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A Pharmacist's Role in the Prevention and Management of Perioperative Atrial Fibrillation and Flutter

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Goal:

This home-study CPE has been developed to educate pharmacists about recently published guidelines for perioperative atrial fibrillation and flutter management and prevention, and discuss the role a pharmacist can have in the care of these patients.

At the conclusion of this lesson, successful participants should be able to:

Objectives for Pharmacists:

1. Summarize the complications of post-operative atrial fibrillation (POAF)
2. Define POAF in terms of electrocardiogram (EKG) findings and clinical signs and symptoms
3. List rate control agents and their mechanism of action and monitoring parameters
4. List rhythm control agents and their limitations
5. Identify potential candidates for rhythm control of POAF
6. Justify the preventative strategies recommended by the POAF guidelines
7. Formulate an appropriate treatment plan for new-onset POAF
8. Discuss management of anticoagulation for patients with preexisting atrial fibrillation

Objectives for Technicians:

1. Understand some of the complications of post operative Atrial Fibrillation
2. List rate control agents and what they are used for
3. List rhythm control agends and what they are used for
4. Learn preventative strategies recommended by POAF guidelines

Introduction

Although thoracic surgeries save the lives of thousands of people every year, they are also associated with an increased risk of cardiac arrhythmias, such as atrial fibrillation (Afib). High risk procedures, such as lung transplantations and esophagectomies have been found to have greater than a 15% incidence of Afib following surgery.[1] Atrial fibrillation/flutter is the most common sustained arrhythmia associated with thoracic surgery.[1] This adverse outcome is potentially preventable, and pharmacological therapy can play key role in the care plan of these patients.

Afib is an irregular heart rhythm caused by chaotic contracting of the atria of the heart. This lack of synchronized beating can result in poor perfusion of the body due to insufficient blood flow and increases the risk of emboli formation due to venous stasis. Common clinical signs and symptoms of Afib may include hypotension, dizziness, decreased urinary output, and fatigue.[1] On an electrocardiogram (EKG), Afib is characterized by no discernible P waves and an irregularly irregular rhythm.

Postoperative/perioperative atrial fibrillation/flutter (POAF) is Afib that occurs specifically during the postoperative period and can be due to several factors. The risk factors for the development of POAF are the same as those for the development of Afib in nonsurgical patients.[1] Oftentimes, the stress of the surgery alone can be a risk factor for experiencing an arrhythmia.[1] The onset of POAF most commonly occurs between two and four days following surgery, and up to 98% of cases resolve after six weeks.[1] This adverse outcome is a concern, however, because it can lead to hemodynamic instability, thrombus formation and even heart failure due to sustained tachycardia. Risk of POAF varies with the intensity of the cardiothoracic surgery, higher risk coinciding with more invasive and intense procedures. Other risk factors include older age, hypertension, obesity, and smoking.[1] See Table 1 for a more complete list of modifiable and non-modifiable risk factors. The most serious adverse event of POAF is formation of thromboemboli, which can lead to stroke and/or acute limb ischemia.

Post-operative Afib is associated with an increased length of stay in the hospital, increased morbidity and mortality, and increased healthcare costs.[1] Some studies have shown POAF to result in increased length of stay by an average of three days, and increased costs of care by up to 30%.[2] It is important for the pharmacist to be informed of the current best practices in the management and prevention of POAF to lead to better treatment outcomes in this patient population.

Guidelines

Previously, management and prevention of POAF has been directed by the Society of Thoracic

Surgeons (STS) guidelines published in in the Journal of Thoracic and Cardiovascular Surgery in 2011.[3] In September of 2014 the American Association for Thoracic Surgery (AATS) published guidelines for POAF, titled "2014 AATS guidelines for the prevention and management of perioperative atrial fibrillation and flutter for thoracic surgical procedures" in the Journal of Thoracic and Cardiovascular Surgery.[1] These guidelines discuss new information and advances in POAF therapy and provide updated recommendations on the management of this condition.

The clinical guidelines start by providing definitions for POAF as both an electro-physiologic and clinical diagnosis. They recommend that the diagnosis of POAF include clinically significant POAF that requires treatment in addition to an EKG reading of Afib lasting longer than 30 seconds.[1] Patients at risk for arrhythmias or those who have substantial risk factors for stroke should be continuously monitored via EKG telemetry during the postoperative period to detect any changes in rhythm.

The guidelines go on to recommend and review various strategies for preventing POAF. Next, for patients in whom new-onset POAF occurs, potential treatment options are identified. The specifics of these recommendations are discussed in the following sections and are the bulk of these clinical guidelines. Finally, recommendations for patients with preexisting Afib are provided, particularly with regards to anticoagulation management.

