8. Talwar S, Bansal A, Choudhary SK, Kothari SS, Juneja R, Saxena A, et al. Results of Fontan operation in patients with congenitally corrected transposition of great arteries. *Interact Cardiovasc Thorac Surg*. 2016;22:188-93.
9. Karl TR. The role of the Fontan operation in the treatment of congenitally corrected transposition of the great arteries. *Ann Pediatr Cardiol*. 2011;4:103-10.
10. Ravishankar C. L-Transposition of the great arteries. *Pediatr Crit Care Med*. 2016;17(8 Suppl 1):S344-6.
11. Spigel Z, Binsalamah ZM, Caldarone C. Congenitally corrected transposition of the great arteries: anatomic, physiologic repair, and palliation. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2019;22:32-42.
12. Rajeswaran J, Blackstone E, Ehrlinger J, Ishwaran H, Parides M. Probability of atrial fibrillation after ablation: using a parametric nonlinear temporal decomposition mixed effects model. *Stat Methods Med Res*. 2019;27:126-41.
13. Blackstone EH, Naftel DC, Turner ME. The decomposition of time-varying hazard into phases, each incorporating a separate stream of concomitant information. *J Am Stat Assoc*. 1986;81:615-24.
14. Snapinn SM, Jiang Q, Iglewicz B. Illustrating the impact of a time-varying covariate with an extended Kaplan-Meier estimator. *Am Stat*. 2005;59:301-7.
15. Andersen P, Borgan O, Gill R, Keiding N. Chapter 4: nonparametric estimation. In: *Statistical Models Based on Counting Processes*. New York, NY: Springer-Verlag; 1993:176-331.
16. Gaies MG, Goldberg CS, Ohye RG, Devaney EJ, Hirsch JC, Bove EL. Early and intermediate outcome after anatomic repair of congenitally corrected transposition of the great arteries. *Ann Thorac Surg*. 2009;88:1952-60.
17. Murtuza B, Barron DJ, Stumper O, Stickley J, Eaton D, Jones TJ, et al. Anatomic repair for congenitally corrected transposition of the great arteries: a single-institution 19-year experience. *J Thorac Cardiovasc Surg*. 2011;142:1348-57.e1.
18. Lenoir M, Bouhout I, Gaudin R, Raisky O, Vouhé P. Outcomes of the anatomical repair in patients with congenitally corrected transposition of the great arteries: lessons learned in a high-volume centre. *Eur J Cardiothorac Surg*. 2018;54:532-8.
19. Shin'oka T, Kurosawa H, Imai Y, Aoki M, Ishiyama M, Sakamoto T, et al. Outcomes of definitive surgical repair for congenitally corrected transposition of the great arteries or double outlet right ventricle with discordant atrioventricular connections: risk analyses in 189 patients. *J Thorac Cardiovasc Surg*. 2007;133:1318-28.
20. Hsu K-H, Chang C-I, Huang S-C, Chen Y-S, Chiu I-S. 17-year experience in surgical management of congenitally corrected transposition of the great arteries: a single-centre's experience. *Eur J Cardiothorac Surg*. 2016;49:522-7.
21. Mainwaring RD, Patrick WL, Arunamata A, Chan F, Newman B, Rosenblatt TR, et al. Left ventricular retraining in corrected transposition: relationship between pressure and mass. *J Thorac Cardiovasc Surg*. 2020;159:2356-66.
22. Hraska V, Duncan BW, Mayer JE Jr, Freed M, del Nido PJ, Jonas RA. Long-term outcome of surgically treated patients with corrected transposition of the great arteries. *J Thorac Cardiovasc Surg*. 2005;129:182-91.

Key Words: congenital, great vessels, outcomes, transposition

Discussion

Presenter: Dr Aisha Zia

Dr Glen S. Van Arsdell *(Los Angeles, Calif)*. Thank you for that clear presentation. This is a really complex topic. You have corrected transposition with no associated lesions. You have varying associated lesions, some that can lead to a need for a single-ventricle repair or a choice for a single-ventricle repair. And it's a rare lesion; that's 240 patients over 65 years. If you look at a prevalence, it's about 0.3% to 0.4% of all surgical cases.

