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Managing arrhythmias in coronary artery disease

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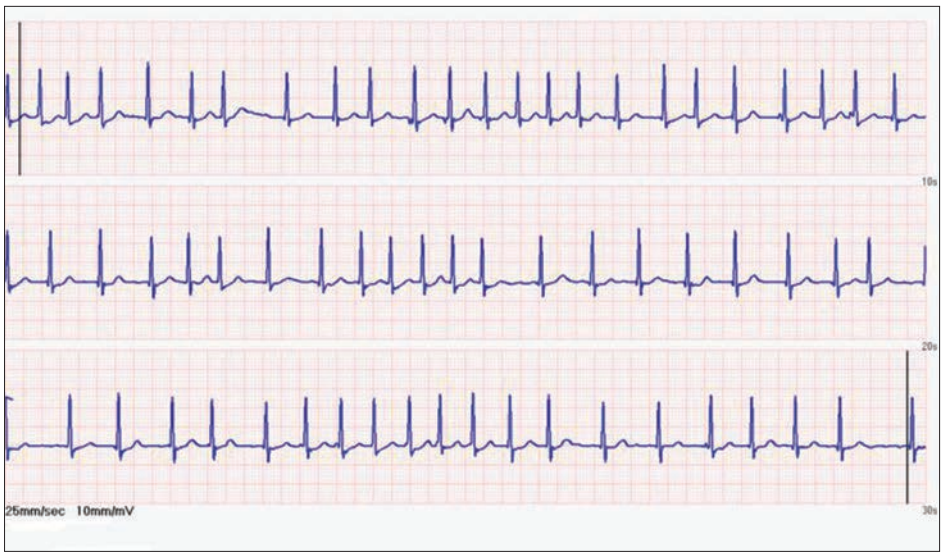

FIGURE 1
Patient event monitor recording of atrial fibrillation during symptoms of palpitations

What are the common arrhythmias?

How should patients be investigated?

What are the management strategies?

CORONARY ARTERY DISEASE (CAD) IS THE LEADING CAUSE OF DEATH IN THE UK ACCOUNTING for approximately 15% of male deaths and 10% of female deaths. It also causes significant morbidity.[1] The broad condition of CAD encompasses presentation with acute coronary syndromes (ACS) and chronic stable disease. Important associated arrhythmias include atrial fibrillation (AF) and atrial flutter, ventricular tachycardia (VT) and ventricular fibrillation (VF), ventricular ectopy, and bradyarrhythmias. Arrhythmias occurring in hospital following admission with an ACS are associated with significant morbidity and mortality and will require immediate evaluation.[2,3]

Patients with a prior myocardial infarction (MI) or stable chronic coronary disease remain at risk of cardiac arrhythmias and particular importance must be attached to the care of those with impaired left ventricular systolic function and thus assessment of left ventricular function informs many management decisions. It is these groups that are of particular relevance to the primary care setting.

CLINICAL ASSESSMENT

Table 1, p18, outlines the key aspects of assessment common to all patients with CAD and suspected arrhythmias. A detailed history is vital to elucidate red flag symptoms necessitating urgent specialist assessment. Palpitations are common. However, patients often describe them in different ways and they can include irregular sensations in AF, rapid and regular palpitations of atrial flutter or VT, and skipped beats typical of ventricular ectopics. In AF, symptoms may be nonspecific and manifest as dyspnoea or fatigue.

Red flag symptoms in patients with CAD include syncope and presyncope, particularly in patients with concomitant left ventricular systolic dysfunction in whom rapid palpitations should raise strong suspicions for VT. Palpitations with severe chest pain and breathlessness also warrant urgent assessment.

Clinical examination will focus on the cardiovascular system particularly looking for signs of heart failure and murmurs suggestive of heart valve disease.

However, patients with CAD are often older with multiple comorbidities. A holistic approach is crucial to detecting and managing accompanying conditions that often precipitate arrhythmias including hypertension, obesity, diabetes mellitus, obstructive airways disease and thyroid dysfunction. Key aspects of clinical investigations and management are highlighted in reference to specific arrhythmias below.