Prevention of Postoperative Atrial Fibrillation

Postoperative Afib is a potentially serious complication of thoracic surgery and can be a preventable incident. Recent evidence indicates that prevention strategies previously reserved for high risk patients may in fact be effective in all thoracic surgical patients. The strongest preventative recommendation provided by the 2014 AATS guidelines is that all patients taking β-blockers before surgery should continue them in the postoperative period (class I recommendation, indicating that the benefit outweighs the risk).[1] This recommendation is resultant of several large meta-analyses and randomized studies, mostly from cardiac surgery literature, that have shown withdrawal of β-blockers prior to surgery increases the risk of developing POAF.[1] It is thought that elevated levels of norepinephrine in patients taking β-blockers preoperatively with an interruption in therapy is associated with this higher risk.[4] This recommendation is in agreement with the 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft (CABG) Surgery which also suggest that beta-blockers be used both pre and post-operatively.[5] A second POAF prevention recommendation for all thoracic surgery patients, level class IIb (benefit ≥ risk), is to replenish serum magnesium stores when levels are depleted with intravenous magnesium supplementation.[1] Finally, the guidelines classify the use of digoxin as a class III recommendation, advising against its use for preventing POAF.[1] This is based off of current literature showing that digoxin has been ineffective in preventing perioperative Afib.[6] This is supported by the Guidelines for CABG Surgery, which state that both digoxin and nondihydropyridine calcium channel blockers (non-DHP CCBs) are not indicated for prophylaxis of POAF.[5] It is important for the pharmacist to recognize these pharmacological recommendations made by AATS so that they can ensure the presence of evidence-based therapy in preoperative patients to minimize risk.

For patients with an intermediate to high risk for POAF additional strategies are offered. The guidelines suggest that diltiazem can be considered as a prophylactic agent in patients who are not taking β-blockers preoperatively, as a class IIa recommendation (benefit outweighs the risk).[1] Diltiazem generally does not have the same blood pressure lowering effects that β-blockers can have, and may be a good alternative for patients in whom postoperative hypotension is a concern. Its ability to decrease the risk of POAF is thought to be related to its ability to decrease pulmonary vascular resistance.[7] Other pharmacological interventions discussed in the guidelines for these higher risk patients include the use of intravenous amiodarone postoperatively and initiation of atorvastatin in statin-naïve patients for the prevention of POAF.[1] The practice of using amiodarone postoperatively as prophylaxis is frequently seen in cardiovascular surgeries. This is largely due to the recommendations provided by the Guidelines for CABG Surgery, which also suggest that amiodarone can be used to decrease the risk of POAF.[2] AATS specifically recommends this practice for pulmonary resection and esophagectomy procedures in this publication. The recommendation for initiation of atorvastatin is derived from the analysis of several studies investigating this indication. It is thought that statins down-regulate the renin angiotensin system, and that

it is through this mechanism that this class reduces risk of Afib.[8] Other novel prophylactic strategies continue to be studied for additional options of POAF prevention in these patients.

Management Strategies for New-onset POAF

For patients in whom POAF occurs, possible triggering causes should be carefully considered. Although the irritation from the thoracic surgery itself is often enough to explain new-onset POAF, other factors should be considered so that they can be reduced or removed if present. Examples of this include bleeding, pulmonary embolism, airway compromise, and infection. In addition the guidelines recommend that catecholaminergic inotropic agents, such as dobutamine, be reduced or stopped when hemodynamics allow. Careful management of fluids and electrolytes is also advised in patients with new-onset POAF, as an imbalance in these can be a trigger. These strategies are all class I recommendations found in the 2014 guidelines, again indicating that the benefit outweighs the risk.[1] Once possible triggers of Afib are assessed and removed where possible, treatment of the arrhythmia should be addressed. There are two approaches that can be considered for the treatment of Afib: rate control or rhythm control. The 2014 AATS guidelines recommend that rate control therapy be used first-line for stable patients with POAF.[1] This recommendation is based largely off of a landmark study named the AFFRIM trial that was published in 2002 in the New England Journal of Medicine. This study showed that rate control was as effective as rhythm control for the primary endpoints of death and incidence of ischemic stroke, with fewer adverse drug events (ADEs) occurring in the rate control group.[9] It is important to note, however, that regardless of which treatment method is used anticoagulation for patients who have been having episodes of Afib lasting longer than 48 hours should be strongly considered. The guidelines recommend using the CHA2DS2-VASc scoring system to determine stroke risk in these patients. This scoring system is shown in Figure 1. Pharmacists should be aware of the different treatment options and their clinical pearls, since many of the medications used in these approaches have several side effects and monitoring parameters. The following sections discuss the two treatment approaches, emphasizing the medications that fall under each category.

Rate Control Recommendations

The 2014 AATS POAF guidelines recommend that rate control therapy be initiated as the first-line treatment option in hemodynamically stable patients in whom POAF occurs. The following agents are endorsed by the guidelines as being effective for rate control. Rate control in POAF can be achieved using intravenous (IV) or oral agents. IV β-blockers and non-DHP CCBs, such as diltiazem and verapamil, are commonly used since they can often achieve rate control faster than other agents. This section discusses the mechanisms of action of the agents, as well as common side effects, dosing recommendations, and contraindications/limitations. Important monitoring parameters for these medications include EKG telemetry monitoring, vital signs including blood pressure and heart rate, electrolytes, and other labs such as serum creatinine (SCr) and complete blood count (CBC). A summary of these medications can be found in Table 2.

β-blockers:

β-blockers are Vaughan Williams class II agents. Classification of the Vaughn Williams agents is shown in Figure 2. These agents block the response to β-adrenergic stimulation thereby decreasing heart rate. Metoprolol is a commonly used β-blocker in Afib that is β-1 selective and as a result mainly affects only cardiac tissue. IV dosing of metoprolol tartrate (Lopressor) is 2.5-5.0 mg IV bolus over 2 min for a maximum of three doses.[10] Esmolol (Brevibloc) is a nonselective β-blocker with a quick onset and shorter duration of action compared to metoprolol. Esmolol is dosed intravenously at 0.5 mg/kg IV bolus over 1 min, then 0.05-0.3 mg/kg/min IV continuous infusion.[11] Both medications reduce ventricular response in patients with Afib within 5 minutes of administration. Significant limitations and known side effects of β-blockers include bradycardia, hypotension, bronchospasm due to β-2 blocking activity, and avoidance of use during heart failure exacerbation. Patients with systolic heart failure and/or CAD have a compelling indication for β-blocker therapy including the use of carvedilol, metoprolol succinate, and bisoprolol as these have favorable mortality data.

