

## Disability and quality of life in elderly people with diabetes

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### **Abstract**

To implement preventive policies of disability in older diabetic people, the role of diabetes in the disablement process should be investigated. Diabetes mellitus is consistently associated with a higher prevalence of disability at all states, as well as with a progression in disability states and may be considered as a brake on recovery. This association is partially explained by existing complications, associated conditions (obesity, depression, hypertension) treatment burden, and other social characteristics (lower income, lower educational level). Finally, in the disablement process, the role of altered muscle metabolism due to diabetes, aging, nutrition and sedentary lifestyle may represent a major target for interventions to improve functions and potentially activities in elderly people.

The elderly part of the population is now concerned with the worldwide diabetes epidemic. In France, it is estimated that, among people with diabetes taking hypoglycemic medications, half are older than 65 y and a quarter are older than 75 y [1]. The prevalence of diabetes is 11% in people older than age 65 y living in France, and ranges, in the world, between 10 and 25 % in that age-group. The increasing prevalence of obesity and the trend towards an increasing life expectancy are likely to accentuate this phenomenon. Projections for France predict that in 2016, about 1 million more people will have diabetes, raising the prevalence from 3.16 to 4.49 %, overall, or from 11,15 to 12,75% in the age group over 65 y. In this model, 41 % of this increase will be due to population aging, 47% to obesity and 12% to the population increase [2].

Diabetes mellitus is a well-known disability-inducing-condition in young people, and is recognized as a frailty condition in the older ones [3]. However, the relationships between diabetes on one hand and disability and quality of life on the other hand have not been fully explored. Potential interactions of comorbidities, diabetes complications, diabetes treatments, as well as aging itself, may well interfere with this relationship. To reach population expectations for active and healthy aging, and to lower the social costs induced by disability, the challenge of modern social society and of the health care system is to promote efficient ways to increase disability-free life expectancy, including for people with diabetes.

In this review, we aimed to describe the role of diabetes mellitus in the disablement process in people older than 65 y and to identify possibilities of disability prevention in elderly people.

## ***Disability: concepts of functional limitations and activity restrictions***

### Definitions

The model of the disablement process usually distinguishes four linked phenomena: 1) an active pathology or disease, 2) impairment, 3) disability and 4) social handicap/disadvantage [4]. In the International Classification of Functioning, disability and health (ICF) (Figure 1), disability has been further broken down into functional limitations and activity restrictions due to these limitations: it is possible to maintain activities despite functional limitation owing to compensatory strategies and to interventions such as rehabilitation or assistance [5]. Handicap or social disadvantage refers for a given person to limitations to fulfill a normal social role.

### International Classification of Functioning, disability and health (ICF)

Recently, the World Health Organization (WHO) constructed the new ICF to provide a comprehensive tool to delineate the different components of disability in various chronic conditions. This tool is recommended by WHO in health research and surveillance [6]. In ICF 2001, the term “handicap” is replaced with “participation restriction”, which better describes social consequences of disability. The ICF includes extensive lists of items describing body structures, body functions, activities and participation, and environmental factors. The use of ICF to explore the consequences of a given condition in public health relies on specific models. For instance, WHO organized a consensual construction of specific ICF core sets [7], including a specific ICF core set for people with diabetes mellitus [8] and for geriatric patients in post-acute care [9]. However, to our knowledge, no research paper has used these two sets until now, probably because of their lack of organized assessment scales, because of their exhaustivity and lack of organized assessment scales.

### Other disability scales

In the elderly population, functional limitations and activity restriction have been previously explored in epidemiological research using several tools. The more severe level of disability is a restriction in activities of daily living, expressed as ADL, [10], which includes

activities as bathing, dressing, indoor locomotion, toileting and eating. Continence is also often included in ADL scales, while it may be more considered as a functional limitation rather than a restricted activity. However, social disadvantage associated with this limitation is well recognized.

A commonly used generic ADL scale is referred as the Barthel index [11], which was initially built for people with stroke, and includes 2 items related to continence and climbing stairs. The functional independence measure (FIM) is a mixed scale evaluating ADL, communication and social participation [12].

A previous step in disability severity may be identified as a restriction in instrumental activities of daily living (IADL)[13]. These activities are mainly linked to cognitive capacities and include abilities for telephoning, shopping, transferring using transportation, and managing medications and finances.

Lastly, mobility restriction for heavy tasks may be assessed using the Rosow and Breslaw scale: doing heavy housework, walking half a mile and climbing stairs [14]. It is possible to construct a hierarchical model of disability, ranging from full independence to severe disability [15]. Restriction in mobility is named mild disability, restriction in both mobility and IADL is named moderate disability, and severe disability involves the three levels of activity restriction.

#### Indicators of social disadvantage, participation restriction and quality of life

Assessment studies of social participation in the elderly are scarce. The Assessment of Life Habits (LIFE-H) is a scale which includes 77 items in 12 domains, 6 ADL and IADL measures and 5 social roles such as responsibilities, interpersonal relationships, community life and recreation tested in various populations and in particular in the elderly [16]. Assessment of difficulties in carrying out these roles is based on the subject personal judgment.

Quality of life questionnaires are mostly used in epidemiological or clinical research to assess the subject social participation. The MOS 36-Item Short-Form Health Survey (SF-36) [17] is now widely used. It includes one multi-item scale that assesses eight health concepts: limitations in physical activities because of health problems; limitations in social activities because of physical or emotional problems; limitations in usual role activities because of physical health problems; bodily pain; general mental; limitations in usual role activities because of emotional problems; vitality; and general health perceptions.

