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Cardiovascular Disorders in the Older Adult

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Disclosure

- Elizabeth Pogge has nothing to disclose.
- None of the planners for this activity have relevant financial relationships to disclose with ineligible companies.

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Learning Objectives

- Determine therapeutic options for hypertension, hyperlipidemia, anticoagulation and heart failure in the older adult.
- Interpret cardiovascular clinical findings and incorporate functional status into therapeutic decision-making.
- Resolve and/or prevent cardiovascular medication-related problems.
- Apply cardiovascular therapy recommendations and person-specific goals to older persons.

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Approaching Cardiovascular Disorders in the Older Adult

- Treatment/management of disease may be similar in young and old; however, need to individualize treatment more in older patients due to side effects and co-morbidities
- Clinical trial data may not include an adequate number of older adults
- Atypical presentation; patient may have less symptom awareness
- Medications are still a valuable tool, but they come with their own risks
- Aspirin for primary prevention of cardiovascular disease is not recommended in older adults (age >60-70 years)

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Kitzman DW et al. Effects of Aging on Cardiovascular Structure and Function. In: Halter JB et al. Hazzard's Geriatric Medicine and Gerontology, 7th edition. New York, NY: McGrawn Hill; 2016.

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Non-pharmacological Strategies to Reduce Cardiovascular Disease

- Consume a dietary pattern that emphasizes intake of vegetables, fruits, legumes, nuts, whole grains, and fish
- Replaced saturated fats with monounsaturated and polyunsaturated fats; avoid trans fats
- Reduce cholesterol and sodium; increase potassium
- Minimize processed meats, refined carbohydrates, and sweetened beverages
- Weight loss, if overweight or obese
- Low or no alcohol intake
- Exercise at least 150 minutes per week
- Stop smoking

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Arnett DK, Blumenthal RS, Albert MA et al. 2019 ACC/AHA guideline on the primary prevention of cardiovascular disease: A report of the American college of cardiology/American heart association task force on clinical practice guidelines. J Am Coll Cardiol 2019; 74(10):e177-2e32.

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Treatment Considerations: Polypharmacy

- Cardiovascular disease has a high rate of mortality
- Consider "*Lag time to benefit*"
  - The time between when an intervention is initiated and when improved health outcomes occur
- To identify which patients are more likely to be helped vs harmed
  - Focusing on age does not account for comorbidities and baseline health
  - Compare lag time vs life expectancy
  - https://eprognosis.ucsf.edu

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Lee SJ Leipzig MR, Walter LC, et al. Incorporating lag time to benefit into prevention decisions for older adults. JAMA. 2013;310(24):2609-2610.

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Hypertension

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Age-Related Physiologic Changes

- Increased arterial stiffness
- Decreased baroreceptor sensitivity
- Increased sympathetic nervous system activity
- Decreased α and β- adrenergic receptor responsiveness
- Endothelial dysfunction
- Decreased ability to excrete sodium load
- Low plasma renin activity
- Resistance to insulin's effect on carbohydrate metabolism
- Central adiposity

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Kitzman DW et al. Effects of Aging on Cardiovascular Structure and Function. In: Halter JB et al. Hazzard's Geriatric Medicine and Gerontology, 7th edition. New York, NY: McGrawn Hill; 2016.

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Primary Hypertension

- ~90% of hypertensive cases
- Cannot be cured, but can be controlled
- Potential mechanisms include genetic and environmental factors
- Isolated systolic hypertension (ISH)
  - Most common form of hypertension in the elderly
  - Defined as elevated systolic blood pressure (SBP ≥ 140 mmHg) with normal or low diastolic blood pressure (DBP < 90 mmHg)
  - Due to diminished arterial compliance
  - Caution: lowering diastolic BP <60 mmHg could contribute to worsening outcomes- J curve phenomenon

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Kitzman DW et al. Effects of Aging on Cardiovascular Structure and Function. In: Halter JB et al. Hazzard's Geriatric Medicine and Gerontology, 7th edition. New York, NY: McGrawn Hill; 2016.
Denardo SJ, Gong Y, Nichols et al. Blood pressure outcomes in very old hypertensive coronary artery disease patients: a INVEST substudy. Am J Med 2010;128:719-26.

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Hypertension Treatment

- Hypertension is poorly controlled in older adults
- Screen for secondary causes; reverse any reversible risk factors
- Emphasis on accurate blood pressure measurement (rest arm on desk)
- Emphasis on lifestyle changes
- Lower BP goals in patients with atherosclerotic cardiovascular disease (ASCVD) risk, diabetes, & chronic kidney disease (CKD)
- Lower blood pressure slowly in older adults to prevent adverse effects
- Evidence for intensive BP control in older adults: SPRINT-Senior, HVET, STEP

Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2018; 71:e127-48.
Mancia G, Kreutz R, Brunstrom M et al. 2023 ESH guideline for the management of arterial hypertension the Task Force for the management of arterial hypertension of the ESH: endorsed by the ISH and the European Renal Association. J Hyperten 2023;41:1874-2071.
Unger T, Borghi C, Charchar F, et al. 2020 ISH global hypertension practice guideline. Hypertension. 2020;75:1334-1357.

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Guideline Recommendations for Older Adults

	Year Published	Age Specified	BP Goal, mm Hg
ISH	2020	≥ 65 years- individualize BP target in the context of frailty, independence and tolerability of treatment	< 140 / 90
ACC/AHA	2017	≥ 65 years; non-institutionalized, ambulatory, community-living	< 130 / 80
ESH	2023	65-79 years ≥ 80 years	< 140/80 (< 130/80 if tolerated) < 140-150/< 80

ISH – International Society of Hypertension; ACC – American College of Cardiology; AHA – American Heart Association; ESH – European Society of Hypertension; BP – blood pressure

Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2018; 71:e127-48.
Mancia G, Kreutz R, Brunstrom M et al. 2023 ESH guideline for the management of arterial hypertension the Task Force for the management of arterial hypertension of the ESH: endorsed by the ISH and the European Renal Association. J Hyperten 2023;41:1874-2071.
Unger T, Borghi C, Charchar F, et al. 2020 ISH global hypertension practice guideline. Hypertension. 2020;75:1334-1357.

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Evidence for Intensive Blood Pressure Control in Older Adults

SPRINT-Senior

Randomized <120 mmHg vs <140 mmHg

Reduction in incidence of combined primary endpoint (CV death, MI, CVA, HF) HR 0.66 (0.51-0.85); all-cause mortality 0.67 (0.49-0.91)

Adults ≥ 75 years (mean 79.9 years)

STEP

Randomized 110-130 mmHg vs 130-150 mmHg

Reduction in incidence of combined, primary endpoint (CV death, MI, CVA, HF, coronary revascularization, atrial fibrillation) HR 0.74 (0.60-0.92)

Average age 66 years

Meta Analysis 6 Trials

120-140 mmHg vs 140-160 mmHg

Reduction in incidence of combined CV outcome HR 0.71 (0.62-0.82); CV death HR 0.65 (0.49-0.86)

Adults ≥ 65 years; mean age 71 years

Intensive blood pressure control did not increase the risk of renal failure or serious adverse events

MI – myocardial infarction; CVA – cerebrovascular accident; HR – hazard ratio; CV – cardiovascular; HF – heart failure

Williamson JD, Supiano MA, Applegate WB et al. Intensive vs standard blood pressure control and cardiovascular disease outcomes in adults >75 years: a randomized clinical trial. JAMA 2016; 315:2673-82.
Zhang W, Zhang S, Deng Y, et al. Trial of intensive blood pressure control in older patients with hypertension. N Engl J Med. 2021; 385(14):1268-1279.
Seidu S, Willis H, Kunutsor SK, et al. Intensive vs standard blood pressure control in older persons with and without diabetes: a systematic review and meta-analysis of randomized controlled trials. J R Soc Med 2023; 116(4):133-142.

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Hypertension Treatment

- In lower risk patients, consider ~3-month trial of lifestyle changes before initiation of medication therapy
- Consider low dose combination therapy with 2 first line agents, especially in patients with co-morbidities or those who need >20 mmHg systolic blood pressure lowering
  - First-line therapy should be optimized (ACEi/ARB + diuretic + CCB) before initiating 2nd line agents
- In frail older adults, may start with monotherapy
- Aldosterone antagonist therapy is recommended in resistant hypertension if eGFR >30 ml/min/1.73m^2

ACEi – angiotensin-converting enzyme inhibitor; ARB – angiotensin II receptor blocker; CCB- calcium channel blocker

Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2018; 71:e127-48.
Mancia G, Kreutz R, Brunstrom M et al. 2023 ESH guideline for the management of arterial hypertension the Task Force for the management of arterial hypertension of the ESH: endorsed by the ISH and the European Renal Association. J Hyperten 2023;41:1874-2071.
Unger T, Borghi C, Charchar F, et al. 2020 ISH global hypertension practice guideline. Hypertension. 2020;75:1334-1357.

