

Atrial arrhythmias and special circumstances

Louise Harris MBChB FRCPC¹, Robert M Gow MB BS FRACP², Joel A Kirsh BSc MSc MD FRCPC¹
George J Klein MD FRCPC³, Samuel C Siu MD SM FRCPC¹

L Harris, RM Gow, JA Kirsh, GJ Klein, SC Siu. Atrial arrhythmias and special circumstances. *Can J Cardiol* 2005;21(Suppl B):51B-60B.

The present paper discusses the general principles of management of atrial fibrillation and atrial flutter under special circumstances. Management recommendations, which encompass initial assessment, initial arrhythmia management and chronic pharmacological therapy, are outlined for patients with hypertrophic cardiomyopathy, Wolff-Parkinson-White syndrome and congenital heart disease. Recommendations are also made for pregnant patients and pediatric patients without congenital heart disease. Discrepancies between the authors' recommendations and those from the American College of Cardiology/American Heart Association/European Society of Cardiology are discussed.

Key Words: Atrial arrhythmias; Atrial arrhythmias in a pediatric population; Congenital heart disease; Hypertrophic cardiomyopathy; Intra-atrial reentrant tachycardia; Pregnancy; Wolff-Parkinson-White syndrome

RECOMMENDATIONS FOR MANAGEMENT OF ATRIAL FIBRILLATION IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

Class I

- 1) Anticoagulate patients with paroxysmal, persistent or permanent atrial fibrillation (AF) with warfarin (international normalized ratio 2.0 to 3.0) (level of evidence B).

Class IIa

- 1) Strategies to maintain sinus rhythm are generally preferred over rate control (level of evidence C).
- 2) Amiodarone is generally the preferred antiarrhythmic agent for maintenance of sinus rhythm (level of evidence C).

DISCUSSION

AF is the most common arrhythmia in hypertrophic cardiomyopathy (HCM), occurring in 20% to 25% of patients, and is generally associated with increased risk of complications including sudden and nonsudden death, heart failure and stroke (1-9). The results of the Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial notwithstanding (10), restoration and maintenance of sinus rhythm has been considered an important priority because of the increased morbidity and mortality associated with AF in

Arythmie auriculaire et situations particulières

Le présent article porte sur les grands principes du traitement de la fibrillation auriculaire et du flutter auriculaire dans des situations particulières. On y traitera plus précisément de la prise en charge recommandée de ce type d'arythmie, comprenant l'évaluation initiale, le traitement de départ et le traitement médicamenteux prolongé, dans les cas de myocardiopathie hypertrophique, de syndrome de Wolff-Parkinson-White et de cardiopathie congénitale. À cela s'ajoutent des recommandations sur les femmes enceintes et les enfants non porteurs d'une cardiopathie congénitale. Enfin, il sera question des différences entre les recommandations des auteurs et celles de l'*American College of Cardiology*, de l'*American Heart Association* et de la Société européenne de cardiologie.

HCM (1,11). Although rigorous comparative studies are not available, amiodarone has been considered the most effective and safest drug for the maintenance of sinus rhythm (12-15). Other antiarrhythmics have been used, but disopyramide has been recommended (16) in the absence of large comparative trials, possibly due to its reported favourable hemodynamic effects in patients with obstruction (17). Rate-control, when desired, is achieved with the usual agents, namely, beta-blockers and calcium channel blockers such as verapamil. Digoxin has theoretical disadvantages in obstruction and is less effective in most contexts. Nonpharmacological therapies including operative and catheter ablation have not been specifically evaluated in HCM, but their role in management of AF in this context is likely to increase.

Finally, the high incidence of stroke in HCM (4,11,18) has led to a prevalent recommendation for anticoagulation with warfarin (1,16) even in the absence of a large specific trial in HCM. There are as yet insufficient data to recommend use of oral antithrombin agents in this context.

Discrepancies with American College of Cardiology/American Heart Association/European Society of Cardiology guidelines

These recommendations are comparable with those of the American College of Cardiology/American Heart Association/European Society of Cardiology (ACC/AHA/ESC) (16). We do not, however, recommend disopyramide specifically over other

¹University of Toronto, Toronto; ²University of Ottawa, Ottawa; ³University of Western Ontario, London, Ontario

Correspondence: Dr Louise Harris, Department of Medicine, Toronto General Hospital, PMCC3 562-200 Elizabeth Street, Toronto, Ontario M5G 2C4. Telephone 416-340-3324, fax 416-595-1811, e-mail louise.harris@uhn.on.ca

agents due to insufficient data supporting its preferential use. We also recommend a preferential rhythm control strategy supported in the body of the text of the ACC/AHA/ESC guidelines but not listed as a recommendation.

RECOMMENDATIONS FOR MANAGEMENT OF AF IN THE WOLFF-PARKINSON-WHITE SYNDROME

Class I

- 1) Catheter ablation of the accessory pathway is recommended in symptomatic patients with AF (level of evidence B).
- 2) Operative ablation of the accessory pathway is indicated in patients with problematic or life-threatening AF where catheter ablation is not feasible (level of evidence B).
- 3) Antiarrhythmic therapy with amiodarone, sotalol, disopyramide, flecainide, propafenone, quinidine or procainamide is recommended when corrective ablation is not feasible (level of evidence C).
- 4) Immediate electrical cardioversion is recommended where AF occurs with a rapid ventricular response and hypotension (level of evidence B).
- 5) Intravenous procainamide or ibutilide is recommended in AF with predominantly preexcited complexes when the patient is hemodynamically stable (level of evidence C).
- 6) Verapamil, diltiazem or beta-blockers are indicated for rate control when AF occurs without preexcitation (level of evidence C).

Class III

Intravenous beta-blocking agents are not generally useful and digitalis, diltiazem or verapamil is contraindicated in patients with a rapid ventricular response related to preexcitation (level of evidence B).

DISCUSSION

The unique feature of AF in the Wolff-Parkinson-White (WPW) syndrome is the presence of one or more accessory pathways in addition to the normal atrioventricular (AV) conduction system that may allow conduction to the ventricles. Accessory pathways may have extremely short effective refractory periods, allowing very rapid ventricular rates in the event of AF (19). This may result in ventricular fibrillation and sudden death (20). AF in a patient with WPW may result from any cause unrelated to the preexcitation, and ablation of the accessory pathway in such instances may not prevent subsequent AF (21). However, AF in WPW is most frequently related to supraventricular tachycardia which then degenerates into AF (20). A second unique feature in the WPW syndrome is the nature of the accessory pathway. Unlike the AV node, accessory pathways are composed of working muscle fibres. Consequently, drugs that usually prolong AV node refractoriness such as digitalis, verapamil and beta-blockers do not prolong refractoriness in accessory pathways. AV node-blocking drugs are contraindicated in patients with AF and predominantly preexcited QRS complexes because they do not slow the ventricular rate and may be

detrimental. Intravenous verapamil in particular may precipitate hemodynamic collapse due to its negative inotropic effect and by accelerating the ventricular rate probably due to a reflex sympathetic effect (22). Intravenous sodium- and potassium-blocking drugs such as procainamide and ibutilide prolong the refractory period of the accessory pathway and slow the ventricular response in preexcited AF (22,23). They may also result in conversion to sinus rhythm. Intravenous amiodarone has not been extensively evaluated for acute treatment of arrhythmias related to WPW. It has been shown to terminate AV reentrant tachycardia and prolong the effective refractory period of the accessory pathway (23,24). At best, it would not be expected to be very useful for acute treatment because of the slow onset of its antiarrhythmic effect. Ventricular fibrillation has been reported during administration of intravenous amiodarone during preexcited AF (25).

Catheter ablation of the accessory pathway is currently the treatment of choice for symptomatic WPW syndrome. Where catheter ablation is not feasible, surgical ablation of the accessory pathway is advised in patients with life-threatening AF.

