HealthManagement.org
The Journal
LEADERSHIP • CROSS-COLLABORATION • WINNING PRACTICES
VOLUME 19 • ISSUE 4 • 2019 • € 22
ISSN = 1377-7629

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Cardiovascular Disease Prevention 2019: **Quo Vadis?**

Summary: Cardiovascular disease prevention strategies in 2019 remain a major healthcare issue, requiring an individualised approach for diagnostic and therapeutic decision making.

Introduction

Since investigators from the Framingham Heart Study first confirmed the existence and importance of cardiovascular disease (CVD) risk factors in 1961 (Kannel et al. 1961), scientists and clinicians have been seeking to refine the prediction of risk for CVD. More than 50 years later, age, gender, and traditional CVD risk factors, including hypertension, diabetes, hypercholesterinaemia, smoking, and adiposity are predominantly used in daily clinical routine for risk prediction and stratification into risk groups. Based on these risk factors, multiple risk scoring algorithms (eg the Framingham Heart Score, the European SCORE, or the ASCVD-Score) have been established over the last decades. These allow the classification of patients into risk groups (low, middle, high), combining the information from traditional risk factors. However, the current algorithms only imprecisely predict the individual's future risk, especially in the intermediate-risk group, which is also acknowledged by current guidelines (Grundy et al. 2018). For further risk stratification, risk enhancement via assessment of carotid artery plaque burden, ankle brachial index, and most importantly, the coronary artery calcification (CAC) score is suggested by current guidelines (Grundy et al. 2018; Piepoli et al. 2016). The present article provides an overview of state of the art cardiovascular risk prediction strategies in 2019 and gives a perspective on innovative approaches that may improve future prevention algorithms.

Risk Scores

Risk scoring algorithms are established in clinical routine for assessment of cardiovascular disease risk based on traditional risk factors. For many years, the Framingham Risk Score was the leading risk score in clinical routine (Pencina et al. 2009). However, several studies have outlined its limitations to distinguish the risk for CVD (Ajani and Ford 2006; Brindle et al. 2003; Akosah et al. 2003). In the U.S., the Framingham Risk Score has been widely replaced by the Pooled Risk Equation, which is recommended according to the current AHA/ACC guidelines (Grundy et al. 2018). In Europe, the ESC advises the utilisation of the SCORE, which has been established based on European cohort studies and differentiates into high and low-risk countries. In contrast to most other algorithms, the SCORE assesses the risk of cardiovascular mortality only instead of overall cardiovascular event risk (Piepoli et al. 2016). Based on different approaches, multiple additional risk scores are available, eg for estimation of lifetime risk (Jaspers et al. 2019). However, the predictive ability of risk scores based on traditional risk factors is limited, providing an area under the ROC curve of around 0.7. Inclusion of modern risk markers such as the CAC score may improve the predictive ability (McClelland et al. 2015), but need to find their way into daily clinical routine.

Statin Therapy for Primary Prevention – Differences in European vs. U.S. Guidelines

In patients aged ≥40 years without known cardiovascular disease, AHA/ACC-guidelines advise statin therapy when the risk for atherosclerotic cardiovascular disease (ASCVD) is ≥7.5% in 10 years, while statin therapy can be considered in patients with 10-year ASCVD risk of ≥5% (Grundy et al. 2018). But the ASCVD-Score, which is based on U.S. population-based studies, leads to a relevant overestimation of 10-year risk in European cohorts (de Las Heras Gala et al. 2016). Therefore, application of AHA/ACC compared to ESC-guidelines results in a tremendously higher rate of indication for statin therapy (Mahabadi et al. 2017; Kavousi et al. 2014). In contrast, according to European guidelines, a relevant amount of patients experiencing cardiovascular events would have been classified into low or intermediate risk groups prior to disease manifestation (Mahabadi et al. 2017). This makes approaches for individualised risk estimation and personalised treatment recommendations indispensable, allowing improved prevention strategies in the future.

