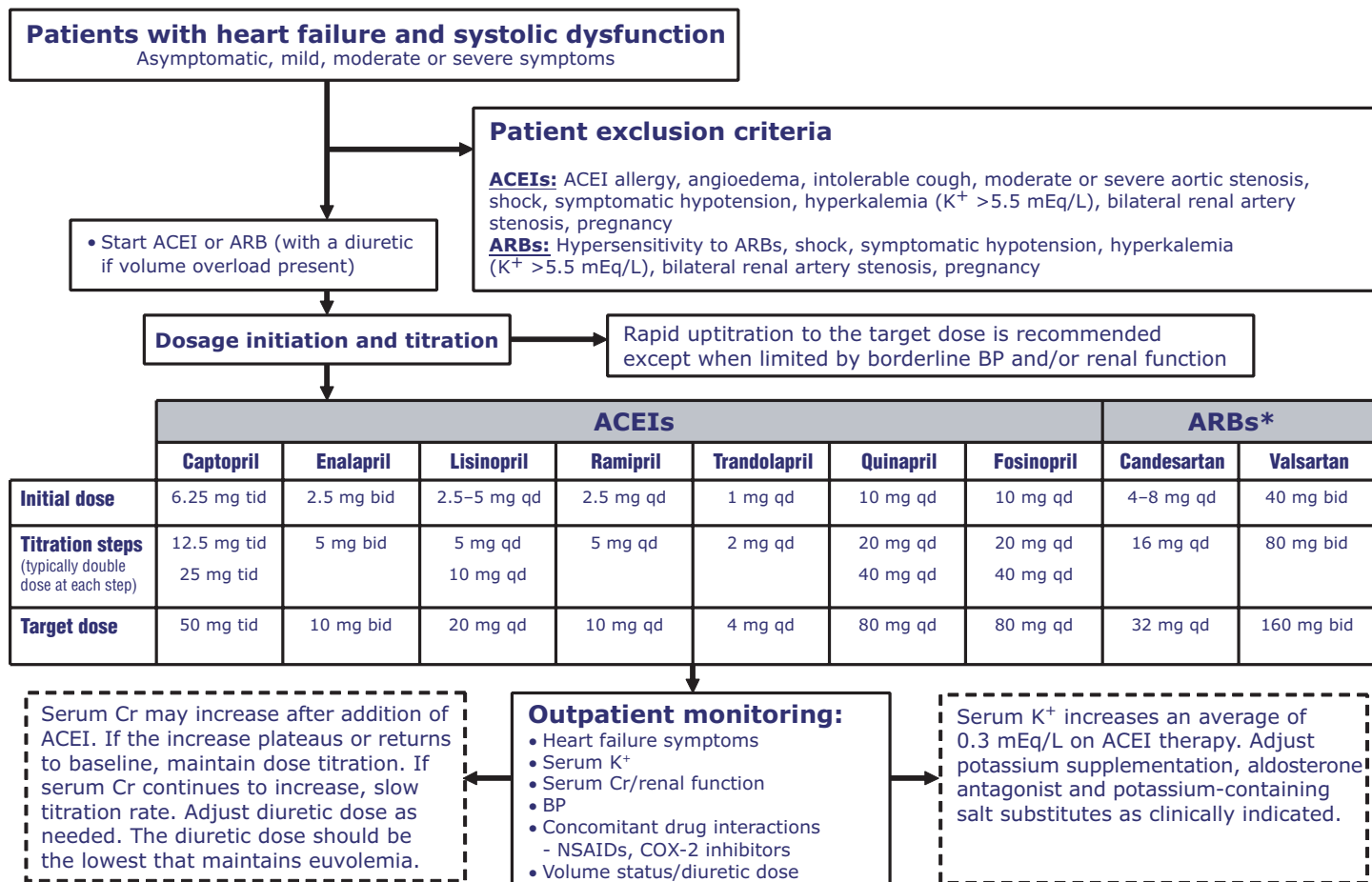


Angiotensin-Converting Enzyme Inhibitor (ACEI)/ Angiotensin Receptor Blocker (ARB) Treatment Algorithm



Note: Careful consideration of patient characteristics and choice of drugs is warranted.

* ARBs are most frequently used in place of ACEIs when side effects limit ACEI use (intolerable cough may occur in as many as 20% of patients receiving ACEIs).

Routine combined use of an ACEI, ARB, and aldosterone antagonist is not recommended for patients with current or prior symptoms of HF and reduced LVEF.