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First Line Agents

Class	Adverse Effects	Clinical Pearls in Older Adults
Thiazide diuretics	Electrolyte abnormalities, hyperuricemia, glucose intolerance	-Reduced efficacy with CrCl <30 mL/min -Can cause hyponatremia
ACEi	Hyperkalemia, dry cough, angioedema, renal dysfunction	-Increased risk for acute kidney injury and hyperkalemia -If serum creatinine (SCr) increased ≥ 30%, consider discontinuing therapy
ARB	Hyperkalemia, renal dysfunction, less cough/angioedema as compared to ACEi	
CCB	Edema, headache, constipation	-Long acting DHP-CCBs are preferred (i.e., amlodipine, nifedipine XL); non-DHP CCBs are 2nd line -non-DHP CCBs reduce heart rate

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DHP-CCB = dihydropyridine calcium channel blocker

Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2018; 71:e127-48.

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2nd Line Agents

Class	Adverse Effects	Clinical Pearls in Older Adults
Diuretics (loops*, "potassium sparing", aldosterone antagonists*)	Electrolyte abnormalities, hyperuricemia, glucose intolerance	-"Potassium sparing" are given in combination with thiazides (i.e., triamterene/HCTZ) to limit hypokalemic effects -Avoid "potassium sparing/aldosterone antagonists" with eGFR <30 ml/min/1.73m^2
Beta-blockers*	Fatigue, depression, dyslipidemia, glucose intolerance, sexual dysfunction	-Not first line for hypertension -Utilize in patients with ischemic heart disease or heart failure -Caution in reactive airway disease (non-selective)
Direct renin inhibitor (aliskiren)	Hyperkalemia, renal dysfunction	-Mixed evidence in older adults
Direct vasodilators (i.e. hydralazine)	Sodium and water retention, syncope	-Use cautiously in older adults due to syncope

*These agents will be discussed in detail in the heart failure section

Whelton PK, Carey RM, Aronow WS et al. 2017 ACC/AHA guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2018; 71:e127-48.

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2nd Line Agents: Avoid per the American Geriatrics Society (AGS) Beers Criteria®

Medication Class	Rationale	Recommendation
Peripheral Alpha-1 Blockers; i.e., doxazosin, prazosin, terazosin	High risk of orthostatic hypotension; alternative agents have superior risk-benefit profile	-Avoid use as an antihypertensive -Considered 2nd line in those with benign prostatic hyperplasia
Centrally Acting Alpha Agonists; i.e., clonidine, methyldopa	High risk of central nervous system effects; may cause bradycardia and orthostatic hypotension	-Avoid clonidine as a first-line antihypertensive -Avoid others if possible
Nifedipine – Immediate Release	Potential for hypotension; risk of causing myocardial ischemia	-Avoid

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AGS. American Geriatric Society 2023 updated AGS BEERS Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023:1-30.

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Monitoring

- Electrolytes and renal function should be monitored 7-14 days after starting therapy and following any dose escalation
- Electrolyte disturbances are more frequent in older adults
- Recommend out-of-office blood pressure monitoring to assess response and check for evidence of white coat hypertension
- Follow-up monthly until adequate blood pressure control is achieved
- Consider moving medications to evening dosing and/or separating blood pressure medications for best efficacy

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Patient Case

DX is a 69-year-old male who is seen in the clinic for follow-up of his blood pressure. He lives independently with his wife. He is active and walks 2 miles daily. He states that he is adherent to his medications and does not complain about any adverse effects.

Past Medical History:

- Myocardial infarction
- Hypertension
- Dyslipidemia

Labs and Vitals:

- BP 146/78 mmHg
- HR 74-80 bpm
- Lab results
  - SCr – 1.0 mg/dL
  - K – 3.6 mEq/L

Current Medications:

- Metoprolol tartrate 50 mg twice daily
- Lisinopril 10 mg/day
- Aspirin 81 mg/day
- Atorvastatin 40 mg/day

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Self-Assessment Question

Which of the following is the best treatment recommendation for DX?

A. Continue current therapy
B. Add clonidine
C. Titrate lisinopril to 20 mg daily
D. Discontinue metoprolol

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Adverse Effect: Orthostatic Hypotension

- Defined as a 20 mmHg fall in systolic blood pressure OR at least a 10 mmHg fall in diastolic pressure
- Occurs in 20% of older adults with hypertension
- Increases the risk of falling
- Supine and standing pressures should be measured in older adults prior to initiation of therapy and periodically throughout therapy

Management: Discontinue or lower dose of offending agent(s), change dosing schedule, ensure adequate hydration, modification of daily activities

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Hypertension Clinical Pearls

- Blood pressure is poorly controlled among older adults
- Blood pressure reduction should always be gradual (exceptions are hypertensive emergency/urgency)
- Caution with lowering DBP < 60 mm Hg (coronary hypoperfusion)
- Consider risk vs benefit of intensive blood pressure lowering

Kitzman DW et al. Effects of Aging on Cardiovascular Structure and Function. In: Halter JB et al. Hazzard's Geriatric Medicine and Gerontology, 7th edition. New York, NY: McGrawn Hill; 2016.
Denardo SJ, Gong Y, Nichols et al. Blood pressure outcomes in very old hypertensive coronary artery disease patients: a INVEST substudy. Am J Med 2010;128:719-26.

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Heart Failure (HF)

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Diagnosis of HF in Older Adults

- Vast majority of those newly diagnosed with HF are ≥ 65 years old
- HF is the leading cause of hospitalization, morbidity, and mortality among older adults
- Classical symptoms of HF (fatigue, dyspnea, reduced exercise tolerance) are common among older adults and frequently overlooked making diagnosis difficult
- Two main types of heart failure
  - Heart failure with reduced ejection fraction (HFrEF)- EF <40%
  - Heart failure with preserved ejection fraction (HFpEF)- EF ~55-65%

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Benjamin EJ, Blaha MJ, Chieve SE et al. Heart disease and stroke statistics-2017 updated: A report from the AHA. *Circulation*. 2017;135(10):e146-e603.

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Drugs That Can Induce/Exacerbate HF

Rationale	Agent
Negative inotropic effects- **HFrEF only**	Antiarrhythmic agents (exceptions are amiodarone & dofetilide) Beta-blockers (benefits with certain agents long-term) Non-DHP CCB (diltiazem, verapamil)
Cardiotoxin	Alcohol, excessive amounts in predisposed patients Chemotherapeutics (e.g., anthracyclines, cyclophosphamide, paclitaxel) Amphetamines (cocaine, methamphetamine, pseudoephedrine OTC)
Sodium & water retention	Androgens / estrogens COX-2 inhibitors Glucocorticoids NSAIDs Salicylates (high doses) Thiazolidinediones (rosiglitazone, pioglitazone)
Miscellaneous	TNF antagonists (e.g., etanercept, infliximab) DPP-4 inhibitors (FDA warning for saxagliptin, alogliptin- likely a class effect) Doxazosin

Always ask about NSAID therapy- especially in older persons

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Parker B, Nappi JM, Cavallari LH. Chronic heart failure. In: DiPiro JT et al. Pharmacotherapy: A Pathophysiologic Approach, 11th edition. New York, NY: McGraw-Hill; 2019.

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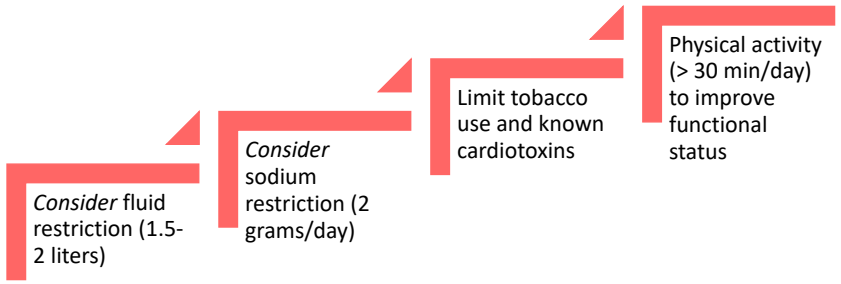
Lifestyle Changes for HF



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Heidenreich PA, Bozkurt B, Aguilier D, et al. 2022 AHA/ACC/HFSA guidelines for the management of heart failure: a report of the ACC/AHA task force on practice guidelines. Circulation. 2022; 145(18):e895-e1032.

