MEDICAL MANAGEMENT OF ARRHYTHMIAS

KEY POINTS:

1. Patients requiring anti-arrhythmic drug treatment for cardiac arrhythmia should receive this treatment from cardiologists who are familiar with all the available treatment options, and concomitant cardiac drug treatments. Clinicians prescribing antiarrhythmic drug therapy should be familiar with the potential side effects, in particular pro-arrhythmic capabilities, or the ability of such drugs ***to cause*** arrhythmias.
2. Clinicians should also be aware that some non-antiarrhythmic drugs can cause arrhythmias. These range from conduction disturbances in elderly patients on b-blockers to acquired Long QT changes with some antibiotics and antihistamines. Sudden cardiac deaths have been known to result.
3. Anti-arrhythmic drug treatment is appropriate for patients with arrhythmias and no structural heart disease, for example in PSVT, (see Chapter 14). However, failure of drug treatment or side effects of treatment should prompt referral for consideration of curative catheter ablation.
4. Long-term anti-arrhythmic drug treatment may be appropriate where an interventional approach has failed or is not possible, but only after a thorough consideration of the options in consultation with a Consultant Cardiac Electrophysiologist.
5. Adjunctive anti-arrhythmic drug treatment may be needed in patients who have received appropriate interventional treatment in whom either symptoms or perceived risk persists, and thus could form part of a hybrid approach to rhythm management in complex cases.
6. Anti-arrhythmic drug treatment is commonly needed, along with other cardiac drugs, in patients at high risk of sudden cardiac death who have an ICD, but is unlikely to be appropriate for sudden cardiac death risk-reduction as a stand-alone therapy.
7. In rare conditions such as the congenital Long QT syndrome, anti-arrhythmic drug treatment may be appropriate as a stand-alone treatment e.g. long-term beta-adrenergic blockade.

INTRODUCTION

The National Service Framework (NSF) for heart disease will now include clear standards for the management of cardiac arrhythmias and their consequences that will lead to improvement in access to high quality care. This document sets out standards for the appropriate use of medical approaches as set out under the following headings:

- The aims
- The standard
- The rationale
- Current interventions
- Service models
- Immediate priorities
- Milestones and goals
- Holding the NHS to account – performance indicators

AIMS

This chapter sets out how the NHS can best use medical approaches in the management of arrhythmias especially drug treatments and describes:

- The impact of life-style on cardiac arrhythmia.
- Currently available drug treatments and the cautions required for their best use.
- Models of care that ensure the best use of drugs for cardiac arrhythmia.
- Milestones marking progress in NSF goals.
- Measures that will be used to mark progress.

STANDARD

The standard that the NHS should aim for

Patients requiring drug treatment for cardiac arrhythmia should receive this treatment from physicians who are familiar with all the available treatment options and the possible downsides of a drug approach. Drug treatment will usually be reserved for the following situations [1 2]:

- Short-term treatment until an appropriate definitive treatment option can be applied.
- Long-term treatment where an interventional approach is not possible after a thorough consideration of the options usually in consultation with a specialist.
- Adjunctive treatment in patients who have received appropriate interventional treatment in whom either symptoms or perceived risk persists.
- In rare conditions such as the genetic Long QT syndrome in which eg long term beta-adrenergic blocker use has been found to be effective.

RATIONALE

Medical management of arrhythmia is defined as treatment based on lifestyle advice or drug therapy [3]. Increasingly such treatment will be used in combination with *non-pharmacological treatments* using either implantable devices or ablation techniques. The objective of medical management is usually to enhance quality-of-life with efficacy determined from a review of the history with in occasional patients other tests e.g. ambulatory electrocardiograms being useful. Several years ago

invasive assessments of cardiac electrophysiology were advocated but serial *invasive* tests of this sort are now almost never used [4].

There is little evidence that drug treatment can prolong life as a result of the amelioration of arrhythmias and indeed antiarrhythmic drugs may be life threatening [4]. The main limiting factor in achieving effective medical management is drug side effects. These can be intolerable with extra-cardiac side effects also occasionally being life-threatening, for example, pulmonary fibrosis or thyrotoxicosis due to amiodarone [5] .