The management of the asymptomatic individual with WPW is only peripherally related to the current guidelines and will not be discussed in detail. Although an argument can be made for recommending catheter ablation in such an individual (26,27), the risk of catheter-related complications with ablation is at least comparable with the risk of sudden death as an initial presentation (28). Catheter ablation can nonetheless be offered to the patient who, after a balanced discussion, prefers a small procedural risk to a comparable but more long-term risk related to WPW.

Discrepancies with ACC/AHA/ESC guidelines

These guidelines do not differ substantively from other guidelines. Some discrepancies are as follows:

- 1) Operative therapy is suggested where ablation is technically not feasible.
- 2) Medical therapy is recommended where neither catheter nor operative accessory pathway ablation is feasible.
- 3) AV nodal blocking drugs are recommended in patients with AF and non-preexcited QRS while ACC/AHA/ESC guidelines do not include this in final recommendations.
- 4) While AV node-blocking drugs such as verapamil are contraindicated in preexcited AF with a rapid ventricular response, the rationale cited in the text of the ACC/AHA/ESC guidelines for this suggests that the mechanism is related to prolonging AV node refractoriness resulting in preferential accessory pathway conduction (16). It is our view that the AV node is not relevant when there is rapid preexcited AF (due to repetitive retrograde concealment into the AV node related to rapid preexcited response) and that the major factors related to deterioration include the delay resulting from an ineffective intervention combined with the negative inotropic effect of verapamil in particular.

RECOMMENDATIONS FOR THE MANAGEMENT OF AF IN PREGNANCY

Class I

- 1) Control the rate of ventricular response with digoxin, a beta-blocker or a calcium channel antagonist (level of evidence C).
- 2) Perform electrical cardioversion in patients who become unstable due to AF (level of evidence C).
- 3) Administer antithrombotic therapy (anticoagulant or acetylsalicylic acid [ASA]) throughout pregnancy in all patients with persistent or paroxysmal AF (level of evidence C).
- 4) In patients at risk of thromboembolism, administer heparin during the first trimester and after 36 weeks' gestation. Unfractionated heparin may be administered by intravenous infusion or by twice-a-day subcutaneous injection (dose adjusted to maintain an activated partial thromboplastin time two to three times the control value). Alternately, low molecular weight heparin can be used (dose adjustment guided by anti-Xa levels) (level of evidence C).
- 5) Administer warfarin or heparin during the second trimester to patients with AF and at high thromboembolic risk (level of evidence C).

Class IIa

- 1) For symptomatic patients or those with poorly tolerated AF, pharmacological or electrical cardioversion may be considered (level of evidence C).

DISCUSSION

AF during pregnancy is usually associated with the presence of maternal structural heart disease or hyperthyroidism (29-32). A rapid ventricular response to AF can have deleterious effects on both mother and fetus.

In a pregnant woman who develops AF, diagnosis and treatment of the underlying condition causing AF is the first priority (33). The ventricular rate should be controlled with digoxin, a beta-blocker or a calcium channel antagonist (33-35). All currently available antiarrhythmic drugs have the potential to cross the placenta and to be excreted in breast milk. Sotalol, quinidine, mexilitine, flecanide and amiodarone have been used successfully during pregnancy in a small number of cases (35-39). Amiodarone may impair neonatal thyroid function and should be reserved for situations in which alternative antiarrhythmic agents are either contraindicated or ineffective (40,41). In the event of hemodynamic instability, electrical cardioversion can be performed without fetal damage (42).

The optimal antithrombotic regimen for pregnant women with AF has not been defined. Because the risk of thromboembolism resulting from AF is high in the presence of structural heart disease, anticoagulation should be administered in pregnant women with structural heart disease and AF.

Warfarin should be avoided especially in the first trimester (risk of embryopathy) and last month (risk of intracranial hemorrhage during vaginal delivery) (43). The risk of embryopathy may be dose-dependent; in one study (44), no embryopathy was reported when the daily warfarin dose was 5 mg or less. Heparin, which does not cross the placenta, is the anticoagulant of choice

at some centres as an extension of its use in pregnant women with prosthetic heart valves or venous thromboembolism. However, the relative efficacy of unfractionated heparin, low molecular weight heparin, or warfarin in the prevention of thromboembolism in pregnant women with AF has not been defined.

AF in the absence of structural heart disease (lone AF) is uncommon during pregnancy. Because serum levels of several coagulation factors are increased during pregnancy (45), pregnant women with lone AF may not be at as low a risk of thromboembolism as nonpregnant individuals. Decisions for the treatment of lone AF during pregnancy (no treatment versus ASA) will need to be tailored for the individual patient.

RECOMMENDATIONS FOR MANAGEMENT OF ATRIAL ARRHYTHMIAS IN PATIENTS WITH CONGENITAL HEART DISEASE

Atrial tachycardias (ATs) are being recognized increasingly as an important cause of morbidity in patients with repaired, palliated or untreated congenital heart disease. The arrhythmia is most frequently a macroreentrant AT. Although often labelled as atrial flutter, it is now preferably called intra-atrial reentrant tachycardia (IART). However, multiple mechanisms for atrial arrhythmias exist in these patients and AF is also well described. Many of the medical issues that are important in adults with AF are relevant to the patient with congenital heart disease and AT – the potential for 1:1 AV conduction, a predisposition to thrombus formation and the potential for further compromise of heart function. Therefore, the more generic term (AT) will be used for the purpose of the following recommendations to encompass these different arrhythmias.

Recommendations for cardioversion of AT

Class I

- 1) Immediately perform electrical cardioversion in patients with AT who are hemodynamically unstable (level of evidence C).

Class IIa

- 1) Electrical cardioversion for the early restoration of sinus rhythm is advisable in patients with newly diagnosed AT after appropriate anticoagulation. For patients with pacemakers, cardioversion may also be accomplished by overdrive pace termination of AT (level of evidence C).
- 2) All patients with congenital heart disease and AT should be managed as patients with AF and structural heart disease with respect to anticoagulation (level of evidence C).
- 3) In addition, all patients with complex heart lesions require a transesophageal echocardiogram before elective cardioversion if no prior anticoagulation or if anticoagulation is subtherapeutic, independent of arrhythmia duration. (A complex heart lesion in this setting is defined as one with excessive atrial enlargement [in particular, right atrial enlargement] and scarring, sluggish blood flow and predisposition to atrial thrombus formation even in sinus rhythm, often accompanied by systemic ventricular dysfunction and/or right to left shunting – as such, it most commonly applies to the patient post-Fontan operation but can

also be encountered in other clinical situations such as Ebstein's anomaly) (level of evidence C).

- 4) Strategies to maintain sinus rhythm are generally preferred over rate control (level of evidence C).

Class IIb

- 1) Pharmacological cardioversion of AT may be considered in patients who are hemodynamically stable and who have a controlled ventricular rate (level of evidence C).

Recommendations for pharmacological therapy to maintain sinus rhythm

Class I

- 1) Patients placed on antiarrhythmic drugs require periodic ambulatory monitoring to identify proarrhythmia, in particular, bradycardia (level of evidence C).

Class IIa

- 1) Class III drugs (amiodarone and sotalol) are generally the preferred antiarrhythmic agents for the maintenance of sinus rhythm (level of evidence C).

Class IIb

- 1) If a class Ic drug is to be used for preventing recurrence of AT, the concomitant administration of drugs to modify AV node conduction is advised. Consideration should be given to commencing antiarrhythmic drug therapy under electrocardiographic monitoring in hospital (level of evidence C).

Recommendations for heart rate control

Class I

- 1) Patients with persistent or permanent AT should have heart rate control assessed at rest and with exercise (level of evidence C).
- 2) Beta-blockers or calcium channel blockers are to be administered to slow the ventricular response rate in patients with persistent or permanent AT with rapid ventricular response not requiring immediate electrical cardioversion (level of evidence C).

