



Martial Coutaz*

Department of Geriatric, Valais Hospital, 1920 Martigny, Switzerland

Received: 06 September, 2019

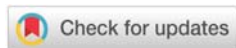
Accepted: 05 November, 2019

Published: 06 November, 2019

***Corresponding author:** Dr. Martial Coutaz, MD, Geriatric Department, Valais Hospital, Av De la Fusion 27, CH-1920 Martigny, Switzerland, Tel: 0041 27 603 96 06; Fax: 00041 27 603 96 06; E-mail: martial.coutaz@hopitalvs.ch

Keywords: Overtreatment; Therapeutic target; Individualized treatment; Elderly; Diabetes

<https://www.peertechz.com>



Review Article

Hypoglycemia and overtreatment of diabetes in elderly subjects: observations from 3 studies over a period of 12 years

Abstract

Purpose: Despite recent new recommendations from professional societies regarding the management of diabetes in older adults, it is clear that in routine practice, treatment targets are often ill-suited to the health state of polymorbid elderly diabetic patients.

Methods and results: Over these last 12 years, we have performed one prospective and two retrospective studies investigating the treatment of diabetes in our 200-bed Geriatric Care unit.

There is a trend towards overtreatment, with the mean glycated haemoglobin (HbA1c) level ranging from 6.5% to 6.9% in the three cohorts of octogenarians we studied. In the first study, we observed an incidence of 24% of hypoglycemic episodes occurring within 24 hours of admission. Categorizing patients by health state as per the American Diabetes Association definition (robust, vulnerable and frail) in the next study, we observed in 257 patients included that 81% had a HbA1c level more than 0.5% below the upper limit of the target range (and only 4% of subjects were robust). In the third study, a retrospective analysis of 2,205 diabetic patients followed for 5 years, we observed that 12% suffered a fracture after a fall, and 79.3% of these had a HbA1c level that was more than 0.5% below the upper limit of the target range.

Conclusions: Our study findings over a 12-year period suggest that elderly patients with diabetes are treated too aggressively, and there may be a need to review practices and implement individualized treatment goals.

Introduction

Diabetes is common in elderly individuals, and it is estimated that in the United States of America, 25% of those aged over 65 years suffer from diabetes, while in Europe, average prevalence is around 20%, with marked differences between countries (ranging from 15% to 18% in the United Kingdom, and from 15 to 26% in Italy) [1,2].

Several features of diabetes are specific to older individuals, notably the increase in insulin resistance related to adiposity, sarcopenia and physical activity, as well as reduced insulin secretion by the pancreas, a high number of comorbidities (40% of diabetics have more than 4 associated comorbidities), the concomitant presence of geriatric syndromes (polypharmacy, falls, cognitive disorders, persistent pain, urinary incontinence, depression), as well as a high risk of micro- and macrovascular complications [3-8].

Since landmark randomized studies mostly excluded diabetic subjects aged over 75 years, most professional societies have issued guidelines for these patients since 2010 (and the American Geriatric Society even started as early as 2003), while the American Diabetes Association proposes an annual update. According to these recommendations, only an individualized approach focusing simultaneously on life expectancy, comorbidities, functional and cognitive status, degree of autonomy and the patient's wishes (e.g. refusal of strict glycemic control or constraints related to a special diet) can achieve adequate management of elderly diabetic subjects, by prioritizing treatment objectives and by taking account of the time necessary to achieve the expected benefit (8 to 10 years for a reduction in microvascular complications) [1,4].

This individualized, priority-based approach is the cornerstone of good geriatric management, and is the strategy we have been implementing in daily practice at the Geriatric Medicine Department of the Valais Hospital (200 beds) in

Switzerland since 2007. Over these last 12 years, we have performed 3 studies investigating the treatment of diabetes in our unit [9-11] and taken together, the results indicate that there is persistent over-treatment of diabetes that has been ongoing for several years.