Potential benefits of antiarrhythmic drug therapy
Decreased mortality (little evidence)
Improved quality-of-life

Risks of antiarrhythmic drug therapy
New or worsened arrhythmia
Heart Failure
Increased mortality with long term treatment
Non-cardiovascular

Mechanisms of drug action

Most cardiac arrhythmias are the result of increased excitability of the myocardium. The abnormal rhythms of the heart travel round in a circus movement pattern, so-called re-entrant excitation. The actions of antiarrhythmic drugs differ and alter the electricity of the heart to make it less excitable and reduce the likelihood of arrhythmias. Some of the drugs such as flecainide and propafenone slow the conduction through the muscle whereas other increase the time taken by the heart cells to recover [6].

Ideal drug characteristics

Most antiarrhythmic drugs modify the function of cardiac ion channels that allow the passage of the electricity into and out of the heart cells. Drug classifications such as that introduced by Vaughan-Williams and Singh are now largely redundant and consideration of specific agents, their individual actions and side effect profiles is probably the best pragmatic approach when using these drugs. The characteristics of the ideal antiarrhythmic agent have not been attained and include: antiarrhythmic efficacy, suppression of triggers, efficacy in diseased tissue, effective at all heart rates, few side effects etc.

Ongoing research in academic laboratories and in industry is aimed at creating new and effective drug reagents for clinical use [7].

Antiarrhythmic drugs may cause arrhythmias (proarrhythmia)

The main concern with the use of antiarrhythmic drugs is that they may of themselves provoke an arrhythmia [8 1 9 10 11]. There are ways of reducing this risk. For example, drugs that slow conduction through the heart such as Flecainide should not be given to patients with structural heart disease as this is known to be potentially risky. In those patients with atrial arrhythmias. Flecainide should almost always be used with a drug that will slow conduction through the atrioventricular node (e.g. a beta adrenergic receptor blocker or a calcium channel blocker) as rapid conduction to the ventricle may otherwise be possible.

The main risks of proarrhythmia with current drugs is with so-called class III agents, such as Sotalol, that block heart potassium channels and prolong the action

potential generating a drug-induced (acquired) Long QT syndrome [12]. The risks of this condition can be reduced by careful use that will include careful prior examination of the electrocardiogram looking for evidence of congenital QT prolongation, an echocardiogram, and serum potassium and creatinine estimation. Dose titration will then be needed with serial electrocardiograms to assess the individual's response to the drug. Some patients will need to start drug treatment in hospital. Many non-cardiac drugs may also cause the same problem (e.g. erythromycin, thioridazine) and these are listed in a separate section in the BNF, which should be consulted. The risks of developing proarrhythmia of this sort is thought to be genetically determined and is being examined as a possible early application of pharmacogenomics [13] [14].

CURRENT INTERVENTIONS

Lifestyle advice

Although many patients will avoid caffeine and alcohol as they find these may induce symptoms of cardiac arrhythmia the objective evidence to support such an approach is lacking [15]. Excess consumption of alcohol should be discouraged especially if there is any evidence of ventricular dilatation possibly indicative of early cardiomyopathy. If caffeine avoidance is proving helpful then this should continue. Weight gain may be associated with a net increased risk of arrhythmia however whether weight loss is beneficial is unclear. Anecdotal evidence would suggest that moving from a stressful job might help with symptoms of paroxysmal atrial fibrillation.

Antiarrhythmic drugs

General principles

The pattern of drug use has changed substantially in recent years [16]. Although there is no systematic data from the United Kingdom that from the United States [17] indicates increasing use of Amiodarone and the virtual extinction of drugs such as quinidine (ref). In the United Kingdom four drugs are commonly used with in addition certain drugs used in small numbers of patients. The main concern with the use of antiarrhythmic drugs is that they may provoke an arrhythmia, so-called proarrhythmia [8] [9] [10].

Specific Antiarrhythmic drugs

The following drugs are commonly used in the United Kingdom:

Flecainide and Propafenone are termed 1c agents and slow the conduction through the heart muscle. They are used mostly in patients with paroxysmal atrial arrhythmias and supraventricular tachycardia in those patients waiting for definitive treatment. They are quite effective [18] and are associated with few side effects although certain patients are totally intolerant of these drugs. They are thought to be contraindicated in those who have evidence of structural heart disease on echocardiography. Accordingly:

- Only Consultant Cardiologists should initiate these drugs in those patients who have been shown to have a normal heart on echocardiography. Flecainide is generally used in the United Kingdom although the adjunctive beta-adrenergic blocking action of propafenone may be useful or even a contra-indication in some patients.

