Diabetes, comorbidities and increased long-term mortality in older patients admitted for geriatric inpatient care

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Abstract

Aims. – To study the specific impact of diabetes on long-term mortality in very old subjects with multiple comorbidities and functional disabilities.

Methods. – The prevalence of vascular disorders, global comorbidity load (cumulative illness rating scale [CIRS]) and functional disabilities (activities of daily living [ADL] and Lawton’s instrumental ADL [IADL] scores) were determined according to diabetes status in a cohort of 444 patients (mean age 85.3 ± 6.7 years; 74.0% women) admitted to our geriatric service. Also, the specific impact of diabetes on 4-year mortality was analyzed using Cox proportional-hazards models.

Results. – Diabetic patients had higher BMI scores (27.1 ± 4.9 vs. 23.4 ± 4.7 kg/m² in controls; P < 0.001), and higher prevalences of hypertension (81.9% vs. 65.1%, respectively; P = 0.003) and ischaemic heart disease (33.7% vs. 22.2%, respectively; P = 0.033), but not of stroke and renal insufficiency. They also had more comorbidities (CIRS score excluding diabetes: 15.1 ± 4.5 vs. 13.8 ± 4.8, respectively; P = 0.016) and functional disabilities. Diabetes was associated with mortality (HR: 1.42, 95% CI: 1.02–1.99; P = 0.041) after adjusting for age, gender and BMI, and this persisted after adjusting for individual vascular comorbidities, but disappeared after adjusting for CIRS, ADL or IADL scores.

Conclusion. – Diabetes was associated with 4-year mortality after adjusting for the inverse relationship between mortality and BMI. This association was better accounted for by the global comorbidity load and functional disabilities than by the individual vascular comorbidities. These findings suggest that the active management of all – rather than selected – comorbidities is the key to improving the prognosis for older diabetic patients.

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Keywords: Diabetes; Mortality; Comorbidities; Elderly

Résumé

Impact du diabète et des comorbidités sur la mortalité des patients âgés hospitalisés.

Objectif. – Étudier l’impact du diabète sur la mortalité des patients âgés atteints de comorbidités et d’incapacités fonctionnelles.

Méthodes. – Nous avons déterminé la prévalence des atteintes vasculaires, des comorbidités cumulées (score Cumulative illness rating scale [CIRS]) et des incapacités fonctionnelles (scores ADL et IADL) selon la présence d’un diabète dans une population de 444 patients (âge moyen 85,3 ± 6,7 ans, 74,0 % femmes) admis dans notre service de gérontologie. Nous avons ensuite étudié l’impact du diabète sur la mortalité à quatre ans par des modèles de régression de Cox.

Résultats. – Les patients diabétiques avaient un IMC (27,1 ± 4,9 vs 23,4 ± 4,7 kg/m², P < 0,001) et une fréquence d’hypertension (81,9% vs 65,1 %, P = 0,003) et de maladies coronaires (33,7% vs 22,2 %, P = 0,033) plus élevés, mais une même fréquence d’accidents vasculaires cérébraux et d’insuffisance rénale. Ils avaient davantage de comorbidités cumulées (score CIRS sans diabète 15,1 ± 4,5 vs 13,8 ± 4,8, P = 0,016) et d’incapacités fonctionnelles. Le diabète était associé à une augmentation de la mortalité (Hazard Ratio 1,42, IC 95% 1,02–1,99, P = 0,041) après ajustement pour l’âge, le sexe et l’IMC. Cette association persistait après ajustement pour les comorbidités vasculaires individuelles mais disparaissait après ajustement pour les scores CIRS, ADL et IADL.

Abbreviations: CIRS, cumulative illness rating scale; ADL, activities of daily living; IADL, instrumental activities of daily living; IHD, ischaemic heart disease.

