A call to incorporate the prevention and treatment of geriatric disorders in the management of diabetes in the elderly


For The Alfediam/SFGG French-speaking group for study of diabetes in the elderly

Abstract

The prevalence of type 2 diabetes increases with age. However, the management of diabetes in the elderly has received surprisingly little attention. Diabetes in the elderly is associated with a high risk of geriatric syndromes including malnutrition and sarcopenia, functional impairments, falls and fractures, incontinence, depression and dementia. Tight glycaemic control for the prevention of vascular complications is often of limited value in the elderly. However, glycaemic control and non-pharmacological therapy may prevent diabetes symptoms and delay geriatric syndromes. The prevention, screening and treatment of both conventional diabetic complications and geriatric syndromes should be integrated in a management plan to optimize the patients’ overall health status and quality of life.

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Keywords: Diabetes; Elderly; Dementia; Malnutrition; Review

Résumé

La prévalence du diabète de type 2 augmente avec l’âge. Cependant, la prise en charge du diabète dans la personne âgée a été peu étudiée. Le diabète est associé à un risque élevé de syndromes gériatriques tels que la malnutrition et la sarcopénie, les incapacités fonctionnelles, les chutes et les fractures, l’incontinence, la dépression et la démence. Le contrôle glycémique intensifié a souvent un intérêt limité en termes de prévention des complications vasculaires chez le diabétique âgé. Pourtant, le contrôle glycémique et les traitements non pharmaco-logic peuvent prévenir les symptômes du diabète et retarder la survenue de syndromes gériatriques. La prévention et le dépistage des complications classiques du diabète et des syndromes gériatriques doivent être intégrés dans la prise en charge des patients âgés, afin d’optimiser leur état de santé global et leur qualité de vie.

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Mots clés : Diabète ; Personne âgée ; Démence ; Malnutrition ; Revue

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1. Introduction

The prevalence of diabetes keeps increasing with age, reaching a plateau at 10–20% (depending on study populations, screening strategies and diagnostic criteria) in people over 70 years old [1–3]. In the coming decades, the prevalence of diabetes is expected to rise sharply worldwide [1]. The so-called diabetes pandemic is often blamed on obesity and sedentary lifestyles. However, a substantial part of the increase in diabetes prevalence can be attributed to aging per se [1]. Thus diabetes in the elderly is a frequent clinical problem that will take even more prominence in the near future.

The management of diabetes in the elderly has received surprisingly little attention. Several recent studies have emphasized diabetes as a risk factor for many geriatric syndromes. However, the benefits of glycaemic control and cardiovascular (CV) risk factor management, as well as the epidemiology and treatment of diabetic complications have been little studied. Beyond the lack of data, a major problem is the heterogeneous situations encountered in elderly persons with diabetes. It is often problematic to extrapolate from young adult to the elderly and further from the elderly to the frail or dependent elderly. Treatment goals, monitoring and therapy of diabetes and its complications will naturally vary with diabetes duration, overall health status and coexisting disorders: heterogeneous situations call for individualized approaches to diabetes management.

With these issues in mind, we will attempt to propose an approach to diabetes management that integrates the prevention of geriatric syndromes into conventional diabetes treatment and monitoring.

1.1. Glycaemic control and the prevention of vascular complications

Over the last 20 years much research has focused on the benefits of tight glycaemic control in terms of prevention of CV complications. However, since no study has directly dealt with elderly patients (>70 years old), we have to extrapolate from studies conducted in younger patients.

