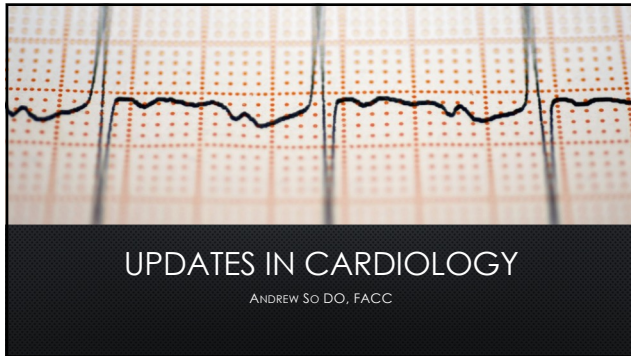
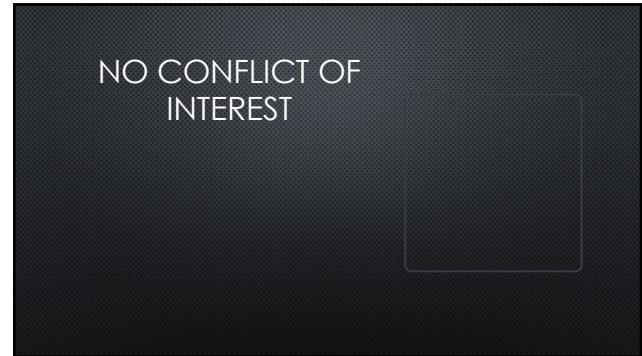
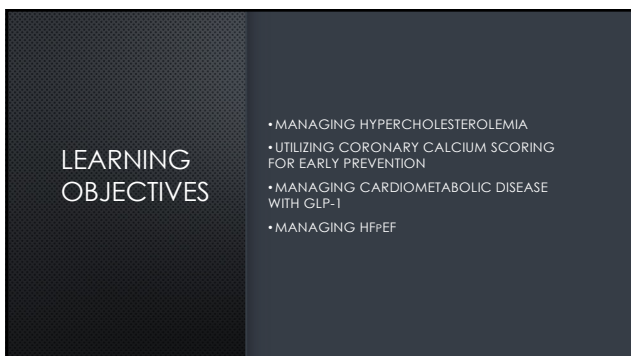




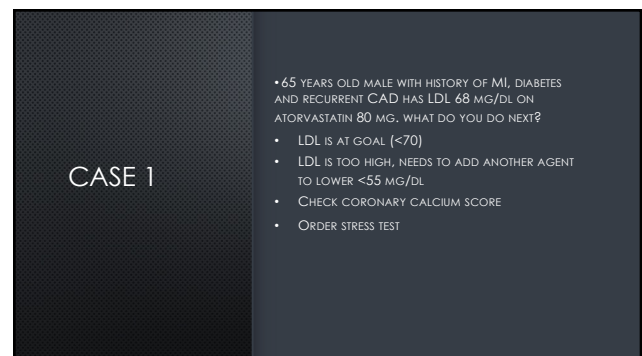
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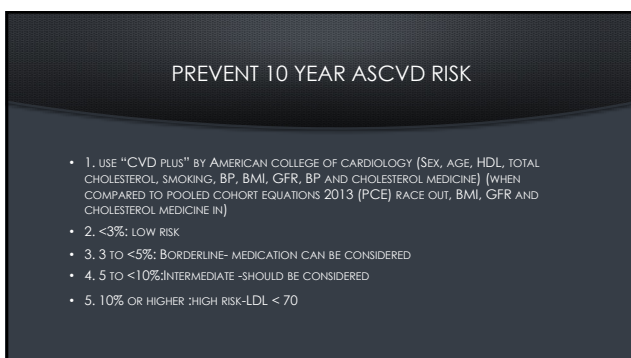
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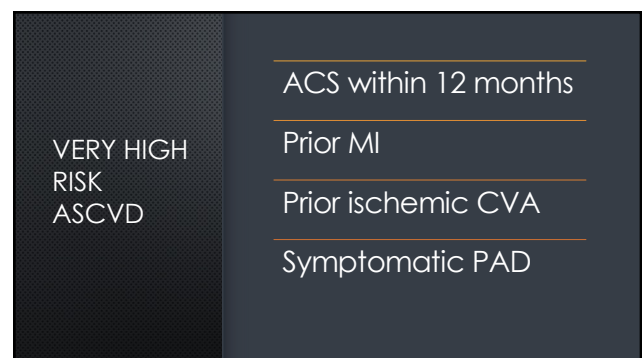
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4