Non-DHP CCBs:

Diltiazem (Cardizem) is a non-DHP CCB and class IV Vaughan Williams agent. IV diltiazem administered

as a bolus and continuous infusion can control ventricular response in 70-90% of patients with recent-onset Afib. The onset of action of diltiazem is 2-7 min. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) trial found oral diltiazem efficacious in controlling rest and exercise heart rate in approximately 60% of patients.[9] Recommended IV dosing of diltiazem is 0.25 mg/kg IV loading dose over 2 min, then 5-15 mg/hour IV continuous infusion.[12] A second non-DHP CCB used for rate control is verapamil (Calan). The recommended IV dosing for verapamil is 0.075 to 0.15 mg/kg (~ 5 to 10 mg for a 70-kg patient) administered as a bolus over 2 minutes; may give an additional 10 mg after 30 minutes if no response, then 0.005 mg/kg/minute as a continuous infusion.[13] Common side effects of the non-DHP CCBs include hypotension, bradycardia, and constipation. Limitations of non-DHP CCBs include use during heart failure exacerbations as this class of medication can worsen heart failure.

Digoxin (Lanoxin):

Digoxin's mechanism of action is inhibition of sodium potassium ATPase. This enzyme, commonly known as the sodium-potassium pump, is responsible for transporting sodium ions out and potassium ions into cells. Inhibition of this pump causes increased intracellular sodium concentrations which leads to increased intracellular calcium concentrations. Digoxin increases the force and velocity of myocardial systolic contraction but also slows heart rate. Digoxin has positive inotropic and negative chronotropic effects. This is significant since it does not cause hypotension which is a limitation to many of the other Afib medications. The loading dose for IV digoxin is 0.5 to 0.75 mg bolus followed by 0.25 mg IV every 2-6 hours to a maximum dose of 1.5 mg over 24 hours. This dosing has an onset of action of 30 minutes to 2 hours.[14] The maintenance dose is based on lean body weight, renal function, age, and concomitant medications. Digoxin is effective for rate control at rest but requires concomitant use with either a β-blocker or non-DHP CCB to achieve exercise rate control. Therefore, digoxin should only be used as combination therapy rather than monotherapy. Also, digoxin should not be used for prophylaxis against Afib. It is important to monitor electrolytes in patients taking digoxin since digoxin toxicity is potentiated by hypokalemia, hypomagnesemia, or hypercalcemia. Symptoms of digoxin toxicity include nausea and vomiting with possible anorexia, dizziness, weakness, mental disturbances (such as confusion or hallucinations) and blurred or yellow vision. In addition, concomitant use of digoxin with amiodarone, dronedarone, or verapamil can worsen symptoms of toxicity as these medications can increase serum digoxin levels. The mechanism of interaction is likely due to inhibition of P-glycoprotein (P-gp) resulting in increased bioavailability of digoxin. Patients that present with symptoms of toxicity should have their serum drug concentration checked as this medication has a narrow therapeutic window. The goal therapeutic range of digoxin for the indication of Afib is 0.8 to 2.0 ng/mL.[14] There is no added treatment benefit with serum concentrations above 2.0 ng/mL; however, risk for toxicity increases substantially beyond that point. Furthermore, it is possible for patients to fall in the therapeutic range but still present with symptoms of toxicity. Digoxin serum concentrations should be drawn at least 6 hours after the last dose if given IV or at least 8 hours after the last dose if given orally. Levels should not be drawn within 2 hours of exercise because of increased skeletal muscle uptake of digoxin. Digoxin accumulates in acute kidney injury and chronic kidney disease so it is justified to check serum drug concentration after one week of therapy. Patients with recurrent hospitalization for HF exacerbation, hypotension, or who are sedentary/bed-bound have compelling indications for treatment with digoxin.

Rhythm Control Recommendations

Rhythm control therapy can be considered in patients who have symptomatic POAF but are hemodynamically stable. Restoration of normal sinus rhythm (NSR) through pharmacologic cardioversion will generally eliminate symptoms of POAF and may lead to better overall patient satisfaction. This method of POAF treatment may also be considered in patients where rate control agents are ineffective or intolerable. This section reviews antiarrhythmic agents, their mechanisms of action, potential ADRs, dosing recommendations, and contraindications/limitations. Specific agent choice depends on several factors, including presence of underlying structural heart disease, renal function, potential toxicities, and provider experience. These medications require careful monitoring to minimize ADRs and toxicities, which can lead to additional arrhythmias, extracardiac toxicities, and increased length

of hospital stay. Important monitoring parameters for these medications include EKG telemetry monitoring with QTc interval measurement, vital signs including blood pressure and heart rate, electrolytes, and other labs such as serum creatinine (SCr) and complete blood count (CBC). Additionally, signs and symptoms of toxicities should be assessed frequently. A summary of these medications can be found in Table 3.

