limited in older patients with CKD.

Meglitinides

Meglitinides have rapid onset time and short half-life, and when taken before meals, they can control postprandial hyperglycemia [65, 73•, 74]. Compared with sulphonylureas, they are associated with a lower risk of hypoglycemia [65]. While nateglinide is contraindicated in patients with an eGFR < 60 mL/min/1.73 m^2 [73•], repaglinide can be used without dose adjustment [75]. Among patients with CKD treated with repaglinide, a clearance as low as 20 mL/min was not associated with hypoglycemia [76]. Meglitinides, however, are costly and require frequent dosing, which may limit their use in the elderly population.

Incretins

Incretins (glucagon-like peptide-1 [GLP-1] receptor agonists and dipeptidyl peptidase-4 [DPP-4] inhibitors) have garnered more attention in recent years, with large clinical trials providing evidence on the efficacy and safety of these agents.

GLP-1 Receptor Agonists Although there is evidence of the efficacy and safety of GLP-1 receptor agonists (exenatide, liraglutide, dulaglutide, lixesenatide, and albiglutide), there have been no studies specifically conducted in older adults with diabetes and CKD. However, there is no reason to believe that there would be major differences in the efficacy and safety profiles between older and young patients [77]. GLP-1 receptor agonists carry a low risk of hypoglycemia and can encourage weight loss, but they are costly and need to be delivered by injection. GI upset is common, which may not be tolerable in older patients. Impaired kidney function reduces the clearance of exenatide, and its use should be avoided in patients with an eGFR < 30 mL/min [78]. Although guideline recommendations vary, no dose adjustments are needed for liraglutide, dulaglutide, lixesenatide, or albiglutide in CKD patients, but caution is advised in the advanced stages given a lack of data in this population [67, 73•].

DPP-4 Inhibitors DPP-4 inhibitors (sitagliptin, saxagliptin, linagliptin, and alogliptin) reduce blood glucose by decreasing glucagon secretion and blocking the breakdown of GLP-1, an incretin hormone [70, 71]. These drugs then stimulate insulin secretion in a glucose-dependent fashion and reduce gastric emptying [78, 79].

DPP-4 inhibitors are associated with a low risk of hypoglycemia and are weight neutral. Several clinical trials have shown the efficacy, safety, and tolerability of these agents in older adults with CKD [80–82]. All DPP-4 inhibitors except linagliptin are excreted via the kidneys to some extent. As such, these agents require dose adjustment according to eGFR [83]. Older adults prescribed DPP-4 inhibitors, including sitagliptin, do not appear to be at an increased risk of pancreatitis compared with those prescribed other antihyperglycemic medications [84].

SGLT-2 Inhibitors

Sodium-glucose cotransporter 2 inhibitors reduce glucose uptake from the kidney, and their antihyperglycemic action depends on urinary glucose excretion. As such, their glycemic-lowering potential is reduced in patients with CKD [83].

Only a few randomized trials have examined the efficacy or safety of canagliflozin and dapagliflozin in older adults (mean age of 67–69 years) with diabetes and CKD [85, 86]. As anticipated, these studies showed that the glycemic-lowering potential of SGLT-2 inhibitors was reduced in older adults, particularly in those with impaired kidney function [87]. Studies were limited to patients who were relatively healthy, without any serious comorbid conditions or cognitive impairment.

In addition to lowering blood sugar and inducing weight loss by promoting a negative calorie balance, reduction of

blood pressure has been reported due to osmotic diuresis [85]. For this reason, SGLT-2 inhibitors may be beneficial in older patients with uncontrolled hypertension, but they should not be used in those with hypotension.

It is currently suggested that canagliflozin should not be used in patients with an eGFR < 45 mL/min/1.73 m^2, and dapagliflozin is not recommended for patients with an eGFR < 60 mL/min/1.73 m^2 [87]. No more than 100 mg once daily of canagliflozin should be used in patients with eGFR 45–59 mL/min/1.73 m^2 [73•]. While the hypoglycemia risk of these agents is low in middle-aged patients, the incidence of hypoglycemia is increased in older adults, particularly among those with later stages of CKD [85–89]. These agents are also expensive with a 30-day supply estimated to cost $350–400 US dollars. As such, older adults on fixed incomes may have difficulty affording these therapies [83].

