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Emergency Department Management of Recent-Onset Atrial Fibrillation

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ABSTRACT
Atrial fibrillation (AF) is the most common tachyarrhythmia managed in the emergency department (ED). Visits to the ED for a presentation of AF have been increasing in recent years, with an admission rate that exceeds 60% in the United States and contributes substantially to health care costs. Recent-onset AF—defined as symptom onset less than 48 hr—is a common ED presentation for which rate control or acute electrical or pharmacological cardioversion may be appropriate treatment modalities depending on patient-specific circumstances. The focus of this review is to discuss the current recommendations regarding the management of recent-onset nonvalvular AF in the ED, discuss medication administration considerations, and identify implementation strategies in the ED to optimize throughput and reduce hospital admissions. **Key words:** atrial fibrillation, emergency medicine, procainamide, rhythm

ATRIAL FIBRILLATION (AF) is the most common tachyarrhythmia for which patients present to the emergency department (ED; January et al., 2014). Visits to the ED for a presentation of AF have been increasing in recent years, with an admission rate of 64% in one analysis (McDonald, Pelletier, Ellinor, & Camargo, 2008). For those who are admitted, the average hospital stay is approximately 4 days at a mean hospital cost of $7,000 per patient (Dell'Orfano, Patel, Wolbrette, Luck, & Naccarelli, 1999). Most AF management in the ED occurs in recent-onset nonvalvular AF in those with a known and unknown history of this condition (Stiell, Macle, & CCS Atrial Fibrillation Guidelines Committee, 2011). The focus of this review is to discuss the current recommendations regarding the pharmacotherapy management of recent-onset nonvalvular AF in the ED, discuss medication administration considerations, and identify ED implementation

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strategies to optimize throughput and reduce hospital admissions.

Atrial fibrillation is a supraventricular tachyarrhythmia that characteristically presents with irregular R-R intervals and an absence of distinct repeating P waves. The etiology may not be readily apparent, and patients may present asymptomatically or symptoms can be profound, including fatigue, palpitations, syncope, dyspnea, hypotension, and even worsening heart failure leading to hemodynamic instability (January et al., 2014). Regardless of symptoms, all patients with AF are at an increased risk of cerebral infarction secondary to the formation of atrial thrombi. Atrial fibrillation can be classified as paroxysmal, persistent, or permanent (January et al., 2014). Paroxysmal AF describes AF that terminates spontaneously, or with intervention, within 7 days of onset. Persistent AF is continuous for greater than 7 days, and permanent AF characterizes instances in which the patient and the provider have made a conscious decision to stop further attempts to restore normal sinus rhythm. Atrial fibrillation can also be classified on the basis of the presence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve, or mitral valve repair (valvular AF).

Patients presenting to the ED with recent-onset AF should be rapidly triaged and evaluated for hemodynamic stability (Stiell et al., 2011). It is important to ascertain any underlying cause and conduct a complete review of the patient's past medical history and current medication regimen. These factors will provide critical information to assist in determining the most appropriate therapeutic strategy for treating the patient in the ED and the subsequent need for hospital admission.

UNSTABLE PATIENTS

Although uncommon, patients presenting with AF who are hemodynamically unstable (e.g., active ischemia, hypotension, severe heart failure) should emergently undergo synchronized electrical cardioversion (January et al., 2014). Repeated electrical cardioversions should be considered if sinus rhythm can be maintained for a clinically meaningful period between procedures. The priority should be to support hemodynamic stability. In unstable patients with a high risk of stroke, anticoagulation should be considered immediately before or after electrical cardioversion.

STABLE PATIENTS

In hemodynamically stable patients presenting with recent-onset AF, a rate control or cardioversion strategy (pharmacological or electrical) can be considered (Stiell et al., 2011). A rate control strategy focuses on reducing the heart rate to improve tachycardia-related symptoms such as palpitations or dyspnea and reduce the risk of tachycardia-associated heart failure. β-Blockers (BBs) or nondihydropyridine calcium channel blockers (CCBs) are used to target a resting heart rate of 80–100 beats per minutes at rest (January et al., 2014; Stiell et al., 2010). A cardioversion strategy on the other hand includes electrical cardioversion or the use of antiarrhythmic medications in an attempt to restore or maintain sinus rhythm (January et al., 2014). Although the establishment of normal sinus rhythm may appear to be a logical and perhaps superior goal in recent-onset AF, data suggest that there are no differences in the risk of stroke, death, or any adverse outcomes between these two strategies (Carlsson et al., 2003; Van Gelder et al., 2002; Wyse et al., 2002). Hence, the appropriate treatment strategy should be based on patient-specific comorbidities, timing of symptom onset, and following shared decision-making between the provider and the patient.

