

## Original Article

# Intracardiac thrombus in adults with the Fontan circulation

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**Abstract Objectives:** To determine the treatment and outcomes of a cohort of adults with the Fontan circulation diagnosed with intracardiac thrombus. **Background:** Formation of thrombus is common after the Fontan operation, albeit little has been published on the treatment and outcomes of these patients once they have developed an intracardiac thrombus. **Methods:** We identified all patients who had been converted to the Fontan circulation from the cardiology database at the Toronto Congenital Cardiac Centre for Adults, Toronto, and The Royal Brompton Hospital, London, studying the period from 1981 to 2003. We then reviewed the relevant echocardiograms and medical records. **Results:** Intracardiac thrombus was identified in 28 of 235 patients with the Fontan circulation, the patients having an average age of 27 plus or minus 9 years. Of the patients, 21 were initially medically treated, 19 with heparin or warfarin, and 2 with thrombolysis, whereas 7 patients underwent immediate surgical removal of the clot. Overall mortality was 18%, with residual clots seen in 39% of surviving patients at 1 year of follow up. At presentation, the haemodynamic stability of each patient with intracardiac thrombus dictated initial strategies for management, with 17% of those with stable presentations undergoing immediate surgical treatment, as opposed to 75% of those with unstable presentations (p-value equals 0.04), as well as correlating with ultimate clinical outcome. The rate of death was 8% in haemodynamically stable patients, versus 75% in haemodynamically unstable patients (p value equals 0.01). **Conclusion:** Formation of intracardiac thrombus is not rare in adults with the Fontan circulation, and carries a significant risk of death, especially in clinically unstable patients. Emphasis on prevention of formation of the clot is warranted.

Keywords: Treatments; outcomes; functionally univentricular circulation

THE FONTAN OPERATION, HAVING UNDERGONE several modifications since its development, is currently used for palliation of a wide variety of complex cyanotic congenital cardiac malformations where biventricular repair is not feasible.<sup>1</sup> Atrial arrhythmias, hepatic dysfunction, protein-losing enteropathy, ventricular failure, formation of thrombus, and thromboembolic events all

cause significant morbidity and mortality in these patients.<sup>2–5</sup> While much research has been focused on the diagnosis, risk factors for, and strategies for prevention of thromboembolic events,<sup>6–9</sup> little has been published regarding the treatment and clinical outcome of patients having intracardiac thrombus. The aim of our study was to review the treatment and outcome of these patients presenting with intracardiac thrombus, and to evaluate the effect of clinical presentation and size of the thrombus on initial strategies for management, as well as to identify risk factors related to poor clinical outcome.

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## Methods

### *Patient population*

We retrospectively identified all patients with the Fontan circulation encountered between January, 1981, and November, 2003, at the Toronto Congenital Cardiac Centre for Adults, and the Royal Brompton Adult Congenital Heart Programme, using the computerized databases of the 2 centres. Approval was obtained from the Research Ethics Boards at both the Toronto General Hospital and the Royal Brompton Hospital. Medical records of all patients identified were reviewed, and patients diagnosed with an intracardiac thrombus selected. All patients had routine yearly transthoracic echocardiograms. Demographics and surgical history were gathered from chart review, as was clinical information on age and symptoms at presentation, previous history of arrhythmia, medications, as well as management of the thrombus and outcome of the patient.

### *Echocardiography*

Transthoracic and transoesophageal echocardiograms were reviewed when available. Transthoracic and transoesophageal echocardiograms were performed using different commercially available machines following a standardized protocol by experienced sonographers. An experienced blinded echocardiographer (OS) made measurements of right atrial size, size of any right atrial clots, and systemic ventricular ejection fraction by visual estimation. Longitudinal measurements of the right atrium and clots within it were taken from apical four-chamber views, whereas left ventricular ejection fraction was graded I to IV, when I is greater than 60%, II equals 40 to 60%, III equals 20 to 30%, and IV is less than 20%, by visual estimation from all available views. Transthoracic echocardiograms were reviewed at 1 year for evidence of resolution of the clot.