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1. Introduction

Many studies have demonstrated that diabetes is associated with an increase in both cardiovascular and all-cause mortality [1–4]. A recent report from the Emerging risk factors collaboration emphasized the association of diabetes with various non-vascular causes of death, including neoplasm and infection [5]. In the US National health and nutrition examination survey (NHANES), diabetes was associated with mortality in subjects 35–75 years old. The relative risk of death decreased with advancing age, but the absolute mortality attributable to diabetes was higher in the older age groups due to a higher overall death rate [1]. However, the impact of diabetes on mortality in very old populations with a high comorbidity load has been little studied. Indeed, the increase in mortality related to ageing and to diverse comorbidities may well overwhelm the specific impact of diabetes.

The impact of diabetes on mortality is further compounded by the inverse relationship observed between obesity and mortality in older populations [6–8]. There are even data to suggest that obesity is associated with lower mortality in older diabetic subjects [9,10]. As obesity is frequently seen in diabetic patients, it must be taken into account as a possible confounder in the association between diabetes and mortality. Diabetes has also been associated with functional disabilities in several older populations [11,12]. Although usually not attributable to a single identifiable cause, these functional disabilities are nevertheless strong predictors of all-cause mortality in such populations [13].

Older patients in medical or geriatric care represent a population with a particularly high prevalence of comorbidities and functional disabilities. Several authors, including the present team, have previously shown that diabetes in such patients is generally characterized by unexpectedly good glycaemic control, albeit in the context of malnutrition and/or comorbidities [14,15]. It is unclear whether diabetes per se remains associated with mortality in such a population. We have previously carried out a prospective study in a cohort of very old geriatric inpatients to determine the impact of cognitive disorders on outcomes and mortality [16]. Using data from that cohort, the present study was performed to determine the relative impact of diabetes, obesity, vascular disorders and other comorbidities on all-cause mortality after hospital discharge.

2. Methods

2.1. Patients and data collection

The prospective study was carried out in a 294-bed geriatric hospital where 22.7% of patients were directly admitted from the community, 54.0% were referred by the emergency unit and 23.3% were transferred from other inpatients services. Patients and data collection have been described elsewhere [17]. Briefly, a representative sample of all patients aged more or equal to 75 years, consecutively admitted between January 2004 and December 2005, were selected by randomization at a sampling fraction of 30%, using a computer-generated randomization table. The Ethics committee of the Geneva university hospitals approved the protocol, and patients, their families or legal representatives provided signed written informed consent. Demographic data for the patients studied did not significantly differ from those for all patients admitted to the hospital during the recruitment period. Our sample was therefore representative of all patients admitted to this hospital, demonstrating the reliability of the randomization procedure used in this study.

2.2. Clinical parameters

Patients’ medical history was recorded on standardized forms, and the same physician (D.Z.) conducted a comprehensive geriatric assessment of all patients. Sociodemographic data included age, gender, marital status and living arrangements. Diabetes status was abstracted from comorbidity scores, and confirmed by review of the individual patient’s hospital charts based on ongoing treatment, HbA1c more than 7.0% and/or a previous physician’s diagnosis. Antidiabetic treatments and any available HbA1c values were also collected at this time. The body mass index (BMI, kg/m²) was calculated from measured weight and height on admission. Arterial hypertension was defined by a physician’s diagnosis and/or ongoing treatment. Ischaemic heart disease (IHD) was defined as myocardial infarction based on previous medical history and/or ongoing treatment, and was confirmed by review of the hospital charts. Stroke was identified by medical history and physical examination, and confirmed by cerebral imaging. The presence of atrial fibrillation was determined by standard electrocardiography (ECG) on admission.

Comorbidities were assessed with the Cumulative illness rating scale for geriatrics (CIRS-G), obtained from medical charts after discharge. The scale integrates previous and present acute medical conditions, and was previously validated in our hospital, and shown to predict length of stay, institutionalization and death [16]. It incorporates 14 disease categories (heart disease, hypertension, haematopoietic, respiratory, eye and ear, upper gastrointestinal, lower gastrointestinal, liver, kidney, genitourinary, musculoskeletal, neurological, endocrine/metabolic and psychiatric/dementia), rated on a scale from 0 to 4. The total CIRS score is calculated as the sum total of the 14 scores. To avoid any effect of diabetes status on the comorbidity

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score, a modified score was generated that excluded the endocrine/metabolic item (CIRS-noDM).

