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Review ofAtrial FibrillationEvaluation in Patients with Pacemaker Implantation

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ABSTRACT

Atrial fibrillation (AF) is the commonest sustained cardiac arrhythmia and has shown incremental prevalence and incidence with age. Atrial fibrillation is directly associated with multifold increased risk of stroke, heart failure, myocardial infarction, dementia, and death. The pathophysiology of atrial fibrillation may involve a complex interplay of electrophysiologic factors and changes, which include increased automaticity, rapid electrical firing from focal anatomical sites such as the pulmonary veins, abnormal autonomic ganglionic plexuses discharges, pathological slow electrical conduction of impulses and reentry in the atria. Management of patients with atrial fibrillation thus poses significant challenges. On the other hand, permanent pacemakers are frequently implanted in patients with atrial fibrillation, and even in a general pacemaker population atrial fibrillation can develop frequently and progressively over time.The goal of this article is review the incidence of AF in patients with pacemaker implantation without previously documented AF and to detect high risk groups vulnerable for development of atrial fibrillation

Keywords: Atrial Fibrillation; ECG;Pacemaker Implantation

INTRODUCTION

Atrial fibrillation (AF) is supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and therefore ineffective atrial contraction. Electrocardiographic characteristics of AF include irregular R-R intervals (when atrioventricular conduction is not impaired), absence of distinct repeating P waves, andirregular atrial activations **(1).**

Currently used terms of AF involves: symptomatic or asymptomatic AF that is documented by surface ECG. The minimum duration of an ECG tracing of AF required establishing the diagnosis of clinical AF is at least 30 seconds, or entire 12-lead ECG. AHRE (Atrial High rate Episodes), subclinical AF that Refers to individuals without symptoms attributable to AF in who clinical AF is not previously detected **(2).**

Screening for atrial fibrillation

Multiple factors as increasing AF prevalence, previously unknown AF detection in about 10% of all ischemic strokes, high prevalence of asymptomatic AF, potential to prevent AF-related strokes with appropriate treatment and increasing availability of AF detection tools) had encouraged international initiatives to implement screening for AF

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in clinical practice. Asymptomatic clinical AF has been independently associated with increased risk of stroke and mortality compared with symptomatic AF **(3)**.

Advances in wearable technology were likely yield inexpensive and practical options as a Screening tool for AF detection and AF burden assessment in the near future. Mobile health technologies are rapidly developing for AF detection and other purposes (>100 000 mHealth apps and >_400 wearable activity monitors are currently available) **(4).**

Caution is needed in their clinical use, as many are not clinically validated. Several studies evaluated AF detection using smartwatches, thus opening new perspectives for AF detection targeting specific populations at risk. Machine learning and artificial intelligence may be capable of identifying individuals with previous AF episodes from a sinus rhythm ECG recording, which would be a major technological breakthrough in AF detection **(5)**.

The Huawei Heart study included 187,912 individuals (mean age 35 years, 86.7% male), of whom 0.23% received a 'suspected AF' notification. Of those effectively followed up, 87.0% were confirmed as having AF. Of those with identified AF, 95.1% entered an integrated AF management program using a mobile AF App **(6).**When AF is detected by a screening tool, including mobile or wearable devices, a single-lead ECG tracing of >_30 s or 12-lead ECG showing AF analyzed by a physician with expertise in ECG rhythm interpretation is necessary to establish a definitive diagnosis of AF (devices capable of ECG recording enable direct analysis of the device-provided tracings). A confirmatory ECG diagnosis has to be obtained using additional ECG recording **(7).**

Mechanism and pathophysiology:

The exact mechanisms that lead to the onset and persistence of AF have not completely explained. But few mechanisms are available:The focal mechanism theory with fibrillatory conduction" stands on the concept that AF is initiated by the rapid firing of a single or multiple ectopic foci."The single circuit re-entry theory of AF" assumes the presence of a single dominant re-entry circuit "mother rotor "with a break-up of emanating waves in the atrial tissue of variable electrical properties."The multiple wavelet theory of AF" assumes the presence of multiple reentry circuits with randomly propagating wave fronts that must find receptive tissue in order to persist **(8).**

Atrial and Electrophysiological Remodeling:

Arrhythmogenic remodeling refers to changes in function or structure that enhances arrhythmias. Remodeling is the corner stone to most acquired forms of AF.AF itself can cause progressive changes in atrial electrophysiology such as substantial refractory period shortening, which further facilitate occurrence of the arrhythmia , Electrical remodeling and its reversal occur in humans in patients undergoing electrical cardioversion of persistent AF. It shortened right atrial refractory periods lengthened again within four weeks after cardioversion**(9).**

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Increased LV stiffness augments LV filling pressure so elevated LV filling pressure raises the LA wall stress which leads to LA remodeling. LA remodeling, which is characterized by alterations in atrial conduction, interstitial fibrosis, and dilatation, may then lead to AF so early stage of diastolic dysfunction could start with a decreased DWS even in patients with normal LV diastolic function**(10).**

Stratification of Stroke Risk in Atrial Fibrillation

Atrial fibrillation(AF) is estimated to affect 33 million people worldwide, this number is likely to be an underestimate since many people do not know that they have AF until they develop symptoms or present with an ischemic thromboembolic stroke or systemic thromboembolism. A rising prevalence is related to an increase in elderly population and the increased prevalence of risk factors, such as diabetes, hypertension, obesity, and alcohol consumption**(11).**

AF is one of the ten potentially modifiable risk factors associated with acute stroke, In Egypt , this arrhythmia may be responsible for >70,000ischemic strokes each year representing 10%–12% of all ischemic strokes. The risk of stroke in patients with AF has been estimated at between 1% and 20% annually. So risk stratification for the risk of stroke in AF and early initiation of therapy that aims to reduce the risk of AF-associated stroke is a crucial component in the management of this arrhythmia**(12)**.

Management of AF

The management of atrial fibrillation (AF) is focused on preventing circulatory instability and to prevent stroke and other ischemic events. The most important factors determining AF treatment are duration and evidence of hemodynamics instability. Cardioversion is indicated with new onset AF less than 48 hours and with hemodynamics instability. If rate and rhythm control cannot be maintained by medication or cardioversion, it may be necessary to perform electrophysiological studies with ablation of abnormal electrical pathways(**13).**

a) Anticoagulation:

Most patients with AF are at increased risk of stroke. The possible exceptions are those with lone AF (LAF), characterized by absence of clinical or echocardiographic findings of other cardiovascular disease (including hypertension), related pulmonary disease, or cardiac abnormalities such as enlargement of the left atrium, and age under 60 years **(14).**The CHA_2DS_2VASC score is a well-validated simple clinical prediction rule for determining the risk of stroke; it assigns points maximum 9 points depending on the presence or absence of co-morbidities. The following treatment strategyis based on the CHA_2DS_2VASC score **(15)**.

- **Acute anticoagulation:**

If anticoagulation is required urgently (e.g., for cardioversion), heparin or similar drugs achieve rapid level of protection. In the initial stages after an embolic stroke, anticoagulation may be risky, as the damage of the brain is relatively prone to bleeding (hemorrhagic transformation) **(16).**

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- **Chronic anticoagulation:**

Warfarin treatment requires frequent monitoring to INR usually every month. In AF, the usual target INR is between 2.0 and 3.0. A high INR may increase bleeding risk, while a low INR would precipitate stroke **(17)**.

Novel oral anticoagulants:

The Novel oral anticoagulants (NOACs) for stroke prevention in AF are oral direct thrombin inhibitors (e.g. dabigatran) and oral direct factor Xa inhibitors (e.g. rivaroxaban, apixaban, etc.)**(18).**

b) Left atrial appendage occlusion:

Left atrial appendage occlusion is an alternative to anticoagulants. During cardiac catheterization, a device (such as the Watchmandevice) consisting of an expandable nitinolframe is introduced into the left atrialappendage, the source of blood clots in more than 90% of cases. This May considered in patients with high risk for stoke and at the same time has contraindication from oral anticoagulation. Left atrial appendage surgical removal may be considered in patient undergoing open heart surgery being acritical site for thrombus formation **(19).**

c) Rate control versus rhythm control:

There are two ways to control AF symptoms using drugs: rate control and rhythm control. Rate control aims to reduce the heart rate usually from 60 to 100 bpm, without trying to convert to a regular rhythm. Rhythm control aims to do cardioversion to regain sinus rhythm and maintain it by drugs. rhythm control is mainly done in newly diagnosed AF, while rate control is more important in the chronic phase **(20).**

Cardioversionis a non-invasive conversion of an irregular heartbeat to normal heartbeat using electrical or chemical means. Electrical cardioversion: through the application of a DC electrical shock. Chemical cardioversion: is performed with drugs such as amiodarone, dronedarone, procainamide, propafenone or flecainide. The main risk of cardioversion is systemic embolization of a thrombus from the previously fibrillating left atrium. Cardioversion should not be performed without adequate anticoagulation in patients with more than 48 hours or unknown duration of AF **(21).**

Rate control is achieved with medications that work through increasing the degree of AV node block.This can be done with Beta blockers (preferably the "cardio selective" beta blockers such as metoprolol, atenolol, bisoprolol). Calcium channel blockers (i.e. diltiazemor verapamil). Cardiac glycosides (i.e. digoxin)**(22).**

Indications for permanent cardiac pacing:

The decision to implant a pacemaker usually is based on symptoms of a bradyarrhythmia or tachyarrhythmia in the setting of heart disease. Symptomatic bradycardia is the most common indication. It has been defined as a “documented bradyarrhythmia that is directly responsible for the development of the clinical manifestations of frank syncope or near syncope, transient dizziness or light-

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headedness, and confusional states resulting from cerebral hypoperfusion and attributable to low heart rates**.**Other symptoms that may result from severe bradycardia include fatigue, reduced exercise capacity, and frank congestive heart failure. Physiologic sinus bradycardia, which can occur in highly trained athletes, must be excluded and should not be confused with pathologic bradyarrhythmias**(23).**

Table (1):Recommendations for pacing in sinus node dysfunction (24):

Recommendations	Class	Level
In patients with SND and a DDD pacemaker, minimization of unnecessary ventricular pacing through programming is recommended.	I	A
Pacing is indicated in SND when symptoms can clearly be attributed to bradyarrhythmias.	I	B
Pacing is indicated in symptomatic patients with the bradycardiatachycardia form of SND in order to correct bradyarrhythmias and enable pharmacological treatment, unless ablation of the tachyarrhythmia is preferred	I	B
In patients who present chronotropic incompetence and have clear symptoms during exercise, DDD with rate-responsive pacing should be considered.	IIa	B
AF ablation should be considered as a strategy to avoid pacemaker implantation in patients with AF-related bradycardia or symptomatic preautomaticity pauses, after AF conversion, taking into account the clinical situation.	IIa	C
In patients with the bradycardia tachycardia variant of SND, programming of atrial ATP may be considered.	IIb	B
In patients with syncope, cardiac pacing may be considered to reduce recurrent syncope when asymptomatic pause(s) >6 s due to sinus arrest is documented.	IIb	C
Pacing may be considered in SND when symptoms are likely to be due to bradyarrhythmias, when the evidence is not conclusive.	IIb	C
Pacing is not recommended in patients with bradyarrhythmias related to SND that are asymptomatic or due to transient causes that can be corrected and prevented.	III	C

Table (2): Recommendations for pacing for atrioventricular block (25)

Recommendations	Class	Level
Pacing is indicated in patients in SR with permanent or paroxysmal third- or second-degree type 2, infranodal 2:1, or high-degree AVB, irrespective of symptoms.	I	C
Pacing is indicated in patients with atrial arrhythmia (mainly AF) and permanent or paroxysmal third- or high-degree AVB irrespective of symptoms.	I	C
In patients with permanent AF in need of a pacemaker, ventricular pacing with rate response function is recommended.	I	C
Pacing should be considered in patients with second-degree type 1 AVB that causes symptoms or is found to be located at intra- or infra-His levels at EPS.	IIa	C
In patients with AVB, DDD should be preferred over single-chamber ventricular pacing to avoid pacemaker syndrome and to improve quality of life.	IIa	A
Permanent pacemaker implantation should be considered for patients with persistent	IIa	C

