„Cross-border cooperation in the prevention and complex treatment of cardiovascular and peripheral vascular diseases in Békés-Timis counties"
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Acute heart failure
Diagnostoc and management protocol

1. Definition, epidemiology

Acute heart failure has wide-reaching implications not only in terms of mortality and morbidity for affected individuals but also for the infrastructure required to provide care for these patients been the leading cause of hospitalization in patients over 65 years old. Although estimates vary depending on the study population, the prevalence of HF is approximately 1–2% and rises to >10% among people over the age of 70 years. [1] 4 weeks mortality is reported up to 40-60% in cardiogenic shock and 15% in other forms of heart failure. Heart failure represents a diagnostic end also therapeutic emergency.

Although estimates vary depending on the study population, the prevalence of HF is approximately 1–2% and rises to >10% among people over the age of 70 years.[1] This numbers may underestimate the true impact of disease as the estimated prevalence of those with asymptomatic left ventricular (LV) systolic dysfunction in those aged over 65 years is 5.5% .[2]

Heart failure is defined as a clinical syndrome characterized by a constellation of symptoms such as dyspnea, ankle swelling and fatigue that may be accompanied by signs like elevated jugular venous pressure, pulmonary crackles and peripheral oedema caused by a structural and/or functional cardiac dysfunction, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during structure. The underlying cardiac is frequently a myocardial abnormality causing systolic and/or diastolic ventricular dysfunction. However, heart failure can be caused by abnormalities of the valves, pericardium, endocardium, heart rhythm and conduction. Identification of the underlying cardiac problem is crucial for therapeutic reasons, as the precise pathology determines the specific treatment used (e.g. valve repair or replacement for valvular disease, specific pharmacological therapy for HF with reduced EF, reduction of heart rate in tachycardiomyopathy, etc.).

Acute heart failure (AHF) refers to rapid onset or worsening of symptoms and/or signs of HF.[3] It is often a potentially life-threatening condition, requiring hospitalization, and emergency treatment is aimed predominantly at managing fluid overload and hemodynamic compromise. The AHF term includes patients presenting for the first time with typical symptoms and signs of heart failure (de novo AHF) and also, more frequently, those with worsening of their pre-existing heart failure (acute decompensated heart failure).

De novo AHF occurs when there is a sudden increase in intracardiac filling pressures and/or acute myocardial dysfunction which can lead to decreased peripheral perfusion and

pulmonary oedema. Acute myocardial dysfunction (ischaemic, inflammatory or toxic), acute valve insufficiency or pericardial tamponade are among the most frequent acute primary cardiac causes of AHF.[4]

Decompensation of chronic HF (ADHF) can occur without known precipitant factors, but more often with one or more factors, such as infection, uncontrolled hypertension, rhythm disturbances or non-adherence with drugs/diet (table 1). Unlike de novo AHF, patients with ADHF tend to present with signs and symptoms of congestion and fluid retention (weight gain, exertional dyspnea, orthopnea, dependent oedema) rather than with pulmonary oedema or cardiogenic shock that characterize acute LV systolic dysfunction as a result of the neuro-humoral compensatory mechanisms which act to maintain a hemodynamic status quo despite worsening LV function. Decompensation occurs when the balance tips towards fluid overload as the compensatory mechanisms prove inadequate or indeed fail all together (Demographics, clinical characteristics, and outcomes of patients hospitalized for decompensated heart failure: observations from the IMPACT-HF registry.[5]

Table 1**.** Precipitating factors of AHF

Acute coronary syndrome (ACS)
Tachyarrhythmia
Excessive rise in blood pressure
Bradyarrhythmia
Infection
Non adherence with salt/fluid intake or medication
Drugs (Nonsteroidal anti-inflammatory drugs, corticosteroids, negative inotropic substances)
Surgery and perioperative complications
Pulmonary embolism
Toxic substances (alcohol, recreational drugs)
Cerebrovascular insult
Increased sympathetic drive, stress related cardiomyopathy
Metabolic/hormonal derangements
Acute mechanical cause (myocardial rupture complicating ACS, chest trauma, cardiac intervention, acute native or prosthetic valve incompetence secondary to endocarditis, aortic dissection or thrombosis)

Moreover, 2 main mechanisms causing organ dysfunction in AHF are congestion, which is very frequent, and hypoperfusion, which is rather rare. Classification based on bedside clinical examination evaluates the symptoms or signs of congestion (“dry” vs. “wet”) and/or peripheral hypoperfusion (“warm” vs. “cold”). [4] This approach divides the patients into 4 groups, which helps guide the treatment in the initial phase and also has prognostic value (Figure 1).[5-6] Classifications based on clinical presentation are intended to provide personalized care for the AHF patient and may be helpful to guide therapy in the initial phase and carries prognostic information.