### *Statistical analysis*

Comparison for continuous variables was made using the independent t test, equal variances not being assumed. Fisher's exact test was used to compare categorical variables. Values are expressed as mean plus or minus 1 standard deviation. A p-value less than 0.05 is considered significant (two sided).

## Results

We identified a total of 244 patients with the Fontan circulation. Of these, complete medical records were available for 235 (96%). Review of these records identified 28 (12%) patients with intracardiac thrombus.

Table 1. Demographics and surgical characteristics of patients.

Variables	Number of patients (% of 28 patients)
Male sex	16 (57%)
Initial diagnosis:	
Tricuspid atresia	19 (68%)
Functionally univentricular physiology	4 (14%)
Right outflow tract obstruction	4 (14%)
Others	1 (4%)
Palliation surgery	23 (82%)
Mean age (years)	2 plus or minus 2
Blalock-Taussig shunt	17 (74%)
Type of surgical procedure	
Right atrium to right pulmonary artery	22 (79%)
Bjork	6 (21%)
Mean age at creation of Fontan circuit (years)	14 plus or minus 8
Surgical revision	10 (36 percent)
Mean age at revision (years)	29 plus or minus 10

Their baseline characteristics are shown in Table 1. Of the 28, 23 (82%) had undergone palliative operations prior to construction of the Fontan circulation. The average age at initial palliation was 2 plus or minus 2 years, with the majority of patients (74%) undergoing a Blalock-Taussig shunt. A second palliative surgery, a Blalock Taussig shunt in 64%, was performed in 14 (50%) of the patients.

The Fontan circulation was created at a mean age of 14 plus or minus 8 years. An anastomosis between the right atrium and the pulmonary arteries was the most common type of procedure performed, in 79%. Of these patients, 36% required revision at an average age of 29 plus or minus 10 years because of atrial arrhythmias or obstruction, with equal numbers in each category. A second revision was needed in 3 patients (11%), in all because of recurrent obstruction within the Fontan circuit.

The clinical characteristics at the time of presentation with the thrombus are shown in Table 2. The average age at presentation of thrombus was 27 plus or minus 9 yrs. Of the patients, 5 (18%) had a history of intracardiac thrombus before commencing follow-up at the adult congenital heart centre. The majority (82%) had a diagnosis of supraventricular tachycardia at some point in their lives. The average age at development of an arrhythmia was 24.5 plus or minus 9 years, a mean of 2.9 plus or minus 6 years before the appearance of the thrombus.

At the time of presentation of their thrombus, 12 patients (43%) were on rate-control medication, 11 with digoxin and 1 with atenolol, 4 patients (14%) were treated with antiarrhythmic medication, 3 with sotalol, and 1 with amiodarone, and

8 patients (28%) were on warfarin. The mean international normalized ratio available in 3 patients on warfarin was 3.02. A further 5 patients (18%) were taking antiplatelet agents, 3 aspirin, 1 dipyridamole, and 1 clopidogrel.

Most patients (79%) were symptomatic at the time of presentation (Fig. 1). Transthoracic echocardiography

Table 2. Characteristics at presentation with thrombus. Characteristics at presentation with thrombus.

Variables	Number of patients (% of 28 patients)
Mean age at thrombus diagnosis (years)	27 plus or minus 9
History of arrhythmia	23 (82%)
Atrial fibrillation/flutter	17 (61%)
Atrial tachycardia	4 (14%)
Other	2 (7%)
Medication	
Antiarrhythmic	4 (15%)
Warfarin	8 (31%)
Anti-platelet agent	5 (19%)
Echocardiography: systemic ventricular function	22 patients
Left ventricular function greater than grade II	9 (41%)
(Left ventricular function (visually estimated): grade I equals ejection fraction greater than 60 percent, grade II equals 40 to 60 percent, grade III equals 20 to 40 percent, grade IV less than 20 percent.)	
Mean thrombus size (millimetre)	
Pedunculated thrombus (21 patients):	
Longitudinal	43 plus or minus 24
Transverse	29 plus or minus 20
Laminated Thrombus (5 patients):	
Thickness	14 plus or minus 6

was performed in 19 patients, and diagnosed intracardiac clots in 14 (74%). Transoesophageal echocardiography diagnosed clots in the remaining 5 patients, along with an additional 6 patients who underwent transoesophageal echocardiography directly. Thrombus was diagnosed in 1 patient on computed tomographic scanning, and another on magnetic resonance imaging, while the diagnosis of a right atrial clot was made at surgery in 1 patient, who was undergoing surgery to replace a conduit.