Class IIa

- 1) Adjunctive therapy with digoxin may be used to control the ventricular rate. Use of digoxin alone is not recommended (level of evidence C).

Recommendations for long-term antithrombotic management in patients with congenital heart disease and AT

Class I

- 1) Anticoagulation with adjusted-dose warfarin is advised in patients with complex high-risk lesions who have had an episode of AT (level of evidence C).

Class IIa

- 1) Anticoagulation with adjusted-dose warfarin should be considered in all other patients with congenital heart disease and recurrent episodes of AT (level of evidence C).

Class IIb

- 1) The usefulness of anticoagulation or ASA in patients with congenital heart disease who have minimal residual lesions and who have experienced a single episode of AT is uncertain. The decision to initiate anticoagulation with adjusted-dose warfarin should then be based on conventional risk factors (see Connolly and Gillis, pages 71B-73B) (level of evidence C).

Recommendations for the nonpharmacological management of patients with congenital heart disease and AT

Class I

- 1) Cardiac pacing should be considered in patients with sinus node or AV node conduction disorders when pharmacological management causes symptomatic or hemodynamically relevant bradycardia (level of evidence C).
- 2) Ablation therapy directed at the arrhythmia substrate is beneficial and should be considered in selected patients with recurrent episodes of AT in whom there is a reasonable expectation of success (level of evidence C).

Class IIa

- 1) Ablation therapy directed at the arrhythmia substrate can be useful in patients with recurrent AT following the Fontan operation (level of evidence C).

Recommendations for surgery in patients with congenital heart disease and recurrent AT

Class I

- 1) All patients presenting with AT require full clinical assessment and investigation to evaluate anatomically correctable abnormalities (level of evidence C).
- 2) Concomitant atrial arrhythmia surgery is recommended in patients with symptomatic, recurrent AT who will be undergoing an operative procedure to correct anatomical abnormalities (level of evidence C).

Class IIa

- 1) Arrhythmia mapping and surgery as primary indications for surgery are reasonable and may be considered in patients with arrhythmias refractory to medical and ablation therapy without a coexisting anatomical/hemodynamic indication for surgery (level of evidence C).

DISCUSSION

Description of mechanism of IART

The mechanism for the atrial arrhythmias in congenital heart disease has been well studied and new insights have arisen with the advent of current sophisticated mapping techniques. In general, IART is considered to be a macroreentrant tachycardia that is dependent on both functional and fixed barriers such as scar tissue, suture lines and anatomical structures such as the crista terminalis (46-48). Typical atrial flutter may coexist with IART (49). Similarly, AF is also well described and has been shown to occur in nearly one-third of patients being referred for electrical cardioversion (50). While IART is encountered in both children and adults with congenital heart

disease, AF is uncommon in children. Risk factors for the development of AF appear to be residual left-sided disease and long-term palliation.

Description of electrocardiography findings of IART

IART is an atrial arrhythmia that is independent of the AV conducting system. The marked variability of the reentrant circuits makes the electrocardiographic appearance quite variable. In general, there is discernable atrial activity with slower rates than are seen with typical atrial flutter. The cycle lengths are usually more than 260 ms and less than 450 ms. There is an increased likelihood of 1:1 AV conduction with the longer atrial cycle lengths (51).

Prevalence

Significant atrial arrhythmias occur with different prevalence depending on the underlying anatomical and surgical substrate. Examples of high-risk situations are previous Mustard/Senning operation, previous Fontan operation, atrial septal defect (ASD) repair and Ebstein's anomaly. Long-term follow-up data show that IART develops in 30% of patients following the Mustard/Senning operation (52), in 50% following the Fontan operation (53,54) and in 23% following ASD repair (54). Despite previous emphasis on ventricular arrhythmias, patients with repair of tetralogy of Fallot also appear to be at increased risk of symptomatic atrial arrhythmias (55).

Clinical impact of atrial arrhythmias

There is a significant clinical consequence of atrial arrhythmias in patients with congenital heart disease and IART; reduction in exercise capacity has been well documented and, in part, appears to be due to more rapid AV conduction during exercise (56). Similarly, overall functional status deteriorates and is demonstrated by a reduction in Ability Index (57). Important residual hemodynamic abnormalities are found in over 80% of patients in some studies (57). Recurrent IART is also associated with an increased risk of sudden death (58).

Thrombus formation

Investigation by transesophageal echocardiogram has shown thrombus formation in up to 33% of patients who are asymptomatic after the Fontan operation (59,60). There appears to be abnormalities of procoagulant and anticoagulant factors, as well as increased factor VIII levels (58). Some of these have been shown to precede surgery (61). These findings have implications for the management of patients who may require electrical or pharmacological cardioversion. A much higher index of suspicion needs to exist to suggest that a clot may form during an atrial arrhythmia, and appropriate steps need to be taken. Thrombi have been identified by transesophageal echocardiogram in up to 42% of patients with congenital heart disease and nonfibrillation atrial arrhythmias (62). Recent guidelines advise the same anticoagulation management for patients with atrial flutter and AF (63).

Medical management

There have been few, if any, controlled trial data looking at the efficacy of different antiarrhythmic agents in converting IART to sinus rhythm, or looking at efficacy of control of ventricular

rate in chronic IART. Sotalol has been shown in one series to convert atrial flutter to sinus rhythm in 85% of children, with the majority occurring within 24 h (64). Long-term management with sotalol showed that only 63% were free from recurrence at two years (65). Amiodarone is considered to be the most effective single agent in some studies (66) but its use is limited by the well-known side effects. Adults with congenital heart disease appear to be particularly susceptible to amiodarone-induced thyroid abnormalities, with 36% of patients demonstrating dysfunction in one report (67). Because of the younger age of many of the congenital patients with IART, and the slower atrial rate, 1:1 AV conduction may be seen in as many as 50% of episodes (68). Recommendations for control of the ventricular rate including using beta-blockers, calcium channel blockers and digoxin are extrapolated from adult studies in AF. Ibutilide and dofetilide have proven to be effective and relatively safe for the conversion of atrial flutter in adults, with conversion rates as high as 63% (69). However, no comprehensive data are available describing their use in patients with IART and congenital heart disease.

Pacemaker therapy

Pacemakers are predominantly inserted for sinus node or AV node conduction disease, which is common in many postoperative patients. Pacemakers may be required in patients who are prescribed antiarrhythmic medication to treat IART. An improvement in arrhythmia frequency has been observed after pacing alone in patients in whom the IART appeared to be bradycardia-dependent (70). Initial results with antitachycardia pacemakers were encouraging before their withdrawal from the market (71). The current generation of antitachycardia pacemakers appears promising as an adjunctive therapy. Overall efficacy is 54%, and there appears to be higher success in Mustard/Senning operation patients (68). One limitation is that episodes with 1:1 AV conduction are not treated for safety reasons, and misclassification of arrhythmia is common. Standard permanent pacemakers may be used to successfully overdrive IART (72) and success with atrial defibrillators has been described (73).

Catheter-based ablation therapy

Catheter techniques have evolved quite rapidly from a diagnostic to therapeutic tool. They have also been responsible for a rapid increase in our understanding of the substrates involved in the maintenance of macroreentrant circuits within the atria of patients with repaired congenital heart disease. Essentially, structural (eg, the orifices of the great veins, crista terminalis, AV valve rings) and surgically induced obstacles (eg, suture lines, scars) provide the pathways for circuits which are often dependent on narrow pathways between adjacent obstacles (74). These narrow pathways, or isthmuses, are ideal sites for ablation of critical parts of the arrhythmia circuit.

