Atrial Fibrillation (AF) & Flutter complicating critical illness

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introduction

What this chapter is about

- AF is the most common arrhythmia encountered in the ICU. (29627355) The two most common scenarios are:
  - (1) A patient with chronic AF develops critical illness.
  - (2) A patient who was previously in sinus rhythm develops new-onset AF (NOAF) while in the ICU, secondary to the physiologic stress of critical illness (e.g., secondary to sepsis or pulmonary embolism).
- These situations are different from AF in other contexts, for example:
  - ICU patients are often hemodynamically tenuous, so they may respond poorly to the usual AF therapies (e.g., diltiazem).
  - DC cardioversion alone has a low success rate among critically ill patients (patients will usually revert back into AF).
The optimal heart rate for critically ill patients is unknown, but some patients may benefit from a mild compensatory tachycardia. Immediately pushing the heart rate down to a “normal” range (e.g., <100) can be dangerous.

- The below excerpt from the 2014 AHA/ACC guideline on atrial fibrillation provides a nice summary of AF in the context of critical illness. (24685669 [https://pubmed.ncbi.nlm.nih.gov/24685669/]) Unfortunately, this is all that the AHA/ACC guidelines have to say about AF in the ICU – so we will have to work to fill in the blanks.

### 7.6. Acute Noncardiac Illness

A number of acute noncardiac conditions are associated with AF (e.g., hypertension, postoperative state, pulmonary embolism, viral infections). **Management of the underlying condition and correction of contributing factors as first-line treatment is common to all of these scenarios** (487), and for many of these patients AF will spontaneously terminate with correction of the underlying condition. However, during acute illness, patients may require rate control with cardioversion, AV nodal blockers, and/or antiarrhythmic drugs if AF is poorly tolerated or rate control is not feasible. The specific rate- or rhythm-control agent(s) will depend on the underlying medical condition. Of note is that an elevated catecholamine state is common to many of these clinical circumstances, and unless contraindicated, a beta blocker is the preferred initial drug. **The role of anticoagulation is less clear** and likely disease specific and needs to be addressed on the basis of risk profile and duration of AF.

2014 AHA/ACC/HRS Guideline for the management of patients with AF

### diagnosis of AF

#### general

- AF may be suspected on the basis of an irregularly irregular heart rate (either on clinical examination or telemetry).
- AF diagnosis should always be confirmed with a full 12-lead EKG.

#### diagnostic criteria for AF on EKG

1. There should be no regularity.
   - At very high rates, the heart rate may appear to be regular (“pseudo-regularization”).
   - When in doubt, calipers may help determine whether there is any regularity.
2. No P waves are seen; instead these may be replaced by fibrillation waves.
   - Fibrillation waves may be best seen in the inferior and right-sided precordial leads.
   - In some patients, fibrillation waves may be small and difficult to distinguish from artifact.
   - If it is unclear whether there are P waves or fibrillation waves, consider obtaining a **Lewis Lead EKG** [https://emcrit.org/emcrit/lewis-lead/]. Also consider comparison to P wave morphology in prior EKGs (if the patient previously had large, well-defined P-waves and now they’re gone, then this supports an AF diagnosis).
- (One exception to these criteria is that if AF is combined with heart block, then the ventricular response may be regular.)

#### heart rate among patients in AF

- For most patients who aren’t on medications that suppress the AV node, AF will have a heart rate of ~120-180.
- If the heart rate is >>200, consider the possibility of an accessory tract (AF plus Wolff Parkinson White).
If the heart rate is <100, conduction disease is likely.

Be careful when cardioverting patients with a heart rate <100, as there may be an increased risk of bradycardia.

**prevention of AF**

AF prevention has been studied extensively following cardiac surgery. Most of this literature isn't applicable to the general ICU population. However, measurement of magnesium levels and repletion may be considered. In the context of post-surgical AF, RCTs have demonstrated that magnesium administration reduced the incidence of AF with an odds ratio of 0.55 (22520937, 23440790). Hypomagnesemia is common among critically ill patients, so detection and treatment of hypomagnesemia makes sense in this population. (More on hypomagnesemia [here](https://emcrit.org/ibcc/hypomagnesemia/).)

**evaluating the etiology of new-onset AF**

**common causes of new-onset AF**

- Electrolyte abnormalities (especially hypokalemia and hypomagnesemia)
- Toxicology / Medications
  - Alcohol (holiday heart syndrome)
  - Substance use (especially cocaine, amphetamine, methamphetamine)
  - Beta-agonists (norepinephrine, epinephrine, dobutamine, etc.)
  - Theophylline
  - Fluid overload (yes, fluid is a medication – and sometimes it’s used as a poison)
- Swan-Ganz catheterization
- Adrenergic states
  - Alcohol withdrawal
  - Pain, agitation
  - Primary neurologic disorders (intracranial hemorrhage, ischemic stroke)
- Respiratory failure
  - Pulmonary embolism
  - Pneumonia, COPD, hypoxemia, hypercapnia
- Myocardial ischemia
- Sepsis
- Thyrotoxicosis

**evaluation**

- Basic evaluation:
  - EKG
  - Electrolytes, including magnesium
  - Review of medication list
  - Review of the presence of any indwelling cardiac devices
  - Echocardiogram
- Additional tests *as clinically warranted*. For example:
  - If thoughtful review of EKG and history suggests ischemia, then obtain troponin.
  - If there is other evidence suggesting PE, CT angiography may be indicated.
  - TSH should be considered if there is no obvious cause of AF, or if other clinical features suggest thyrotoxicosis.