ATRIAL FIBRILLATION

Assessment

AF is associated with increased mortality particularly due to heart failure and sudden death.[4,5] Early detection and management is therefore crucial. Undiagnosed AF is common, particularly in older populations, which overlap significantly with those with CAD. Although there are no specific studies in patients purely with CAD, broader studies of screening in older populations appear cost effective and use a combination of pulse palpation and single lead ECG.[6] The European Society of Cardiology guidelines recommend opportunistic screening using these methods in patients over 65 years of age, which encompasses many patients with CAD.[2]

The management of AF consists of three essential components:

- Thromboembolic risk assessment and stroke prevention
- Control of symptoms through either rate or rhythm control
- Management of associated comorbidities and risk factors

If an irregular pulse is detected, a 12-lead ECG should be carried out to confirm and document the presence of AF as well as identify the ventricular rate. Radial palpation should not be relied upon for assessment of ventricular rate. It is important to note that high ventricular rates will often result in an »

element of ST segment depression and this alone does not signify significant ischaemia. Moreover, it may cause a small elevation in cardiac troponins, even in people with no coronary atheroma. However, if ongoing angina is suspected then referral for repeated ischaemia evaluation may be required.[2,3]

Antithrombotic therapy

Thromboembolic risk should be assessed in all patients using the CHA_2DS_2VASc score (see table 2, opposite). Bleeding risk should also be assessed with particular emphasis on detecting and correcting modifiable risk factors (see table 2, opposite).

All patients with CAD will have a CHA_2DS_2VASc score of at least 1 and oral anticoagulation should therefore be considered.[2] Although both vitamin K antagonists (VKA) and direct oral anticoagulants (DOAC) are effective in stroke risk reduction, evidence suggests superior efficacy of DOACs particularly through lower risk of haemorrhagic stroke. Bleeding risk is also lower with DOACs and should therefore be considered first line.[2,7]

Importantly, patients with CAD are also prescribed antiplatelet agents. Combination therapy with anticoagulation significantly increases bleeding risk, particularly in the case of triple therapy with dual antiplatelet agents and oral anticoagulation where risk is increased by 79-134%.[8,9]

In patients with stable CAD without an ACS or percutaneous coronary intervention (PCI) in the preceding 12 months then oral anticoagulation alone should be used. In the context of ACS or recent (preceding 12 months) PCI then decisions on combination therapy should be undertaken in collaboration with the interventional cardiology team. A period of one to six months of triple therapy may be indicated, influenced by the specific stents used, coronary anatomy and patient specific bleeding risk. Dual

Table 1

Assessment of patients with suspected arrhythmias

History

Symptoms
- Palpitations
- Dyspnoea
- Chest pain
- Peripheral oedema
- Presyncope/syncope
- Exercise tolerance

Important comorbidities/ past medical history
- Hypertension
- Heart failure
- Valve disease
- Angina/ACS/PCI
- Thyroid dysfunction
- Obesity
- Diabetes mellitus
- Obstructive sleep apnoea
- Chronic airways disease
- Chronic kidney disease

Medications
- Anticoagulants
- Antiplatelets
- NSAIDs
- Heart failure drugs
- Antihypertensives

Social history
- Alcohol
- Smoking
- Exercise
- Occupation and driving

Examination

General
- Height, weight/BMI
- Oxygen saturations

Cardiovascular
- Pulse palpation
- BP
- JVP
- Murmurs
- Pulmonary congestion/ pleural effusions
- Peripheral oedema

Respiratory
- Chest hyperexpansion
- Expiratory wheeze

Thyroid
- Tremor
- Thyroid goitre

Investigations

Test/investigation	Indications/important considerations of tests
Blood tests: ● Full blood count ● Renal function/electrolytes ● Liver function ● Thyroid function	● Identify anaemia ● Guide drug dosing ● Inform bleeding risk ● Identify reversible causes
12-lead ECG	● Confirm diagnosis and assess ventricular rate ● Identify signs of ischaemia ● Identify conduction disease ● Identify signs of structural heart disease (e.g. BBB)
Ambulatory monitoring ● Continuous ECG monitoring ● External event recorders Including Zio patch and Kardia AliveCor device ● Implantable loop recorders	● Important to detect AF paroxysms ● Assess rate control ● Identify and assess burden of PVCs or NSVT ● Continuous monitoring of limited duration
Transthoracic echocardiography	● Assess LV systolic function ● Identify valve disease ● LVH as sign of hypertension ● LA size