Reference Sources:

- Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005;112:1825-1852.
- Garg R, Yusuf S. Overview of randomized trials of angiotensin-converting-enzyme inhibitors on mortality and morbidity in patients with heart failure. Collaborative Group on ACE Inhibitor Trials. *JAMA*. 1995;273:1450-1456.
- Young JB, Dunlap ME, Pfeffer MA, et al. Mortality and morbidity reduction with candesartan in patients with chronic heart failure and left ventricular systolic dysfunction: results of the CHARM low-left ventricular ejection fraction trials. *Circulation*. 2004;110:2618-2626.
- Pfeffer MA, McMurray J, Velazquez EJ, et al for the Valsartan in Acute Myocardial Infarction Trial Investigators. Valsartan, captopril, or both in myocardial infarction complicated by heart failure, left ventricular dysfunction, or both. *N Engl J Med*. 2003;349:1893-1906.

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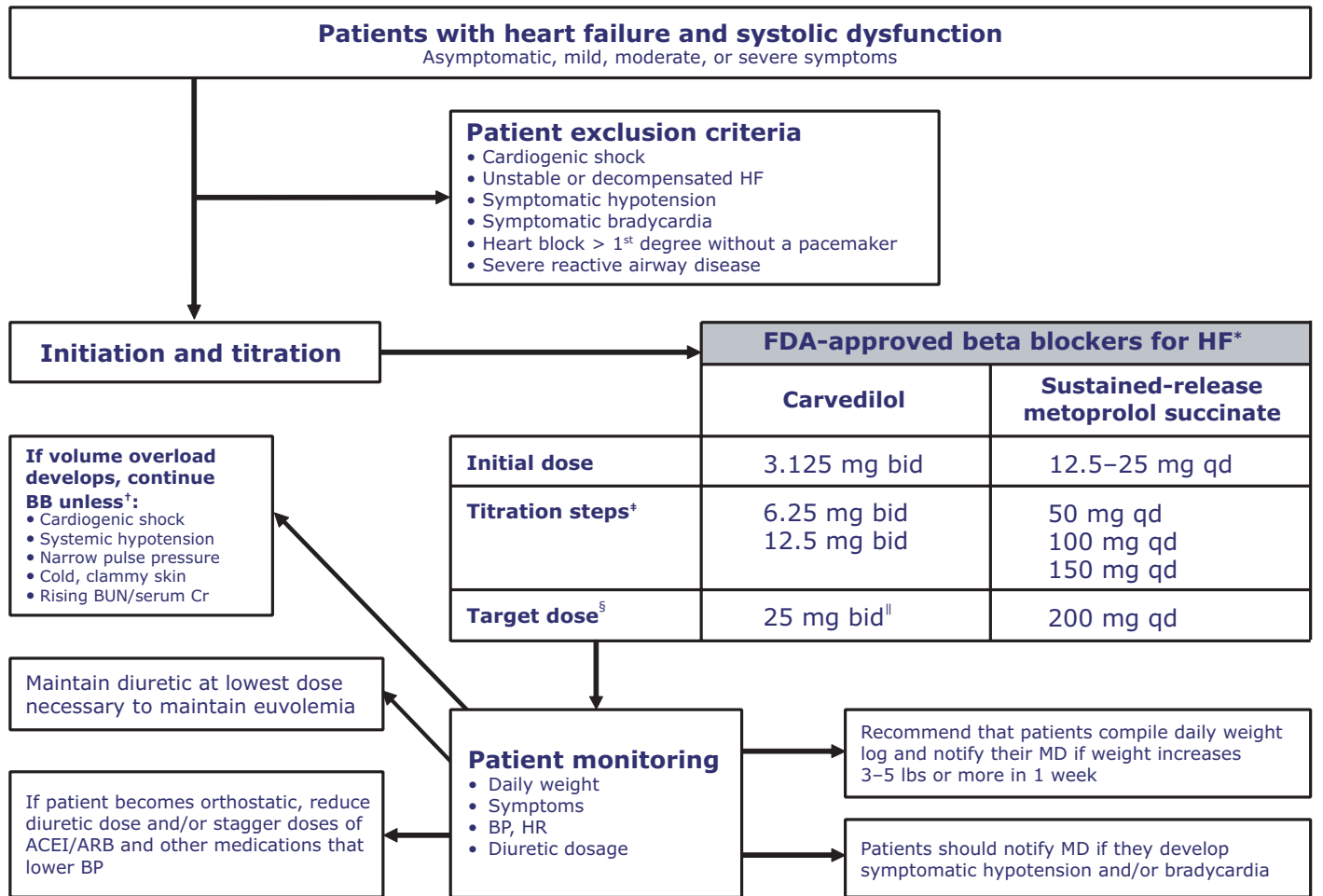
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Beta Blocker Treatment Algorithm



*ACC/AHA 2005 guidelines recommend using only those beta blockers proven to be effective in heart failure (carvedilol, sustained-release metoprolol succinate, and bisoprolol) at the doses studied in large clinical trials. If patient is currently on a beta blocker other than those listed, consider switching.

[†] Applies to both outpatients and those hospitalized for heart failure.