**overall approach to AF**
The following figure will serve as a general framework for approaching a critically ill patient with AF:

(emcrit.org/ibcc/af/attachment/afalgor2/)

emergent cardioversion

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how much is AF actually contributing to the patient’s instability?

(https://emcrit.org/ibcc/af/attachment/afguilty/)

- The key question is: *What is driving the instability?* Is the atrial fibrillation causing the patient to be unstable? Or is atrial fibrillation merely triggered by underlying instability?
- Some key pieces of information can help:
  - (1) **Heart rate**: As a general rule, heart rates <150 are less likely to cause hemodynamic instability. The faster the heart rate is, the more likely it is causing trouble.
  - (2) **Structural heart abnormalities** (especially pulmonary hypertension, mitral stenosis, or diastolic heart failure) may render patients dependent on atrial kick. Such patients may tolerate AF poorly.
  - (3) **Overall clinical context**
- Trying to sort this out is important:
  - DC cardioversion will stabilize the patient only if the AF is *causing* the instability.
  - ⚠️ If fast heart rate is due to an underlying process, then overly aggressive attempts to reduce the heart rate to a “normal” range may make matters worse (because a mild degree of tachycardia may actually have a *compensatory*, beneficial effect).
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consider immediate DC cardioversion

- DC cardioversion is indicated if new-onset AF clearly caused the patient to be severely unstable. *This is unusual* – for most critically ill patients, the AF isn’t the primary driver of instability.

- Even if cardioversion is successful, patients will usually revert to AF subsequently.

- If possible, pretreatment or post-treatment with amiodarone +/- magnesium may enhance the likelihood of achieving and maintaining sinus rhythm.

AF with an accessory pathway (Wolff Parkinson White)

- An accessory pathway is an aberrant electrical connection between the atria and the ventricles that shouldn’t exist.

- Normally, when in AF the heart rate is limited by the refractory period of the AV node. Although the AV node may allow for a *fast* heart rate (e.g. ~120-180), these heart rates are usually tolerated reasonably well.

- When AF occurs in the context of an accessory pathway, *both* the AV node *and* the accessory pathway can transmit beats to the ventricles. Since the accessory pathway often has a shorter refractory period than the AV node, it may drive the ventricle very rapidly (e.g. >200). This is dangerous because the extremely fast and uncoordinated contractions of the ventricle can promote ventricular tachycardia or cardiovascular collapse.

- AF with an accessory pathway produces a fairly distinctive pattern of EKG findings:
  - Irregularly irregular heart rate that may be extremely fast (e.g. >200).
  - Wide-complex beats can result from transmission over the accessory pathway.
  - Morphology *varies* between different beats (some beats are *fusion complexes* if the AV node and the accessory pathway fire at a similar time).

- AF with an accessory tract *shouldn’t* be treated with medications that impair the AV node (e.g. beta-blockers, calcium channel blockers, or amiodarone). Blockade of the AV node may merely cause a greater dominance of the accessory pathway, exacerbating matters (to a certain extent, the AV node and the accessory pathway are competing for control of the ventricle). Antiarrhythmics which may be used are procaainamide or ibutilide.

- This is a unique situation where DC cardioversion is usually the treatment of choice (based on its efficacy and speed). If a patient with AF and an accessory pathway is displaying instability, proceeding directly to DC cardioversion is indicated.

universal AF stabilization package

The most important intervention for critically ill patients with AF is usually treating the causes of AF. There is a risk of getting overly focused on antiarrhythmics and cardioversion, but the most important interventions are often as follows:

hemodynamic optimization

- (1) Discontinue beta-adrenergic vasopressors as able.
  - Especially epinephrine and dobutamine may increase heart rate and should be weaned if possible.

- (2) For hypotension, add pressors that don’t stimulate beta receptors.
  - Phenylephrine is a good choice if needed to support blood pressure, without driving tachycardia. Phenylephrine infusions are often avoided due to fear that they will reduce the cardiac output, but they generally *don’t* reduce the cardiac output. Phenylephrine usually increases preload by causing venoconstriction, thereby balancing out the effects of increasing the afterload. *(discussed here)*

  - Vasopressin is another option.

- (3) Optimize volume status.
  - AF may be caused by volume overload, which causes atrial dilation. If volume overload is present, diuresis may be beneficial.
  - If frank hypovolemia is present, then volume administration may be beneficial. However, note that hypovolemia is relatively uncommon among patients who are admitted to ICU.

treatment of pain/anxiety/withdrawal

- Untreated distress can drive sympathetic tone and aggravate AF.
Pain and anxiety should always be treated adequately. However, uncontrolled AF may serve as a reminder to make especially sure that these issues are being attended to (see chapters on anxiety and pain).