RATE CONTROL STRATEGY

One advantage of a rate control strategy is that it can be applied regardless of the timing of symptom onset (January et al., 2014). Importantly, rate control is the only appropriate therapy in patients with permanent AF, elderly patients, patients with onset greater

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than 48 hr, patients with history of valvular disease, or patients with recent transient ischemic attack (TIA)/stroke. In a rate control strategy, BBs or CCBs reduce atrioventricular (AV) conduction and prolong AV node refractoriness, which reduces the rate of AF but does not alter the rhythm (January et al., 2014).

Within the broad class of BBs, metoprolol is often considered the BB of choice secondary to its β_1 receptor specificity in the heart, sparing β_2 receptor action that could lead to hypotension or a worsening of the patient's clinical status (see Table 1; January et al., 2014; Stiell et al., 2010). Furthermore, metoprolol is available both as intravenous and oral formulations, allowing for its emergent implementation in the ED, followed by a rather natural transition to oral therapy on an outpatient basis. β-Blockers have been shown to be effective in approximately 70% of patients in this setting (Olshansky et al., 2004). It is typically given as an intravenous bolus over 2 min of 2.5–5 mg for up to three doses (January et al., 2014; Stiell et al., 2010). Patients should be monitored for bradycardia and hypotension following administration.

Calcium channel blockers exist in two forms, dihydropyridine CCBs (e.g., amlodipine, nicardipine) and nondihydropyridine CCBs (e.g., diltiazem, verapamil) (January et al., 2014). In this setting, only the nondihydropyridine CCBs are recommended because of their heart rate-lowering effects. Within this group, diltiazem is the preferred agent due to its ability to reduce heart rate with a minimal impact on blood pressure (Allen, 2003). Diltiazem has been shown to be effective in approximately 83% of patients with AF (Ellenbogen, Dias, Plumb, Heywood, & Mirvis, 1991). Similar to metoprolol, it is available in both oral and intravenous forms, allowing for an easier transition of care. The recommended dosing of intravenous diltiazem is 0.25 mg/kg over 2 min, with an optional subsequent bolus dose of 0.35 mg/kg over 2 min if initial control is not achieved. This is then followed by a continuous infusion of 5–15 mg/hr (January et al., 2014; Stiell et al., 2011). The most common side effects of therapy are hypotension and bradycardia.

Selection between these two rate control classes should largely be based upon individual patient characteristics and the patient's past medical history (January et al., 2014; Stiell et al., 2011). For example, metoprolol is the preferred rate control agent in the setting of nondecompensated heart failure (January et al., 2014). The use of BBs does have the potential to cause acute decompensation of heart failure, exacerbate chronic obstructive pulmonary disease, and accelerate conduction in patients with preexcitation (January et al., 2014). Secondary to their negative inotropic effects, diltiazem and verapamil should not be used in patients with left ventricular systolic dysfunction (BBs preferred) or decompensated heart failure (electrical cardioversion preferred) (January et al., 2014). However, they may be used in patients with heart failure and preserved left ventricular systolic function. They also should not be used in patients who have preexcitation secondary to accelerated cardiac conduction (e.g., Wolff–Parkinson–White syndrome). In otherwise healthy individuals, diltiazem was found in one study to be 40% more successful in achieving a target heart rate than metoprolol at 5 min, and 50% more successful at 30 min, with a nonsignificant difference in the incidence of adverse effects in both groups (Fromm et al., 2015).