[‡] Beta blocker titration steps are generally at 2-week intervals. BP and HR should be carefully monitored. If SBP is <80 mmHg or HR is <55 bpm, assess the dose and recheck patient carefully for signs of hypoperfusion. Recheck status as needed.

[§] Patients who cannot achieve target dose of the beta blocker should be maintained on the highest tolerated dose.

^{||} For patients weighing >85 kg, carvedilol 50 mg bid may be used.

Reference Sources:

- Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005;112:1825-1852.
- Packer M, Coats AJ, Fowler MB, et al. Effect of carvedilol on survival in severe chronic heart failure. *N Engl J Med*. 2001;344:1651-1658.
- Hjalmarson A, Goldstein S, Fagerberg B, et al. The MERIT-HF Study Group. Effects of controlled-release metoprolol on total mortality, hospitalizations, and well-being in patients with heart failure (MERIT-HF). *JAMA*. 2000;283:1295-1302.

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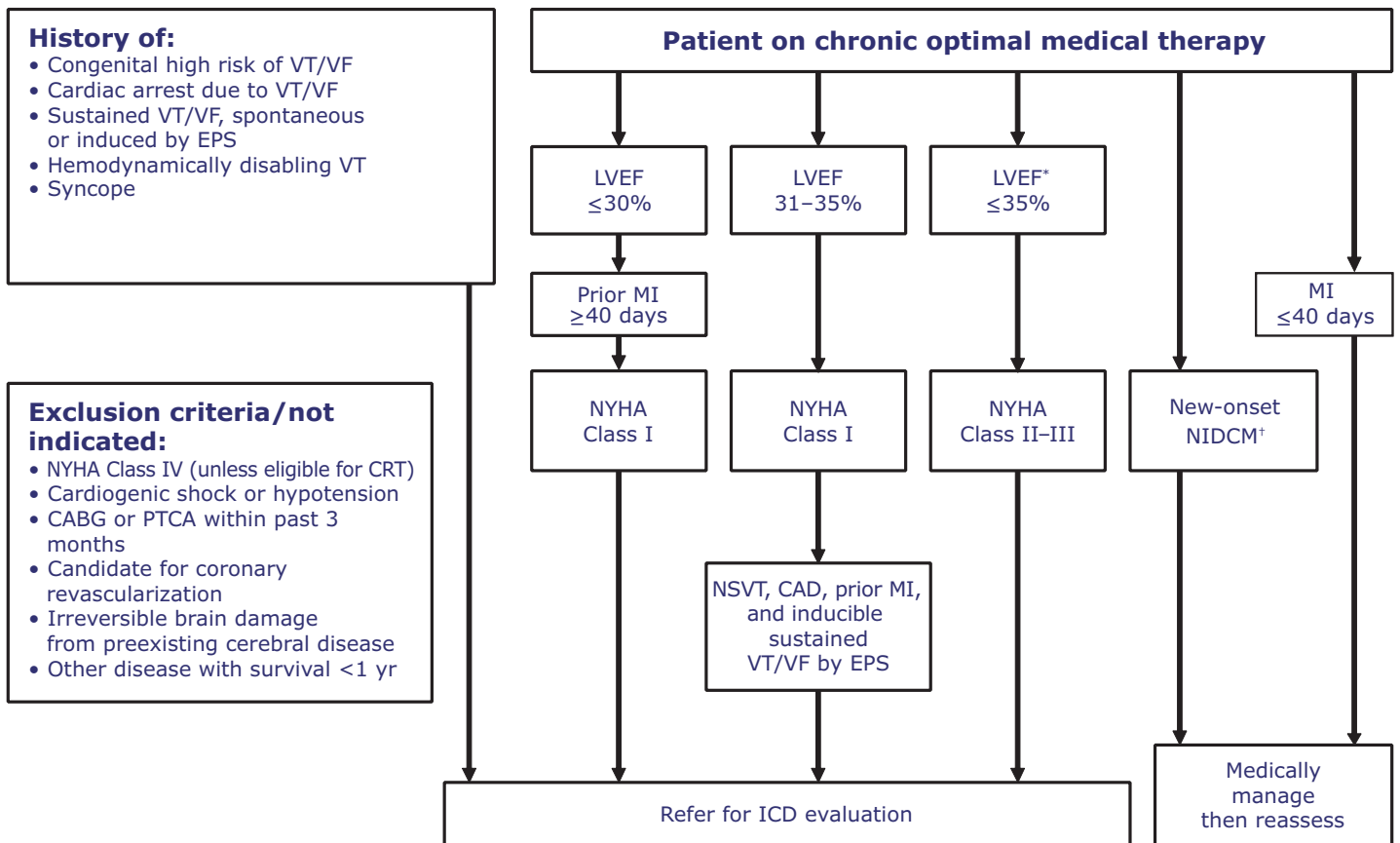
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Implantable Cardioverter Defibrillator (ICD) Therapy Algorithm



* LVEF ≤30%: Class I recommendation; LVEF 31–35%: Class IIa recommendation.