Treatment and outcome of the patients are presented in Figure 2. In 21 patients, treatment was initially medical, 19 having heparin or warfarin, and 2 undergoing thrombolysis, whereas 7 patients underwent immediate surgical removal of the clot. The initial medical treatment failed in 2 patients, both requiring thrombolysis, along with another patient needing surgery for removal of the

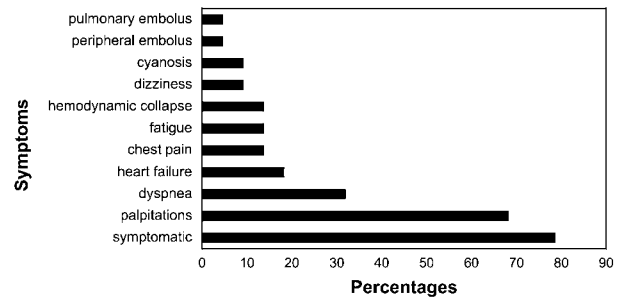
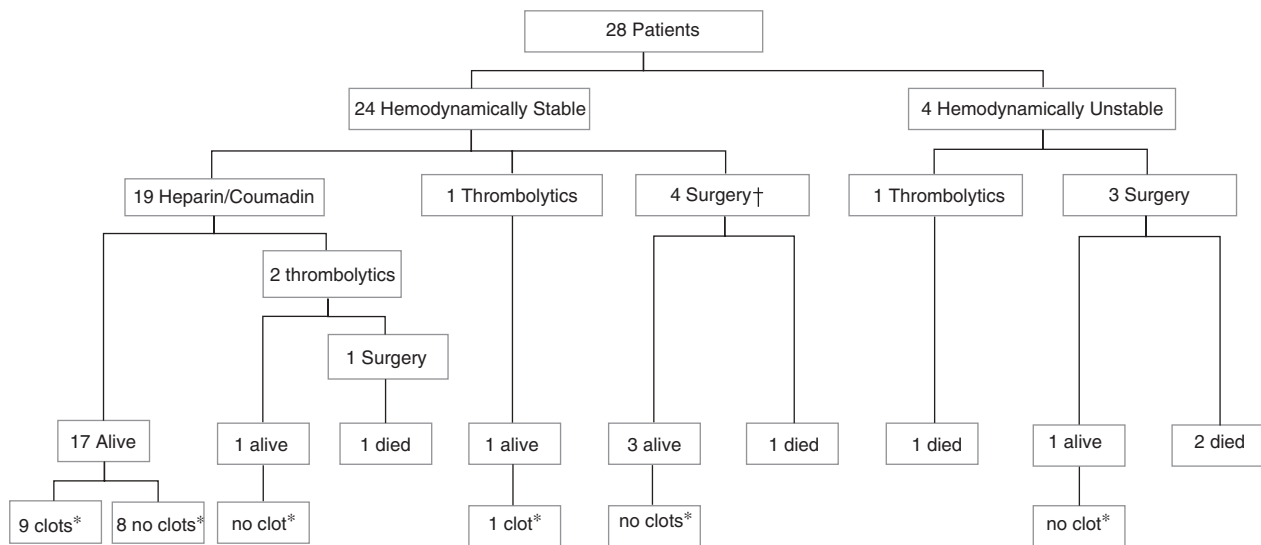


Figure 1. Symptoms at presentation with intracardiac thrombus.



\*Presence or absence of thrombus on echocardiogram one year after treatment.  
 †One case was identified incidentally during surgery, that patient died.

Figure 2. Presentation, treatment and outcomes.

clot. Treatment was escalated in one patient from oral anticoagulants to thrombolytics to surgery as magnetic resonance imaging found the clot increasing in size despite treatment. The second patient was considered to have failed initial medical therapy as he re-presented to the emergency department with worsening symptoms of dyspnoea, cyanosis and fatigue, and required thrombolytics. Overall mortality in the group of patients initially treated medically was 10%, with 2 patients dying. Residual thrombus was seen in 9 (39%) of the patients at follow-up transthoracic echocardiography after one year.