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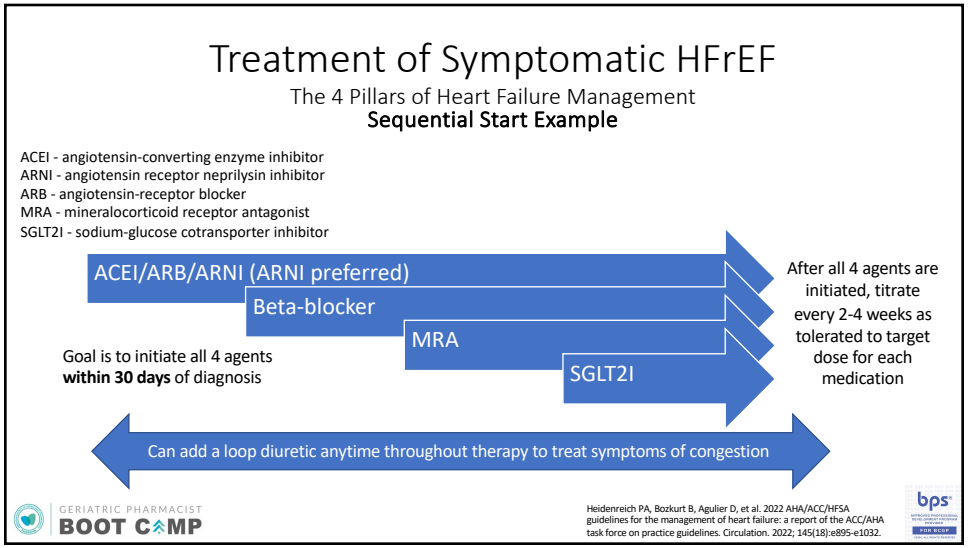
Treatment of Symptomatic HFrEF
The 4 Pillars of Heart Failure Management
Sequential Start Example
ACEI - angiotensin-converting enzyme inhibitor
ARNI - angiotensin receptor neprilysin inhibitor
ARB - angiotensin-receptor blocker
MRA - mineralocorticoid receptor antagonist
SGLT2I - sodium-glucose cotransporter inhibitor
ACEI/ARB/ARNI (ARNI preferred)
Beta-blocker
MRA
SGLT2I
After all 4 agents are initiated, titrate every 2-4 weeks as tolerated to target dose for each medication
Goal is to initiate all 4 agents within 30 days of diagnosis
Can add a loop diuretic anytime throughout therapy to treat symptoms of congestion
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Heidenreich PA, Bozkurt B, Aguilier D, et al. 2022 AHA/ACC/HFSA guidelines for the management of heart failure: a report of the ACC/AHA task force on practice guidelines. Circulation. 2022; 145(18):e895-e1032.
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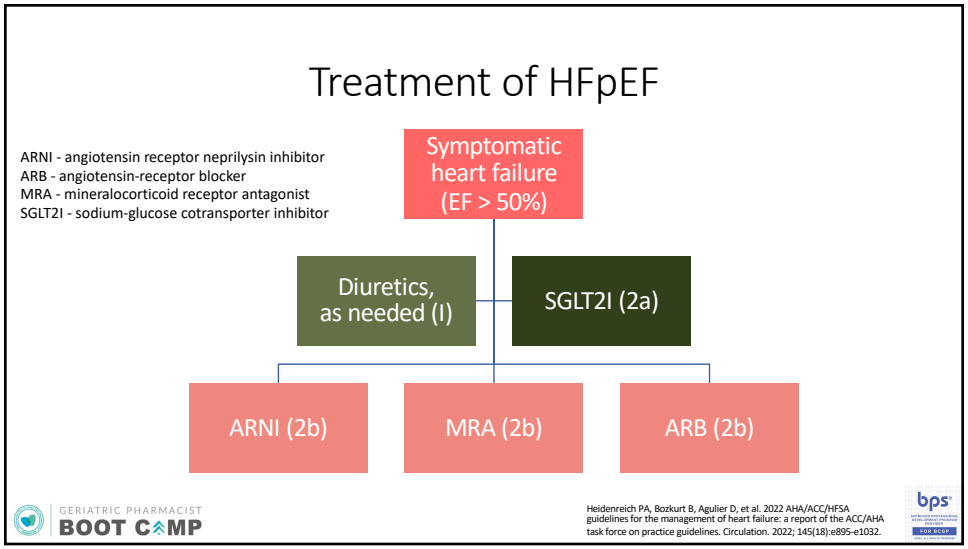
Treatment of HFpEF
ARNI - angiotensin receptor neprilysin inhibitor
ARB - angiotensin-receptor blocker
MRA - mineralocorticoid receptor antagonist
SGLT2I - sodium-glucose cotransporter inhibitor
Symptomatic heart failure (EF > 50%)
Diuretics, as needed (I)
SGLT2I (2a)
ARNI (2b)
MRA (2b)
ARB (2b)
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Heidenreich PA, Bozkurt B, Aguilier D, et al. 2022 AHA/ACC/HFSA guidelines for the management of heart failure: a report of the ACC/AHA task force on practice guidelines. Circulation. 2022; 145(18):e895-e1032.
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Guideline Directed Medical Therapy (GDMT)

GDMT	Key adverse effects	Cost	Clinical Pearls
ACEi/ARB/ARNi (class effect)	ACEi/ARNi: cough/angioedema All agents: Hyperkalemia, renal dysfunction	ARNi>ACEi/ARB	Do not use ACEi/ARNi in patients with a history of angioedema
MRA spironolactone, eplerenone	Spironolactone: gynecomastia, breast tenderness. Class effect: Hyperkalemia, renal dysfunction	eplerenone >spironolactone	Close monitoring is required to reduce risk of hyperkalemia Avoid if CrCl < 30 mL/min
SGLT2i (class effect)	Mycotic yeast infections, urinary tract infections, hypovolemia	high	Remain hydrated to prevent adverse effects
Beta-blocker carvedilol, metoprolol succinate, bisoprolol	Carvedilol: Bronchospasms Class effect: Fatigue, exercise intolerance, bradycardia	low	Only use evidence-based agents; May worsen heart failure symptoms when starting or up-titrating

Abbreviations: Angiotensin-Converting Enzyme Inhibitors (ACEi)/Angiotensin Receptor Blockers (ARB)/Angiotensin Receptor–Neprilysin Inhibitors (ARNi), Beta-Blocker (BB), Mineralocorticoid receptor antagonist (MRA), Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2i)

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Heidenreich PA, Bozkurt B, Aguilier D, et al. 2022 AHA/ACC/HFSA guidelines for the management of heart failure: a report of the ACC/AHA task force on practice guidelines. Circulation. 2022; 145(18):e895-e1032.

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ARNi Therapy: Sacubitril/valsartan (Entresto®)

- Sacubitril is a neprilysin inhibitor that increases the availability of natriuretic peptides (ANP, BNP, CNP) in the body
  - This will increase diuresis; may need to adjust diuretics when starting sacubitril
- Higher risk of hypotension as compared to ACEi/ARB
- ACEi → sacubitril/valsartan → ACEi; requires 36-hour washout
- Starting dose is 24/26 mg BID; start at 49/51 mg BID in those on >50% target dose ACEi/ARB
- Approved for HFrEF and HFpEF
  - In HFpEF, benefits are more favorable in women and those with EF below normal

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Entresto® [package insert]. New Jersey: Novartis; 2021.

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Resu Statistics Review al

Primary outcomes of the PARADIGM-HF Trial				
Outcome	Sacubitril/valsartan (n=4187)	Enalapril (n=4212)	Hazard ratio (95% CI)	P value
Death from cardiovascular cause or first hospitalization for worsening heart failure	914 (21.8)	1117 (26.5)	0.80 (0.73-0.87)	<0.001

How to calculate the relative risk reduction using event rates (raw calculation with no adjustments)

Control event rate: 1117/4212 = 0.265 = 26.5%

Experiment event rate: 914/4187 = 0.218 = 21.8%

RRR = (CER – EER) / CER = (0.265-0.218)/0.265= .177 = 18%

Above; 1-RR = 1-0.80 = 20%

These numbers are close but not identical due to the statistical model adjustments in the clinical trials

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McMurray JJV, Packer M, Desai AS et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. N Engl J Med. 2014; 371(11):993-1004.
DeMuth, JE. Basic statistics and pharmaceutical statistical applications, 3rd edition. CRC press. 2014

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Patient Case

DX is a 73-year-old male who is seen in the clinic for follow-up. He was seen 1 month ago. He is still experiencing fatigue and shortness of breath. He reports stable home weight, and he has 1+ pitting edema.