Functional disabilities were assessed according to the basic and instrumental Activities of daily living (ADL and IADL, respectively) scores [18,19]. These were determined using the 2 weeks before admission as the reference period, and based on the patients’ medical history or information supplied by their informal or formal caregivers. The ADL assesses the patient’s ability to manage basic activities such as bathing, dressing, going to the toilet, maintaining continence, feeding and transferring (six items). The IADL assesses the ability to use the telephone, shop, use transportation, cook, do housework, take medication and handle finances (eight items). For both scales, 0 indicates total dependence and the maximum score (6 or 8) indicates total independence.

The short form version of the Mini nutritional assessment (MNA-SF) was also administered, again using the 2 weeks prior to admission as the reference period (www.mna-elderly.com). In addition, haemoglobin, serum albumin, creatinine and an endocrine/metabolic item (CIRS-noDM).

Functional disabilities were assessed according to the basic and instrumental Activities of daily living (ADL and IADL, respectively) scores [18,19]. These were determined using the 2 weeks before admission as the reference period, and based on the patients’ medical history or information supplied by their informal or formal caregivers. The ADL assesses the patient’s ability to manage basic activities such as bathing, dressing, going to the toilet, maintaining continence, feeding and transferring (six items). The IADL assesses the ability to use the telephone, shop, use transportation, cook, do housework, take medication and handle finances (eight items). For both scales, 0 indicates total dependence and the maximum score (6 or 8) indicates total independence.

The short form version of the Mini nutritional assessment (MNA-SF) was also administered, again using the 2 weeks prior to admission as the reference period (www.mna-elderly.com). In addition, haemoglobin, serum albumin, creatinine and random plasma glucose levels were determined by the standard techniques. Glomerular filtration rate (GFR, mL/min/1.73 m²) was calculated using the Cockcroft-Gault formula, adjusted for body surface area, as previously described [14]. Finally, cognitive function was assessed by the Folstein test or Mini-mental state examination (MMSE) [20], and depression by the Geriatric Depression Scale (GDS) [21]. The same neuropsychologist assessed all subjects at least 1 week after admission to eliminate cases of delirium.

2.3. Outcome

The outcome of interest was death from any cause by 31 December 2009, other words, at least 4 years after hospital discharge. Information regarding this outcome was obtained through phone calls to the patients, their families and/or general practitioners. Data were also confirmed through access to the population registry of the State of Geneva.

2.4. Statistical methods

Data for continuous variables are presented as means ± 1 standard deviation (SD). Kaplan-Meier survival curves were used to examine the impact of diabetes on mortality, and the univariate relationship between each independent variable and 4-year mortality was also measured. In addition, Cox proportional-hazards models were applied to account for the time to death. The independent variables assessed as possible predictors included age, gender, diabetes status, BMI, cardiovascular comorbidities (hypertension, IHD, stroke and atrial fibrillation), renal function, total comorbidities (CIRS score) and functional disabilities (ADL and IADL scores). All independent variables and 4-year mortality were entered as dependent variables in the multivariate Cox regression models. Hazard ratios (HR) and 95% confidence intervals (CI) were calculated. Continuous variables were included as such (age, ADL, IADL, albumin and GFR), whereas binary variables were gender and cardiovascular risk factors. BMI was used either as a continuous variable or grouped into four categories:

- 20 kg/m²;
- 20–25 kg/m² (reference);
- 25–30 kg/m²;
- > 30 kg/m².

Statistical analyses were performed using Stata software, version 11.1 (StataCorp LP, College Station, TX, USA).

3. Results

3.1. Patients’ characteristics according to diabetes status

The present analysis included 444 patients for whom full data were available (mean age 85.3 ± 6.7 years; 74.0% women), representing more than 90% of the patients initially recruited. A diagnosis of diabetes was found in 83 (18.7%) of these patients, among whom 20.5% were taking no drug therapy, 44.6% were taking oral hypoglycaemic agents (OHAs), 28.9% were using insulin, and 6.0% were taking combined insulin and OHA treatment.

