Lee Benson, MD

A pediatric interventional cardiologist talks about stenting for aortic coarctation, PFO closure, and device approvals.

When it comes to stenting—both covered and uncovered—for coarctation, what can interventionists expect in terms of acute and late outcomes?

Percutaneous stenting for arch coarctation is a significant advance in the treatment algorithm for this lesion. It is no longer solely a surgical lesion for the majority of patients, once they are a certain weight and age. In the neonatal period, coarctation is still a surgical disease. After the neonatal period, up until the child is around 20 to 25 kg, balloon angioplasty works very well. If the patient weighs > 25 kg, there are stents that you can place transfemorally that have a low risk of compromise to the femoral vessels, which was the initial reason for its limited application.

I think that the stenting outcomes have been very good—as good as, if not better than (in some cases), surgery. We're very fortunate in Canada to have covered stents available through the Special Access Program (a request-based regulatory exemption that allows use of otherwise noncommercially available drugs and medical devices), which are available in Europe but not the United States. Covered stents have added a level of safety to the procedure because they protect the wall of the vessel as it is expanded by the stent.

Acute outcomes have been very good. Late outcomes, when the stents are expanded to full diameters, have also been very good. Stents that are implanted in younger patients must be monitored because the stents have to be re-expanded as the child grows (around 5 to 7 years after the initial implant, depending on the child's growth rate).

In patients with stented coarctation, how should blood pressure and echocardiographic parameters be used to guide long-term care?

Unfortunately, repairing the coarctation, whether it's with a stent or surgery, does not cure the disease. These patients inevitably have an aortopathy—in other words, the structure of their arch vessels is different from normal, so for monitoring, they should have 24-hour ambulatory blood pressure monitors periodically throughout their lives to detect whether or not they develop hypertension. Many of these patients have some form of hypertension—resting, exercise-induced, or are normotensive in the office, but hypertensive on monitoring—so it can sneak up on you.

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A recent article from the Mayo Clinic tried to identify the cause of death in a coarctation population. Many years ago, there was a suggestion that patients with coarctation had a higher incidence of developing coronary artery disease (CAD), and they developed CAD and died. As it turns out from this case-controlled study, the risk factors for CAD and the coarctation population were exactly the same. The problem was that the patients with coarctation had hypertension, and that was what killed them.

If you (the physician) are vigilant, monitor patients, and control their hypertension if it occurs, you may take them out of the high-risk, sudden-death group or high-risk group for cardiac events. Additionally, at some point in their lives, patients should have a brain MRI; aneurysms of the Circle of Willis occur in approximately 10% of the coarctation population, and some need neurosurgical intervention. Whether the coarctation was stented or surgically repaired, patients should be scanned both as children and as adults, because it could be a developmental problem.

There are now more adults with congenital heart disease than children. What is the reason for this? Are more preventative measures being taken to reduce the incidence of congenital defects?

This is due to improved surgical and medical management. For children who had heart disease that would have died 30 or 40 years ago, there are now techniques to correct their heart lesions—at least the plumbing part of it. There were lesions that didn't have any form of therapy 20 years ago, and now these children are undergoing staged surgeries and are able to live relatively normal lives.

Do you think that more needs to be done to identify causes of congenital lesions in the neonatal period?

There are a couple of things. First, there has to be more comprehensive fetal echocardiography to identify lesions in utero, when the families can be given management options appropriately. There also has to be better postnatal screening, so children with congenital heart disease can be identified early. I think those two steps will be very significant in identifying infants with structural lesions.

Addressing the genetic issues is on the horizon; genetic profiling is not quite here yet. I think that's still a ways away. Although there are many noncardiac lesions that can be identified by genetic testing, I don't think we're there yet for congenital heart lesions.

What is on the top of your wish list for pediatric devices? Why do you think there is less innovation in this market, and what do you think can be done in the future to encourage innovation?

