

Disclaimer

Ambulatory Care Case-Based Reviews

Chronic Cardiovascular Disorders

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Basic Rules

- Learning should be
 - Easy to understand clinically relevant
 - Evidence-based
 - Oriented to the patient but
- It also should be FUN

Introduction



Anthony Busti, MD, PharmD, MSc, FNLA, FAHA



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Agenda

- Case with 5 primary care indications
- A special coupon code & feedback
- Live Q&A

Integrated Case-Reviews

- Case 1 -



Case 1

- A 54-year-old female with a PMH of DM2, HTN, HFrEF, chronic low-back pain comes in by EMS with reports of waking up this morning with a sudden onset of shortness of breath and found to have flash pulmonary edema in the context of uncontrolled HTN and known HF.
- The patient was stabilized, underwent diuresis, and was sent home.
- What was the patient's cause for exacerbation?



Case 1

- Drugs to use with Caution -

TABLE 12 Selected Prescription Medications That May Cause or Exacerbate HF

Drug or Therapeutic Class	Associated With HF		Magnitude of HF Induction or Precipitation	LOE for HF Induction or Precipitation	Possible Mechanism(s)	Onset
	Causes Direct Myocardial Toxicity	Exacerbates Underlying Myocardial Dysfunction				
COX-2, nonselective inhibitors (NSAIDs)		X	Major	B	Prostaglandin inhibition leading to sodium and water retention, increased systemic vascular resistance, and blunted response to diuretics	Immediate
COX-2 selective inhibitors (COX-2 inhibitors)		X	Major	B		
Thiazolidinediones	X		Major	A	Possible calcium channel blockade	Intermediate
Saxagliptin	X		Major	A	Unknown	Intermediate to delayed
Alogliptin	X		Major	A		
Flecainide	X		Major	A	Negative inotrope, proarrhythmic effects	Immediate to intermediate
Disopyramide	X		Major	B		
Sotalol	X		Major	A	Proarrhythmic properties, beta blockade	Immediate to intermediate
Dronedarone	X		Major	A		
Alpha-1 blockers						
Doxazosin	X		Moderate	B	Beta-1-receptor stimulation with increases in renin and aldosterone	Intermediate to delayed
Diltiazem	X		Major	B	Negative inotrope	Immediate to intermediate
Verapamil	X		Major	B		
Nifedipine	X		Moderate	C		

JACC 2022;79(77):e263-e421.

Case 1

- Drugs to use with Caution -

- What other common drugs were missing from that chart?
 - Chemo (Anthracyclines): Doxorubicin, Daunorubicin
 - Antifungals: amphotericin B, +/- Itraconazole
 - _____

Circulation 2016;134:e32-e69.

Case 1

- Risk Factors for HF -

- What are the *most common* risk factors for HF in the US?
 - HTN
 - Ischemic heart disease
 - Valvular disorders
 - Others:
 - Chemotherapy
 - Viral myocarditis
 - OSA

Case 1

- Comprehensive Care -

- What other information do we need at this point?
 - Ethnicity → _____
 - Past medical history → _____
 - Current Medications → _____
 - Vital signs → _____
 - Dry weight → _____
 - What about other "weights"? → _____

Case 1

- Comprehensive Care -

- What other data do we need at this point?
 - Cardiopulmonary exercise testing → _____
 - Labs → _____
 - When might BNP be falsely low?
 - Chest radiograph → _____
 - ECG → _____
 - ECHO results → _____
 - Our patient: Baseline (_____%) vs. Current (_____%)

Integrated Case-Reviews

- Evaluation & Work-Up: Case 1 -



Table 6. Classification of Overweight and Obesity by BMI and Waist Circumference (31 [EL 4; NE])