Digoxin had previously been a mainstay of therapy in the acute management of AF because it slows the ventricular activity through its suppression of AV node conduction. However, its onset of action is up to 6 hr—making it less ideal for use in the ED—and has a relatively large adverse effect profile (January et al., 2014). With more effective alternatives available, it is no longer considered a first-line therapy and its primary utility is in those with concomitant hypotension due to its minimal impact on blood pressure. Given its adverse effect profile, its use should occur in consultation with a specialist (January et al., 2014; Stiell et al., 2011).

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Table 1. Pharmacotherapy for the emergency department management of recent-onset atrial fibrillation

Medication	Mechanism of action	Dose	Frequency/titration	Side effect monitoring
Rate control agents				
Metoprolol	β-blockade	2.5–5 mg intravenous bolus over 2 min	Every 2 min until target HR achieved (max 15 mg)	Bradycardia; hypotension
Diltiazem	Calcium channel blockade	0.25 mg/kg intravenous bolus over 2 min	Optional dose of 0.35 mg/kg if target HR not achieved after 15 min	Bradycardia; hypotension
Digoxin	Suppression of atrioventricular node conduction	0.25 mg intravenous bolus over 5 min	May repeat dose every 2 hr (max 1.5 mg)	Bradycardia; digitalis toxicity
Rhythm control agents				
Procainamide	Blocks sodium channels	15–17 mg/kg intravenously over 60 min; alternatively, 1,000 mg intravenously over 60 min	N/A	Hypotension; bradycardia; torsades de pointes
Flecainide	Blocks sodium channels	Less than 70 kg: 200 mg PO More than 70 kg: 300 mg PO	N/A	Headache; dizziness; tremor
Propafenone	Blocks sodium channels	Less than 70 kg: 450 mg PO More than 70 kg: 600 mg PO	N/A	Hypotension; QRS widening; nausea; metallic taste in mouth
Ibutilide	Prolongs action potential in cardiac tissue	Less than 60 kg: 0.01 mg/kg intravenously over 10 min More than 60 kg: 1 mg intravenously over 10 min	N/A	Hypotension; bradycardia; torsades de pointes
Amiodarone	Prolongs action potential in cardiac tissue; nonselective inhibition of α- and β-receptors	150 mg in 10 min, followed by 1 mg/min for 6 hr and then 0.5 mg/min for 18 hr	N/A	Phlebitis; hypotension; bradycardia

Note. From Stiell et al. 2011; January et al., 2014. HR = heart rate; N/A = not applicable; PO = orally.

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ACUTE CARDIOVERSION STRATEGY

An acute cardioversion strategy in appropriate patients with recent-onset AF may be advantageous to rate control because it restores sinus rhythm, which eliminates AF symptoms. This includes electrical and pharmacological cardioversion. Several studies have shown that when a cardioversion strategy is selected, more patients are safely discharged from the ED than those with a rate control strategy (Stiell et al., 2007, 2010, 2017). In the United States, where rate control is the most common strategy regardless of timing of symptom onset, the average admission rate for AF approaches 70%. This contrasts with several Canadian and U.S. studies that found that an acute cardioversion strategy in patients with recent-onset AF resulted in 85%–97% of patients discharged. Thus, in many cases of recent-onset AF, an acute cardioversion strategy may safely reduce hospital admissions (Cohn, Keim, & Yealy, 2013; Scheuermeyer et al., 2012; Vinson, 2012). One study using this strategy documented sinus rhythm conversion rates of 80.1%, ED discharge rates of 91%, and 30-day adverse event rates of 10.5% (Stiell et al., 2017; Vinson, Hoehn, Graber, & Williams, 2012; White, Heller, Kahoud, Slade, & Harding, 2015). A similar study found a 94% cardioversion rate compared with historical cardioversion rate of 28% and found a hospital discharge rate of 93% compared with a historical rate of 40% ($p < 0.001$; White et al., 2015).