ACS = acute coronary syndrome; BBB = bundle branch block; BMI = body mass index; BP = blood pressure; JVP = jugular venous pressure; LA = left atrium; LV = left ventricle; LVH = left ventricular hypertrophy; PCI = percutaneous coronary intervention

therapy with oral anticoagulation and clopidogrel should then be continued up to 12 months followed by anticoagulation alone. Prasugrel or ticagrelor are avoided in combination with anticoagulation given their increased risk of bleeding but DOACs are generally recommended in place of warfarin because of their lower bleeding risk.[2,10]

Rate vs rhythm control

Although there are no specific trials in patients with CAD, there is no clear evidence that a rhythm control strategy offers any significant long-term benefits.[11,12] The appropriate strategy is therefore determined primarily by the symptomatic burden of AF. In patients with well tolerated or infrequent episodes a rate control strategy is recommended. In those with paroxysmal AF a detailed correlation of contemporaneously recorded symptoms and arrhythmias during ambulatory recording is key, and in those with persistent AF cardioversion to assess the symptomatic benefit of a period of sinus rhythm may be required.

Management options for rate or rhythm control are outlined in table 3, p20. Rate control is based on slowing AV nodal conduction. As beta-blockers are indicated for many patients with CAD, particularly following an ACS, this should be considered first line. The appropriate initial target heart rate should be < 110. Evidence suggests that this lenient target, compared with a strict target of < 80 is equally effective and significantly easier to achieve.[13]

Importantly, although flecainide is commonly prescribed for patients with paroxysmal AF it is contraindicated in patients with CAD because of an increased risk of sudden death.[14] When clinically suspected, CAD should be excluded prior to commencing flecainide.

Patients with AF and heart failure with left ventricular systolic dysfunction should be referred to secondary care. AF may be the primary cause of heart failure often as a result of tachycardia mediated cardiomyopathy. This can be difficult to establish and is confirmed by demonstrating improved ejection fraction following a period of good rate control or sinus rhythm. In this setting, a rhythm control strategy is recommended. Calcium channel blockers are contraindicated. Beta-blockers and digoxin are used for rate control while amiodarone is used for rhythm control.

Studies have not specifically evaluated patients with CAD, but catheter ablation is increasingly used as part of a rhythm control strategy in patients refractory to pharmacological management and is effective in reducing AF recurrence.[2,15]

The recent CASTLE-AF trial evaluated catheter ablation compared with pharmacological therapy (rate or rhythm control) in patients with AF and heart failure with reduced ejection fraction. Nearly half, 46%, of patients had an ischaemic aetiology and catheter ablation was shown to result in significantly reduced rates of death or hospitalisation for heart failure. Catheter ablation should therefore particularly be considered in patients with severe symptoms and/or LV dysfunction.[16]

Risk factor modification

Risk factor modification is a crucial facet of CAD management and should include blood pressure control and lifestyle adjustments such as weight loss and exercise, which have been demonstrated to result in a significant reduction in AF burden and symptoms, as well as positive cardiac remodelling.[17] Studies of beta-adrenoceptor antagonists or renin-angiotensin-aldosterone system inhibitors have demonstrated reduced incidence of AF.[18]

Drugs in these classes are also indicated to reduce mortality following MI and in patients with left ventricular systolic dysfunction, and will therefore also be indicated in many patients with chronic CAD.[19]

Post coronary artery bypass grafting

AF occurs in up to 50% of patients following coronary artery bypass grafting (CABG). However, it is often self-limiting within the first 4-6 weeks.[10] Rhythm control is generally recommended in the early postoperative period and amiodarone is the most frequently used antiarrhythmic drug in this setting. This should be reviewed within six weeks of hospital discharge and can usually be stopped at this stage if sinus rhythm has been maintained. Ongoing arrhythmias should be managed with specialist input. There are no clear guidelines on anticoagulation in this patient group and decisions should be taken on a case by case basis considering ongoing bleeding and thromboembolic risk.[3]

