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Molecular markers for cardiovascular disease: cardiovascular biomarkers to proteomic discovery

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The level of interest in the research and discovery of new cardiovascular biomarkers has steadily grown. With new 'proteomic' technologies, namely mass spectrometers, becoming increasingly available there are growing expectations that isolation of new protein biomarkers will become possible. With efforts ongoing at the global level, we don't yet know how the newly discovered biomarkers will impact clinical medicine. In addition to these developments, we've seen great advances in protein-based diagnostics that have made biomarker testing more readily available both in the clinic and at the bedside. These technical advancements lie at two extremes of the spectrum—the bench and the bedside. Here we examine the cutting-edge, high-tech equipment in development, and the advantages of dissemination of these technologies in the clinical setting.

Laboratory-standard testing for proteins has reached a sophisticated stage whereby the testing unit can be brought to the office or clinic, thus enabling 'point-of-care' use. For cardiovascular diseases that often manifest as emergencies, such as ischemic heart disease, heart failure and coagulation disorders, patients have benefited greatly from the availability of technology that can measure levels of a spectrum of appropriate markers. Chest pain will, of course, remain one of the key manifestations of cardiac disease; however, accuracy of disease identification would be improved if a biomarker or biomarkers for aortic dissection were to be isolated and become available for testing. Advances have been made in this field, by our study group and others, which show that proteins such as smooth muscle myosin heavy chain, elastin and D-dimer could be useful as biomarkers of aortic dissection. Aortic dissection will remain a field for further development of biomarkers on the basis of presently available technologies, namely enzyme immunoassays.

By contrast, new technologies such as mass spectrometry are expected to facilitate the discovery of new proteins and analytes. Whether the presently available hardware *per se* will be useful in the diagnostic laboratory given the technical expertise needed for operation, however, remains to be seen. Furthermore, questions have been raised regarding the reproducibility and quantitative ability of this technology. Despite these reservations, mass spectrometry has importantly allowed us to investigate aspects of proteins and their lifecycle that were never before possible, such as processing and modifications. Protein processing is not a new concept, but the technology for its detection has not been readily available previously. As exemplified by the landmark discoveries of endostatin and angiostatin, both endogenous inhibitors of angiogenesis, and fragments of the seemingly ordinary proteins collagen and plasminogen, respectively, protein fragments initially thought to be benign can in fact possess bioactive properties and have diagnostic implications. As mentioned previously, modifications are also an important aspect of potential mass-spectrometry-based discoveries. Glycosylation of proteins remains a heavily researched field, especially in oncology, but mass spectrometry could also be applied to cardiovascular diseases, in which nitrosylation and oxidation might be of great importance. Once we have a better understanding of the technical requirements necessary for the detection of such proteins and their derivatives, hardware better suited for diagnostic use will be developed. This development still lies a few years ahead; currently available technology will be used to find new and important biomarkers in the meantime. Ultimately, these cutting-edge technologies could be incorporated into treatment algorithms, enabling them to be brought to the bedside.

We are in a rapidly evolving era for protein-based diagnosis of cardiovascular disease. Technological advancements will enable the discovery of new biomarkers and bring diagnostic technology closer to the clinic, with the common objective of improving clinical cardiovascular care.

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