The patients’ characteristics according to diabetes status are shown in Table 1. Predictably, the patients with diabetes had higher BMI scores, and higher prevalences of hypertension and IHD, but there was no difference in the prevalence of renal insufficiency. The diabetes patients also had a higher incidence of comorbidities according to the CIRS score, even after the exclusion of diabetes from the score, as well as more functional disabilities, as evidenced by lower ADL and IADL scores. There were no significant differences in the prevalences of cognitive impairment and depression between diabetic and non-diabetic subjects.

The low mean HbA1c value noted in our diabetic patients was in agreement with previous observations [15,22]. The MNA-SF was slightly higher in diabetic patients, a finding most likely accounted for by their higher prevalence of obesity. However, by its design, the MNA, which includes a low BMI as a key item, is not suitable for comparing the prevalence of malnutrition in diabetic/obese subjects with a control population [15]. For this reason, this parameter was left out of the subsequent mortality analysis.

3.2. All-cause mortality according to diabetes status

Survival according to diabetes status was analyzed using Kaplan-Meier curves. Of the 444 patients included, 225 (51%) died within 4 years of discharge, 23 (5.2%) of which died during hospitalization. The mortality rates were 57.8% and 49.0% in diabetic and non-diabetic patients, respectively (P = 0.13 by log-rank test) (Fig. 1). In the simple Cox models, a low BMI, but not diabetes, was associated with 4-year mortality (Table 2, Model 0). However, in a multiple model including age, male gender, diabetes and BMI, the association between diabetes and mortality became apparent (HR: 1.42, 95% CI: 1.02–1.99; P = 0.041), and

Table 1
Patients’ characteristics according to diabetes status.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No diabetes (n = 361)</th>
<th>Diabetes (n = 83)</th>
<th>P value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>85.4 ± 6.6</td>
<td>84.2 ± 7.2</td>
<td>0.169</td>
</tr>
<tr>
<td>Female (n, %)</td>
<td>275 (76.2%)</td>
<td>53 (63.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.4 ± 4.7</td>
<td>27.2 ± 4.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Random PG (mmol/L)</td>
<td>6.50 ± 1.45</td>
<td>9.62 ± 3.45</td>
<td></td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td></td>
<td>6.85 ± 1.17</td>
<td></td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>235 (65.1%)</td>
<td>68 (81.9%)</td>
<td>&lt;0.003</td>
</tr>
<tr>
<td>Ischaemic heart disease (n, %)</td>
<td>80 (22.2%)</td>
<td>28 (33.7%)</td>
<td>0.033</td>
</tr>
<tr>
<td>Stroke (n, %)</td>
<td>44 (12.2%)</td>
<td>13 (15.7%)</td>
<td>0.369</td>
</tr>
<tr>
<td>Atrial fibrillation (n, %)</td>
<td>102 (28.3%)</td>
<td>24 (28.9%)</td>
<td>0.893</td>
</tr>
<tr>
<td>GFR (mL/min/1.73 m²)</td>
<td>44.4 ± 17.1</td>
<td>47.1 ± 18.8</td>
<td>0.250</td>
</tr>
<tr>
<td>&lt; 30</td>
<td>69 (19.1%)</td>
<td>11 (13.2%)</td>
<td>0.219&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>30–60</td>
<td>230 (63.7%)</td>
<td>52 (62.7%)</td>
<td></td>
</tr>
<tr>
<td>&gt; 60</td>
<td>62 (17.2%)</td>
<td>20 (24.1%)</td>
<td></td>
</tr>
<tr>
<td>Known dyslipidaemia (n, %)</td>
<td>42 (11.6%)</td>
<td>15 (18.1%)</td>
<td>0.144</td>
</tr>
<tr>
<td>Cigarette-smoking (n, %)</td>
<td>95 (26.3%)</td>
<td>24 (28.9%)</td>
<td>0.680</td>
</tr>
<tr>
<td>CIRS-G</td>
<td>14.1 ± 4.8</td>
<td>17.3 ± 4.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CIRS-noDM</td>
<td>13.8 ± 4.8</td>
<td>15.1 ± 4.5</td>
<td>0.016</td>
</tr>
<tr>
<td>MMSE</td>
<td>21.0 ± 5.3</td>
<td>21.1 ± 4.9</td>
<td>0.809</td>
</tr>
<tr>
<td>ADL</td>
<td>5.0 ± 1.1</td>
<td>4.6 ± 1.4</td>
<td>0.013</td>
</tr>
<tr>
<td>IADL</td>
<td>4.5 ± 2.3</td>
<td>3.9 ± 2.4</td>
<td>0.044</td>
</tr>
<tr>
<td>Depression: GDS &gt; 0 (n, %)</td>
<td>111 (30.8%)</td>
<td>18 (21.7%)</td>
<td>0.101</td>
</tr>
<tr>
<td>MNA-SF</td>
<td>9.0 ± 2.8</td>
<td>10.0 ± 2.3</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>33.3 ± 6.1</td>
<td>33.2 ± 5.6</td>
<td>0.816</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>124.3 ± 18.2</td>
<td>123.1 ± 18.1</td>
<td>0.560</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>48.0 ± 52.4</td>
<td>46.3 ± 45.4</td>
<td>0.775</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SD unless otherwise indicated; statistically significant results are shown in boldface. PG: plasma glucose; GFR: glomerular filtration rate; CIRS-G: cumulative illness rating scale for geriatrics; CIRS-noDM: modified CIRS score excluding diabetes mellitus; MMSE: mini-mental state examination; ADL: activities of daily living; IADL: Lawton’s instrumental activities of daily living; GDS: geriatric depression scale; MNA-SF: mini nutritional assessment-short form.