Pediatric cardiology is a boutique subspecialty; we're like orphans in a way, because our population is very limited. I can count on one hand the number of companies that focus entirely or partially on products for pediatric cardiology. Unfortunately, it is all due to the bottom line. Although there might be a product or a product line that has enormous potential for saving children's lives, it's not pursued or developed—money doesn't go in that direction.

The latest wave in pediatric devices is in biodegradable implants. In the United States, there is a US Food and Drug Administration (FDA) initiative looking at biodegradable implants (ie, stents) for coarctation and pulmonary artery stenosis, as well as biodegradable surgical implants. I think that kind of technology could change the way we look at implanting devices in children. It also has an impact on adults—wouldn't it be nice if you could have your patent foramen ovale (PFO) closed and then 2 years later, the device disappears?

Due to pediatrics' small numbers compared to adults with coronary artery disease, randomized studies are difficult to perform, but there are ways. The FDA has agreed that they could do studies that don't randomize in the traditional sense, but use operational performance guidelines and develop trials based on retrospective data. There are a lot of different ways of dealing with trials for children. I think that it's possible to do randomized trials, but numbers are difficult.

Compared to the United States, what is the device approval process like in Canada?

It's like night and day. I think that the Canadian government and the Medical Devices Bureau for Health Canada are enlightened. The structure of the programs, especially the Special Access Program, looks toward the patients' best interests based on recommendations from physicians. So if a device that has a CE Mark and good track record in Europe, and you have a patient population in need here, you can apply for use of the device in Canada as long as you follow the rules and regulations of the Special Access Program. It's a very good way of getting technology to Canada for the betterment of our patient population.

For example, covered stents are not approved devices in Canada but are available through the Special Access Program. As long as we don't abuse it, they will continue to support availability. Americans are disadvantaged by the rigors of the FDA, certainly compared to the Europeans, who are way out on the extreme end of having devices available. There is some review and regulation here in Canada, the government will not let just anything in and depends on careful review.

How do you see the RESPECT trial's data guiding clinical practice? What is next for PFO closure?

The RESPECT trial was interesting in that, if you didn't think PFO closure worked, it supported that view; if you thought that it worked, then it proved it effective. It all depends on how you look at the data. At our adult hospital, we close PFOs for recurrent stroke prevention. The number of closures didn't go down after CLOSURE-1 came out, and they certainly didn't decline after the RESPECT trial. I think that when you look at the numbers and the protocol-driven analysis, there is an enormous difference between treated (device) and medically treated groups.

The purists among us would say the intention-to-treat analyses showed no difference, but there were patients who were randomized to device implant but never received a device and had a stroke. That's why the intention-to-treat analysis was nonsuperior to

medical management. You certainly can make a very good argument that if you're conducting a device trial, the patient has to receive the device in order for you to test it. It's like having a drug trial and being randomized to the drug, but you don't take the drug and have an event; what are you supposed to do about that data?

If you look at the protocol-driven analysis, the recurrence rate was significantly less in the device group. In longer follow-up, I think there is going to be even greater separation in the intention-to-treat group because those patients who were device-assigned but not implanted will be washed out, with the medically managed patients having recurrent strokes. Only time will show the difference.

From my read, it's clear that closure does work. If I had a stroke and a PFO, there would be no doubt that I'd have a device implanted and take aspirin for the rest of my life.

Tell us a little about your institution and your current areas of research.

The cardiology program at the Hospital for Sick Children was started after the Second World War and is one of the largest programs in North America. The division has always led the way in many areas of pediatric cardiology. The interventional program was the first in the country, and it's also one of the largest in North America. We offer a full gamut of procedures for children with congenital heart lesions, both diagnostic, interventional, and electrophysiological. The program has led the way in many areas of therapy—in diagnosis, imaging, and intervention.

My areas of research focus on interventional procedures. I also have a special interest in hypertrophic cardiomyopathy and heart failure. ■

Lee Benson, MD, FRCP(C), FACC, FSCAI, is the Director of Cardiac Diagnostic and Interventional Unit for The Hospital for Sick Children in Toronto, Ontario, Canada. He has stated that he has no financial interests related to this article. Dr. Benson may be reached at benson@sickkids.ca.

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