The DCCT trial (in young type 1 diabetic patients) [4] and the UKPDS study (in newly diagnosed type 2 diabetic patients, mean age 53 years) [5,6] have demonstrated that tight glycaemic control reduces the incidence of microvascular complications, but has at best minor benefits on the risk of CV events over 6.5 and eight years respectively. However, posttrial follow-ups have shown the persistence of vascular benefits several years after the active intervention period. In the EDIC (post-DCCT) study, patients from both intensive and standard treatment groups had similar glycaemic control during follow-up (mean HbA1c approx. 8.0%). However, patients from the former intensive therapy group still had a lower incidence of microvascular complications over the next four years [7], and during the whole 17 years of follow-up the incidence of CV events was also reduced by 42% [8]. Similarly, during the 10 years following the completion of the UKPDS study, the lower incidence of microvascular complications persisted in patients from the former intensive therapy group, and an approximately 15% decrease in the risk of death and myocardial infarction became apparent [9]. These data suggest that there is a lag phase of several years between the implementation of tight glycaemic control and the observed clinical benefits, a phenomenon now called the “legacy effect”.

The ADVANCE study, performed on older patients (mean age 66 years, diabetes duration eight years), compared the effects of tight versus “standard” glycaemic control strategies on clinical outcomes over five years. Low mean HbA1c levels (6.5 and 7.3% respectively) were achieved in both groups. After five years, there was no significant difference in the risk of death or CV events. However, a 20% reduction in the incidence of nephropathy – but not retinopathy – was observed [10]. The ACCORD study compared “standard” treatment (aiming an HbA1c 7.0–7.9%) with an intensive strategy targeting an HbA1c < 6.0%. in patients with a mean age of 62 years and a diabetes duration of 10 years [11]. After 3.5 years, total and CV mortality were actually higher in the intensive therapy group, likely due to a much higher risk of severe hypoglycaemia. However, total mortality was lower than expected in both groups. These studies essentially indicate the lack of effect of a three-to-five year intervention when it is initiated in patients with previous greater than 8–10 year exposure to hyperglycaemia.

In conclusion, it appears that the benefits of tight glycaemic control on the risk of CV events are most significant when implemented right from the diagnosis and pursued consistently over time. The “legacy effect” implies that the benefits may be small if tight control is started late in life, in patients with a long diabetes history or a reduced life expectancy.

1.2. Diabetes and geriatric syndromes

Diabetes is associated with an increased incidence of most important geriatric syndromes.

1.2.1. Functional impairments

Diabetes has been associated with functional impairments, such as difficulties with walking a quarter mile, climbing 10 steps, heavy household work, shopping, preparing meals [12–17]. Functional impairment may be due to diabetes itself, or to accumulated complications. However, most longitudinal studies have shown an effect of diabetes even after adjustment for all measured comorbidities in subjects with or without preexisting disabilities [13,16].

1.2.2. Falls and fractures

Diabetes is associated with an increased risk of falls, recurrent falls and fractures in subjects with or without preexisting disabilities; this risk is particularly high in long-standing diabetes. Among diabetic patients, reported risk factors include female gender, impaired mobility, orthostatic hypotension, high body mass index (BMI) and poor diabetic control but not hypoglycaemia [18–20]. Although yet undocumented, other likely diabetes-related risk factors include visual loss, peripheral neuropathy, foot deformities (including previous amputation) and polypharmacy.
The increased risk of falls translates into an increased risk of fractures. This is not necessarily expected as diabetic patients with overweight/obesity tend to have a higher bone mass. In the “Study of Osteoporotic Fractures”, women with diabetes had an increased risk of hip, proximal humeral fractures (relative risk RR around 2.0) but not in vertebral fractures, after adjustment for age, body mass index, and bone density among other factors [21]. The health ABC study also found an increased risk of fractures among diabetic patients (RR 1.64) after adjustment for hip bone mineral density and other fracture risk factors.

1.2.3. Urinary incontinence

Diabetes is associated with a high prevalence of urinary incontinence in women. The association with severe incontinence is particularly pronounced [22–24]. Risk factors include diabetes duration, neuropathy and albuminuria. Obesity is also a strong risk factor for incontinence, and may account in part for the association with diabetes [25]. Weight loss reduces the incidence of new incontinence [26]. Although poor glycaemic control has not emerged as a major risk factor in epidemiological studies, it seems obvious that poorly controlled diabetes can cause symptoms of polyuria, high urinary frequency and incontinence.

