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EDITORIAL COMMENT

Cardiovascular disease in diabetes: Do we need to look behind the mirror?

Doença cardiovascular na diabetes – precisamos de olhar para trás do espelho?

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Cardiovascular disease (CVD) is a common complication of diabetes and a major cause of death, permanent disability and resource expenditure. Advances in knowledge and technology, novel treatments and greater accessibility have dramatically changed the overall panorama, with a much more favorable short- and long-term prognosis for people with diabetes and CVD.

It is interesting to look at how the concept of cardiovascular (CV) risk in diabetes has changed over the last 30 years or so. From CV risk in diabetes being considered equivalent to coronary disease,[1] the estimated risk for people with diabetes went to double that of the general population.[2] The standpoint now is different. CVD risk in diabetes is strongly related to CV risk factors for ischemic heart disease, but less so for heart failure, for which age is a strong contributor.[3] Furthermore, other modifiers like duration of diabetes, target organ damage and other diabetes complications (especially nephropathy), can exponentially increase the risk of progressive and widespread CVD.

Perhaps, at this point, we should start looking at CVD in diabetes in a more comprehensive and wide-ranging way. How should CVD be defined? Should we wait for a person to suffer a major event like myocardial infarction, stroke or amputation, to consider that they have CVD? At that point, it is already too late for many preventive measures and the first window of opportunity is already past; between 13 and 17 years of life have been lost in women and men, respectively.[4]

So, in our view, in the appropriate group of individuals with diabetes (those at very high risk), it is time to be more proactive in finding subclinical CVD, whether hidden atherosclerosis in different vascular beds or silent myocardial dysfunction. The challenge for most clinicians is to successfully select individuals at sufficient risk to justify a cost-benefit approach. Available risk charts are scarce, unsuitable or untested in general populations.[5] Imaging modalities and biomarkers are still not totally accepted (despite clear evidence in the case of the former) by the experts who develop practice guidelines.[6] There is an enormous task to undertake in the coming years.

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This reflection is prompted by the article by Cardoso et al., on behalf of the PICT2RE investigators, published in this issue of the *Journal*.[7] The paper addresses the prevalence of CVD and CV risk factors among people with diabetes in a hospital setting. The results presented are not surprising. Although the number of patients included in the study is relatively small compared to previously published large registries, its overall findings are in line with what could be expected from a population in hospital care, with longer duration and more severe expression of disease. Obesity was present in a large proportion of participants, as expected, and 80% of the cohort had multiple associated CV risk factors, as is usually found in this type of population.

The prevalence of CVD was relatively high (40%), but might have been even higher if subclinical disease had been investigated. This contrasts with lower rates observed in general care settings, in which people with milder forms of disease are generally followed.

Importantly, about half of CVD was due to ischemic heart disease and only 21.5% to heart failure, much less than would have been expected.[8] This raises questions concerning the inclusion criteria. I believe, since this was a retrospective study, that the only criteria used were clinical. If so, for example, were angina and heart failure symptoms supported by any subsequent tests? Were other etiologies of chest pain or dyspnea sought? The same is true for the diagnosis of peripheral arterial disease and carotid disease. What were the criteria? More than 50% stenosis in a carotid artery, measurement of ankle-brachial index, or lower limb Doppler findings?

Regarding intervention, the results presented are also in line with many other registries. Most patients were treated with several antidiabetic agents (predominantly insulin and metformin, but also about a third with one of the newer therapies, sodium-glucose co-transporter-2 inhibitors or glucagon-like peptide-1 receptor agonists). In spite of this, metabolic control was clearly suboptimal, with a mean glycated hemoglobin of 7.7%, clearly above the recommended target. There were few hypoglycemic events, perhaps due to the low use of sulfonylureas. On the other hand, hyperglycemic episodes were more frequent, which is in accordance with the inadequate level of metabolic control reported.