- Medium - or long-term management by primary practitioners may be possible but shared care guidelines should be in place. In general long-term monitoring is not needed although if patients' clinical status changes (for example, the patient

suffers a myocardial infarction and then has evidence of structural heart disease) then re-consideration of drug treatment may be needed under the supervision of a Consultant Cardiologist.

- In general drug interactions are few but should be routinely reviewed against national guidelines as noted in the British National Formulary.

Sotalol is a class III agent and impairs the recovery of excitability of heart cells but in addition also is a beta-adrenergic blocker and therefore causes the class side effects of that group of drugs with tiredness and lack of energy being prominent. Accordingly many patients are intolerant of this therapy. In addition it may cause life-threatening arrhythmias (see above), which may be a major problem especially in elderly patients with impairment of renal function. Accordingly:

- Sotalol should only be initiated by a Consultant Physician and ideally a Consultant Cardiologist fully familiar with its use. The patient should be fully assessed beforehand with a careful assessment of the relative risks and benefits. The assessment will include an ECG with a careful evaluation of the QT interval, an echocardiogram and blood tests of renal function.

- Any dose increment should be actioned only by the managing Consultant and will need monitoring with electrocardiograms.

- Although it is a potentially dangerous drug medium- to long-term, shared care with primary care providers may be possible with proper guidelines in place. Any change in the health status of the patient such as the development of renal failure or of structural heart disease should prompt a re-evaluation of the appropriateness of the treatment. Acute illness that may drop the serum potassium concentration (e.g. vomiting, diarrhoea) may be dangerous and the drug may need to stop for a period of time.

Amiodarone is a complex but widely used drug [5]. The use of the agent has increased enormously in recent years despite some very severe, potentially life threatening adverse effects [19]. In view of safety concerns and according to the summary of product characteristics (SPC) amiodarone 'should be initiated and normally monitored only under hospital of specialist supervision'. The responsibility for prescribing and monitoring often falls to non-specialist and hence the development and application of shared care guidelines should be encouraged. In general:

- Amiodarone should be considered a drug of last resort and only started by a Consultant Cardiologist who has considered all the options including interventional treatments. It may interfere with the proper delivery of interventional curative treatments and this is a major concern.

- Shared care guidelines should be in place to be sure that monitoring for toxicity in particular is efficiently and effectively achieved. Patients should all receive information leaflets and be encouraged to report potential adverse events due to skin, thyroid or lung toxicity.

- Primary care practitioners need to periodically check thyroid function in all patients taking amiodarone. The current recommendation is each six months but more regular checks may be needed in certain patient groups.

Newer antiarrhythmic drugs. Many new agents (e.g. Dofetilide [20], Azimilide [21] [22], Ibutilide) have not been released in the United Kingdom. It is hoped that the increased availability of arrhythmia specialists following the NSF will make the

United Kingdom an increasingly attractive market place and that these agents that provide benefit in individual patients will become available. There is a major effort being made by the pharmaceutical industry to develop drugs with useful actions that may target ion channels concentrated in specific tissue types especially the atria. The idea is that these drugs would able to treat the arrhythmia without causing ventricular arrhythmia.

Other drugs with antiarrhythmic actions

- Beta-adrenergic blockers
- Calcium channel blockers
- Digoxin
- ACE inhibitors
- Spironolactone

Antithrombotic interventions [23]

- Aspirin
- Warfarin
- Newer antithrombotic treatments

SERVICE MODELS

This chapter deals exclusively with arrhythmias and issues of syncope prophylaxis are covered elsewhere (see Chapter 10). Specific antiarrhythmic drugs should only be started under the instructions and guidance of Consultant Cardiologists. In most cases the patients should have had a recent echocardiogram to assess the heart function. Most drugs can be started in outpatients in those with normal heart function including Flecainide, Propafenone and Amiodarone. Drugs having substantial actions to prolong the cardiac action potential may need to be started in hospital and this should be a specific consideration with Sotalol especially when used in patients with other evidence of heart disease (e.g. left ventricular hypertrophy, heart failure).

Acute Management of Cardiac Arrhythmias

It is hoped that prior to the next revision of the NSF all Medical Admission Units will have adopted nationally agreed guidelines on best standards of care for the acute management of cardiac arrhythmias. In general the following basic principles will apply:

- Patients with a history of structural/coronary heart disease presenting with a broad complex tachycardia should be regarded as having ventricular tachycardia. If they are unwell with a low blood pressure or have evidence of an impaired pumping ability of the heart then they should immediately undergo DC cardioversion. If the tachycardia is well tolerated then some of these patients may be candidates to receive intravenous amiodarone to bring the rhythm under control. This decision should be made in conjunction with a Consultant Physician familiar with the management of acute cardiac emergencies.

