Prediction of 14-year cardiovascular outcomes by dobutamine stress 99mTc-tetrofosmin myocardial perfusion SPECT; methodological issues in prediction studies

It was interesting to read the paper by Roest S and colleagues published in Feb 2018 issue of the Journal of Nuclear Cardiology.[1] Dobutamine stress myocardial perfusion imaging (MPI) is a useful alternative for the evaluation of coronary artery disease (CAD). Those authors aimed to evaluate the long-term prognostic value of dobutamine stress MPI in elderly patients unable to perform an exercise test. They included 247 elderly patients (mean age 71 ± 5 years) who underwent dobutamine stress single-photon emission computed tomography (SPECT) MPI. A summed stress score (SSS) was obtained to estimate the extent and severity of perfusion defects. End points during follow-up were all-cause mortality, cardiac mortality, and nonfatal myocardial infarction (MI). They reported that during a median follow-up of 14 years (range 12–16), 168 (68%) patients died (all-cause mortality), of which 56 (23%) occurred due to cardiac causes. They further reported that Kaplan-Meier survival curves showed that MPI provided optimal risk stratification in patients with normal and abnormal MPI. Multivariable analysis identified an abnormal MPI as a strong significant predictor of all-cause mortality and cardiac events.[1] They concluded that dobutamine stress ^{99m}Tc-tetrofosmin SPECT provides incremental prognostic information for the prediction of long-term cardiovascular outcomes in elderly patients, unable to perform exercise testing.

However, these results are not the most appropriate approach for prediction of cardiac mortality and especially all-cause mortality in elderly patients.[2–7] First, for prediction studies, we need data from two different cohorts or at least from one cohort divided into two to first to develop a prediction model and subsequently validate it. Misleading results are generally the main outcome of research that fails to validate its prediction models. Validation of a prediction model can be done by applying different approaches such as split file, bootstrapping, or other well-known validation methods. Moreover, for prediction of cardiac mortality and especially all-cause mortality, we must assess the interactions between important variables. Final results can be impacted dramatically when qualitative interactions are present.[2–7] This means that most of the time, without assessing the interaction terms, prediction studies will mainly produce misleading messages. It is crucial to know that by applying a multivariable analysis, we are actually dealing with possible confounding factors such as sex, etc. However, effect modification (interaction) should also be investigated by stratified analysis to detect any possible modification effect of important variables such as sex, since cardiac mortality is more frequent in female than male. That is why for prediction of cardiac mortality, we should not rely on Kaplan-Meier curves because the comparison is actually between groups. To make it brief, in prediction studies, the main purpose is to provide a model, index, or score applicable to individual (patient). Finally, associations, even though statistically significant, do not guarantee prediction.

In this letter, I discussed methodological issues on prediction studies. Any prediction, especially all-cause mortality, should be supported by the above-mentioned methodological issues.

Disclosures

The author has no competing interests to declare.

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