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SHORT COMMUNICATION

Patient/disease features and glycemic targets in type 2 diabetes: Where do we stand?

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Once again in 2015, the ADA and the EASD have opportunely pointed the need of a patient-centered approach for the management of hyperglycemia in individuals with type 2 diabetes (T2DM) [1]. A HbA_{1c} cut off <7 % has been suggested with more or less stringent targets to be individually pursued according to patient/disease features (PDFs), including: (a) risks associated with hypoglycemia; (b) disease duration; (c) life expectancy; (d) comorbidities; (e) vascular complications; and (f) patient's attitude. Since the ADA/EASD made clear that scale for such approach "is not designed to be applied rigidly but to be used as a broad construct to guide clinical decision making," many clinicians will appreciate to be told how to measure the above-mentioned PDFs. We addressed this issue by firstly proposing a way to score individual PDFs and then investigating the distribution of such scores in a real-life clinical set.

Data from 400 consecutive out-patients with T2DM attending two research-based hospitals in Central-Southern Italy, "Casa Sollievo della Sofferenza," Scientific Institute in San Giovanni Rotondo (SGR, $n = 200$) and "Sapienza" University Policlinico Umberto I Hospital in Rome (Rome, $n = 200$) were collected.

Each of the six ADA/EASD suggested PDF was scored equal to 0 (good), 1 (intermediate) or 2 (poor). Scoring criteria (Table 1) were pre-specified in a collaborative fashion by all authors and then used independently by four authors who are experienced diabetologists (i.e., taking care of >20 patients/week since 10–35 years; AP, SDC in SGR; MF, SM in Rome). Within each hospital, concordance between scores attributed to each single PDF in each patient was observed in more than 95 % cases. In the absence of agreement, the final score was attributed upon confrontation between the two examiners. Mean values attributed to each single PDF were summed to obtain the total individual PDFs score.

Patients' clinical features are summarized in Table 2.

Median value of individual PDFs score was 6, with only one patient scoring 0 and no patients scoring 11 or 12. Patients were then grouped according to score 0–2, ($n = 41$, 10.2 %), 3–4 ($n = 85$, 21.2 %), 5–6 ($n = 136$, 34.0 %), 7–8 ($n = 111$, 27.8 %) and 9–10 ($n = 27$, 6.8 %), arbitrarily defined as "very good," "good," "intermediate," "poor" and "very poor," respectively.

According to ADA/EASD patient-centered approach, which patients should be targeted to an intensive anti-diabetes therapy ($HbA_{1c} < 7$ %)? Probably, only those with "very good" or "good" PDFs scores? If so, more than two-thirds of our patients should be targeted to more relaxed attempts ($HbA_{1c} < 7.5$ % or more). In fact, the majority of study patients had a score ranging from "intermediate" to "very poor," while only 31.4 % show a "very good" or "good" score. A similar conclusion could have been drawn according to a totally independent ADA suggestion,

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Table 1 Scoring criteria of the six patient/disease features, ranging from 0 (good) to 1 (intermediate) or 2 (poor)

Score	0	1	2
Duration of diabetes (years)	<5	5–10	>10
Age (years)	<45	45–65	>65
or			
Life expectancy (years)[a]	>10	5–10	<5
Comorbidities	Absent	Mild[b]	Severe[c]
Cardiovascular disease	Absent	Present without clinical events	Present with clinical events[d]
or			
Advanced microangiopathy			
Hypoglycemic episodes	Never	Moderate	Severe[e]
Patient's attitude[f]	Good	Intermediate	Poor

[a] According to the risk defined by our previously published risk engine for predicting all-cause mortality in patients with type 2 diabetes (De Cosmo et al. Diabetes Care 2013; 36:2830–2835. doi: 10.2337/dc12-1906; also available as a free web-based calculator at http://www.operapadrepio.it/rcalc/rcalc.php): high risk was given a score equal to 2, intermediate risk equal to 1 and low risk equal to 0

[b] Hearing impairment, arthritis, chronic obstructive bronchitis, depression, gastrointestinal and musculoskeletal diseases, obesity

[c] Congestive heart failure, hip fracture, tumors, memory or cognitive impairment, vision reduction

[d] Myocardial infarction, heart failure, pulmonary edema, stroke, diabetic foot, amputation, blindness, retinal detachment, nephrosis, acute renal failure, end stage renal disease

[e] Requiring assistance of another person to actively administer carbohydrate, glucagon, or other resuscitative actions