† CMS coverage for primary prevention ICD implants: patients with nonischemic dilated cardiomyopathy (NIDCM) >9 months, NYHA Class II and III heart failure, and measured LVEF ≤35%. Patients with NIDCM >3 months and <9 months, NYHA Class II or III heart failure, and measured LVEF ≤35% at this time are only covered by Medicare if these patients are enrolled in an FDA-approved category B IDE clinical trial, a trial under the CMS clinical trial policy, or the American College of Cardiology National Cardiovascular Data Registry (ACC-NCDR).

Reference Sources:

- Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005;112:1825-1852.
- Gregoratos G, Abrams J, Epstein AE, et al. ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiarrhythmia devices: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/NASPE Committee on Pacemaker Implantation). *Circulation*. 2002;106:2145-2161.
- Bardy JB, Lee KL, Mark DB, et al, for the Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an implantable cardioverter-defibrillator for congestive heart failure. *N Engl J Med*. 2005;352:225-237.
- Moss AJ, Hall WJ, Cannom DS, et al. Improved survival with an implanted defibrillator in patients with coronary disease at high risk for ventricular arrhythmia. *N Engl J Med*. 1996;335:1933-1940.
- Moss AJ, Zareba W, Hall WJ, et al. The Multicenter Automatic Defibrillator Implantation Trial II Investigators. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. *N Engl J Med*. 2002;346:877-883.
- Buxton A, Lee K, Fisher J, et al. A randomized study of the prevention of sudden death in patients with coronary artery disease. *N Engl J Med*. 1999;341:1882-1890.
- Hohnloser SH, Kuck KH, Dorian P, et al. Prophylactic use of an implantable cardioverter-defibrillator after acute myocardial infarction. *N Engl J Med*. 2004;351:2481-2488.

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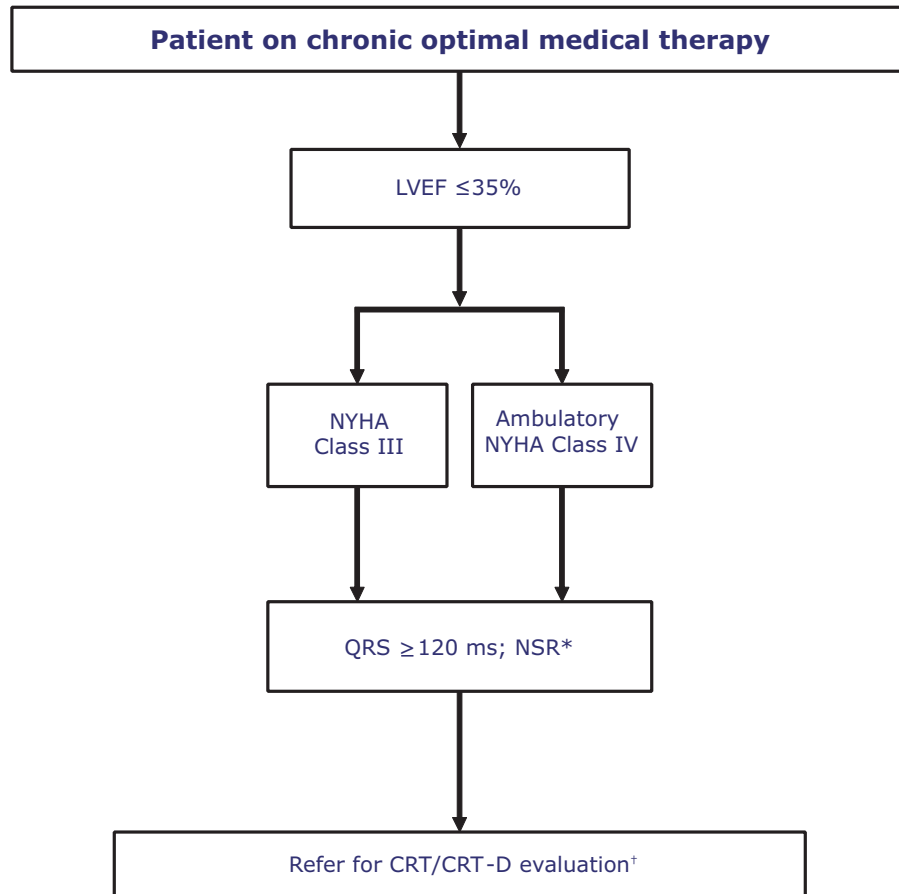
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Cardiac Resynchronization Therapy (CRT) Algorithm



Note: Ongoing clinical trials are evaluating the benefit of CRT in NYHA Class II patients.