#### ***Social disadvantage in elderly people with diabetes***

It has been shown in various populations that people with diabetes have a lower income and a lower level of education than others [18, 19]. The socio-economic level itself may impact disability. Relationships between social activities/quality of life and disability could be reciprocal. In a study involving about 9,000 elderly people with diabetes with no ADL disability at baseline, social disengagement was measured at the initial examination using SF-36 and two questions with graduate responses: 1 “During the past 4 weeks, to what extent has your health or emotional problems interfered with your social activities?”, 2 “During the past 4 weeks, how much of the time has your health or emotional problems interfered with your social activities?”. The 2-year incidence of ADL disability was proportionally related to the degree of social disengagement, when controlled for age, sex, depression and other comorbidities [20]. However, this finding may not be specific of diabetes and is probably shared with other chronic diseases.

Hospitalization rates may increase with diabetes condition, even in the oldest age. Compared to people without diabetes of similar age, hospitalizations were more frequent in people with diabetes. While this difference decreased with age, it remained significant in the oldest age group within a north-American study.[21]. The costs related to hospitalizations or

other resources were 60 % higher in older Medicare beneficiaries with diabetes than in their counterparts without diabetes [19].

It has been shown in one study that personal health goals expressed by elderly people with diabetes were to maintain functional independence and to control blood glucose levels [22]. However, patients may anticipate different ways to achieve these goals than what their medical practitioners would recommend. In this latter study, patients were mainly focused on drug regimen but had poor adherence to diet and exercise, which are particularly recommended in this population.

Diabetes treatment may induce differences in quality of life in older people with diabetes. In a study, older people treated with insulin had a lower well-being and treatment satisfaction than those on diet or tablets, but this difference was not significant when controlled for diabetes duration. In this study, subjects were relatively young (age: 71 +/- 7 y, and 69 +/-7 y) [23]. Another study showed improvement in well-being and treatment satisfaction after 7 months of insulin therapy in people ranging from 39 to 81 y old [24]. Specific investigations of quality of life with respect to treatment in very old people with diabetes are lacking.

In the elderly population, an indicator of extreme social disadvantage due to disability could be the admission to geriatric institutions. Indeed, it reflects the need for sustained assistance due to severe activity restrictions. In elderly people with diabetes, insulin treatment in particular may lead to IADL dependence for treatment management and to institutionalization. A previous level of social disadvantage is the need for human help at home, either for nursing, for treatment monitoring or for supervision.

#### Remarks

It is important to note that the level of disability may be assessed at different examinations. Owing to possible changes in body structure, function, or adaptation, disability can move from one level to another one. The recognition of transitions from a level to another one, either less or more severe, necessitates close iterative assessments. The study of Hardy and coll., using monthly phone assessments of ADL, has shown that disability periods occurred frequently in elderly subjects and that an initial low gait speed is a bad prognostic factor for such transitions [25].

In the case of diabetes, to examine the disablement process in people older than 65 y implies to closely monitor potential confounding factors for the diabetes-disability relationship, such as comorbidities, diabetes complications and associated conditions, diabetes treatments, as well as aging itself.

#### ***Impact of diabetes characteristics on disability within populations with diabetes including elderly people***

It comes readily to mind that, within populations with diabetes, diabetes complications and associated disorders such as cardiovascular diseases, hypertension, obesity or depression induce several alterations to body functions and structures (Table 1). The consequences of heart (Beauduceau, Verny), eye (Kaloustian) and feet (Visher) alterations in structure and function have been well delineated, and we previously reported on the impact of diabetes on cognition, stroke and depression [26]. These alterations seem in day to day practice largely sufficient to explain the observed activity restrictions.

In the diabetic population of all ages of the Fremantle Australian cohort, independent 4.5-year predictors of new mobility disability were an older age, cerebrovascular disease, current smoking, insulin treatment, microalbuminuria, neuropathy, arthritis, unmarried status, and not exercising [27]. Independent predictors of ADL disability were an older age, cerebrovascular diseases, not exercising, intermittent claudication, mobility problems,

depression, and social difficulties. Within this population, baseline HbA1c was not related to disability occurrence.

Depression, and particularly major depression, has been confirmed as an additional factor of motor disability in people with diabetes of all ages [28]. Depression can be considered as an associated condition to diabetes [26]. Psychological factors can interact on several ways with the occurrence of complications. It has been shown in 370 people with diabetes older than 65y and followed-up for 3 years that the absence of a positive attitude toward aging was an independent risk factor for stroke [29]. In this latter study, a longer duration of diabetes, but not baseline HbA1c level, was also associated with a stroke risk increase.

### ***Impact of diabetes on disability in cross-sectional population-based studies including elderly people***

To study the effect of diabetes on disability and control for comorbidities and aging, it is important to compare disability levels in people with and without diabetes. In most of cross-sectional studies of general populations, diabetes is associated with mild to severe disability. For example, in the French PAQUID study which involved a large (4000) representative sample of people older than 65 y, diabetes was associated with ADL, IADL and mobility disability at the baseline examination [18]. Similar results were found according to these three types of activity restriction in elderly Chinese [30], African-Americans [31], and in Italians for ADL, with no information for IADL and mobility in the latest [32].

In Hispano-Americans aged older than 65 y of the EPESE study, diabetes (prevalence 22%), as well as obesity and underweight (Body mass index, BMI < 21 kg/m<sup>2</sup>), arthritis, cancer, cardiovascular diseases, age over 75 y, visual impairment, and female sex were independently associated with decreased performance in balance and gait [33]. Hip and knee motions impairments were limiting factors for gait. It has been reported in other studies that the relationship between diabetes or arthritis and these motion impairments were fully explained by obesity or increased BMI [34]. Increased plasma IL-6 concentration, a marker of chronic inflammation, was linked with each domain of activity restriction in the 1737 elderly people of the EPESE cohort. In this latter study, hypertension and smoking, but diabetes, were predictive of increased IL-6 [35].

