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Review

On the importance of global cardiovascular risk assessment in people with type 2 diabetes

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ABSTRACT

This narrative review examines the concept of diabetes as a cardiovascular disease (CVD) risk equivalent, the rationale and approaches to absolute CVD risk estimation in type 2 diabetes. In people with diabetes, CVD risk follows a gradient. Reliably capturing this gradient depends on the combination of several risk factors. Existing CVD risk tools applicable to people with diabetes have shown a modest-to-acceptable performance. Future improvements may include updating existing models or constructing new ones with improved predictive accuracy. Ultimately, developed models should be tested in independent populations, and the impact of their uptake on clinical decision making and the outcome of care assessed.

Contents

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1. Introduction

Cardiovascular disease (CVD) is the leading cause of ill-health and mortality in people with type 2 diabetes (T2DM). T2DM is associated with twice the risk of incident coronary heart disease (CHD) and ischemic stroke and 2–4 times increased risk of CHD and stroke mortality compared with diabetes-free individuals [1–3]. Implementation of CVD risk reducing therapies over the last decades has considerably improved the cardiovascular health of people with diabetes [4–7]. However, CVD has remained the leading cause of death in people with diabetes [1,2], raising more interest for new strategies to achieve further reduction in CVD risk in this population.

During the last decade, strategies for CVD prevention in diabetes have been guided by the consideration that people with diabetes had future risk of CVD equivalent to that in non-diabetic CVD survivors. Such a consideration qualified them for risk reducing therapies without prior CVD risk assessment. This consideration was based on evidence from earlier cohort studies [8–10]. However, subsequent studies have shown variable results, with more indication that diabetes status may not be a CVD equivalent in all circumstances [11]; thus highlighting the need for multivariable approach as an appropriate basis for risk stratification for CVD prevention in people with diabetes. This is even more relevant in the current context characterized by a gradual shift in the management of diabetes mellitus from a glucocentric focus to an intensive multifactorial strategy targeting reduction in the risk of both macrovascular and microvascular complications of diabetes [12,13].

In this paper, we critically review the concept of diabetes mellitus as a CVD risk equivalent from both methodological and therapeutic perspectives. We then elaborate on the rationale and strategies for global CVD risk estimation in people with diabetes, emphasizing on the specificities and limitations of those strategies. We aim to contribute to the debate on the importance of global CVD risk assessment in people with diabetes, as the basis for initial prescription and subsequent intensification of risk reducing therapies.

1.1. Evidence acquisition

For this narrative review, we searched PubMed for English-language studies published up to April 2012 that addressed cardiovascular risk estimation among people with diabetes. We did not limit by country. We excluded non-human studies and studies focusing on cardiovascular risk estimation among people with type 1 diabetes (T1DM), as there are fundamental differences in cardiovascular risk levels in people with T1DM and those with T2DM, which are related to the age groups affected, the time course of the conditions, their pathophysiology, as well as the interactions with complications, especially renal disease [14]. We also examined the reference lists of articles identified. We relied on good-quality systematic reviews to assess the performance of CVD risk estimation prognostic models [15,16]. Global cardiovascular risk assessment in people with diabetes is a complex and vast question which incorporates many different and heterogeneous questions (e.g., rationale, approaches to tools building, performance of tools, etc.), and spans many areas. We examined papers across a broad range of pathophysiology, clinical and public health literature, incorporating various types of studies, which may be difficult to target with a single and unifying search strategy. Thus, this review does not systematically assess every published article addressing this subject; rather, we seek to provide a synthesis of the most up-to-date, relevant literature regarding the key concepts underlying the notion of global cardiovascular risk assessment among people with type 2 diabetes, using prognostic models.

2. The concept of diabetes as a CVD risk equivalent

2.1. Origins of the concept

The concept of CVD risk equivalent originates from a study by Haffner et al. [8], in which a non-significant difference was found in the risk of death from CHD when diabetic subjects without prior myocardial infarction (MI) were compared with non-diabetic subjects with a history of MI (adjusted hazard ratio [HR]: 1.4; 95% confidence interval [95% CI]: 0.7–2.6). The enthusiasm for this seemingly "elegant concept" was further reinforced by findings from randomized trials showing that statins lower the risk of CVD events among people with diabetes irrespective of the baseline levels of LDL-cholesterol [9,10,17]. Consequently, many have argued for an aggressive treatment for CVD risk factors, including the widespread use of statins and aspirin in everyone with T2DM for primary CVD prevention regardless of starting cholesterol levels.

2.2. Evidence for and against the coronary heart disease/cardiovascular risk equivalent concept from cohort studies

The seminal study by Haffner et al. on diabetes as a CHD risk equivalent had important limitations [8]. Firstly, it was