The clinical presentation of 7 patients who underwent immediate surgical treatment is shown in Table 3. Of the 7 patients who underwent immediate surgical therapy, 3 were considered haemodynamically unstable at presentation, this being defined as systemic hypotension, with systolic blood pressure less than 90 mmHg, tachycardia with heart rate greater than 100 beats per minute, or significant hypoxemia, with oxygen saturation less than 90 percent. In 3 further patients, revisions and/or thrombectomies had been planned, and one patient did not improve during the day, so surgery was performed. The overall rate of mortality in this group was 43%, with 3 patients dying. No residual clots were found in any of the surgical survivors at follow up.

Overall death rate for the entire cohort was 18%, with 5 patients dying (Table 4). The initial size of the clot did not seem to dictate initial management, this being 36 plus or minus 18 mm in the medical group versus 58 plus or minus 32 mm in the surgical group (p-value equals 0.17), was not predictive of residual clots in the medically treated patients (40 plus or minus 5 mm in patients with residual clots versus 25 plus or minus 19 mm in patients with no residual clots, p-value equals 0.17) and did not significantly correlate with clinical outcome (36 plus or minus 19 mm in survivors versus 71 plus or minus 24 mm in deceased patients, p-value equals 0.05). Furthermore, initial strategies for management did not predict clinical outcome (10% mortality in the medical group versus 43% in the surgical group, p-value equals 0.08).

Haemodynamic stability of these patients at presentation with their intracardiac thrombus did influence initial treatment choice, as 17% of those who were haemodynamically unstable at presentation were treated medically, versus 75% of those with unstable presentation treated surgically (p-value equals 0.04). Haemodynamic stability at presentation also predicted outcome, as 2 of the 24 patients (8%) who were haemodynamically stable at presentation died, versus 3 of the 4 patients (75%)

Table 3. Indications for immediate surgical treatment.

Patient	Presentation	Outcome
1	No haemodynamic compromise. Planned conduit revision. Clot found incidentally.	Died
2	No haemodynamic compromise. Planned thrombectomy and conduit revision.	Survived
3	Presented with clot associated with atrial fibrillation. Was haemodynamically unstable.	Survived
4	Presented with atrial fibrillation. Was moribund on presentation.	Died
5	Presented with pacemaker failure. Required massive resuscitation on arrival.	Died
6	Progressed over one day from atrial fibrillation to congestive heart failure.	Survived
7	No cardiovascular compromise. Thrombus found on magnetic resonance imaging. Thrombectomy planned.	Survived

Table 4. Patient deaths.

Patient	Treatments	Course	Death
1	Heparin, warfarin, thrombolytics, surgery	Treatment was accelerated as serial magnetic resonance imaging indicated increasing clot size. At surgery no clot was found.	During surgery the patient required inotropic support and then had a cardiac arrest from which he did not recover.
2	Thrombolytics	Patient appeared to stabilize with thrombolytics. Unfortunately his hypoxemia worsened and was associated with liver congestion.	The patient suffered an asystolic arrest from which he did not recover.
3	Surgery	Clot found incidentally during conduit revision surgery.	Died during surgery due to persistently low cardiac output.
4	Surgery	Urgent surgery for removal of clot and conduit revision.	Died 6 hours post-operatively in the intensive care unit from multi-organ failure and low cardiac output.
5	Surgery	Urgent surgery for clot removal.	Died during the surgery after failing to come off cardiac bypass.

who were haemodynamically unstable at presentation died ( $p$ -value equals 0.01).

## Discussion

We have found right atrial thrombus in one-eighth of adults with the Fontan circulation, and an associated overall mortality rate of 18%. Patients who were haemodynamically unstable at presentation were more likely to undergo immediate surgical removal of the clot, and carried a worse prognosis.

