Atrial arrhythmias have for decades been recognized as a principal late complication of the Fontan procedure. A specific connection between the 2 was recognized soon after the procedure emerged as a standard clinical pathway for patients with single ventricle physiology. Intra-atrial reentrant tachycardia (IART) is a major cause of morbidity in the form of recurring symptoms and need for medical intervention in these patients. Early on, risk factors for future IART were identified, most notably the occurrence of atrial arrhythmia in the perioperative period. The relationships between organized atrial tachycardias and comorbidities such as thromboembolism, heart failure, and mortality have been investigated and are now well established. These observational associations were established through retrospective studies, which could not allow for attribution of causality. Despite this weakness of this type of clinical evidence, IART has been clearly identified in multiple concordant studies as one of the bad actors predictive of poor long-term outcome in patients undergoing the Fontan procedure.

One such approach proposed as means by which arrhythmia prophylaxis (along with other theoretical hemodynamic benefits) could be achieved is to exclude the right atrium altogether, by using an extracardiac conduit to complete the specific connection between the 2 was recognized soon after the procedure emerged as a standard clinical pathway for patients with single ventricle physiology. Intra-atrial reentrant tachycardia (IART) is a major cause of morbidity in the form of recurring symptoms and need for medical intervention in these patients. Early on, risk factors for future IART were identified, most notably the occurrence of atrial arrhythmia in the perioperative period. The relationships between organized atrial tachycardias and comorbidities such as thromboembolism, heart failure, and mortality have been investigated and are now well established. These observational associations were established through retrospective studies, which could not allow for attribution of causality. Despite this weakness of this type of clinical evidence, IART has been clearly identified in multiple concordant studies as one of the bad actors predictive of poor long-term outcome in patients undergoing the Fontan procedure.

The findings of their study are to be honest a bit disappointing, in that they show neither clear benefit nor harm to the technique: IART was observed in only 2 patients in each group, a total of 4 altogether in 114 patients followed up. The overall IART prevalence of 3.5% was considerably lower than the prevalence that would be necessary to demonstrate a difference between the treated and untreated group with any
reasonable statistical power. Thus, the use of this approach remains unproven.

This is not the first time this question has been asked. The clinical feasibility of this was acutely demonstrated by Collins et al.\(^1\) in a similarly prospective but much smaller study of this approach, with electrophysiological demonstration that effective lines of block could be achieved without significant surgical risk. This study was more recently followed up, albeit with small numbers of patients and also inconclusively, by Atallah et al.\(^1\)

In planning a study like this, we look to historical data on prevalence to help us determine necessary sample sizes and follow-up periods. The incidence of IART a decade after surgery was already known to be low. Unfortunately—at least from the point of view of study design—only a limited number of qualified Fontan patients are available to begin with, and calculations of statistical power on which this study was based were likely to have been marginal from the start. A back of the envelope power calculation presuming the observed true prevalence of 3.5% and looking for an efficacy of \(\pm 50\%\) (treated 2.3% and untreated 4.7%) would require >350 patients enrolled to have 80% likelihood of detecting a difference in outcome.

This easily understood problem with prospective study of this intervention is a common one in adult congenital heart disease. IART is only rarely an early complication of Fontan. It more commonly emerges in the second or third decade after completion of the surgery, and even at that late date, its prevalence seems to be decreasing with time. This is a recurring theme in the history of clinical research on outcomes of patients with congenital heart disease. It is an impressive feat that Law et al have accumulated 927 patient-years of follow-up in this prospectively enrolled group, with 86% rate of follow-up. They should receive kudos for their patience in letting this mature, but still, the median follow-up per patient in this group is 8.2 years—by arrhythmogenesis standards, still a young Fontan.

The network of care that surrounds patients with complex palliations of congenital heart disease is constantly evolving. By the time that data on late outcomes is available, the procedures have changed and, possibly more important, many aspects of the environment that support the surgical procedures—both perioperative management and lifelong clinical approaches to care and support—have also changed. As we attempt to plan clinical research studies, the goalposts that we use to define our outcomes are constantly and surreptitiously moving in new directions and to more distant locations.

In this current study of IART prophylaxis, the likelihood of a type II statistical error occurrence—failure to find statistical evidence of a difference between treatment and control groups where in fact a difference was truly present—was already substantial if initial assumptions about arrhythmia outcomes were correct. As the late incidence of IART has apparently fallen, at least in comparison to the historical data used to inform these calculations at the time of the study, the power of this study to detect a difference has decreased even further. Thus, this is a classic situation in which absence of evidence of a beneficial prophylactic effect of atriotomy modification should not be misconstrued as evidence of its absence.

It would be a great asset to the field to nail down the answer to this question, which would more closely tie together the role of the surgeon and the electrophysiologist in charting the future evolution of patients requiring Fontan palliation for single ventricle physiology. We have not achieved that in the current study, but this work still teaches us several useful things. First, it confirms that modifying atriotomy technique in this way is likely to be safe. In neither clinical study of this approach has there been any indication that acute or chronic adverse effects are noted in the treatment group. Second, it underlines the fact that IART prevalence in all Fontans seems to be falling. This informs design of future research in this area, and provocatively raises the question as to which other potentially modifiable clinical features of our Fontan population may also be changing that observation.

Finally, this study highlights the important, general difficulties that we face as we attempt to design meaningful research informing our care of adult congenital heart patients. It is difficult to draw meaningful and valid connections between the dramatic events and interventions that occur to children born with complex congenital heart disease and the results of those early clinical events as they gradually evolve and play themselves out over decades of life. During these long periods, patients are inevitably lost to follow-up in significant proportions. Surgical and medical practice evolve and change in ways that make it difficult to know not only whether a patient enrolled at the beginning of a study is the same as one enrolled at the end but also whether the results will even be relevant to practice 10 years in the future! A continuing challenge for researchers in this field is the design of well-grounded clinical studies that recognize the difficulties and limitations of study design in this special population. We must look to new models of long-term outcome assessment and effective proxies for those outcomes, which will help us to identify effective interventions for patients with congenital heart disease, which may take decades to express their value.

**Disclosures**

None.

**References**


Key Words: Editorials • atrial flutter • comorbidity • Fontan procedure
Moving the Goalposts: Prevention of Atrial Arrhythmias After Congenital Heart Surgery
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