- Patients presenting with a regular narrow complex tachycardia with no evidence of heart disease usually have a supraventricular tachycardia. They should generally receive intravenous adenosine in an incremental dosing regimen as recommended in the BNF. Occasional patients with severe bronchial asthma or those with previous intolerance of adenosine should receive intravenous verapamil.

- Patients presenting with atrial fibrillation should be managed dependent on the duration of the history and their current condition. If the history is very short then cardioversion should be attempted either by intravenous drugs or electrical cardioversion. Drugs would be preferred if the patient is haemodynamically stable and has a normal heart on echocardiography with intravenous flecainide a reasonable choice. If the patient is stable but with an abnormal echocardiogram then intravenous amiodarone may be used. If there is evidence of haemodynamic instability and a short history then electrical cardioversion may be preferred. If there is any doubt regarding the length of the history then the patient should be anticoagulated first with heparin and then with Warfarin and the rate controlled with digoxin. Beta-adrenergic blockers or calcium channel blockers.

Subsequent management of each of these groups of patients should involve a Consultant Cardiologist and is described in the relevant Chapters.

Prophylactic Drug Treatment

- Now regarded as stepping stone to definitive treatment with non-pharmacological treatments.
- Occasionally patients will be on long-term prophylactic treatment e.g. non-hypotensive VT with good left ventricular function.
- Amiodarone should be avoided in most patients with arrhythmias in whom radiofrequency ablation is contemplated. In these patients this drug will not allow full diagnostic electrophysiology study and is likely to compromise the result and therefore the treatment of the patient.
- Prophylactic drugs of choice in different settings are described in the chapters covering atrial fibrillation, supraventricular tachycardia, ventricular tachycardia etc.

Adjunctive Drug Treatments

Hybrid treatment of atrial arrhythmias [24]

- In conjunction with atrial ablation e.g. flutter ablation.
- In conjunction with pacemakers for bradycardia.
- Reduction of the defibrillation threshold prior to DC cardioversion of atrial fibrillation.

Adjunctive treatment patients with ICDs

The aim here would generally be to reduce the possibility of ICD device discharge [25]. The following drugs currently achieve this objective:

- Amiodarone.
- Sotalol.[26]
- Newer drugs currently not available in the United Kingdom: Azimilide, [21] [22] Dofetilide [20]

Patients with genetic causes of cardiac arrhythmias

Those patients identified as having a specific genetic cause of cardiac arrhythmia or perceived risk of sudden cardiac death should be managed by individuals identified as having a specific interest in this area of medicine. These patients will include those with Hypertrophic Cardiomyopathy, Long QT syndrome and Brugada syndrome. Information guiding drug treatment in these patients is evolving and will become increasingly targeted as we learn more about the genetic basis of these conditions.

Prophylaxis following cardiothoracic surgery

- Cardiac surgery. [27]
- Thoracic surgery.

IMMEDIATE PRIORITY

The immediate priorities for implementing this area of the NSF are delivering the early milestones. This will be monitored through performance management processes.

MILESTONES AND GOALS

The milestones and goals set out below refer to primary, secondary and tertiary care.

Milestones for drug use by non-specialists

Milestone 1

Clear guidance re the appropriate pattern of referral should have been made available to all practitioners likely to encounter patients with cardiac arrhythmia. All patients taking antiarrhythmic drugs should be reviewed within the context of these new guidelines. Shared care guidelines for all relevant drugs should have been developed and applied. No patient should be taking an antiarrhythmic drug unless there has been prior review by a Consultant Cardiologist.

Milestone 2

No patient should be taking an antiarrhythmic drug without appropriate consultation with an arrhythmia specialist as to the best options for arrhythmia management in that individual.

Milestones for drug use by specialists

Milestone 1

Every hospital should have applied guidelines for the best use of antiarrhythmic drugs.

- Patients presenting with acute cardiac arrhythmia to an acute admissions unit will receive care as described in nationally agreed guidelines.
- No patient should be taking a prophylactic antiarrhythmic drug unless there has been prior review by a Consultant Cardiologist.
- Patients presenting with drug-induced arrhythmia should be reported to the national database (British Heart Foundation-funded DARE study, St George's Hospital Medical School).

