Clinical Research

Determinants of Atrial Arrhythmia Late After the Atriopulmonary Fontan Operation

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Introduction: Adults palliated with the atriopulmonary Fontan operation suffer frequent atrial tachyarrhythmias. Control of these arrhythmias is difficult and may eventually require surgical intervention. We evaluated factors related to arrhythmic status in this adult population in order to gauge optimal timing and selection criteria for surgical intervention.

Methods: We identified all patients in our database with atriopulmonary 'Fontan' circulations who had cardiovascular magnetic resonance scans between 1994-2000. Scans were analysed with regard to right atrial dimensions, left atrial volume, Fontan circuit obstruction, pulmonary artery stenosis, pulmonary vein compression, ventricular function and AV valve regurgitation. These indices were compared in patients with and without atrial tachyarrhythmias.

Results: Twenty-two patients (14 males, aged 25 ± 7 years) who had undergone Fontan surgery at age 13 ± 7 years were studied. Seventeen had a history of sustained atrial tachyarrhythmia and 5 had no previous tachyarrhythmia. The only factors significantly related to arrhythmic status were the sum of the right atrial dimensions (p=0.03) and the product of the right atrial dimensions (p=0.048). There was a tentative relationship between arrhythmia and patient age (p=0.056) and ventricular function (p=0.054).

Conclusions: Right atrial size is the most important factor associated with atrial tachyarrhythmias after the Fontan operation. Our data support the continuing use of the total cavopulmonary connection and may suggest that a strategy of early conversion from atriopulmonary Fontan to total cavopulmonary connection based on right atrial size should be considered.

S ince its introduction in the early 1970s, the Fontan operation has become the major surgical route for the management of patients with congenital heart disease of univentricular physiology.[1] There is now a large group of young adults palliated with the atriopulmonary Fontan operation and its variants who are experiencing late complications, the most frequent being atrial tachyarrhythmias.[2-6] These arrhythmias are often refractory to medical therapy and may eventually necessitate surgical intervention in the form of conversion to total cavopulmonary connection. This comprises a bidirectional cavopulmonary anastomosis combined with either a lateral tunnel or extracardiac conduit, with right atrial reduction and a modified Maze procedure.[7-11] The optimal timing of this major surgical intervention is difficult to determine and selection criteria remain unclear. Furthermore, persistent arrhythmias may lead to ventricular dysfunction and are often associated with toxicity secondary to antiarrhythmic drug therapy.[12]

We studied a group of adult survivors of the Fontan operation using cardiovascular magnetic resonance (CMR) imaging to assess predictors of atrial tachyarrhythmias in this population.

Patients and Methods

We identified from our database all patients with atriopulmonary "Fontan" circulations followed up at the Royal Brompton Hospital adult congenital heart unit. Patients were included in the study if they had had a CMR scan performed at our centre between 1994–2000 and had a complete cardiac rhythm history available at the time of the CMR scan. Complimentary echocardiographic data were utilised to assess atrioventricular valve regurgitation. The design of the study was cross-sectional using heart rhythm data available at the time of the CMR scan.

Magnetic resonance imaging scans were performed using a Picker 0.5T or a Picker Edge 1.5T scanner (Marconi Medical Systems, Cleveland, Ohio). Spin echo multislice images were acquired in transaxial and coronal planes. Gradient echo cine images, time to echo (TE) = 14 ms, were acquired in planes aligned with the atriopulmonary connection and the atrioventricular valve and the long-axis of the ventricle. Slice thickness was 8-10mm and in-plane resolution 1.5 x 1.5 mm. CMR scans were analysed with regard to right atrial dimensions, left atrial volume, obstruction of the Fontan circuit, branch pulmonary artery hypoplasia or stenosis, pulmonary vein compression, ventricular function and atrioventricular valve regurgitation.

Pulmonary artery hypoplasia/stenosis was defined as ≥50% narrowing relative to the adjacent normal vessel or the other branch pulmonary artery. Pulmonary vein compression was similarly defined as ≥50% narrowing. Because of the difficulty of analysing ventricular function in the functional single-ventricle heart, this was defined using a binary index as either good function or impaired function according to the subjective impression of the reporting physician. Atrioventricular valve regurgitation was graded on a scale from 0 (no regurgitation) to 4 (severe regurgitation). Echocardiographic data were used to complement CMR data regarding atrioventricular valve regurgitation where this was incomplete (4 cases), for example due to signal loss from an atrial septal defect device. Left atrial volume was calculated by measuring the area of multiple contiguous slices through the atrium and using a modified Simpson's rule to calculate volume. Volume measurements were not possible for the right atrium due to incomplete coverage by multislice acquisitions, therefore maximal right atrial dimensions were measured from CMR scans in 3 orientations (antero-posterior, trans-verse and supero-inferior). The sum and the product of the three dimensions were also calculated. The physician reporting CMR scans (PK) was blinded to rhythm data. For patients in sinus rhythm, P-wave amplitude, P-wave duration and PR interval were measured manually from 12-lead surface ECGs obtained at the last clinic visit before the CMR scan.