Hypoglycaemia of the elderly subject with diabetes: A silent disease? [9]

With increasing age, there are changes in the counter-regulatory response to hypoglycaemia, with the adrenergic symptom profile (shakiness, palpitations, anxiety) being replaced by neuroglycopenic symptoms (behavioural changes, fatigue, confusion). These symptoms are non-specific and may mistakenly be attributed to other comorbidities (such as neurological or psychiatric disorders), and consequently, there is a probable under-estimation of the frequency of hypoglycaemia in this population.

In order to better assess the risk of hypoglycaemia, we prospectively included 100 patients with diabetes hospitalised in the acute geriatric care ward, and treated with oral anti-diabetic agents and/or insulin. Of note, 77% of these patients were transferred to the acute geriatric care ward from the internal medicine ward after being stabilized, and 23% were admitted directly from their home for a geriatric work-up. Five capillary glycemia measurements were performed (at 7.00am, 11.00am, 5.00pm, 10.00pm and 3.00am) within the first 24 hours of admission, without modifying the usual treatment. Hypoglycemia was defined as a glycemia value <4mmol/L. The incidence of hypoglycaemia was found to be very high, at 24%, during the first 24 hours. In total, 24 patients presented 33 episodes of hypoglycaemia (nadir glycemia 1.9 mmol/L), of which one third occurred at 3.00am, and most episodes went unnoticed by the patient. According to our results, the usual risk factors for hypoglycaemia described in elderly patients with diabetes (such as insulin therapy, older age, renal insufficiency, polypharmacy and frailty) showed no significant statistical relation with the occurrence of hypoglycaemia (Table 1) and appear to be insufficient to help detect hypoglycaemia. Furthermore, the average value of glycated haemoglobin (HbA1c) of 6.5% is too low a treatment target, and unsuited to the age of our study population (mean 79 years), and to their general characteristics (average Barthel's index 61/100, average Mini Mental State Examination (MMSE) score 24/30, polypharmacy with more than 8 drugs per day).

In the last 10 years, guidelines have evolved, to take into account the idea of "biological age", including cognitive status, comorbidities, functional status and life expectancy. Recommendations now propose therapeutic targets and treatment strategies for three different health states, namely for robust, vulnerable and frail (Table 2) (adapted from [12]). For robust patients, with intact functional and cognitive status, and a life expectancy of around 10 years, the suggested reasonable HbA1c range is 7.5% or less, with a view to preventing cardiovascular complications. In frail patients, with multiple comorbidities, and moderate to severe cognitive impairment (MMSE <17), or in long-term care, the target HbA1c is 8.5% or less, with a view to avoiding the effects of overtreatment

Table 1: Characteristics of the population in the first study in our unit to show evidence of overtreatment [9].

Characteristic	All (N=100)	No hypoglycemia (N=76)	Hypoglycemia (N = 24)	p-value
Age	79.29±7.1	79.66±7.1	78.13±6.8	0.35
MMSE	24.07±5.15	24±5.35	24.29±4.57	0.80
Barthel's index	61.24±25.53	60.51±25.98	63.54±24.47	0.61
Albumin, g/L	35.34±4.83	35.30±4.81	35.48±5	0.87
Creatinine clearance, ml/min	62.07±29.32	62.16±29.27	61.8±30.11	0.96
Drugs per day	8.37±3.07	8.47±3.17	8.04±2.76	0.52
Treatment				0.08
-Insulin	22%	59% (13/22)	41%(9/22)	
-Oral antidiabetic agents	67%	81% (54/67)	19%(13/67)	
-Both	11%	82% (9/11)	18%(2/11)	
Diet-control	22%	59% (13/22)	41%(9/22)	0.07
HbA1c %	6.51±1.79	6.38±1.53	6.91±2.42	0,32

MMSE, Mini Mental State Examination.

Table 2: Patient classification criteria according to health status, with corresponding HbA1c goals (Adapted with permission from [12]).