ATRIAL FLUTTER

Atrial flutter is an organised atrial arrhythmia. The most common form observed in patients with CAD involves a band of tissue between the inferior vena cava and tricuspid annulus termed the cavotricuspid isthmus (CTI). This is identified by typical 'saw tooth' flutter waves visible in the inferior ECG leads. Catheter ablation involves creation of a linear lesion through the CTI thereby interrupting the reentry circuit and is both safe and effective.[20] Catheter ablation is therefore widely considered as the first-line treatment option. Importantly, atrial flutter and fibrillation often coexist and thromboembolic risk is considered similar. The same »

Table 2

Managing thromboembolic risk

Thromboembolic risk

CHA_2DS_2VASc	Score
Congestive heart failure/ LV systolic dysfunction	+1
Hypertension	+1
Age 75 or older	+2
Diabetes mellitus	+1
Prior **S**troke, TIA or systemic embolism	+2
Vascular disease (MI, peripheral arterial disease or aortic plaque)	+1
Age 65-74 years	+1
Sex: female	+1

Bleeding risk

Modifiable factors	Non-modifiable factors
● Hypertension	● Age
● Labile INR (if on VKA)	● Previous major bleeding
● Antiplatelet or NSAID use	● Stroke
● Excess alcohol	● Dialysis dependent renal disease or transplant
● Impaired renal function	● Cirrhotic liver disease
● Impaired liver function	● Malignancy
● Thrombocytopaenia	

Recommendations according to CHA_2DS_2VASc
0 (male) **1** (female) – Anticoagulation not recommended
1 (male) **2** (female) – Consider anticoagulation
2 (male) **3** (female) – Recommend anticoagulation

recommendations for antithrombotic therapy should therefore be followed.

Specific patient groups, particularly those who have previously undergone cardiac surgery or catheter ablation are susceptible to different forms of atrial flutter arising from both the left and right atria. These patients require specialist assessment.

However, the broad principles of initial management are the same for patients with any atrial flutter or AF and involve assessment of haemodynamic compromise, control of ventricular rate and stroke prevention.

VENTRICULAR ECTOPY

Premature ventricular complexes (PVC) and non-sustained VT (NSVT) are frequently observed in patients with an ACS, particularly during revascularisation for STEMI. However, PVCs are also frequently observed in primary care and are therefore commonly seen in patients with stable CAD. In this context reassurance is usually all that is required.

In patients with particularly bothersome symptoms of skipped or extra beats then pharmacological therapy with beta-blockers may be indicated. In patients with a very high burden of ectopy, severe symptoms or associated presyncope or syncope, and when associated with heart failure or significant ECG abnormalities (e.g. abnormal QRS morphology or bundle branch block) specialist assessment should be sought.

VENTRICULAR ARRHYTHMIAS

Ventricular arrhythmias in the context of CAD include monomorphic and polymorphic ventricular tachycardia (VT) and ventricular fibrillation (VF). These will often result in significant haemodynamic compromise or cardiac arrest resulting in sudden death. In the case of resuscitated cardiac arrest or sustained VT, management is undertaken in secondary care and may involve any, or a combination, of revascularisation, antiarrhythmic drug therapy, catheter ablation and device implantation. For patients in primary care, management should focus on identifying those at greatest risk of sudden death who will benefit from an implantable cardioverter defibrillator (ICD).