Past Medical History:

- **Heart failure X 6 months (EF ~30%)**
- MI (2020)
- Hypertension
- Dyslipidemia

Labs and Vitals:

- BP 138/76 mmHg
- HR 64-66 bpm
- Lab results
  - SCr – 1.3 mg/dL
  - K – 4.6 mEq/L

Current Medications:

- Carvedilol 6.25 mg twice daily
- Lisinopril 40 mg/day
- Aspirin 81 mg/day
- Atorvastatin 40 mg/day
- Furosemide 40 mg/day
- Potassium 10 mEq/day

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Patient Case

The decision is made to switch DX from lisinopril 40 mg to sacubitril/valsartan. Which of the following statements is true with regards to sacubitril/valsartan therapy in DX?

a. DX should be instructed to stop lisinopril and start sacubitril/valsartan 12 hours later
b. The starting dose of sacubitril/valsartan in DX should be 49/51 mg twice daily
c. Sacubitril/valsartan is contraindicated in DX due to his history of myocardial infarction
d. Sacubitril/valsartan can cause hypokalemia so his potassium dose should be doubled

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SGLT-2 Inhibitors in Heart Failure

- Dapagliflozin, empagliflozin, and sotagliflozin are approved to treat HFrEF and HFpEF
- Side effects
  - Genital mycotic infections
  - Urinary tract infections
  - Hypotension/volume depletion
  - Euglycemic diabetic ketoacidosis- in patients with diabetes
- Do not use at ~ eGFR < 25 mL/minute/1.73 m^2
- BEERS Criteria® 2023; Use with caution due to risk of urogenital infections

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Anker SD, et al. N Engl J Med. 2021; 385:1451-1461, Solomon S, et al. N Engl J Med. 2022; 387(12): 1089-1098. Bhatt DL, et al. N Engl J Med. 2021; 384:117-128.

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Loop Diuretics in Heart Failure

- Indicated for symptom management to reduce fluid overload
- Dosing is on a sigmoidal curve; double the dose until adequate urine output is seen (3-4L of urine output with each dose)
- Diuretic resistance can occur; double the dose, switch to an alternative diuretic, or add metolazone 30 minutes prior to the loop
- Furosemide 40 mg = torsemide 20 mg = bumetanide 1 mg = ethacrynic acid 50 mg
- Monitor for electrolyte loss
  - Sodium, potassium, magnesium

Be cautious with high dose metolazone in the elderly. Recommend 2.5 mg twice to three times weekly

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Pham D, Grodin JL. Dilemmas in dosing of heart failure drugs: titrating diuretics in chronic heart failure. Card Fail Rev 2017; 3:108-12.

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Other Therapies for HFrEF

- Use in addition to GDMT or in patients who are intolerant to GDMT
- Hydralazine/isosorbide dinitrate
  - Add on therapy in African American patients
  - Alternative to an ACEi/ARB if patient is intolerant due to hypotension or renal insufficiency
- Digoxin
  - 2023 AGS Beers Criteria® state digoxin is not first line therapy
  - The maximum dose of digoxin is 0.125 mg in older adults
- Ivabradine
  - Consider if heart rate of ≥ 70 BPM and patient is in normal sinus rhythm
- Vericiguat
  - Recent hospitalization or need for IV diuretics

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Yancy CW, Jessup M, Bozkurt B et al. 2017 ACC/AHA/HFSA focused updated of the 2013 ACCF/AHA guidelines for the management of heart failure: a report of the ACCF/AHA task force on practice guidelines. J Am Coll Cardiol 2017; 70:776-803.
AGS. American Geriatric Society 2023 updated AGS BEERS Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023:1-30.

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Hypotension

- Hypotension often limits or prevents up-titration of guideline directed pharmacotherapy
- Screen all patients for reversible causes of hypotension
  - Unnecessary blood pressure medications
  - Medications that lower blood pressure as a side effect (e.g., alpha-1 blockers for BPH)
  - Hypovolemia due to over-diuresis
- Substitute agents with less risk of hypotension
  - ARNi > ACEi/ARB
  - Carvedilol > metoprolol succinate

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Heart Failure Clinical Pearls

- The diagnosis of HF in older adults can be complicated by the presence of multi-morbidity, polypharmacy, cognitive impairment, frailty, and generalized symptoms with a large differential
- Morbidity and mortality of HFrEF is reduced by targeting the involved neurohormones
- When treating HFpEF, agents provide hospitalization benefits
- Older adults oftentimes will not tolerate target dose medications
  - Lower doses of multiple first-line medications preferred over high dose of a single agent
- Reassess diuretic therapy continually for efficacy and safety as older adults are more likely to experience side effects
  - -Hypotension may limit the ability to uptitrate evidence-based medications
  - -It is imperative to identify and treat electrolyte disturbance

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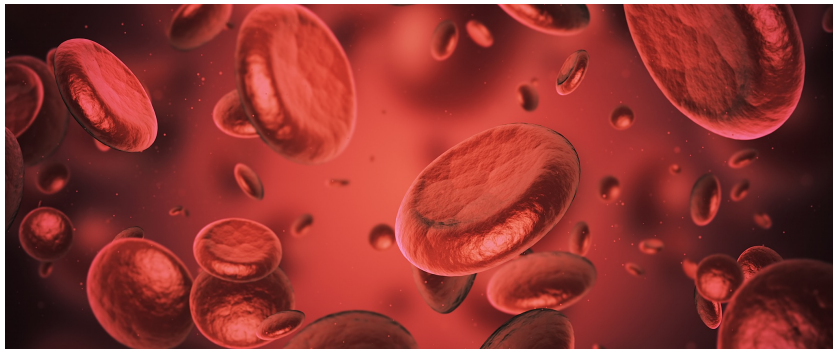
Anticoagulation



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Oral Anticoagulation Therapy Indications

Atrial fibrillation (AF)

Warfarin or direct oral anticoagulation* (DOAC)

Venous Thromboembolism (VTE)

Warfarin or DOAC

Valvular heart disease

Warfarin

*DOACs indicated in AF without presence of mechanical valve replacement or moderate to severe mitral valve stenosis (eg, non-valvular AF)

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Assessing Stroke Risk in Atrial Fibrillation

CHA_2DS_2-VASc Condition	Points
Congestive heart failure or LV dysfunction	1
Hypertension; (diagnosis regardless of BP)	1
Age ≥75 years	2
Diabetes mellitus	1
Stroke or TIA or thromboembolism	2
Vascular disease (Defined as prior MI, PAD, or aortic plaque)	1
Age 65-74 years	1
Sex **C**ategory (female sex)	1

↑ Score = ↑ Risk

For older adults (age ≥ 65) → recommend anticoagulation (age is worth 1-2 pts on CHA_2DS_2-VAS_C Score)

Risk Factors	CHA_2DS_2VASc Score	Recommended Agent
A. Fib plus 2 or more non gender risk factor	≥2 in men ≥3 in women	Anticoagulation strongly recommended
A. Fib plus 1 or more non gender risk factor	1 in men 2 in women	Anticoagulation is reasonable
A. Fib plus 0 non gender risk factors	0 in men 1 in women	No antithrombotic therapy preferred
If patients with AF who are a candidate for anticoagulation therapy and do not have an indication for antiplatelet therapy, aspirin or aspirin + clopidogrel is NOT recommended as an alternative to anticoagulation therapy.		

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Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the management of heart failure: a report of the ACCF/AHA joint committee on clinical practice guidelines Circulation 2024; 149(1):e1-e156.

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Treatment of Atrial Fibrillation Symptoms

- Symptom control is needed in atrial fibrillation
- Rate control (medications or non-pharmacological options to control the heart rate)
  - Pharmacological: B-blockers, non-DHP CCB, digoxin
  - Non-pharmacological: ablation of the AV node with implantation of ventricular pacemaker
- Rhythm-control (restore and maintain sinus rhythm)
  - Pharmacological: Anti-arrhythmic medications (see cardiovascular reference sheet for agents and adverse effects)
  - Non-pharmacological: Direct current cardioversion (DCC), open-heart surgery (MAZE procedure), catheter ablation (pulmonary vein isolation), implantable atrial defibrillators

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Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the management of heart failure: a report of the ACCF/AHA joint committee on clinical practice guidelines Circulation 2024; 149(1):e1-e156.

