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Half of patients with type 2 diabetes mellitus are at very high cardiovascular risk according to the ESC/EASD: data from a large Mediterranean population

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In terms of cardiovascular (CV) risk, diabetes, and CV disease (CVD) have been described as 'two bad companions'.[1] However, whether the risk of subsequent adverse CV events in patients with diabetes equals to that of those with previous CVD has been long debated. In this regard, some studies showed that the risk of patients with type 2 diabetes mellitus (T2DM) was similar to those with established coronary artery disease (CAD), thus in clinical practice T2DM might be considered as a 'CAD equivalent',[2–4] but this concept was at odds with other studies.[5–7] Two outstanding studies helped to unravel the controversy.[6,7] In 2002, Evans *et al.*[6] found that patients with T2DM were at lower risk of CV outcomes than patients with CAD during an 8-year follow-up. In 2011, Wannamethee *et al.*,[7] in 4045 men with T2DM aged 60–79 years and followed up for a mean of 9 years, provided evidence that only early-onset patients appeared to be a 'CAD equivalent'. Notably, the results of these landmark studies were based on old cohorts of T2DM patients that were recruited in UK before year 2000. Thus, what we have learned is that risk levels approach CAD risk equivalence in T2DM patients after a decade or in those with target organ damage (proteinuria, estimated glomerular filtration rate <30 mL/min/1.73 m^2, left ventricular hypertrophy or retinopathy) or three or more CV risk factors.[8] These concepts are reflected in recent European Guidelines on diabetes, pre-diabetes, and CVD from the European Society of Cardiology (ESC) and the European Association for the Study of Diabetes (EASD)[8] and allow the classification of patients with diabetes into three categories: very high, high, and moderate CV risk. Hence, the identification of T2DM patients at very high CV risk has important clinical and therapeutic implications.

In relation to the concept of 'CAD equivalent' and applying the recommendations of the latest European Guideline,[8] we hypothesized in the present study that most of T2DM patients might be at very high CV risk analysing a large population in a region of a low-risk European country.

This is a cross-sectional study that used the Information System for the Development of Research in Primary Care (SIDIAP) database in a Mediterranean region (Catalonia) in Spain.[9] Healthcare is organized in Spain in the framework of a National Health System that is financed by general taxes. People are assigned to a family physician that works in geographically organized primary healthcare teams. The Catalonian Health Institute is the main provider of primary healthcare services in Catalonia, managing 286 primary care teams, including 74% of the total population. Primary care professionals of the Catalonian Health Institute use the same electronic medical record system (e-CAP). The SIDIAP database was created for research purposes and contains anonymous, longitudinal, patient information extracted from the e-CAP. The study population consisted of patients aged ≥18 years ($N = 373\,185$, mean age 70.1 ± 12.3 years, 45.2% female) with a diagnosis of T2DM (International Classification of Diseases–ICD, 10th Revision, codes E11, E11.0–E11.9, E14, and E14.0–E14.9) by 31 December 2016. We further applied specific ICD codes 10th Revision to identify subjects with previous CV disease or target organ damage recorded in the database. We excluded patients with a diagnosis of type 1 diabetes, gestational diabetes mellitus, and any other type of diabetes. In accordance with the Spanish regulations, this retrospective study conducted using anonymized data did

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Table 1 Distribution of patients with type 2 diabetes according to cardiovascular mortality risk categories in primary healthcare services in Catalonia (Spain)

ESC cardiovascular mortality risk categories[a,b]		Total (*N* = 373 185) N % (95%CI)	Female (*N* = 168 478) N % (95%CI)	Male (*N* = 204 707) N % (95%CI)
Very high risk	With CVD	99 527 26.7 (26.4–26.9)	37 635 22.3 (21.9–22.8)	61 892 30.2 (29.9–30.6)
	Target organ damage[c] or ≥3 risk factors[d]	99 575 26.7 (26.4–27.0)	47 702 28.3 (27.9–28.6)	51 873 25.3 (25.0–25.7)
High risk[e]		147 779	71 879	73 577
		39.6 (39.2–40.0)	42.7 (42.3–43.1)	35.9 (35.6–36.3)
Moderate risk[f]		26 304	11 262	17 365
		7.0 (6.7–7.4)	6.7 (6.2–7.1)	8.5 (8.1–8.9)