Falls are major events on the way between disability and participation restriction. It has been demonstrated that elderly people with diabetes could be at increased risk for falls, which was partially explained by visual impairment, pain and light touch misperception [31]. Among the adult female population older than 20 years of the NHANES study (diabetes prevalence 16.8%), incontinence was twice as frequent in diabetic women than in others. Furthermore, incontinence was related to the presence of microvascular complications such as neuropathy or nephropathy [36].

In the Women's Health and Aging study, Leveille and coll. investigated the impairment at the origin of restriction of any activity as recognized by women themselves [37]. The authors stated that, unless they are severely cognitively impaired, people are likely to know why they had to stop a given activity, and that people best identify the last impairment that occurred in the loss of this activity. In this study, women with diabetes complained from weakness as the origin of their ADL incapacity. Women with cardiovascular diseases reported a limitation due to loss of endurance capacities.

In another study, Spanish people older than 65 y were likely to attribute their disability (ADL impairment) to arthritis and old age, but not diabetes. However, 10 % of this population had diabetes, which ranked fourth in ADL deficiency predictors (OR: 2.75, 95% CI 1.65-4.56) behind cerebrovascular disease, depression and anxiety disorders, and heart disease [38]. Thus, awareness of diabetic people about diabetes impact on their quality of life may be

low. Self-reported mental health (reported anxious feelings and tiredness) has also been studied in people with diabetes of all ages [39]. Symptoms of anxiety were more frequent in people with diabetes aged 45-74 y than in healthy people of similar age; however, in the oldest age group (75-84 y), no difference was found. Conversely, the difference in tiredness between people with and without diabetes was more pronounced in the 65-84 y range of age than in the youngest group.

To estimate the part of a disability attributable to a chronic disease or impairment is required for prevention. Indeed, a given condition can induce a major disability, but the real population impact depends on the prevalence of this condition. In the Leiden 85-plus study, which included people older than 85 y living in Netherlands, walking disability [40] was measured using a standardized timed 3-meter and walking back and forth at quick speed. The total walking speeds were divided into quartiles respectively in men and women and walking disability was defined by a speed below the 25th lowest quartile. In multivariate cross-sectional analyses, diabetes mellitus was associated with a 2.1 (95% CI: 1.0-4.4) increased prevalence of stroke and a 2.5 (95% CI: 1.5- 4.3) increased prevalence of walking disability, but a 4.1 (95% CI: 2.1-7.7) increase in cognitive impairment and a 3.5 (95% CI: 2.0-6.1) increase in depressive symptoms. Diabetes mellitus contributed to 9 % of walking disability, cardiovascular diseases to 21 %, cognitive impairment to 24 % and depressive symptoms to 27 %. However, this transversal study can not provide the true responsibility of a given condition in the process leading to disability, which is time-dependent.

The Rotterdam study provided another cross-sectional analysis of locomotion disability predictors. It included the assessment of 6 functions related to lower limbs: walking, climbing stairs, getting in and out of bed, bending and rising from a chair [41]. Subjects were much younger with a mean age about 69 y ranging from 55 to 94 y. The prevalence of diabetes was 11.5% and increased with age. The fraction of locomotion disability attributable to diabetes mellitus was 17.8% in men and 26.6% in women. Vascular complications, hypertension, obesity, or visual impairment were included in the model but did not fully explain the role of diabetes.

### ***Impact of diabetes on disability in longitudinal population-based studies including elderly people***

Longitudinal studies are better settings to study a potentially causal relationship between diabetes and incidence of disability, and several studies are available. In all community dwelling subjects older than 65 y living in a city in Japan and without baseline functional limitations, a 7-year longitudinal study assessed disability using scale mixing impairments and activity restrictions in four domains: mobility, toileting, mental status (behavior mainly) and nutrition [42]. This study showed that among chronic conditions, diabetes was a risk factor for the occurrence of disability in women (multivariate analysis, RR 1.5, 95% CI, 0.2-13.2) but not in men.

In the study of the Osteoporotic Fracture, about 6000 women older than 65 y were investigated, among whom 6.8% had diabetes. The age-adjusted risk for falls was 1.53 (95% CI 1.14-2.04) for people with diabetes and 3.98 for the sub-group on insulin treatment (95% CI 2.27-7.05) [43]. While the authors controlled for several risk factors for fall and neuropathy, they did not adjust for diabetes duration, and the association was significant only in women on insulin treatment. In another study, we showed that fall was a potent risk factor for institutionalization among elderly hospitalized people [44]. Thus, when providing medical care for elderly people with diabetes, particular attention should be given to the risk of falling, keeping in mind the goal of preventing a wide range of social disadvantages.

In the large Nurses' Health Study, including women aged 30-55 y at baseline, the risk for 20-y incident self-reported urinary incontinence was increased if diabetes has been

reported at any visit of the follow-up (RR 1.21, 95% CI 1.02-1.43) [45]. Particularly the risk of severe incontinence incidence, defined as at least weakly leakage of a quantity of urine enough to wet outer clothing or the floor, was increased in diabetic women. Furthermore, the risk of incontinence was associated with diabetes duration [45].