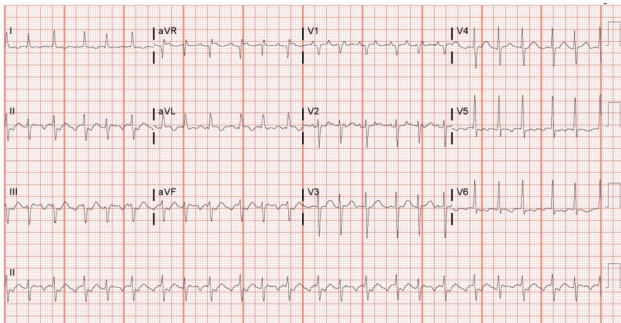
Classification	BMI		Waist	
	BMI (kg/m ²)	Comorbidity Risk	Waist Circumference and Comorbidity Risk	
			Men ≤40 in (102 cm) Women ≤35 in (88 cm)	Men >40 in (102 cm) Women >35 in (88 cm)
Underweight	<18.5	Low but other problems		
Normal weight	18.5–24.9	Average		
Overweight	25–29.9	Increased	Increased	High
Obese class I	30–34.9	Moderate	High	Very high
Obese class II	35–39.9	Severe	Very high	Very high
Obese class III	≥40	Very severe	Extremely high	Extremely high

Abbreviations: BMI = body mass index; in = inches.

ACE Obesity Guidelines 2016

Case 1

- Evaluation & Workup -



Case 1

- Evaluation & Workup -

- 54-yr-old female (Hispanic)
- PMH:
 - DM2, HTN, HFrEF
- Current Meds:
 - Metformin, glyburide, lisinopril, metoprolol tartrate, furosemide
- Current VS:
 - T = 98.7, P = 68, BP = 145/91, RR = 14, O2Sat = 96%
 - Ht: 5' 7", Wt = 95 kg, Waist circumference = 42"
 - IBW = ___ kg and BMI = _____

Case 1

- Evaluation & Workup -

- Labs:
 - CBC = nml
 - BMP: Cr = 1.1, Glucose = 145 (fasting)
 - HgbA1C = 7.8%
 - TSH = 2.1
 - Lipids: TC = 205, HDL = 32, TG = 210, LDL = 131
 - BNP = 140 pg/mL
- ECHO:
 - EF: Baseline (___ %) vs. Current (___ %)
- NYHA Class II:
 - Mild symptoms & limitations during ordinary activity

Case 1

- Evaluation & Workup -

- Problem List:
 - ➔ – HFrEF by history, labs, and ECHO
 - HTN (uncontrolled?)
 - Hyperlipidemia (uncontrolled and untreated)
 - DM2 (uncontrolled)
 - Obesity

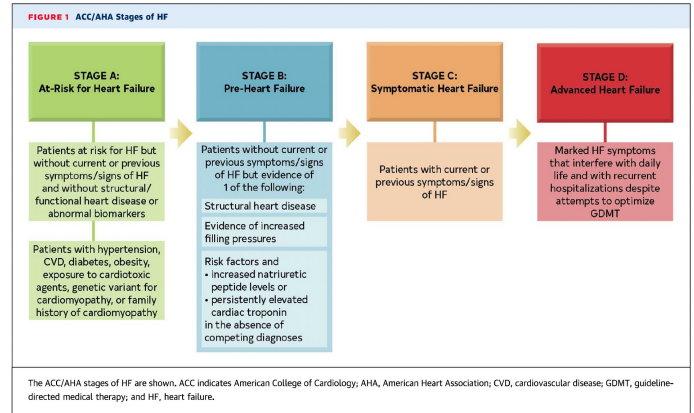
Level of Evidence

TABLE 2 Applying American College of Cardiology/American Heart Association Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

CLASS (STRENGTH) OF RECOMMENDATION	BENEFIT >>> RISK	LEVEL (QUALITY OF EVIDENCE)
CLASS 1 (STRONG)	Benefit >>> Risk	LEVEL 1 • High-quality evidence from more than 1 RCT • Meta-analysis of high-quality RCTs • One or more RCTs conducted by high-quality registry studies
CLASS 2a (MODERATE)	Benefit >> Risk	LEVEL 1-R (Randomized) • Moderate-quality evidence from 1 or more RCTs • Meta-analysis of moderate-quality RCTs
CLASS 2b (MODERATE)	Benefit >> Risk	LEVEL 1-NR (Nonrandomized) • Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analysis of such studies
CLASS 2c (WEAK)	Benefit = Risk	LEVEL 1-LD (Limited Data) • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analysis of such studies • Physiological or mechanistic studies in human subjects
CLASS 3 (No Benefit) (MODERATE) (Generally, LOE A or B use only)	Benefit = Risk	LEVEL 1-EO (Expert Opinion) • Consensus of expert opinion based on clinical experience
CLASS 3a (MODERATE)	Benefit >> Risk	LEVEL 2 • High-quality evidence from more than 1 RCT • Meta-analysis of high-quality RCTs • One or more RCTs conducted by high-quality registry studies
CLASS 3b (MODERATE)	Benefit >> Risk	LEVEL 2-R (Randomized) • Moderate-quality evidence from 1 or more RCTs • Meta-analysis of moderate-quality RCTs
CLASS 3c (MODERATE)	Benefit >> Risk	LEVEL 2-NR (Nonrandomized) • Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analysis of such studies
CLASS 3d (WEAK)	Benefit = Risk	LEVEL 2-LD (Limited Data) • Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analysis of such studies • Physiological or mechanistic studies in human subjects
CLASS 3e (WEAK)	Benefit = Risk	LEVEL 2-EO (Expert Opinion) • Consensus of expert opinion based on clinical experience

