COMMENTARY

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Will Cardio-Virology Be the Next Cardio-Oncology?

Remarkable advancements in therapeutic effectiveness over the past 30 years have created new cohorts of patients not previously seen. Once imminently fatal illnesses are now chronic manageable conditions, often treated with ongoing pharmacotherapy. The prolonged longevity enjoyed by these patients, combined with complicating factors from their diseases and/or treatments, expose patients to other conditions that were of little significance in past generations when life expectancy was very limited. Patients with congenital heart diseases, chronic heart failure, many forms of cancer, and human immunodeficiency virus (HIV) infection and others are at risk for serious comorbid conditions—in many cases, more likely to cause morbidity and mortality than their "primary" diagnoses. The specifics of care for these new patient groups, including differences in character and severity of the comorbid conditions, differences in treatment efficacy and tolerability in these individuals, and the significant likelihood of drug-induced disease and drug–drug interactions all suggest that specialization in providing their care may result in additional clinical benefits.

In cardiovascular disease, cardio-oncology is an excellent example of this concept.[1] With more efficacious and better-tolerated drug, radiation, and surgical treatments, many cancer patients are enjoying longer lifespans. Certain cancers are now themselves chronic diseases, with their sufferers enjoying markedly better survival but, consequently, a greater risk of dying from conditions other than cancer. Cardiovascular disease in particular may be influenced by complications of the malignancy, often by complications of the therapies, and sometimes by adverse drug interactions with the chemotherapeutic agents. Hence, the need for cardiologists to become experts in treating heart disease in oncology patients is now accepted. These specialists have gone far to establish cardio-oncology as a defined subspecialty of cardiovascular diseases and are to be applauded for their efforts.[2]

Persons living with HIV constitute another new population with many similarities to the oncology patients discussed above. Approximately 1.1 million people in the United States are infected, with more than 37,000 new cases diagnosed each year.[3] Most HIV+ patients have a life expectancy nearing that of their uninfected counterparts,[4] and infected patients are about as likely to die from HIV-independent comorbidities as from HIV/acquired immunodeficiency syndrome.[5] The average age of these patients has progressively increased (with one-third now over age 45 years),[4,6] placing many in the high-risk age range for atherosclerotic cardiovascular disease and hard major adverse cardiovascular events. Additionally, HIV+ patients seem to have an earlier onset of cardiovascular disease.[7] Human immunodefiency virus infection itself is associated with a 50%-100% greater cardiovascular risk,[8] even after controlling for traditional risk factors.[9] Traditional risk factors seem to convey risk enhancements in HIV patients equal to those in noninfected patients[10]—though some (eg, smoking) may be comparatively more common in this population. The mechanism mediating this elevated independent risk is ill defined, though mounting evidence suggests vascular inflammation as contributory,[8] whereas direct cellular infection and a dysregulated host immune response are possible additional influencing factors. Patients living with HIV also suffer from metabolic syndrome and diabetes, dyslipidemias, hypertension,[11] and conditions such as osteoporosis that can limit their ability to perform regular exercise. Some antiretroviral agents/classes seem to accelerate atherosclerosis directly (protease inhibitors[12]) or indirectly through worsening dyslipidemia (nonnucleoside reverse transcriptase inhibitors[13]). Yet, data are clear that effective HIV therapy, confirmed by maintenance of minimum CD4+ counts and low or unmeasurable viral loads, is essential to reduce the event rate.[14] The risk of drug interactions between antiretroviral drugs and many classes of cardiovascular medications is high, particularly for drugs metabolized through CYP 3A4. Statins reduce event rates in HIV+ patients,[15] though many patients cannot receive the high-intensity therapy recommended by guidelines for the general population, owing to pharmacokinetic interactions.[16] Ezetimibe seems safe in these patients,[17]

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but outcome data for this population are lacking. No data are available for newer lipid-lowering agents (PCSK-9 inhibitors[18]) or anti-inflammatory drugs, such as the interleukin-1β inhibitor canakinumab,[19] for either primary or secondary prevention in HIV+ patients.

Our ability to predict future major adverse cardiovascular events risk remains limited because risk equations developed for general populations, even with the addition of calibration constants, tend to underestimate higher-risk patients and overestimate lower-risk patients.[20] One system, derived from the Data Collection on Adverse Events of Anti-HIV drugs (D:A:D),[21] includes a full model including some antiretroviral drug information. However, the highly questionable impact of abacavir on the myocardial infarction rate may invalidate this model.[22] A reduced D:A:D model (that does not use antiretroviral drug information) may be the best available at this time.[6]

Thus, as more data are collected on details of atherosclerotic mechanisms, treatment variances, and modifiable risk factor management and newer, more accurate risk estimation models are developed, the specific knowledge base for providing patient-specific cardiovascular care to patients with HIV will continue to grow. This, combined with the growing number of HIV+ patients at moderate-to-high cardiovascular risk, suggests that "cardio-virology" could be the next target population-based subspecialty in cardiology.

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