In the Women's Health and Aging study, disabled people were enrolled in a 3-year follow-up study of cognitive and physical decline if they had baseline MMSE score higher than 24 and gait speed higher than 0.4 m/s [46]. The association between diabetes diagnosis and physical decline, i.e. decrease in gait speed, was not significant while baseline low gait speed, smoking, and IADL impairment predicted physical decline. Anemia, baseline MMSE and IADL impairment, and current smoking were independent predictors of combined physical and cognitive decline in these elderly women. In the physically impaired group of these women, diabetes majored the risk of disability worsening, which was partially explained by other comorbidities [47]. Adjustment on HbA1c level reduced the risk of ADL impairment by 65% [48]. The authors noticed that the differences in dependency progression according to diabetes appeared after a period of 18 months. In the same cohort, peripheral nerve dysfunction was extremely frequent, concerning 58% of these women [49]. A woman older than 85 y had about a two-fold risk of peripheral neuropathy, and this risk was even increased in case of diabetes diagnosis [50]. This was associated with higher frequency of impairment in gait and balance but not with change in muscle strength. In a model predicting gait and balance impairment, diabetes was not a significant contributor when controlled for peripheral neuropathy.

In the British Medical Research Council Cognitive and Ageing study, 10,582 people were included who were not disabled at baseline and were followed up to two years for ADL and IADL disability incidence. The prevalence of treated diabetes was 4.8% in people older than 65 y. Diabetes predicted disability independently of cerebro- and cardiovascular diseases, hypertension, sensory problems, cognitive impairment, marital status, social class and level of education [51].

The clinical trial PROSPER investigated the effects of pravastatin in a cohort of 70-82 y old people with cardiovascular risk factors. In this study, diabetes and female sex were predictors of 3-year ADL and IADL decline independently of non fatal strokes or myocardial infarction [52].

In the 7-year follow-up of the Mexican-American study, H-EPESE, the prevalence of self-reported diabetes was 18.9% and mean diabetes duration was 11 years, among 1835 people aged older than 65 y reporting no ADL limitation at baseline [53]. ADL limitation, mobility limitation or gait time higher than 9.0 s for a 2.5 m walk defined a lower body disability. Diabetes was associated with the occurrence of all lower body disability items, independently of age, sex, visual or cognitive impairment, cardiovascular diseases, stroke, hypertension, arthritis, obesity, hip fracture or cancer. Among people with diabetes, an older age and an amputation were factors associated with an increased of any lower body disability item but none other covariate was associated with diabetes.

Similar results were found in a cohort of women followed during 12 years with measurement of IADL and mobility limitation [54]. The authors estimated the effects of diabetes to those of a crude 7.4 year-aging and 4.5 year-aging when controlled for co-factors. A strong interaction between age and diabetes was found. In the oldest age range (> 80 y), the effect of diabetes on increasing disability was not significant (see Figure 2). The authors advocated a survival bias or a selective loss of follow-up of the oldest women with diabetes compared to their counterparts without diabetes. However, this explanation is not convincing, because the authors did not estimate the potential selective attrition of the cohort.

In the majority of these reports, the effect of diabetes is independent of stroke. However, strokes can only be spotted in epidemiological surveys if they involve a large area

of infarction or hemorrhage. The impact of lacunae infarctions is much less easily investigated. One 5-year prospective study reported that diabetes was associated with a two-fold risk of progression of Parkinson-like syndrome and gait disorders in a population aged 65-75 y old at baseline [55].

The H-EPESE cohort was investigated to analyze changes in lower body disability according to changes in body weight [56]. Of the 1,737 subjects, 21.7% lost 5% or more of their initial weight, 20.6% gained 5% with no difference according to diabetic status. In univariate analyses, weight loss or weight gain > 5% was predictive of two-year ADL disability. However, after adjusting for chronic medical conditions including diabetes and arthritis, weight changes were no more independent risk factors for disability. The authors suggested that weight changes, which usually are not voluntary, were associated with worsening of the health status mostly due to the chronic conditions.

The AHEAD survey included 3 waves of assessment in households including at least one person older than 70 y to study the disablement process during a 5-year period. About 4200 subjects were explored at each visit. The originality of this study was to describe baseline medical conditions and onset of conditions. Behavioral, ethnic and social conditions were also included in the model to analyze ADL and IADL impairment [57]. A baseline diagnosis of diabetes significantly altered autonomy for bathing and bed transfer for ADL limitations and use of the phone and grocery shopping for IADL. The onset of diabetes in between waves had a significant effect only on toileting for ADL and using the phone for IADL. However, no interpretation of these specific alterations was put forward by the authors or comes into mind.

### Transitions in disabilities

Transitions in disabilities have been much less examined. In the 10-year follow-up of the French PAQUID study, transitions between four levels of disability, defined as none (state 0), mild (state 1), moderate (state 2) and severe (state 3), were analyzed. People were evaluated 6 times during a 10-year period and thus, only long-term changes were described [15]. In the model, pathologies such as cardiovascular disease, stroke and diabetes, and impairments such as cognitive and visual impairments and dyspnea were included. Behavioral factors (wine and tobacco consumption), social factors, depressive symptoms, and other health indicators such as multiple drug consumption and hospitalization during the previous year were also included. In all models, diabetes was a significant risk factor for progression from a disability state 1 to 2 (TIR transition intensity ratio, 1.4, 95% CI 1.1-1.6) and a negative factor for recovery from state 1 to 0 (TIR, 0.6, 95% CI 0.4-0.8). Other risk factors for disability progression were an age over 80 y, stroke, cognitive impairment and depressive symptoms at all states, while female gender, cognitive and visual impairments, and dyspnea were negative factors for recovery at all states. A high level of education was also associated with a lower rate of disability progression.

As a summary of population-based studies on the relationship between diabetes and disability in elderly people, diabetes mellitus is consistently associated with a higher prevalence of disability at all states, as well as with a progression in disability states. Diabetes is also often associated with a lower rate of health recovery and with a weakness feeling. Thus, diabetes mellitus may be well considered as a frailty factor. However, the reasons and mechanisms of these deleterious effects of diabetes on disability need to be clarified.