The exact location of these critical pathways varies with the underlying anatomical substrate and the precise nature of the surgery performed. Enough knowledge has been gained that some prediction is possible and more focused attempts at ablation considered. For example, the tricuspid valve region is the critical region in the majority of patients with previous Mustard/Senning operations and in those with repaired congenital heart disease (eg, tetralogy of Fallot) (75). Patients

with previous Fontan operation tend to have IART, which is dependent on the lateral right atrial wall (75).

Initial attempts at ablation using standard fluoroscopic bipolar electrogram techniques showed a reasonable acute success with a high recurrence rate. The evolution of sophisticated computerized mapping techniques has resulted in improved acute and long-term success (76,77). Acute, in laboratory success is as high as 80% to 90% (77). Recurrence rate depends to some extent on the underlying anatomy. Rates vary from 12% in patients with previous Mustard/Senning operations (78) to 62% for patients with previous Fontan operations and multiple circuits (79).

Overall, catheter ablation techniques are a reasonable option in patients with recurrent IART in whom a relatively high success rate, with low risk, can be anticipated. Examples are patients with previous ASDs, repaired congenital disease with IART or typical atrial flutter (eg, repair of tetralogy of Fallot), and patients with previous Mustard/Senning operations. The decision is less clear in patients with previous Fontan operation who may have multiple circuits and who have a much higher chance of early recurrence.

Cardiac surgery and congenital heart disease

Surgery for hemodynamic indications: in the patient with congenital heart disease, the onset of atrial arrhythmias often heralds a change in the hemodynamic status of the patient – for example, worsening pulmonary and/or tricuspid regurgitation in the patient with previous tetralogy of Fallot repair. The AT should therefore not be managed in isolation and it is recommended that all patients presenting with AT undergo full clinical assessment and investigation to identify anatomically correctable abnormalities.

Surgery for management of IART: The surgical approach to the management of recurrent IART is receiving more attention. Although arrhythmia surgery alone is considered occasionally, most reports describe the arrhythmia surgery taking place with concomitant surgery to improve abnormal hemodynamics or repair structural abnormalities (80-83). The actual approach may differ with variations of the right atrial Maze operation being most common.

Diagnostic electrophysiology and hemodynamic studies are usually performed preoperatively, although this is not universal. The atrial lesions may be created by cryoablation (81), radiofrequency ablation (84) or surgical incisions (83). Right-sided surgery is usually done alone for IART, although the left side may be included if there is left atrial dilation. Pulmonary vein isolation or left atrial Maze operation may be performed if there is clinical AF. The overall mortality rate may be as low as 0% (81,83), and as high as 13% for complex Fontan revision at the time of arrhythmia surgery (82).

Recurrence rates also vary between 0% and 25%. Although direct comparative data are not available, in general, the arrhythmia recurrence rate appears to be less than that after catheter-based ablation procedures. It has been suggested that older patients having surgery to correct hemodynamic abnormalities should have 'prophylactic' right atrial Maze operation (81). There are no data to support this position. It is recommended that arrhythmia surgery in this patient population be performed at an appropriately experienced centre.

AF AND ATRIAL FLUTTER IN THE PEDIATRIC PATIENT WITHOUT CONGENITAL HEART DISEASE

The strength of recommendations is compromised by the absence of level I and level II studies, making all recommendations level of evidence C.

Recommendations: Acute management

Class I

- 1) Perform electrical cardioversion if there is severe hemodynamic compromise.
- 2) Unless otherwise contraindicated, anticoagulate with heparin for urgent cardioversion in patients in whom the duration of arrhythmia is greater than 48 h or is uncertain.
- 3) Administer beta-blockers, calcium channel blockers and, less frequently, digoxin to achieve acute rate control. Intravenous calcium channel blockers should be avoided in infants who are more susceptible to their negative inotropic effects.
- 4) Consider transesophageal atrial pacing, which has been shown to be particularly effective in terminating neonatal atrial flutter.
- 5) In patients not on anticoagulation or subtherapeutically anticoagulated, perform transesophageal echocardiography before cardioversion if arrhythmia has been present for greater than 48 h or is of uncertain duration.
- 6) In stable patients with duration of AF greater than 48 h or of uncertain duration in whom a decision has been made to attempt cardioversion, optimize rate control and anticoagulate to an international normalized ratio of 2.0 to 3.0 for three weeks before cardioversion.

Class IIa

- 1) Transesophageal echocardiography is recommended in individuals in whom it is considered that the transthoracic echocardiogram has not provided sufficient imaging quality to rule out thrombus.

Recommendations: Chronic management

Class IIa

- 1) Consider drugs with class IC and class III actions as preferred agents for prevention of recurrence of atrial arrhythmias. AV node blockade should be considered as adjunctive therapy when using class IC drugs.
- 2) Consider radiofrequency ablation of recurrent atrial flutter.
- 3) Antithrombotic therapy with ASA, if not contraindicated, may be considered in young patients with recurrent episodes who are considered low risk of stroke.

Investigation

Class I

- 1) Echocardiography to rule out cardiomyopathy and/or structural heart disease is recommended in patients with newly presenting atrial flutter and AF.

- 2) Holter monitoring and exercise testing should be performed in young patients with chronic atrial arrhythmia because of the increased occurrence of 1:1 conduction.

DISCUSSION

This review focuses on AF and atrial flutter in children, and in young adults without congenital heart disease. Atrial arrhythmias in children with congenital heart disease have been discussed in conjunction with the adult patient. Most of the management issues have been addressed in detail elsewhere in this consensus report. AF is rarely seen in the pediatric patient without congenital heart disease, and the largest series, published nearly 30 years ago, was able to identify only 35 cases over a 22-year period (85). Other pediatric studies have combined AF and atrial flutter, making it difficult to ascertain the frequency of fibrillation in many conditions.

PREDISPOSING FACTORS

Structurally normal heart

Children with structurally normal hearts may have atrial flutter or AF. This is particularly true for fetal and neonatal atrial flutter which is infrequently associated with congenital heart disease (86). In older children, however, an underlying cardiac abnormality is the norm. Lone AF was seen in only one patient in Radford and Izukawa's study (85), and a collaborative study showed that only 8% of 380 children with atrial flutter had a normal heart (60). Familial AF has been described (87), with fetal presentation being documented in one case (88).

WPW

Children with WPW syndrome may develop AF, although this is much more common in adults. Clinical AF was found during follow-up in only three of 105 children with WPW syndrome (89), and has only rarely been described in young children (90,91). The inducibility of AF during an electrophysiology study in children depends on the clinical circumstances. AF was induced in 12 of 14 patients who presented with syncope and preexcitation (92), and in more than 90% of those who presented with a life-threatening event or clinical AF (93). AF is induced infrequently in children younger than six years of age, and most frequently in children older than 12 years of age (94). There were two other important observations from the paper by Bromberg et al (93). First, a slow ventricular response during induced AF was not observed. Second, there was a large discrepancy between the shortest preexcited RR intervals during induced AF and the shortest preexcited intervals during rapid atrial pacing. This last observation suggests that using pacing techniques alone (such as esophageal pacing) may not accurately risk-stratify children with an antegradely conducting accessory pathway. It is still advisable, however, to attempt to define the conduction properties of an accessory pathway as completely as possible.

Cardiomyopathy

AF occurs in children with various cardiomyopathies. Isolated case reports have included cases of restrictive cardiomyopathy (95); however, HCM and dilated cardiomyopathy are the most important in this patient population. McKenna et al (96) found an 8% incidence of nonsustained AT in 53 children with HCM. One other child had pre-excitation and recurrent

AV reentry tachycardia and one developed AF during follow-up. Invasive electrophysiological studies have helped to define the mechanisms of supraventricular arrhythmia in HCM. In 55% of patients with clinical AF the arrhythmia could be induced, whereas it was induced in only 7% of those without the clinical arrhythmia.

