Over the past several decades, great strides have been made in the care of patients with congenital heart disease (CHD). As a result of the tremendous improvements in medical and surgical care, the focus is shifting from survival of infants with cyanosis to quality of life and maintenance of good health for patients with CHD throughout adolescence and adulthood. Along with increased survival has come a host of comorbid medical conditions related to aging and to the sequelae of the congenital heart condition or treatments for it. Among the recently raised concerns is the development of cancer in the population with CHD.

The article by Mandalenakis et al1 is the latest in a small but growing series of articles describing increased cancer risk among patients with CHD. This Swedish group used administrative data to evaluate the association between CHD and cancer, and, given the robust data available in Sweden, the authors were able to match each patient with CHD to 10 healthy control participants by birth year, sex, and county. With this method, they found an increased risk of cancer among patients with CHD across all types of CHD and multiple types of cancer.

The use of administrative data in the Swedish study is similar to that in other studies done in Canada2 and Taiwan,3 where patients with CHD were selected from national health care databases and the prevalence of cancer was determined using International Classification of Diseases, Ninth Revision diagnosis codes. Another study4 was done in children in the United States using data from California records of birth defects and the California cancer registry. The authors of these studies using administrative data have appropriately recognized the limitations of this approach, particularly as it relates to diagnosis validation and clinically available information. For example, information regarding lifestyle-related factors, such as primary or secondary smoking exposure, family medical history, dietary habits, and physical activity, is critically important to understanding cancer epidemiology among patients with CHD and is not available in administrative records.

Despite the limitations of administrative data and the different geographic, ethnic, and cultural populations across studies, the estimates of increased risk and increased prevalence of cancer in the population with CHD have been fairly consistent. It is now time, however, to move forward from association alone and to further explore the underpinnings of the connection between CHD and cancer. There are several plausible mechanisms that may relate CHD to cancer, and it is possible that there is more than 1 mechanism involved in the development of cancer among patients with CHD. The mechanism that has been studied the most is exposure to low-dose ionizing radiation. Low-dose ionizing radiation is a known carcinogen, and multiple studies have tried to review or estimate its effects on the population with CHD.5 This is particularly pertinent for CHD because both pediatric and adult patients are exposed to low-dose ionizing radiation in multiple diagnostic and therapeutic cardiac procedures, including computed tomography scans, cardiac catheterizations, and nuclear medicine studies.

However, alternative and/or additive mechanisms influencing the association between CHD and cancer must also be considered. These include multiple examples of overlap in the potential genetic origins of cancer and CHD, such as gene abnormalities in the RAS mitogen–activated protein kinase signaling pathway leading to CHD, a predisposition to cancer in patients with Noonan syndrome (PTPN11 mutation),6 and the association of variants in NOTCH1 with both CHD and cancer.7,8 Along with genetics, exposure to toxic compounds (eg, industrial air pollutants and pesticides) and...
radiation in utero also has the potential to be both teratogenic and carcinogenic. Our understanding of how genetics and environmental exposures may influence the association between CHD and cancer is still in the early stages.

From a clinical and public health perspective, it is also critical to understand whether patients with CHD are undergoing cancer screening at the recommended times. This issue may be less applicable for the younger cohort addressed in the study by Mandalenakis et al but is very important for middle-aged and older adults with CHD. Prior work has found that adult women with CHD underwent Papanicolaou tests, mammography, and colonoscopy for cancer screening at rates significantly lower than the national averages and those for adults without CHD in the same practice. Historically, only a few patients with CHD survived to adulthood. Now that adult survival is the norm, it is important that patients establish care with a primary care physician and undergo at least the minimum cancer prevention strategies and screenings recommended by the American Cancer Society and the US Preventive Services Task Force.

Although new research is ongoing, interpretation of the currently available data requires caution. The overall prevalence of cancer remains fairly low, and most people with CHD will not develop or die from cancer. However, cancer is a morbid and potentially fatal condition with available treatment and prevention strategies, and early identification is critical to optimal treatment. Because the population with CHD is large and diverse, with different patterns of care, interventions, exposures, and genetic predispositions, it is essential to develop more-specific information before drawing conclusions and implementing care strategies regarding cancer risk. Even if causal associations are identified, the timing and cost-effectiveness of screening strategies will need to be determined.

As we await more information, there are important strategies that can be implemented to decrease concerning exposures and potentially increase timely diagnosis. For example, cardiologists specializing in CHD can continue the emphasis on minimizing exposure to low-dose ionizing radiation by using noninvasive testing with magnetic resonance imaging and echocardiography when possible, as well as working with the catheterization and electrophysiology laboratories and computed tomography imaging sites to minimize radiation doses for necessary studies. In addition, cardiologists and other health care professionals for patients with CHD need to strongly encourage patients to seek routine primary care and ask about cancer screening at regular cardiology appointments to ensure that patients meet the screening requirements for the general population.

Thus far, most of the literature on the association between CHD and cancer has used administrative data but has established consistent associations, and the studies have hypothesized plausible mechanisms. It is now time to move beyond associations to explore clinical and translational research to determine better screening and treatment models for the population of patients with CHD. Although this will take time and larger numbers of patients to determine conclusions, cardiologists specializing in CHD, primary care clinicians, and patient and family organizations can continue to advocate for further research in this important area, mitigation of concerning exposures, and accomplishment of recommended cancer screening for patients with CHD.

ARTICLE INFORMATION
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