Amiodarone (Nexterone - IV, Pacerone - Oral):
Amiodarone prolongs the action potential by inhibiting the inward potassium current and is therefore a Vaughan Williams class III agent. It is also a noncompetitive α- and β-adrenergic inhibitor. Amiodarone can be used for cardioversion from Afib to sinus rhythm or for maintenance of sinus rhythm. Cardioversion dosing consists of 150 mg IV over 10 minutes, then 1 mg/minute for 6 hours, then 0.5 mg/minute for 18 hours or change to oral maintenance dosing of 100-400 mg daily.[15] The 2014 AATS Guidelines for POAF recommend prophylactic amiodarone dosing of 300 mg IV bolus, then 600 mg orally twice daily for 3-5 days. The IV bolus and first oral dose of 600 mg are to be given together immediately after surgery. A variety of regimens for preventing POAF have been used in clinical trials but the AATS guideline recommendation is based on the dosing regimen utilized in a randomized, double-blinded, placebo controlled trial in patients undergoing surgery for lung cancer.[16] Amiodarone has an unpredictable time course of effect so loading doses should only be administered in a hospital setting. Acute adverse effects of amiodarone include bradycardia, QT interval prolongation, arrhythmias, and hypotension. Heart rate and blood pressure should be monitored regularly. Baseline QT interval should be measured with additional follow up measurements throughout the course of treatment along with electrolytes. More serious adverse effects are seen in long-term amiodarone use like pulmonary toxicity, hepatic disorders, hyper or hypothyroidism, neurologic disorders including fatigue and peripheral neuropathy, blue skin discoloration, and visual disturbances. Additional monitoring includes baseline chest x-ray, pulmonary function tests, liver function test, and thyroid function. These should also be monitored periodically during therapy along with routine eye exams. Amiodarone should be used cautiously in patients on oral anticoagulation as it inhibits the metabolism of warfarin and inhibits the elimination of the new oral anticoagulants. There is no well-established relationship between plasma concentration and effectiveness so serum drug concentration monitoring is not warranted.

Flecainide (Tambocor):
Flecainide is a Vaughan Williams class IC antiarrythmic agent. It slows conduction in cardiac tissue by altering transport of ions across cell membranes. Flecainide is only manufactured as an oral dosage form in the United States. Dosing for conversion to sinus rhythm is 200-300 mg as a single oral dose and sinus rhythm is maintained by 50-150 mg orally every 12 hours.[17] Adverse effects include dizziness and visual abnormalities such as blurred vision and difficulty focusing. Flecainide is less tolerated in patients with structural heart disease as these patients may experience ventricular proarrhythmias. Flecainide is contraindicated in patients with heart failure with reduced ejection fraction (HFrEF), due to potent negative inotropic activity, and in coronary artery disease (CAD)/structural heart disease. Additionally, class IC antiarrythymic medications are listed in the Beers Criteria so they are not first-line treatment for Afib in the geriatric population.[18] Select patients are eligible for the "pill-in-the-pocket" administration approach for cardioversion. Eligible candidates for this approach have infrequent paroxysmal atrial fibrillation with no other cardiac symptoms and have no structural heart disease. These patients take either flecainide or propafenone on an as-needed instead of scheduled basis. This therapy demonstrated a significant reduction in emergency room visits and hospitalizations in a clinical trial.[19]

Dofetilide (Tikosyn):
Dofetilide is a Vaughan Williams class III antiarrythmic agent. The mechanism of action is to create a prolonged action potential as a result of delayed repolarization by blocking IKr channels. Dofetilide may not be an ideal choice for cardioversion to sinus rhythm in the postoperative setting as it may take 2-3 days to cardiovert and would therefore require anticoagulation therapy for stroke prevention. Maintenance dosing for dofetilide depends on renal function as follows: 0.5 mg orally every 12 hours for CrCl >60 mL/min, 0.25 mg orally every 12 hours for CrCl 40-60 mL/min, and 0.125 mg for CrCl 20-40 mL/min. Dofetilide is contraindicated in patients with CrCl <20

mL/min and for QTc interval >470 msec in men or >480 msec in women.[20] Other side effects include QT prolongation and torsades de pointes (TdP), especially in patients with heart failure. Dofetilide carries a unique treatment initiation limitation as it must be started in the inpatient setting to complete 2 hours of EKG monitoring after each dose for at least 3 days of therapy.

Dronedarone (Multaq):

Dronedarone is a Vaughan Williams class III antiarrhythmic and has a similar mechanism of action to amiodarone which inhibits multiple ion currents including sodium, potassium, and calcium currents. Additionally, dronedarone is a noncompetitive β-adrenergic inhibitor. Dronedarone was associated with an increased incidence of mortality compared to amiodarone and is therefore contraindicated in patients with NYHA class III to IV heart failure, unstable NYHA class II heart failure, and in patients with permanent Afib.[21] Furthermore, efficacy of dronedarone for maintenance of normal sinus rhythm has only been shown in patients with nonsurgical paroxysmal Afib and therefore does not qualify as a potential treatment for POAF.