* CRT is guideline recommended for patients with normal sinus rhythm (NSR). Further study is necessary in patients with atrial fibrillation or complete atrioventricular block. Preliminary data suggest a possible functional improvement in these patients.

† Inclusion of defibrillator to be based on ICD algorithm and physician discretion.

Reference Sources:

- Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005;112:1825-1852.
- Strickberger SA, Conti J, Daoud EG, et al. Patient selection for cardiac resynchronization therapy. *Circulation*. 2005;111:2146-2150.
- Bristow MR, Feldman AM, Saxon LA. Heart failure management using implantable devices for intraventricular resynchronization: Comparison of Medical Therapy, Pacing, and Defibrillation in Chronic Heart Failure (COMPANION) Trial. *J Card Fail*. 2000;6:276-285.
- Abraham WT. Rationale and design of a randomized clinical trial to assess the safety and efficacy of cardiac resynchronization therapy in patients with advanced heart failure: the Multicenter InSync Randomized Clinical Evaluation (MIRACLE). *J Card Fail*. 2000;6:369-380.
- Young JB, Abraham WT, Smith AL, et al. The Multicenter InSync ICD Randomized Clinical Evaluation (MIRACLE ICD) Trial Investigators. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD Trial. *JAMA*. 2003;289:2685-2694.
- Cleland JGF, Daubert JC, Erdmann E, et al. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med*. 2005;352:1539-1549.

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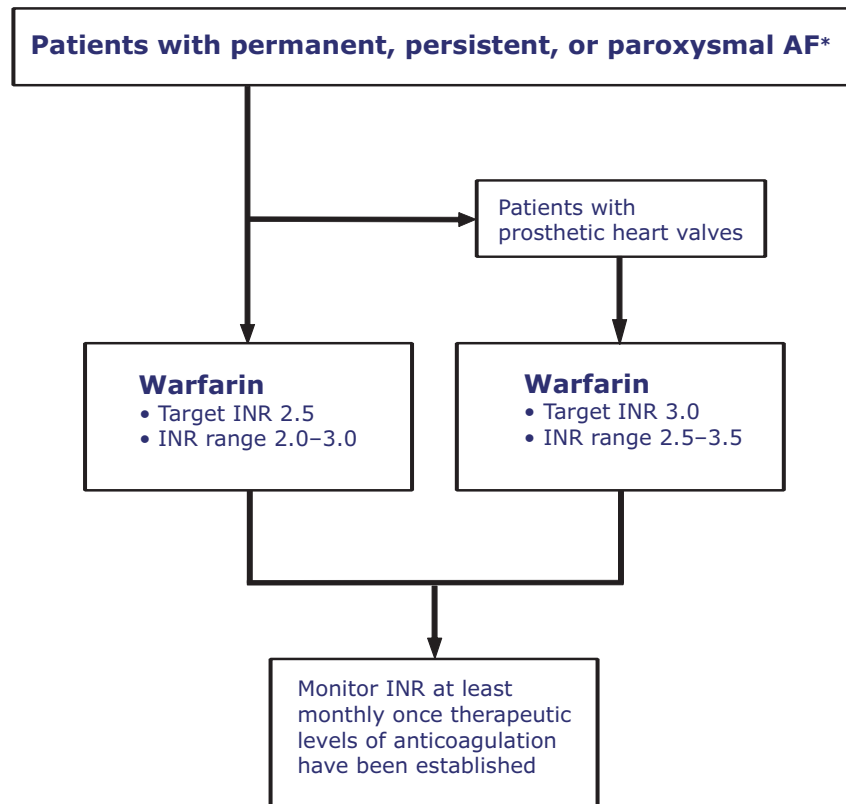
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Anticoagulation Therapy in Atrial Fibrillation Algorithm



*Atrial flutter should be similarly treated.

- Contraindications to warfarin include:
 - Allergy
 - Pregnancy
 - Risk of bleeding (such as active peptic ulcer disease); hemorrhagic stroke; other hemorrhage; hepatic failure; bleeding disorder; metastatic cancer; recent or planned surgery or biopsy procedure; other physician-documented bleeding risk
 - Risk of fall documented by physician
 - Psychosocial concerns (such as active psychosis; terminal illness/comfort care only; alcoholism or drug abuse)
 - Other potential contraindication (such as seizure disorder; malignant hypertension; intracranial aneurysm, repaired or unrepaired)
- Aspirin should be used in patients with absolute contraindications to oral anticoagulation.