Milestone 2

Every hospital with an electrophysiology service should have completed an audit of the current pattern of antiarrhythmic drug use

- Clinical audit data for each drug used, documenting diagnosis, reasons for choice of drug as opposed to interventional approach, appropriate adherence to e.g. NICE guidance for management of atrial fibrillation (or, if outside NICE guidance, additional reason or evidence for drug use).

HOLDING THE NHS TO ACCOUNT

The Commission for Health Improvement and Regional Offices of the NHS Executive will use both local and national indicators to judge the performance of individual organisations.

NHS organisations will be expected to demonstrate that, in implementing this NSF, they are making full use of the available information and guidelines for improving the use of antiarrhythmic drugs. This includes ensuring that local

systems for clinical governance and life-long learning to optimise the use of these drugs.

LAY SUMMARY

Heart drugs for suppressing heart rhythm disorders are appropriate for some but not all patients. Modern treatments for heart rhythm disorders include the ability to cure many patients with arrhythmias, (see Chapter 14, 16, 18). In the UK curative catheter ablation procedures are very undersupplied, and many patients may spend longer than they should on drug treatment, when a cure could be achieved. Patients with normal hearts and arrhythmias commonly have conditions that can be cured, because often the arrhythmia is an electrical short-circuit involving a tiny area. Heart rhythm drugs are generally reasonably safe, especially if the heart is normal other than for an electrical fault. Seemingly

paradoxically, all antiarrhythmic drugs have the ability to cause a heart rhythm disorder that was not there in the first place, because of the way in which they act on the heart. Sometimes, this effect can be life threatening, and all doctors should be aware of this.

It may be appropriate therefore to be on heart rhythm drug treatment in the short-term to see if symptoms are controlled. If they are not controlled or side effects occur, then there should be referral to a cardiologist with an interest in cardiac arrhythmias, (electrophysiologist), for consideration of other treatments that would include curative catheter ablation or the use of implantable devices such as pacemakers or ICDs.

Long-term rhythm drug treatment may be appropriate if a catheter ablation has failed or is not possible, but only after a thorough consideration of the options in consultation with a cardiac electrophysiologist. Antiarrhythmic drug treatment may be needed in patients used in conjunction with catheter ablation in some complicated cases.

Heart rhythm drug treatment is commonly needed, along with other cardiac drugs, in patients with life-threatening heart damage who have an ICD. However, patients at such high-risk should not be receiving heart rhythm drug treatment alone. An exception to this rule exists in some rare conditions such as the congenital Long QT syndrome, then heart rhythm drug treatment alone may be appropriate e.g. beta-blockers.

REFERENCES:

1. Roden DM. Risks and benefits of antiarrhythmic therapy. *N Engl J Med*. 1994;331:785-91.
2. Podrid PJ. Redefining the role of antiarrhythmic drugs. *N Engl J Med*. 1999;340:1910-2.
3. Roden DM. Antiarrhythmic drugs: past, present and future. *J Cardiovasc Electrophysiol*. 2003;14:1389-96.
4. Huikuri HV, Castellanos A, Myerburg RJ. Sudden death due to cardiac arrhythmias. *N Engl J Med*. 2001;345:1473 82.
5. Connolly SJ. Evidence-based analysis of amiodarone efficacy and safety. *Circulation*. 1999;100:2025-34.