Treatment of hypertension and dyslipidemia was also as expected. In general, patients with documented CVD had better control of concomitant CV risk factors, with the exception of lipid control. This seems to indicate a discrepancy between medical advice and the real world. The guidelines are in use everywhere, but control rates, especially for lipids, are well below targets in about 70% of the population.[9] What is the problem? It is due to a mix of reasons that include patient adherence, physician inertia, awareness, patient education and deficient team work. A gigantic task for all of us, since these problems have been unresolved for the last 20–30 years.

When we look at complications, there is one item that deserves attention. Neuropathy in diabetes is a complex entity. Peripheral neuropathy is responsible for many lower limb amputations and is easily detected with traditional screening methods. By contrast, cardiac autonomic neuropathy (CAN) is more obscure, insidious and difficult to diagnose at the bedside. The reported number of patients with neuropathy (about one quarter) appears to refer only to peripheral neuropathy. We believe a much larger number of patients could have undiagnosed CAN, at different levels of involvement. This can change the perspective, the level of risk and the association with underlying subclinical CVD,[10] potentially changing the approach to screening for hidden disease and the prevalence of CVD in this cohort.

Studies of diabetes and CVD in Portuguese patients like this one are welcome, since the findings could be substantially different from populations in other parts of the world. The study published here also reflects how diagnosis, practice and intervention are being carried out in this country. The results are not surprising in general, and are similar to other published registries. The limited number of individuals included (clearly below the number needed for high confidence levels) may to some extent limit the final conclusions to be drawn.

The purpose of the study was to compare a group with previous documented CVD with a follow-up group. The definition of the two groups would therefore seem to be of utmost importance. In this editorial we have underlined the need for more precise definition of CVD in its different clinical and subclinical expressions. It is clear that if we wait for major events, a window of opportunity for prevention is lost and prognosis for survival is significantly impaired.

Our ambition should be to appropriately select who to screen for subclinical disease, to set stricter targets for intervention, and to build global multiteam strategies to improve prognosis. We need to look behind the mirror.

Conflicts of interest

The author has no conflicts of interest to declare.

References

1. Haffner SM, Lehto S, Ronnemaa T, et al. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med. 1998;339:229–34.
2. Sarwar N, Gao P, Kondapally Seshasai SR, et al. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet. 2010;375:2215–22.
3. Di Angelantonio E, Kaptoge S, Wormser D, et al. Association of cardiometabolic multimorbidity with mortality. JAMA. 2015;314:52–60.
4. Rawshani A, Rawshani A, Franzén S, et al. Risk factors mortality and cardiovascular outcomes in patients with type 2 diabetes. N Engl J Med. 2018;379:633–44.
5. Rossello X, Dorresteijn JAN, Janssen A, et al. Risk prediction tools in cardiovascular disease prevention: a report from the ESC Prevention of CVD Programme led by the European Association of Preventive Cardiology (EAPC) in collaboration with the Acute Cardiovascular Care Association (ACCA) and the Association of Cardiovascular Nursing and Allied Professions (ACNAP). Eur Heart J Acute CV Care. 2019;26:1534–44.
6. Visseren FLJ, Mach F, Smulders YM, et al. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J. 2021;42:3227–337.
7. Cardoso H, Bello CT, Andrade L, et al. High prevalence of cardiovascular disease and risk factors among type 2 diabetes patients followed in a hospital setting in Portugal:

the PICT2RE observational study. Rev Port Cardiol. 2023;42, http://dx.doi.org/10.1016/j.repc.2022.04.011.
8. Shah AD, Rapsomaniki E, Langenberg C, et al. Type 2 diabetes and incidence of cardiovascular diseases: a cohort study in 1.9 million people. Lancet Diab Endocrinol. 2015;3:105−13.
9. Kotseva K, De Backer G, De Bacquer D, et al. Primary prevention efforts are poorly developed in people at high cardiovascular risk: a report from the European Society of Cardiology EURObservational Research Programme EUROASPIRE V survey in 16 European countries. Eur J Prevent Cardiol. 2021;28:370−9.
10. Vinik AI, Maser RE, Mitchell BD, et al. Diabetic autonomic neuropathy. Diabetes Care. 2003;26:1553−79.