### ***Muscle function and diabetes***

An interesting hypothesis for the mechanisms that may partially explain the impact of diabetes on disability relies on muscle function. The Japanese-American men cohort of the

Honolulu heart program reported that conditions such as diabetes (prevalence 17.0%), arthritis, coronary heart disease, stroke, chronic obstructive lung disease were predictive of a 2-year later grip-strength disability in the old age (71-96 y) [58], while hypertension had a protective effect. Grip strength disability was defined by the lowest 10<sup>th</sup> percentiles of old-age handgrip strength, with the cut-off point being 21 kg for these men. In this study, body weight loss during the previous 25-year follow-up, as well as older age, increased the risk of steep handgrip strength decline. The results of this study provides an echo to the women with diabetes who complained of weakness in the Women Health and Aging study [37]. The authors [58] suggested that diabetes could alter strength due to the effects of insulin resistance. However, a limit of this analysis is the late assessment of medical diagnosis, which was undergone in the latest 2 years of the follow-up.

In a population-based transversal study, weight-adjusted handgrip strength decreased with glucose tolerance, from normal glucose tolerance, impaired glucose tolerance to newly diagnosed or known diabetes, in 1,391 men and women [59]. In this study, no consistent relationship was found between fasting insulin and handgrip strength. Insulin resistance was suggested as one of the mechanisms at the origin of muscle mass loss during aging [60].

However, an apparent contradictory result comes from the Health, Aging and Body Composition study which reported that muscle mass was higher in elderly (70-79 y) people with diabetes compared to elderly people without diabetes. Furthermore, in this study, muscle mass was higher when diabetes control was poorer (HbA1c > 7%) [61]. Despite these findings, muscle strength was lower in people with diabetes, suggesting once more a lower muscle quality, particularly in relation with longer diabetes duration and poor glucose control (HbA1c > 8.5%). Indeed, metabolic muscle abnormalities associated with diabetes potentially decrease the quality of muscle defined as the power per unit of muscle mass.

Insulin resistance reduces the rate of glycogen synthesis in muscle, an effect attributed to an increase in plasmatic fatty acids [62]. <sup>13</sup>C magnetic resonance spectroscopy allows an iterative and non-invasive quantitation of glycogen. It has been reported that basal muscle glycogen content was sub-normal in people with diabetes and that post-meal muscle glycogen synthesis was related to post-prandial insulin increment only in controls [63]. Muscle glycogen is used in type II fibers, in type IIb, exclusively using the anaerobic pathway and in type IIa using both anaerobic and aerobic metabolism. High and short intensity muscle contraction is mediated by anaerobic ATP production and the use of glycogen stores instead of glucose could represent energetic cost-effective pathway, associated with less muscle fatigue [64]. Furthermore, the highly-potent type IIa fiber permits sustained efforts, due to the oxidation of glycogen by mitochondrion [65]. Indeed, muscle glycogen content may be particularly decreased in types IIa fibers of people with diabetes [66]. In those people, fuel disposal seems to be of poorer quality than in others due to insulin resistance, and is associated with lower performance.

A high carbohydrate diet has shown efficiency in improving the insulin-stimulated glucose disposal and weight loss in elderly, with no additional effect of exercise [67]. However, concomitant exercise induced a greater muscle glycogen content than diet alone. Another study reported that a 6-month endurance training and aerobic exercising had similar effects in improvement of the insulin sensitivity and strength in older subjects [68]. A higher stimulation of glycogen synthase activity was noticed after aerobic training.

Another source of poor muscle performance is the muscle oxidative capacity due to lower muscle mitochondrial content, with an important role of training. Disuse is reported to induce a decrease in mitochondrion muscle content, but contractile activity produces mitochondrial biogenesis, inducing an increase in the total muscle oxidative capacity [69]. Clinically, the steady state of mitochondrial density was achieved within 6 weeks of training or disuse. Indeed, using <sup>31</sup>P magnetic resonance spectroscopy, we previously reported that

muscle oxidative capacity was related to ADL score in frail non-diabetic hospitalized subjects, and that the higher ADL disability, the lower oxidative capacity [70]. Another source of decreased oxidative capacities could be insulin resistance itself [60]. Insulin has been shown as a modulator of mitochondrial protein synthesis and insulin resistance could break mitochondrial biogenesis.

Thus exercise training could improve muscle performance through at least two pathways: improving insulin sensitivity and increasing the muscle oxidative capacities. In elderly people, this may have an effect independent of diabetes complications. However, the effect of exercise on muscle metabolism and function has not been fully investigated in elderly people with diabetes.

## **Conclusions**

With population aging, people expectancies for active and healthy aging, and our health care resource limits, a major challenge relies on the promotion of efficient ways to increase disability-free life, including for people with diabetes. More research in this area should be undergone.

Several scales exist to precisely measure disability, and a new tool, the ICF 2001 [6] has been recently developed by WHO, with a specific adaptation to elderly people and those with diabetes. When studying the relationship between diabetes and disability, one should consider measuring potential confounding factors, such as diabetes complications, associated conditions and comorbidities, and different age groups. Cohort studies should produce iterative measurements of disability and transitions analysis.

In previous studies, diabetes not only represented a risk factor for disability but also a brake on health/autonomy recovery in elderly people. However, this association is partially explained by the impact of diabetes complications and associated conditions on disability (Table 1). Discrepancies in studies have been found about the true impact of glucose control on the onset of disability. The impact of diabetes on disability may decrease in the very old age range. However, in this very old group, the analysis is more and more difficult as the number of comorbidities increases.