Imaging for Reclassification of Cardiovascular Risk

Several measures of subclinical atherosclerosis have been suggested for potential risk reclassification in primary prevention cohorts. Most importantly, the CAC score, quantified from non-

contrast cardiac computed tomography (CT), has demonstrated its ability to improve the prediction of cardiovascular events as well as allows reclassification of risk groups (Mahabadi et al. 2017; Yeboah et al. 2012). The CAC score also outperforms other markers of subclinical atherosclerosis such as the ankle brachial index and the carotid intima media thickness (Geisel et al. 2017). A CAC score of zero reclassifies patients to a category in which guidelines no longer recommend treatment according to population-based cohort studies (Nasir et al. 2015; Mahabadi et al. 2017). Therefore, CAC scoring can be used to down-classify selective patients as statin therapy in primary prevention cohorts may be withheld or delayed if the CAC score is zero. In contrast, recent data suggests that the detection of subclinical atherosclerosis by a CAC score of greater than zero increases the likelihood of lifestyle modification and initiation or continuation of pharmacological therapy (Gupta et al. 2017). Likewise, within the framework of ESC-guidelines, one in three individuals with a recommendation for lipid-lowering therapy can be reclassified to a lower risk group by CAC scoring (Bittencourt et al. 2018). But in addition, assessment of the CAC score also has the added value of identifying patients without indication for statin therapy, who indeed are at increased risk (Mahabadi et al. 2017). When following ESC recommendations, CAC scoring can be used to both down- and up-classify patients with and without indication for statin therapy in appropriate risk groups. Therefore, CAC scoring has the ability to improve the prediction of cardiovascular risk on an individualised level and leads to a significant improvement in reclassification, allowing personalised treatment decisions in primary prevention settings.

Innovative Imaging Technologies for Risk Prediction

The CAC score is quantified based on the Agatston method, which was described in 1990 and accounts for size and density of calcified lesions (Agatston et al. 1990). However, over the last 30 years, imaging technology for visualisation of cardiovascular structures has relevantly improved. In addition, once cardiac CT is performed, assessment of other structures of the heart and the vasculature may improve risk prediction in addition to the CAC score. These include the sizes of cardiac chambers and the great vessels as well as visceral adipose tissues within the thorax (Dykun et al. 2015; Kalsch et al. 2013). Most importantly, the epicardial adipose tissues have gained interest over the last two decades as a potential modulator of local inflammation. Epicardial fat can be quantified from computed tomography, magnetic resonance imaging, or echocardiography of the heart. Recent data suggests that both the volume as well as the CT derived attenuation of epicardial fat is associated with cardiovascular risk, independent of traditional cardiovascular risk factors and the CAC score (Oikonomou et al. 2018; Mahabadi et al. 2013; Balcer et al. 2018). When contrast-enhanced CT coronary angiography is performed, information on the presence or absence of obstructive CAD can be obtained, which may improve the patient's outcome in high-risk cohorts (Scot-Heart Investigators et al. 2018). Moreover, from contrast-enhanced CT, composition of plaque burden can be evaluated, allowing the detection of established high-risk plaque features, which may further increase the predictive value of this imaging technology (Ferencik et al. 2018). In addition, novel imaging technologies such as molecular imaging on inflammation and metabolism provide first promising results and may play a relevant role in the future (Schlosser et al. 2013; Nensa et al. 2015).

Conclusion

Despite cardiovascular disease being the number one reason for morbidity and mortality in the industrialised world, primary prevention strategies remain a major challenge in both research as well as clinical practice. Based on traditional risk factors, multiple risk scoring algorithms are established and broadly used in daily routine. However, these algorithms only imprecisely assess the individual patient's risk. The CAC score currently is the best imaging derived measure for redefining risk, allowing personalised treatment decisions in primary prevention. But multiple new approaches are on the horizon that will challenge the role of CAC scoring in the future. ■

Conflict of Interest

There are no conflicts of interest to disclose.

KEY POINTS

- The predictive ability of risk scores based on traditional risk factors is limited
- Inclusion of modern risk markers may improve cardiovascular risk prediction in daily clinical routine
- Application of AHA/ACC compared to ESC-guidelines results in a tremendously higher rate of indication for statin therapy
- CAC scoring has the ability to improve the prediction of cardiovascular risk on an individualised level and can allow personalised treatment decisions in primary prevention settings
- Novel imaging technologies such as molecular imaging on inflammation and metabolism provide first promising results and may play a relevant role in the future

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