So it's hard to come to the right answers, given the numbers of patients and the heterogeneity of presentation and treatment. You focus particularly on 80 anatomic corrections with the survival of just more than 80% at 10 to 12 years, and it was very equivalent to the physiologic repair survivals, although the age of presentation was remarkably different.

It's clear that our profession seems to have a bias to move toward anatomic repair over the past 20 years. Yet the results have not yielded what had been hoped. Contrast that to simple transposition, where anatomic repair delivered remarkably, and it delivered it across the world. The Toronto data that were presented at in Washington a few years back showed outcome curves that were essentially the same as yours, and there was a similar number of treatment patients in each arm since 2000 showing equivalent outcomes for anatomic and physiologic repairs.

What it demonstrated was that operative mortality wasn't really the issue. The issue was development of ventricular dysfunction over time. And interestingly enough, those patients who did not require any repair and who were not operated on had a 95% survival at 30 years. When you put all these things together, it tells us there's something different about corrected transposition. We can do accurate surgery; we can show that in the operating room. Early operative mortality is not the same as simple transposition, but it's not prohibitive. Yet we develop late heart failure and if we don't move on to death, there's risk of death, because we know ventricular dysfunction is a risk for mortality.

It leaves us to ask the question: Maybe we need to develop a perfect criteria for doing an anatomic correction, as with Fontan palliation. Kirkland developed the perfect Fontan criteria a number of years ago. So in that spirit, I ask: Were you able to gather any insights in what might have correlated to later failures? Things that have been shown, for example, have been bands versus no bands in preparation. Or development of heart block or not getting heart block.

Do you have any insights into that that you might share with us?

Dr Tara Karamlou *(Cleveland, Ohio)*. Thank you very much, Glen. I think we're going to tag-team this, given that Aisha did a fantastic job but hasn't spent years in congenital heart surgery. Even among an experienced study group such as our moderators and our discussant, we still have not come to a consensus as to how best to manage the collective anatomy

that defines congenitally corrected transposition.

What we can say from this series is that it is clear that the age at presentation as you mentioned is likely a critical factor in determining outcome. And in some cases it's going to be a determining factor because when the patients present, as in the physiologic repair group, they may be presenting at a time when their right ventricle is already failing or when their tricuspid valve is already a problem. So in some ways, the favoritism toward anatomic repair may be due to the anticipatory nature of those surgeries, in so far as they are planned. Regarding characteristics that may potentially improve the outcome of anatomic repair, our age at repair was slightly younger than the majority of series, although there are series where the median age approximates ours. This may be a reason for slightly better outcomes. However, we didn't have a huge event rate among this population; it is too small to look in detail at the demographic characteristics, including age, that may influence outcomes long-term.

With regard to retraining, what we can say about our group is that in general, our favoritism was to do early repair rather than put patients down or retraining pathway. If you looked at the Stanford data (and they are probably the group that has studied this in the most rigorous way), most patients followed a retraining pathway that was relatively predictable, with the caveat that some patients developed left ventricle hypertrophy that was out of proportion potentially to the pressure load that was applied, suggesting that certain phenotypic or even genetic components that may mediate the type of hypertrophic response actually was at play here.

Ultimately, we have a lot of data among our specialty collectively. I think synthesizing it into a cohesive message with small patient numbers that are usually treated at 1 center in a nonprospective fashion has hampered our ability to really answer the question about optimizing retraining that you're rightly posing. With regard to the arrhythmia issue, we have no data, but I think resynchronization therapy, QRS intervals, and looking at the morphology of the QRS could give us some guidance as to which patients may benefit, but in some ways that's rearranging furniture and I'm not sure that the durability of that technique is going to influence the overall outcome.

Dr Van Arsdell. I'll pose 2 more questions. You gave us outcomes for a perfect patient. What about the imperfect patient? Let's say you have a 2-year-old patient who presents with some mitral regurgitation, some mild ventricular dysfunction, but is a candidate for an upfront Rastelli Mustard.

How do you think about that patient? Should we be doing a double switch? What should we do—or do we not know? As a follow-up to that, given that we have this ongoing risk of development of ventricular failure, which seems to be in all series that follow this longitudinally (there may be some data out there that we don't know about, but at least in what's published): Do you think that we should be thinking about putting all these patients on prophylactic heart failure medications?