Reference Sources:

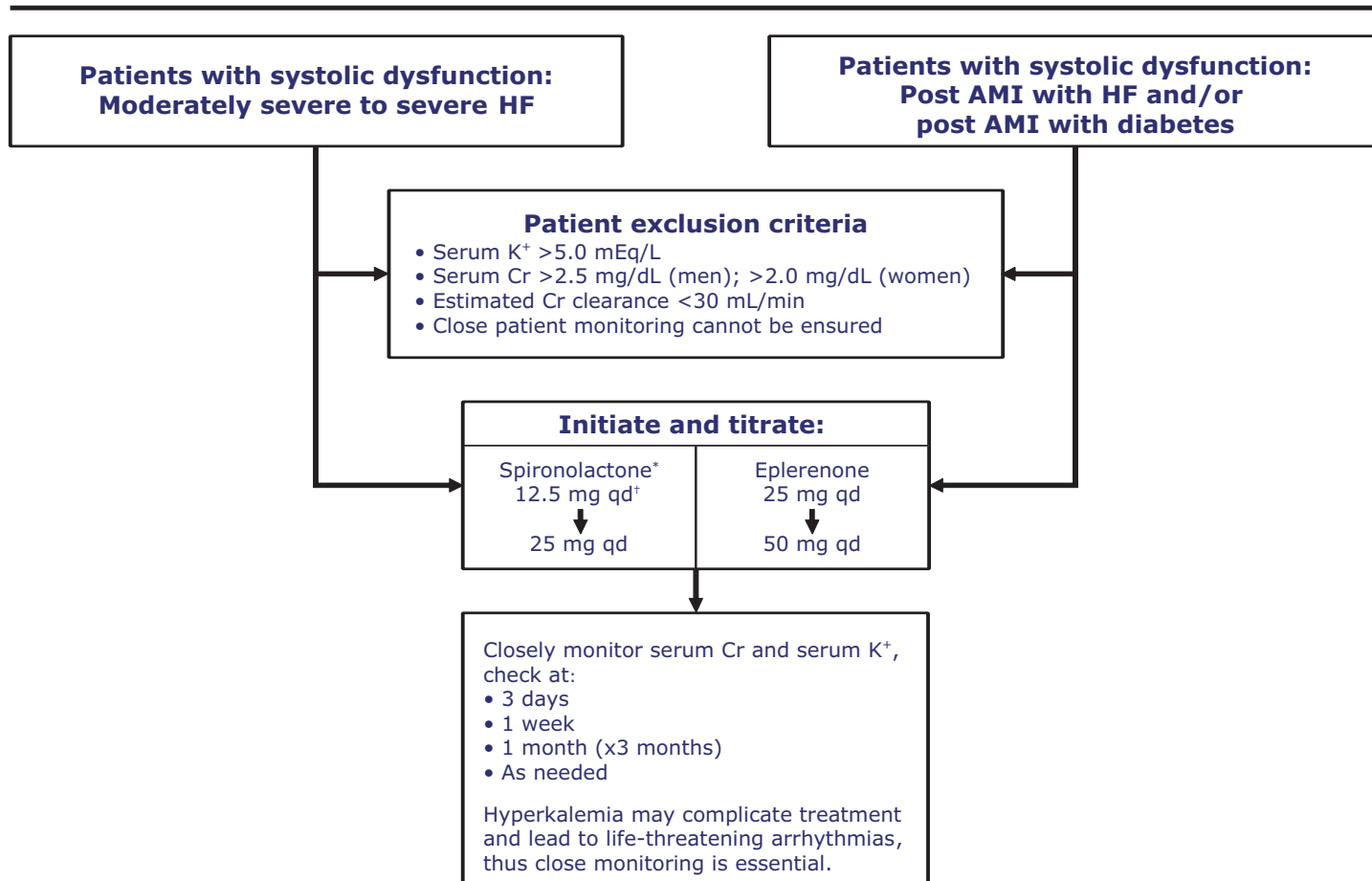
- Singer DE, Albers GW, Dalen JE, et al. Antithrombotic therapy in atrial fibrillation: The Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. Chest. 2004;126:429S-456S.
- Bonow RO, Bennett S, Casey DE Jr, et al. ACC/AHA clinical performance measures for adults with chronic heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Performance Measures (Writing Committee to Develop Heart Failure Clinical Performance Measures) endorsed by the Heart Failure Society of America. J Am Coll Cardiol. 2005;46:1144-1178.
- Fonarow GC. Quality indicators for the management of heart failure in vulnerable elders. Ann Intern Med. 2001;135:694-702.

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Aldosterone Antagonist Treatment Algorithm



Note: Ongoing clinical trials are evaluating the benefit of aldosterone antagonists in patients with mild heart failure.

* Switch to eplerenone if signs of gynecomastia.

† Start at 6.25 mg qd in patients at high risk for hyperkalemia.

- Impaired renal function is a risk factor for hyperkalemia during treatment with aldosterone antagonists. The risk of hyperkalemia increases progressively when serum Cr >1.6 mg/dL.
- Hyperkalemia risk is increased with concomitant use of higher doses of ACEIs or ARBs.
- NSAIDs and COX-2 inhibitors should be avoided.
- Potassium supplements should be discontinued or reduced.
- Dehydration, by diarrhea or other causes, should be addressed emergently.