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symptoms similar to those of pacemaker syndrome and clearly attributable to first-degree AVB (PR >0.3 s).		
Pacing is not recommended in patients with AVB due to transient causes that can be corrected and prevented.	III	C

Table (3):Recommendations for pacing in patients with bundle branch block (26):

Recommendations	Class	Level
In patients with unexplained syncope and bifascicular block, a pacemaker is indicated in the presence of either a baseline HV of >_70 ms, second- or third-degree intra- or infra-Hisian block during incremental atrial pacing, or an abnormal response to pharmacological challenge.	I	B
Pacing is indicated in patients with alternating BBB with or without symptoms.	I	C
Pacing may be considered in selected patients with unexplained syncope and bifascicular block without EPS (elderly, frail patients, high-risk and/ or recurrent syncope).	IIb	B
Pacing is not recommended for asymptomatic BBB or bifascicular block.	III	B

Table (4):Recommendations for pacing for reflex syncope (27):

Recommendations	Class	Level
Dual-chamber cardiac pacing is indicated to reduce recurrent syncope in patients aged >40 years, with severe, unpredictable, recurrent syncope who have:spontaneous documented symptomatic asystolic pause(s) >3 s or asymptomatic pause(s) >6 s due to sinus arrest or AVB; orcardioinhibitory carotid sinus syndrome; orasystolic syncope during tilt testing.	I	A
Dual-chamber cardiac pacing may be considered to reduce syncope recurrences in patients with the clinical features of adenosine-sensitive syncope.	IIb	B
Cardiac pacing is not indicated in the absence of a documented cardioinhibitory reflex.	III	B

Table (5):Recommendations for cardiac pacing after transcatheter aortic valve implantation (28):

Recommendations	Class	Level
Permanent pacing is recommended in patients with complete or high-degree AVB that persists for 24 - 48 h after TAVI.	I	B
Permanent pacing is recommended in patients with new-onset alternating BBB after TAVI.	I	C
Earlyc permanent pacing should be considered in patients with pre-existing RBBB who develop any further conduction disturbance during or after TAVI.	IIa	B
Ambulatory ECG monitoringe or EPSf should be considered for patients with new LBBB with QRS >150 ms or PR >240 ms with no further prolongation during the >48 h after TAVI.	IIa	C

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Ambulatory ECG monitoringe or EPSf may be considered for patients with a pre-existing conduction abnormality who develop prolongation of QRS or PR >20 ms.g	IIb	C
Prophylactic permanent pacemaker implantation is not indicated before TAVI in patients with RBBB and no indication for permanent pacing.	III	C

Table (6):Recommendations for cardiac pacing in patients with congenital heart disease (29):

Recommendations	Class	Level
In patients with congenital complete or highdegree AVB, pacing is recommended if one of the following risk factors is present: symptoms; pauses >3 the cycle length of the ventricular escape rhythm;broad QRS escape rhythm; prolonged QT interval; complex ventricular ectopy; mean daytime heart rate <50 b.p.m.	I	C
In patients with congenital complete or high degree AVB, permanent pacing may be considered even if no risk factors are present.	IIb	C
In patients with persistent post-operative bifascicular block associated with transient complete AVB, permanent pacing may be considered.	IIb	C
In patients with complex CHD and asymptomatic bradycardia (awake resting heart rate <40 b.p.m. or pauses >3 s), permanent pacing may be considered on an individual basis.	IIb	C

Pacing Modes:

In selecting the ideal pacing mode, the patient's overall physical condition, associated medical problems, exercise capacity, and chronotropic response to exercise must be considered along with the underlying rhythm disturbance **(30).**

Single chamber pacing: Early pacemakers were designed to sense and pace in a single chamber. Ventricular pacing can prevent ventricular bradyarrhythmias or asystole of any etiology. Atrial pacing can be used in patients with isolated sinus node dysfunction or sick sinus syndrome (SSS) and intact AV conduction **(31).**

VVI or VVIR pacing:Ventricular demand pacing (ventricle paced, ventricle sensed, and pacemaker inhibited in response to a sensed beat) remains the most commonly used pacing mode. Advantages of ventricular demand pacing include the requirement for only a single lead and the ability to protect the patient from dangerous bradycardias of any etiology. If sinus node function is intact, dual chamber (DDD) pacing preserves AV synchrony and maintains the patients natural heart rate response to activity. This approach is optimal and should use whenever possible **(32).**