There has been concern that AF heralds a poor prognosis and that symptomatic deterioration occurs with the onset of rapid atrial rates. Indeed, Stafford et al (97) reported a youth who developed ventricular fibrillation as a consequence of rapid ventricular conduction during AF. Overall, the current evidence supports the observations of increased complications, including sudden death, in patients with HCM who develop AF. Therefore, the preferred management is for rhythm rather than rate control as per these and other guidelines (1). Careful assessment of hemodynamics is important after establishing sinus rhythm.

Although a variety of supraventricular arrhythmias have been described in dilated cardiomyopathy, AF is particularly frequent and occurs in 10% to 20% of patients. Atrial arrhythmias were diagnosed in 22% of the pediatric patients described by Friedman et al (98). AF and atrial flutter were found in 70% of these (16% of all patients), but were not predictive of a poor prognosis. Ventricular arrhythmias were found in 24% of all patients, with ventricular tachycardia being documented in 46% of these. Other studies (99) have shown that the presence of arrhythmias (atrial and ventricular combined) is a risk factor and that AF was common. However, atrial arrhythmias have not been shown to be an independent indicator of a poor outcome in children. Although it is theoretically important to maintain sinus rhythm in any child with dilated cardiomyopathy for as long as possible, there is no data to support this strategy as being superior to rate control if AF develops. In adults, the AFFIRM trial (10) found that a rhythm control strategy was associated with a higher risk of death in patients with congestive heart failure.

Patients with some neuromuscular disorders may manifest cardiac disease (100). AF has been described in patients with cardiac involvement in Emery-Dreifuss muscular dystrophy (101), fascioscapulohumeral muscular dystrophy (102) and muscular dystrophy (103). Atrial flutter and AF were associated with a worse outcome in pediatric patients following heart transplant (104).

Miscellaneous factors

AF occurs in up to 40% of adults with rheumatic mitral valve disease, and although progressive mitral valve disease may occur in childhood, the incidence of AF is less than 5% (105). Hyperthyroidism has only rarely been implicated in causing AF in children (106). In one study (107), none of 92 hyperthyroid patients younger than 40 years of age developed AF. Methylprednisolone pulse therapy has caused AF in children (108). Other causes that have been implicated are electric injury (109) and alcohol ingestion (110). Although pericarditis has been suggested as an independent cause of AF (111), this is disputed (112).

MANAGEMENT

The general principles of management of AF and atrial flutter for children do not differ from those for adult patients. Common ground will only be touched on, while any special issues relating to children will be dealt with in more detail. As

stated previously the strength of recommendations in this patient group is compromised by lack of level I and level II studies. Thus, the recommendations can only be classified as level of evidence C.

Initial assessment

The immediate evaluation includes a clinical assessment of the hemodynamic impact of the arrhythmia, electrocardiographic documentation and basic blood work as suggested for adult patients. Esophageal or epicardial wire studies, with or without adenosine, can be used to sort out difficult diagnoses. This technique is particularly useful in neonates who often have rapid (300 beats/min) reentrant supraventricular tachycardias that may be difficult to differentiate from atrial flutter by routine electrocardiography (113). A stable patient with atrial flutter and AF who is being admitted for assessment should be monitored with a 24 h Holter tape to assess periods of rapid conduction that may not be apparent. Recommendations for echocardiography are as for adult patients. Young children with excellent transthoracic imaging may not require transesophageal echocardiography.

Initial arrhythmia management

Immediate cardioversion may be required in a hemodynamically compromised patient with rapidly conducting atrial flutter or AF. Consideration should be given to initiating anticoagulation before cardioversion. In more stable patients, control of AV conduction can be achieved with intravenous calcium channel blockers, or beta-blockers (114). Intravenous calcium channel blockers should be avoided in infants younger than one year of age because they are more sensitive to their negative inotropic and vasodilator effects. Intravenous digoxin may be used in young patients. Esophageal pacing may also be used to terminate atrial flutter, and is particularly effective in neonates (113). If transesophageal pacing is not effective and rapid conduction

continues, cardioversion is the treatment of choice. Older children can be managed with initial rate control and elective cardioversion. Children with AF who require anticoagulation need AV rate control, and the principles do not differ from those for adult patients.

Chronic pharmacological therapy

The question of using pharmacological therapy to maintain sinus rhythm following successful reversion of AF in children/adolescents has not been studied. It seems appropriate to follow the adult management guidelines. AF due to reversible causes (such as alcohol ingestion) does not require ongoing therapy. Neonatal atrial flutter tends not to recur, and ongoing therapy is usually not indicated. The choice of rate or rhythm control depends to some extent on patient preference, and whether there is a significant compromise of quality of life during recurrence of AF. Appropriate attention to rate control in the younger population who is more likely to have rapid ventricular rates during exercise is required. Analysis of the adult data indicates a preference for atenolol, metoprolol, diltiazem or verapamil (115). Digoxin should only be used as a secondary medication (116). The choice of pharmacological therapy to maintain sinus rhythm is unclear because no controlled studies have been performed in children. Based on adult studies the type III drugs (sotalol or amiodarone) could be considered the preferred initial prophylactic drug therapy (114). Type IC agents (flecainide and propafenone) may be used. The role of radiofrequency ablation in this group of patients (excluding those with WPW) has not been defined. Chronic anticoagulation with warfarin may be required in some young patients but ASA can be considered if they do not have risk factors for thromboembolism. Unfortunately, these factors have not been as clearly delineated in the young patient as in the adult. Anticoagulation in patients with congenital heart disease is discussed in the relevant section.

REFERENCES

- Maron BJ, McKenna WJ, Danielson GK, et al. American College of Cardiology/European Society of Cardiology clinical expert consensus document on hypertrophic cardiomyopathy. A report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents and the European Society of Cardiology Committee for Practice Guidelines. *J Am Coll Cardiol* 2003;42:1687-713.
- Favale S, Pappone C, Nacci F, Fino F, Resta F, Dicandia CD. Sudden death due to atrial fibrillation in hypertrophic cardiomyopathy: A predictable event in a young patient. *Pacing Clin Electrophysiol* 2003;26:637-9.
- Boriani G, Rapezzi C, Biffi M, Branzi A, Spirito P. Atrial fibrillation precipitating sustained ventricular tachycardia in hypertrophic cardiomyopathy. *J Cardiovasc Electrophysiol* 2002;13:954.
- Olivetto I, Cecchi F, Casey SA, Dolara A, Traverse JH, Maron BJ. Impact of atrial fibrillation on the clinical course of hypertrophic cardiomyopathy. *Circulation* 2001;104:2517-24.
- Doi Y, Kitaoka H. Hypertrophic cardiomyopathy in the elderly: Significance of atrial fibrillation. *J Cardiol* 2001;37(Suppl 1):133-8.
- Lopez Gil M, Arribas F, Cosio FG. Ventricular fibrillation induced by rapid atrial rates in patients with hypertrophic cardiomyopathy. *Europace* 2000;2:327-32.
- Suzuki M, Hirayama T, Marumoto K, Okayama H, Iwata T. Paroxysmal atrial fibrillation as a cause of potentially lethal ventricular arrhythmia with myocardial ischemia in hypertrophic cardiomyopathy – a case report. *Angiology* 1998;49:653-7.
- Shigematsu Y, Hamada M, Mukai M, Matsuoka H, Sumimoto T, Hiwada K. Mechanism of atrial fibrillation and increased incidence of thromboembolism in patients with hypertrophic cardiomyopathy. *Jpn Circ J* 1995;59:329-36.
- Albanesi Filho FM, Girardi JM, Castier MB, Ginefra P. [Influence of atrial fibrillation in the natural history of hypertrophic cardiomyopathy.] *Arq Bras Cardiol* 1994;62:337-41.
- Wyse DG, Waldo AL, DiMarco JP, et al. A comparison of rate control and rhythm control in patients with atrial fibrillation. *N Engl J Med* 2002;347:1825-33.
- Maron BJ, Olivetto I, Bellone P, et al. Clinical profile of stroke in 900 patients with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 2002;39:301-7.
- McKenna WJ, Harris L, Rowland E, et al. Amiodarone for long-term management of patients with hypertrophic cardiomyopathy. *Am J Cardiol* 1984;54:802-10.
- Sugrue DD, Dickie S, Myers MJ, Lavender JP, McKenna WJ. Effect of amiodarone on left ventricular ejection and filling in hypertrophic cardiomyopathy as assessed by radionuclide angiography. *Am J Cardiol* 1984;54:1054-8.
- Robinson K, Frenneaux MP, Stockins B, Karatasakis G, Poloniecki JD, McKenna WJ. Atrial fibrillation in hypertrophic cardiomyopathy: A longitudinal study. *J Am Coll Cardiol* 1990;15:1279-85.
- Spirito P, Seidman CE, McKenna WJ, Maron BJ. The management of hypertrophic cardiomyopathy. *N Engl J Med* 1997;336:775-85.
- Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation: Executive Summary. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation) Developed in Collaboration With the North American Society of Pacing and Electrophysiology. *Circulation* 2001;104:2118-50.
- Pollick C, Kimball B, Henderson M, Wigle ED. Disopyramide in hypertrophic cardiomyopathy. I. Hemodynamic assessment after intravenous administration. *Am J Cardiol* 1988;62:1248-51.
- Maron BJ. Hypertrophic cardiomyopathy: A systematic review. *JAMA* 2002;287:1308-20.