Dr Karamlou. Yeah, it's an interesting question. I think again, the most honest and transparent answer is that we don't know what the best modality is in terms of pathway for patients with imperfect anatomy. We can safely say that patients who have more-than-moderate mitral insufficiency or who have left ventricle dysfunction that it is moderate initially are probably not good candidates for anatomic pair.

However, if you look at our curves, an interesting point is that as valvular and ventricular function progressed, albeit slowly, but survival seemed to plateau, and that was an interesting finding to us. This was in contradistinction to the physiologic repairs where attrition seemed to mirror the trajectories of right ventricle dysfunction and the development of tricuspid regurgitation.

So again, not to avoid your question, but I think the best answer is: We don't know. I think prophylactic heart failure therapy is an interesting concept. It has been used successfully in single-ventricle patients. Some of the data on digoxin have been favorable, angiotensin-converting enzyme inhibitors, but the population of congenitally corrected transposition of the great arteries is so varied, it would probably take a prospective study for us to understand that.

Dr Van Arsdell. Thank you.

Dr Karamlou. Thank you, Glen.

Dr Kristine J. Guleserian *(Dallas, Tex)*. Aisha and Tara, 1 obvious question. We have a 65-year time period. Was there any era effect that you were able to observe, even though overall these numbers are small on an annual basis?

Dr Aisha Zia *(Cleveland, Ohio)*. More patients were operated on during the Roger Mee era, which was in 1995 to 2000. Before 1983, there were only 3 patients, and we lost them because they died and we were unable to include them in our cohort. We have done about 5 patients more recently, all of whom underwent double anatomic repair here.

There are definitely differences in approach and an era effect, but we did not specifically look at that because the preponderance of patients were done in an earlier era. Something to do in the upcoming study.

Dr Karamlou. The short answer is no, Kris, we weren't able to look at that.

Dr Guleserian. What is your management strategy for the neonate with corrected transposition who doesn't have

any significant valvular disease, valvular dysfunction, or ventricular dysfunction? Are you recommending neonatal repair or another pathway? How do we deal with these patients?

Dr Karamlou. I think it depends on the associated lesions, Kris. As you well know, if there's no ventricular septal defect, if there's no pulmonary stenosis, you might want to manage those patients differently. In a patient who's balanced, you could probably avoid doing things very early on, with the caveat that you may need to retrain them. An interesting thing to bring up that is somewhat provocative: If you look at David Quinn's data from 2008, patients who require retraining did better than patients who did not require retraining, and that is different among different studies. So I think it's a very interesting question: Do you band early, do you do nothing, or do you go ahead and do a double switch? My own bias, quite frankly, is based on the data that we have, it's very difficult to recommend a pre-emptive operation in a patient who may be balanced and who may be wonderful for many, many years.

Among the curves we didn't show because our time zero was intervention (therefore excluding the patients not receiving any therapy), was the nonintervention patients. The patients who despite their diagnosis seems to live a normal life (nearly), asymptomatic with very little restrictions on their exercise, and so on. We had 6 deaths only in our 46 medically managed patients.

It's hard to beat that. That's 15%, which is actually better than the anatomic repairs.

Dr Emile Bacha *(New York, NY).* That's actually a very, very important piece of information. The on-treatment arm, that's a hugely important arm. You could do nothing for that 4-year-old and let him be if he's asymptomatic.

Dr Karamlou. Absolutely, Emile.

Dr Bacha. A lot of cardiologists would argue that.

Dr Guleserian. Right, and I think when we talk to families, we have to include the nonmanagement strategy when we are offering management.

Dr Karamlou. I couldn't agree more. And I think, obviously we were little bit pressed due to some of our resources getting deployed to likely much more important things given the present circumstance, but this is something that we will definitely touch on in the manuscript.

I think Rohit Loomba and Andrew Redington's editorial that commented on Brizard's 2017 article was really prescient and very important and we have to have a very circumspect approach with a lesion in which the uncertainties are probably greater than the certainties.

Dr Guleserian. Well, thank you again for a wonderful presentation and best of luck in your pediatrics residency this summer. Great job.

Dr Zia. Thank you.

Dr Karamlou. She's fantastic.