Case 1

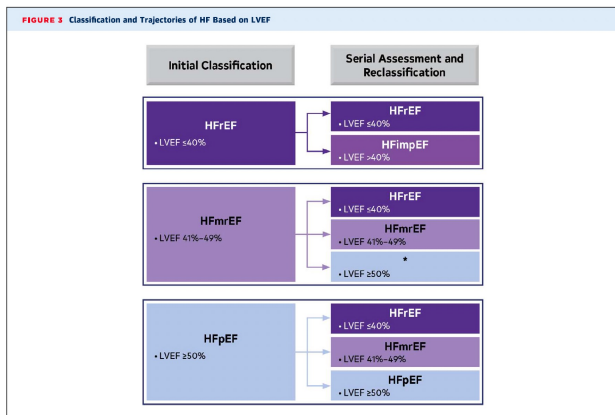
- Classification of HF -



JACC 2022;79(77):e263-e421.

Case 1

- Classification of HF -



JACC 2022;79(77):e263-e421.

Case 1

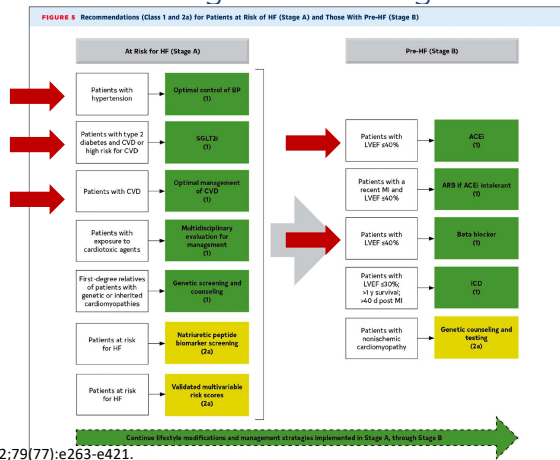
- Evaluation & Workup -

Problem List:

- HFrEF (Stage C)
- HTN (uncontrolled?)
- Hyperlipidemia (uncontrolled and untreated)
- DM2 (uncontrolled)
- Obesity

Case 1

- Management Strategies -



JACC 2022;79(77):e263-e421.

Case 1

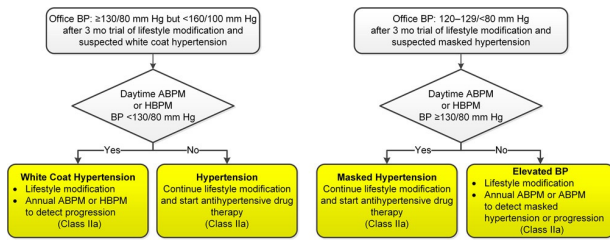
- Evaluation & Workup -

Problem List:

- HFrEF (Stage C)
- HTN (uncontrolled?)
- Hyperlipidemia (uncontrolled and untreated)
- DM2 (uncontrolled)
- Obesity