Patients were divided into 2 groups on the basis of their cardiac rhythm. Patients in group 1 were in sinus rhythm and had never had sustained atrial tachyarrhythmias; patients in group 2 had documented sustained atrial tachyarrhythmias in the form of atrial flutter or atrial fibrillation. We included both typical and atypical atrial flutter (the latter also called atrial re-entry tachycardia) under the same umbrella. Sustained tachyarrhythmia was defined as atrial tachyarrhythmia which was clinically apparent and was documented by ECG, Holter recordings (lasting for >30 seconds) or ECG strips prior to electrical cardioversion. Group 2 was further subdivided into those with paroxysmal atrial tachyarrhythmias (group 2A) and those with permanent atrial tachyarrhythmias (group 2B). Permanent tachyarrhythmia was defined as that which could not be converted, other than transiently, into sinus rhythm using direct current cardioversion or pharmacological methods. The data were analysed in order to determine any relationship between anatomical or functional factors and arrhythmic status.

Statistical analysis

Group values for continuous variables are presented as mean ± standard deviation. Non-parametric variables are presented as median and range. Analysis of continuous variables (atrial dimensions and ECG parameters) was performed using an unpaired two-tailed t-test. Non-parametric variables were analysed using Fisher's exact test. Statistical significance was inferred at $p < 0.05$.

Results

CMR scans were performed on 22 patients (14 men/8 women), aged 25 ± 7 years, who had undergone atriopulmonary Fontan surgery at age 13 ± 7 years. The underlying anatomical diagnoses and previous interventions are summarised in table 1. Five patients were in sinus rhythm and had never had documented sustained atrial tachyarrhythmias (group 1). The remaining 17 patients had had documented atri-

Table 1. Patient diagnoses and previous interventions

Diagnoses

Tricuspid atresia	17
DILV	3
DIRV	2

Previous Interventions

Blalock-Taussig shunt(s)	15
Waterston shunt	3
Central shunt	2
Pulmonary artery band	2
Pulmonary valvotomy	1
Glenn shunt	4
Fontan	22
Re-do Fontan	4

DILV - double inlet left ventricle, DIRV - double inlet right ventricle.

al tachyarrhythmias (group 2). When group 2 was subdivided, there were 15 patients with paroxysmal atrial tachyarrhythmias (group 2A) and 2 patients with permanent atrial tachyarrhythmias (group 2B). Twelve patients in group 2 were receiving amiodarone, 2 flecainide, 2 digoxin and 1 sotalol. No patients in group 1 were on antiarrhythmic therapy.

The study results are summarised in table 2. All right atrial dimensions were greater in group 2 than group 1. The only indices that were significantly different between the two groups were the sum of the right atrial dimensions (p=0.034) (Figure 1) and the product of the right atrial dimensions (p=0.048) (Figure 2). When group 2 was subdivided, these variables were also substantially greater in group 2B than group 2A, although neither variable reached statistical significance: sum of right atrial dimensions p=0.089 (Figure 1), product of right atrial dimensions p=0.064 (Figure 2). The left atrial dimensions were not significantly different between group 1 and group 2.

P-wave amplitude, P-wave duration and PR interval were all greater in group 2 than group 1. This only approached significance for P-wave duration: 125 ± 33 ms versus 105 ± 11 ms (p=0.06).

Group 2 was subjected to further subgroup analysis according to whether patients had atrial flutter (n=9) or atrial fibrillation (n=8) (Table 3). None of the measured factors differed significantly in patients with the different atrial arrhythmias. In particular, the sum of the right atrial dimensions was 245 ± 31 mm in the group with atrial flutter, compared to 250 ± 34 mm in the group with atrial fibrillation (p=0.78), and the left atrial volume was 102 ± 43 ml in the flutter

Table 2. Anatomical and functional indices - differences between tachyarrhythmia group and arrhythmia-free group.