Finally, in the disablement process, the role of altered muscle metabolism due to diabetes, aging, nutrition and sedentary lifestyle may represent a major target for interventions to improve functions and activities in elderly people.

## References

1. Fagot-Campagna A, Bourdel-Marchasson I, Simon D. Burden of diabetes in an aging population: prevalence, incidence, mortality, characteristics and quality of care. *Diabetes Metab* 2005;31 Spec No 2:5S35-5S52
2. Bonaldi C, Romon I, Fagot-Campagna A. Impacts du vieillissement de la population et de l'obésité sur l'évolution de la prévalence du diabète traité : situation de la France métropolitaine à l'horizon 2016. *Bull Epidemiol Hebd* 2006: 69-71
3. Bourdel-Marchasson I, Berrut G. Caring the elderly diabetic patient with respect to concepts of successful aging and frailty. *Diabetes Metab* 2005; 31 Spec No 2: 13-9
4. WHO. Internal Classification of impairments, disabilities and handicaps: a manual of classification relating to the consequences of disease. Geneva: WHO, 1980
5. Jagger C, Barberger-Gateau P, Robine JM. Disability in older people--indicators, process and outcomes. *Disabil Rehabil* 2005; 27: 209-12
6. WHO. Internal Classification of Functioning, Disability and Health: ICF. Geneva: WHO, 2001
7. Ustun B, Chatterji S, Kostanjsek N. Comments from WHO for the Journal of Rehabilitation Medicine Special Supplement on ICF Core Sets. *J Rehabil Med* 2004: 7-8
8. Ruof J, Cieza A, Wolff B, et al. ICF Core Sets for diabetes mellitus. *J Rehabil Med* 2004:100-6
9. Grill E, Hermes R, Swoboda W, Uzarewicz C, Kostanjsek N, Stucki G. ICF Core Set for geriatric patients in early post-acute rehabilitation facilities. *Disabil Rehabil* 2005;27: 411-7
10. Katz S, Downs TD, Cash HR, Grotz RC. Progress in development of the index of ADL. *Gerontologist* 1970; 10:20-30
11. Mahoney FI, Barthel DW. Functional Evaluation: The Barthel Index. *Md State Med J* 1965; 14:61-5
12. Guide for the Uniform Data Set for Medical rehabilitation (Adult FIM), version 4.0. Buffalo: State University of New York at Buffalo, 1993
13. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; 9: 179-86
14. Rosow I, Breslau N. A Guttman health scale for the aged. *J Gerontol* 1966; 21: 556-9
15. Peres K, Verret C, Alioum A, Barberger-Gateau P. The disablement process: factors associated with progression of disability and recovery in French elderly people. *Disabil Rehabil* 2005; 27: 263-76
16. Desrosiers J, Noreau L, Rochette A. Social participation of older adults in Quebec. *Aging Clin Exp Res* 2004; 16: 406-12
17. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992; 30: 473-83
18. Bourdel-Marchasson I, Dubroca B, Manciet G, Decamps A, Emeriau JP, Dartigues JF. Prevalence of diabetes and effect on quality of life in older French living in the community: the PAQUID Epidemiological Survey. *J Am Geriatr Soc* 1997; 45: 295-301.
19. Salas M, Bubolz T, Caro JJ. Impact of physical functioning of health status on hospitalizations, physician visits, and costs in diabetic patients. *Arch Med Res* 2000; 31: 223-7
20. Kuo YF, Raji MA, Peek MK, Goodwin JS. Health-related social disengagement in elderly diabetic patients: association with subsequent disability and survival. *Diabetes Care* 2004; 27: 1630-7
21. Naslafkih A, Sestier F. Diabetes mellitus related morbidity, risk of hospitalization and disability. *J Insur Med* 2003; 35: 102-13