1.2.4. Depression

Depression may be caused or favoured by the burden of diabetes and diabetes care. Conversely, depression can be detrimental to diabetes self-management and to coping with diabetes or its complications. Diabetes is associated with a high (approximately doubled) prevalence of depression, and diabetic patients are overrepresented in clinical trials of depression therapy [27,28]. Among diabetic patients, the presence of coexisting depression is associated with increased mortality [29]. Similarly, in patients presenting with an initial foot ulcer, depression is frequent, and associated with increased mortality [30]. While treatment with antidepressive drugs appears to be less effective in elderly than in young diabetic patients, the efficacy of non-pharmacological approaches to the treatment of depression in the elderly is not affected by the presence of coexisting diabetes [27,31].

1.2.5. Impaired cognitive function and dementia

Several studies have shown that diabetes accelerates the rate of decline in cognitive function in both elderly men and women [32,33]. The role of glycaemic control in cognitive function is not well studied. Several small, observational studies have shown that hyperglycaemia is associated with worse cognitive function (measured by tests of complex motor skills, abstract reasoning and memory), and that improved glycaemic control improves cognitive function [34–37]. In the DCCT trial, recurrent severe hypoglycaemia was not associated with cognitive impairment over 18 years, but some aspects of cognitive function (such as motor speed and psychomotor efficiency) were associated with poor glycaemic control [38].

Diabetes is also a strong and probably underestimated risk factor for dementia. Early studies had actually suspected a negative association between diabetes and dementia [39]. However, these observations are probably explained by recruitment bias in dementia clinics and mortality bias in diabetic subjects. More recent longitudinal studies have shown a quite consistent association between diabetes and incident dementia (reviewed in [40]). Diabetes assessed in midlife (approx. 50 years) predicts dementia in the elderly in the majority of studies. Due to the long interval (more than two to three decades) between diabetes and dementia assessment, different drop-out rates, selective survival and incident diabetes during follow-up may all lead to underestimate the association. Associated CV risk factors, including hypertension, dyslipidemia and smoking are additive dementia risk factors [41]. Studies in which diabetes was assessed after age 65 show that diabetes is associated with any dementia and Alzheimer’s disease in most studies (relative risk approx. 1.4–2.0), and vascular dementia in all studies (relative risk approx. 2.0–3.0) [40]. The prevention of dementia, in particular vascular dementia, must be seen as an essential and underestimated outcome for diabetes and CV prevention in midlife, while glycaemic control likely remains important even in old age for optimal cognitive function.

1.2.6. Malnutrition and sarcopenia

Type 2 diabetes in young adults is essentially linked to insulin resistance and obesity, secondary to a sedentary lifestyle and excessive caloric intake. The Diabetes Prevention program (DPP) study has clearly shown that simple lifestyle changes (increased physical activity, reduced fat and calorie intake) strongly reduce the risk of diabetes in subjects with impaired glucose tolerance [42]. The effectiveness of lifestyle changes was greatest among the oldest patients enrolled in this study. However, the relationship between obesity and diabetes evolves with age. Aging is associated with a decline in body weight and a marked decrease in food intake [43]. Whether these phenomena are pathological or physiological (associated with the aging process), they imply that the central role of obesity and insulin resistance in diabetes and other health outcomes must be reconsidered in elderly subjects.