	Group 1 (n=5)	Group 2 (n=17)	p value
Age (years)	21 (15-26)	27 (19-43)	0.056
Time since Fontan (years)	12 (9-17)	13 (8-26)	0.39
Antero-posterior RA dimension (mm)	68 ± 4	82 ± 15	0.075
Transverse RA dimension (mm)	62 ± 12	71 ± 14	0.20
Supero-inferior RA dimension (mm)	83 ± 9	95 ± 16	0.15
Product of RA dimensions (mm^3 x 10^3)	353 ± 97	559 ± 202	0.048*
Sum of RA dimensions (mm)	213 ± 19	247 ± 30	0.034*
LA volume (ml)	74 ± 24	110 ± 46	0.15
Obstructed Fontan circuit	2/5	3/16	0.62
PA hypoplasia / stenosis	1/5	9/17	0.32
Pulmonary vein compression	1/5	4/17	1.0
Impaired ventricular function	0/5	9/17	0.054
Atrioventricular valve regurgitation	2/5	14/17	0.59
Mean P-wave amplitude (mV)	0.15 ± 0.05	0.22 ± 0.12	0.11
Mean P-wave duration (ms)	105 ± 11	125 ± 33	0.06
Mean PR interval (ms)	189 ± 17	214 ± 44	0.26

* p<0.05
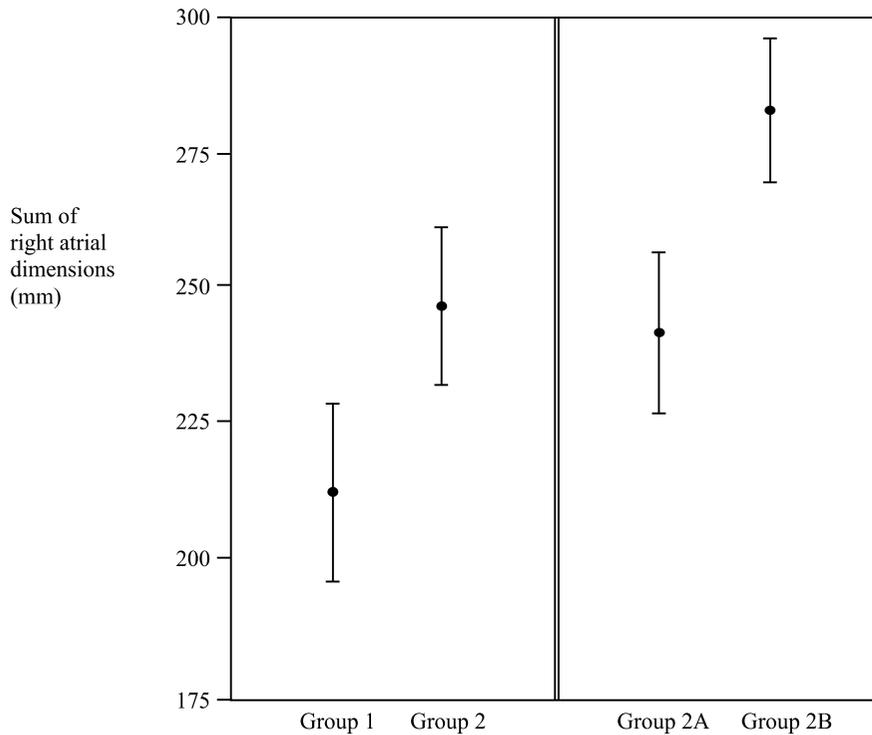LA – left atrium, PA – pulmonary artery, RA – right atrium

Figure 1. Sum of right atrial dimensions: comparisons of arrhythmia-free group (1) with tachyarrhythmia group (2), and further comparison between those with paroxysmal tachyarrhythmia (2A) and permanent tachyarrhythmia (2B). The figure shows group means and 95% confidence limits.

group compared to 118 ± 50 ml in the fibrillation group (p=0.49).

Discussion

Previous studies have suggested that length of follow-up, impaired ventricular function and high atrial pressure are factors influencing the development of arrhythmias after the Fontan procedure.[5,13-15] Our study demonstrates that with more precise 3-dimensional assessment of atrial size using CMR, dilatation of the right atrium is the most important determinant of atrial tachyarrhythmias and that arrhythmia control with medical therapy becomes extremely difficult for adult patients with the most dilated atria.

Atrial tachyarrhythmia is a potentially life-threatening complication in this group of patients.[2-6] The Fontan physiology results in a limitation of cardiac output and is often complicated by suboptimal haemodynamics. These patients are less able to tolerate loss of atrioventricular synchrony and may therefore decompensate quickly following the onset of atrial tachyarrhythmias.[5,6,13] General anaesthesia for direct current cardioversion may also carry an increased risk. The incidence of atrial clot formation is higher than in subjects with biventricular physiology,[5] thereby increasing the risk of embolic complications.