Ibutilide (Corvert):

Ibutilide is a Vaughan Williams class III antiarrhythmic agent. It delays repolarization by activation of slow, inward sodium current and IKR. Ibutilide is only available as an IV dosage form and is therefore only used for cardioversion to NSR and not for maintenance of NSR. This medication is dosed based on weight as follows: 1 mg IV over 10 min for weight ≥60 kg or 0.01 mg/kg IV administered over 10 min for weight <60 kg.[22] Side effects that limit the use of ibutilide include QT interval prolongation and TdP. The risk for TdP is 2 to 3 fold higher in patients with systolic heart failure. A small prospective randomized pilot study compared ibutilide to propafenone and a rate control arm. The study found that while every patient given ibutilide was successfully cardioverted, 90% of these patients also experienced recurrent Afib.[23] This was statistically significant compared to the lower rate of recurrence for both propafenone and the rate control arm. Ibutilide may be considered for patients with structural heart disease and new-onset POAF without hypotension or CHF. Patients must be monitored for at least 6 hours after receiving ibutilide.

Procainamide (Procainamide HCl):

Procainamide is a Vaughan Williams class 1A antiarrhythmic agent. It blocks fast sodium channels which increases the effective refractory period of the atria, and to a lesser extent the ventricles. It is only available as an IV formulation and is therefore only indicated for the conversion of Afib to sinus rhythm but not for maintenance of sinus rhythm. Additionally, procainamide has only been shown effective for conversion in nonoperative Afib as conversion after noncardiac thoracic surgery has not been investigated. Dosing of procainamide is more difficult and requires close monitoring to assess appropriate dose. It is dosed at 20-50 mg/min IV continuous infusion until Afib terminated, hypotension occurs, QRS duration prolonged by 50%, or cumulative total dose of 15 mg/kg reached. Alternative dosing includes 100 mg IV every 5 minutes until Afib terminated or previous mentioned conditions are met.[24] Procainamide is contraindicated in patients with systolic heart failure or pretreatment QTc interval >470 ms in men or >480 ms in women.

Propafenone (Rythmol):

Propafenone is a Vaughan Williams class 1C antiarrhythmic agent. It reduces upstroke velocity of the action potential which is phase 0. A single oral dose of 450-600 mg is effective for conversion of nonsurgical Afib to sinus rhythm. Propafenone is also effective for maintenance of sinus rhythm in patients with nonoperative Afib at doses of 150-300 mg (immediate release) orally every 8 hours or 225-425 mg (extended release) orally every 12 hours.[25] There are only oral formulations of propafenone. Side effects include dizziness, blurred vision, sinus bradycardia, and AV block. Propafenone is contraindicated in patients with systolic heart failure or CAD/structural heart disease.

Sotalol (Betapace AF):

Sotalol has both Vaughan Williams class II and class III antiarrhythmic properties since it is a racemic mixture. Sotalol is noncardioselective as it blocks β-1 and -2 receptors leading to decreased heart rate and AV nodal conduction. Sotalol also prolongs atrial and ventricular action potentials by inhibition of the IKr channels that satisfy class III properties. The class III effects are only seen at oral doses ≥160mg/day. Sotalol is only formulated as an oral dosage form with a

maintenance dose of 40-160 mg orally every 12 hours with the interval requiring adjustment based on kidney function. For CrCl 30-59 mL/min, administer dose every 24 hours. Administer dose every 36-48 hours in patients with CrCl of 10-29 mL/min.26 Side effects of sotalol include sinus bradycardia, AV block, QT interval prolongation, TdP, heart failure, and bronchospasm. Sotalol has been used to reduce the risk of Afib after CABG surgery but is not used for conversion of Afib to sinus rhythm. Sotalol is contraindicated in patients with pretreatment QTc interval >470 ms in men or >480 ms in women.

Quinidine (Quinidine gluconate - IV):

Quinidine is a Vaughan Williams Class 1A antiarrhythmic agent. It inhibits both sodium and potassium channels. Quinidine can induce QT interval prolongation that leads to TdP and may increase mortality. Therefore, quinidine has fallen out of favor for use in management of Afib as there are safer and more efficacious agents available.

Management of Patients with Preexisting Afib

Elderly patients, who commonly have multiple comorbidities due to their advanced age, are a large portion of patients requiring cardiothoracic surgery. Oftentimes this patient population will present with preexisting Afib preoperatively. The 2014 AATS POAF guidelines recommend that cardiology consultations be obtained for these patients, and that they should be treated according to the existing guidelines for non-surgical Afib, namely the recently released 2014 AHA/ACC/HRS guidelines for Afib management.[15]

AATS recommends that for patients with preexisting Afib, decisions regarding interruption of anticoagulation for surgery be made based on the patient's stroke risk versus bleed risk.[1] This is done with the guidance of the CHA2DS2-VASc score (Figure 1). In patients with a high risk for stroke (equating to a CHA2DS2-VASc score of ≥2), history of a prior stroke, or mechanical heart valve, perioperative bridging with a parenteral anticoagulant (i.e. enoxaparin) is reasonable. For patients with a lower risk, short-term withdrawal without bridging may be appropriate.

Conclusion

Postoperative atrial fibrillation is a major complication of thoracic surgery that, with evidence-based practice, is often preventable. This complication has several implications, the most worrisome being thromboemboli formation resulting in stroke. The guidelines presented here have provided the most up-to-date recommendations on prophylaxis for POAF, treatments strategies, and anticoagulation in patients presenting with chronic Afib. It is important that pharmacists understand the current treatment guidelines for critical care patients such as those undergoing cardiothoracic surgery. Ensuring the proper pharmacological therapy in these patients will help establish better treatment outcomes, decrease hospital length of stay, and save money and resources.