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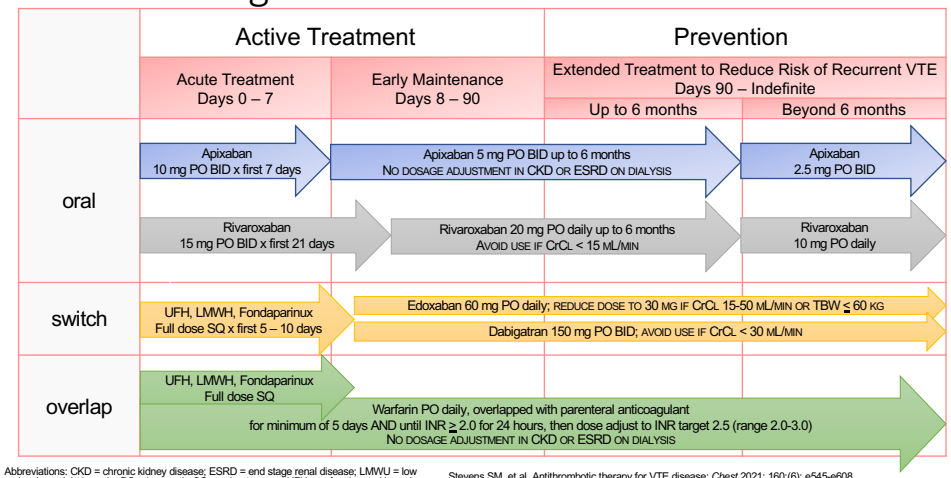
Anticoagulation for the Treatment of VTE



Abbreviations: CKD = chronic kidney disease; ESRD = end stage renal disease; LMWU = low molecular weight heparin; PO = by mouth; SQ = subcutaneous; UFH = unfractionated heparin

Stevens SM, et al. Antithrombotic therapy for VTE disease: *Chest* 2021; 160:(6): e545-e608.
Drug package inserts. https://dailymed.nlm.nih.gov/dailymed/

43

Duration of Anticoagulation Therapy Based on Indication

Indication	Therapy Duration	Comments
PROVOKED VTE	3 to 6 months	▪ Provoked VTE implies that clot formation secondary to a transient or reversible risk factor (e.g., trauma, surgery, oral contraceptives)
VTE that is UNPROVOKED or PROVOKED BY A CHRONIC RISK FACTOR	Indefinite*	▪ Indefinite duration implies no scheduled stop date of therapy ▪ Continue oral anticoagulation if patient is not at high risk of bleeding and adherent to therapy
Atrial fibrillation **Mechanical heart values**	Indefinite*	▪ Treat based on risk of stroke; for most patients, indefinite duration implies no scheduled stop date therapy ▪ Continue oral anticoagulation if patient is not at high risk of bleeding and adherent to therapy

*Risk vs. benefit of indefinite therapy should be reassessed periodically, especially if bleeding event occurs or with change in status of comorbidity requiring additional antithrombotic therapy

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Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the management of heart failure: a report of the ACCF/AHA joint committee on clinical practice guidelines Circulation 2024; 149(1):e1-e156.
Stevens SM, et al. Antithrombotic therapy for VTE disease: Chest 2021; 160:(6): e545-e608.

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First-line Anticoagulation Recommendations

- Direct oral anticoagulants (DOAC) are recommended over warfarin for non-valvular AF and VTE
- Aspirin is not a good alternative to anticoagulation for AF or VTE
- If warfarin is used, goal time in therapeutic range (TTR) is ≥ 70%
  - If TTR <65% consider DOAC or strategies to improve TTR
  - SAMe-TT_2R_2 score can be used to predict those who might do better on warfarin (only validated in Caucasian)
- Dosing is variable based on indication and renal function
- Inappropriate dosing is common, specifically underdosing in older adults

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Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the management of heart failure: a report of the ACCF/AHA joint committee on clinical practice guidelines Circulation 2024; 149(1):e1-e156.
Stevens SM, et al. Antithrombotic therapy for VTE disease: Chest 2021; 160:(6): e545-e608.

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Anticoagulation Recommendations: Special Populations

	Active Cancer	Older adults	Antiphospholipid syndrome	Severe obesity BMI >40	End stage renal disease on dialysis
Anticoagulation Recommendations	*(pts without GI malignancies):* apixaban or edoxaban or rivaroxaban > LWMH; *(pts with GI malignancies):* LMWH > DOAC	Apixaban or edoxaban > dabigatran > warfarin or rivaroxaban	Warfarin	rivaroxaban or apixaban > warfarin or LMWH or fondaparinux	apixaban or warfarin
*All agents given at standard treatment dose; LMWH/UFH is weight based dosing					

AGS. American Geriatric Society 2023 updated AGS BEERS Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023:1-30.

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Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the management of heart failure: a report of the ACCF/AHA joint committee on clinical practice guidelines Circulation 2024; 149(1):e1-e156.
Stevens SM, et al. Antithrombotic therapy for VTE disease: Chest 2021; 160:(6): e545-e608.

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Overview of DOAC Regimens Based on Indication

Indication	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Prevention of MACE in CAD/PAD	Not FDA approved	2.5 mg BID	Not FDA approved	Not FDA approved
VTE treatment	150 mg BID following 5-10 days of initial treatment with parenteral anticoagulant	15 mg BID for 21 days, then 20 mg daily with large meal; may reduce to 10 mg daily for extended treatment ≥6 months	10 mg BID for 7 days, then 5 mg BID; may reduce to 2.5 mg BID for extended treatment ≥6 months	60 mg daily following 5-10 days of initial treatment with parenteral anticoagulant
VTE prophylaxis	110 mg x1 (optional), then 220 mg daily ORTHOPEDICS ONLY	10 mg daily MEDICAL AND ORTHOPEDICS	2.5 mg BID ORTHOPEDICS ONLY	Not FDA approved
Nonvalvular AF	150 mg BID	20 mg daily with large meal (food ↑ bioavailability)	5 mg BID	60 mg daily
Dose adjustments	**VTE treatment/prophylaxis:** Avoid if CrCl <30 mL/min	**CAD/PAD and VTE treatment/prophylaxis:** Avoid if CrCl <15 mL/min	**VTE treatment/prophylaxis:** No dosage adjustment is recommended	**VTE treatment:** If TBW ≤60 kg or CrCl 15-50 mL/min or take P-gp inhibitors, reduce to 30 mg daily
	AF: If CrCl 15-30 mL/min, reduce to 75 mg BID	**AF:** If CrCl 15-50 mL/min, reduce to 15 mg with large meal	**AF:** If ≥ 2 of the following, reduce to 2.5 mg BID: age ≥80 years, TBW ≤60 kg, SCr ≥1.5 mg/dL	**AF:** CrCl 15-50 mL/min: 30 mg daily; Not recommended if CrCl >95 mL/min or <15 mL/min

Abbreviations: AF= atrial fibrillation, CAD = coronary artery disease, CrCl = creatinine clearance, FDA = food and drug administration, MACE = major adverse cardiac events, PAD = peripheral arterial disease, P-gp = P-glycoprotein, SCr = serum creatinine, TBW = total body weight, VTE = venous thromboembolism.

Drug package inserts. https://dailymed.nlm.nih.gov/dailymed/

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Patient Case

DX is a 76-year-old male who is seen in the clinic for follow-up of his new onset atrial fibrillation. He was diagnosed by his cardiologist via EKG earlier this morning and is sent to you for management. He is not complaining of any symptoms of atrial fibrillation.

Past Medical History:

- **Atrial fibrillation**
- Heart failure
- MI (2020)
- Hypertension
- Dyslipidemia

Labs and Vitals:

- BP 118/68 mmHg
- HR 62-64 bpm
- Lab results
  - SCr – 1.3 mg/dL
  - K – 4.5 mEq/L

Current Medications

- Carvedilol 12.5 mg twice daily
- Sacubitril/valsartan 97/103 mg twice daily
- Aspirin 81 mg/day
- Atorvastatin 40 mg/day

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Self-Assessment Question

Which of the following medication changes would be best to make in DX today?