For uncontrolled anxiety, dexmedetomidine may be considered as an anxiolytic that will reduce sympathetic tone and decrease heart rate.

**treatment of electrolyte abnormalities**

- **Hypokalemia** and **hypomagnesemia** may promote AF, so if present these should be treated aggressively.

- If magnesium hasn’t been checked recently, it is reasonable to empirically give 2-4 grams of magnesium sulfate provided that the patient’s renal function is normal. The magnesium level **should** be checked, but administration of magnesium doesn’t need to wait until the level returns. For patients with substantial hypomagnesemia, a magnesium infusion may help rapidly replete total body stores of magnesium and settle down the AF (see the magnesium infusion protocol here).

**respiratory support**

- Hypoxemia or respiratory distress may be drivers of AF.

- Respiratory failure should be aggressively treated (e.g., CPAP for heart failure, BiPAP for COPD, HFNC for pneumonia).

**evaluation and treatment of other causes of hemodynamic instability**

- Avoid anchoring excessively on AF as the cause of the patient’s hemodynamic instability.

- For ongoing instability, evaluate broadly and treat appropriately. For example, uncontrolled AF could be a manifestation of sepsis, PE, thyrotoxicosis, or any cause of shock.

  - If AF is being driven by another underlying process, focusing solely on suppressing the heart rate with medications will fail – and may actually make the patient worse.

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**rate control versus rhythm control**

**overview of evidentiary basis for rate control vs. rhythm control**

- No RCTs have been performed comparing rate control vs. rhythm control in a general ICU population. However, several RCTs have been performed in other contexts (e.g., emergency department patients, patients status post cardiac surgery).

- Available studies show no differences in hard endpoints (e.g., mortality or stroke). However, this doesn't exclude the possibility that some subgroups of patients might benefit more from one strategy.

- Overall, both strategies are generally reasonable and the choice may depend on patient specifics.

**factors favoring a rate-control strategy**

- **Chronic AF** is perhaps the strongest indicator for a rate-control strategy. AF leads to electrical remodeling, which leaves the atria less able to convert to sinus rhythm. The longer patients are in AF, the harder it is to convert to sinus rhythm.

- **Onset of AF >48 hours previously, in a patient who isn't anticoagulated:** In this situation, conversion to sinus rhythm may theoretically increase the risk of stroke due to dislodging a clot from the atrial appendage.

**factors favoring a rhythm-control strategy**

- **Inability to tolerate AF hemodynamically:** AF can cause hemodynamic instability, especially in patients with chronic pulmonary hypertension, mitral stenosis, or diastolic dysfunction (situations where the atrial kick may be especially beneficial).

- **New-onset AF:** Patients often develop new AF in the context of critical illness. If this occurs while being monitored in the hospital, it may warrant an attempt at rhythm control (explored further in the next section).

- **Atrial flutter:** This is often a transitional state, as the atria is deciding whether to settle down into sinus rhythm or atrial fibrillation. Atrial flutter is often difficult to treat using rate control, since the rate tends to be stubbornly stuck at around 150. (More on atrial flutter below.)

**argument for attempting rhythm control in critically ill patients with new-onset AF (NOAF)**

- What is NOAF?
• New-onset AF (NOAF) refers here to AF that began during hospitalization for critical illness, in a patient who previously did not have chronic or paroxysmal AF. A common example is in patients with septic shock, wherein the prevalence of NOAF is ~10%. ([32983720](https://pubmed.ncbi.nlm.nih.gov/32983720/))

• The natural history of NOAF is usually to revert to sinus rhythm on its own, as the underlying critical illness resolves.

• NOAF correlates with worse outcomes, including mortality. However, it remains murky whether the NOAF causes worse outcomes, whether the NOAF merely is a marker of sicker patients, or both. ([31089761](https://pubmed.ncbi.nlm.nih.gov/31089761/))

• There is no high-quality evidence regarding the optimal approach to NOAF in the context of general critical illness (e.g., sepsis). However, several arguments can be made for attempting rhythm control in these patients:
  
  (#1) Most patients with NOAF will eventually revert back into sinus rhythm on their own. However, the risk of stroke may relate to the duration of time that the patient spends in AF (e.g., >48 hours in NOAF may increase stroke risks). If we can convert patients out of NOAF rapidly, this ought to reduce the risk of stroke.

  (#2) Not all patients with NOAF will spontaneously revert back into sinus rhythm (for example, one series found that 44% of patients were discharged in AF). ([32983720](https://pubmed.ncbi.nlm.nih.gov/32983720/)) The longer AF is allowed to continue, the less likely it is to revert to sinus rhythm. Ongoing atrial fibrillation causes electrical remodeling of the atria, which perpetuates the atrial fibrillation (hence the clinical adage, “AF begets AF”). Prompt cardioversion out of NOAF could theoretically increase the likelihood that the patient could successfully revert to sinus rhythm and stay in sinus rhythm on a long-term basis.

  (#3) AF may impair cardiac function in a subset of patients, due to impaired atrial kick. Cardioversion out of NOAF might therefore improve cardiac function in some patients, allowing them to compensate better for their acute critical illness.