In populations over 70 years old, the BMI no longer predicts CV and all-cause death [44]. Some population studies have even shown an inverse association between the BMI and survival [45]. We have recently shown that mortality is inversely related to BMI, diastolic blood pressure, total and LDL-cholesterol and insulin resistance in a population of very old patients in geriatric care facilities [46]. The likeliest explanation is that in elderly and/or frail patients the interpretation of the BMI and other parameters of the metabolic syndrome are compounded by malnutrition and/or sarcopenia, the age-related decline in skeletal muscle mass. Malnutrition and sarcopenia are strong determinants of muscle strength and functional capacities. Diabetic patients are at high risk for sarcopenia, as the rate of skeletal muscle mass and strength loss in type 2 diabetes is accelerated 1.5–2.0 fold [47]. Malnutrition, sarcopenia and obesity may coexist, and there is some evidence that sarcopenia is a stronger predictor of functional impairment than obesity [48]. The use of BMI to define obesity assumes that the body weight is narrowly associated with the fat mass. This assumption is not warranted in elderly persons. One epidemiological study has shown that...
mortality is inversely associated with the BMI but positively with the waist-to-hip ratio, suggesting that factors unrelated to adiposity are involved [49]. Weight loss between age 60 and 70 predicts mortality over the subsequent 10 years, an effect most pronounced in diabetic persons [50]. Interestingly, the study of Allison et al. has shown that weight loss predicts mortality, but that fat mass loss is associated with decreased mortality [51]. Weight cycling is associated with net lean body mass loss and increased mortality [52]. Taken together these observations indicate that in both the non-diabetic and diabetic elderly the prevention of malnutrition and sarcopenia should take precedence over weight reduction in both diabetic and non-diabetic patients.

1.3. Approaches to diabetes management in the elderly

From the above considerations it is obvious that care of the elderly person with diabetes cannot be restricted to the management of hyperglycaemia, associated risk factors and specific diabetic complications. An integrated approach must assess the presence of associated diseases and of geriatric syndromes, in particular malnutrition and cognitive impairment. It must then establish treatment priorities that are tailored to the need of the individual patients and sometimes adjusted to the available resources.

1.3.1. Treatment of hyperglycaemia and related metabolic disturbances

1.3.1.1. Targets for glycaemic control. As reviewed above, tight glycaemic control for the prevention of vascular complications becomes a low priority issue in many elderly diabetic patients. However, glycaemic control offers other important clinical benefits. The potential for improving symptoms, including reversible cognitive impairments, is easily underestimated [35,53] Glycaemic control is also of paramount importance for the preservation of an adequate nutritional status, via avoidance of glycosuria (and the ensuing caloric loss) and possibly the direct anabolic effects of insulin. Glycaemic control is also a potential tool for the prevention of geriatric syndromes and the promotion of successful aging. The heterogeneity in clinical situations makes the establishment of simple, universal treatment guidelines impossible. The guidelines published by the European Union of Geriatric Medical societies (EUGMS: http://www.eugms.org/index.php; see table) distinguish patients with a single disorder (in “apparent good health”), and frail patients, affected by multiple pathologies (“unsuccessful aging”).

<table>
<thead>
<tr>
<th>Older diabetic patient “in good health”</th>
<th>“Frail” older diabetic patient</th>
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<tr>
<td>Fasting blood glucose between 0.9 and 1.26 g/l</td>
<td>Fasting blood glucose between 1.26 and 1.60 g/l</td>
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<tr>
<td>HbA1c between 6.5 and 7.5%</td>
<td>HbA1c between 7.5 and 8.5%</td>
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These guidelines should be interpreted with flexibility: tight glycaemic control should never be implemented at the expense of frequent hypoglycaemia. Conversely, while these guidelines recognize that it is unnecessary to target near-normoglycaemia in frail patients, they also imply that poor glycaemic control (HbA1c > 8.5–9.0%) should be treated for possible relief of symptoms, irrespective of the overall health status.

1.3.1.2. Non-pharmacological treatment. Beyond its benefits on blood glucose control, non-pharmacological treatment is essential for the prevention of malnutrition, sarcopenia and functional impairments. Dietary advice given to older people with diabetes is intended to maintain an adequate nutritional status [54]. Food intake should provide about 30 kcal/kg ideal body weight/day, divided into three proper daily meals. Weight loss is not desirable as it can affect muscle mass and function. Dietary advice should take into account the patient’s personal tastes, and consider the pleasure and social aspects of meals. Simple (non-starch) carbohydrates can usually be permitted if they are counted as part of the daily allowance.