Patient health status	Characteristics	Reasonable HbA1c target range
Robust	Relatively healthy, 1-2 coexisting chronic illnesses, intact functional and cognitive status (MMSE ≥ 25)	≤7.5%
Vulnerable	Intermediate health status, ≥3 coexisting chronic illnesses or mild to moderate cognitive impairment (MMSE 18-24)	≤8.0%
Frail	Very poor health status, long-term care or end-stage chronic illnesses or severe impairment of functional status or moderate to severe cognitive impairment (MMSE ≤17)	≤8.5%

(falls, fracture, cognitive impairment or fainting due to hypoglycaemia) or under-treatment (dehydration, electrolyte disturbances, fatigue or infection due to hyperglycemia). Despite these recommendations, treatment intensity is rarely adapted to the health status of elderly patients, and overtreatment is often observed [3,4].

Overtreatment of frail elderly patients with diabetes [10]

Using this definition of the therapeutic targets, we performed a retrospective study comparing the glycemia measurement, and the guidelines-recommended targets, in all diabetic patients hospitalized in the geriatric medicine unit in 2014 (376 diabetic patients among 2,272 patients hospitalized). The final study population comprised 257 patients after exclusion of patients with untreated diabetes and those with unreliable HbA1c measurements. Average age was 80.9 years, and the distribution across the three health states defined by the ADA was as follows: 3.1% were robust, 61.1% were vulnerable and 35.8% were frail (Table 3). Average HbA1c in the population was 6.85%±1.26%; values were comparable across the three health state groups. Overall, 81% had a HbA1c value that was below the recommended target for their health state, and most were 0.5% below the upper limit of the target range (Figure 1). Furthermore, 50.4% were treated by sulfonylurea or

insulin (or both), and were thus at high risk of hypoglycaemia. These findings confirm that a substantial proportion (81% in our sample) of elderly diabetics with significant comorbidities are over-treated, as assessed by the HbA1c level.

Fractures in elderly diabetic patients : A link with over-treatment ? [11]

We retrospectively analysed data from a period of 5 years (from 1 January 2002 to 31 December 2016) from 2,259 diabetic patients hospitalised in the acute geriatric care ward, and recorded those who suffered a fracture after a fall (N=275, 12% of the overall population), according to their health state (robust, vulnerable or frail), using the same methodology as in our previous study [10]. We excluded 77 patients (28%) due to the absence of any anti-diabetic treatment, an unreliable HbA1c value, or because of fracture unrelated to a fall. The average age

of the final study population was 81.7 years, mean MMSE score 21.7, and 18.2% of patients had documented hypoglycaemia (Table 3). Among the 198 patients included, only 4% were robust, 50% were vulnerable, and 46% were frail. The average HbA1c of the overall population was 6.9%. Here again, we noted that 79.3% of patients had a HbA1c value that was at least 0.5% lower than the upper limit of the target range for their health state, suggesting the possibility of overtreatment that may have contributed to their falls (Figure 1).

Discussion

Our experience of three studies carried out over a period of 12 years indicates that there is potential overtreatment of diabetes in elderly hospitalized patients. Although it is established that HbA1c is a poor predictor of the occurrence of severe hypoglycaemia, several randomized, controlled studies have shown that strict control of diabetes strongly increases the risk of hypoglycaemia [5]. According to our observations, more than 96% of hospitalized elderly patients with diabetes are classed as vulnerable or frail, and according to established guidelines, there is clearly overtreatment of diabetes in these patients since the HbA1c level is more than 0.5% lower than the upper limit of the target range in 72 to 88% of them [10,11].

The occurrence of hypoglycaemia is a probable consequence of overtreatment and represents a major challenge in the management of elderly diabetic subjects. According to the Diabetes and Aging Study, the rate of complications and mortality in elderly diabetics depends on both duration of diabetes and increasing age [7]. Indeed, in that study, the sex and race-adjusted incidence of diabetes complications in older adults with more than 10 years duration of type 2 diabetes was 9.62 events/1,000 person-years (95% confidence interval (CI) 8.7–10.64) in those aged 60–69 years; 15.88 (95%CI 14.56–17.32) in those aged 70–79 years, and 19.60 (95%CI 17.48–21.98) in those aged 80 and over [7]. Thus, for most elderly diabetic patients, lowering HbA1c to below 7.5% likely induces more harm than benefit [5].