6. Camm AJ, Savelieva I. Advances in antiarrhythmic drug treatment of atrial fibrillation: Where do we stand now? *Heart Rhythm*. 2004;1:244-246.
7. Sanguinetti MC, Bennett PB. Antiarrhythmic drug target choices and screening. *Circ Res*. 2003;93:491-9.
8. Selzer A, Wray HW. Quinidine Syncope. Paroxysmal Ventricular Fibrillation Occurring During Treatment of Chronic Atrial Arrhythmias. *Circulation*. 1964;30:17-26.
9. Grace AA, Camm AJ. Quinidine. *N Engl J Med*. 1998;338:35-45.
10. Yap YG, Camm J. Risk of torsades de pointes with non-cardiac drugs. Doctors need to be aware that many drugs can cause qt prolongation. *Bmj*. 2000;320:1158-9.
11. Roden DM. Drug-induced prolongation of the QT interval. *N Engl J Med*. 2004;350:1013-22.
12. Cobbe SM. Class III Antiarrhythmics: put to the SWORD? *Heart*. 1996;75:111-3.
13. Roses AD. Genome-based pharmacogenetics and the pharmaceutical industry. *Nat Rev Drug Discov*. 2002;1:541-9.
14. Deloukas P, Bentley D. The HapMap project and its application to genetic studies of drug response. *Pharmacogenomics J*. 2004;4:88-90.
15. Falk RH. Atrial fibrillation. *N Engl J Med*. 2001;344:1067-78.
16. Fuster V, Ryden LE, Asinger RW, Cannom DS, Crijns HJ, Frye RL, Halperin JL, Kay GN, Klein WW, Levy S, McNamara RL, Prystowsky EN, Wann LS, Wyse DG, Gibbons RJ, Antman EM, Alpert JS, Faxon DP, Gregoratos G, Hiratzka LF, Jacobs AK, Russell RO, Smith SC, Jr., Alonso-Garcia A, Blomstrom-Lundqvist C, de Backer G, Flather M, Hradec J, Oto A, Parkhomenko A, Silber S, Torbicki A. 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.
17. Fang MC, Stafford RS, Ruskin JN, Singer DE. National trends in antiarrhythmic and antithrombotic medication use in atrial fibrillation. *Arch Intern Med*. 2004;164:55-60.
18. Nichol G, McAlister F, Pham B, Laupacis A, Shea B, Green M, Tang A, Wells G. Meta-analysis of randomised controlled trials of the effectiveness of antiarrhythmic agents at promoting sinus rhythm in patients with atrial fibrillation. *Heart*. 2002;87:535-43.
19. Hohnloser SH, Klingenheben T, Singh BN. Amiodarone-associated proarrhythmic effects. A review with special reference to torsade de pointes tachycardia. *Ann Intern Med*. 1994;121:529-35.
20. Mounsey JP, DiMarco JP. Cardiovascular drugs. Dofetilide. *Circulation*. 2000;102:2665-70.

21. Pratt CM, Singh SN, Al-Khalidi HR, Brum JM, Holroyde MJ, Marcello SR, Schwartz PJ, Camm AJ. The efficacy of azimilide in the treatment of atrial fibrillation in the presence of left ventricular systolic dysfunction: results from the Azimilide Postinfarct Survival Evaluation (ALIVE) trial. *J Am Coll Cardiol*. 2004;43:1211-6.
22. Singer I, Al-Khalidi H, Niazi I, Tchou P, Simmons T, Henthorn R, Holroyde M, Brum J. Azimilide decreases recurrent ventricular tachyarrhythmias in patients with implantable cardioverter defibrillators. *J Am Coll Cardiol*. 2004;43:39-43.
23. Hankey GJ, Klijn CJ, Eikelboom JW. Ximelagatran or warfarin for stroke prevention in patients with atrial fibrillation? *Stroke*. 2004;35:389-91.
24. McNamara RL, Brass LM, Drozda JP, Jr., Go AS, Halperin JL, Kerr CR, Levy S, Malenka DJ, Mittal S, Pelosi F, Jr., Rosenberg Y, Stryer D, Wyse DG, Radford MJ, Goff DC, Jr., Grover FL, Heidenreich PA, Peterson ED, Redberg RF. ACC/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with atrial fibrillation: a report of the American College of

Cardiology/American Heart Association Task Force on Clinical Data Standards (Writing Committee to Develop Data Standards on Atrial Fibrillation). *Circulation*. 2004;109:3223-43.
25. Curtis AB. Filling the need for new antiarrhythmic drugs to prevent shocks from implantable cardioverter defibrillators. *J Am Coll Cardiol*. 2004;43:44-6.
26. Pacifico A, Hohnloser SH, Williams JH, Tao B, Saksena S, Henry PD, Prystowsky EN. Prevention of implantable-defibrillator shocks by treatment with sotalol. d,l-Sotalol Implantable Cardioverter-Defibrillator Study Group. *N Engl J Med*. 1999;340:1855-62.
27. Villareal RP, Hariharan R, Liu BC, Kar B, Lee VV, Elayda M, Lopez JA, Rasekh A, Wilson JM, Massumi A. Postoperative atrial fibrillation and mortality after coronary artery bypass surgery. *J Am Coll Cardiol*. 2004;43:742-8.