The acute cardioversion strategy is not appropriate for all AF presentations. Acute cardioversion is contraindicated in patients with a mechanical heart valve, history of rheumatic heart disease, recent TIA or stroke, significant signs of heart failure, or an alternative primary illness (e.g., sepsis). To reduce the risk of stroke, it should not be used in patients with AF of more than 48 hr or of unknown duration. In patients taking anticoagulation therapy for established AF, cardioversion can be attempted if compliant on anticoagulation for at least 3 weeks. Patients taking warfarin must additionally have a therapeutic international normalized ratio (January et al., 2014; Stiell et al., 2011). Several factors increase acute cardioversion success including younger age, fewer comorbidities, and first or infrequent episodes of AF (January et al., 2014). In contrast, acute cardioversion success is less likely in elderly patients, those with many comorbidities, and those with frequent episodes of AF (January et al., 2014). Studies have shown that when an acute cardioversion strategy is used within 48 hr of onset, there is a less than 1% risk of stroke or death (Cohn et al., 2013; Stiell et al., 2010, 2017).

As previously mentioned, electrical cardioversion is always the modality of choice in the setting of a hemodynamically unstable patient. However, it may also be optimal in a stable patient when cardioversion is desired. It has a substantially higher success rate (89%–96%) than pharmacological cardioversion (50%–83%) and has an immediate result rather than the delay associated with waiting for the pharmacological action of a medication (Stiell et al., 2011; Stiell, Healey, & Cairns, 2015). Electrical cardioversion has fewer side effects and, unlike several pharmacological agents, can be used in those with structural or functional heart disease (January et al., 2014). However, electrical cardioversion is not without risks. Procedural sedation prior to electrical cardioversion has infrequent but serious potential adverse effects including hypotension and respiratory depression. In addition, although electrical cardioversion is rarely if ever dangerous as a therapy, many patients express severe preprocedural anxiety associated with the thought of an electrical "shock" (January et al., 2014; Stiell et al., 2011).

Alternatively, pharmacological cardioversion eliminates the need for procedural sedation and its associated risks. From a patient comfort perspective, this alternative may be less painful and unpleasant. Each antiarrhythmic has unique mechanisms, onset of actions, and side effect profiles (January et al., 2014; Stiell et al., 2011). The ideal agent in the ED setting should have a rapid onset of action, require limited monitoring, and have minimal

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adverse effects. The selection of the appropriate agent for each patient should be based on the comorbidities and past medical history of the patient.

Procainamide has been used with increasing frequency in recent-onset AF (Stiell et al., 2010). This Class IA sodium channel blocker has demonstrated cardioversion rates in the ED of 58%–65%, typically in less than 60 min (Madrid et al., 1993; Michael, Stiell, Agarwal, & Mandavia, 1999). It is given as a single intravenous dose over 60 min at a weight-based dose of 15–17 mg/kg or a flat-based dose of 1,000 mg (Stiell et al., 2010, 2011). The most common associated side effect with therapy has been transient hypotension (5%–8%).

Flecainide and propafenone are commonly used agents in the outpatient setting with similar mechanisms of action (Stiell et al., 2011). Both block sodium channels and slow conduction in addition to exerting a negative inotropic effect. The reported success of flecainide in this setting is 51%–72% and that of propafenone is 56%–83% in 3–8 hr (Boriani, Diemberger, Biffi, Martignani, & Branzi, 2004; Boriani, Martignani, Biffi, Capucci, & Branzi, 2002; Khan, 2001). This delayed onset of action limits its usability in a busy ED setting where throughput is critical. In addition, these agents should not be used in patients with structural or functional heart disease, heart failure, sick sinus syndrome, bundle branch blocks, or AV blocks (January et al., 2014). Flecainide is typically given as an oral dose of 300–400 mg and propafenone is given at a dose of 450–600 mg orally (Stiell et al., 2011). Common side effects of both agents include hypotension and bradycardia.