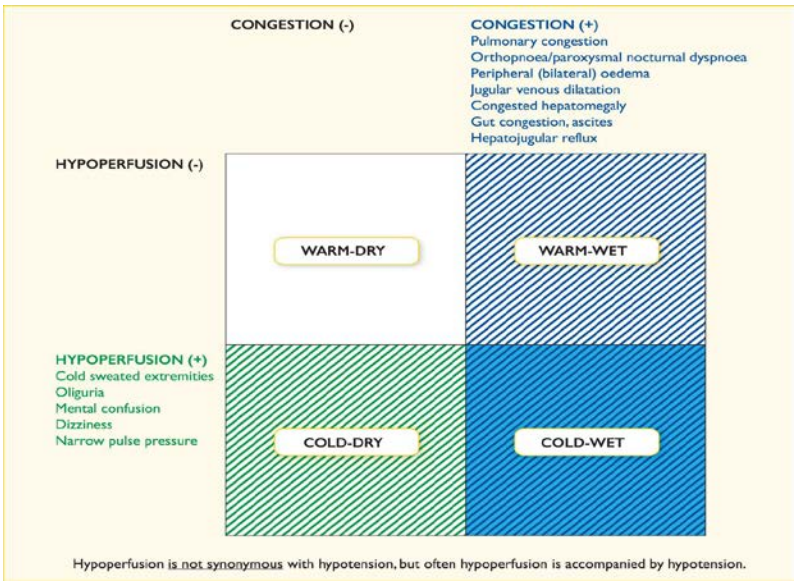

Figure 1. Clinical profiles of patients with acute heart failure based on the presence/absence of congestion and/or hypoperfusion

2. Diagnosis

The diagnostic workup needs to be started as soon as possible, in the pre-hospital setting or in the emergency unit in order to establish the diagnosis in a timely manner and initiate appropriate management. Typically, the first step in the diagnostic workup of AHF is to rule out alternative causes for the patient's symptoms and signs (i.e. pulmonary infection, severe anemia, acute renal failure).

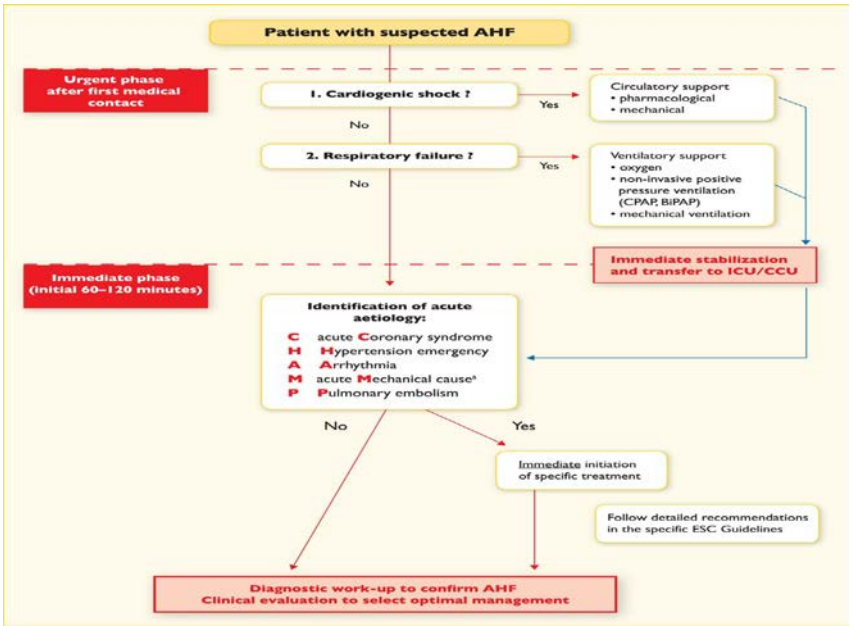

Figure 2. Initial management of a patient with acute heart failure.[5]