  (#4) Attempts at rhythm control for NOAF will typically involve magnesium and amiodarone (more on this below). Even when these strategies fail to achieve cardioversion, they will generally achieve rate control – so they may remain clinically beneficial.

• Related supporting evidence:

  • Evidence from postoperative AF provides some support for pursuing a rhythm control strategy in other critically ill patients. For example, a multicenter RCT found that for AF following cardiac surgery, a rhythm control strategy increased the likelihood of being free from atrial fibrillation two months later (94% vs. 98%; p = 0.02). ([27043047](https://pubmed.ncbi.nlm.nih.gov/27043047/))

  • A recent multicenter RCT among outpatients found that a rhythm-control strategy among patients with onset of AF within <1 year led to a lower risk of adverse cardiovascular outcomes. ([32865375](https://pubmed.ncbi.nlm.nih.gov/32865375/)) Likewise, the J-RHYTHM trial, a multicenter study involving patients with AF onset within <48 hours, found that rhythm control was associated with an improvement in composite outcomes. ([19060419](https://pubmed.ncbi.nlm.nih.gov/19060419/))

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**rhythm control strategy for critically ill patients**  
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#1 magnesium

• Rationale for magnesium in rhythm control:

  • Among critically ill patients, magnesium seems to have similar efficacy when compared to other antiarrhythmics. In one RCT, a continuous magnesium infusion was actually superior to amiodarone. ([7587256](https://pubmed.ncbi.nlm.nih.gov/7587256/))

  • Magnesium has an excellent safety profile, with one meta-analysis detecting no reported adverse events due to magnesium within any study. ([32209631](https://pubmed.ncbi.nlm.nih.gov/32209631/)) The combination of reasonable efficacy plus a largely unparalleled safety record makes magnesium a rational front-line agent for critically ill patients. ([29627355](https://pubmed.ncbi.nlm.nih.gov/29627355/))

  • Even when magnesium alone doesn't cause cardioversion, it still offers the patient potential benefits. Magnesium augments the efficacy of other antiarrhythmic agents or DC cardioversion. ([23731344](https://pubmed.ncbi.nlm.nih.gov/23731344/), [21815963](https://pubmed.ncbi.nlm.nih.gov/21815963/), [32861384](https://pubmed.ncbi.nlm.nih.gov/32861384/)) If rhythm control fails, magnesium also has some efficacy at reducing the heart rate. ([15795711](https://pubmed.ncbi.nlm.nih.gov/15795711/))

• Nuts and bolts

  • For patients with adequate renal function (GFR > 30 ml/min), a protocoled magnesium infusion may be used as shown below. Most of the administered magnesium will be excreted, so a continuous infusion may be required to effectively replete intracellular magnesium levels. ([18320707](https://pubmed.ncbi.nlm.nih.gov/18320707/))

  • For patients with renal insufficiency, intermittent boluses of magnesium may be utilized (targeting a level of ~3-4 mg/dL).
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Cardiac Magnesium Infusion Protocol

[1] Loading dose & starting infusion
  - Load with 4 grams magnesium sulfate over 1 hour
  - Then start infusion at 1 gram/hour

[2] Monitor electrolytes & magnesium q6hr x 24 hours
  - Magnesium:
    - Target level = 3.6-4.9 mg/dL
    - If Mg 5-7 mg/dL => reduce infusion rate by 50%
    - If Mg >7 mg/dL => stop infusion (do not re-start)
  - Potassium: replete for target K>4 mM

  - For weakness or somnolence, obtain Mg level
  - For bradycardia or respiratory distress, stop infusion and check Mg level

[5] Stop magnesium infusion after 24 hours

#2a) attempt chemical cardioversion with amiodarone

- Amiodarone may be utilized if magnesium infusion is ineffective. Depending on the situation, amiodarone might be initiated within ~12 hours of starting the magnesium infusion, if the patient remains in atrial fibrillation.
  - Even if the magnesium has failed to work alone, continuing the magnesium infusion may still remain beneficial in combination with amiodarone. The combination of aggressive magnesium loading plus adequate doses of amiodarone achieved a cardioversion rate of 90% in one series of critically ill patients. ([18320707](https://pubmed.ncbi.nlm.nih.gov/18320707/))
- Start with ~150-300 mg amiodarone load and an infusion of 1 mg/min. If unsuccessful, one or more reloading doses may be given (up to a total of ~450-600 mg in the form of IV boluses).
  - Note that the dose of amiodarone required for chemical cardioversion is often large (e.g., some sources recommend 5-7 mg/kg infused over an hour). ([11568824](https://pubmed.ncbi.nlm.nih.gov/11568824/)) Many patients won't cardiovert in response to a 150-mg loading dose of amiodarone, but may nonetheless respond to additional loading doses.
  - Even if amiodarone fails to work immediately, continue the infusion, as some patients may have delayed cardioversion (e.g., within the first 24 hours after starting the amiodarone infusion).