Even though the risk factors for falls are multidimensional (e.g. polypharmacy, lack of muscle strength, neuropathy), several authors have suggested that HbA1c <7% may be associated with an increased risk of falls and fractures, in particular in frail elderly subjects [3,13]. In a Swedish study involving almost 430,000 individuals (mean age 80.8±8.2 years), followed-up from 2008 to 2014, the risk of falls was increased in all treated diabetics, and there was a 24% increase in the risk of hip fracture in patients with diabetes treated by insulin (adjusted hazard ratio (HR) [95% CI] 1.24 [1.16–1.32]) [14]. Glycemia-lowering treatments are strongly associated with Emergency Department (ED) visits due to insulin-related hypoglycemia and errors. In a nationally representative public health surveillance of adverse drug events among insulin-treated patients seeking ED care in the United States, Geller et al found that insulin-treated patients aged 80 years or older were more than twice as likely to visit the ED and nearly 5 times as likely to be subsequently hospitalized for insulin-related hypoglycaemia and medication errors than those aged 45 to 64 years [15]. Furthermore, it was shown in a population

Table 3: Characteristics of the study populations of two studies from our unit [10,11].

Patient characteristics	Overtreatment of elderly diabetic patients	Fractures in elderly diabetic patients
Number of patients	257	198
Mean (±SD) age, years	80.9±7	81.7±7.2
Female sex, %	50.2	72.2
Mean MMSE score	22.7(5.1)	21.7(5.5)
Mean (±SD) Barthel index at discharge	73.2(24.7)	67.7(21.2)
Anti-diabetic treatment, %		
· Insulin	22.6	16.7
· Oral antidiabetics	77.4	65.6
· Both	12.1	17.7
Health state, %		
· Robust	3.1	4
· Vulnerable	61.1	50
· Frail	35.8	46
Mean (±SD) HbA1c, %		
* All patients	6.85(1.26)	6.9(1.24)
* Robust	6.75(1.48)	6.86(0.74)
* Vulnerable	6.79(1.23)	6.94(1.20)
* Frail	6.93(1.3)	6.86(1.33)



Figure 1: Percentage of patients with HbA1c more than 0.5% below target, at target or above target, across the health states (robust, vulnerable, frail) in the study by Deletre S et al (left hand bar of each health state) and in the study by Jacques A et al (right hand bar of each health state).

with a mean age of 74 years, followed for 12 years, that severe hypoglycaemia doubled the risk of developing dementia [16].

Despite the publication of guidelines for the management of diabetes in elderly subjects, it is clear that the recommendations are not complied with in daily practice, and the intensity of anti-diabetic treatment is not routinely adapted according to the patient's health state [4]. Lipska et al. also suggested the possible presence of overtreatment in a population of 1,288 diabetic patients aged on average 73 years, and followed for 10 years, with 61% of the population having a HbA1c level below 7%, and 56.4% of subjects classed as frail [17]. It is also noteworthy that in that study, among those with a HbA1c <7%, 54.9% were treated by insulin or sulfonylureas [17]. In a retrospective cohort study involving 20,329 patients older than 65 years with type 2 diabetes admitted to Veterans Affairs nursing homes, the 100-day mortality rate was 83%, 67% of the population had a mean HbA1c <7.9%, and 50% were below 7% [18]. Finally, data from the Diabetes Collaborative Registry, an observational study in the USA that examined glycemic control in 43,000 patients with type 2 diabetes and aged 75 years or older from 2014 to 2016, found that 30,396 (72%) patients were taking glucose-lowering medications. Among these, 26% had a HbA1c level <7% when taking at least one agent at high risk of hypoglycaemia (insulin, sulfonylureas or meglitinides) [19].

Our studies have some limitations that deserve to be underlined. The study populations were relatively small, and were comprised of hospitalized patients, who likely have a poorer state of health than an ambulatory population of the same age. Furthermore, although low HbA1c values suggest potential overtreatment, we cannot draw any firm conclusions regarding the existence of a causal link between hypoglycaemia, falls and fractures. Indeed, hypoglycaemia often goes undiagnosed in this population (with few symptoms), and numerous other complications, linked for example to the duration of diabetes (not recorded in our studies) or to other comorbidities (peripheral neuropathy, secondary visual impairment, orthostatic hypotension, polypharmacy). could also be responsible for an increased risk of falls and fractures.

