Cardiovascular risk prediction models with myocardial perfusion imaging in chronic kidney disease: ACCESSing digits or focusing on the patient?

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Received Jul 4, 2018; accepted Jul 5, 2018
doi:10.1007/s12350-018-1367-8

See related article, pp. 41–50

Cardiovascular disease (CVD) remains the leading cause for mortality worldwide.[1] Prevention strategies and the pursuit for predictors of CVD as well as the associated mortality have given rise to several statistical models and algorithms[2] aiming to predict future events. The multifactorial nature of CVD and the interactions between genetic, social, and environmental risk factors complicate accurate risk assessment.[3] Commonly, multiparametric prediction models include well known risk factors such as age, gender, smoking, dyslipidemia, hypertension, and diabetes and have been shown to improve our ability for prevention and enhanced screening of patients at risk for cardiovascular events.[4-6]

Nevertheless, in the clinical world such prediction models face several issues that humper its implementation. While the demand for population-adjusted risk scores has increased, the dynamic nature of the disease as well as of the risk factors aggravates the creation of an integrated risk assessment scoring system for all populations.[7] In addition to the eminent Framingham study[4] numerous different models have been investigated such as the Europe British/Scottish Regional HeartStudies[5] or the Munster Cardiovascular Study (PROCAM).[6] On top of clinical risk factors, incorporation of cardiac imaging test results has been shown to possess incremental value for the development of new risk stratification strategies. To that end, nuclear imaging primarily with the stress myocardial perfusion single-photon emission-computed tomography (SPECT) myocardial perfusion imaging (MPI)[8] represents one of the best investigated modality for risk assessment with regards to myocardial infarction.[9-11] In addition to sole risk stratification, SPECT-MPI further influences management decisions since patients with moderate to large areas of inducible ischemia are more likely to have a survival benefit from revascularization therapy vs. medical treatment.[12]

In order to develop a risk score for the Japanese population, the J-ACCESS studies-family, that initiated close to 20 years ago, established a database including more than 4000 patients and investigated the prognostic value of ^{99m}Tc-tetrofosmin SPECT-MPI in the prognosis of patients with ischemic heart disease.[13,14] Cardiac event risk estimation was based amongst others on myocardial perfusion defects during stress (using summed stress score), left ventricular ejection fraction (LVEF), age, and presence of diabetes mellitus. Although annual cardiovascular events were significantly lower in Japan compared to those in the USA and Europe, it was shown that cardiovascular event rates were higher in patients with larger perfusion defects and reduced LVEF.[14] Follow-up studies, such as the J-ACCESS-3 demonstrated the ability and usefulness of SPECT-MPI to predict 3-year outcomes in patients with chronic kidney disease (CKD), a condition well associated with the risk of death, hospitalization as well as cardiovascular events.[15]

To complement these previous findings, in the current issue of the *Journal*, Nakajima et al.[16] investigated the accuracy of three risk models derived from the J-ACCESS study to predict major events in a new cohort

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J Nucl Cardiol 2020;27:51–2.
1071-3581/$34.00

of 526 patients with CKD. One four- and two five-parametric models were utilized, with the latter two including information on the stage of CKD (as absolute estimated glomerular filtration rate (eGFR) numbers and as categorical values, respectively). Using the actual 3-year outcomes of the J-ACCESS 3 study as a reference, all three risk models were shown to perform well with regards to risk stratification. The authors elegantly demonstrated that the J-ACCESS risk models can correctly stratify CKD patients with eGFR$\geq$15 mL/min/1.73m^2 into low, intermediate, or high risk of developing major cardiac events while patients with end-stage disease (eGFR<15 mL/min/1.73m^2) are at high risk, as expected, regardless of estimated risk values. The study focused solely on patients with CKD G-stage 3-5 and notably, the receiver-operating characteristics analysis for cardiac events prediction were rather moderate (with area under the curve values $\sim$ 0.66) for all three models. Furthermore, although inclusion of eGFR improved risk estimation, all three risk models underestimated the actual outcomes of patients with CKD.

Risk scores are designed to assist physicians in clinical decisions by simplifying perplex relationships. Increased complexity of a score with diverse inclusion and exclusion criteria blunders the purpose of the score itself. This could very well be one of the reasons for the relative underutilisation of risk scores in clinical practice. Nevertheless, the identification and potential future implementation of additional clinical or non-clinical parameters (as for example SPECT-MPI) can enhance the accuracy of risk stratification analysis allowing for improved understanding of CVD and enabling more opportunities for prevention. The study by Nakajima et. al.[16] represents a further step towards a more accurate prediction of cardiovascular events by combining SPECT-MPI findings and clinical risk factors for the Japanese population.

The quest for the perfect risk score will definitely carry on and the authors have added yet a small stone into building patient-specific risk models. Notwithstanding the relevance of cardiovascular risk assessment it still remains an estimate. An estimate that can facilitate therapeutic decisions but will always contain a level of uncertainty. Risk scores hold great potential with regards to epidemiologic assessment; as physicians treat individuals and not entire populations, novel risk scores are highly valuable, they shall not however replace our clinical evaluation and drift the focus away from the patient.

Disclosure

The University Hospital Zurich holds a research contract with GE Healthcare.

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