AAI or AAIR pacing: Atrial demand pacing (atrium paced, atrium sensed, and pacemaker inhibited in response to sensed atrial beat) is appropriate for patients with sinus node dysfunction who have intact AV nodal function. Pacemaker upgrade can be technically more difficult than original placement of a dual chamber pacemaker, and the second procedure obviously entails additional cost and patient risk. Assessment prior to use of an AAI system should include incremental atrial pacing at the time of pacemaker implant. Although criteria vary among institutions and implanting clinicians, the adult patient should be capable of 1:1 AV nodal conduction

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to rates of 120 to 140 beats/min. Patients who are chronotropically incompetent can be programmed in the AAIR mode **(33).**

Acute complications of pacemaker implantation:

- **Pneumothorax**: may be asymptomatic and detected only by chest radiograph. A small pneumothorax can resolve without intervention. However, the presence of severe symptoms, a pneumothorax >10%, or an expanding or persistent pneumothorax often necessitates placement of a chest tube **(34).**
- **Cardiac and central venous perforation:** may leadto pericardial effusion and cardiac tamponade. A chest radiograph may reveal an enlarged cardiac silhouette or an extracardiac lead tip. A change in the paced ventricular morphology, particularly a right bundle branch pattern, may indicate ventricular lead migration. The hemodynamically unstable patient with tamponade will require urgent pericardiocentesis and drainage of the effusion **(35**).
- **Pacemaker pocket Haematoma:** This is one of the most common complications of pacemaker implantation and is often due to a small vessel venous bleeding inside the pacemaker pocket. Bleeding may also arise from arterial vessels or retrograde flow of venous blood along the pacemaker leads into the pocket. Small haematomas may be managed conservatively while larger ones need surgical drainage **(36).**
- **Diaphragmatic stimulation.** Stimulation of the left diaphragm may occur with a pacing lead at the RV apex, particularly at high pacing outputs. The possibility of cardiac perforation should be considered. Stimulation of the right diaphragm may occur due to stimulation of right phrenic nerve by a displaced atrial lead. Reduction in pacemaker output voltage or lead repositioning may be necessary **(35**).
- **Local muscular stimulation.** This may occur with a unipolar pacemaker configuration, particularly if the pulse generator is positioned upside down within the pocket (whereby a node is directed in contact with the pectoralis muscle).A pacing lead fracture may result in leakage of current into the surrounding tissue, resulting into local muscle stimulation **(34).**
- **Pacemaker malfunction.** The pulse generator may be defective or may have been damaged at the time of implantation (e.g., by electrocautery or direct current [DC] defibrillation). Improper fixation of the terminal pins of the pacing leads into the pulse generator (e.g., loose-Set Screws) may result in complete or intermittent pacemaker malfunction with high impedance measurements **(36).**
- **Lead dislodgement:** usually occurs within two days following implantation of a permanent pacer and may be seen on chest radiography (if the lead is floating freely in the ventricle, malignant arrhythmias may develop)**.** Pacing leads may become dislodged soon after implantation before the lead has a chance to become more fixed in place through clotting and fibrosis. Lead dislodgement may be suspected by noncapture, High lead impedance, undersensing, or oversensing on telemetry or ECG and may be confirmed by chest radiography or formal pacemaker testing **(37).**

Hence, it is not surprising that a considerable amount of interest exists in exploring pacemakers' role in the therapeutic and preventive aspects of atrial fibrillation

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CONCLUSION

Management of patients with atrial fibrillation thus poses significant challenges. Pacemakers play a potentially important role in the non-pharmacological management of atrial fibrillation (AF).

Antiarrhythmic drugs and nonpharmacological ablation methods have failed to show satisfactory long-term atrial fibrillation-free survival, and as such they may not be suitable for many elderly patients.

Pacemakers may prevent atrial fibrillation by mechanisms such as correction of bradycardia-induced dispersion of atrial repolarization, suppression of atrial fibrillation triggers, change in atrial activation patterns, and prevention of electromechanically related atrial stretch.

No Conflict of interest.

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