Table 1. Modifiable and nonmodifiable risk factors for postoperative atrial fibrillation.[1]

Modifiable	Nonmodifiable
Hypertension	Increasing age
Myocardial Infarction	African American (protective)
Valvular Heart Disease	Family History
Heart Failure	Genetic Variance
Obesity	Male Sex
Obstructive Sleep Apnea	History of Arrhythmias
Smoking	
Exercise	
Alcohol use	
Hyperthyroidism	
Increased Pulse Pressure	
Mitral Regurgitation Left Ventricular Hypertrophy	

Figure 1. CHA_2DS_2-VASc scoring system for the prediction of stroke risk in patients with a fibrillation. A maximum score of 9 is possible. Scores of ≥2 are considered high risk. Adapte 2014 AATS POAF guidelines.[1]
LV=left ventricular, BP=blood pressure, HTN=hypertension, TIA=transient ischemic attack, MI=myocardial infarction, PVD= disease

	Condition	Points
C	**Congestive heart failure** (or LV dysfunction)	1
H	**Hypertension** BP>140/90 (or treated HTN)	1
A_2	**Age** ≥75 years	2
D	**Diabetes Mellitus**	1
S_2	**Prior stroke** or **TIA** or **Thromboembolism**	2
V	**Vascular disease** (MI, PVD, Aortic plaque)	1
A	**Age** 65-74 years	1
Sc	**Sex Category** (female)	1

Figure 2. Vaughan Williams classification of agents. [27]

Vaughn-Williams Classification
Class I Sodium-channel-blocking drugs:
Class IA - Moderately slow conduction, moderately prolonged action potential duration: Quinidine Procainamide Disopyramide
Class IB - Minimally slow conduction, shortened action potential duration: Tocainide Lidocaine Mexiletine Phenytoin
Class IC - Markedly slow conduction, minimally prolonged action potential duration: Flecainide Encainide Propafenone Moricizine
Class II Beta-blocking drugs
Class III Potassium-channel-blocking drugs - prolonged action potential duration: Amiodarone Bretylium Sotalol Ibutilide
Class IV Calcium-channel-blocking drugs

Table 2. Rate control agents and their clinical pearls.[1]

Name	Renal Adjust*	Monitoring	ADEs	Clinical Pearls
Esmolol (Brevibloc)	No	HR, BP, telemetry/EKG	Hypotension, bradycardia, AV block, fatigue, dizziness	Titrate dose to goal HR
Metoprolol (Lopressor)	No	HR, BP, telemetry/EKG	Hypotension, bradycardia, AV block, fatigue, dizziness	Oral dosage form available for long-term maintenance
Diltiazem (Cardizem)	No	HR, BP, telemetry/EKG	Hypotension, bradycardia, AV block, worsening of HF, peripheral edema, constipation	Titrate dose to goal HR
Digoxin (Lanoxin)	Yes	K^+, Mg^{2+}, serum drug level, HR, telemetry/EKG	N/V, anorexia, confusion, visual disturbances, AV block, ventricular arrhythmias	Therapeutic serum concentration: 0.8-2ng/mL, does not appreciably effect BP, synergistic with βB/CCB

HR= heart rate, BP= blood pressure, EKG=electrocardiogram, AV=atrioventricular, HF=heart failure, K^+=potassium, Mg^{2+}=magnesium, N/V=nausea/vomiting, βB=beta-blocker, CCB=calcium channel blocker,

Table 3. Rhythm control agents and their clinical pearls.[1]

Name	Renal Adjust*	Monitoring	ADEs	Clinical Pearls
Amiodarone (Nexterone)	No	HR, BP, QTc interval, telemetry/EKG	Bradycardia, hypotension, QTc prolongation, AV block	DDI with warfarin
Flecainide (Tambocor)	Yes	HR, BP, telemetry/EKG	Dizziness, blurred vision, bradycardia, AV block	CI in HFrEF and CAD/structural heart disease
Dofetilide (Tikosyn)	Yes	HR, BP, QTc interval, telemetry/EKG	QTc prolongation, TdP	Must be started as an inpatient
Dronedarone (Multaq)	No	HR, BP, telemetry/EKG	GI upset, dizziness, bradycardia	CI in HF and permanent Afib
Ibutilide (Corvert)	No	HR, BP, QTc interval, telemetry/EKG	QTc prolongation, TdP	Not indicated for maintenance of SR
Procainamide	Yes	HR, BP, QTc interval, telemetry/EKG	Hypotension, QTc prolongation, TdP	CI in HFrEF, Not indicated for maintenance of SR
Propafenone (Rhythmol)	No	HR, BP, telemetry/EKG	Dizziness, blurred vision, bradycardia, AV block	CI in HFrEF and CAD/structural heart disease
Sotalol (Betapace AF)	Yes	HR, BP, QTc interval, telemetry/EKG	Bradycardia, AV block, QTc prolongation, worsening HF	May be used with a "pure beta blocker"

HR= heart rate, BP= blood pressure, QTc=corrected QT interval, EKG=electrocardiogram, AV=atrioventricular, DDI=drug-drug interaction, CI=contraindicated, HFrEF=heart failure with reduced ejection fraction, CAD=coronary artery disease, GI=gastrointestinal, TdP=torsades de point, SR=sinus rhythm, HF=heart failure

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ACPE UAN# 0100-0000-15-044-H03-P; 0100-0000-15-044-H03-T

