Conflict of Interest Statement
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Discussion

Dr F. Fynn-Thompson *(Boston, Mass)*. I want to congratulate Dr Carins for an excellent and clear presentation, and I want to commend our colleagues in Australia and New Zealand for creating this Fontan registry, which I believe is the largest of its kind and which with each analysis is advancing our knowledge of contemporary Fontan outcomes.

In your study, you identified arrhythmias in approximately 20% of patients, but the overall survival was similar after the onset of tachyarrhythmia or bradyarrhythmia among the various types of Fontans. Your analysis identified the first episode of an arrhythmia as a tipping point that is often followed by progressive deterioration in systemic ventricular function. Although medical management, including direct cardioversion, could mitigate the clinical sequelae of these symptoms as related to the arrhythmias, the ventricular function did not appear to recover in most of those patients, and those patients were less likely to be alive with Fontan circulation at 20 years. Some 40% of those patients with a decrease in ventricular function had a major adverse event within 5 years. This is an important study and has significant potential implications for how we manage and expectantly treat arrhythmias in our Fontan cases.

I want to point out 2 important characteristics of this study population and registry that you did not present but were available in your article, and these are different from previous reported case series, including the Pediatric Heart Network (PHN) Fontan Cross-Sectional Study, looking at long-term Fontan outcomes.

The median age for the Fontan operation in your patient population was approximately 5 years. It was 3.3 years in the PHN study and 2.3 years in the study just presented from the group at Children's Hospital of Philadelphia (CHOP). Also, the morphologic characteristics of the group are different in that only 8% of your registry population had hypoplastic left heart syndrome versus 20% in the PHN study and as high as 50% again in the just presented CHOP study.

It has been suggested by a number of studies, including one from our center, looking at cohorts of earlier era Fontan cases that heart failure and sudden death presumed to be from arrhythmias were more likely in patients with single right ventricle morphology, particularly those with hypoplastic left heart syndrome.

Can you provide us with some insight as to the skewed demographic and morphologic makeup of your Fontan population, the fewer number of hypoplasts, and if you think that has any impact on your analysis of the rate of arrhythmias and long-term results?

Dr d'Udekem. So you want to know how much the skewing of our population compared with the previous series is affecting outcomes, and the real answer is we don't know, obviously. There are a few interesting things that we're learning today. The previous talk was interesting in showing that in terms of survival at 20 years, even Philadelphia cannot prove that having a single right ventricle is worse than having a single left ventricle.

Now, you're saying that in terms of sudden death, our incidence may be less than other groups because our population is skewed. I would contend that most of us here do not know the cause of death and failure in Fontan populations. The only 2 articles that have described the cause of death that I know of is the famous Khairy article saying that one third of the patients died of sudden death, and we had the same conclusion in a study that we did in Melbourne in 2005. I went back, as a surgeon, to look at all the files of the patients who died. The type of sudden death I encountered was an atriopulmonary connection Fontan in someone with complete heart block who died suddenly while he was swimming, not really an unexpected death. The only 2 sudden deaths I could find were in patients with pulmonary atresia intact septum and right ventricle–dependent coronary circulations. I think the idea that these patients die suddenly of arrhythmia is a myth, but we have to do more exploration.

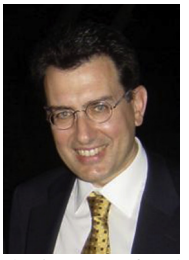
Dr Fynn-Thompson. My second and final question relates to a central question, much like Dr Kirklin's question, which I think is a focus in all our minds, I expect, and that is, what are we to do with this information? Your results are excellent, 20-year survivals even after first onset of tachyarrhythmia and bradyarrhythmia are 72% and 81%, respectively. This is obviously pretty good and better than expected.

As you're aware, there is a growing enthusiasm in our field for staged biventricular repair rather than single-ventricle palliation. A lot of that enthusiasm is rooted in the old, historical results of Fontan outcomes. So my question is, how has this information affected your practice? Do you think results like this should have us reconsider how we view the Fontan operation, how we counsel our patients and families?

Dr d'Udekem. I have to confess that when I directed the study at the start, I had a personal agenda. My agenda was to say I believe that when these patients start to have arrhythmia, their health is going to decrease in a matter of years, and we have to start performing reoperations in them. I wanted to do a conversion as soon as they had arrhythmia and bring the arguments for that. I thought that ablation therapy was absolutely hopeless, we should stop doing it, and we should do conversion in all of these patients. I found out that the results were better than I expected. So to answer your question, I'm more confused now than before the study. All we need to do is to find out at what time we should reintervene in these patients. Now it's even more difficult because, yes, they have symptomatic relief for quite a while.

Dr G. Stellin *(Padua, Italy)*. Some of the patients with a single-ventricle morphology in the context of the heterotaxy syndrome will develop some bradyarrhythmia. I'm talking about the polysplenia syndrome in which there is not a well-defined sinus node. I wonder if you found a correlation between early onset of arrhythmias and heterotaxy syndrome?

Dr d'Udekem. We did not find any predictive value of this parameter in our previous analysis. We didn't repeat the risk prediction analysis for tachyarrhythmia or bradyarrhythmia in this analysis because the goal was mainly to identify late outcomes after the onset of arrhythmia. But it's a good point, because now that we have identified bradyarrhythmia, that's a study that we should do.



Dr G. Sarris *(Athens, Greece)*. It was not clear to me from the presentation, perhaps the information was there and I did not get it. Once an arrhythmia is identified, if it is a bradyarrhythmia, I imagine a pacemaker is probably in the works and perhaps for some of the tachyarrhythmias as well. Considering the impact of arrhythmias on adverse outcome development, are you implanting pacemaker leads at the time of the Fontan to use them should arrhythmias develop or do you just do the procedure later on if the arrhythmia develops?