19. Wellens HJ, Durrer D. Wolff-Parkinson-White syndrome and atrial fibrillation. Relation between refractory period of accessory pathway and ventricular rate during atrial fibrillation. *Am J Cardiol* 1974;34:777-82.
20. Klein GJ, Bashore TM, Sellers TD, Pritchett EL, Smith WM, Gallagher JJ. Ventricular fibrillation in the Wolff-Parkinson-White syndrome. *N Engl J Med* 1979;301:1080-5.
21. Hamada T, Hiraki T, Ikeda H, et al. Mechanisms for atrial fibrillation in patients with Wolff-Parkinson-White syndrome. *J Cardiovasc Electrophysiol* 2002;13:223-9.
22. Gulamhusein S, Ko P, Carruthers SG, Klein GJ. Acceleration of the ventricular response during atrial fibrillation in the Wolff-Parkinson-White syndrome after verapamil. *Circulation* 1982;65:348-54.
23. Kuga K, Yamaguchi I, Sugishita Y. Effect of intravenous amiodarone on electrophysiologic variables and on the modes of termination of atrioventricular reciprocating tachycardia in Wolff-Parkinson-White syndrome. *Jpn Circ J* 1999;63:189-95.
24. Soult JA, Munoz M, Lopez JD, Romero A, Santos J, Tovaruela A. Efficacy and safety of intravenous amiodarone for short-term treatment of paroxysmal supraventricular tachycardia in children. *Pediatr Cardiol* 1995;16:16-9.
25. Boriani G, Biffi M, Frabetti L, et al. Ventricular fibrillation after intravenous amiodarone in Wolff-Parkinson-White syndrome with atrial fibrillation. *Am Heart J* 1996;131:1214-6.
26. Pappone C, Santinelli V, Manguso F, et al. A randomized study of prophylactic catheter ablation in asymptomatic patients with the Wolff-Parkinson-White syndrome. *N Engl J Med* 2003;349:1803-11.
27. Pappone C, Santinelli V, Rosanio S, et al. Usefulness of invasive electrophysiologic testing to stratify the risk of arrhythmic events in asymptomatic patients with Wolff-Parkinson-White pattern: Results from a large prospective long-term follow-up study. *J Am Coll Cardiol* 2003;41:239-44.
28. Todd DM, Klein GJ, Krahn AD, Skanes AC, Yee R. Asymptomatic Wolff-Parkinson-White syndrome: Is it time to revisit guidelines? *J Am Coll Cardiol* 2003;41:245-8.
29. Mendelsohn CL. Disorders of the heartbeat during pregnancy. *Am J Obstet Gynecol* 1956;72:1268-301.
30. Siu SC, Sermer M, Harrison DA, et al. Risk and predictors for pregnancy-related complications in women with heart disease. *Circulation* 1997;96:2789-94.
31. Silversides CK, Colman JM, Sermer M, Siu SC. Cardiac risk in pregnant women with rheumatic mitral stenosis. *Am J Cardiol* 2003;91:1382-5.
32. Forfar JC, Miller HC, Toft AD. Occult thyrotoxicosis: A correctable cause of "idiopathic" atrial fibrillation. *Am J Cardiol* 1979;44:9-12.
33. Fuster V, Ryden LE, Asinger RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: Executive summary. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines and Policy Conferences (Committee to Develop Guidelines for the Management of Patients With Atrial Fibrillation): Developed in Collaboration With the North American Society of Pacing and Electrophysiology. *J Am Coll Cardiol* 2001;38:1231-66.
34. Page RL. Treatment of arrhythmias during pregnancy. *Am Heart J* 1995;130:871-6.
35. Chow T, Galvin J, McGovern B. Antiarrhythmic drug therapy in pregnancy and lactation. *Am J Cardiol* 1998;82:581-621.
36. Lownes HE, Ives TJ. Mexiletine use in pregnancy and lactation. *Am J Obstet Gynecol* 1987;157:446-7.
37. Wagner X, Jouglard J, Moulin M, Miller AM, Petitjean J, Pisapia A. Coadministration of flecainide acetate and sotalol during pregnancy: Lack of teratogenic effects, passage across the placenta, and excretion in human breast milk. *Am Heart J* 1990;119:700-2.
38. Ovadia M, Brito M, Hoyer GL, Marcus FI. Human experience with amiodarone in the embryonic period. *Am J Cardiol* 1994;73:316-7.
39. Magee LA, Downar E, Sermer M, Boulton BC, Allen LC, Koren G. Pregnancy outcome after gestational exposure to amiodarone in Canada. *Am J Obstet Gynecol* 1995;172:1307-11.
40. Bartalena L, Bogazzi F, Braverman LE, Martino E. Effects of amiodarone administration during pregnancy on neonatal thyroid function and subsequent neurodevelopment. *J Endocrinol Invest* 2001;24:116-30.
41. Blomstrom-Lundqvist C, Scheinman MM, Aliot EM, et al. ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias – executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (writing committee to develop guidelines for the management of patients with supraventricular arrhythmias) developed in collaboration with NASPE-Heart Rhythm Society. *J Am Coll Cardiol* 2003;42:1493-531.
42. Leung CY, Brodsky MA. Cardiac arrhythmias and pregnancy. In: Elkayam U, Gleicher N, eds. *Cardiac Problems in Pregnancy*. New York: Wiley-Liss, 1998:155-74.
43. Ginsberg JS, Greer J, Hirsh J. Use of antithrombotic agents during pregnancy. *Chest* 2001;119:122S-31S.
44. Vitale N, De Feo M, De Santo LS, Pollice A, Tedesco N, Cotrufo M. Dose-dependent fetal complications of warfarin in pregnant women with mechanical heart valves. *J Am Coll Cardiol* 1999;33:1637-41.
45. Ozanne P, Linderkamp O, Miller FC, Meiselman HJ. Erythrocyte aggregation during normal pregnancy. *Am J Obstet Gynecol* 1983;147:576-83.
46. Rodefeld MD, Bromberg BI, Schuessler RB, Boineau JP, Cox JL, Huddleston CB. Atrial flutter after lateral tunnel construction in the modified Fontan operation: A canine model. *J Thorac Cardiovasc Surg* 1996;111:514-26.
47. Gandhi SK, Bromberg BI, Rodefeld MD, et al. Spontaneous atrial flutter in a chronic canine model of the modified Fontan operation. *J Am Coll Cardiol* 1997;30:1095-103.
48. Love BA, Collins KK, Walsh EP, Triedman JK. Electroanatomic characterization of conduction barriers in sinus/atrially paced rhythm and association with intra-atrial reentrant tachycardia circuits following congenital heart disease surgery. *J Cardiovasc Electrophysiol* 2001;12:17-25.
49. Akar JG, Kok LC, Haines DE, DiMarco JP, Mounsey JP. Coexistence of type I atrial flutter and intra-atrial re-entrant tachycardia in patients with surgically corrected congenital heart disease. *J Am Coll Cardiol* 2001;38:377-84.
50. Kirsh JA, Walsh EP, Triedman JK. Prevalence of and risk factors for atrial fibrillation and intra-atrial reentrant tachycardia among patients with congenital heart disease. *Am J Cardiol* 2002;90:338-40.
51. Muller GI, Deal BJ, Strasburger JF, Benson DW Jr. Electrocardiographic features of atrial tachycardias after operation for congenital heart disease. *Am J Cardiol* 1993;71:122-4.
52. Gelatt M, Hamilton RM, McCrindle BW, et al. Arrhythmia and mortality after the Mustard procedure: A 30-year single-center experience. *J Am Coll Cardiol* 1997;29:194-201.
53. Bink-Boelkens MT, Velvis H, van der Heide JJ, Eygelaar A, Hardjowijono RA. Dysrhythmias after atrial surgery in children. *Am Heart J* 1983;106:125-30.
54. Gelatt M, Hamilton RM, McCrindle BW, et al. Risk factors for atrial tachyarrhythmias after the Fontan operation. *J Am Coll Cardiol* 1994;24:1735-41.
55. Roos-Hesselink J, Perloth MG, McGhie J, Spitaels S. Atrial arrhythmias in adults after repair of tetralogy of Fallot. Correlations with clinical, exercise, and echocardiographic findings. *Circulation* 1995;91:2214-9.
56. Li W, Somerville J, Gibson DG, Henein MY. Effect of atrial flutter on exercise tolerance in patients with grown-up congenital heart (GUCh). *Am Heart J* 2002;144:173-9.
57. Li W, Somerville J. Atrial flutter in grown-up congenital heart (GUCh) patients. Clinical characteristics of affected population. *Int J Cardiol* 2000;75:129-37.
58. Garson A Jr, Bink-Boelkens M, Hesslein PS, et al. Atrial flutter in the young: A collaborative study of 380 cases. *J Am Coll Cardiol* 1985;6:871-8.
59. Balling G, Vogt M, Kaemmerer H, Eicken A, Meisner H, Hess J. Intracardiac thrombus formation after the Fontan operation. *J Thorac Cardiovasc Surg* 2000;119:745-52.
60. Odegard KC, McGowan FX Jr, Zurakowski D, et al. Procoagulant and anticoagulant factor abnormalities following the Fontan procedure: Increased factor VIII may predispose to thrombosis. *J Thorac Cardiovasc Surg* 2003;125:1260-7.
61. Odegard KC, McGowan FX Jr, Dinardo JA, et al. Coagulation abnormalities in patients with single-ventricle physiology precede the Fontan procedure. *J Thorac Cardiovasc Surg* 2002;123:459-65.
62. Feltes TF, Friedman RA. Transesophageal echocardiographic detection of atrial thrombi in patients with nonfibrillation atrial tachyarrhythmias and congenital heart disease. *J Am Coll Cardiol* 1994;24:1365-70.
63. Blomstrom-Lundqvist C, Scheinman MM, Aliot EM, et al. ACC/AHA/ESC guidelines for the management of patients with supraventricular arrhythmias – executive summary: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Supraventricular Arrhythmias). *Circulation* 2003;108:1871-909.
64. Beaufort-Krol GC, Bink-Boelkens MT. Effectiveness of sotalol for atrial flutter in children after surgery for congenital heart disease. *Am J Cardiol* 1997;79:92-4.
65. Beaufort-Krol GC, Bink-Boelkens MT. Sotalol for atrial tachycardias after surgery for congenital heart disease. *Pacing Clin Electrophysiol* 1997;20:2125-9.