Case 1 - Hypertension -

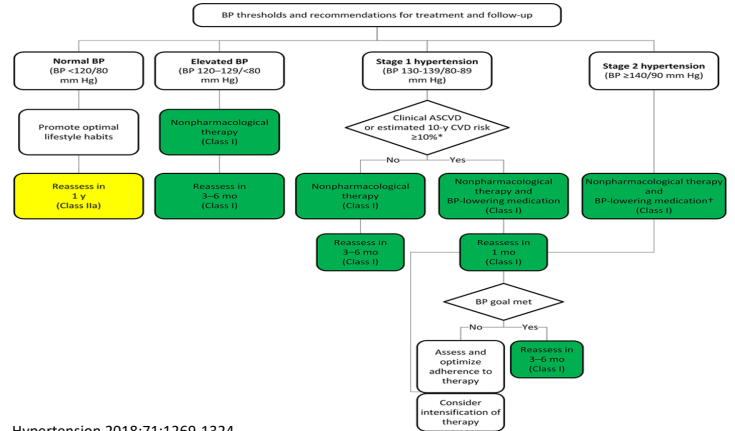
- Does our patient have uncontrolled HTN?



Hypertension 2018;71:1269-1324.

ACC/AHA/AAPA/ABC/ACPM/AGS/ASH

- Hypertension Guidelines -



Hypertension 2018;71:1269-1324.

ACC/AHA/AAPA/ABC/ACPM/AGS/ASH

- Hypertension Guidelines -

Patient Group	Blood Pressure (mm Hg)	Initial Treatment Options
Normal	< 120 / < 80	
Elevated	120 – 129 / < 80	Lifestyle Modifications
Stage 1	130 – 139 / 80 - 89	Thiazide diuretics* CCBs* ACE or ARBs
Stage 2	≥ 140/90	Combination with 2 first line agents of different classes

* Preferred if black adults

What drug classes are missing?

What are the ideal antihypertensive medications?

Hypertension 2018;71:1269-1324.



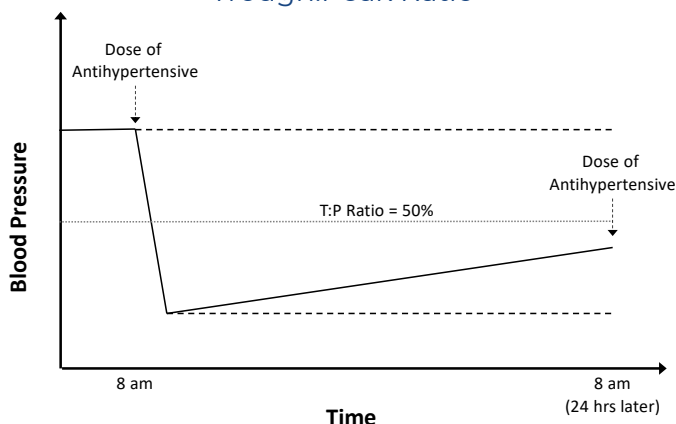
Ideal Antihypertensives

Trough:Peak Ratio

- Goal: Maintain antihypertensive effects over the entire 24-hour period.
 - Trough:Peak ratio.
 - The trough is the decrease in blood pressure maintained at the end of the dosing interval versus the peak lowering, usually around the Cmax. To offer 24-hour control, drugs need a T:P ratio of _____