Routine combined use of an ACEI, ARB, and aldosterone antagonist is not recommended for patients with current or prior symptoms of HF and reduced LVEF.

Reference Sources:

- Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005;112:1825-1852.
- Swedberg K, Cleland J, Dargie H, et al. Guidelines for the diagnosis and treatment of chronic heart failure: executive summary (update 2005): The Task Force for the Diagnosis and Treatment of Chronic Heart Failure of the European Society of Cardiology. *Eur Heart J*. 2005;26:1115-1140.
- Pitt B, Remme W, Zannad F, et al. Eplerenone, a selective aldosterone blocker, in patients with left ventricular dysfunction after myocardial infarction. *N Engl J Med*. 2003;348:1309-1321.
- Pitt B, Zannad F, Remme WJ, et al. The effect of spironolactone on morbidity and mortality in patients with severe heart failure. Randomized Aldactone Evaluation Study Investigators. *N Engl J Med*. 1999;341:709-717.

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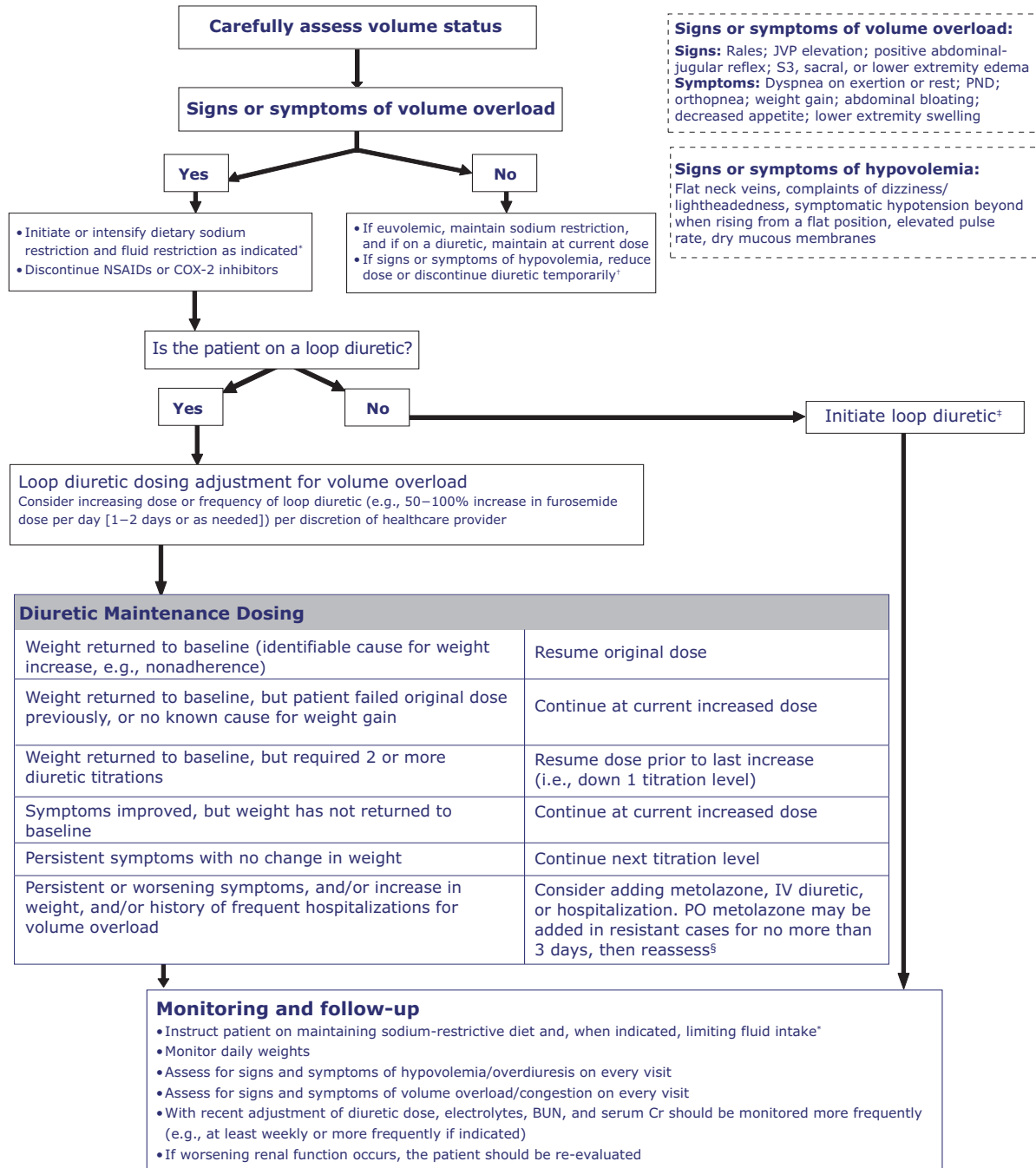
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Management of Volume Overload Algorithm



* Fluid restriction (<2 L/day) is recommended in patients with moderate hyponatremia (serum sodium <130 mEq/L) and should be considered to assist in treatment of fluid overload in other patients.