22. Huang ES, Gorawara-Bhat R, Chin MH. Self-reported goals of older patients with type 2 diabetes mellitus. *J Am Geriatr Soc* 2005; 53: 306-11
23. Petterson T, Lee P, Hollis S, Young B, Newton P, Dornan T. Well-being and treatment satisfaction in older people with diabetes. *Diabetes Care* 1998; 21: 930-5
24. Wilson M, Moore MP, Lunt H. Treatment satisfaction after commencement of insulin in Type 2 diabetes. *Diabetes Res Clin Pract* 2004; 66: 263-7
25. Hardy SE, Dubin JA, Holford TR, Gill TM. Transitions between states of disability and independence among older persons. *Am J Epidemiol* 2005; 161: 575-84
26. Bauduceau B, Bourdel-Marchasson I, Brocker P, Taillia H. The brain of the elderly diabetic patient. *Diab Metabolism* 2005; 31 Spec No 2 : 5S92-5S97
27. Bruce DG, Davis WA, Davis TM. Longitudinal predictors of reduced mobility and physical disability in patients with type 2 diabetes: the Fremantle Diabetes Study. *Diabetes Care* 2005; 28: 2441-7
28. Egede LE. Diabetes, major depression, and functional disability among U.S. adults. *Diabetes Care* 2004; 27: 421-8
29. Araki A, Murotani Y, Kamimiya F, Ito H. Low well-being is an independent predictor for stroke in elderly patients with diabetes mellitus. *J Am Geriatr Soc* 2004; 52: 205-10
30. Chou KL, Chi I. Functional disability related to diabetes mellitus in older Hong Kong Chinese adults. *Gerontology* 2005; 51: 334-9
31. Miller DK, Lui LY, Perry HM, 3rd, Kaiser FE, Morley JE. Reported and measured physical functioning in older inner-city diabetic African Americans. *J Gerontol A Biol Sci Med Sci* 1999; 54: M230-6
32. Maggi S, Noale M, Gallina P, et al. Physical disability among older Italians with diabetes. The ILSA study. *Diabetologia* 2004; 47: 1957-62
33. Perkowski LC, Stroup-Benham CA, Markides KS, et al. Lower-extremity functioning in older Mexican Americans and its association with medical problems. *J Am Geriatr Soc* 1998; 46: 411-8
34. Lichtenstein MJ, Dhanda R, Cornell JE, Escalante A, Hazuda HP. Modeling impairment: using the disablement process as a framework to evaluate determinants of hip and knee flexion. *Aging (Milano)* 2000; 12: 208-20
35. Cohen HJ, Pieper CF, Harris T, Rao KM, Currie MS. The association of plasma IL-6 levels with functional disability in community-dwelling elderly. *J Gerontol A Biol Sci Med Sci* 1997; 52: M201-8
36. Brown JS, Vittinghoff E, Lin F, Nyberg LM, Kusek JW, Kanaya AM. Prevalence and risk factors for urinary incontinence in women with type 2 diabetes and impaired fasting glucose: findings from the National Health and Nutrition Examination Survey (NHANES) 2001-2002. *Diabetes Care* 2006; 29: 1307-12
37. Leveille SG, Fried LP, McMullen W, Guralnik JM. Advancing the taxonomy of disability in older adults. *J Gerontol A Biol Sci Med Sci* 2004; 59: 86-93
38. Valderrama-Gama E, Damian J, Ruigomez A, Martin-Moreno JM. Chronic disease, functional status, and self-ascribed causes of disabilities among noninstitutionalized older people in Spain. *J Gerontol A Biol Sci Med Sci* 2002; 57: M716-21
39. Wandell PE, Brorsson B, Aberg H. Psychic and socioeconomic consequences with diabetes compared to other chronic conditions. *Scand J Soc Med* 1997;25:39-43
40. Bootsma-van der Wiel A, Gussekloo J, De Craen AJ, Van Exel E, Bloem BR, Westendorp RG. Common chronic diseases and general impairments as determinants of walking disability in the oldest-old population. *J Am Geriatr Soc* 2002; 50: 1405-10
41. Odding E, Valkenburg HA, Stam HJ, Hofman A. Determinants of locomotor disability in people aged 55 years and over: the Rotterdam Study. *Eur J Epidemiol* 2001; 17: 1033-41

42. Okochi J. Increase of mild disability in Japanese elders: a seven year follow-up cohort study. *BMC Public Health* 2005; 5: 55
43. Schwartz AV, Hillier TA, Sellmeyer DE, et al. Older women with diabetes have a higher risk of falls: a prospective study. *Diabetes Care* 2002; 25: 1749-54
44. Bourdel-Marchasson I, Vincent S, Germain C, et al. Delirium symptoms and low dietary intake in older inpatients are independent predictors of institutionalization: a 1-year prospective population-based study. *J Gerontol A Biol Sci Med Sci* 2004; 59: 350-4
45. Lifford KL, Curhan GC, Hu FB, Barbieri RL, Grodstein F. Type 2 diabetes mellitus and risk of developing urinary incontinence. *J Am Geriatr Soc* 2005; 53: 1851-7
46. Atkinson HH, Cesari M, Kritchevsky SB, et al. Predictors of combined cognitive and physical decline. *J Am Geriatr Soc* 2005; 53: 1197-202
47. Volpato S, Blaum C, Resnick H, Ferrucci L, Fried LP, Guralnik JM. Comorbidities and impairments explaining the association between diabetes and lower extremity disability: The Women's Health and Aging Study. *Diabetes Care* 2002; 25: 678-83
48. Volpato S, Ferrucci L, Blaum C, et al. Progression of lower-extremity disability in women with diabetes. *Diabetes Care* 2002; 26: 70-75
49. Resnick HE, Vinik AI, Schwartz AV, et al. Independent effects of peripheral nerve dysfunction on lower-extremity physical function in old age: the Women's Health and Aging Study. *Diabetes Care* 2000; 23: 1642-7
50. Resnick HE, Vinik AI, Heimovitz HK, Brancati FL, Guralnik JM. Age 85+ years accelerates large-fiber peripheral nerve dysfunction and diabetes contributes even in the oldest-old: the Women's Health and Aging Study. *J Gerontol A Biol Sci Med Sci* 2001; 56: M25-31
51. Spiers NA, Matthews RJ, Jagger C, et al. Diseases and impairments as risk factors for onset of disability in the older population in England and Wales: findings from the Medical Research Council Cognitive Function and Ageing Study. *J Gerontol A Biol Sci Med Sci* 2005; 60: 248-54
52. Kamper AM, Stott DJ, Hyland M, Murray HM, Ford I. Predictors of functional decline in elderly people with vascular risk factors or disease. *Age Ageing* 2005; 34: 450-5
53. Al Snih S, Fisher MN, Raji MA, Markides KS, Ostir GV, Goodwin JS. Diabetes mellitus and incidence of lower body disability among older Mexican Americans. *J Gerontol A Biol Sci Med Sci* 2005; 60: 1152-6
54. Gregg EW, Mangione CM, Cauley JA, et al. Diabetes and incidence of functional disability in older women. *Diabetes Care* 2002; 25: 61-7
55. Arvanitakis Z, Wilson RS, Schneider JA, Bienias JL, Evans DA, Bennett DA. Diabetes mellitus and progression of rigidity and gait disturbance in older persons. *Neurology* 2004; 63: 996-1001
56. Al Snih S, Raji MA, Markides KS, Ottenbacher KJ, Goodwin JS. Weight change and lower body disability in older Mexican Americans. *J Am Geriatr Soc* 2005; 53: 1730-7
57. Reynolds SL, Silverstein M. Observing the onset of disability in older adults. *Soc Sci Med* 2003; 57: 1875-89
58. Rantanen T, Masaki K, Foley D, Izmirlian G, White L, Guralnik JM. Grip strength changes over 27 yr in Japanese-American men. *J Appl Physiol* 1998; 85: 2047-53
59. Sayer AA, Dennison EM, Syddall HE, Gilbody HJ, Phillips DI, Cooper C. Type 2 diabetes, muscle strength, and impaired physical function: the tip of the iceberg? *Diabetes Care* 2005; 28: 2541-2
60. Guillet C, Boirie Y. Insulin resistance: a contributing factor to age-related muscle mass loss? *Diabetes Metab* 2005; 31 Spec No 2: S20-S26