5



6

LDL TARGETS ARE OFFICIALLY BACK

- 1. PERCENTAGE REDUCTION LESS IMPORTANT, ABSOLUTE NUMBER IS MORE IMPORTANT
- 2. BORDERLINE, INTERMEDIATE RISK: <100 MG/DL
- 3. HIGH RISK PRIMARY PREVENTION: <70 MG/DL
- 4. **ASCVD, VERY HIGH RISK: <55 MG/DL**
- 5. ASCVD, HIGH RISK: <70 MG/DL

7

CPR APPROACH

CALCULATE->PERSONALIZE->RECLASSIFY WITH CAC WHEN APPROPRIATE

8

PERSONALIZE WITH RISK ENHANCERS

- FAM HX
- ELEVATED LP(A)
- APOB
- Hs-CRP
- CHRONIC INFLAMMATION
- CKD
- OBESITY
- HYPERTRIGLYCERDEmia

9

MEASURE LP(A)

At least once

>50 mg/dl->1.4% x ASCVD risk

>100 mg/dl->2.0% x ASCVD risk

Genetic and stable

10

USE CAC

Man	Goal	Target	Defer
Man >40, women >45 yo with borderline / intermediate risk	Goal <100	Target lower as CAC burden increases	CAC=0: possibly defer medication

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CORONARY ARTERY CALCIUM

Any->LDL <100 mg/dl

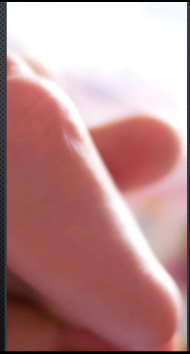
100-999->LDL < 70 mg/dl

>1000->extremely high risk->LDL < 55 mg/dl

12

EARLIER TREATMENT

- AGE 9-11
- YOUNG ADULTS WITH LDL >160 MG/DL
- STRONG FAMILY Hx



13

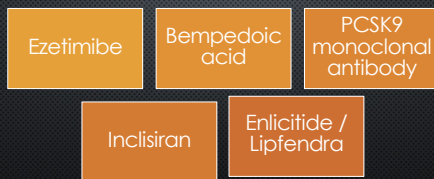
TREAT REGARDLESS OF PREVENT SCORE

- TYPE 1 OR 2 DIABETES
- CKD, STAGE 3 OR 4
- HIV



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COMBINATION TX ENCOURAGED SOONER



15

LDL REDUCTION

Ezetimibe: 20%
Moderate intensity Statin: 30-50%
High intensity statin: >50%
Bempedoic acid: 20%
PCSK9 monoclonal antibody: 50-60%
Inclisiran: 50%

16

EZETIMIBE

- Blocks cholesterol absorption in the small intestine
- Inhibits NPC1L1 transporter on intestinal cells
- Liver pulls more LDL particles from blood through increased LDL-receptor activity
- 20% LDL, 5-10% triglyceride reduction

17

BMPEDOIC ACID
(NEXLETOL)

- Combination with Ezetimibe (Hexlert)
- 180 mg daily
- Inhibits ATP-citrate lyase (ACLY), an enzyme in the liver's cholesterol production pathway. ACLY works upstream from HMG-CoA reductase, the enzyme inhibited by statins.
- For statin intolerance, partial statin intolerance, preference over injections
- CV outcome evidence
- Hyperuricemia and gout, tendon rupture, liver, muscle.

18

PCSK9 MONOCLONAL ANTIBODIES

- Evolocumab (Repatha), Alirocumab (Praluent)
- Binds circulating PCSK9 (LDL receptor destroyer) → LDL receptors to be recycled.
- Recheck 1-2 months
- Homozygous FH: less effective since there is no functional LDL receptors

19

INCLISIRAN (LEQVIO)

- SMALL INTERFERING RNA (siRNA), BINDS PCSK9 MESSENGER RNA → DESTROYED → LESS PCSK9 PROTEIN
- TARGETS PRODUCTION OF PCSK9 IN THE LIVER
- Q 6 MONTHS
- 50% LDL REDUCTION
- INJECTION BY HEALTH CARE PROVIDER
- NO MUSCLE TOXICITY, NO MAJOR LIVER ISSUES