Conclusion

Twelve years after the first surprising observation that the mean HbA1c value in 100 hospitalized, elderly patients with diabetes was 6.5%, and that 1 in 4 patients presented hypoglycaemia within 24 hours after admission, suggesting probable overtreatment in view of their age and state of health, it is clear that the latest guidelines for the treatment of elderly subjects with diabetes are not widely applied in our region, as in many other parts of the world.

Despite repeated communication of these findings in conferences and publications targeting primary care physicians, and publications from national experts emphasising the guidelines from professional societies, an unacceptably high proportion of frail elderly subjects continue to be treated too aggressively, without taking account of their physical or cognitive status or their life expectancy. When a frail patient of 85 years of age is re-admitted in the same year for a third

hypoglycaemia-related event after the patient's diabetologist re-introduced a basal-bolus treatment regimen (4 injections per 24-hour period), it is legitimate to wonder about the level of knowledge and the rate of implementation of guidelines for geriatric care. In line with the example of onco-geriatric consultations, perhaps diabeto-geriatric consultations might be useful, targeting elderly (>75 years) subjects with diabetes, to perform global geriatric assessment with a view to developing an individualized treatment approach. By taking into consideration the patient's life expectancy, comorbidities, functional and cognitive status, degree of autonomy and wishes and preferences, the therapeutic management of elderly diabetic patients could be enhanced, defining targets that are congruent with our oath to "primum non nocere".

References

- American Diabetes Association (2019) 12. Older Adults: Standards of Medical Care in Diabetes-2019. *Diabetes Care* 42: S139-S147. [Link: http://bit.ly/2JSsSb8](http://bit.ly/2JSsSb8)
- Sesti G, Incalzi RA, Bonora E, Consoli A, Giaccari A, et al. (2018) Management of diabetes in older adults. *Nutr Metab Cardiovasc Dis* 28: 206-218. [Link: http://bit.ly/36wYxbY](http://bit.ly/36wYxbY)
- Sinclair A, Dunning T, Rodriguez-Manas L (2015) Diabetes in older people: new insights and remaining challenges. *Lancet Diabetes Endocrinol* 3: 275-285. [Link: http://bit.ly/2NEYVVD](http://bit.ly/2NEYVVD)
- Huang ES (2016) Management of diabetes mellitus in older people with comorbidities. *BMJ* 353: i2200. [Link: http://bit.ly/34uDxaj](http://bit.ly/34uDxaj)
- Lipska KJ, Krumholz H, Soones T, Lee SJ (2016) Polypharmacy in the Aging Patient: A Review of Glycemic Control in Older Adults With Type 2 Diabetes. *JAMA* 315: 1034-1045. [Link: http://bit.ly/2NllpDT](http://bit.ly/2NllpDT)
- Kirkman MS, Briscoe VJ, Clark N, Florez H, Haas LB, et al. (2012) Diabetes in older adults. *Diabetes Care* 35: 2650-2664. [Link: http://bit.ly/2qnodqS](http://bit.ly/2qnodqS)
- Huang ES, Laiteerapong N, Liu JY, John PM, Moffet HH, et al. (2014) Rates of complications and mortality in older patients with diabetes mellitus: the diabetes and aging study. *JAMA Intern Med* 174: 251-258. [Link: http://bit.ly/2JLCV1R](http://bit.ly/2JLCV1R)
- Coutaz M (2017) Hypertension, diabetes, hyperlipidemia : what are the treatment goals for the elderly?. *Rev Med Suisse* 13: 1924-1930. [Link: http://bit.ly/2PQdD6u](http://bit.ly/2PQdD6u)
- Coutaz M, Nicod M, Chassot M, Morisod J (2007) Monitoring hypoglycemia in elderly diabetic patients: a prospective study. *Rev Med Suisse* 3: 1071-1076. [Link: http://bit.ly/2POauEn](http://bit.ly/2POauEn)
- Deletré S, Coutaz M (2016) Diabetes: glycemic targets and over-treatment in older patients. *Rev Med Suisse* 12: 461-464. [Link: http://bit.ly/36CbEIK](http://bit.ly/36CbEIK)
- Jacques A, Coutaz M (2019) Fractures in the elderly subject with diabetes: A consequence of overtreatment?. *Rev Med Suisse*.
- American Diabetes Association (2015) Standards of Medical Care in Diabetes. (10) Older adults. *Diabetes Care* 38: S67- S69. [Link: http://bit.ly/2qIW4k8](http://bit.ly/2qIW4k8)
- Nelson JM, Dufraux K, Cook PF (2007) The relationship between glycemic control and falls in older adults. *J Am Geriatr Soc* 55: 2041-2044. [Link: http://bit.ly/2JPCBUK](http://bit.ly/2JPCBUK)
- Wallander M, Axelsson KF, Nilsson AG, Lundh D, Lorentzon M (2017) Type 2 Diabetes and Risk of Hip Fractures and Non-Skeletal Fall Injuries in the Elderly: A Study From the Fractures and Fall Injuries in the Elderly Cohort (FRAILCO). *J Bone Miner Res* 32: 449-460. [Link: http://bit.ly/34qPDLc](http://bit.ly/34qPDLc)