<sup>a</sup> By t-test for continuous variables and Fisher’s test for binary variables.

<sup>b</sup> By Kruskal-Wallis test for comparison of GFR levels.

the inverse relationship between BMI and mortality persisted (Table 2, Model 1).

Of the vascular comorbidities, hypertension, IHD and stroke were not associated with mortality. However, atrial fibrillation and low GFR were both associated with mortality (Table 2, Model 0). In the multiple models, diabetes remained associated with mortality after the subsequent inclusion of these five variables (Table 2, Model 2). The CIRS (or CIRS-noDM) score and low serum albumin, which reflects global comorbidity and/or acute disease load, were both associated with mortality in simple models (Table 2, Model 0). Furthermore, when the CIRS-noDM score and serum albumin were added to the model, only the CIRS-noDM score and low BMI remained associated with mortality. In contrast, diabetes and individual comorbidities were no longer significantly associated with mortality (Table 2, Model 3).

ADL and IADL scores were inversely related to mortality (Table 2, Model 0). Also, when entered into a multiple Cox model along with diabetes, BMI and vascular comorbidities, they remained significantly inversely related to mortality. However, the association between either diabetes status or BMI and mortality disappeared (data not shown).

4. Discussion

The present results indicate that diabetes is associated with an elevated global comorbidity load, as assessed by CIRS score. There were also higher prevalences of overweight/obesity,
hypothesis and IHD, but not of stroke and renal insufficiency. Diabetes patients also had higher prevalences of low ADL and IADL scores. Thus, diabetes is associated with comorbidities and functional disabilities in a geriatric inpatient population with a poor overall health status. These findings in a hospital setting are similar to those of previous studies involving older outpatients [11,12].

The specific impact of diabetes on 4-year mortality in this population was relatively weak, and was apparent only after adjusting for age, gender and BMI. A high BMI has paradoxically been associated with survival in several geriatric populations [6]. Our findings indicate that the protective effect of a high BMI tends to mask the specific impact of diabetes on long-term mortality. Strikingly, the individual vascular comorbidities (hypertension, IHD and stroke) were not associated with 4-year mortality, and did not account for the impact of diabetes on mortality. In contrast, the CIRS score was higher in diabetic patients (even after exclusion of the diabetes item), and did account for the impact of diabetes on mortality. The observation that the global comorbidity score is a better indicator of diabetes-related mortality than individual vascular comorbidities was not totally unexpected. An important recent report has re-emphasized that diabetes is associated not only with cardiovascular mortality, but also with death due to multiple non-vascular causes, including cancers, infections, mental disorders and falls [5]. A high prevalence of multiple disorders ultimately leading to death due to the combined effects of these diverse causes should therefore be expected in diabetes patients requiring geriatric care. Our results suggest that the active care of all – rather than selected – comorbidities is the key to improving the prognosis for such patients.