My other question pertains to your recommendation for ablation. How do you manage that if, as I saw in your slide, most of the Fontan operations that are being done now are extracardiac, limiting access to the atria?

Dr d'Udekem. I'm not aware of any extracardiac conduit Fontan procedure that needed and had an ablation in Australia and New Zealand. Like you, we're wondering what we're going to do when the time comes, and we don't know yet. There is nobody in Australia and New Zealand who would put pacemaker leads in advance just in the case that they will be needed later. It may have been done, but it would be anecdotal.

Dr P. Eghtesady *(St Louis, Mo)*. Regarding the data, the time to the first onset of the tachyarrhythmias, was it approximately 10 to 11 years, is that correct, or did I get that incorrectly, the first episode?

Dr d'Udekem. So we look at it as a time-related event?

Dr Eghtesady. From the time of the Fontan.

Dr Carins. We didn't actually present those data today. We have calculated the median onset from tachyarrhythmias after the Fontan operation. I think from memory it's approximately 10 years.

Dr Backer. Was that the same for the lateral tunnel and extracardiac?

Dr d'Udekem. In a time-related event, it was the same for the lateral tunnel and the extracardiac. The atriopulmonary Fontan had a higher incidence.

Dr Eghtesady. So it's interesting. The reason I bring that up, or I ask it, is the presentation we got from CHOP, and sort of some of the data just looking at it, it's interesting you look at that data and at approximately 10 years is when you start seeing the curve starting to slip. It makes me wonder, is this tachyarrhythmia a sign, if you will, of the volume overload of that atrium from the collaterals, the burden of collaterals that develop over time, and essentially that's when you start slipping down the slippery slope. I find it coincidentally interesting that you guys in your cohort have seen it at approximately 10 to 11 years, because that's what I noticed on their graphs when they presented it.

Dr J. Mayer, Jr *(Boston, Mass)*. A few questions have occurred to me, and the first is whether or not the arrhythmia is the sign of ventricular dysfunction rather than it being necessarily the other way around? Do you have any data on what the ventricular function was at the time of onset of the first arrhythmia? Is there any difference at the same time interval after the Fontan between those patients who did and did not develop the arrhythmia at the same time interval after the Fontan?

Dr Carins. By looking at the echocardiogram reports, the majority of patients had subjectively good ventricular function before their arrhythmias, then developed their arrhythmia, and then had decreased ventricular function, although it is subjective.

Dr Mayer. The question really is what is the chicken and what's the egg, right? If the ventricular function is deteriorating and then there is an arrhythmia, then the arrhythmia is a manifestation of the ventricular dysfunction. Part of my thinking is influenced by our electrophysiologists at Children's who all say that they are the final common pathway for all failed congenital heart disease repairs. Therefore, I am curious what your thoughts or observations might be.

Dr d'Udekem. It's an interesting question. When I listened to the talk yesterday, Dr Rychik was explaining the mechanism of failure in Fontans, and we talk about pump failure. I think the evidence that these Fontan cases have, strictly speaking, a pump failure, a myocardial dysfunction with time, is very weak. When you perform transplantations in them, they have quite a bit of muscle there, it's contracting well, and when you look at the time lapse for them to develop ventricular dysfunction after the onset of arrhythmia, it's quite slow again. It takes a long time for them to develop ventricular dysfunction. But when they have ventricular dysfunction, my personal experience from looking at files is that they're going down clinically very quickly. So I don't think there is a lot of unmasked ventricular dysfunction in these patients.

Dr Mayer. The other aspect of ventricular function that we cannot measure well is diastolic function, and that may be more related to arrhythmia onset than necessarily systolic dysfunction.

Dr C. Backer *(Chicago, Ill)*. Yves, before you leave I want to pin you down a bit on your indications for Fontan conversion in the atriopulmonary Fontan cases. I believe you presented an article at the European meeting that discussed earlier referral having better outcomes. When you looked at your different centers, the ones that had a strategy of earlier conversion had better outcomes than those with a strategy of later conversion. Are you changing your views a bit on the basis of these data? Are you still recommending referring within 3 years of developing an arrhythmia, while the patients are still New York Heart Association II and before starting a second antiarrhythmic medication?

Dr d'Udekem. I'll secretly reveal some data that I just had last week. I had another student working on the atriopulmonary Fontans. We have different geographic eras, one that is doing early Fontan conversion and the rest are doing late Fontan conversions. If you have an atriopulmonary connection, because now we've been able to compare with the whole population of atriopulmonary Fontan cases, if you have a conversion in the geographic era where you have an early conversion, you have twice the chance of surviving than if you don't have a Fontan conversion. If you're in the geographic era where you do late conversions, if you have a Fontan conversion, you have 5 times the chance of dying or needing a heart transplantation compared with another atriopulmonary connection. So I think with that article and research, we'll bring strong evidence that you have a window of opportunity to do the Fontan conversion, and if you miss it, actually, you shouldn't do it because you're going to do them more harm than good.

Dr Backer. That's an important point. The window of opportunity. I think the other point is to have it done at a center such as yours that has the experience and expertise with the Fontan conversion procedure. The problem now may be that it is becoming too late for early referral because most of those patients who underwent an atriopulmonary connection have died, had a heart transplant, or, as you point out, it is now too late to refer them.

Dr d'Udekem. The clock is ticking. So if you have some of them, just work on them, I think.