Fat intake should not be restricted at the expense of palatability. This being said, an exceedingly liberal approach must be avoided, and the specified meal schedule must be respected, especially in patients on insulin therapy.

The difficulty of ensuring an adequate food in the elderly must be remembered. Elderly subjects have an impaired feeling of hunger [55]. Past, lifelong negative attitudes toward food intake may persist in the elderly [56,57]. Prior dietary advice, meal plans, and attempts at intentional weight loss may all predispose patients with long-standing diabetes to reduced food intake in old age. Attention should also be paid to oral and dental health [58]. Protein supplements can be beneficial in patients at high risk of malnutrition, although no study has properly addressed this important issue [59].

Physical activity must always be encouraged, but specific advice should be adapted to the patient’s capabilities, and to any motor or sensory impairment (peripheral neuropathy, history of stroke, osteoarthritis, etc). Endurance training (treadmill, rowing machine, or just walking) can promote fat mass loss. Resistance training (upper and/or lower body muscle workouts raising moderate weights, usually offered as a structured program in a gymnasium) increases the muscle mass and reduces the fat mass, improving both autonomy and quality of life. The studies with the most successful results are rather short-term (a few weeks), while the efficacy of resistance training (combined with nutritional supplements) is more difficult to demonstrate in long-term studies, not least because of difficulties with patient compliance [60,61]. In the context of disability, only resistance training (low-intensity physical therapy) should be envisaged, but at this stage the priority is to limit the risk of a transition to dependence. Thus physical activity remains of great importance at all stages of life in diabetic patients. However, its actual aims evolve with time, progressing from weight loss to the maintenance of muscle mass and function.

1.3.1.3. Drug therapy. The pharmacological treatment of hyperglycaemia in the elderly relies on the same principles and the same molecules than in younger patients. A detailed review of drug treatment is beyond the scope of this review. Treat-
• GLP-1 agonists or DPP-IV inhibitors are attractive in some specific points.

• Metformin is very frequently used in elderly diabetic patients. The risk of metformin-induced lactic acidosis is rare in the absence renal insufficiency [62]. Its use can be limited by digestive symptoms. Metformin is also associated with a reduced energy intake and possibly with vitamin B12 mal-absorption, which is important to consider in elderly patients at risk of malnutrition [63,64].

• Sulfonylureas are associated with a significant risk of hypoglycaemia, due to their direct effect on insulin secretion [65,66]. This risk is particularly high in elderly patients (>80 y.o.) or in the presence of chronic renal insufficiency. It is greatest with drugs that have a long elimination half-life (notably glyburide, carbutamide and glipizide), and can be minimized by choosing molecules with a short half-life [66]. Repaglinide and nateglinide are attractive alternatives, as they have a short half-life and probably less effect on insulin secretion in the absence of glucose [67,68]. However, they cannot be formally recommended for patients over 75 years old, due to the lack of data. They can be an occasional alternative to insulin in patients with renal failure [69].

• Alpha-glucosidase inhibitors inhibit the degradation of complex carbohydrates into simple hexoses. Although they often cause gastro-intestinal side effects, they are frequently used because of the absence of contra-indications and the low risk of hypoglycaemia.

• Glitazones are quite attractive as a specific treatment of insulin resistance. However, glitazone use is associated with an increased risk of salt/water retention and heart failure [70]. Age, renal failure or previous CV events are recognized risk factors for this complication [71,72]. Furthermore, glitazone use has been associated with a higher risk of osteoporosis and fractures in elderly women [73–75]. Thus, glitazones must unfortunately be avoided in most elderly patients.

• GLP-1 agonists or DPP-IV inhibitors are attractive in some situations but no specific information about their use in older diabetic patients is yet available.