#2b) amiodarone contraindicated: may consider ibutilide

- Amiodarone is usually the preferred antiarrhythmic for ICU patients due to its ability to both cardiovert patients and subsequently prevent recurrent AF. For patients in whom amiodarone is contraindicated, ibutilide may be considered. ([21209348](https://pubmed.ncbi.nlm.nih.gov/21209348/), [10763074](https://pubmed.ncbi.nlm.nih.gov/10763074/)). The main drawback of ibutilide is that, unlike amiodarone, ibutilide doesn't provide ongoing antiarrhythmic support to prevent AF recurrence.
  - One very small RCT found that amiodarone and ibutilide were equally effective. The advantage of ibutilide was a reduced rate of hypotension, whereas the advantage of amiodarone was a reduced rate of recurrent AF. ([12682468](https://pubmed.ncbi.nlm.nih.gov/12682468/))
  - Ibutilide may be superior to procainamide among critically ill patients, because it has greater efficacy and no negative hemodynamic effects. ([9581743](https://pubmed.ncbi.nlm.nih.gov/9581743/), [9416896](https://pubmed.ncbi.nlm.nih.gov/9416896/), [15773423](https://pubmed.ncbi.nlm.nih.gov/15773423/)). Ibutilide may not be preferred in emergency departments due to the requirement to observe patients for 4 hours, but this isn't an issue among patients already admitted to the ICU. ([28969929](https://pubmed.ncbi.nlm.nih.gov/28969929/))
  - Ibutilide is an effective antiarrhythmic in its own right. However, combining ibutilide with magnesium can improve its safety and efficacy:
    - The main side effect of ibutilide is prolongation of QTc, which cause Torsades de Pointes. Coadministration with a magnesium infusion will dramatically reduce the risk of Torsades. ([20723644](https://pubmed.ncbi.nlm.nih.gov/20723644/))
    - Administration of magnesium has been shown to substantially improve the efficacy of ibutilide ([14652979](https://pubmed.ncbi.nlm.nih.gov/14652979/), [32861384](https://pubmed.ncbi.nlm.nih.gov/32861384/)). If ibutilide is being utilized following initiation of a magnesium infusion, ibutilide's efficacy may be maximized by delaying ibutilide administration until the magnesium level has risen over ~3.8 mg/dL. ([32861384](https://pubmed.ncbi.nlm.nih.gov/32861384/)).
Ibutilide is contraindicated in QT prolongation, hypokalemia, hypomagnesemia, ejection fraction <30%, or severe LV hypertrophy. The standard dose is 1 mg infused over 10 minutes (or 0.01 mg/kg for patients <60 kg). This can be repeated once if needed. Patients should be monitored for ~4 hours subsequently (although arrhythmias will generally occur within the first hour after administration).

#3) DC cardioversion might be considered among intubated patients

- Most patients with NOAF will cardiovert in response to steps #1-2 above (especially if ~24 hours are allowed for the magnesium and amiodarone infusions to take effect).
- Failure of magnesium and amiodarone to work suggests that the patient’s heart doesn’t want to go into a sinus rhythm (e.g., perhaps due to significant chronic atrial dilation, underlying structural heart disease, or profound systemic inflammation). In this situation, it’s difficult to know whether to accept atrial fibrillation or continue efforts towards conversion to normal sinus rhythm.
  - For intubated patients, an attempt at cardioversion may be reasonable (since the risks of sedation are minimal).

**Follow-up care after cardioversion to sinus rhythm**

- If the patient does cardiovert in response to amiodarone, consider continuing the amiodarone infusion until they are substantially improved (e.g., for about a week). If amiodarone is stopped early (while the patient is still critically ill), patients are likely to revert into AF. One multicenter study found that amiodarone had an 87% success rate at achieving cardioversion, but 42% of patients reverted back to AF during their ICU stay. More on amiodarone dosing below.

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**Rate control**

**#1/3: set a safe target heart-rate goal**

Cardiac Output = \( \text{(Heart Rate)} \times \text{(Stroke Volume)} \)

- The target heart rate for outpatients is often regarded to be <110 (based on the RACE II trial).
- However, nobody knows what the ideal heart rate is for critically ill patients. Some patients may benefit from a mild degree of compensatory tachycardia.
  - As shown above, cardiac output is equal to heart rate multiplied by stroke volume. At very fast heart rates (>150), diastolic filling will become impaired, so the stroke volume will fall. However, at heart rates below ~150, the diastolic filling may often be OK, so the dominant driver of cardiac output may be the heart rate. Thus, for example, causing a drop in the heart rate from 130 to 90 may often cause a drop in the cardiac output.
  - Trying to “normalize” the heart rate (e.g., targeting a rate below 100) may increase the risk of iatrogenic harm in patients with tenuous hemodynamics.
  - For many critically ill patients, a heart rate goal below ~130 might be reasonable. The target may vary depending on patient specifics and clinical response. The optimal target may also vary over time – for example, initially a target of <130 may be reasonable, but as the patient recovers a lower target may become appropriate.