66. Kanter RJ, Garson A Jr. Atrial arrhythmias during chronic follow-up of surgery for complex congenital heart disease. *Pacing Clin Electrophysiol* 1997;20:502-11.
67. Thorne SA, Barnes I, Cullinan P, Somerville J. Amiodarone-associated thyroid dysfunction: Risk factors in adults with congenital heart disease. *Circulation* 1999;100:149-54.
68. Stephenson EA, Casavant D, Tuzi J, et al. Efficacy of atrial antitachycardia pacing using the Medtronic AT500 pacemaker in patients with congenital heart disease. *Am J Cardiol* 1990;65:871-6.
69. Gallik D, Altamirano J, Singh BN. Restoring sinus rhythm in patients with atrial flutter and fibrillation: Pharmacologic or electrical cardioversion? *J Cardiovasc Pharmacol Ther* 1997;2:135-44.
70. Silka MJ, Manwill JR, Kron J, McAnulty JH. Bradycardia-mediated tachyarrhythmias in congenital heart disease and responses to chronic pacing at physiologic rates. *Am J Cardiol* 1990;65:488-93.
71. Fukushige J, Porter CB, Hayes DL, McGoan MD, Osborn MJ, Vlietstra RE. Antitachycardia pacemaker treatment of postoperative arrhythmias in pediatric patients. *Pacing Clin Electrophysiol* 1991;14:546-56.
72. Chiu CC, McCrindle BW, Hamilton RM, Griffiths JE, Gow RM. Clinical use of permanent pacemaker for conversion of intraatrial reentry tachycardia in children. *Pacing Clin Electrophysiol* 2001;24:950-6.
73. Timmermans C, Rodriguez LM, Reuter D, et al. Management of atrial arrhythmias secondary to severe congenital heart disease with the Atrioverter. *Pacing Clin Electrophysiol* 2000;23:1181-3.
74. Nakagawa H, Shah N, Matsudaira K, et al. Characterization of reentrant circuit in macroreentrant right atrial tachycardia after surgical repair of congenital heart disease: Isolated channels between scars allow "focal" ablation. *Circulation* 2001;103:699-709.
75. Collins KK, Love BA, Walsh EP, Saul JP, Epstein MR, Triedman JK. Location of acutely successful radiofrequency catheter ablation of intraatrial reentrant tachycardia in patients with congenital heart disease. *Am J Cardiol* 2000;86:969-74.
76. de Groot NM, Schalij MJ, Zeppenfeld K, Blom NA, Van der Velde ET, Van der Wall EE. Voltage and activation mapping: How the recording technique affects the outcome of catheter ablation procedures in patients with congenital heart disease. *Circulation* 2003;108:2099-106.
77. Triedman JK, Alexander ME, Love BA, et al. Influence of patient factors and ablative technologies on outcomes of radiofrequency ablation of intra-atrial re-entrant tachycardia in patients with congenital heart disease. *J Am Coll Cardiol* 2002;39:1827-35.
78. Kanter RJ, Papagiannis J, Carboni MP, Ungerleider RM, Sanders WE, Wharton JM. Radiofrequency catheter ablation of supraventricular tachycardia substrates after mustard and senning operations for d-transposition of the great arteries. *J Am Coll Cardiol* 2000;35:428-41.
79. Deal BJ, Mavroudis C, Backer CL, Buck SH, Johnsrude C. Comparison of anatomic isthmus block with the modified right atrial maze procedure for late atrial tachycardia in Fontan patients. *Circulation* 2002;106:575-9.
80. Mavroudis C, Backer CL, Deal BJ, Johnsrude CL. Fontan conversion to cavopulmonary connection and arrhythmia circuit cryoblation. *J Thorac Cardiovasc Surg* 1998;115:547-56.
81. Deal BJ, Mavroudis C, Backer CL. Beyond Fontan conversion: Surgical therapy of arrhythmias including patients with associated complex congenital heart disease. *Ann Thorac Surg* 2003;76:542-53.
82. Vignati G, Crupi G, Vanini V, Iorio FS, Borghi A, Giusti S. Surgical treatment of arrhythmias related to congenital heart diseases. *Ann Thorac Surg* 2003;75:1194-9.
83. Theodoro DA, Danielson GK, Porter CJ, Warnes CA. Right-sided maze procedure for right atrial arrhythmias in congenital heart disease. *Ann Thorac Surg* 1998;65:149-53.
84. Kopf GS, Mello DM, Kenney KM, Moltedo J, Rollinson NR, Snyder CS. Intraoperative radiofrequency ablation of the atrium: Effectiveness for treatment of supraventricular tachycardia in congenital heart surgery. *Ann Thorac Surg* 2002;74:797-804.
85. Radford DJ, Izukawa T. Atrial fibrillation in children. *Pediatrics* 1977;59:250-6.
86. Casey FA, McCrindle BW, Hamilton RM, Gow RM. Neonatal atrial flutter: Significant early morbidity and excellent long-term prognosis. *Am Heart J* 1997;133:302-6.
87. Brugada R, Tapscott T, Czernuszewicz GZ, et al. Identification of a genetic locus for familial atrial fibrillation. *N Engl J Med* 1997;336:905-11.
88. Tikanoja T, Kirkinen P, Nikolajev K, Eresmaa L, Haring P. Familial atrial fibrillation with fetal onset. *Heart* 1998;79:195-7.
89. Gillette P, Blair H, Crawford F. Preexcitation syndromes. In: Gillette P, Garson A Jr, eds. *Pediatric Arrhythmias: Electrophysiology and Pacing*. Philadelphia: WB Saunders Company, 1990:360-79.