20

LIPFENDRA

- FDA APPROVED 7/2024
- ORAL PCSK9 BLOCKER
- LDL REDUCTION 55-60%
- MACROCYCLIC PEPTIDE THAT BINDS CIRCULATING PCSK9
- EMPTY STOMACH, 30 MIN BEFORE EATING (OTHERWISE 50% DRUG EXPOSURE REDUCTION)
- NO CV OUTCOME DATA
- EXCELLENT SAFETY PROFILE

21

30 YEARS OLD MALE WITH WELL CONTROLLED TYPE I DIABETES. LDL 65, ASYMPTOMATIC. STATIN?

1. START STATIN
2. CORONARY CALCIUM SCORE THEN DECIDE
3. HOLD SINCE LDL < 70
4. ONLY IF THERE ARE RISK ENHANCERS (FAMILY HX, ELEVATED Lp(A), APOB, CRP, CKD, OBESITY, OR HYPERTRIGLYCERIDEMIA)

22

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23

TREAT REGARDLESS OF PREVENT SCORE

- TYPE 1 OR 2 DIABETES
- CKD, STAGE 3 OR 4
- HIV

24

45 YEARS OLD MALE SMOKER WHO SUFFERS FROM CLAUDICATION. LDL 55. PREVENT SCORE IS LOW (1.3% 10% RISK OF ASCVD)

- START STATIN
- HOLD STATIN SINCE LDL IS 55 AND PREVENT SCORE IS LOW
- HOLD UNTIL CAC RESULT
- CHECK ONLY IF OTHER RISK ENHANCERS ABNORMAL

25

45 YEARS OLD MALE SMOKER WHO SUFFERS FROM CLAUDICATION. LDL 55. PREVENT SCORE IS LOW (1.3% 10% RISK OF ASCVD)

- **Start Statin**
- HOLD STATIN SINCE LDL IS 55 AND PREVENT SCORE IS LOW
- HOLD UNTIL CAC RESULT
- CHECK ONLY IF OTHER RISK ENHANCERS ABNORMAL

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VERY HIGH
RISK
ASCVD

ACS within 12 months

Prior MI

Prior ischemic CVA

Symptomatic PAD

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- 5. ASCVD, HIGH RISK: <70 MG/DL

28

60 YEARS OLD MALE WITH LDL 150, SMOKER, ON HTN MEDICATION (INTERMEDIATE 10 YEARS RISK: 6.2%). HE IS WORRIED ABOUT SIDE EFFECTS FROM CHOLESTEROL MEDICATIONS, ESPECIALLY STATIN. WHAT TO DO NEXT?

- 1. START NON STATIN MEDICATION TO BRING LDL <100
- 2. CHECK FOR RISK ENHANCER AND LOWER LDL ACCORDINGLY WITH NON-STATIN MEDICATION
- 3. CAC AND LOWER LDL ACCORDINGLY
- 4. TRY RED YEAST RICE

29

60 YEARS OLD MALE WITH LDL 150, SMOKER, ON HTN MEDICATION (INTERMEDIATE 10 YEARS RISK: 6.2%). HE IS WORRIED ABOUT SIDE EFFECTS FROM CHOLESTEROL MEDICATIONS, ESPECIALLY STATIN. WHAT TO DO NEXT?

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- 2. **CHECK FOR RISK ENHANCER AND LOWER LDL ACCORDINGLY WITH NON-STATIN MEDICATION**
- 3. **CAC AND LOWER LDL ACCORDINGLY**
- 4. TRY RED YEAST RICE

30

THERE ARE NO RISK ENHANCERS BUT CAC SCORE WAS 1200. THE CALCIUM IS MOSTLY IN PROXIMAL LAD. NOW WHAT?

1. START MAXIMUM DOSE STATIN
2. START PCSK9 INHIBITOR AND EZETIMIBE OR BEMPEDOIC ACID
3. CONSULT CARDIOLOGY FOR ISCHEMIC EVALUATION AND FURTHER MANAGEMENT
4. CARDIAC CTA AND MEASURE FFR TO MAKE SURE THERE IS NO "WIDOW MAKER"

31

THERE ARE NO RISK ENHANCERS, BUT CAC SCORE WAS 1200. THE CALCIUM IS MOSTLY IN PROXIMAL LAD. NOW WHAT?