• Insulin therapy is indicated in case of oral agent failure or severe, uncontrolled diabetes. All sorts of insulin regimens can be used, depending on the aims of the treatment, the risks of nocturnal hypoglycaemia and practical issues. The flexibility of the rapid-acting analogues and the simplicity of use of the long-acting analogues are advantages. Except in symptomatic uncontrolled diabetes, a moderate starting dose (0.25–0.35 units/kg/day) is recommended. Insulin requirements often decline with age, due in part to progressively worsening renal function leading to slower insulin degradation. Malnutrition may also decrease insulin resistance and insulin requirements [76]. Elderly patients tend to eat more in the morning than in the evening [77], which could decrease night-time insulin requirements. Insulin therapy can help to improve the general and nutritional status of older diabetic patients. It can justify a daily visit for injection by a nurse, which may improve overall care and thus help to avoid institutionalisation. More often than in the young, insulin therapy in the elderly is necessary due to contra-indications to oral agents, in particular renal failure. However, it cannot be taken for granted that insulin therapy has a lower risk of hypoglycaemia than oral agents [65]. The safety of insulin therapy clearly depends on proper administration, careful monitoring and education of the patient and his caregivers [78].

1.3.2. Treatment of arterial hypertension

The prevention of CV disease, in particular stroke is a major issue in the care of elderly diabetic subjects. However, there are no clinical trials specifically testing the effects of antihypertensive treatments in elderly diabetic subjects. Several trials have shown the efficacy of antihypertensive therapy is isolated systolic hypertension in subjects over 60 y.o. (average age approx. 70 years). The Syst-Eur trial using calcium-channel blockers and ACE inhibitors showed a non-significant reduction in the risk of myocardial infarction and mortality, but a large decrease in the risk of stroke (~42% over four years) [79]. A reanalysis of the diabetic subgroup showed a large reduction in the risk of stroke, other CV events and death. The absolute risk reduction was approx. 2% per year for stroke, an impressive figure [80]. Similar results, indicating particularly high benefits in diabetic patients, were obtained in the SHEP study, using a drug regimen including thiazide diuretics and betablockers [81,82]. In the Syst-Eur trial antihypertensive therapy had no detrimental effect on renal function and reduced the risk of incident proteinuria [83]. Several studies performed in type 2 diabetic patients aged 50–70 have shown a reduced risk of CV events, but their results must be extrapolated to elderly patients with caution [84–86]. The safety of antihypertensive in the very old (>80 years) remains a source of concern. A meta-analysis of the subgroups over 80y.o. from all major clinical trials has suggested a persistent benefit on the risk of stroke, but an increase in total mortality [87]. Reassuringly, the recently published HYVET trial testing the effects of indapamide (a diuretic) and perindopril (an ACE inhibitor) in patients over 80 y.o. has shown a reduction in the risk of stroke, heart failure and mortality [88]. However, this study included relatively low risk hypertensive patients with little comorbidity. Most studies in the elderly have included patients with a systolic blood pressure (SBP) over 160 mmHg. The effectiveness of treatment when the SBP at inclusion is between 140 and 160 mmHg remains uncertain.

In summary, the treatment of hypertension in the very old remains an attractive prevention of stroke, heart failure and CV events. Diabetes defines a high-risk category likely to derive particularly high benefits. The selection of antihypertensive drugs depends more on safety and tolerance than on specific pharmacological properties. Contrary to glycaemic control, antihypertensive therapy is beneficial within a relatively short time frame (1–5 years). However, in frail patients the benefits of treatment must be weighed against the risks of drug side-effects (polypharmacy) and the limited life expectancy.