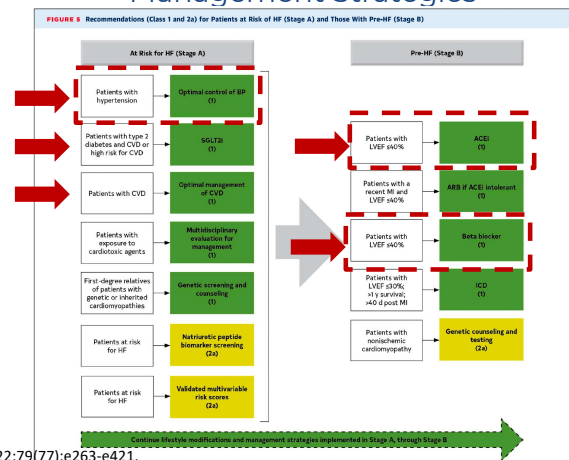
Ideal Antihypertensives

Trough:Peak Ratio



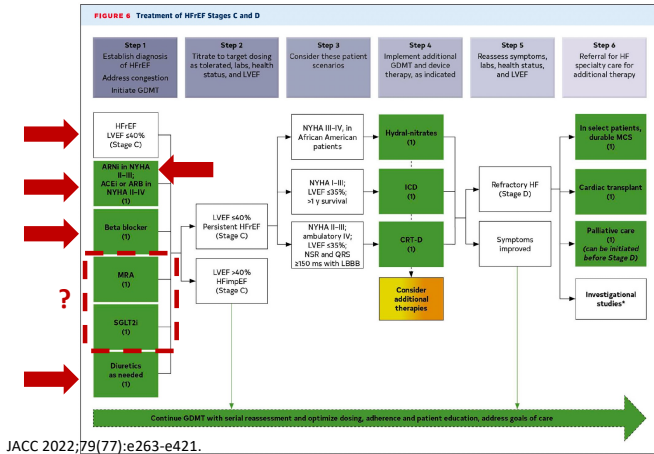
Case 1

- Management Strategies -



JACC 2022;79(77):e263-e421.

Case 1 - Management Strategies -



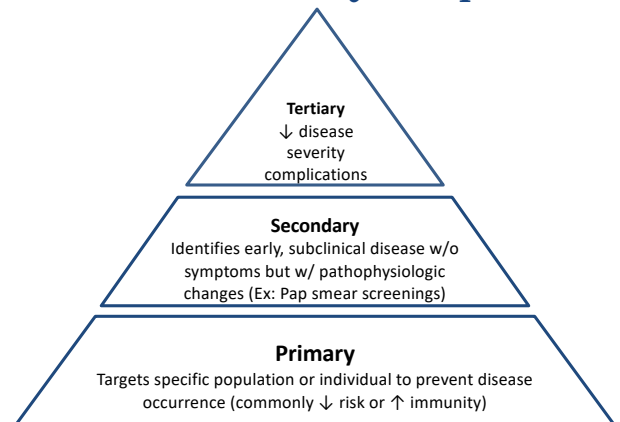
Case 1 - Evaluation & Workup -

- Problem List:
 - HFREF (Stage C)
 - HTN (uncontrolled?)
 - Hyperlipidemia (uncontrolled and untreated)
 - DM2 (uncontrolled)
 - Obesity

Case 1 - Hyperlipidemia -

- Does our patient need primary, secondary, or tertiary prevention?

USD-HHS Healthy People 2030



Kisling LA, Das J. Prevention Strategies. In: StatPearls [Internet].

Case 1 - Hyperlipidemia -

- What is our patient's risk for ASCVD?

AMERICAN COLLEGE OF CARDIOLOGY ASCVD Risk Estimator Plus

Estimate Risk Therap

10.3% Current 10-Year ASCVD Risk*
Lifetime ASCVD Risk: 50% Optimal ASCVD Risk: 1.2%

Current Age: 54, Sex: Female, Race: White

Systolic Blood Pressure: 145, Diastolic Blood Pressure: 91

Total Cholesterol: 208, HDL Cholesterol: 32, LDL Cholesterol: 131

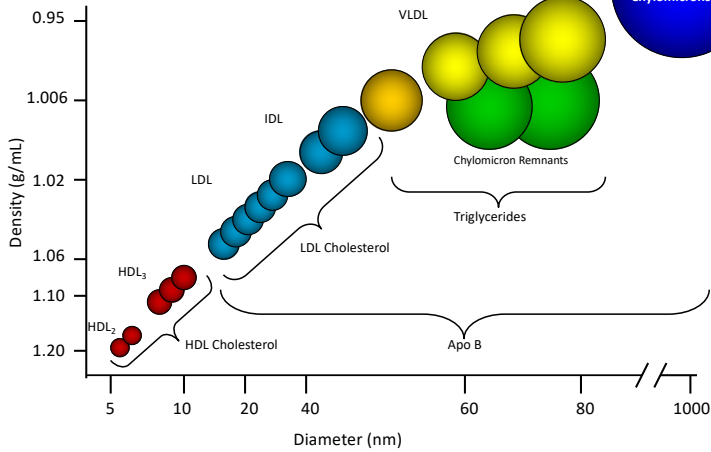
History of Diabetes: Yes, Smoker: Former, On a Statin: Yes, On Aspirin: Yes, On Aggrify Therapy: No

Note: These estimates may underestimate the 10 year and lifetime risk for persons from some racial/ethnic groups, especially American Indians, some Asian Americans (e.g., of south Asian ancestry), and some Hispanics (e.g., Puerto Ricans) and may overestimate the risk for others, including some Asian Americans (e.g., of east Asian ancestry) and some Hispanics (e.g., Mexican Americans). Because the primary use of these risk estimates is to facilitate the very important discussion regarding risk reduction through lifestyle change, the impression introduced is small enough to justify proceeding with lifestyle change counseling informed by these results.