A. Discontinue aspirin and initiate apixaban
B. Continue aspirin and initiate warfarin
C. Discontinue carvedilol and initiate amiodarone
D. Add amiodarone to his current therapy

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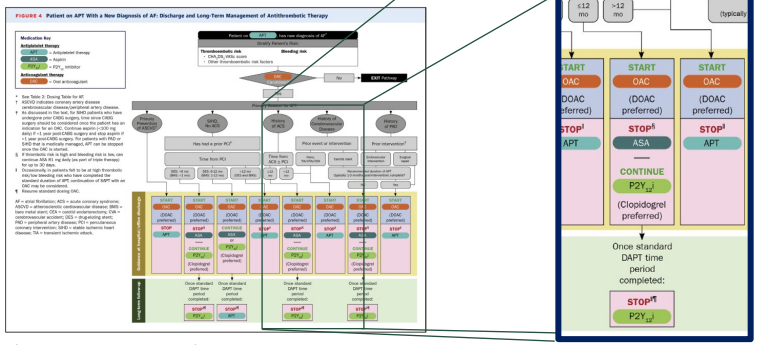
ACC Expert Consensus Decision Pathway



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Kumbhani DJ, Cannon CP, Beavers CJ, et al. 2020 ACC Expert Consensus Decision Pathway for Anticoagulant and Antiplatelet Therapy in Patients With Atrial Fibrillation or Venous Thromboembolism Undergoing Percutaneous Coronary Intervention or With Atherosclerotic Cardiovascular Disease: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021 Feb 9;77(5):629-658.

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Antiplatelet Therapy + Anticoagulation

- When using dual or triple therapy, the following is recommended
  - DOACs are preferred over warfarin
  - Clopidogrel is the preferred P2Y12 inhibitor
  - Aspirin is recommended at a low dose
- Triple therapy (anticoagulation, aspirin, P2Y12-inhibitor) should be limited to 4 weeks
- Dual therapy (anticoagulation + P2Y12-inhibitor) should be limited to 1 year
- Patient with chronic coronary artery disease (CAD) (>1 year after revascularization or CAD without revascularization) without history of stent thrombosis or stable peripheral arterial disease, monotherapy with anticoagulation is recommended

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Kumbhani DJ, Cannon CP, Beavers CJ, et al. 2020 ACC Expert Consensus Decision Pathway for Anticoagulant and Antiplatelet Therapy in Patients With Atrial Fibrillation or Venous Thromboembolism Undergoing Percutaneous Coronary Intervention or With Atherosclerotic Cardiovascular Disease: A Report of the American College of Cardiology Solution Set Oversight Committee. J Am Coll Cardiol. 2021 Feb 9;77(5):629-658.

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Anticoagulation in older adults

- Anticoagulation therapy is underused in older adults
- The most frequent reason for non-prescribing of anticoagulation in older adults with ≥ 6 comorbidities is frequent falls or frailty; due to concerns related to bleeding
- 2023 BEERS criteria® recommendations for long-term treatment of VTE and atrial fibrillation
  - Avoid rivaroxaban due to high risk of major bleeding and gastrointestinal (GI) bleeding
  - Avoid warfarin due to high risk of major bleeding (particularly intracranial bleeding)
  - Caution with dabigatran due to high risk of GI and major bleeding

GERIATRIC PHARMACIST BOOT CAMP

Volgman et al. Management of atrial fibrillation in patients 75 years and older: A JACC state-of-the-art review. J Am Coll Cardiol. 2022;79(2):166-179.
AGS. American Geriatric Society 2023 updated AGS BEERS Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023:1-30.

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DOAC Drug–Drug Interactions

- **Pharmacokinetic**
  - All DOACs are P-gp substrates
  - Apixaban and rivaroxaban are CYP3A4 substrates
  - DOACs interact with strong inhibitors (↑ DOAC level) or inducers (↓ DOAC level) of CYP3A4 and/or P-gp
    - **Enzyme inhibitors: consider a reduced dose of the DOAC**
    - **Enzyme inducers: avoid use of DOACs**
- **Pharmacodynamic**
  - Medications that increase the risk for bleeding
  - Antiplatelet drugs, NSAIDs, systemic steroid therapy, other anticoagulants

GERIATRIC PHARMACIST BOOT CAMP

Steffel J, Collins R, Antz M, et al. 2021 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Europace. 2021;23(10):1612-1676.

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Drug–Drug Interactions

Strong P-gp and/or CYP3A4 Inhibitors	Strong P-gp and/or CYP3A4 Inducers
Amiodarone	Carbamazepine
Clarithromycin/erythromycin	Levetiracetam
Diltiazem/verapamil	Phenytoin/phenobarbital
Dronedarone	Rifampin
Cyclosporine/tacrolimus	St John's wort
Fluconazole/ketoconazole/itraconazole	
HIV protease inhibitors*	
Anticancer agents*	

*Several agents within these drug classes interact; see Steffel et al for details.

GERIATRIC PHARMACIST BOOT CAMP

Steffel J, Collins R, Antz M, et al. 2021 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Europace. 2021;23(10):1612-1676.

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DOAC Clinical Implications

Dabigatran is given in an acidic core→ low oral bioavailability

- Potential PPI drug–drug interaction (decreased average drug exposure by ~20%-25%)
- Increases the risk of GI upset and dyspepsia
- Store in original container- NOT pill boxes

Rivaroxaban bioavailability ↑ with food

- Take with the largest meal of the day

Edoxaban efficacy decreases with high renal function

- For atrial fibrillation, do not use with CrCl >95 mL/min

Apixaban and rivaroxaban may be crushed

GERIATRIC PHARMACIST BOOT CAMP

Steffel J, et al. 2021 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Europace 2021; 23(10):1612-76.
AGS. American Geriatric Society 2023 updated AGS BEERS Criteria® for potentially inappropriate medication use in older adults. J Am Geriatr Soc. 2023:1-30.

55

Clinic Anticoagulation Management

- Guidelines recommend warfarin management be performed systematically, using dosing algorithms
- Systematic review of pharmacist-managed warfarin vs standard of care showed improved anticoagulation management with pharmacists
  - Improved quality of anticoagulation control (time in therapeutic range)
  - Lower or equivalent major bleeding or thromboembolic events
  - Lower rate of hospitalizations or emergency department visits
  - Cost savings
- DOAC clinics: increasingly popular to help improve efficacy and safety of DOAC

GERIATRIC PHARMACIST BOOT CAMP

Manzoor. BS, Cheng W, Lee JC, et al. Quality of pharmacist-managed anticoagulation therapy in log-term ambulatory settings: A systematic review. Ann Pharmacother. 2017;51:1122-1137.

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DOAC Risk Reduction Strategies and Checklist

	Interval	Comments
Adherence/ reassess appropriateness	Each visit	Bring medications/list, counsel/educate about importance of adherence, review for appropriate dosing, consider insurance coverage
Thromboembolism	Each visit	Has the patient had any changes to their condition (e.g., TIA, stroke)?
Bleeding	Each visit	Any evidence of bleeding? Does the patient know what to look for? Reinforce education and make adjustments as necessary
Side effects	Each visit	In relation to the anticoagulant, do changes need to be made?
Drug interactions	Each visit	Include prescription and over-the-counter medications
Blood sampling (CBC and CMP)	Every 1-2 months	CrCl <30 mL/min, severe liver disease
	Every 3 months	CrCl 30-59 mL/min, moderate liver disease, high bleeding risk (HASBLED ≥3)
	Every 6 months	CrCl ≥60 mL/min, mild or no liver disease, low or moderate bleeding risk (HASBLED 0-2)
Manage modifiable risk factors for bleeding	Each visit	Based on current guidelines, control hypertension, reduce medications that can increase risk, alcohol

*Cockcroft-Gault method preferred using actual body weight

GERIATRIC PHARMACIST BOOT CAMP

Steffel J, et al. 2021 European Heart Rhythm Association practical guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation. Europace 2021; 23(10):1612-76.

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Interactions with Warfarin

- Screen frequently and often for pharmacokinetic and pharmacodynamic interactions
- Pharmacokinetic interactions; Absorption, distribution, metabolism, excretion
  - Absorption alteration
  - 99% plasma protein bound; mainly to albumin
  - Induction and inhibition of metabolism
    - S enantiomer is > 4-fold more potent than R enantiomer
    - S enantiomer is metabolized in part by CYP2C9, 2C19
    - R enantiomer is metabolized in part by CYP1A2, 3A4
- Pharmacodynamic interactions
  - Dietary supplements and vitamin K
  - Antiplatelet drugs, NSAIDs, systemic steroid therapy, other anticoagulants

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Holbrook A, Schulman S, Witt D, et al. Evidenced-based management of anticoagulant therapy. CHEST 2012: 141 (E152S-E184S).