Maintenance of sinus rhythm is therefore of paramount importance for patients after the Fontan operation.

Mechanism of arrhythmias

Our data show that right atrial size is the most important determinant of atrial tachyarrhythmia in this population. This would be consistent with the concept that a larger atrial circumference allows greater potential for intra-atrial macro re-entrant circuits to be initiated and sustained.[16] Although atrial scarring alone can induce atrial re-entry, our data suggest that an additional substrate is required for clinical arrhythmia, that of right atrial dilatation. Although we do not have longitudinal CMR data, clearly marked right atrial dilatation is not present from the outset following the atriopulmonary Fontan procedure, but rather progresses with time. The association between older patient age and arrhythmia from our data, albeit weak, would also support this thesis and may also assist in the timing of potential surgical interventions.

In contrast to the right atrium, there was no statistical difference in left atrial volumes between patients with atrial flutter/fibrillation and those without. Furthermore, there was no difference in left
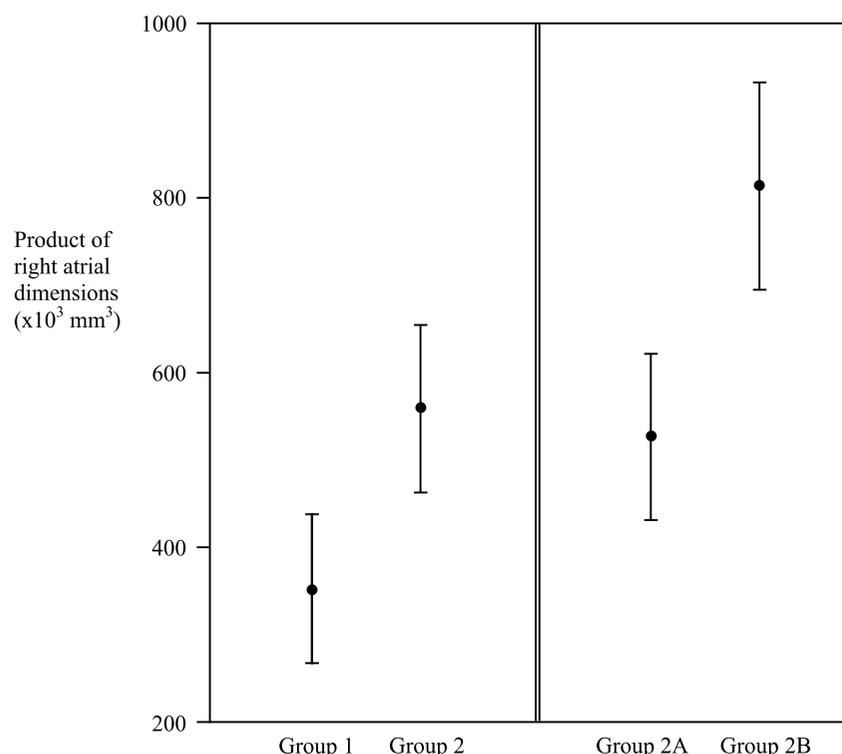
Figure 2. Product of right atrial dimensions: comparisons of arrhythmia-free group (1) with tachyarrhythmia group (2), and further comparison between those with paroxysmal tachyarrhythmia (2A) and permanent tachyarrhythmia (2B). The figure shows group means and 95% confidence limits.

atrial volumes between patients with atrial flutter and patients with atrial fibrillation. It is possible that the commonly accepted mechanism of atrial fibrillation arising from the pulmonary veins in patients with acquired heart disease does not apply in the Fontan circulation. Furthermore, these patients do not have excessive pulmonary blood flow, as do patients with large atrial septal defects, which in turn results in pulmonary venous dilatation, thus potentially creating another substrate for atrial fibrillation.

It may be that the grossly dilated and often hypertrophied right atria in older patients with an atriopulmonary Fontan, as reported here, have the potential not only for atrial flutter but also for atrial fibrillation.[17]

Therapeutic implications

For many patients in this group, amiodarone is the only drug that gives temporary cardiac rhythm con-

Table 3. Anatomical and functional indices - differences between atrial flutter subgroup and atrial fibrillation subgroup.