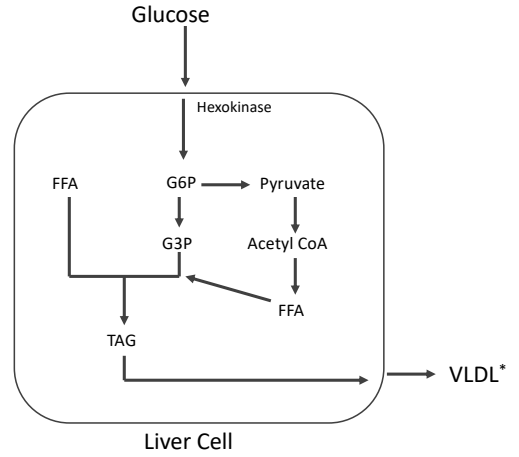


What do we make of the lipid profile?

Lipoprotein Subclasses

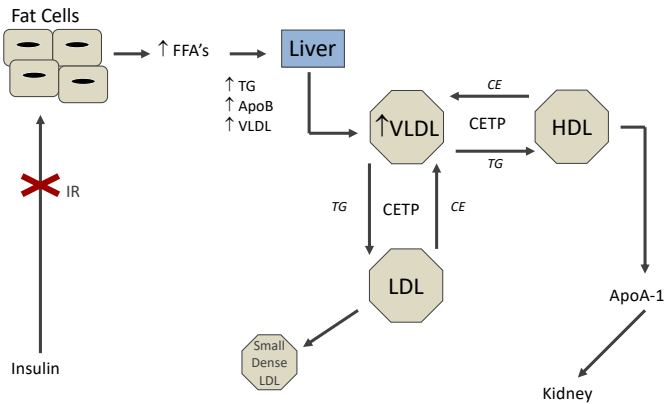


Pathology of Type 2b Dyslipidemia



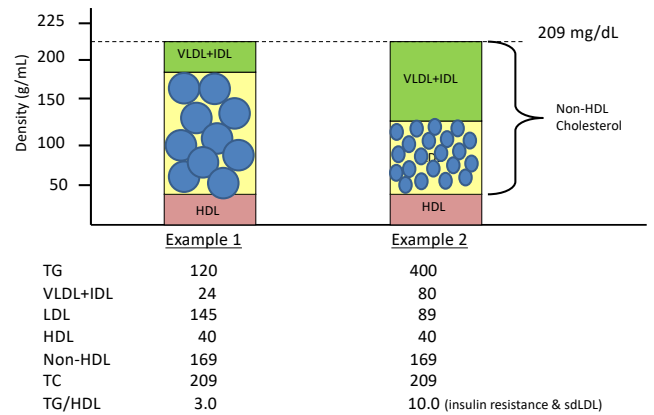
* VLDL = TG/5

Small LDL Patterns & HDL Removal

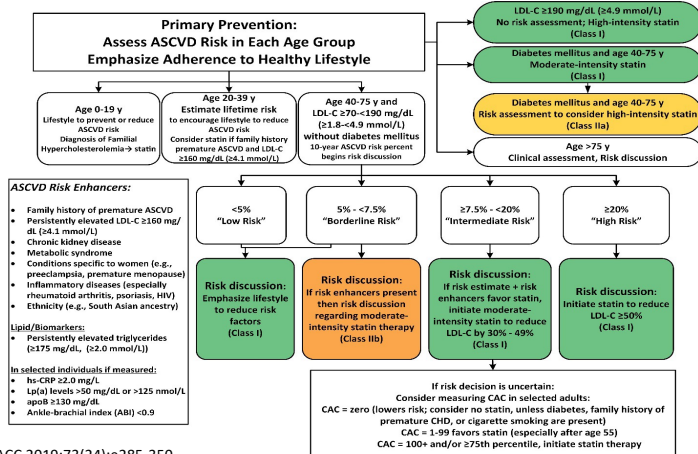


Ginsberg HN. J Clin Invest 2000;106:453-458.

