European Geriatric Medicine
https://doi.org/10.1007/s41999-021-00594-1

BRIEF REPORT

Large discrepancy in glycaemic control appropriateness in geriatric patients with type 2 diabetes according to major clinical practice guidelines

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Received: 12 August 2021 / Accepted: 17 November 2021

Key summary points

Aim This study compared glycaemic control appropriateness across three major clinical practice guidelines

Findings Large discrepancy exists in glucose-lowering appropriateness classification between clinical practice guidelines, particularly in overtreatment detection.

Message This finding relates to the absence in the clinical practice guidelines from the American Diabetes Association 2021 of a lower HbA1c value, which may be an obstacle to the prevention of hypoglycaemia.

Abstract

Purpose In geriatric patients with type 2 diabetes (T2D), appropriate glycaemic control is crucial to avoid overtreatment and hypoglycaemia. This study compared glycaemic control appropriateness across three major clinical practice guidelines (CPGs).

Methods Retrospective study of geriatric older inpatients with T2D and glucose-lowering treatment before admission. Patients were classified as appropriately treated, overtreated or undertreated using CPGs from Diabetes Canada 2018 (DC18), the Endocrine Society 2019 (ES19) and the American Diabetes Association 2021 (ADA21).

Results Of the 318 geriatric patients (median age 84 years, 54% women, 66% in poor health), 46%, 25% and 82% were appropriately treated, while 38%, 57% and 0% were overtreated, based on DC18, ES19 and ADA21, respectively.

Conclusion Large discrepancy of glycaemic control appropriateness was detected across these CPGs and concerned mainly overtreatment. This finding relates to the absence in ADA21 of a lower HbA1c value, which may be an obstacle to the prevention of hypoglycaemia.

Keywords Type 2 diabetes · Clinical practice guidelines · Geriatric patients · Glycaemic control appropriateness · Overtreatment · Glucose-lowering treatment

Introduction

In older patients with type 2 diabetes (T2D), hypoglycaemic events are associated with adverse outcomes, such as functional impairment, deterioration of health status or death [1, 2], which are even more damaging for older patients who are frail or in poor health [3].

Hypoglycaemic events are induced by too tight glycaemic control using glucose-lowering drugs at high risk of hypoglycaemia, namely insulins, sulfonylureas or glinides (i.e. overtreatment) [2, 4, 5].

While avoiding overtreatment is, therefore, crucial, reaching appropriate glycaemic control is a challenge for geriatric

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Published online: 25 November 2021

people with T2D. Due to the wide heterogeneity of health status existing in this population, the treatment objectives should be individualised according to some patient's characteristics (such as their comorbidities, functional or cognitive status, or residual life expectancy) [6, 7].

Despite a lack of strong scientific evidence in this field [8], some major clinical practice guidelines (CPGs) provided these last years recommendations on the individualised management of glycaemic control in older people [9]. This study aimed at comparing glycaemic control appropriateness in geriatric patients with type 2 diabetes according to major these CPGs.

Methods

Study design and participants

This retrospective study includes consecutive patients aged ≥ 75 years hospitalised in a geriatric ward (Brussels, Belgium) between 2008 and 2015 [10], with type 2 diabetes, glucose-lowering treatment (GLT) before hospital admission, and HbA1c measured during the hospital stay. A patient was included only once. Type 2 diabetes was defined according to the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [11].

Data collection and definition of variables

Socio-demographic, biomedical, geriatric and medication data were collected from patients' medical records at hospital admission. Geriatric features included functional impairment (≥ 2 impairments in five basic activities of daily living including eating, bathing, toileting, transferring and dressing) [12], severe polypharmacy (≥ 10 drugs/day), cognitive impairment (dementia or Mini-Mental State Examination < 24/30), recent falls (≥ 2 falls within last year), malnutrition (diagnosed by a fulltime dietician after taking an anamnesis about patient's appetite loss, weight loss, eating habits as their evolution over time), and residency in a nursing home. HbA1c was expressed in % (NGSP nomenclature. Concerning GLT, agents with a high risk of hypoglycaemia (i.e. insulin, sulfonylureas and glinides) were distinguished from agents with a low risk of hypoglycaemia (i.e. biguanides, GLP1-receptor agonists, DPP4-inhibitors, thiazolidinediones and alpha-glucosidase inhibitors).

CPGs and glycaemic control appropriateness

Three major recent CPGs about diabetes management on older patients were used: Diabetes Canada 2018 (DC18) [13], the Endocrine Society 2019 (ES19) [12] and the American Diabetes Association 2021 (ADA21) [14]. These three CPGs recommend that glycaemic control management should be individualised according to patient's health status. Each CPG categorises global health status in three tiers (good, intermediate or poor) using different criteria related to the number of comorbidities, functional and cognitive status or place of residency [9].