Primary prevention

Left ventricular ejection fraction (LVEF) $\leq$ 35% increases the risk of sudden death. All patients with CAD should therefore undergo assessment of LVEF usually by transthoracic echocardiography. This is particularly important at least six weeks following presentation with ST-elevation ACS.[19]

Recommendations for ICD implantation are derived from chronic heart failure guidelines and overlap with

Table 3

Management strategies for rate or rhythm control of atrial fibrillation (AF)

Therapy	Indication	Special considerations
Flecainide	**Contraindicated** in patients with CAD	Increased risk of sudden death
Beta-blockers	Rate control Indicated post ACS and in heart failure	Considered first line
Calcium channel blockers (diltiazem and verapamil)	Rate control	Contraindicated in heart failure with reduced ejection fraction. Avoid combination of verapamil and beta-blocker (risks severe bradycardia or AV block)
Digoxin	Rate control	Limited efficacy during exercise
Amiodarone	Maintenance of sinus rhythm	Requires careful counselling and checking/monitoring of TFTs, LFTs and lung function. Titrate to lowest effective dose
Sotalol	Maintenance of sinus rhythm	Confers risk of arrhythmia and sudden death Avoid in heart failure with reduced ejection fraction
Dronedarone	Maintenance of sinus rhythm (third line to amiodarone and sotalol)	Avoid in heart failure with reduced ejection fraction Requires close LFT monitoring. Avoid if AF becomes persistent
Catheter ablation	Maintenance of sinus rhythm: — Severe drug refractory symptoms — AF mediated LV dysfunction	Carries significant risk of complications and patient selection important to confer most benefit
AV node ablation and pacemaker implantation	Patients with severely symptomatic drug refractory AF unsuitable for/declined AF ablation Patients with heart failure and CRT in order to optimise biventricular pacing	May be useful in patients with ischaemia and symptoms related to difficult rate control

Table 4

ICD/CRT treatment options for heart failure with ejection fraction ≤ 35%, adapted from NICE TA134[21]

QRS duration (ms)	NYHA class I	NYHA class II	NYHA class III	NYHA class IV
< 120	ICD if there is a high risk of sudden cardiac death			ICD and CRT not indicated
120-149 (without LBBB)	ICD	ICD	ICD	CRT-P
120-149 (with LBBB)	ICD	CRT-D	CRT-P or CRT-D	CRT-P
≥ 150 (with or without LBBB)	CRT-D	CRT-D	CRT-P or CRT-D	CRT-P

ICD = implantable cardioverter defibrillator; CRT-D = cardiac resynchronisation therapy with ICD; CRT-P = cardiac resynchronisation therapy with pacing

recommendations for cardiac resynchronisation therapy (CRT).

QRS duration and morphology has been demonstrated to identify those who will benefit from CRT with those with QRS >150 ms and left bundle branch block most likely to benefit. However, left ventricular systolic dysfunction and heart failure are also associated with high rates of non-sudden cardiac death. Patients with severe heart failure (NYHA class IV) have a particularly poor prognosis and are therefore less likely to benefit from ICD implantation.

Table 4, above, outlines guidelines for cardiac device implantation but it should also be stressed that optimisation of medical therapy including renin-angiotensin-aldosterone inhibitors, angiotensin-receptor-neprilysin inhibitors and beta-blockers is of paramount importance and confers significant reduction in mortality.[19,21]

Secondary prevention

Patients with sustained ventricular arrhythmias require emergency assessment and secondary care management. In patients with severe LV impairment symptoms of rapid palpitations or syncope should raise strong clinical suspicions of ventricular arrhythmias and urgent specialist assessment is required.

The majority of patients with CAD who experience ventricular arrhythmias will require ICD implantation. A proportion of patients with an ICD will require antiarrhythmic drug therapy or catheter ablation to reduce the frequency of ICD shocks.

Those with sustained monomorphic VT without haemodynamic compromise and preserved LV systolic function may be managed with antiarrhythmic drug therapy or catheter ablation alone without requiring ICD implantation.[22]

Table 5

When to refer patients with arrhythmias

Arrhythmia	When to refer
Atrial fibrillation/flutter	● Symptomatic arrhythmia in whom rhythm control considered ● Symptoms of severe chest pain and/or dyspnoea ● Concomitant LV systolic impairment (new or preexisting) ● Guidance on appropriate antiplatelet combination therapy required ● New onset atrial flutter ● Ongoing arrhythmia six weeks post CABG
Ventricular arrhythmias/ heart failure	● Presyncope, syncope or rapid palpitations with known LV impairment ● Symptoms/signs of heart failure in patient with previous ACS ● New marked ECG abnormalities (e.g. new BBB)
Ventricular ectopy	● Severe symptoms or associated syncope ● High burden on ambulatory monitoring (> 10%) ● Associated LV systolic impairment ● New marked ECG abnormalities (e.g. new BBB)
Bradyarrhythmia	● Symptomatic sinus bradycardia despite reduction/cessation of rate limiting medications ● Second- or third-degree AV block