[f] Based on the personal judgment of experienced physicians

Table 2 Clinical features of the 400 study patients with type 2 diabetes

Sex (M/F)	249/151
Age (years)	66.8 ± 10.3
Body mass index (kg/m^2)	29.0 ± 5.3
Smokers [*n* (%)]	58 (14.5)
Duration of diabetes (years)	12.8 ± 9.5
Glycated hemoglobin (%)	7.6 ± 1.7
Anti-hyperglycemic therapy	
Diet alone [*n* (%)]	44 (11.0)
Oral antidiabetes drugs [*n* (%)]	198 (49.5)
Insulin ± oral antidiabetes drugs [*n* (%)]	88 (39.5)
Anti-hypertensive treatment [*n* (%)]	314 (78.5)
Anti-dyslipidemic treatment [*n* (%)]	252 (63.0)

Data are number (*n*) and percentage (%) or mean ± SD

specifically devoted to elderly people (>65 years). In this subgroup, the ADA recommends a level of $HbA_{1c} < 7.5$ % rather than 7 % if patients are otherwise healthy with intact cognitive and functional status, more relaxed targets are indicated for elderly with comorbidities ($HbA_{1c} < 8.0$ % or even <8.5 %) [2]. Of note, 255 (63.7 %) of our study patients were in fact ≥65 years old, a finding which is similar to that reported in larger epidemiological surveys, and thus candidates, by the only virtue of age, to a relaxed HbA_{1c} target (<7.5 % or more). Such a proportion is similar to that obtained by using the PDFs score (68.6 % of our patients scored as "intermediate," "poor" or "very poor" score), thus somehow validating the results obtained by PDFs score and reinforcing the idea that, in our clinical set, intensive anti-diabetes therapy is suggestible for a minority of patients.

Are our findings interpretable in the context of meta-analyses of trials addressing the impact of intensive glucose lowering therapy on all-cause mortality which showed, quite unexpectedly, no benefit at all? Probably yes; in fact, among possible explanations of such counterintuitive negative result is certainly—on one side—the deleterious role of severe hypoglycemia [3, 4], which is ineludibly associated with intensive anti-diabetes therapy, but—on the other side—also the possibility that intensive treatment should be limited to younger patients, with short disease duration and lack of major chronic complications and comorbidities, all patients whose PDFs score would conceivably be defined as "very good" or "good" by our scoring method.

Although we recognize that our scoring method does not derive from objective standardized measurements (especially the one referring to patient's attitude, which is only based on personal judgment of experienced diabetologists), it is of note that more than 95 % agreement was observed between the two examiners within the each hospital, thus internally validating it.

A further limitation of our scoring method, which is based on the arbitrary assumption of an equivalent role played by each PDF, is that the contribution of each feature is not "weighted" according to its own importance in determining the level of treatment intensiveness. This might end up to different individual HbA_{1c} targeting. For example, it is conceivable, and probably agreeable, that individuals with previous major cardiovascular events, even in the absence of other counter-indications (thus scoring only 2), should be preferentially targeted to a relaxed glycemic control. It is worth noting that, under this scenario (or similar ones), our scoring method, if any, underestimates the proportion of patients targetable to more relaxed HbA_{1c} levels. In all, though some suggestions from experienced people have been recently offered [5], specifically designed prospective studies aimed at objectively addressing the individual weight to be attributable to each PDF are definitively needed.

In conclusion, despite the above-mentioned limitations, we believe our present report has the merit of proposing a method for measuring ADA/EASD suggested PDFs to eventually be used for pursuing a patient-centered glucose lowering treatment. According to the proposed method, in the real-life clinical set of Central-Southern Italy, the majority of patient attending diabetes clinics from research-based hospitals seems not to be eligible to intensive anti-diabetes treatments. Additional attempts are needed to address the generalizability of our finding and to better shape the specific weight of each single PDF in determining the degree of intensiveness of anti-diabetes treatments.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standard The study was approved by local ethical committee.

Human and animal rights statement All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008.

Informed consent statement Informed consent was obtained from all patients for being included in the study.

References

1. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M et al (2015) Management of hyperglycemia in type 2 diabetes, 2015: a patient centered approach update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 38:140–149
2. American Diabetes Association (2015) Glycemic targets. Sec. 6. in standards of medical care in diabetes 2015. Diabetes Care 38:S33–S40
3. Yeh JS, Sung SH, Huang PC, Hsu PF, Huang HM, Yang HL, You LK, Chuang SY, Cheng HM, Chen CH (2015) Hypoglycemia and risk of vascular events and mortality: a systematic review and meta-analysis. Acta Diabetol. doi:10.1007/s00592-015-0803-3
4. Nicolucci A, Pintaudi B, Rossi MC, Messina R, Dotta F, Frontoni S, Caputo S, Lauro R (2015) The social burden of hypoglycemia in the elderly. Acta Diabetol 52:677–685
5. Cahn A, Raz I, Kleinman Y, Balicer R, Hoshen M, Lieberman N, Brenig N, Del Prato S, Cefalu WT (2015) Clinical assessment of individualized glycaemic goals in patients with type 2 diabetes: formulation of an algorithm based on a survey among leading worldwide diabetologists. Diabetes Care 38:2293–2300