Thrombosis is a major cause of morbidity and mortality after the Fontan procedure. The prevalence of intracardiac thrombus found in this study falls within the range from 3 to 33% reported by several cross-sectional studies.<sup>4,9-13</sup> As the majority of clots were diagnosed via methods other than transoesophageal echocardiography, this may represent an underestimation of the true prevalence.<sup>12,14</sup>

We found that initial size of the thrombus did not dictate the initial strategy for management, nor was it predictive of clinical outcome. The location of the thrombus, specifically its proximity to the atrio-pulmonary connection, may have had a greater impact on the haemodynamic state of the patient and the decision concerning management than did its size. A long laminated stable thrombus on the lateral aspect of the right atrial wall in an asymptomatic patient would lend itself to a more conservative medical treatment, as the physician may not perceive it as an immediate threat to the life of the patient. A small but protruding clot in or close to the connection between the right atrium and the pulmonary arteries, in contrast, may be seen to herald more imminent problems, and lend itself to a more urgent aggressive surgical approach.

Initial size of the clot did not correlate with residual size at follow up 1 year later. We postulate that the response of the intracardiac thrombus to medical therapy may be more related to the age of the thrombus than the size of the thrombus itself, the more recent thrombus presumably responding better to heparin and thrombolysis than older thrombus.<sup>13</sup> This remains speculative, however, as it was not possible to ascertain the age of many of the clots in this retrospective study.

The initial method of treatment did not seem to influence clinical outcome, although there was a trend for a greater mortality in the patients treated with immediate surgery. Patients who did undergo immediate surgical removal were more haemodynamically unstable at presentation, and haemodynamic instability was associated with a greater mortality. Indeed, haemodynamically unstable patients had the highest mortality rate of the whole

cohort. Whether the haemodynamic instability of the patient in itself contributes to a worse clinical outcome, or the emergency nature of the surgery confers a greater risk, remains to be determined.

Currently, there is no consensus regarding the role of prophylactic anticoagulation in patients with the Fontan circulation. Results of cohort studies on the effect of aspirin and/or warfarin are contradictory.<sup>7-9</sup> In a study of 72 postoperative patients, operated at a median age of 25 months, treated with aspirin only, no thrombus was detected with transthoracic echocardiography at a mean follow up of 40 months.<sup>7</sup> Conversely, the follow up study from Coon and colleagues<sup>9</sup> of 552 patients using transthoracic echocardiography showed that almost one-tenth of patients developed atrial thrombus while on aspirin or warfarin at a median follow up of 22 months.

Furthermore, serious bleeding with the use of warfarin has been documented at a rate of 0.5 percent per patient year in a young adult population.<sup>15</sup> Compliance with medication in this age group can also be an issue.<sup>2</sup> Without proper randomized controlled studies, the benefits and risks of routine prophylactic anticoagulation in these patients will remain controversial.<sup>6</sup> In our study, 31% of patients with clots were on anticoagulative therapy, and 19% were taking antiplatelet agents at the time of their presentation. Unfortunately, the international normalized ratio was not always available in these patients at the time of presentation. Whether this represents true failure of warfarin, or is the manifestation of a subtherapeutic regimen of anticoagulation, remains unknown.

Whether patients undergoing acute surgery for removal of clot should undergo concomitant conversion to a total cavopulmonary connection, or insertion of an extracardiac conduit, has not been addressed by our study.

There are several limitations to the study. The referral bias of the two institutions involved in this study may have resulted in an overestimation of the incidence of adult patients presenting with an intracardiac thrombus. Conversely, superspecialized care received in these hospitals providing quaternary care may have led to an underestimation of the overall mortality associated with intracardiac thrombus. More importantly, the retrospective nature of this study, and the modalities employed to detect thrombus, mainly transthoracic echocardiography, may have underestimated the incidence of thrombus. The success of identifying intracardiac thrombus through the imaging modalities used, and the associated mortality found in our study, were concordant with those cited in the literature. Lastly, the decisions made at these institutions with regards to medical or surgical therapy were not



standardized, but based on the clinical circumstances and the experience of the attending physician.

In conclusion, intracardiac formation of thrombus is not rare in adults with the Fontan circulation. When found, it carries a significant mortality. Patients who are haemodynamically unstable at presentation are more likely to receive immediate surgical care, and have a worse prognosis. Emphasis on prevention of the development of the clot is warranted.

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