To receive CPE credit you must complete the quiz and evaluations on page 41 & 42

CONTINUING EDUCATION QUIZ QUESTIONS

I. Comparing the 2013 ACC/AHA & 2014 NLA Dyslipidemia Guidelines and their Impact on Clinical Decision Making

ACPE UAN# 0100-0000-15-043-H04-P; 0100-0000-15-043-H04-T

1. The ACC/AHA recommends utilizing which risk assessment calculator?
a. Pooled Cohort equations
b. Framingham risk calculator
c. Framingham long-term risk calculator
d. A & B
e. All of the above

2. AD is a 56 year-old male who presents to the lipid clinic for evaluation of his cholesterol. He has never had a fasting lipid panel performed and was referred to the clinic by his primary care physician. According to the NLA, which component of a fasting lipid panel is considered a primary target for modification?
a. LDL-C
b. Non-HDL-C
c. apoB
d. HDL-C

3. AD's fasting lipid panel results reveal an LDL-C of 196mg/dL. How would you classify AD's risk based on his LDL-C level alone, based on the NLA recommendations?
a. Low risk
b. Moderate risk
c. High risk
d. Very high risk

4. Based on AD's above risk category, what pharmacotherapy would you recommend initiating, per the NLA recommendations?
a. Atorvastatin 40mg daily
b. Pravastatin 20mg daily
c. Lovastatin 40mg daily
d. Simvastatin 20mg daily

5. Which of the following is/are considered clinical ASCVD?
a. Myocardial infarction
b. Stroke/TIA
c. Peripheral artery disease
d. All of the above

6. Which of the following medications should be selected for a patient with Type II diabetes and a non-HDL-C of 128 mg/dL according to the NLA recommendations?
a. Fenofibrate 145 mg daily
b. Niacin 100 mg TID
c. Atorvastatin 20 mg daily Ezetimibe 10 mg daily

7. MJ is a 44 year-old male who has been referred to your facility's lipid clinic for the management of his dyslipidemia. He has a LDL-C of 164 mg/dL and a HDL-C of 58 mg/dL. The patient reports that his father passed away at 54 years of age from a heart attack, but his mother is healthy without any significant health concerns. He has hypertension with a blood pressure reading of 158/92 mm Hg today at his follow-up visit. How many risk factors for ASCVD does this patient have?
a. 0
b. 1
c. 2
d. 3

8. Which of the following statements is true about non-HDL-C and Apo B?
a. Both are considered a secondary target in the treatment of atherogenic cholesterol in the NLA recommendations for the treatment of dyslipidemia.
b. Neither of the two requires fasting prior to a lipid panel for accurate assessment.
c. Apo B has shown superiority to non-HDL-C in randomized controlled trials in predicting ASCVD risk.
d. The treatment goals for non-HDL-C and Apo B are the same despite which risk category the patient falls under.

9. You are a pharmacist on rounds with a physician in the hospital setting. Your primary responsibility this morning as the pharmacist is to provide recommendations for the renal dose adjustment of medications in a patient with stage 4 chronic kidney disease. The patient is 65 years old, smokes one pack of cigarettes per day and has stage II hypertension. The results of the lipid panel confirm that the patient has dyslipidemia with a non-HDL-C of 155 mg/dL and an LDL-C of 110 mg/dL. The physician wants to start a statin in this patient but is unfamiliar with the new NLA recommendations and what risk category the patient falls under. He also wants to know what the patient's goal non-HDL-C is based on his risk category. What is the correct response to the physician?
a. The patient is at moderate risk with a non-HDL-C goal of <130 mg/dL
b. The patient is at very high risk with a non-HDL-C goal of <100mg/dL
c. The patient is at high risk with a non-HDL-C goal of <130 mg/dL
d. You cannot give an appropriate answer at this time because quantitative risk scoring is required to further assess the patient's risk category and cholesterol goals.

10. Comparing the 2013 ACC/AHA guidelines and the 2014 NLA recommendations what is/are the major differences?
a. The NLA recommendations use of non-HDL-C, LDL-C, and Apo-B target goals in the treatment of dyslipidemia where the ACC/AHA guidelines do not utilize treatment goals.
b. The NLA recommendation of using Apo-B as the primary lipid measure to target treatment goals as opposed to LDL-C by the ACC/AHA guidelines.
c. The NLA recommendation of using fibrates as an initial treatment option in patients that fall into the moderate risk ASCVD group compared to the ACC/AHA guidelines that recommend statin use first line.
d. A and C

11. Which of the following statements of the NLA recommendations is true:
a. Patients that fall into the very high risk ASCVD category should have an initial TLC trial prior to pharmacotherapy initiation.
b. The NLA does not recommend the use of quantitative risk scoring in patients being evaluated for dyslipidemia that fall into the high and very high risk categories as it typically underestimates their risk for an ASCVD event.
c. TLC changes such as initiating or increasing exercise regimens to 30 minutes/day, adding 5-10g of viscous fiber to diet, and 5-10% weight loss for all patients should be started at initial evaluation for patients who have dyslipidemia.
d. The NLA recommends fibrates, nicotinic acids, and statins to be considered first line therapy in treating patients newly diagnosed with dyslipidemia.