Ibutilide and amiodarone are antiarrhythmics that work primarily through the prolongation of the action potential within the heart (January et al., 2014; Stiell et al., 2011). Although evidence supports the use of ibutilide in the ED setting, the success rates are lower than those with other therapies (27%–40%) and its utility is challenging because of the requirement of an extended monitoring time frame of at least 4 hr (Ellenbogen et al., 1996; Kowey, Marinchak, Rials, & Filart, 1998; Kowey, VanderLugt, & Luderer, 1996; Vinson et al., 2018). It is typically administered intravenously at a dose of 1–2 mg over 10–20 min and to minimize side effects patients are often pretreated with intravenous magnesium sulfate (Stiell et al., 2011). Up to 3% of patients may experience torsades de pointes. Amiodarone is a commonly used agent; however, it has similarly low conversion rate, has a substantial side effect profile, and requires the patient to receive multiple doses over an extended period of time, complicating its use in the ED and typically resulting in hospital admission (January et al., 2014; Stiell et al., 2011). It does however provide an option for those with left ventricular dysfunction who are not eligible for other therapies. It is often given as an intravenous bolus of 150 mg over 10 min, followed by an intravenous infusion of 1 mg/min for 6 hr and then 0.5 mg/min for 18 hr; however, multiple dosing schemes exist (January et al., 2014; Sardar, Saeed, & Kowey, 2014). Amiodarone does have a substantial risk of hypotension and bradycardia, associated with both the dose and the infusion rate.

Although not technically an antiarrhythmic, magnesium can be an adjunctive agent for AF as it reduces conduction through the AV node (Ganga, Noyes, White, & Kluger, 2013; January et al., 2014; Rasmussen & Thomsen, 1989). In addition, intracellular magnesium deficiency has been noted in patients with arrhythmias (Shah et al., 2008). Studies have demonstrated that the prophylactic use of magnesium in combination with ibutilide has increased the conversion rates associated with this therapy and decreased the incidence of side effects (Kalus et al., 2003; Tercius, Kluger, Coleman, & White, 2007). If utilized in this setting, the typical dose is 1–2 g of magnesium sulfate administered intravenously as a rapid infusion (Stiell et al., 2011). The most common side effect is hypotension, typically associated with the infusion rate.

ANTICOAGULATION

Patients with AF are at an increased risk of ischemic stroke. Therefore, all patients

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presenting to the ED who are not already on anticoagulation therapy should be evaluated for stroke risk by the CHA_2DS_2-VASc score. This risk stratification tool assesses 1-year risk of stroke. Low-risk patients (score less than 1) are considered low risk and should not be anticoagulated. High-risk patients (score 2 or more) should be anticoagulated. Patients with a score of 1 should undergo shared decision-making with their provider, and either an anticoagulant or low-dose aspirin should be considered. (January et al., 2019). Multiple anticoagulation options can be utilized for patients with a high CHA_2DS_2-VASc score. Warfarin, following a low-molecular-weight heparin (LMWH) bridge, has been the mainstay of therapy for many years. More recently, a spectrum of direct oral anticoagulants (e.g., apixaban, rivaroxaban) has been used with increasing frequency. Various patient-specific factors influence agent selection, including renal dysfunction and the presence of mechanical heart valves. In many cases, these newer agents have displayed a superior safety and, at worst, equivalent efficacy, compared with warfarin. In the most recent American Heart Association guidelines, they are actually recommended as first-line agents over warfarin (January et al., 2019). In the ED setting, patients with an increased risk of stroke who undergo electrical or pharmacological cardioversion should be administered anticoagulation prior to, or immediately after, cardioversion with intravenous heparin, LMWH, oral factor Xa inhibitor (e.g., rivaroxaban, apixaban), or an oral direct thrombin inhibitor (e.g., dabigatran). In addition, high-risk patients with stroke should receive long-term anticoagulation following the restoration of normal sinus rhythm for at least 4 weeks (January et al., 2019).

DISCHARGE MANAGEMENT

For patients who are successfully rate controlled or cardioverted and stable for discharge, a rate control agent (e.g., metoprolol, diltiazem) should be prescribed. If already taking a rate control agent, providers should consider increasing the patient's home dose in order to prevent recurrence of AF. In addition, if the CHA_2DS_2-VASc score is elevated, patients should be prescribed an anticoagulant (e.g., apixaban, rivaroxaban; Stiell et al., 2011). Prior to discharge, appropriate counseling on medication adverse effects is critical, especially bleeding risk.

Despite the busy, often chaotic, emergency setting, the importance of assessing patients' ability to afford and comply with prescription medications as well as follow-up with an outpatient provider cannot be overstated. For instance, warfarin is inexpensive but requires relatively expensive LMWH bridging and frequent monitoring. On the other hand, despite the higher cost of direct oral anticoagulants, the dosing is easier and they do not require frequent laboratory monitoring. Fortunately, most direct oral anticoagulant manufacturers provide financial assistance programs to assist those who are unable to afford their medications. Emergency departments should partner with case managers, social workers, and pharmacists to ensure that these resources are in place for patients.