BRADYARRHYTHMIAS

Bradycardia secondary to advanced atrioventricular (AV) conduction block may occur in the context of STEMI. However, bradycardia in patients with stable CAD is most frequently related to rate limiting drugs such as beta-blockers resulting in sinus bradycardia with or without PR prolongation. In the absence of symptoms no intervention is required. The observation of second- or third-degree AV block requires specialist assessment.

CONCLUSION

Arrhythmias, particularly AF and VT/VF with associated risk of sudden death are common in patients with CAD. Identification of patients with AF is important particularly to institute appropriate anticoagulation for stroke prevention. Further management involving either rate control or rhythm control is determined primarily by patient symptoms as well as the effect of AF on LV systolic function and must incorporate a holistic approach to treat concomitant conditions and lifestyle factors. LVEF should be assessed in all patients with CAD to identify those at risk of sudden cardiac death who may benefit from ICD »

key points

SELECTED BY

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A detailed history is essential in patients with coronary artery disease (CAD) to elucidate red flag symptoms necessitating urgent specialist assessment. Red flags include syncope and presyncope, particularly in patients with concomitant left ventricular systolic dysfunction. Palpitations with severe chest pain and breathlessness also warrant urgent assessment.

Undiagnosed atrial fibrillation (AF) is common in older populations. In patients with stable CAD without an acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI) in the preceding 12 months oral anticoagulation alone should be used. In the context of ACS or recent (preceding 12 months) PCI decisions on combination therapy should be undertaken in collaboration with the interventional cardiology team. Triple therapy for 1-6 months may be indicated, influenced by the specific stents used, coronary anatomy and patient specific bleeding risk. Dual therapy with oral anticoagulation and clopidogrel should then be continued up to 12 months followed by anticoagulation alone.

There is no clear evidence that a rhythm control strategy offers any significant long-term benefits in AF. The appropriate strategy is therefore determined primarily by the symptomatic burden of AF. Rate control is based on slowing AV nodal conduction. As beta-blockers are indicated for many patients with CAD, particularly following an ACS, this should be considered first line. The initial target heart rate should be < 110. Flecainide is commonly prescribed for paroxysmal AF. It is contraindicated in patients with CAD because of an increased risk of sudden death. Catheter ablation should therefore particularly be considered in patients with severe symptoms and/or LV dysfunction. AF occurs in up to 50% of patients post CABG, but is often self-limiting within the first 4-6 weeks.

Premature ventricular complexes are also frequently observed in primary care and are therefore commonly seen in patients with stable CAD. In this context reassurance is usually all that is required. In patients with particularly bothersome symptoms of skipped or extra beats then beta-blockers may be indicated.

Left ventricular ejection fraction (LVEF) ≤35% is a predictor of increased risk of sudden death. All patients with CAD should therefore undergo assessment of LVEF, usually by transthoracic echocardiography. This is particularly important at least 6 weeks following presentation with ST-elevation ACS. Most patients with CAD who experience ventricular arrhythmias will require an ICD.

Bradycardia in patients with stable CAD is most frequently related to rate limiting drugs such as beta-blockers resulting in sinus bradycardia with or without PR prolongation. In the absence of symptoms no intervention is required. The observation of second- or third-degree AV block requires specialist assessment.

implantation for primary prevention.

Evidence in this area is continually evolving. Screening for AF is likely to develop further and trials to identify the optimal anticoagulation strategies in combination with antiplatelet agents are currently ongoing. Risk stratification for sudden death remains challenging and current interest in the use of cardiac MRI and scar assessment may prove advantageous.

Competing interests: None

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