† Consider also loosening the degree of dietary sodium restriction, then reassess.

‡ Initial dose of loop diuretic at physician discretion. Careful observation for the development of side effects, including electrolyte abnormalities, symptomatic hypotension, and renal dysfunction, is recommended in patients treated with diuretics. Patients should undergo routine laboratory studies and clinical examination as dictated by their clinical response.

§ Addition of chlorothiazides or metolazone, once or twice daily, to loop diuretics should be considered in patients with persistent fluid retention despite high-dose loop diuretic therapy. But chronic daily use, especially of metolazone, should be avoided if possible because of the potential for electrolyte shifts and volume depletion. These drugs may be used periodically (every other day or weekly) to optimize fluid management. Volume status and electrolytes must be monitored closely when multiple diuretics are used. Consider administering metolazone 30–60 min before administration of loop diuretic.

Reference Sources:

- Hunt SA, Abraham WT, Chin MH, et al. ACC/AHA 2005 guideline update for the diagnosis and management of chronic heart failure in the adult—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Update the 2001 Guidelines for the Evaluation and Management of Heart Failure). *Circulation*. 2005;112:1825-1852.
- Adams KF, Lindenfeld J, Arnold JMO, et al. HFSA 2006 comprehensive heart failure practice guideline. *J Card Fail*. 2006;12:e1-e122.
- Cody RJ, Covit AB, Schaer GL, et al. Sodium and water balance in chronic congestive heart failure. *J Clin Invest*. 1986;77:1441-1252.

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Overview of Heart Failure Therapies for Left Ventricular Systolic Dysfunction*

	ACE Inhibitor	Beta Blocker	Aldosterone Antagonist	Diuretic	Angiotensin Receptor Blocker	Digitalis	Hydralazine/ Isosorbide Dinitrate	ICD	CRT
Asymptomatic LV Dysfunction (Stage B and Stage C, NYHA Class I)	Indicated	Indicated [‡]	Recent MI	Indicated, if fluid retention	If ACEI intolerant	For atrial fibrillation requiring rate control [§]	Not indicated	Post-MI LVEF ≤30% [#]	Not indicated
Symptomatic HF - Mild (Stage C, NYHA Class II)	Indicated [‡]	Indicated [‡]	Recent MI (consider in others) [†]	Indicated, if fluid retention	If ACEI intolerant or consider in addition to ACEI [†]	For atrial fibrillation requiring rate control [§]	Not indicated	Indicated LVEF ≤35% [#]	Not currently indicated ^{**}
Symptomatic HF - Moderate to Severe (Stage C, NYHA Class III–IV)	Indicated [‡]	Indicated [‡]	Indicated [‡]	Indicated, if fluid retention	If ACEI intolerant or consider in addition to ACEI [†]	For atrial fibrillation requiring rate control; consider in others	Indicated in black patients on standard medical therapy including ACEI and BB [¶]	Indicated LVEF ≤35% [#]	Indicated, if QRS ≥120 ms, LVEF ≤35% ^{††}
Advanced Late-Stage HF (Stage D, NYHA Class IV)	Indicated [‡]	Indicated [‡]	Indicated [‡]	Indicated, if fluid retention; may need combination	If ACEI intolerant or consider in addition to ACEI [†]	Indicated	Indicated in black patients on standard medical therapy including ACEI and BB [¶]	Not indicated (unless eligible for CRT)	Indicated, if QRS ≥120 ms, LVEF ≤35% ^{††}

Note: Please see individual algorithms for references.

* In patients without absolute contraindications, see individual algorithms for details.

† Routine combined use of an ACEI, ARB, and aldosterone antagonist is not recommended for patients with current or prior symptoms of HF and reduced LVEF.

‡ Using one of the three BBs proven to reduce mortality: bisoprolol, carvedilol, and sustained-release metoprolol succinate.

§ In patients that are Stage C, NYHA Class I or II or who previously required digoxin for symptoms, digoxin may be continued at physician discretion.

|| Patients who are Stage C, NYHA Class I or II and previously required hydralazine/isosorbide dinitrate for more severe symptoms should be continued on therapy.

¶ Others may benefit similarly but this has not yet been tested; the addition of hydralazine/isosorbide dinitrate is reasonable for other patients who are already taking an ACEI and BB and have persistent symptoms.

At least 40 days post-MI.

** At present the use of CRT in patients with minimal HF symptoms is not universally recommended and is the focus of ongoing clinical trials.

†† CRT indicated only in ambulatory NYHA Class IV patients.

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