90. Belhassen B, Pauzner D, Blieden L, et al. Intrauterine and postnatal atrial fibrillation in the Wolff-Parkinson-White syndrome. *Circulation* 1982;66:1124-8.
91. Pagis B, Villain E, Hidden-Lucet F, Frank R, Sidi D. Wolff-Parkinson-White syndrome in the child. A case report with associated atrial fibrillation. *Arch Pediatr* 2003;10:38-41.
92. Paul T, Guccione P, Garson A Jr. Relation of syncope in young patients with Wolff-Parkinson-White syndrome to rapid ventricular response during atrial fibrillation. *Am J Cardiol* 1990;65:318-21.
93. Bromberg BI, Lindsay BD, Cain ME, Cox JL. Impact of clinical history and electrophysiologic characterization of accessory pathways on management strategies to reduce sudden death among children with Wolff-Parkinson-White syndrome. *J Am Coll Cardiol* 1996;27:690-5.
94. Vignati G, Balla E, Mauri L, Lunati M, Figini A. Clinical and electrophysiologic evolution of the Wolff-Parkinson-White syndrome in children: Impact on approaches to management. *Cardiol Young* 2000;10:367-75.
95. Miyazaki A, Ichida F, Suzuki Y, Okada T. Long-term follow-up of a child with idiopathic restrictive cardiomyopathy. *Heart Vessels Suppl* 1990;5:74-6.
96. McKenna WJ, Franklin RC, Nihoyannopoulos P, Robinson KC, Deanfield JE. Arrhythmia and prognosis in infants, children and adolescents with hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1988;11:147-53.
97. Stafford WJ, Trohman RG, Bilsker M, Zaman L, Castellanos A, Myerburg RJ. Cardiac arrest in an adolescent with atrial fibrillation and hypertrophic cardiomyopathy. *J Am Coll Cardiol* 1986;7:701-4.
98. Friedman RA, Moak JP, Garson A Jr. Clinical course of idiopathic dilated cardiomyopathy in children. *J Am Coll Cardiol* 1991;18:152-6.
99. Lewis AB, Chabot M. Outcome of infants and children with dilated cardiomyopathy. *Am J Cardiol* 1991;68:365-9.
100. Sachdev B, Elliott PM, McKenna WJ. Cardiovascular Complications of Neuromuscular Disorders. 2002;4:171-9.
101. Boriani G, Gallina M, Merlini L, et al. Clinical relevance of atrial fibrillation/flutter, stroke, pacemaker implant, and heart failure in Emery-Dreifuss muscular dystrophy: A long-term longitudinal study. *Stroke* 2003;34:901-8.
102. Stevenson WG, Perloff JK, Weiss JN, Anderson TL. Facioscapulohumeral muscular dystrophy: Evidence for selective, genetic electrophysiologic cardiac involvement. *J Am Coll Cardiol* 1990;15:292-9.
103. Lazarus A, Varin J, Babuty D, Anselme F, Coste J, Duboc D. Long-term follow-up of arrhythmias in patients with myotonic dystrophy treated by pacing: A multicenter diagnostic pacemaker study. *J Am Coll Cardiol* 2002;40:1645-52.
104. Collins KK, Thiagarajan RR, Chin C, et al. Atrial tachyarrhythmias and permanent pacing after pediatric heart transplantation. *J Heart Lung Transplant* 2003;22:1126-33.
105. Okubo S, Nagata S, Masuda Y, Kawazoe K, Atobe M, Manabe H. Clinical features of rheumatic heart disease in Bangladesh. *Jpn Circ J* 1984;48:1345-9.
106. Perry LW, Hung W. Atrial fibrillation and hyperthyroidism in a 14-year-old boy. *J Pediatr* 1971;79:668-71.
107. Iwasaki T, Naka M, Hiramatsu K, et al. Echocardiographic studies on the relationship between atrial fibrillation and atrial enlargement in patients with hyperthyroidism of Graves' disease. *Cardiology* 1989;76:10-7.
108. Ueda N, Yoshikawa T, Chihara M, Kawaguchi S, Niinomi Y, Yasaki T. Atrial fibrillation following methylprednisolone pulse therapy. *Pediatr Nephrol* 1988;2:29-31.
109. Arya KR, Taori GK, Khanna SS. Electrocardiographic manifestations following electric injury. *Int J Cardiol* 1996;57:100-1.
110. Thornton JR. Atrial fibrillation in healthy non-alcoholic people after an alcoholic binge. *Lancet* 1984;2:1013-5.
111. Ristic AD, Maisch B, Hufnagel G, et al. Arrhythmias in acute pericarditis. An endomyocardial biopsy study. *Herz* 2000;25:729-33.
112. Spodick DH. Arrhythmias during acute pericarditis. A prospective study of 100 consecutive cases. *JAMA* 1976;235:39-41.
113. Dunnigan A, Benson W Jr, Benditt DG. Atrial flutter in infancy: Diagnosis, clinical features, and treatment. *Pediatrics* 1985;75:725-9.
114. Luedtke SA, Kuhn RJ, McCaffrey FM. Pharmacologic management of supraventricular tachycardias in children. Part 2: Atrial flutter, atrial fibrillation, and junctional and atrial ectopic tachycardia. *Ann Pharmacother* 1997;31:1347-59.
115. McNamara RL, Tamariz LJ, Segal JB, Bass EB. Management of atrial fibrillation: Review of the evidence for the role of pharmacologic therapy, electrical cardioversion, and echocardiography. *Ann Intern Med* 2003;139:1018-33.
116. Snow V, Weiss KB, LeFevre M, et al. Management of newly detected atrial fibrillation: A clinical practice guideline from the American Academy of Family Physicians and the American College of Physicians. *Ann Intern Med* 2003;139:1009-17.