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Warfarin Sample Dose Adjustment Algorithm
Target Range 2.5 (2.0-3.0)

Patient's INR	<1.5	1.5 - 1.9	2.0 - 3.0	3.1 – 3.9	4.0 – 4.9	5.0 – 5.9	6.0 – 10.0	> 10.0
Dose Change	Increase weekly dose 10-20%. Consider extra dose	Increase weekly dose 5-10%	No change	Decrease weekly dose 5-10%	Consider 1-2 day hold and decrease weekly dose 5-15%	Hold 1-2 days and decrease weekly dose 10-20%	Hold anti-coagulant	Hold anti-coagulant. Give 2.5 mg – 5 mg of oral vitamin K
Next INR	7-10 days	7-14 days	Follow up Algorithm	7-14 days	7-14 days	2-10 days	Next business day	Next business day

Consecutive In-range INRs	Repeat INR in
1	2-3 weeks
2	3-4 weeks
3 or greater	4 weeks
*After institution of antibiotics/antifungals that interact with warfarin	3-5 days

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Holbrook A, Schulman S, Witt D, et al. Evidenced-based management of anticoagulant therapy. CHEST 2012: 141 (E152S-E184S).

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Anticoagulation Management During Procedures

Anticoagulant	Procedure Bleeding Risk	Day -6	Day -5	Day -4	Day -3	Day -2	Day -1	Surgery/Procedure (Day 0)	Day +1	Day +2	Day +3	Day +4
Apixaban Edoxaban Rivaroxaban Dabigatran (CrCl ≥ 50 ml/min)	High											
	Low/moderate											
Dabigatran (CrCl <50)	High											
	Low/moderate											
Warfarin	High											
	Low/moderate											

Anticoagulation therapy interruption should occur for high/moderate/low bleeding risk procedures; Interruption is not required for minimal bleed risk procedures (dental, dermatological, ophthalmologic, pacemaker or cardioverter-defibrillator device implantation)

No anticoagulation administered this day

Resume anticoagulation ~48-72 hours after high-bleed risk procedures

GERIATRIC PHARMACIST BOOT CAMP

Douketis JD, et al. Perioperative management of antithrombotic therapy: An American College of Chest Physicans clinical practice guideline. CHEST. 2022; 162(5):e207-e243

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Bleeding Risk Scores

- HASBLED
- HEMORR$_2$HAGES
- ATRIA

A high-risk assessment score is NOT a reason to withhold anticoagulation
It is a reason to assess patient for modifiable risk factors

MODIFIABLE RISK FACTORS FOR BLEEDING

Alcohol use, anemia, chronic steroid therapy, chronic NSAID therapy, antiplatelet therapy, labile INR, uncontrolled comorbidities (e.g., peptic ulcer disease, hypertension, diabetes)

Antidotes

- Idarucizumab for dabigatran
- Andexanet alfa for factor Xa inhibitors

NSAID = non-steroidal anti-inflammatory drugs; INR = international normalized ratio

Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS guidelines for the management of heart failure: a report of the ACCF/AHA joint committee on clinical practice guidelines Circulation 2024; 149(1):e1-e156.

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Statistics in Practice: GARFIELD-AF Registry

Clinical Outcom
Insights from

Population

- 1318 sites, 35 countries, March 2010-Augu
- 52,018 newly diagnosed (2 weeks) with AF
- More patients were female if ≥ 75 (75-84, 52.9%, ≥ 85, 61.2%)

Post-hoc data from databases
Prospective vs retrospective
Good way to draw conclusions for older adults and see what is being done in practice
Can be used to make risk score calculators

Age	< 65 (n=15,691)	65-74 (n=16,946)	75-84 (n=15,252)	≥ 85 (n=4,129)
CHA_2DS_2-VASc	1.8 ±1.2	3.2 ±1.2	4.4 ±1.3	4.5 ±1.3
HAS-BLED	0.6 ±0.7	1.7 ± 0.7	1.8 ± 0.8	1.9 ± 0.8
Antiplatelet Therapy (%)	5,854 (37.9)	5,833 (34.9)	5,015 (33.4)	1,401 (34.2)

Goldhaber SZ, Bassand JP, Camm AJ et al. GARFIELD-AF Investigators. Clinical Outcomes in Older Patients with Atrial Fibrillation: Insights from the GARFIELD-AF Registry. Am J Med. 2024 Feb;137(2):128-136.e13. doi: 10.1016/j.amjmed.2023.10.027.

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Statistics in Practice: GARFIELD-AF Registry

- Based on GARFIELD registry data
- Designed to assess mortality, ischemic stroke, and major bleeding risk in patients newly diagnosed with atrial fibrillation for up to 24 months

	Mortality	Ischemic stroke or systemic embolism	Major bleeding including hemorrhagic stroke
No oral anticoagulation treatment	10.2%	2.5%	1.3%
Warfarin	8.6%	1.8%	2.3%
Direct oral anticoagulant	6.9%	1.4%	1.6%
The percentage is the chance of experiencing the event at 1 year			

Adapted from The Garfield-AF registry. Available at: https://af.garfieldregistry.org/garfield-af-risk-calculator

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Anticoagulation Clinical Pearls

- DOACs are recommended over warfarin for most patients with indications for anticoagulation therapy
- Bleeding can be reducing by managing reversible risk factors
- Pharmacists play an important role in anticoagulation management, including but not limited to appropriate dosing, compliance, drug/drug interactions, and procedure management

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Hyperlipidemia

https://www.freepik.com/vectors/bad

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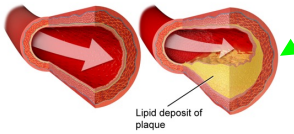
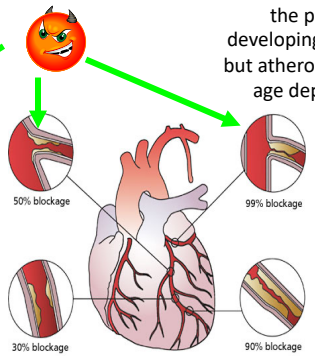
Cholesterol & Heart Disease

~80% of cholesterol in our body is made in the liver
~20% comes from the diet

Physiological changes that occur with aging increase the probability of developing atherosclerosis; but atherosclerosis is not an age dependent event



Coronary Artery Disease



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Assessment of ASCVD Risk

- Assess patient's medical history, lipid panel,* and other ASCVD risk factors
  - Major risk factors include smoking, age, hypertension, and hyperglycemia
- Primary prevention patients with LDL < 190 mg/dL
  - Calculate 10-year ASCVD risk score with the pooled cohort equation
  - Other popular risk scoring tools include PREVENT, SCORE, and MESA score

*Guidelines allow a non-fasting or fasting lipid panel for baseline LDL if TG < 400 mg/dL

http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

GERIATRIC PHARMACIST BOOT CAMP

Grundy SM, Stone NJ, Bailey JL et al. 2018 AHA/ACC guideline on the management of blood cholesterol: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2019; 73:e285-350.

67

Cholesterol Guideline Highlights

- Statins are recommended as first line therapy, with maximally tolerated statin being recommended in most adults
- For adults ≤ 75 years, start high intensity statin (see supplemental handout for review of dosing)
- For adults >75 years, start moderate intensity statin
- Recently, there is a renewed emphasis on LDL goals in which to initiate non-statin therapy

GERIATRIC PHARMACIST BOOT CAMP

Aygun S, Tokgozoglu. Comparison of current internation guideline for the management of dyslipidemia. J Clin Med. 2022;11(23):7249.

68

Guideline Recommendations for LDL Goals

	Secondary Prevention	Familial hypercholesterolemia	Primary prevention
CCS	LDL <70 mg/dL	LDL <97 mg/dL	LDL <77 mg/dL
ACC/AHA	Very high-risk: LDL < 55 mg/dL High risk: LDL <70 mg/dL	LDL <100 mg/dL	LDL <70 mg/dL
ESC	LDL < 55 mg/dL	Very high-risk <55 mg/dL No risk factors <70 mg/dL	Very high-risk <55 mg/dL High risk <70 mg/dL Moderate-risk <100 mg/dL Low-risk <116 mg/dL

CCS- Canadian cardiology society; ACC – American College of Cardiology; AHA – American Heart Association; ESC – European Society of Cardiology;

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Aygun S, Tokgozoglu. Comparison of current internation guideline for the management of dyslipidemia. J Clin Med. 2022;11(23):7249.