For each health status tier, CPGs suggest the most appropriate HbA1c target range. Based on this interval, patients were classified in three groups of glycaemic control appropriateness: appropriately treated (patient's HbA1c in-target), overtreated (patient's HbA1c below the target range) and undertreated (patient's HbA1c above the target range) (Fig. 1). Each CPG has its own HbA1c target ranges suggestion as shown in Fig. 1.

Data analysis

Continuous variables were presented as medians [P25;P75]. Categorical variables were expressed as number (*n*) and percentages (%).

The degree of concordance among the CPGs (i.e. the raters) on patients' health status or on glycaemic control appropriateness was assessed using inter-rater reliability methods of Kappa coefficient. Cohen's kappa coefficient was used for assessment between two CPGs, while Fleiss's kappa coefficient was used for assessment between three CPGs. The level of concordance between CPGs was interpreted according to McHugh's recommendations: None ($\kappa \leq 20\%$), Minimal ($21\% \leq \kappa \leq 40\%$), Weak ($41\% \leq \kappa \leq 60\%$), Moderate ($61\% \leq \kappa \leq 80\%$), Strong ($81\% \leq \kappa \leq 90\%$) and Almost perfect ($\kappa \geq 91\%$).

Statistical analyses were performed using R studio software (R × 64 version 3.4.1). A p value < 0.05 was considered as statistically significant.

Ethical consideration

This study was approved by the Institutional Review Board Committee (Commission d'Ethique Hospitalo-Facultaire, Cliniques universitaires Saint-Luc, Brussels, Belgium, IRB Agreement Nb. IRB00001530).

Results

Patients' characteristics

General characteristics of the 318 included geriatric patients (median age: 84 years; 54.1% female) are presented in Table 1. The majority of the patients had functional impairment (63.2%) and cognitive impairment (57.5%). HbA1c was lower than 6.1% in a quarter of the patients (median = 6.9%). One-fourth of the patients were prescribed GLT bi- or