**#2/3: select an agent for rate control**
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[https://emcrit.org/ibcc/af/](https://emcrit.org/ibcc/af/)

**general approach to selecting an agent**

- Four agents are generally used for rate control: digoxin, amiodarone, beta-blockers, or diltiazem.
- The primary consideration when selecting an agent is often how stable the patient is (since most of these agents can cause hypotension).
  - For the most unstable patients (especially patients with severe systolic heart failure and longstanding AF), digoxin may be a consideration.
- Amiodarone is generally a solid choice for ICU patients with the potential for hemodynamic instability (as is true for most ICU patients).
- For patients with more robust hemodynamics and lower risk of hypotension, either a beta-blocker or diltiazem may be chosen – more on this below.
- Other considerations in selecting an agent are shown here:

[https://emcrit.org/ibcc/af/attachment/selectionavn/](https://emcrit.org/ibcc/af/attachment/selectionavn/)

**beta-blocker (usually metoprolol) vs. diltiazem?**

- One of the longstanding controversies in AF management has always been selecting between metoprolol and diltiazem. There is no good data regarding this, specifically:
  - (1) There is no RCT-level evidence regarding the comparison of these agents for rate control in the ICU.
  - (2) There is no RCT-level evidence comparing metoprolol versus a diltiazem infusion (all available RCTs involve only a bolus of diltiazem, which is likely safer than starting a continuous infusion).
- As suggested in the 2014 AHA/ACC guidelines above, many critically ill patients develop AF due to increased sympathetic tone. ([24685669](https://pubmed.ncbi.nlm.nih.gov/24685669/)) This implies a greater utility of beta-blockers among ICU patients. Some additional data support the utility of beta-blockers for AF among ICU patients:
  - One before/after study ([https://journals.lww.com/ccmjournal/Citation/2020/01001/278__EVALUATION_OF_METOPROLOL_VERSUS_DILTIAZEM_FOR_245.aspx](https://journals.lww.com/ccmjournal/Citation/2020/01001/278__EVALUATION_OF_METOPROLOL_VERSUS_DILTIAZEM_FOR_245.aspx)) following a diltiazem shortage found that transitioning from diltiazem to metoprolol led to improved success and reduced rates of...
hypotension among ICU patients. A retrospective study among critically ill patients likewise found a lower rate of failure when using metoprolol, when compared to diltiazem. (28328711) One RCT comparing metoprolol versus diltiazem among patients in the emergency department found that diltiazem was more effective. (25913166) However, this study didn’t involve a continuous infusion of diltiazem, so it doesn’t reflect the reality of diltiazem utilization among critically ill patients.

Overall, available evidence suggests that beta-blockers may have an edge among ICU patients. However, both options are entirely reasonable.

More important than the drug selection might be proper dose titration. Specifically, continuous diltiazem infusions can cause problems if they are up-titrated and subsequently allowed to accumulate over time. Alternatively, intermittent dosing of metoprolol naturally encourages nurses to think about each dose and hold doses in patients who are beginning to become hypotensive (the active act of giving each metoprolol dose incorporates a fail-safe mechanism).

### #3/3: if the patient continues to have a fast ventricular rate:

- Re-evaluate to make sure there isn’t an underlying problem (e.g. sepsis, hypovolemia). Ensure that the patient has been provided the full AF stabilization package.
- Consider adding additional magnesium.
- Try a different agent:
  - Avoid combining beta-blockers and calcium-channel blockers (overlapping these agents may increase the risk of hypotension).
  - Adding on amiodarone is often useful here (it is more hemodynamically stable and less likely to cause synergistic hypotension in combination with other agents).

### Optimal candidates for digoxin have:

- (1) Chronic AF (digoxin tends to perpetuate AF, rather than favoring cardioversion back to normal sinus rhythm).
- (2) Heart failure with reduced ejection fraction
  - Digoxin is the only agent which reduces heart rate while simultaneously functioning as a positive inotrope.
  - Digoxin may be uniquely beneficial for patients with heart failure whose hemodynamics are very tenuous, who may have difficulty tolerating a negative inotrope.
- (3) Mild or moderate tachycardia for which immediate control isn’t necessary (digoxin takes several hours to work and it’s not tremendously potent).
- (4) Adequate renal function
  - The presence of preserved renal function makes dosing of digoxin easier and a bit safer.
  - This isn’t an absolute requirement, because careful dosing and monitoring within the ICU allow digoxin to be given safely even in the presence of renal dysfunction.

### IV digoxin loading (digitalization)

- Digoxin takes a little while to work, but if given intravenously it may take effect within several hours. When initiated in the ICU, digoxin will nearly always be started with intravenous loading doses.
- Total IV loading dose: (package insert) . Normal renal function: 8-12 mcg/kg ideal body weight (usually ~600-1,000 mcg).
- Renal insufficiency: 6-10 mcg/kg ideal body weight.
- Err on the lower end in patients with renal dysfunction, hypothyroidism, and/or reduced muscle mass.
- Typically, 50% of the total loading dose is given initially, followed by 25% given twice, every six hours. The first IV dose (typically ~400-600 mcg) takes effect within roughly 1-4 hours. Monitor for effect. If an adequate heart rate is achieved, then subsequent doses may be omitted. If bradycardia occurs, further administration should be held.
maintenance doses