Why TG & non-HDL Goals?



Guidelines



JACC 2019;73(24):e285-350.



High-Yield Clinical Integration

What is the evidence for statins in primary vs. secondary prevention?

Landmark Primary Prevention Trials

Study	Year	n	Drug	Results
LRC-CPPT	1984	1,906	cholestyramine	CHD incidence ↓ 18.9%
HHS	1987	2,051	Gemfibrozil	CHD incidence ↓ 34%
WOSCOPS	1995	3,302	Pravastatin	Death from all CVD ↓ 32%; non-fatal MI ↓ 31%
AFCAPS/ TexCAPS	1998	3,304	Lovastatin	First acute event ↓ 37%
PROSPER	2002	3,239 / 5804	Pravastatin	HR, 0.94 (0.77-1.15; p=0.19). Combined CVD no different
ASCOT-LLA	2003	10,305	Atorvastatin	Stopped early. Nonfatal MI & fatal CHD ↓ 36%. Fatal & non-fatal stroke ↓ 27%.
Juniper	2008	17,802	Rosuvastatin	In pts with hsCRP>2 mg/dL; 20% risk reduction in overall mortality

LRC-CPPT = Lipid Research Clinics Coronary Primary Prevention Trial; HHS = Helsinki Heart Study; WOSCOPS = West of Scotland Coronary Prevention Study; AFCAPS/TexCAPS = Air Force/Texas Coronary Atherosclerosis Prevention Study; PROSPER = Propective Study of Pravastatin in the Elderly at Risk; ASCOT-LLA = Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm

Landmark Secondary Prevention Trials

Study	Year	n	Drug	Results
4S	1994	2,221	Simvastatin	CHD mortality ↓ 42%
CARE	1996	2,081	Pravastatin	CHD death or nonfatal MI ↓ 24%
LIPID	1998	4,512	Pravastatin	CHD death ↓ 24%
MIRACL	2001	1,538	Atorvastatin	Recurrent events ↓ 16%; stroke ↓ 50%
PROSPER	2002	2,565	Pravastatin	Elderly pts* (70-82 yrs) Combined CVD ↓ by 22%
HPS	2002	20,536	Simvastatin	All cause mortality ↓ by 13%; Coronary death rate ↓ 18%
PROVE IT	2004	4,162	Atorvastatin vs Pravastatin	Composite CVD ↓ 16%

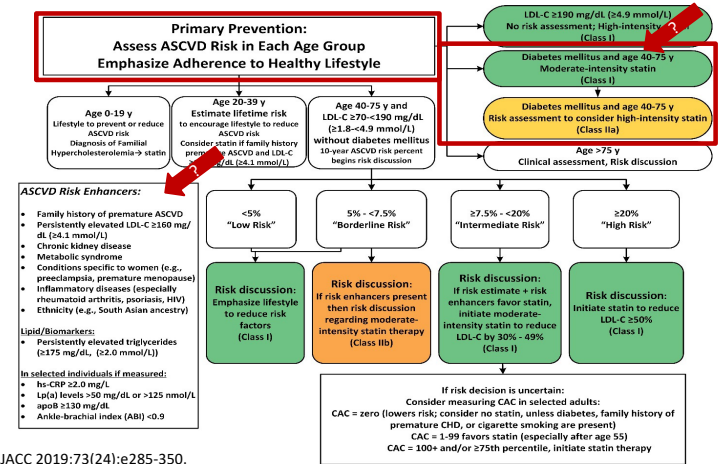
4S = Scandinavian Simvastatin Survival Study; CARE = Cholesterol and Recurrent Events Trial; LIPID = Long-term Intervention with Pravastatin in Ischemic Disease Study; MIRACL = Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering Study; PROSPER = Propective Study of Pravastatin in Elderly at Risk; HPS = Health Protection Study; PROVE IT/TIMI 22 = Pravastatin or Atorvastatin Evaluation and Infection Therapy – Thrombolysis in MI 22 Study.