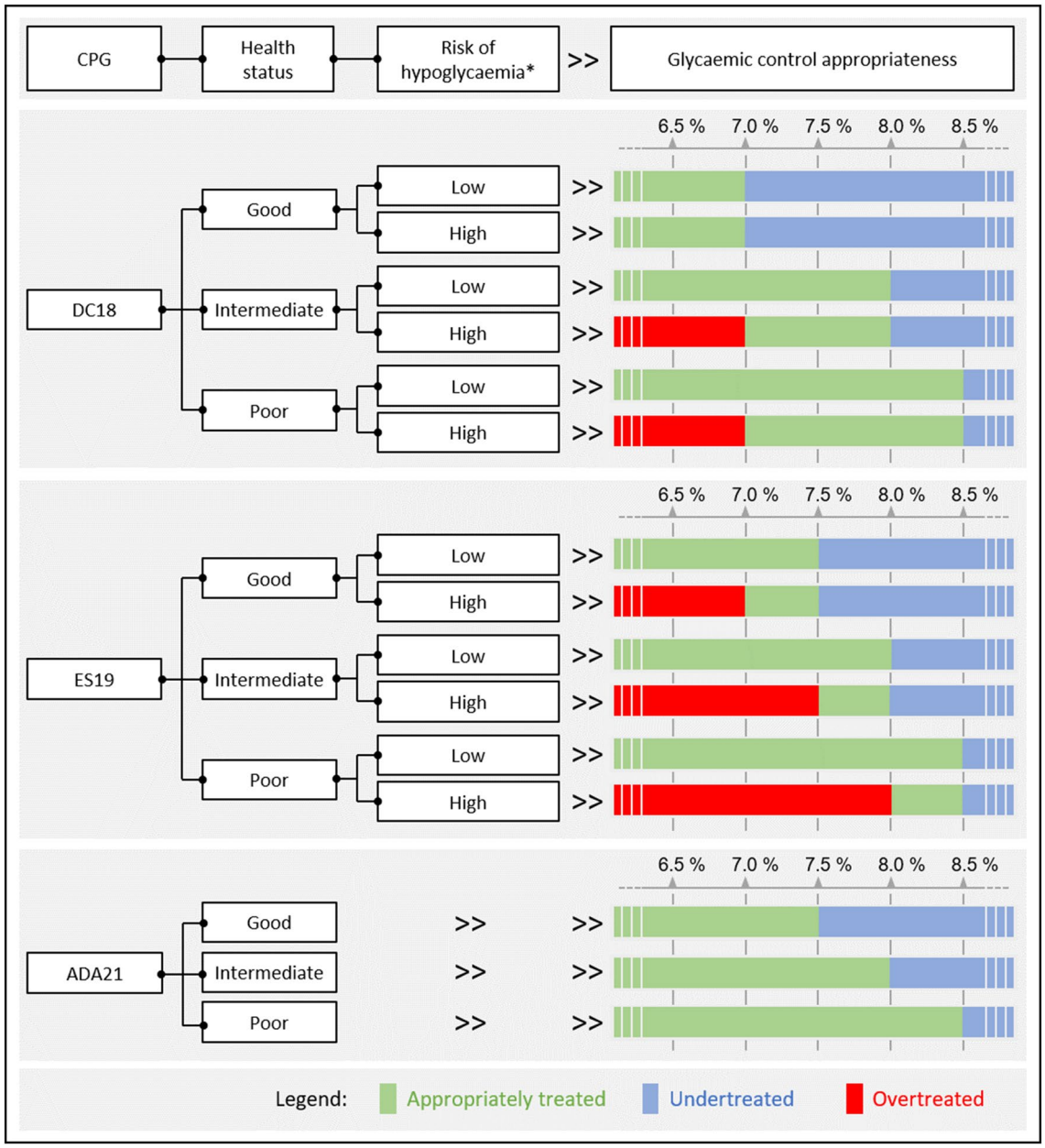

Fig. 1 Classification of patient's glycaemic control appropriateness based on health status and risk of hypoglycaemia, according to three clinical practice guidelines. Legend: CPG: Clinical Practice Guideline; DC18: Diabetes Canada 2018 [13]; ES19: Endocrine Society 2019 [12]; ADA21: American Diabetes Association 2021 [14]; * The risk of hypoglycaemia is high for patients taking glucose-lowering treatment with a high risk of hypoglycaemia (i.e. insulin, sulfonylurea or glinide) and low for other patients

tri-therapy. At least one hypoglycaemic agent was prescribed in 79.6% (Table 1), including insulin (29.9%), sulfonylureas (34.9%) and glinides (18.2%).

Health status definition between CPGs

Overall, each CPG defined one-third of the patients as being in intermediate health status, while two-third of them being in poor health status (Table 2). As ES19 and ADA21 use identical criteria to define patients' health status, no difference between them was observed. A strong concordance was observed between health status definition by DC18 and ES19/ADA21 (Cohen's $\kappa = 0.86$). The change of health status tier between DC18 and ES19/ADA21 occurred, respectively, for 12 patients from intermediate to poor health status and for 9 patients from good to intermediate health status.

Table 1 Patients' general characteristics ($N=318$)

	All patients ($N=318$) N (%) or Median [P25–P75]
Age, in years	84 [80–88]
Female	146 (45.9)
Geriatric features	
Functional impairment[a]	201 (63.2)
Severe polypharmacy[b]	139 (43.7)
Cognitive impairment[c]	183 (57.5)
Recent falls[d]	169 (53.1)
Malnutrition[e]	96 (30.2)
Nursing home residency	71 (22.3)
Diabetes comorbidities	
Arterial hypertension	251 (78.9)
GFR < 30 ml/min	51 (16.8)
Ischaemic heart disease	136 (42.8)
HbA1c, in %	6.9 [6.1–7.8]
< 6%	51 (16.0)
≥ 6% and < 7%	119 (37.4)
≥ 7% and < 8%	80 (25.2)
≥ 8%	68 (21.4)
Use of GLT classes	
Metformin	131 (41.2)
Other non-hypoglycaemic agents[f]	9 (2.8)
Hypoglycaemic agents[g]	253 (79.6)
GLT bi- or tri-therapy	78 (24.5)

GLT Glucose-lowering therapy

[a] ≥ 2 impairments in five basic activities of daily living

[b] ≥ 10 drugs/day

[c] dementia or MMSE < 24/30

[d] ≥ 2 falls within last year

[e] diagnosed by a fulltime dietician

[f] Other non-hypoglycaemic agents included DPP4-inhibitors, GLP1-agonists, thiazolidinediones and alpha-glucosidase inhibitors

[g] Hypoglycaemic agents included insulin, sulfonylureas and glinides

Glycaemic control appropriateness between CPGs

DC18, ES19 and ADA21 classified, respectively, 45.6%, 24.8% and 82.1% of the patients as appropriately treated, 16.7%, 17.9% and 17.9% of the patients as undertreated, and 37.7%, 57.2% and 0% of the patients as overtreated (Table 2). The concordance of glycaemic control appropriateness classification between the three CPGs was minimal ($\kappa = 0.36$).

The majority of patients considered as undertreated by ADA21 were also considered as undertreated by the other CPGs (93% of 57 patients). Of the 182 patients considered as overtreated by ES19, DC18 considered 120 as overtreated, 61 as appropriately treated and 1 as undertreated. ADA21 considered all these 182 patients as appropriately treated.