- Typical maintenance dose:
  - Patients <70 years old with normal renal function: 250 mcg daily.
  - Patients over 70 years old — or — with renal dysfunction: 125 mcg daily.
  - Patients who are both >70 YO — and — have renal dysfunction: 62.5 mcg daily.
- The table below provides typical maintenance doses, based on the patient's renal function and body weight. (Package insert)

Digoxin has a long half-life (~36-48 hours, or longer in renal insufficiency). Therefore, steady state may not be reached until about a week after a dose adjustment.

monitoring digoxin levels

- Drug level must be checked several hours after the last digoxin dose, to allow for distribution (e.g., >8 hours after an oral dose). Ideally this should be a trough level.
- The safest approach to digoxin dosing in the ICU among tenuous or dynamic patients is to closely monitor the digoxin level:
  - Check a trough digoxin level daily with AM labs.
  - Adjust the daily dose as needed, depending on the trough level.
  - As the patient stabilizes, digoxin levels may be spaced out.
- A therapeutic level is ~0.5-2 ng/mL.
  - 0.5-1 ng/mL might be the optimal concentration for outpatients.
  - 1-2 ng/mL levels may improve contractility, so these aren't unreasonable levels for closely monitored ICU patients.

if digoxin fails

- Digoxin is not an extremely powerful agent, so it may fail to achieve optimal heart rate control.
- If digoxin does fail, it may be combined with a beta-blocker or diltiazem.
  - The presence of digoxin may reduce the required dose of beta-blocker or diltiazem, thereby improving hemodynamic stability.
    (31700500) In particular, the combination of digoxin plus a beta-blocker may work well for some patients with systolic heart failure.

amiodarone

amiodarone for rate control

- This may be useful for patients with potential hemodynamic instability, if they aren't good candidates for digitalization (see above).
Achieving rate control may require reloading with 150 mg amiodarone 2-3 times.

- Don’t conclude that amiodarone has failed to work without re-bolusing adequately.
- There is a theoretical risk of causing stroke among patients who aren’t anticoagulated and might cardiovert into sinus rhythm. However, for critically ill patients who are hemodynamically tenuous, this theoretical risk may often be superseded by the need to achieve hemodynamic stability.

**amiodarone dosing**

- **Initial IV dosing**
  - Load with 150 mg bolus, then infuse at 1 mg/minute.
  - May re-load 1-2 times if inadequate response (for a total of 150-450 mg given in the form of boluses).
- **Conversion to oral**
  - Infusion may be converted to oral administration after >24 hours.
  - Start at 400 mg PO BID, until the patient has received a total of 10 grams cumulative dose (both IV and PO). Subsequently, the dose may be decreased to 200 mg daily.
- **Eventually transition to another agent**
  - Chronic use of amiodarone causes a host of side effects.
  - After patients recover from their critical illness, they should be transitioned to a safer long-term regimen (e.g., a beta-blocker).

**beta-blockers**

**selection of beta blocker**

- **IV metoprolol** is usually the agent of choice.
- **IV esmolol** infusion may be used if it’s unclear whether the patient will tolerate a beta-blocker. This has the advantage that if it causes hypotension it can be stopped and will wear off fairly rapidly (over ~10 minutes). If the patient responds well to esmolol, they may be transitioned to a longer-acting beta-blocker.
  - Another simpler option is to use IV metoprolol. If the patient is unable to tolerate beta-blockade, this may be reversed transiently by using an infusion of low-dose dobutamine or epinephrine.

**metoprolol dosing**

- **Initial IV loading** ([University of Wisconsin protocol](https://www.uwhealth.org/cckm/cpg/cardiovascular/related/Atrial-Fibrillation-Mgt---Rate-Control-Drugs-190312.pdf))
  - Usually start with 5 mg IV, which should take effect within ~5 minutes.
  - Additional doses may be given every 5 minutes, titrating to effect (reduction in heart rate, without causing hypotension).
  - Generally, no more than 15 mg total will be used initially.
- **Ongoing IV therapy**
  - For patients without enteral access, scheduled IV doses may be required.
  - The intravenous form wears off faster than the oral form, so more frequent dosing may be required than is usual with oral metoprolol (e.g. the initial loading dose may be repeated q4hr-q6hr, depending on heart rate and blood pressure).
- **Transition to oral administration**
  - The initial oral dose may be estimated based on the IV dose required, based on a 1:2.5 conversion from IV to PO:
    - Response to 5 mg IV → Start metoprolol tartrate 12.5 mg PO q6hr.
    - Response to 10 mg IV → Start metoprolol tartrate 25 mg PO q6hr.
    - Response to 15 mg IV → Start metoprolol tartrate 37.5 mg PO q6hr.
  - The first oral dose can be started 20 minutes after the initial IV dose.
  - Metoprolol tartrate usually isn’t given every six hours. However, starting with more frequent dosing may allow more flexibility in dose adjustment.