Since the sensitivity and specificity of symptoms and signs of heart failure can often be not satisfactory, careful clinical evaluation needs to be followed by these additional investigations:

1. Chest X-ray can reveal pulmonary venous congestion, pleural effusion, interstitial or alveolar oedema and cardiomegaly that are the most specific findings for AHF, although in up to 20% of patients with AHF, chest X-ray is nearly normal.[4] Chest X-ray is also useful to identify alternative non-cardiac diseases that may cause or contribute to the patient's symptoms (i.e. pneumonia, non-consolidative pulmonary infections).
2. ECG is rarely normal in AHF and can identify underlying cardiac disease and potential precipitant factors such as arrythmia or acute myocardial ischemia).
3. An immediate echocardiography is mandatory only in patients with hemodynamic instability and in patients suspected of acute life-threatening structural or functional cardiac abnormalities (mechanical complications, acute valvular regurgitation, aortic dissection). Early echocardiography should be considered in all patients with *de novo* AHF and in those with unknown cardiac function; however, the optimal timing is unknown (preferably within 48 h from admission, if the expertise is available). [4]
4. Laboratory tests:
    - natriuretic peptides (BNP, NT-proBNP) should be measured in all patients with acute dyspnea and suspected AHF to help in the differentiation of AHF from non-cardiac causes of acute dyspnea. Natriuretic peptides have high sensitivity, and normal levels in patients with suspected AHF makes the diagnosis unlikely (thresholds: BNP <100 pg/mL, NT-proBNP <300 pg/mL, MR-proANP <120 pg/mL). On the other hand, elevated levels do not automatically confirm the diagnosis of AHF, there are a wide variety of cardiac and non-cardiac causes that can lead to the increase level of natriuretic peptides .
    - cardiac troponin for detection of ACS as the underlying cause of AHF
    - blood urea nitrogen (BUN) (or urea), creatinine
    - electrolytes (sodium, potassium)
    - liver function tests, thyroid-stimulating hormone (TSH)
    - blood glucose
    - complete blood count
    - D-dimer is indicated in patients with a suspicion of acute pulmonary embolism.
    - arterial blood when a precise measurement of O_2 and CO_2 partial pressures is needed
    - procalcitonin levels in patients with AHF with suspected coexisting infection
    - TSH should be assessed in newly diagnosed AHF

It is recommended to measure creatinine, BUN and electrolytes every 1–2 days while in the hospital and before discharge from the hospital. Pre-discharge assessment of NPs may be considered for prognostic evaluation.

3. Management

AHF is a serious, life-threatening medical condition, that requires a rapid transfer to the nearest hospital, preferably in cardiology department or a coronary care/intensive care unit. Patients with AHF are at high risk of complications during the first hour of the onset of the disease. [7] Therefore, it is increasingly acknowledged that "time-to-treatment" approach, should be considered in AHF to prevent adverse outcomes.

Initial evaluation and continued monitoring of the patient's vital cardiorespiratory functions, including pulse oximetry, blood pressure, respiratory rate and a continuous ECG instituted within minutes, is essential to evaluate whether ventilation, peripheral perfusion, oxygenation, heart rate and blood pressure are adequate. Urine output should also be monitored, although routine urinary catheterization is not recommended.

3.1 Identification of causes leading to heart failure decompensation

- **Acute coronary syndrome.** Patients presenting with ACS should be managed according to the guidelines on non-ST elevation ACS and STEMI. Coexistence of these two clinical conditions (ACS and AHF) always identifies a very-high-risk group where an immediate (i.e. <2 h from hospital admission in patients with NSTEMI, analogous to STEMI management) invasive strategy with intent to perform revascularization is recommended, irrespective of ECG or biomarker findings(4).
- **Rapid arrhythmias or severe bradycardia/conduction disturbance.** Severe rhythm disturbances in patients with AHF and unstable conditions should be immediately corrected with medical therapy, electrical cardioversion or temporary pacing. Electrical cardioversion is recommended if an atrial or ventricular arrhythmia is thought to be contributing to the patient's hemodynamic compromise in order to restore sinus rhythm and improve the patient's clinical condition.
- **Hypertensive emergency.** An immediate reduction in blood pressure should be considered as a primary therapeutic target on order to avoid acute pulmonary oedema. Aggressive blood pressure reduction with i.v. vasodilators in combination with loop diuretics is recommended.
- **Acute mechanical cause underlying AHF.** Echocardiography is essential for diagnosis, and treatment may require circulatory support with surgical or percutaneous intervention.
- **Acute pulmonary embolism.** If acute pulmonary embolism is the cause of shock or hypotension, immediate specific treatment is recommended with primary reperfusion either with thrombolysis, catheter-based approach or surgical embolectomy. Patients presenting with acute pulmonary embolism should be managed according to the appropriate guidelines. [4]