15. Geller AI, Shehab N, Lovegrove MC, Kegler SR, Weidenbach KN, et al. (2014) National estimates of insulin-related hypoglycemia and errors leading to emergency department visits and hospitalizations. *JAMA Intern Med* 174: 678-686. [Link: http://bit.ly/33g38xi](http://bit.ly/33g38xi)
16. Yaffe K, Falvey CM, Hamilton N, Harris TB, Simonsick EM, et al. (2013) Association between hypoglycemia and dementia in a biracial cohort of older adults with diabetes mellitus. *JAMA Intern Med* 173: 1300-1306. [Link: http://bit.ly/2J0I0q2](http://bit.ly/2J0I0q2)
17. Lipska KJ, Ross JS, Miao Y, Shah ND, Lee SJ, et al. (2015) Potential

overtreatment of diabetes mellitus in older adults with tight glycemic control. *JAMA Intern Med* 175: 356-362. [Link: http://bit.ly/2oT0Rcs](http://bit.ly/2oT0Rcs)

18. Petrillo LA, Gan S, Jing B, Lang-Brown S, Boscardin WJ, et al. (2018) Hypoglycemia in Hospice Patients With Type 2 Diabetes in a National Sample of Nursing Homes. *JAMA Intern Med* 178: 713-715. [Link: http://bit.ly/2Cdo1NN](http://bit.ly/2Cdo1NN)
19. Arnold SV, Lipska KJ, Wang J, Seman L, Mehta SN, et al. (2018) Use of Intensive Glycemic Management in Older Adults with Diabetes Mellitus. *J Am Geriatr Soc* 66: 1190-1194. [Link: http://bit.ly/34rVb88](http://bit.ly/34rVb88)

Discover a bigger Impact and Visibility of your article publication with Peertechz Publications

Highlights

- ❖ Signatory publisher of ORCID
- ❖ Signatory Publisher of DORA (San Francisco Declaration on Research Assessment)
- ❖ Articles archived in worlds' renowned service providers such as Portico, CNKI, AGRIS, TDNet, Base (Bielefeld University Library), CrossRef, Scilit, J-Gate etc.
- ❖ Journals indexed in ICMJE, SHERPA/ROMEO, Google Scholar etc.
- ❖ OAI-PMH (Open Archives Initiative Protocol for Metadata Harvesting)
- ❖ Dedicated Editorial Board for every journal
- ❖ Accurate and rapid peer-review process
- ❖ Increased citations of published articles through promotions
- ❖ Reduced timeline for article publication

Submit your articles and experience a new surge in publication services
(<https://www.peertechz.com/submission>).

Peertechz journals wishes everlasting success in your every endeavours.

Copyright: © 2019 Coutaz M. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.