**esmolol dosing**

- Starting esmolol:
  - Load with 0.5 mg/kg IV (e.g. 35 mg for a 70-kg patient).
- Start infusion at 0.05 mg/kg/min (e.g., 3.5 mg/min for a 70-kg patient).
- If ineffective, the infusion may be up-titrated as follows:
  - i) Reload with 0.5 mg/kg IV
  - ii) Increase the infusion rate by 0.05 mcg/kg/min
- Up-titration may be performed about every half hour as needed (up to a maximal infusion rate of 0.2 mg/kg/min).

**diltiazem**

**general comments on diltiazem**

- Diltiazem may be useful in patients who are hypertensive or more hemodynamically robust, especially patients who have been chronically treated with diltiazem as outpatients.
- In the only RCT involving diltiazem infusions among ICU patients, 30% of patients treated with a diltiazem infusions developed hypotension which required the diltiazem to be discontinued. ([11395591](https://pubmed.ncbi.nlm.nih.gov/11395591/))

**diltiazem dosing**

- (1) Initial loading dose
  - Start with 0.25 mg/kg (max dose 25 mg) IV bolus.
  - If inadequate response and blood pressure remains adequate, may re-bolus once after 15 minutes.
- (2) Infusion
  - Infuse at a rate of 2.5-15 mg/hour.
  - Consider a reduction in the infusion rate after the target heart rate is reached. Especially with hepatic dysfunction, diltiazem may accumulate.
- (3) Transition to oral
  - Start diltiazem extended release (diltiazem-ER) at a dose roughly equal to 10\[3(\text{infusion rate in mg/hr}) +3\]. When in doubt, round down. For example:
    - 3 mg/hour -> 120 mg/day diltiazem-ER
    - 5 mg/hour -> 180 mg/day diltiazem-ER
    - 7.5 mg/hour -> 260 mg/day diltiazem-ER
    - 10 mg/hour -> 330 mg/day diltiazem-ER
    - 15 mg/hour -> 480 mg/day diltiazem-ER
  - Wean off infusion over the next few hours.

**anticoagulation?**

**scope of the problem**

- Critically ill patients often have systemic inflammation, and may increase their risk for thromboembolic stroke compared to outpatients.
- Critically ill patients have numerous risk factors for bleeding (e.g., renal dysfunction, use of antiplatelet medications, invasive procedures).
- Risk scores for bleeding and thrombosis haven't been validated in the ICU (e.g., CHAD-VASC, HAS-BLED). This makes it difficult to balance the risks versus benefits of anticoagulation accurately.

**available evidence on new-onset AF**

- There is no high-quality evidence to support anticoagulation for patients with new-onset AF secondary to critical illness.
- Retrospective studies suggest that anticoagulation for atrial fibrillation secondary to critical illness increases the bleeding risk without reducing the incidence of stroke. ([30089566](https://pubmed.ncbi.nlm.nih.gov/30089566/)) This finding appears robust, even if propensity matching is used in attempts to remove confounding variables. ([27487456](https://pubmed.ncbi.nlm.nih.gov/27487456/))
- A survey of intensivists in the UK found that most (64%) don't routinely anticoagulate patients with new-onset atrial fibrillation. ([28929012](https://pubmed.ncbi.nlm.nih.gov/28929012/))

**current practice?**

https://emcrit.org/ibcc/af/
New-Onset AF (NOAF)
- For most patients with new-onset AF due to critical illness, the risks of anticoagulation seem to generally outweigh potential benefits. (32968991, 29627355) However, this remains largely unknown. For some patients at high stroke risk and low bleeding risk, anticoagulation might be beneficial.
- The Canadian 2020 guidelines state that "In some cases, such as sepsis, the acute administration of intravenous anticoagulation increases the risk of bleeding, but does not appear to reduce the risk of ischemic events." (33191198)
- If the AF persists for weeks, then it becomes increasingly likely that the patient may develop ongoing AF. In this situation, anticoagulation may become beneficial.

Chronic AF
- For patients who appear to have chronic AF, anticoagulation may be considered similarly to that of outpatients (e.g., based on CHAD-VASC scores).
- Among patients with long-standing AF who have been previously on anticoagulation, this will often be continued (unless it is necessary to hold it for a procedure or bleeding).

Flutter is usually a short-lived transitional state, which either degenerates into atrial fibrillation or converts to sinus rhythm. As a transitional state, atrial flutter may closely resemble new-onset atrial fibrillation (NOAF).
- The management of atrial flutter is overall very similar to that of AF. However, flutter may lend itself to more of a rhythm-control strategy:
  - Heart rate control is often difficult in flutter, as the heart rate has a tendency to get "stuck" at ~150 (2:1 transmission through the AV node).
  - Cardioversion of atrial flutter is often easier and more successful than cardioversion of AF.

summary
Always look for other causes of instability among patients with AF and shock or difficulty controlling the ventricular rate. In some patients, this may be a "sinus tach equivalent" which is due to an underlying problem (e.g., sepsis, PE). In such patients, successful management depends on treating the underlying problem. Merely trying to squash the heart rate can be dangerous among these patients, as it may suppress a compensatory tachycardia.

ACLS guidelines typically recommend immediate cardioversion for unstable patients with AF. However, among critically ill patients this has a low success rate.

references


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