1.3.3. Screening and management of diabetic complications

1.3.3.1. Geriatric syndromes. As reviewed above, diabetes is a strong risk factor for most geriatric syndromes, including functional disabilities, falls and fractures, incontinence, depression
and dementia, sarcopenia and malnutrition. Treatment strategies combining glycaemic control and regular geriatric assessment have been very little studied so far, and are an essential area for future research [89,90]. We have recently proposed such a strategy, which remains to be evaluated.\(^1\) Even at present, it seems nonetheless obvious that the systematic detection and early care of geriatric syndromes has an enormous potential to improve patients’ functional prognosis and quality of life. A systematic approach is necessary as patients are often quite reluctant to mention symptoms unless specifically asked. In practice the efforts required are modest and often quite rewarding. A history of impaired function (in particular walking), falls, incontinence, weight loss and reduced food intake can easily be elicited in a diabetologist’s consultation. Dementia and depression must be regularly screened for to allow early treatment. They are also possible causes of poor or deteriorating diabetes self-management skills. Their diagnosis should prompt a reorganization of diabetes care, which must sometimes be transferred to family members or professional caregivers.

The importance of pharmacological and non-pharmacological diabetes treatment in the prevention of malnutrition, sarcopenia, falls, fractures and functional impairments has already been emphasized.

1.3.3.2. Diabetic foot disorders in the elderly. The prevention and treatment of diabetic foot disease in the elderly has recently been reviewed [91]. The prevalence of the main risk factors (foot deformities, neuropathy and PAD) increases with age, leading to progressive increase in the risk of foot ulcers or lower extremity amputations [92,93].

Prevention in high-risk subjects basically relies on the same principles than in younger patients. Appropriate footwear, trauma avoidance, regular foot inspection and podiatric care are essential, but must be considered in the context of the patients’ lifestyle. For instance, when prescribing appropriate footwear, the practitioner should consider that many patients spend most of their time at home, usually barefoot. …

The treatment of foot ulcers relies on pressure relief, wound debridement, and the management of infection and ischemia. All these interventions remain just as important in elderly patients. Particular attention should be paid to comorbidities and functional impairments. Many interventions such as sophisticated pressure relief devices or orthopedic and vascular surgery are limited by the patients’ functional status or prognosis. In these cases dedicated wound care is the best approach, even if it tests both the patient’s and the physician’s patience. While the general principles of prevention and care of foot disorders are clear, they must be carefully adapted to the patients’ individual situations.

1.3.3.3. Diabetes-related kidney disorders. The incidence of patients with diabetes and end-stage renal failure has increased progressively in the past decades in all industrialized countries [94,95]. Besides the increasing prevalence of diabetes, a major factor is presumably diminishing mortality from hypertension and cardiovascular causes, so that patients survive long enough to develop kidney failure [94].

Diabetic nephropathy in type 1 diabetes is a predominantly glomerular disease progressing through the stages of hyperfiltration, microalbuminuria (urinary albumin excretion rate 30–300 mg/24 h or urinary albumin/creatinine ratio 30–300 mg/g), overt proteinuria (urinary albumin excretion rate > 300 mg/24 h or urinary albumin/creatinine ratio > 300 mg/g), renal insufficiency (glomerular filtration rate (GFR) 15–60 ml/min), and kidney failure (GFR < 15 ml/min); in this context microalbuminuria is a strong risk factor for more severe nephropathy [96]. However, in type 2 diabetes renal disease can result from other causes, in particular hypertension. Chronic renal insufficiency often presents without microalbuminuria or diabetic retinopathy [97] and is associated with an increased risk of CV events and mortality in elderly populations [98]. Conversely, microalbuminuria cannot be assumed to represent early diabetic nephropathy in type 2 diabetes [99]. It remains a strong predictor of CV events [84,100] but not of chronic renal insufficiency [95,101,102].

From these data it seems logical to screen elderly patients with diabetes for renal disease by yearly determination of both albuminuria and serum creatinine [95]. The latter should be used to calculate creatinine clearance with either the Cockcroft or the MDRD formula, using online calculation tools (http://nephron.com/cgi-bin/MDRDSIdefault.cgi). Indeed, due to age and a decreased muscle mass, a “normal” serum creatinine level does not exclude significant impairment in GFR [103].