3.2. Criteria for hospitalization in ward vs. intensive care/coronary care unit

- The criteria for Intensive care unit or coronary care department ICU/CCU admission include any of the following:
    - need for intubation (or already intubated)
    - signs/symptoms of hypoperfusion
    - oxygen saturation (SpO_2) <90% (despite supplemental oxygen)

- use of accessory muscles for breathing, respiratory rate >25/min
- heart rate <40 or >130 bpm, SBP <90 mmHg. [8]

3.3. Management of the early phase

3.3.1. Oxygen therapy and/or ventilatory support

Monitoring of transcutaneal oxygen saturation is a first class recommendation of the European Society of Cardiology. Oxygen is recommended in AHF patients and SpO2 <90% or PaO2 <60 mmHg (8.0 kPa) to correct hypoxaemia. Oxygen should not be used as routinely treatment in patients with AHF in non-hypoxemic conditions, as it can causes vasoconstriction and a reduction in cardiac output.[4] Hyperoxygenation in patient with chronic obstructive pulmonary disease may increase ventilation–perfusion mismatch that could cause to hypercapnia. During oxygen therapy, acid–base balance and transcutaneous SpO_2 should be monitored.

Non-invasive positive pressure ventilation includes both continuous positive airway pressure (CPAP) and bi-level positive pressure ventilation (PPV). Bi-level PPV also allows inspiratory pressure support that improves minute ventilation. CPAP is a feasible technique in the pre-hospital setting, because it is simpler than pressure support positive end-expiratory pressure (PS-PEEP) and requires minimal training and equipment and can also be continued in hospital in case of acidosis and hypercapnia, particularly in those with a previous history of COPD or signs of fatigue.

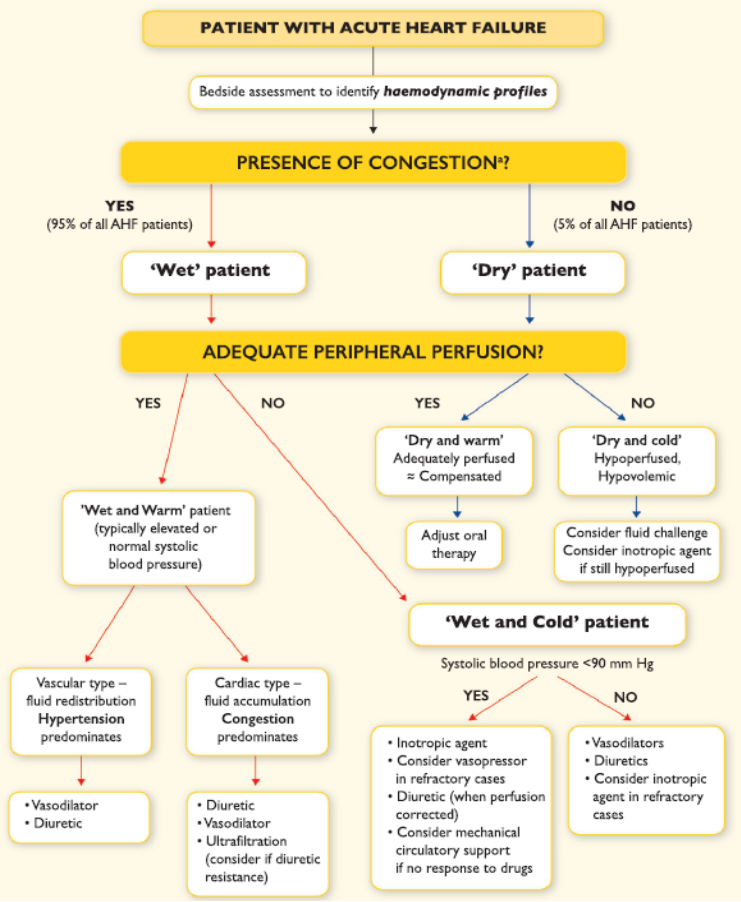

Figure 3. European Society of cardiology recommendation for the management of patients with acute heart failure based on clinical profile during an early phase.[4]