Discussion

This study found a minimal concordance in glycaemic control appropriateness, with a large discrepancy concerning detection of glycaemic control overtreatment between CPGs.

The criteria used to define patient's health status tier are very similar across the three CPGs [9], and even identical between ES19 and ADA21. The excellent agreement between CPGs in health status classification was therefore expected. As the definition of patient's health status tier is determinant for the choice of appropriate HbA1c target, discrepancies found in glycaemic control appropriateness classification are not due to differences in health status.

The main reason for large discrepancies in glycaemic control appropriateness classification between CPGs lies in discrepancies between guidelines regarding values of HbA1c target range, and above all, the definition of a lower bound. DC18 and ES19 guidelines suggest indeed a lower bound to HbA1c target range when GLT includes insulin, sulfonylurea or glinide [12, 13], whereas ADA21 guidelines do not [9, 14] (Figure). Consequently, all patients considered as overtreated using DC18 or ES19 were considered as appropriately treated using ADA21. Interestingly, this pattern of mismatches was similarly highlighted between other former CPGs [15].

More than theoretical considerations, these discrepancies between CPGs about definition of glycaemic control appropriateness (and detection of overtreatment) may have major consequences in clinical practice. The purpose of setting HbA1c targets suggested by CPGs is to adjust patient's GLT, so that the glycaemic control corresponds to what is best suited to the patient according to his or her health characteristics [6, 7]. This proposal enables an individualised therapeutic approach, i.e. a treatment meeting the needs of each patient, while being as safe as possible. In clinical practice, these differences between the three major CPGs involve different attitudes to prescribing and adapting GLT, same patient being considered as overtreated or appropriately treated overtreated according to different CPG, triggering, therefore, GLT-deintensification or no adaptation to the GLT, respectively. These differences may conduct to an opposite and/or unsafe GLT choice for geriatric patients, who are particularly sensitive to hypoglycaemic events and their morbid and fatal consequences.

For all these reasons, the choice of the CPG to follow is particularly important in clinical practice. Given that these three guidelines are supported by major scientific societies, are of good methodological quality and are based on same

Table 2 Health status and glycaemic control appropriateness in the 318 geriatric patients with T2D according to the three major CPGs

	DC18	ES19	ADA21	Concordance estimation (κ)
Health status, *n* (%)				
Good	9 (2.8)	0 (0.0)	0 (0.0)	
Intermediate	108 (34.0)	105 (33.0)	105 (33.0)	0.858
Poor	201 (63.2)	213 (67.0)	213 (67.0)	
Glycaemic control appropriateness, *n* (%)				
Undertreated	53 (16.7)	57 (17.9)	57 (17.9)	
Appropriately treated	145 (45.6)	79 (24.8)	261 (82.1)	0.356
Overtreated	120 (37.7)	182 (57.2)	0 (0.0)	

DC18 Diabetes Canada 2018 [13], *ES19* Endocrine Society 2019 [12], *ADA21* American Diabetes Association 2021 [14]

(and very limited) scientific evidence, it is, therefore, urgent, in the light of the results of this study, to plead for CPGs favouring the safest treatment for patient and of conducting research that provide high level of scientific evidence to rely on.

This study was limited by its retrospective design, preventing the collection of other data of interest, such as duration of diabetes or patient's and/or physician preferences. Strengths of this study are the use of the most recent version of major CPGs focussing on diabetes management in older adults, the use of real life patient's data allowing accurate health status definition, and the focus on a geriatric population.

Conclusion

A large discrepancy in glycaemic control appropriateness was found across the major CPGs on diabetes management in older adults, and mainly concerned the definition of diabetes overtreatment. This is an obstacle to the prevention of threatening hypoglycaemic events that ought to be avoided in this high-risk population.

Author contributions AC designed the study, performed the analysis and interpreted the data under the supervision of SH and BB. AC drafted the manuscript, which was reviewed by SH and BB. All authors read and approved the final manuscript.

Funding This study was supported by a Research Fellow grant [Antoine Christiaens] from the Fund for Scientific Research – FNRS (Belgium). The funding body (Fund for Scientific Research – FNRS, FC23595) played no part in the design of the study and collection, analysis, interpretation of data or in writing the manuscript.

Availability of data and materials The datasets generated and analysed during the current study are not publicly available due to restrictions on patients' anonymity but are available from the corresponding author on reasonable request.

Declarations

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Ethical approval This study was approved by the Institutional Review Board Committee (Commission d'Ethique Hospitalo-Facultaire, Cliniques universitaires Saint-Luc, Brussels, Belgium, IRB Agreement Nb. IRB00001530).

Informed consent Not applicable.

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