- Microalbuminuria is a strong CV risk factor in the elderly. The HOPE study has shown that treatment with ACE inhibitors (Ramipril) is particularly worthwhile in patients with diabetes and microalbuminuria even in the absence of hypertension, in patients with a mean age of 65 [84]. However, it is unclear whether this strategy is effective in older, frail patients.
- Overt proteinuria is a clear risk factor for progression to kidney failure. It requires specific therapy, including treatment with ACE inhibitors or angiotensin receptor blockers [104].
- Moderate renal insufficiency (GFR 30–60 ml/min) does not require specific interventions. However, physicians must be aware of this condition which may require dose adjustments for drugs with renal elimination and puts patients at increased risk from nephrotoxic drugs. Low protein diets can delay the progression of renal insufficiency [95] but may favor malnutrition and sarcopenia.
- The care of patients with severe renal insufficiency (estimated GFR 15–30 ml/min) or with kidney failure (estimated GFR < 15 ml/min) has recently been reviewed [105]. It is essentially the same than in the young, although the decision to enter dialysis or renal transplantation must obviously consider age, comorbidities, life expectancy and local/national health policies among other factors.

1.3.3.4. Eye disease in the elderly. The epidemiology of diabetic retinopathy in the elderly is poorly studied. Several studies have shown a high prevalence of diabetic retinop-
thy (>40%) in elderly diabetic populations. However, the prevalence figures vary widely with age, diabetes duration, diagnostic criteria, survival bias and secular trends [106–108]. The risk of retinopathy is more related to diabetes duration than to age. The progression to (sight-threatening) proliferative retinopathy is actually decreased by age, even though the risk of macular edema persists [107,109]. Proliferative retinopathy is occasionally found in newly diagnosed type 2 diabetes [108].

Other age-related eye disorders must be considered in elderly diabetic patients. Diabetes is a strong risk factor for cataract [110,111]. Diabetes is not a significant risk factor for age-related macular degeneration [112] or glaucoma [113]. However, the prevalence of cataract, glaucoma and age-related macular degeneration all strongly increase with age [114].

There are no age-specific guidelines for the screening of diabetic retinopathy. A yearly complete eye exam, with a first exam at diabetes diagnosis should be performed, as recommended by the American Diabetes Association (ADA) [115]. The possibly lower rate of progression to proliferative retinopathy in the elderly is an argument for less frequent exams. However, regular complete eye exams also allow the screening and early treatment of the other, age-related eye disorders. Early detection of visual loss is of obvious importance for preserving quality of life, and possibly the patients’ diabetes self-management skills. Less frequent exams (every 2–3 years) may be considered following one or more normal eye exams.

There are no major age-related specificities in the treatment of diabetic retinopathy. Concerning prevention, it is important to underline that treatment of hypertension in quite effective also in the prevention of retinopathy [116]. The use of ACE inhibitors or angiotensin II receptor blockers has been advocated for the prevention of retinopathy, even in normotensive subjects. However, according to the recently published DIRECT trial, this approach has quite limited benefits [117]. Diabetic retinopathy is not a contra-indication for the use of antiplatelet drugs for CV prevention [115].

2. Conclusions

We clearly need more research on the epidemiology of diabetes and its complications in the elderly, the impact of diabetes on geriatric syndromes and optimal management strategies. However, it seems clear that elderly patients could derive major benefits from an approach to diabetes management that includes the prevention, screening and management of geriatric syndromes as well as conventional diabetic complications. The treatment of hyperglycaemia, including its non-pharmacological aspects has a great potential impact on diabetic symptoms (including cognitive impairment) and on the prevention of malnutrition, sarcopenia and functional impairments.

Conflict of interest

None of the authors have a conflict of interest to declare individually.

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