3.3.2. Pharmacotherapy

Diuretics

The decongestive treatment should be tailored according to the hemodynamic phenotype and the underlying pathophysiology and administered as soon as possible after presentation to increase its success. Diuretics increase renal salt and water excretion and have some vasodilatory effect. In patients with AHF and signs of hypoperfusion, diuretics should be avoided before adequate perfusion is attained. The peak effect of intravenous loop diuretics occurs within the first hours, however, to maintain the decongestive effect, the administration of diuretics should continue until euvolaemia is achieved, with three or four daily doses or continuous infusion. The diuretic response should be observed by measuring the urinary volume output and spot urinary sodium content within the first hours after loop diuretic administration. [9] The initial i.v. dose should be at least equal to the pre-existing oral dose used at home.

In patients with congestion, an hourly urine output of <100–150 ml during the first 6 hours and/or a spot urinary sodium content of <50–70 mmol 2 hours after loop diuretic administration generally indicates an inadequate response to diuretics.[9] If an increase of loop diuretic dose does not induce incremental diuresis and/or natriuresis, the addition of a different type of diuretic agent should be considered.

To enhance diuresis or overcome diuretic resistance, options include dual nephron blockade by loop diuretics with thiazide diuretics or natriuretic doses of MRAs. with a careful monitoring to avoid hypokalemia, renal dysfunction and hypovolaemia.[10]

Renal replacement therapy may be considered if there are refractory forms, although beside being effective in volume removal it has showed no improved outcomes. [10]

Diuretic treatments should be continued until euvolemia has been achieved and the medications are switched to an oral form, in the lowest dose that can maintain this status.

Vasodilators

Intravenous vasodilators are the second most often used agents in AHF for symptomatic relief; however there is no robust evidence confirming their beneficial effects. I.v. vasodilators should be considered for symptomatic relief in AHF with SBP >90 mmHg (and without symptomatic hypotension), and symptoms and blood pressure should be monitored frequently during administration. Dosing should be carefully controlled to avoid excessive decreases in blood pressure, which is related to poor outcome. Vasodilators should be used with caution in patients with significant mitral or aortic stenosis. [4]

Vasopressors

Use of an inotrope should be reserved for patients with a severe reduction in cardiac output resulting in compromised vital organ perfusion, which occurs most often in hypotensive AHF. Inotropic agents are not recommended in cases of hypotensive AHF if there is an underlying cause of hypovolemia or a potentially correctable factor. Drugs with prominent peripheral arterial

vasoconstrictor action such as norepinephrine or dopamine in higher doses (>5 μg/kg/min) are given to patients with marked hypotension.

Table 2. Positive inotropes and/or vasopressors used to treat acute heart failure as recommended by the European Society of Cardiology Guideline**.** [4]

Vasodilator	Bolus	Infusion rate
Dobutamine[a]	No	2–20 μg/kg/min (beta+)
Dopamine	No	3–5 μg/kg/min; inotropic (beta+)
		>5 μg/kg/min: (beta+), vasopressor (alpha+)
Milrinone[a,b]	25–75 μg/kg over 10–20 min	0.375–0.75 μg/kg/min
Enoximone[a]	0.5–1.0 mg/kg over 5–10 min	5–20 μg/kg/min
Levosimendan[a]	12 μg/kg over 10 min (optional) [c]	0.1 μg/kg/min, which can be decreased to 0.05 or increased to 0.2 μg/kg/min
Norepinephrine	No	0.2–1.0 μg/kg/min
Epinephrine	Bolus: 1 mg can be given i.v. during resuscitation, repeated every 3–5 min	0.05–0.5 μg/kg/min

Thromboembolism prophylaxis

Thrombo-embolism prophylaxis (e.g. with LMWH) is recommended by de European Guideline in patients not already anticoagulated and with no contra-indication to anticoagulation, to reduce the risk of deep venous thrombosis and pulmonary embolism.