Statin Therapy

	High-Intensity Statins	Moderate Intensity	Low Intensity
Primary Prevention	ASCVD Risk of ≥ 20% or "High Risk"	ASCVD Risk of ≥ 7.5% to < 20% or "Intermediate Risk" ASCVD Risk of 5% to < 7.5% or "Borderline Risk" + ASCVD Risk Enhancers	ASCVD Risk of < 5% or "Low Risk"
Secondary Prevention	"Very High Risk" ASCVD	ASCVD + Unable to Tolerate High-Intensity Statins	ASCVD + Unable to Tolerate Moderate-Intensity Statins
LDL-c Lowering	≥ 50%	30% - 49%	< 30%
Statins	<ul style="list-style-type: none"> Atorvastatin 40 – 80 mg Rosuvastatin 20 – 40 mg 	<ul style="list-style-type: none"> Atorvastatin 10 – 20 mg Rosuvastatin 5 – 10 mg Simvastatin 20 – 40 mg Pravastatin 40 – 80 mg Lovastatin 40 – 80 mg Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1 – 4 mg 	<ul style="list-style-type: none"> Simvastatin 10 mg Pravastatin 10 – 20 mg Lovastatin 20 mg Fluvastatin 20 – 40 mg

JACC 2019;73(24):e285-350.

Hyperlipidemia Guidelines



JACC 2019;73(24):e285-350.

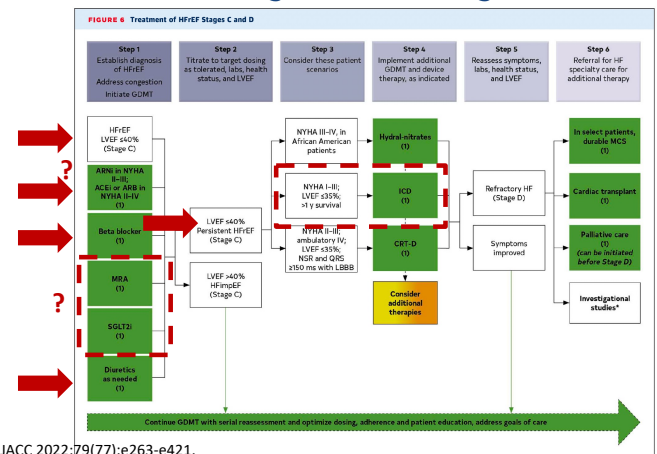
Integrated Case-Reviews

- Other Considerations -



Case 1

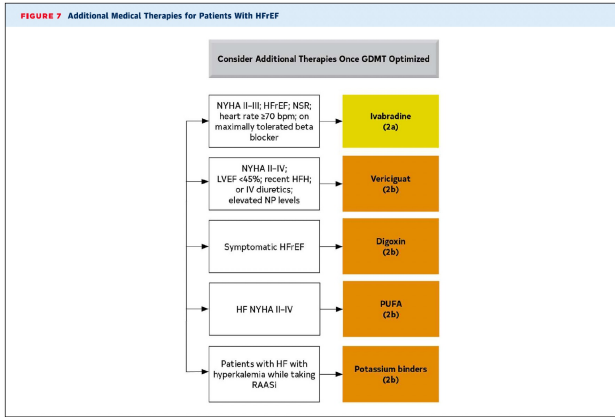
- Management Strategies -



JACC 2022;79(77):e263-e421.

Case 1

- Less Likely Tested But ... -



JACC 2022;79(77):e263-e421.

Case 1

- Evaluation & Workup -

- Problem List:
 - HFrEF (Stage C)
 - HTN (uncontrolled?)
 - Hyperlipidemia (uncontrolled and untreated)
 - ➔ – DM2 (uncontrolled)
 - ➔ – Obesity

Case 1

- Plan -

- Problem List:
 - HFrEF (Stage C)
 - Switch patient from _____
 - Switch metoprolol tartrate to _____
 - Add SGLT2i (Dapagliflozin or _____)
 - +/- MRA
 - Consider ICD placement since HFrEF with EF $< 35\%$ + NYHA II
 - HTN (uncontrolled?)
 - Re-evaluate after the above for HF
 - Hyperlipidemia (uncontrolled and untreated)
 - Improved DM control + weight loss
 - Moderate-intensity statin (atorvastatin, rosuvastatin)
 - DM2 (uncontrolled)
 - SGLT2i
 - What about GLP-1 agonist (DM, HF, & Obesity): _____
 - But NO → _____
 - Obesity

Coupon

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