Editorial

Effectiveness of Biomarkers in Cardiology

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Besides providing diagnostic or prognostic accuracy, a biomarker must be effective to ensure its adequate use in routine clinical implementation. Effectiveness can be defined as an individual's potential to benefit from using the biomarker. This benefit includes the prevention of undesirable clinical outcomes and improvement in an individual's quality of life.

Assessment of a biomarker's effectiveness should include two sequential criteria. First, the biomarker should add prognostic value in relation to basic clinical and laboratory data. Second, the information provided by the biomarker should promote changes in medical conduct in a way that ultimately benefits the patient. Beginning with the analysis of prognostic value, a new biomarker must have a prognostic value independent of conventional risk markers. However, this criterion of statistical significance is not enough to guarantee clinical significance. Once the statistical significance is confirmed by multivariate analysis, it is necessary to proceed and evaluate whether the biomarker increases our ability to identify individuals who will present the undesirable outcome. This is done by incremental analysis of the C-statistic and net reclassification analysis[1]. For example, although high sensitivity C-reactive protein has an independent association with cardiovascular risk, it only slightly increases the discriminatory capacity in Framingham score[2]. The coronary calcium score, on the other hand, can increase the C-statistic of Framingham score, in addition to correctly reclassifying a proportion of patients[3]. This incremental value is an essential condition for a biomarker to be effective, because only then can its result correctly modify clinical decisions.

However, the added value is not enough for defining effectiveness; the result of the biomarker must also promote actions that benefit the patient. To facilitate this discussion, we will use the stress test as an example, which should be considered inappropriate for studying coronary heart disease in asymptomatic individuals[3,4]. Incomprehension by some people as to why this test is classified inappropriate in this situation derives from the incorrect belief that prognostic value itself justifies implementing a test. However, this argument is limited to the first stage of assessing the effectiveness of a biomarker, as described previously. Diagnosing coronary heart disease using biomarkers in asymptomatic patients may be the best diagnostic tool for not modifying the clinical conduct to benefit the patient because strategies to control risk factors are well targeted on the basis of overall risk assessment of the individual and because the possible diagnosis of obstructive coronary disease in asymptomatic patients should not induce invasive strategies aimed at revascularization, as the benefit of this type of treatment lies in controlling symptoms without reducing the risk of heart attack or death[5,6]. Instituting a treatment to control symptoms is not required in an asymptomatic patient. In addition, some of these patients suffer from injury and unwanted outcomes arising from unnecessary procedures[7]. This type of reasoning can be complemented by randomized clinical trials that compare patients outcomes between randomized groups for using a test *versus* control. This is the case of the DIAD study, in which randomized asymptomatic individuals with diabetes underwent or did not undergo myocardial scintigraphy, suggesting that the clinical evaluation of patients was equal, without reduction of cardiovascular events in the scintigraphy group[8]. For this reason, the American Board of Internal Medicine's campaign *Choosing Wisely*, with support from the American College of Cardiology, recommends not using imaging scans for annual survey of coronary disease in asymptomatic patients[9]. For the same reason, the use of PSA for screening prostate cancer was proscribed by the US Prevention Task Force[10]. These are examples of recommendations for the use of diagnostic tests, keeping in mind the concept of effectiveness.

In addition, someone could offer the example of an asymptomatic patient whose (inappropriate) assessment of ischemia led to the diagnosis of a serious illness in the left coronary trunk. If the number of patients benefiting were greater than the number of patients suffering damage (which is not shown), then the cost-effectiveness analysis enters into play. How many patients must take the examination for one to benefit from the use of this biomarker? And at what cost? This can be understood as the revenue (yield) of the examination, often described by the number of individuals that must be tested for one to benefit (NNTestar).

In the article "Biomarkers in Cardiology," we introduce the potential for new tests under the critical eye of the concept of effectiveness.

Keywords

Biological Markers; Effectiveness; Cardiovascular Diseases/genetic; Disease Prevention; Evidence-Based Practice.

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