Digoxin

The co-existence of atrial fibrillation and a rapid ventricular rate (>110 bpm) may require digoxin administration. It can be given in boluses of 0.25–0.5 mg i.v. if not used before (0.0625–0.125 mg may be the dose in case of moderate to severe renal dysfunction). However, in elderly patients or in the presence of co-morbidities or other factors affecting digoxin metabolism the maintenance dose may be difficult to estimate theoretically and it should be established based on the measurements of digoxin concentration in peripheral blood.

Opiates

The role of opiates in AHF can be explained by the effect of relieving dyspnea and also of the anxiety. There is no recommendation of a routine use in AHF but they can be considered in patients with pulmonary edema. Nausea, bradycardia, hypotension and respiratory depression can be side effect of this medication.

Renal replacement therapy

Ultrafiltration is not a first line therapy in patients with AHF. [11] It should be considered in patients with refractory congestion, who failed to respond to diuretic. The criteria that may indicate the need for initiation of renal replacement therapy in patients with refractory volume overload are: oliguria unresponsive to fluid resuscitation measures, severe hyperkaliemia (K^+ >6.5 mmol/L), severe acidemia (pH <7.2), serum urea level >25 mmol/L (150 mg/dL) and serum creatinine >300 μmol/L (>3.4 mg/dL).[4]

Intra-aortic balloon pump

The role of intra-aortic balloon pump (IABP) is to support the circulation before surgical correction of specific acute mechanical, in cases of severe acute myocarditis and in a specific type of patients with acute myocardial ischemia or infarction before, during and after percutaneous or surgical revascularization.

Ventricular assist devices

Ventricular assist devices and other forms of mechanical circulatory support (MCS) may be used as a 'bridge to decision' or longer term in selected patients.[4]

Other interventions

Pleurocentesis may be considered if feasible in order to alleviate dyspnea and ascitic paracentesis in order to reduce the symptoms but also for the reduction of intraabdominal pressure that might contribute to reduce the renal flow and filtration.

3.4 Management of patient with cardiogenic shock

Cardiogenic shock is defined as hypotension (SBP <90 mmHg) despite adequate filling status with signs of hypoperfusion. Patient with cardiogenic shock should be rapidly transferred to a tertiary care center which has a 24/7 service of cardiac catheterization, and ICU/CCU that can provide short-term mechanical circulatory support. An immediate comprehensive assessment of a patient with cardiogenic shock should include: ECG and echocardiography. In patients with cardiogenic shock complicating acute coronary syndrome, an immediate coronary angiography is recommended (within 2 h from hospital admission) with an intent to perform coronary revascularization. [12] Invasive monitoring with an arterial line should be also considered. Pharmacologic management consists of an inotropic agent and a vasopressor as needed.

As a vasopressor, norepinephrine is recommended when mean arterial pressure needs pharmacologic support. Dobutamine is the most commonly used adrenergic inotrope. Levosimendan may also be used in combination with a vasopressor.[4] Levosimendan infusion in cardiogenic shock following acute myocardial infarction on top of dobutamine and norepinephrine improved cardiovascular hemodynamics without leading to hypotension.[12] PDE3 inhibitors may be another option, especially in non-ischemic patients.[4]

4. Recommendations regarding monitoring of clinical status of patients hospitalized due to acute heart failure

Standard non-invasive monitoring of heart rate, rhythm, respiratory rate, oxygen saturation and blood pressure is recommended in patients with acute heart failure. It is also recommended to evaluate the signs and also the symptoms that are relevant to HF. Patients should be daily weighted. Frequent, often daily measurement of renal function (blood urea, creatinine) and electrolytes (potassium, sodium) during i.v. therapy and when renin-angiotensin aldosterone system antagonists are initiated is also recommended. [4] Natriuretic peptides measuring at admission and also at discharge can be helpful.

5. Discharge criteria and follow-up recommendation for the high-risk period

Patients admitted with AHF are medically fit for discharge in this conditions. [13]

- haemodynamically stable patients treated with evidence-based oral medication and with stable renal function for at least 24 hours before discharge;
- individualized education and self-care advice performed
- established follow-up plan communicated to the primary care team;
- reviewed by their general practitioner within 1 week of discharge;
- seen by the hospital cardiology team within 2 weeks of discharge if feasible.

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