Importantly, one study noted that there was an underprescribing of anticoagulation on discharge in patients with an elevated CHA_2DS_2-VASc score (White et al., 2015). This emphasizes the importance of developing a standardized clinical pathway that leverages assistance from a multidisciplinary team who can help ensure that patients' outpatient management is optimized. A simplified sample workflow is depicted in Figure 1.

CONCLUSION

For patients who present to the ED in AF with hemodynamic instability, emergent electrical cardioversion and anticoagulation consideration is indicated. In those patients presenting with recent-onset nonvalvular AF, both rate control and rhythm control strategies can be pursued. The selection of the individual strategy should be based on individual patient characteristics and the goals of care for the patient. Although a rate control strategy is a

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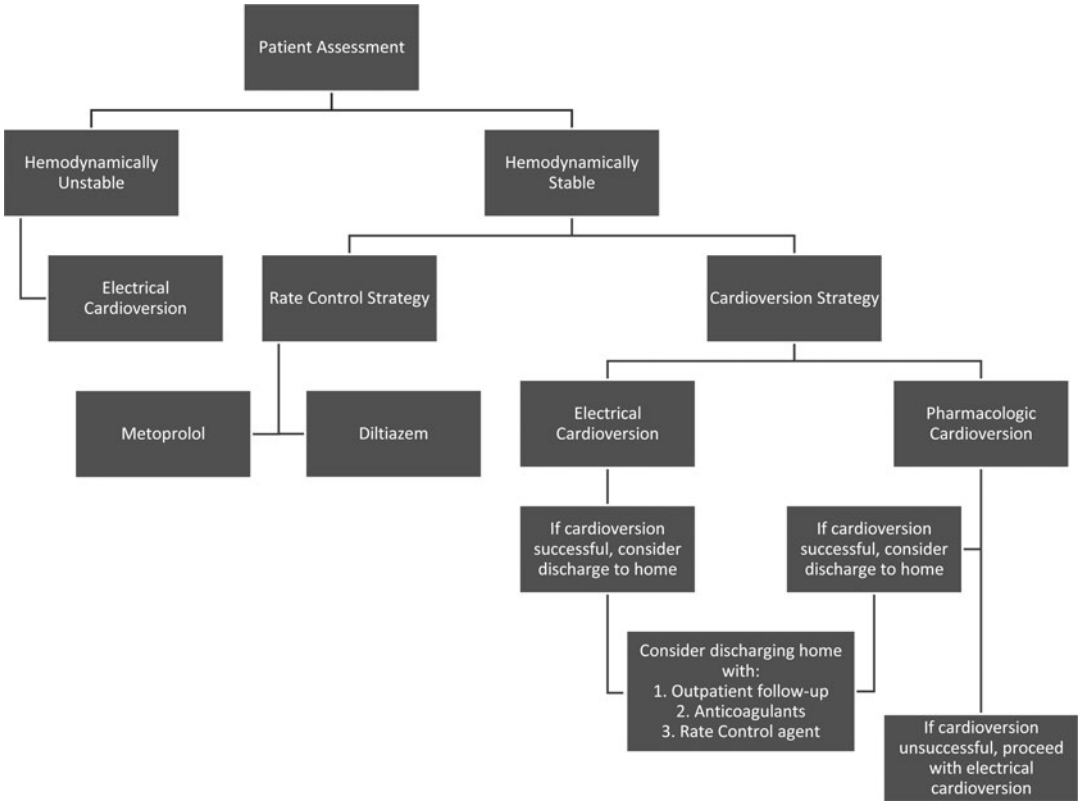

Figure 1. Sample atrial fibrillation workflow.

safer and more universally applicable strategy, a successful cardioversion strategy allows for the patient to be potentially discharged from the ED. For patients who are discharged, it is important to provide the patient with appropriate discharge medication counseling, financial resources, and outpatient follow-up.

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