Insulin

With age comes progressive β-cell function decline, making insulin therapy often necessary in older adults. However, as it is cleared by the kidneys, an initial insulin dosage reduction of 25% is sometimes recommended in patients with eGFR 10–50 mL/min to reduce the risk of hypoglycemia [75]. When long-acting insulin such as glargine or detemir are used, dose reductions of 50% have also been suggested [75]. These long-acting basal insulin analogues might be preferred given they appear to have a lower hypoglycemia risk than NPH or regular insulin, [90] although studies are duly lacking in those with CKD. If needed for post-prandial control, rapid-acting insulin administration after a meal in those with CKD may be beneficial [73•].

Comorbidities, poor physical function, and cognitive impairment can make safe insulin administration difficult. More complicated insulin regimens can increase the odds of dosing error and the risk of hypoglycemia, especially in older patients with cognitive impairment. Between 2007 and 2011 in the USA, there were 97,648 hospital encounters for insulin-related hypoglycemia and errors [38]. Compared with those aged 65–79 and 45–64 years, patients over the age of 80 had higher rates of emergency department visits (34.9 per 1000 insulin-treated patients with diabetes). Almost 2/3 of patients had severe hypoglycemia. [38]

Glycemic Targets

A summary of guideline recommendations for glycemic targets in older adults is included in Table 1.

Some suggest that it is not unreasonable for healthy older patients who have normal life expectancy to aim for the same glycemic targets as younger adults (HbA1c <7%). In older patients with only a few comorbidities and a reasonable life expectancy, < 7.5% is a reasonable goal. There is growing recognition that intensive glycemic control in older frail patients with diabetes has limited benefit and probably causes harm and as such, a target HbA1c of < 8.0% has been suggested. In the severely frail, functional outcomes appear best over 2 years when patients have an HbA1c > 8.0%, and as such, as target of < 8.5% has been proposed in this population [17••].

It is, however, important to prevent severe hyperglycemia in older adults. Hyperglycemia can lead to polyuria, polydipsia and nocturia, visual impairment, dehydration, and can predispose patients to urinary tract infections, candidiasis, and cardiovascular events [17••]. Screening and treatment of potential microvascular complications should also not be disregarded in this age group.

Discussion

Older adults with diabetes are a complex, heterogenous population. Health care professionals who manage these patients should play close attention to their comorbidities and functional status, practice safe and cautious prescribing, individualize their glycemic targets, closely monitor them, involve other care professionals in their management, and provide them with patient-centered care.

Awareness of Comorbidities and Functional Status

Care professionals who treat older adults with diabetes and CKD should be fully aware of their comorbidities and functional status. During their clinical assessments, providers might periodically screen for cognitive dysfunction and depression or involve geriatric teams to help with this screening [94]. Frailty is a recognized complication of diabetes and reduced kidney function but is often not assessed in older adults with diabetes. There are multiple frailty measures available, many of which require minimal training for accurate use [17••].

Attention should also be paid to the risk of nutritional deficiency in older adults [94]. Good nutrition with vitamin D and protein intake (especially the amino acid leucine) has been associated with improvements in muscle mass and function [18]. Physical rehabilitation and multi-component exercise programs incorporating balance exercises, gait re-training, and strength, power, and resistance training have the potential to reverse frailty deficits [18]. Vision and hearing should be screened, and attention should be paid to health literacy and self-management skills [94, 95].