61. De Rekeneire N, Resnick HE, Schwartz AV, et al. Diabetes is associated with subclinical functional limitation in nondisabled older individuals: the Health, Aging, and Body Composition study. *Diabetes Care* 2003; 26: 3257-63
62. Petersen KF, Shulman GI. Pathogenesis of skeletal muscle insulin resistance in type 2 diabetes mellitus. *Am J Cardiol* 2002; 90: 11G-18G
63. Carey PE, Halliday J, Snaar JE, Morris PG, Taylor R. Direct assessment of muscle glycogen storage after mixed meals in normal and type 2 diabetic subjects. *Am J Physiol Endocrinol Metab* 2003; 284: E688-94
64. Shulman RG, Rothman DL. The "glycogen shunt" in exercising muscle: A role for glycogen in muscle energetics and fatigue. *Proc Natl Acad Sci U S A* 2001; 98: 457-61
65. Sherman WM. Metabolism of sugars and physical performance. *Am J Clin Nutr* 1995; 62: 228S-241S
66. He J, Kelley DE. Muscle glycogen content in type 2 diabetes mellitus. *Am J Physiol Endocrinol Metab* 2004; 287: E1002-7
67. Hays NP, Starling RD, Sullivan DH, et al. Effects of an ad libitum, high carbohydrate diet and aerobic exercise training on insulin action and muscle metabolism in older men and women. *J Gerontol A Biol Sci Med Sci* 2006; 61: 299-304
68. Ferrara CM, Goldberg AP, Ortmeier HK, Ryan AS. Effects of aerobic and resistive exercise training on glucose disposal and skeletal muscle metabolism in older men. *J Gerontol A Biol Sci Med Sci* 2006; 61: 480-7
69. Hood DA. Invited Review: contractile activity-induced mitochondrial biogenesis in skeletal muscle. *J Appl Physiol* 2001; 90: 1137-57
70. Bourdel-Marchasson I, Biran M, Dehail P, et al. Muscle phosphocreatine post-exercise recovery rate is related to functional evaluation in hospitalized and community-living older people. *J Nutr Health Aging* 2006; in press

**Table I**

Potential factors associated with disability in elderly people with diabetes

	<b>Common features of elderly people with diabetes</b>
Complications (specific or not specific)	Cerebrovascular diseases (cognition) Visual impairment Heart disease (coronary insufficiency) Neuropathy Ischaemic arterial peripheral disease Podiatric problems and lower limb amputation
Associated conditions	Obesity (arthritis) Hypertension Depression
Treatment burden	Social disadvantage due to treatment
Muscle metabolism	Insulin resistance Sedentary life style or disuse Diet
Social conditions	Lower income Lower education level

Figure 1: International Classification of Functioning, disability and health (ICF) WHO 1980 [4] and WHO 2001 [6]

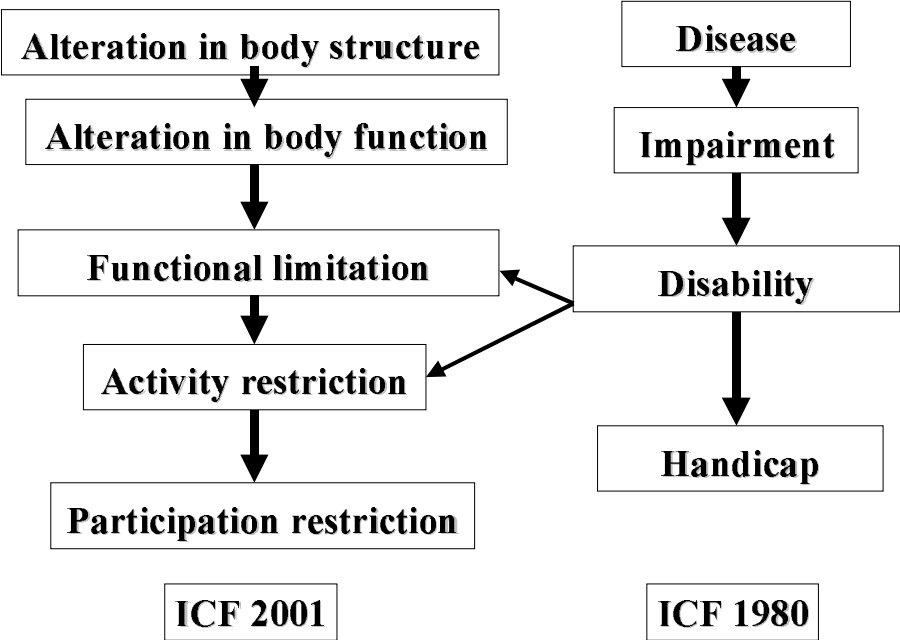


Figure 2: Issued from ref [54]: elderly people with diabetes aged older than 65 y (DM) were at increased risk for incidental disability compared to other elderly people without diabetes (non-DM). In people older than 80 y, no difference was found.