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Clinical Trial Data Related to Statin Therapy in Older Adults

- Secondary prevention
  - Strong evidence that statins provide benefit
- Primary prevention
  - Risk likely outweighs benefit if life expectancy is >2.5 years or if patient has other cardiovascular risk factors
  - Coronary artery calcium score may help identify individuals more likely to gain benefit (MESA score)
  - Consider pleiotropic benefits and cost-effectiveness

Treating 100 adults (aged 50-75 years) without known CV disease with a statin for 2.5 years prevented 1 MACE in 1 adult

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Grundy SM, Stone NJ, Bailey JL et al. 2018 AHA/ACC guideline on the management of blood cholesterol: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2019; 73:e285-350.

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Statin Clinical Pearls

- Rosuvastatin/pravastatin are hydrophilic = may penetrate less tissues/not cross blood-brain barrier
  - Better tolerated in older adults
- Rosuvastatin/atorvastatin have longer half-lives
  - Can do every other day dosing
- Simvastatin/lovastatin have more drug/drug interactions via being CYP3A4 substrates
  - Common interactions include diltiazem/verapamil/ amlodipine/amiodarone/azole antifungals
- Statins should NOT be used with gemfibrozil

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Dipiro, JT, Talbert RL, Yee GC, et al. Pharmacotherapy: A Pathophysiologic Approach, 12th edition. McGraw Hill 2023.

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Side Effects and Tolerability in Older Adults

Hepatotoxicity: Incidence risk < 0.01%

Cognitive function

- No evidence statins or very low LDL leads to cognitive impairment
- Decreased risk of any dementia OR 0.80 (0.75-0.86) and Alzheimer's OR 0.68 (0.56-0.81) with high-potency statins

Diabetes

- Extrapolated data to older adults showed incidence risk 0.12% per year of treatment
- Less of a concern with those ≥ 75

Muscle-related (e.g., myalgia, rhabdomyolysis)

- Difference in incidence < 1 % among statin vs. placebo-treated patients
- Risk is < 0.1%
- Most often due to drug interactions

Not all adverse events have been reproducible in clinical studies!

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Razavi AC, Kelly TN, Budoff MJ, et al. Atherosclerotic cardiovascular disease events among statin eligible individuals with and without long-term healthy arterial aging. Atherosclerosis. 2021 Jun;326:56-62. Jamil YA, Cohen R, Alameddine DK, et al. Cholesterol Lowering in Older Adults: Should We Wait for Further Evidence? Curr Atheroscler Rep. 2024 Sep;26(9):521-536.

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Management of Adverse Effects

- Hold current statin for 2 to 6 weeks
  - Rule out other causes (i.e., other disease state, vitamin D deficiency, drug/drug interactions)
- Once symptoms resolve or liver enzymes return to normal, initiate a different statin, with a different metabolic pathway, at a lower dose
- Consider alternative statin dosing with atorv/rosuv (3X per week)
- Criteria for statin intolerance
  - Symptoms must resolve upon discontinuation and occur upon re-challenge
  - Patients should have tried at least 2 statins, one of which was at the lowest dose, preferably agents from different metabolic pathways and lipophilicity

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Lloyd-Jones DM, Morris PB, Ballantyne CM et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of ASCVD risk: a report of the ACC task force on clinical practice guidelines. J Am Coll Cardiol 2016; 68:92-125.

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Non-statin Therapy: Targeting LDL

- Recommended when LDL goal is not being reached with maximally tolerated statin or patient is statin intolerant
- 1ST line: Ezetimibe: Lowers LDL by inhibiting the absorption of biliary and dietary cholesterol. Reduces LDL 10-30%
- 2nd line: PCSK9 inhibitors: Enhances LDL removal by inhibiting PCSK9 which binds to LDL receptors to promote LDL degradation in the liver
- Alternative agents
  - Bile acid resins: interrupts enterohepatic recycling of bile salts
  - Bempedoic acid: inhibitors cholesterol synthesis in the liver upstream from HMG-CoA
  - Inclisiran: small interfering RNA therapy that prevents the formation of PCSK9

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Grundy SM, Stone NJ, Bailey JL et al. 2018 AHA/ACC guideline on the management of blood cholesterol: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2019; 73:e285-350.

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Management of Elevated Triglycerides (TG)

- Lifestyle modifications (reduce fat, reduce carbohydrates, avoid alcohol, increase physical activity, weight loss)
- Treat reversible risk factors (medications, hyperglycemia)
- Start a statin
- Add non-statin therapy for persistently elevated values (>500 mg/dL)
  - Vascepa® (icosapent ethyl)
  - Lovaza® (omega-3 acid ethyl esters)
  - Fibrate (fenofibrate is the preferred agent to use with a statin)

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Grundy SM, Stone NJ, Bailey JL et al. 2018 AHA/ACC guideline on the management of blood cholesterol: a report of the ACC/AHA task force on clinical practice guidelines. J Am Coll Cardiol 2019; 73:e285-350.

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Overview of Cholesterol Lowering Effects

Medication	LDL-C	HDL-C	Triglyceride
Statins	⇩ **LDL 20-63%**	⇧ HDL 5-15%	⇩ TG's 10-30%
Ezetimibe	⇩ **LDL 18%**	⇧ HDL slightly	⇩ TG's 5-10%
PCSK9 Inhibitors	⇩ **LDL 50-70%**	⇧ HDL 5-10%	⇩ TG's 15-25%
Fish oil	⇧ LDL slightly	⇧ HDL slightly	⇩ **TG's 20-50%**
Fenofibrate	⇩ LDL 10-20%	⇧ HDL 11%	⇩ **TG's 30-50%**
Bile Acid Sequestrants	⇩ **LDL 9-26%**	⇧ HDL 4-8%	⇧ TG's 12-28%
Bempedoic acid	⇩ **LDL 15-20%**	⇧ HDL slightly	⇩ TG's 5-10%
Bempedoic acid/ezetimibe	⇩ **LDL 40-50%**	⇧ HDL slightly	⇩ TG's 5-10%

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Dipiro, JT, Talbert RL, Yee GC, et al. Pharmacotherapy: A Pathophysiologic Approach, 12th edition. McGraw Hill 2023.

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Patient Case

DX is a 77-year-old male who is seen in the clinic for follow-up of his hyperlipidemia. He is complaining of current muscle pain that he feels is due to his atorvastatin.

Past Medical History:

- Atrial fibrillation
- Heart failure
- MI (2020)
- Hypertension
- **Dyslipidemia**

Labs and Vitals:

- BP 118/68 mmHg
- HR 72-74 bpm
- Lab results
  - SCr – 1.3 mg/dL
  - K – 4.5 mEq/L
  - TC – 168 mg/dL
  - LDL – 64 mg/dL
  - HDL – 58 mg/dL
  - TG - 132 mg/dL

Current Medications:

- Carvedilol 12.5 mg twice daily
- Sacubitril/valsartan 97/103 mg twice daily
- Apixaban 5 mg twice daily
- Atorvastatin 40 mg/day
- Amiodarone 200 mg/day

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Self-Assessment Question

Which of the following would be the best option to manage the muscle pain that DX is experiencing?

A. Continue his atorvastatin and have him take naproxen for his muscle pain
B. Discontinue atorvastatin and start rosuvastatin 20 mg
C. Discontinue atorvastatin and start pravastatin 40 mg
D. Discontinue atorvastatin and start ezetimibe 10 mg

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Hyperlipidemia Monitoring

- Fasting lipid panel 4-12 weeks after initiation of any cholesterol medication or change in dose
  - Monitor every 3-12 months thereafter
  - LDL = TC – HDL - (TG/5)
  - Measure a direct LDL if LDL < 70 mg/dL or triglycerides are >400 mg/dL
  - The calculated LDL is less accurate at low LDL values or when triglyceride values are high
- Monitor other values if clinically indicated
  - Creatine kinase, liver enzymes, A1C

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Hyperlipidemia Clinical Pearls

- Statin therapy is often indicated in older adults
  - Limited role of non-statin medications
- Monitor for adverse effects and manage appropriately
  - Assess for interactions and contributing factors
  - Statin-associated adverse effects may improve with a different statin, decreasing the dose or extending the dosing interval

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Cardiovascular Palliative Care

- Consider short and long-term goals of care
- Hypertension; less intensive blood pressure goal
- Heart failure; goal is to provide comfort care
- Anticoagulation; consider risk of stroke vs risk of bleeding
- Hyperlipidemia; may discontinue statin therapy

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