CPQ Medicine (2019) 8:2
Editorial

Biomarkers of Death Prediction: Are We Currently Going Too Far?

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Received: 29 August 2019

Published: 16 December 2019

Keywords: *Biomarkers; Diagnosis; Outcome; Prediction; Respond to Treatment; Death Biomarkers*

Abbreviations

ADA: anti-drug antibodies
AGT: angiotensinogen
AKI: acute kidney injury (AKI)
ANA: antinuclear antibodies
anti-ACPA anti-citrullinated peptide antibodies
anti-CCP: anti-cyclic citrullinated peptide
CAD: coronary artery disease
COPD: Chronic Obstructive Pulmonary Disease
CRP: C reactive protein
CVD: cardiovascular disease
ESR: erythrocyte sedimentation rate
HbA1c: Glycated hemoglobin
IL-18: interleukin 18
KIM-1: kidney injury molecule 1
NGAL: neutrophil gelatinase-associated lipocalin
RA: rheumatoid arthritis
RF: rheumatoid factor
RRT: renal replacement therapy
TIMP-2: tissue inhibitor of metalloproteinase 2
TNF-α: tumor necrosis factor-α

Biomarkers are able to inform about the stage or severity of a particular disorder or differentiate diagnoses. Other biomarkers can predict the evolution and outcome of a disease, or the respond or not to a particular treatment. Currently, there are many biomarkers and they all have a great value as diagnostic and/or prognostic tools.

Some of these examples include rheumatoid factor (RF), erythrocyte sedimentation rate (ESR), C reactive protein (CRP), and the anti-cyclic citrullinated peptide (anti-CCP), used for diagnosis in rheumatoid arthritis (RA); they are associated with the development of a more aggressive disease, extra-articular manifestations and premature mortality in RA patients, and are capable of predicting therapeutic response. Anti-citrullinated peptide antibodies (ACPA) have a predictive role in RA, while antinuclear antibodies (ANA), and have a predictive, prognostic and preventive role [1].

Rare autoantibodies and anti-drug antibodies (ADA) -associated with different disease manifestations and also with a greater incidence of cancer- are predictors of clinical manifestations in systemic sclerosis and systemic lupus erythematosus and are associated with malignancies. The determination of ADA levels may be useful for the assessment of a right management in patients where the clinical efficacy of tumour necrosis factor-alpha (TNF-α) inhibitor has dropped [2].

Metabolite profiling at baseline are useful in the context of examining prospective disease, including myocardial infarction, stroke, and/or cardiovascular disease (CVD) death in the CVD outcome [3,4].

Glycated hemoglobin (HbA1c) for prognostic in overall coronary artery disease (CAD), and let not forget the biomarkers for cancer -for detection, prediction or respond to treatments [5].

Biomarkers of inflammation can help to identify exacerbations that may respond to oral corticosteroids and antibiotics in Chronic Obstructive Pulmonary Disease (COPD), and find the preventative treatment most appropriate. They can also help in the approach and management of exacerbation [6].

In acute kidney injury (AKI), neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule 1 (KIM-1), liver-type fatty acid-binding protein, interleukin 18 (lL-18), insulin-like growth factor-binding protein 7, tissue inhibitor of metalloproteinase 2 (TIMP-2), calprotectin, urine angiotensinogen (AGT), and urine microRNA are useful biomarkers for differential diagnosis, prognostic, as well as for differentiation of patients into risk groups for progressive renal failure, need for renal replacement therapy (RRT), or death [7].

Now, a recent study using a big sample -over 44,000 individuals in a range of age from 18 to 109, of which over 5,500 died during the follow up- has identified 14 metabolic biomarkers independently associating with all-cause mortality, predictors for long-term mortality, reaching 83 percent accuracy [8].

The authors of this research indicate that the information may be useful in helping decide whether or not to do surgery on patients who are frail or could serve as endpoints in new clinical trials.

Finding biomarkers indicators of risk of vulnerabilities and providing information for improvement or better treatment can obviously be helpful. Most of the biomarkers involved in physiological processes -fatty

acid metabolism, fluid balance, or inflammation-, have been used individually, but have never been combined in a single predictive score before. However, the authors also caution that the information cannot be use as yet to estimate the risk of mortality of an individual, and further studies to corroborate the work hypothesis have to take place.

Although such a test would be useful in predicting, for example, the outcome of elderly emergency patients, and therefore improve medication, others have already expressed their concerns about the use of these biomarkers by the health insurer providers.

However, the ability to predict the likelihood of five and 10 year mortality may not be all the beneficial in healthcare that we might initially think. Beside the risk of being used as a punishment in health premiums, we must consider the effect that this knowledge would have in the mental health of certain patients.

Do we really want to know how long we have to live? Maybe that is a personal question that patients -and potentially all of us- should answer before been subjected to these developing tests. This, of course, would involve an important ethical issue in medicine.

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