We also observed that functional disabilities are both more prevalent in diabetes patients and associated with mortality, confirming earlier reports in comparatively healthier outpatients [11,13,23]. Functional disabilities are determined by multiple and overlapping causes, including comorbidities, malnutrition, cognitive impairment and even social isolation [24–27]. Given these multiple causes, it may be inappropriate to draw any conclusions as to the mechanistic and prognostic links between diabetes and functional disabilities. However, it is our opinion that, from a practical viewpoint, the simple observation that diabetes signals a greater risk of functional disabilities is important in itself.

The mortality risk associated with diabetes was weaker in our study that in many previous studies of younger adults [5]. Ageing per se and comorbidities might be expected to overwhelm the specific impact of diabetes on mortality. However, our present results do suggest that diabetes contributes to comorbidity and functional disability. Another possibility is a survival bias in very old patients, whereby patients with long-standing diabetes die before reaching the age of geriatric care, and are ‘replaced’ by patients with comparatively recent-onset diabetes. It would be of great interest to stratify the mortality risk associated with diabetes according to diabetes duration in a larger study.

Few previous studies have addressed the impact of diabetes on mortality in geriatric patients. Diabetes is not included in mortality risk scores in patients with long-term care needs [28].
However, a study in patients with Alzheimer’s disease found that diabetes was associated with mortality even after adjusting for multiple comorbidities (but excluding obesity) [29]. Our present study involved patients admitted for geriatric inpatients care, but we believe that our results may also be relevant for other older populations with a high comorbidity load, such as nursing home residents and patients with long-term care needs. More research on the impact of diabetes in such populations is clearly needed.

The major strengths of our present study were the randomization procedure, which ensured an unbiased sampling of diabetic and non-diabetic patients, and the extensive geriatric evaluation carried out by the same small team of dedicated trained collaborators, who generated data through consistent procedures. Nevertheless, our study also had limitations. The ascertainment of vascular comorbidities was based on the data available in medical charts. Thus, hypertension and previous IHD and stroke may have been subject to misclassification. However, this is a situation faced by clinicians on a daily basis, and it was reassuring that higher prevalences of hypertension and IHD were identified in our diabetic patients, as predicted. This issue was of less concern with stroke, which was confirmed by cerebral imaging. We were not able to obtain information on diabetes duration, which is difficult to collect reliably in the context of cognitive disorders and memory impairment, and limited access to adequate documentation. Diabetes duration may be an important determinant of vascular and other comorbidities, and functional disabilities. As discussed above, our diabetes-associated mortality may have been ‘diluted’ by the inclusion of patients with recent-onset diabetes. However, it is unlikely that diabetes duration would have affected the relative impact of these parameters on mortality.

We have previously suggested that malnutrition is an important prognostic factor in older diabetic patients [15]. However, the relative prevalence of malnutrition is difficult to determine when comparing diabetic (and/or obese) and control patients, and particularly when using diagnostic scores (such as the MNA) that include BMI as a criterion. Indeed, in obese patients, extremely substantial weight loss must occur before achieving a low BMI. Recent reports have emphasized the overlap between malnutrition, cachexia and comorbidities [30,31]. Low serum albumin, classically considered a marker of malnutrition, is better associated with inflammation and comorbidities than with malnutrition per se [14,32]. The prognostic impact of malnutrition, unlike comorbidities, remains to be studied in both diabetic and non-diabetic older patients.

5. Conclusion

Diabetes was associated with 4-year mortality after adjusting for its inverse relationship with BMI. This association is accounted for by the global comorbidity load rather than by the individual vascular diseases. These findings suggest that the active management of all – rather than selected – comorbidities is the key to improving the prognosis for diabetic patients in older high-risk populations.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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