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EDITOR'S PAGE

A First Dilemma in Cardiovascular Medicine

Adherence Versus Personalized Therapy

Valentin Fuster, MD, PhD

Adherence to therapy refers to "the extent to which patients follow a general strategy of medical instructions, this implying an active patient participation about the timing, dosage, and frequency of taking medications, as well as about compliance with health-related behavior or lifestyle modification" (1). Thus, current practice is to advise the same pharmacological therapy or lifestyle modification to a wide range of patients who are all presumed to resemble one another in terms of disease entity or of risk factor lifestyle category. Conversely, personalized or individualized therapy is the art and science of "coupling established clinical-pathological indices with state-of-the-art molecular profiling, to create diagnostic and therapeutic strategies precisely tailored to each patient's requirements" (2). Thus, in the field of oncology, this targeting of unique therapies has met with great successes for a variety of cancers based on patients' molecular profiles. As a result, the promise of personalized medicine or therapy has been excitedly embraced by the medical community at large. However, this excitement is, at present, meeting with much less enthusiasm in cardiovascular medicine for several reasons, but mainly because of medication nonadherence and failure to modify patient behavior. In fact, recent data on the rates of compliance with lifestyle modification and prescribed medication adherence are "alarming" (3). More than 50% of patients, on average, decide to abandon the prescribed treatment, and the objectives to improve their habits (quit smoking, lose weight, or engage in physical activity) are met by an equal or lower adherence percentage.

From the Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York.

Although Brazilian author Paulo Coelho's sentiment—"you shouldn't believe in promises"—may be considered somewhat negative (4), it provides a helpful reminder, especially for clinicians who should remain rooted in science and fact, to not get too swept up in the promise of new ideas. In cardiovascular medicine, we are constantly evaluating new targets to improve patient outcomes. These outcomes must drive our research and practices, not the promise of personalized medicine. For instance, to address the disappointing risk factor control in clinical practice, we evaluated data from 3 large-scale, randomized trials that focused on optimal medical therapy to determine if formalized attempts at risk factor control within clinical trials are effective in achieving guideline-driven treatment goals for diabetic patients with coronary artery disease (5). Including 5,034 diabetic patients, we found that the percentages of patients achieving the 1-year low-density lipoprotein cholesterol targets compared with baseline increased from 55% to 77% in the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial, from 59% to 75% in the BARI 2D (Bypass Angioplasty Revascularization Investigation 2 Diabetes) trial, and from 34% to 42% in the FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes) trial. Although similar improved trends were seen for systolic blood pressure, glycemic control, and smoking cessation, only 18% of the COURAGE diabetes subgroup, 23% of BARI 2D patients, and 8% of FREEDOM patients met all 4 pre-specified treatment targets at 1 year of follow-up. Thus, a significant proportion of diabetic patients with coronary artery disease fail to achieve pre-specified targets for 4 major modifiable cardiovascular risk factors in clinical trials. Based on these

results, we recommend "that fundamentally new thinking is needed to explore approaches to achieve optimal secondary prevention treatment goals" (5).

Similarly, in commenting on a failed study to develop a molecular imaging strategy that can monitor myocardial angiotensin-converting enzyme-1 up-regulation as a function of progressive heart failure, Yancy et al. (6) adeptly stated, "meaningful research focused on increasing our precision in the prescription of evidence-based medical therapies for heart disease should continue. But personalized medicine remains an unfulfilled hope." These types of results may account for why the majority of cardiovascular specialists are not yet incorporating personalized medicine into their clinical "thinking" and therapeutic options (7). There are exceptions, such as pulmonary arterial hypertension or unusual rhythm disturbances, which may require specific individualized therapies. However, a number of our highly esteemed colleagues strongly advocate pursuing personalized cardiovascular treatments, whereas we strongly argue for pursuing better adherence to common therapies, perhaps the highest priority in cardiovascular medicine today.

The pathway to improving patient outcomes may not lie in the field of targeting and personalized therapies. Our task as cardiovascular specialists is far more simple and, yet, far more complex. How can we overcome the lack of medication adherence and lifestyle modification? As an example, research is starting to show that the polypill may overcome some of the adherence barriers in secondary prevention in countries where it is approved. However, pushing the envelope further, the real key to improving our patient outcomes may be truly *personal*, as we attempt to speak to our patients about making better choices, connect with them about the cultural or socioeconomic barriers to better lifestyle habits, or convince them how critically important it is for them to impart these better decisions to their children. We, as cardiovascular specialists, are uniquely positioned to help influence our patients and their families in positive ways—and although these successes may be seen as small, they have the potential to save lives one person at a time. Thus, I am prepared for my next Editor's Page: "A Second Dilemma in Cardiovascular Medicine: Personalized Medicine Versus Personal Interaction with the Patient."

ADDRESS CORRESPONDENCE TO: Dr. Valentin Fuster, Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, New York, New York 10029. E-mail: valentin.fuster@mountsinai.org.

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