JACC: ADVANCES VOL. 3, NO. 10, 2024

EDITORIAL COMMENT

Early Intervention for Tetralogy of Fallot, But at What Cost?

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Cardiac catheterization with fluoroscopic guidance has become indispensable in the care of children and adults with congenital heart disease (CHD) since Werner Forssman first reached the heart with a percutaneously inserted catheter almost 100 years ago. In the past 2 decades there have been rapid advances in minimally invasive treatments for CHD to reduce repeated open heart surgeries. However, with the expanding use of low-dose ionizing radiation (LDIR), we are increasingly aware of the long-term costs of radiation exposure for both patients and the care team in the catheterization laboratory. Not only do children with CHD have more exposure to LDIR, but cardiac catheterizations are by far the highest source of exposure.[1,2] Children with CHD undergoing catheter-based interventions compared to those undergoing surgical interventions have higher rates of chromosomal abnormalities in peripheral lymphocytes which could be a marker of increased cancer risk.[3]

In this issue of *JACC: Advances*, Wong-Siegel et al[4] are the latest group to assess the impact of LDIR exposure for children with CHD. Utilizing the multicenter Congenital Cardiac Research Collaborative registry, the group compared LDIR exposure and lifetime attributable risk of cancer for a group of neonates with tetralogy of Fallot who underwent intervention in the first 30 days of life. Two groups were defined for comparison:staged repair (SR) and primary repair (PR). All medical sources of LDIR exposure (catheterizations, interventional radiology procedures, CT scans, nuclear medicine studies, and conventional x-ray) were assessed and the doses either extracted from the medical record (catheterizations, interventional radiology procedures, CT scans) or calculated based on published norms (nuclear medicine studies, conventional x-ray). Radiation-related cancer risks were calculated and compared to the baseline risk from general U.S. population data using data from the National Cancer Institute, which estimates lifetime attributable risk based on age at exposure, dose, and life expectancy.

Overall, the groups were quite similar, although the SR group were sicker (more inotropic support and mechanical ventilation) and younger at the time of initial intervention. Within the SR group, females and those with pulmonary atresia were more likely to undergo transcatheter palliation. Importantly, only 43% of the SR group underwent an initial transcatheter intervention; the majority underwent an initial surgical palliation.

There was a markedly higher percentage for all cancers attributable to LDIR exposure in both females (0.1%-2% vs 0.3%-7.3%) and males (0.1%-1.1% vs 0.3%-3.8%), with thyroid cancer having the highest rates. Multivariable regression found that SR, a genetic syndrome, preprocedure mechanical ventilation and need for reintervention were associated with higher total LDIR exposure (OR: 2.37, 1.16, 1.20 and 3.90, respectively). There were higher proportions of patients in the SR group who underwent catheterization, interventional radiology procedures, and CT scans, but the differences in frequency of procedures per patient found more conventional x-ray for the SR group and more nuclear medicine studies for the PR group; 71% of SR patients had either a catheterization alone or in combination with a CT scan, compared to only 36% of PR patients. Interestingly, while x-rays might typically be considered more “benign,” the frequency with which they were performed was so high that the LDIR exposure was similar to the amount from the less frequently performed CT scans. Encouragingly, the LDIR dose from catheterization

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The author attests they are in compliance with human studies committees and animal welfare regulations of the author’s institution and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2024.101240

decreased over the study period, though the proportion undergoing catheterization increased over time.

The consequences of early exposure to significant doses of LDIR in the current study are worrying and consistent with prior reports. A review of a Canadian health registry found significantly higher doses of LDIR in children with CHD, higher increases in the amount of LDIR exposure compared to noncongenital cardiac imaging procedures, and a significant decrease in the age of first exposure to LDIR.[5] A second review of the same health system compared adult patients with CHD with and without cancer and suggested an 8% to 10% increase in cancer risk for those adult patients with CHD with a higher number of LDIR procedures and estimated exposure doses.[6] A French registry of pediatric patients who underwent catheterization found that while over 80% only had a single catheterization procedure, there were still significant increases in cancer rates overall, as well as leukemia, lymphoma, and non-central nervous system solid tumors, specifically. Additional research to assess LDIR dose exposure in this population is underway.[7] A review of a U.S. national administrative database found increased rates of breast, lung, and liver cancer occurring at younger ages in adult patients with CHD compared to adults without CHD.[8]

Despite this, our patients are not doomed to suffer from excessive LDIR exposure and increased risks for cancer. Technological advances in fluoroscopic imaging have made significant reductions in LDIR exposure without compromising image quality. Digital angiography and image enhancement have led to more than a 50% reduction in exposure with no other changes in acquisition technique.[9] Comparisons of LDIR generated by fluoroscopy equipment made by different manufacturers identified some differences in dose between the companies, but the most significant difference was between older and newer imaging systems, with improvements in image quality and up to 3 times less radiation needed.[10] Beyond technological advances, increased provider awareness also has a significant impact on LDIR exposure. Single and multicenter quality improvement initiatives increasing provider awareness about radiation dosing and methods to reduce it as well as utilizing institutionally developed methods for radiation reduction have led to decreases in radiation exposure.[11,12] However, despite these interventions, smaller and younger patients (who are at the highest risk for future malignancy) saw no reduction in exposure.[12]

Wong-Siegel's study is further support for our need to be exceedingly vigilant when considering procedures that will expose our patients to LDIR. While the study conclusions are from a predictive model of cancer risk and not definitive diagnoses, and only examined one specific CHD, we cannot ignore the potential impact for our patients. Not only must we be diligent in practicing ALARA LDIR dosing, we should consider whether a given procedure is even needed at all. Practices such as routine daily postoperative chest x-rays that may lead to little change in management can quickly accumulate and produce unwelcome downstream consequences for an already fragile population with complex medical needs.

Treating CHD is a lifelong effort with many medical subspecialties collaborating to maximize the quantity and *quality* of life for our patients. As we continue to extend the lives of children who may never have survived the first year of life, it is vital that we focus on a lifelong plan to ensure they do not just survive their interventions, but are also able to thrive as adults with CHD. We are learning more about this population as they age and while there are many comorbidities and risks that cannot be mitigated, perhaps thoughtful use of LDIR in childhood can modify the future risk of cancer.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

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KEY WORDS cancer, congenital heart disease, ionizing radiation, tetralogy of Fallot