Adults after the Fontan Operation: Which Medications Work?

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Dr. Burchill: Welcome back to "Interview with the Experts", a podcast series from Mayo Clinic, cardiovascular education. My name is Luke Burchill, and I'm leading the Heart Failure Care Pathway here at Mayo Clinic. And joining me today is Dr. Alexander Egbe, the director of research for the Adult Congenital Heart Disease Program. Welcome, Alexander.

Dr. Egbe: Thank you so much for having me.

Dr. Burchill: It's really great to have this opportunity to sit down and talk with you about heart failure. And today we're really gonna focus on those patients who've had the Fontan operation. So maybe we could start, in really general terms, how would you describe the Fontan operation to those patients you see, who have had this operation?

Dr. Egbe: Yeah, the Fontan operation is a very wonderful procedure that's been effective for treating patients with the most complex type of congenital heart disease. So in a nutshell, it directs the blue blood returning to the body directly into the lungs without having to pass through the heart. So normally in the heart, there should be a right side in the heart that pumps blood through the lungs to fill the left side. In, after a Fontan operation, the blood that's returning to the heart from the body goes straight to the lungs. This creates a problem. There is no pump to push blood through the lungs into the left side to go to the body. As a result, that leads to a number of problems. One is the problem of heart failure. So the ventricle, or the pump from the heart to the body now some time does not feel very well, because there's not enough blood returning to it. Additionally, there could be a problem with the systemic ventricle except as a pump to the body. So collectively, all these things reduce the amount of blood that the heart can pump to the body, especially under the strain of exercise. So the first medical problem that we have to deal with would be heart failure. The second problem that also ties very closely to heart failure is the issue of atrial arrhythmias. So atrial arrhythmias, that used to be more common with the older Fontan operation techniques, is less common now with the new one, but it is still a problem. It is estimated that even with the most recent type of Fontan operation, about 22 to 25 percent of the patients will have atrial arrhythmias at some point before age 30. So with the atrial arrhythmia, that sort of depresses the ability of the systemic ventricle to pump blood to the body to meet metabolic demand. That's problem number two. So tying into that is the problem with the lungs. Normally, the blood vessels in the lungs is designed to receive blood being pumped from the right ventricle. So in patients with Fontan operation, because there's no pump, they resist passive flow that goes through the lungs. And that affects the small blood vessels in the lungs, and reduces the ability of those blood vessels to dilate in response to increased demand. This leads to pulmonary vascular disease, similar to what you see in pulmonary hypertension. Because of these, now blood cannot flow through the lungs, and cannot fill the ventricle, and that will also exacerbate heart failure. So I've gone through three problems already. You want me to go on because there's still a lot, a lot more.

Dr. Burchill: Well, I might- Yeah, I'm gonna, I think some repetition is good. So I'm thinking of the cardiologist who's out there in the community who may not have seen so many of these adults, young adults after the Fontan. So I'm just gonna emphasize a few points and then yes, I'll be really interested to talk to you about medical treatment. Also some of your research, I think that you've really been leading the way in understanding medical treatment options for these patients. But just to emphasize, yeah, these are patients, the story that I often hear is that these were children with very complex congenital heart disease. They were born blue. The parents tell me that there was a lot of uncertainty. I've often heard this story, I don't know if you've heard it too, but I've often heard this story of parents being told, "Take this baby home, love this baby. We really don't know if they're gonna survive." And then as you said, like, the Fontan operation is offered, but in those first trailblazers of patients and parents that agreed to the surgery, it was very unclear how it would go. They had the operation, they survived, and then they got through their childhood, and then they were told they may not survive beyond childhood, and yet they did. And then they got beyond 18 years, and they were told, "Well you may not survive beyond 20 something years." and they did. And we are seeing some of these patients now in their thirties, even a few in their forties. And exactly as you said, they're coming in with a form of heart failure that's quite unique to the Fontan circulation. They're coming in with their rhythm problems, and they're coming in with those abnormal changes across their lungs and their pulmonary vessels. And that's really where our treatment is focused. So, let's go on. I think you're about to tell us about some of the other major challenges that we see as a result of living with this so-called single ventricle circulation.

Dr. Egbe: Yes, So with the sluggish flow through the lungs and through the heart, these patients are also prone to thromboembolic events. So, and again to that ties into heart failure, and ties into arrhythmia. So there, the risk of thromboembolsing added to the lungs or to the body causing a stroke is significant. Now with the high pressure in the venous circulation, blood dams backwards to the liver. So this creates one of the most, that's the most other common morbidity that we see in this population, which is chronic liver disease. So about one third of the patients will have something, will have some form of advanced liver disease that are cirrhosis, or they are rarely, they can develop hepatocellular carcinoma. And problem with the liver also ties in to problem with the kidneys, and some, a significant proportion of them will have chronic kidney disease, either due to problem with the liver, or due to problem from inadequate cardiac output.

Dr. Burchill: Yeah. And you mentioned, you know, the Fontan, we call it Fontan associated liver disease, don't we? Or F-A-L-D, FALD. You mentioned the liver cancer. I know that you've led research in this space. It's difficult for us to really have the proper population studies to know the true incidence of liver cancer, but what are your thoughts on that? When you're meeting patients, do you quote 1, 3, 5 or 10 percent? I mean, it's varied across the studies that have been conducted to date.