Use the following patient case to #12-14:
RD is a 63 years old male (70in, 249lbs) with a history of COPD, DM, 1 PPD smoker, total hip replacement and HTN. He is returning after 3 months to the clinic where you the clinical pharmacist have authority to adjust pharmacotherapy in patients with dyslipidemia. RD is complaining of muscle pain and weakness at his follow up visit after he was started on atorvastatin 40mg.
Creatinine Kinase: within normal limits
LFTs: within normal limits Non-HDL cholesterol(baseline/current): 232/156 mg/dL; HDL-C(baseline/current): 40/45 mg/dL
TG (baseline/current): 430/389mg/dL;
Current BP is 132/78; Current meds: Lisinopril 40mg PO daily, amlodipine 10mg PO daily, Metformin 1000mg PO BID, Glipizide 5mg PO BID, Symbicort 160/4.5

2 puffs BID

12. Based on RDs current status the most appropriate change to therapy would be to:

a. Discontinue atorvastatin 40mg as it causing myopathies.
b. Decrease his dose of atorvastatin to 20mg and add long chain omega-3 fatty acids to decrease his TG.
c. Change atorvastatin to rosuvastatin 20mg.
d. Stop all statin use as RD is intolerant to statins and start fenofibrate 135 mg.

13. What therapeutic lifestyle changes (TLC) should be recommended to RD to help him reach his non-HDL-C goal:

a. Counsel RD on smoking cessation and refer him to the Arizona Smokers Helpline (ASH-Line)
b. Suggest moderate exercise for 30 minutes per day, 7 days week, as possible
c. Recommend following DASH diet
d. All of the above are appropriate lifestyle changes

14. RD returns to the clinic after another 3 months after following the recommendations made at his previous visit. His current non-HDL-C is 130mg/dL. Which of the following is false?

a. RDs adherence and tolerability to his pharmacotherapy and TLC need to be assessed.
b. RD has reached his non-HDL-C goal and can discontinue therapy and follow up in 12 months.
c. RD should be evaluated and encouraged for smoking cessation.
d. TLC changes should be discontinued as he has reached his goal non-HDL-C.
e. B and D

II. A Pharmacist's Role in the Prevention and Management of Perioperative Atrial Fibrillation and Flutter

ACPE UAN# 0100-0000-15-044-H03-P; 0100-0000-15-044-H03-T

1. Which of the following is a major complication associated with POAF?

a. Vision changes
b. Insufficient blood flow leading to poor perfusion to the body
c. Moderate to severe skin reactions
d. Increased risk of bleed due to inability to coagulate

2. Which is/are symptoms of POAF?

a. Excessive weight gain
b. Increased thirst (polydipsia) and increased urination (polyuria)
c. Brittle nails
d. Hypotension and fatigue

3. Which of the following statements is TRUE regarding β-blockers?

a. β-blockers are Vaughan Williams class IV agents
b. Tachycardia and hypertension are common side effects of β-blocker therapy
c. IV dosing of metoprolol tartrate (Lopressor) is 12.5-25 mg IV bolus over 2 min for a maximum of three doses
d. Patients with systolic heart failure and/or CAD have a compelling indication for β-blocker therapy

4. JW is a 72 yo M who is currently taking metoprolol tartrate 50 mg BID. He has no history of AF but is undergoing a pulmonary segmentectomy. Which of the following statements is most accurate?

a. JW should be started on digoxin 0.125 mg for AF prophylaxis
b. Metoprolol should be discontinued prior to surgery
c. Continue metoprolol since JW was taking prior to surgery
d. Beta-blocker therapy is contraindicated in thoracic surgeries

5. Which of the following is a unique side effect of diltiazem?

a. Constipation
b. Diarrhea
c. Visual disturbances
d. Alopecia

6. All of the following are monitoring parameters for digoxin EXCEPT:

a. Serum drug concentration (goal: 0.8 - 2.0 ng/mL for Afib)
b. Electrolytes
c. Liver function
d. Kidney function

7. Which of the following statements regarding amiodarone is FALSE?

a. Amiodarone can be used for cardioversion from AFib to sinus rhythm or for maintenance of sinus rhythm.
b. Amiodarone is available in IV and oral formulations.
c. Amiodarone does not cause bradycardia or hypotension.
d. Amiodarone should be used cautiously in patients on oral anticoagulation as it inhibits the metabolism of warfarin and inhibits the elimination of the new oral anticoagulants.

8. Which rhythm control agent must be started in an inpatient setting for a minimum of 3 days?

a. Propafenone
b. Amiodarone
c. Dofetilide
d. Verapamil

LT is a 68 y/o female s/p thoracic surgery. Her BP is 132/88 with a HR of 78. She is hemodynamically stable yet having symptoms of AFib including shortness of breath, fatigue, and confusion. Rate control agents are not sufficiently treating POAF in LT. Use this case for #9 – 10.

9. LT is a candidate for rhythm control for POAF.

a. True
b. False

10. Which of the following medications cannot be used to cardiovert LT?

a. Amiodarone
b. Sotalol
c. Ibutilide
d. All of these can be used to pharmacologically cardiovert.

11. Which of the following is NOT a recommendation provided by the 2014 AATS guidelines for preventing POAF?

a. Supplemental intravenous magnesium should be considered for patients in which serum magnesium levels are low
b. Patients taking beta-blockers prior to surgery to continue to take them in the postoperative period
c. Initiate sotalol preoperatively as prophylaxis for POAF
d. Digoxin should not be used for preventing POAF

GL is a 72 y/o male who will be undergoing a lung transplantation next week. His PMH includes chronic Afib, DM, HTN and gout.

12. GL's CHA2DS2-VASc score is:

a. 1
b. 2
c. 3
d. 4

13. Perioperative anticoagulation bridging should be considered for GL:

a. True
b. False