Values between brackets are 95% confidence intervals.
CVD, cardiovascular disease (includes coronary heart disease, stroke, peripheral arteriopathy, and heart failure).
[a]Modified from the 2016 European Guidelines on cardiovascular disease prevention in clinical practice.[10]
[b]According to the 2019 European Guidelines on diabetes, pre-diabetes, and cardiovascular diseases.[8]
[c]Proteinuria (Albumin-to-creatinine ratio >300 mg/g), severe renal failure defined as estimated Glomerular Filtration Rate (eGFR) <30 mL/min/1.73 m^2, left ventricular hypertrophy, or retinopathy.
[d]Age ≥50 years, hypertension, dyslipidaemia, smoking, obesity (body mass index > 30 kg/m^2).
[e]Type 2 diabetes with duration ≥10 years without target organ damage plus any other additional risk factor.
[f]Type 2 diabetes aged <50 years with duration <10 years without other risk factors.

not require informed consent. Patients were classified in risk categories according to the recent ESC Guidelines.[8] We present the number of patients in each category as counts, percentages, and the 95% CI, calculated with SPSS 21.0 (SPSS Inc., Chicago, IL, USA).

Table 1 depicts the distribution of patients according to ESC/EASD risk categories.[8] The prevalence of CV risk factors was as follows: 72% hypertension, 45% obesity, 60% dyslipidaemia, and 14% current smoking. We found that most patients with T2DM (53.4%, 95% CI 53.1–53.6) were at very high risk of fatal CV events. This observation was more evident for men (55.6%, 95% CI 55.3–55.9) than for women (50.7%, 95% CI 50.3–51.0). Globally, 50% of those with very high risk did not show prior established CVD (including coronary heart disease, stroke, peripheral arteriopathy, and heart failure).

However, in women with T2DM at very high risk, a greater proportion of them did not show established CVD (55.9%). Approximately one in four patients with T2DM show prior CVD (26.7%, 95 CI 26.4–26.9).

Notably, most patients showed high or very high risk of fatal CV events (92.95%, 95% CI 92.87–93.04). Moreover, of those T2DM patients without established CVD, a significant proportion, more than a third (36.4%, 95% CI 36.1–36.7) exhibited very high CV risk and should be considered as 'CAD equivalent' patients.

The results we present here might have significant implications for clinical practice. The finding that in a large cohort of T2DM patients managed in a primary care setting, at least 50% are at very high risk of fatal CV events, is of clinical relevance. One might argue in consequence, albeit provocative, that most of our T2DM patients are 'CAD equivalent'. Moreover, we support the concept that the prevention of CVD should be delivered specially in primary care in line with 2016 European Guidelines on Cardiovascular Prevention.[10] Primary care has a unique role in the identification of individuals at high risk of CVD as we cover a significant proportion of consultations in Spain. The finding that more than half of T2DM patients are at very high CV risk and one in three of T2DM patients without prior CVD exhibit a very high risk—being a 'CAD equivalent'—should fuel the implementation of integrated care, including lifestyle interventions and tighter glucose, lipid and blood pressure controls in most patients with T2DM. Primary care physicians have a crucial role in delivering CVD prevention following the Geoffrey Rose paradigm: small shifts in the risk achieved from a population-based primary care strategy lead to significant reductions in disease burden. It is also important to set goals according to risk level and prioritize anti-diabetic medications that have been shown to reduce CV events.

Author's contributions

A.C. and L.C.S wrote the manuscript; A.C., L.C.S, J.F-N., M.M-C., D.O-B, and D.M. designed and conducted the study, reviewed/edited the manuscript, and contributed to the discussion. M.M-C. had full access to all data in the study and takes responsibility for the integrity of data and the accuracy of the data analysis.

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