Practice Safe, Cautious Prescribing

Before prescribing new medications, the medication lists of older adults with CKD should be reviewed. Where patients are

Table 1 Guideline recommendations for HbA1c targets for older adults with diabetes

American Diabetes Association [91]		Diabetes Canada [92]		International Diabetes Federation [93]	
Healthy: few existing chronic illnesses, intact cognitive, and functional status	< 7.5%	Functionally independent	≤ 7.0%	Functionally independent	7.0–7.5%
Complex/intermediate: multiple coexisting chronic illnesses or ≥ 2 instrumental ADL impairments or mid-to-moderate cognitive impairment	< 8.0%	Functionally dependent	7.1–8.0%	Functionally dependent	7.0–8.0%
Very complex/poor health: long-term care or end-stage chronic illnesses or moderate-to-severe cognitive impairment or ≥ 2 ADL dependencies	< 8.5%	Frail and/or presence of dementia	7.1–8.5%	Functionally dependent with frailty	< 8.5%
		End of life	A1c measurements not recommended. Avoid hypoglycemia and symptomatic hyperglycemia	Functionally dependent with dementia	< 8.5%
				End of life	Avoid symptomatic hyperglycemia

ADL activities of daily living

at increased risk of polypharmacy, their need for prescribed therapies might be re-evaluated, and medications should be reconciled [94]. Providers might also look for nephrotoxic medications and use drug interaction checkers when reviewing their medication lists.

We also suggest that when prescribing antihyperglycemic medications, regimens should be made simple. Prescribers might choose the lowest effective dose of medications, ensure that patients know how to take their drugs [96], and ensure that they can distinguish between therapies to avoid product mix-ups [38]. Although older adults with CKD are frequently excluded from clinical drug studies, it would be reasonable to choose antihyperglycemic medications with a strong benefit to risk ratio for these patients. As they are at increased risk of drug-associated hypoglycemia, it would be important to choose agents with a lower hypoglycemia risk. It is also necessary to consider the cost of antihyperglycemic medications given older adults are frequently on fixed incomes or have limited drug benefits.

Individualization of Glycemic Targets

Glycemic targets should be based upon the individual patient. Given the heterogeneity of older adults with diabetes, there are no age specific recommendations for glycemic control. Targets should depend upon their function, life expectancy, and risk of hypoglycemia [97]. In older adults, it also remains important to identify overtreatment and to de-intensify and de-prescribe to minimize harm [98]. Unfortunately, the overtreatment of older adults remains an issue. In a study of patients > 70 years with type 2 diabetes prescribed sulphonylureas or insulin in the UK [98], almost 1/3 had an HbA1c < 7%. Those with CKD or dementia were overtreated just as commonly as those without these conditions.

Monitor Closely

While HbA1c measurement might be useful to evaluate glycemic trends, attention to capillary and venous blood glucose is important in older adults with diabetes and CKD. The kidney function of these individuals might also be monitored more frequently, given the risk of declining function and AKI.

Involve Family, Healthcare Team

Given their complexity, care professionals might involve multidisciplinary care teams in the management of older adults with diabetes and CKD. Geriatricians can bring expertise in managing multi-morbidity, de-prescribing, falls risk reduction, and rehabilitation [17••]. In older adults, multidisciplinary teams (i.e., geriatricians, diabetes nurse educators, registered dietitians) can improve glycemic control and self-care behaviors when compared with usual diabetes care [99].

Conclusion

Older adults with diabetes and CKD are a complex, vulnerable population. We suggest a patient-centered, individualized approach to their best management. Where the number of patients living with these conditions will continue to increase, more efforts might be taken to understand their outcomes and the ideal therapies and targets to use in this population.

Funding Information Kristin K. Clemens reports grants from the Canadian Institutes of Health Research/Strategy for Patient Oriented Research and grants from Western University. Niamh O'Regan reports a grant from the Academic Medical Organization of Southwestern Ontario. Jinnie J. Rhee reports grants from National Institutes of Health/National Institute of Diabetes and Digestive and Kidney Diseases (K01 Research Scientist Career Development Award).

Compliance with Ethical Standards

Conflict of Interest Kristin K. Clemens received a 2017 Diabetes Canada Junior Investigator Award funded by AstraZeneca outside of the submitted work. She has also received conference support from Merck Inc.

Niamh O'Regan and Jinnie J. Rhee declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- •• Of major importance

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