Dr. Egbe: Yeah, I try to stay away from putting any estimates, because the, the studies that we've published is, there's a lot of selection bias. So at Mayo we see the most severe of cases, and we tend to see more of those. And on the other hand, because most people with hepatocellular carcinoma will have, will present with liver failure and be, and just look like a regular heart failure patient. I have a feeling that most patients die from hepatocellular carcinoma without people actually knowing it. So if you can't make a diagnosis, then the incidence will be zero.

Yeah, it is a problem, so, and it's not common, but when it occurs, the clinical course is very aggressive. So that the, there's a need to think about it, screen for it, and identify it as early as possible.

Dr. Burchill: Yeah, and the abdominal pain is important, isn't it? To ask about in in our patients who have had the Fontan, not necessarily because of hepatocellular carcinoma. It can also be how they present with their so-called failing Fontan circulation, correct? They, yes, they're developing a lot of congestion that may be in their liver, it may be in their gut. I've had a couple of patients referred to surgeons, because their team thought that, in fact, they had gallbladder problems, when in fact, it was them presenting with volume overload and symptoms of congestion, including in the liver, have you had that experience?

Dr. Egbe: Yes, so, it is very non specific. So, and so you have the abdominal distention and discomfort. Can be from the liver, can be from heart failure, can be from hepatocellular carcinoma, Everything, it's all tied in.

Dr. Burchill: Tied in, but low index of suspicion. And usually these are patients who, again, they should be referred to an adult congenital provider, but certainly an ultrasound of the abdomen can be helpful for looking at the liver, for ruling out fluid collection like ascites. which we do see in some of our patients. So, okay, well I wanted to talk to you about what treatment options are available, what's in our toolkit when it comes to treating these young adults with Fontan circulations?

Dr. Egbe: Yeah, that's a difficult part. So, we don't have nearly as much treatment as we would like to have, so let kind of just go through them sequentially. So when I mentioned heart failure, so we think about heart failure in the context of ventricular failure. So since more than half of the older Fontan population will have morphologic left ventricle, there's no reason to believe that the regular guideline directed medical therapy would not work in improving the ventricular function. So we don't have rigorous data showing that it works, but that doesn't mean it wouldn't work. So that would be a good place to start. If there is morphologic left ventricle and there is a solid dysfunction, should try those medications. Regular ACE inhibitor, ARB, Entresto, beta blocker. But the problem you run into here is that these people have low blood pressure to start with. So there is not a lot of room to maneuver. So that's one thing to do. And if there's ventricular dysfunction, you look for structural things that could, that can be addressed. If the AV valve is leaking, then they will need surgery for that if there's surgical candidates. So that's for heart failure. For the pulmonary vascular disease, there is some evidence that pulmonary vasodilators might help in some patients. So in this case the regular things like tadalafil, sildenafil, these are phosphodiesterase-5 inhibitors. They can help, but the effect is very much limited if they have concomitant diastolic dysfunction, which we're beginning to realize is very common in this population. So I mentioned thromboembolism, which is relatively common given their age. And so the options here are to use antiplatelet therapy, vitamin K antagonist, or the DOACs, the direct oral anticoagulants there. So there's sufficient evidence now to show that aspirin by itself, excepting the lowest risk of patient, is not enough to prevent thromboembolic events here. So you can use vitamin K antagonists or the DOACs, where there is, because of the- because there's no need to monitor INRs in this patient. Probably the DOACs might be useful in- for thromboembolic event prevention in this population.

Dr. Burchill: Yeah, I know that there was a lot of, you know, nervousness about going to these newer agents, particularly something like Eliquis or apixaban, but really we've got now a decade of experience and some international trial data that suggests that for the great majority, these can be tolerated, they're relatively safe. And I agree many of our patients have met some indication to be on a blood thinner. So a Fontan patient that's not on a blood thinner is less common these days and it might raise questions as to why they're not. Okay, well, I think that this has been excellent. What do you see coming on the horizon? Are there any other studies, any new research, any new treatments? What would you like to share with us before we sign off?

Dr. Egbe: Yeah, so the other thing that I didn't mention anything about is prevention or treatment of liver disease. And I didn't say anything about it because there's currently nothing that we know that works, right? So there is some evidence that if you can offload- if you can decrease the afterload of the liver by giving pulmonary vasodilators, you can slow the progression of liver disease. And so, so that's something that we did a pilot clinical trial on, that showed that can, this works, but not in everybody. So what is in the pipeline now is trying to actually phenotype the patient. So we don't use one treatment to fit all. And to do that involves doing cardiac catheterization differently, which will be doing it with exercise. There we were able to unmask mechanical obstruction in the pathway, which you can a address with stents or identify people with pulmonary vascular disease who get pulmonary vasodilators. And find out people who have diastolic dysfunction, which not much will work apart from trying diuretics, and deciding when would be the right time to send them for a transplant evaluation. So that's mostly what is in the pipeline now, which is phenotyping and using that to direct therapy in this population.

Dr. Burchill: I think that that's a really great note to end on. We are no longer taking this one size fits all approach to these adult Fontan patients. We're really wanting to understand the unique hemodynamics for each individual. the cardiac catheterization procedures we are doing now respect that these symptoms are occurring and the problems are occurring not just at rest but when people are active. And it's with exercise that we're really uncovering really quite striking issues, whether it's related to that occult diastolic dysfunction, or perhaps we're also seeing that people have a mechanical problem with their Fontan conduit being stenosed or even obstructed. So I think that this is a great time to be looking after these patients when we can offer more than we ever have in the past. And thank you, Dr. Egbe, for the work that you do and the leadership that you are providing with finding these solutions. Thank you so much for your time today.

Dr. Egbe: Thanks so much for having me.

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