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2. START PCSK9 INHIBITOR AND EZETIMIBE OR BEMPEDOIC ACID
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32

GLP-1 (GLUCAGON-LIKE PEPTIDE-1)

- NATURAL INCRETIN HORMONE RELEASED BY INTESTINE AFTER EATING
- STIMULATES INSULIN RELEASE WHEN GLUCOSE IS ELEVATED
- REDUCES GLUCAGON PRODUCTION
- SLOWS STOMACH EMPTYING
- DECREASE APPETITE AND INCREASES SATIETY
- LOWER BLOOD GLUCOSE AND WEIGHT

33

GLP-1 RECEPTOR AGONISTS

- MEDICINES THAT MIMIC GLP-1
- SEMAGLUTIDE: OZEMPIC, WEGOVY, RYBELSUS
- DULAGLUTIDE: TRULICITY
- LIRAGLUTIDE: VICTOZA, SAXENDA
- TIRZEPATIDE: MOUNJARO, ZEPBOUND- ACT ON BOTH GIP AND GLP-1

34

GIP (GLUCOSE-DEPENDENT INSULINOTROPIC POLYPEPTIDE)

- HORMONE RELEASED BY SMALL INTESTINE AFTER EATING
- STIMULATE INSULIN RELEASE WITH ELEVATED GLUCOSE
- REGULATE GLUCAGON DECREASE APPETITE AND FAT METABOLISM

35

GLUTIDES

- OBESITY, BLOOD PRESSURE, DIABETES, KIDNEY, AND CV EVENT
- NAUSEA, VOMITING, CONSTIPATION, DIARRHEA, REFLUX
- PANCREATITIS AND GALLBLADDER DISEASE
- AVOID WITH Hx OF MEDULLARY THYROID CARCINOMA OR MEN2

36

ESTABLISHED CAD, PRIOR STROKE WITH OBESITY

- SEMAGLUTIDE (WEGOVY): REDUCES RISK OF CV DEATHS, NON FATAL MI AND STROKE

37

DM II WITH ASCVD OR HIGH CV RISK

- SEMAGLUTIDE, DULAGLUTIDE AND LIRAGLUTIDE
- REDUCES MAJOR CV EVENTS WHILE CONTROLLING GLUCOSE

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OBESITY RELATED HFPEF

- SEMAGLUTIDE OR TIRZEPATIDE
- WEIGHT LOSS, IMPROVED DYSPNEA, EXERCISE CAPACITY, QOL, INFLAMMATION AND CHF EVENTS.
- NOT CHF TREATMENT FOR HFREF->SGLT2 INHIBITOR

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SGLT2 INHIBITOR (SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITOR)

- BLOCK GLUCOSE AND SODIUM REABSORPTION IN THE KIDNEYS->GLUCOSE, SODIUM AND WATER INTO URINE
- HF AND CKD PATIENTS EVEN WITHOUT DM
- EMPAGLIFLOZIN-JARDIANCE, DAPAGLIFLOZIN-FARXIGA, CANAGLIFLOZIN-INVOKANA

40

GLIFLOZINS

- REDUCE HF HOSPITALIZATION
- BENEFITS HFREF, HFmrEF, AND HFpEF
- SLOW CKD PROGRESSION
- MILD DIURESIS AND LOWER BP
- REDUCE CV DEATH

41

GLIFLOZINS

- GENITAL YEAST INFECTION
- VOLUME DEPLETION
- SMALL eGFR REDUCTION INITIALLY
- RARE EUGLYCEMIC KETOACIDOSIS
- HOLD 3 DAYS BEFORE SURGERY, PROLONGED FASTING, OR SERIOUS ACUTE ILLNESS

42

60 YEARS OBESE (BMI 32 KG/SQM) WOMAN WITH DISTANT HX OF AFIB, TAKING 2 BP MEDICATIONS PRESENTS WITH PROGRESSIVELY WORSENING DOE FOR THE PAST 2 WEEKS. WHAT DO YOU DO NEXT?

- TELL HER TO LOSE WEIGHT AND COME BACK IN 3 MONTHS
- CONSULT CARDIOLOGY FOR FURTHER TESTING AS THIS IS LIKELY HFPEF
- ORDER STRESS TEST TO SEE IF HER SYMPTOM IS DUE TO ISCHEMIA
- CHECK NT-PROBNP, EKG AND ORDER ECHO (EF, PA AND FILLING PRESSURE).

43

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- ORDER STRESS TEST TO SEE IF HER SYMPTOM IS DUE TO ISCHEMIA
- CHECK NT-PROBNP, EKG AND ORDER ECHO (EF, PA AND FILLING PRESSURE).