	Flutter (n=9)	Fibrillation (n=8)	p value
Age (years)	25 (19-43)	31 (19-38)	0.57
Time since Fontan (years)	13 (10-24)	14 (19-38)	0.63
Antero-posterior RA dimension (mm)	81 ± 12	83 ± 20	0.83
Transverse RA dimension (mm)	70 ± 18	72 ± 9	0.75
Supero-inferior RA dimension (mm)	95 ± 15	95 ± 18	0.99
Product of RA dimensions ($mm^3 \times 10^3$)	544 ± 196	577 ± 234	0.75
Sum of RA dimensions (mm)	245 ± 31	250 ± 34	0.78
La volume (ml)	102 ± 43	118 ± 50	0.49
Obstructed Fontan circuit	3/8	0/8	0.20
PA hypoplasia / stenosis	5/9	4/8	1.0
Pulmonary vein compression	3/9	1/8	0.58
Impaired ventricular function	6/9	3/8	0.35

Abbreviations as in Table 2.

trol:[12,16] in our series 70% of patients with arrhythmia were taking amiodarone at the time of the study. The long-term complications of amiodarone are well-known and include thyroid, pulmonary, ocular and hepatic disorders. Thyroid dysfunction is especially troublesome and in one study affected 36% of adult congenital heart disease patients who were taking amiodarone for longer than 6 months, with a particular preponderance amongst patients with previous Fontan procedures.[12] As regards the new generation of class III antiarrhythmic drugs, which are not yet in widespread use, these appear to have significant side-effects and are therefore unlikely to provide a simple solution to the problems of amiodarone for this relatively young population.[18]

Trans-catheter ablation of atrial re-entrant circuits in patients after the Fontan operation is another therapeutic option. However, a high recurrence rate has been reported in most series.[15,19,20] This is probably due to the potential for multiple macro re-entrant pathways in a grossly dilated right atrium.[16,19] It appears that, for many of these patients, the only definitive treatment option is likely to be surgical. Furthermore, surgery in the form of total cavopulmonary conversion conveys additional advantages on top of arrhythmia control, namely preservation of systemic ventricular function and improved functional class.

Conversion to total cavopulmonary connection

The total cavopulmonary connection is expected to have a lower risk of atrial tachyarrhythmias than atriopulmonary connections.[21] This is thought to be due to the lesser degree of right atrial dilatation and scarring. Early studies are beginning to provide data supporting this hypothesis,[7,21-24] and we submit that our study adds further supportive evidence for this. Our data argue that right atrial dilatation is the key element for late atrial tachyarrhythmias in these patients. We would speculate that reduction of right atrial size by conversion of an atriopulmonary Fontan to a lateral tunnel or extracardiac conduit is likely to have a positive impact in terms of late tachyarrhythmias. This is in agreement with preliminary data from the Chicago group with the largest experience of conversion to total cavopulmonary connection.[7]

The selection criteria for total cavopulmonary connection conversion, however, have been somewhat unclear. Conversion has often been delayed until atrial tachyarrhythmias refractory to medical or catheter therapy ensue. Ventricular dysfunction, diastolic and/or systolic, is often established by then and may ultimately compromise outcome. A strategy of earlier total cavopulmonary connection conversion may avoid the need for prolonged treatment with amiodarone or other antiarrhythmic drugs, thus avoiding drug related complications and potentially helping with preservation of ventricular function. Our data demonstrate that severe right atrial dilatation and older patient age are risk factors for atrial tachyarrhythmias, suggesting that earlier conversion to total cavopulmonary connection may be the preferred route for the adult patient. Furthermore, the surgical risks associated with the conversion to total cavopulmonary connection –shown to be relatively low[7-9,11]– may be further increased when surgery is delayed, while at the same time long-term prospects may be compromised.

Study limitations

Our definition of significant atrial tachyarrhythmia was arbitrary. However, our cut off point of 30 seconds identified all patients with clinical arrhythmia from our cohort, whereas patients with asymptomatic short runs -recorded on Holter monitoring- were not included in the arrhythmia group. Ventricular function in patients with single ventricle physiology is difficult to quantify and for this reason we simply used a binary index for normal or abnormal function. More detailed quantitative volumetric information might allow more accurate analysis of the effects of ventricular function and future studies may demonstrate closer relationships between both systolic and diastolic function and atrial dilatation. Additional predictors of atrial tachyarrhythmia may exist, and be identified with a larger patient sample and longer period of observation in future studies.

Conclusions

Right atrial size is the most important factor associated with late atrial tachyarrhythmias after the Fontan operation. Our data support the continuing use of the total cavopulmonary connection and may suggest that a strategy of early conversion from atriopulmonary Fontan to total cavopulmonary connection based on right atrial size should be considered.

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