44

HEART FAILURE WITH PRESERVED EJECTION FRACTION ($\geq 50\%$)
H2FPEF SCORE

- HEAVY: BMI >30 KG/SQM – 2 POINTS
- HYPERTENSIVE: ≥ 2 ANTIHYPERTENSIVE MEDICATIONS – 1 POINT
- ATRIAL FIBRILLATION – 3 POINTS
- PHTN (RASP >35 mmHg) – 1 POINTS
- ELDER: AGE > 60 – 1 POINTS
- FILLING PRESSURE: E/e > 9 – 1 POINTS

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H2FPEF SCORE

- 0-1: UNLIKELY
- 2-5: INTERMEDIATE PROBABILITY; EXERCISE DIASTOLIC ECHO OR INVASIVE EXERCISE HEMODYNAMICS
- 6-9: HIGH PROBABILITY

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HFPEF

- MOST COMMON HF-58% (HFmrEF 16%, HFREF 26%)
- 5 YEAR MORTALITY RATE 76%
- 5 YEAR READMISSION RATE 84%

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WHICH MEDICINE TO AVOID IN HFPEF PATIENT?

- 1. GLP-1 RECEPTOR AGONIST
- 2. SGL2 INHIBITOR
- 3. NSMRA (FINERENONE)
- 4. ARNI (ENTRESTO)
- 5. BETA BLOCKER
- 6. FUROSEMIDE
- 7. ARB

48

WHICH MEDICINE TO AVOID IN HFPEF PATIENT?

- 1. GLP-1 RECEPTOR AGONIST
- 2. SGL2 INHIBITOR
- 3. NSMRA (FINERENONE)
- 4. ARNI (ENTRESTO)
- 5. BETA BLOCKER (USE ONLY IF THERE IS ANGINA OR ARB REQUIRING RATE CONTROL)
- 6. FUROSEMIDE
- 7. ARB

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WHAT'S NEW IN HFPEF?

- PRESERVED EF ALONE DOESN'T DIAGNOSE
- NORMAL BNP DOES NOT EXCLUDE (OBSE PATIENT)
- USE SCORING BUT DON'T REPLACE CLINICAL JUDGEMENT
- SGL2 ARE THERAPEUTICALLY INEFFECTIVE
- FINERENONE IS NEW SECOND PILLAR
- CLODIT IS NOW TARGET, NOT MERELY COMORBIDITY
- DIURETICS ARE SYMPTOM THERAPY
- DO NOT PRESCRIBE BB ROUTINELY
- ARNI / ARB IS SELECTIVE, NOT UNIVERSAL [EF LOWER END, RECURRENT HOSPITALIZATION RISK]

50

65 YO FEMALE WITH LVEF 50%, TOLERATING JARDIANCE. SHE HAS K OF 5.1 AND EGFR OF 24. WHICH MEDICINE TO AVOID?

1. ARNI (ENTRESTO)
2. ARB (LOSARTAN)
3. FUROSEMIDE
4. KERENDIA (FINERENONE)

51

65 YO FEMALE WITH LVEF 50%, TOLERATING JARDIANCE. SHE HAS K OF 5.1 AND EGFR OF 24. WHICH MEDICINE TO AVOID?

1. ARNI (ENTRESTO)
2. ARB (LOSARTAN)
3. FUROSEMIDE
4. KERENDIA (FINERENONE)

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FINERENONE (KERENDIA)

- FOR HFPEF AND HFmrEF AND CKD ASSOCIATED WITH DM II
- NON STEROIDAL MINERALOCORTICOID RECEPTOR ANTAGONIST
- BLOCKS ALDOSTERONE MEDIATED INFLAMMATION AND FIBROSIS IN KIDNEY, MYOCARDIUM.
- NO ANDROGEN OR PROGESTERONE RECEPTOR ACTIVITY- NO GYNCOMASTIA OR SEXUAL DYSFUNCTION
- ONLY MODEST BLOOD PRESSURE LOWERING

53

FINERENONE (KERENDIA)

- 16-18% REDUCTION IN HF HOSPITALIZATION, CV DEATH + TOTAL HF EVENTS
- DO NOT INITIATE IF K > 5 MEQ/L OR eGFR < 25
- DIABETIC CKD TARGET 20 MG DAILY
- HF WITH EF >= 40%; TARGET 40 MG (eGFR >60), TARGET 20 MG IF LESS INITIALLY

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QUESTIONS?

- THANK YOU FOR YOUR ATTENTION