Cardiology Update for Primary Care 2019

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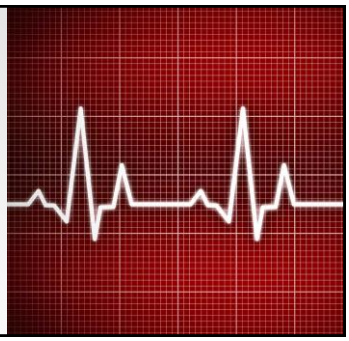

Disclosures

- No financial disclosures
- No conflicts of interest

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Objectives

- Briefly review the new 2019 ACC/AHA primary prevention guidelines
- Review the recent trials in aspirin for primary prevention
- Understand the coronary artery calcium score and its implications in primary prevention
- Understand the utility of PCSK9 inhibitors in cardiovascular disease
- Review the recent trials for SGLT2 inhibitors and GLP1R agonists in cardiovascular outcomes and implications in management
- Review relevant updates to the 2014 atrial fibrillation guidelines
- Discuss the Apple heart study and what it means for primary care
- Review Entresto and when it is used in heart failure treatment
- Review the basics of cardio-oncology and what a primary care physician should know

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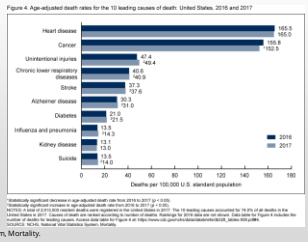
Death Rates for Leading 10 Causes of Death in USA

630,000 Americans died from heart disease in 2015.
366,000 from coronary artery disease.



NCHS, National Vital Statistics System, Mortality.

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Primary Prevention: 2019 Guidelines

- Early and recognition and promotion of lifestyle changes are key to prevent atherosclerotic vascular disease, HF and AF
- Team based approach and determinates of barriers to treatment will aid in success.
- Healthy lifestyle includes tobacco cessation, exercise, glucose, diet and weight loss
- Aspirin should be reserved for high risk patients with appropriate bleeding risk assessment
- Statins are first line therapy for primary prevention in those with risk
- Blood pressure goals on pharmacological therapy are <130/80 mmHg
- Diabetic control with medications such as SGLT2i and GLP1 agonists

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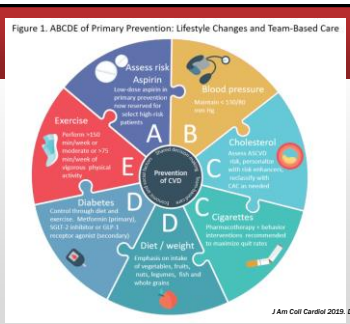

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Primary Prevention: Risk

- ASCVD 10-year risk calculator
  - Low risk: <5%
  - Borderline: 5-7.5%
  - Intermediate: 7.5-19-9%
  - High risk: >20%
- Risk enhancers overcome limitations of pooled cohort equations
- Coronary artery calcium (CAC) can help re-classify patients with borderline or intermediate risk (IIa)
  - MESA risk calculator

Table 1: ASCVD Risk Enhancers

- Family history of premature ASCVD
- Primary hypercholesterolemia
- Chronic kidney disease
- Metabolic syndrome
- Conditions specific to women (e.g. preeclampsia, premature menopause)
- Chronic inflammatory conditions (especially rheumatoid arthritis, psoriasis, HIV)
- Ethnicity (e.g. south Asian ancestry)

Lipid/Biomarkers:

- Persistently elevated triglycerides (≥175 mg/dL)

In selected individuals if measured:

- hsCRP ≥2 mg/L
- Lp(a) levels ≥50 mg/dL or ≥125 nmol/L
- ApoB levels ≥130 mg/dL
- Ankle-brachial index <0.9

J Am Coll Cardiol 2019. DOI:10.1016/j.jacc.2019.03.010

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Cholesterol

High-, Moderate-, and Low-Intensity Statin Therapy*

Table 3

	High-Intensity	Moderate-Intensity	Low-Intensity
LDL-C Lowering†	≥50%	30% to 49%	<30%
Statins	Atorvastatin (40 mg‡) 80 mg Rosuvastatin 20 (40 mg)	Atorvastatin 10 mg (20 mg) Rosuvastatin (5 mg) 10 mg Simvastatin 20–40 mg§	Simvastatin 10 mg
	-	Pravastatin 40 mg (80 mg) Lovastatin 40 mg (80 mg) Fluvastatin XL 80 mg Fluvastatin 40 mg BID Pitavastatin 1–4 mg	Pravastatin 10–20 mg Lovastatin 20 mg Fluvastatin 20–40 mg

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Cholesterol

- Statins, the new aspirin
- With exception of DM and LDL-C >190mg/dL, 40-70y should be screened with PCE to determine if statin should be initiated.
- 2018 statin guidelines integrated
  - High risk (20%): start moderate intensity statin
  - Intermediate (7.5-19.9%)
  - Borderline (5-7.5%):
    - Benefit of starting a statin is uncertain for intermediate and borderline risk groups
    - Assess risk enhancers and consider coronary calcium score.

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Table 3. Risk-Enhancing Factors for Clinician–Patient Risk Discussion

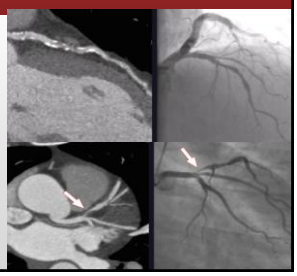
Risk-Enhancing Factors

- **Family history of premature ASCVD** (males, age <55 y; females, age <65 y)
- **Primary hypercholesterolemia** (LDL-C, 160–189 mg/dL [4.1–4.8 mmol/L]; non–HDL-C 190–219 mg/dL [4.9–5.6 mmol/L])*
- **Metabolic syndrome** (increased waist circumference [by ethnically appropriate cutpoints], elevated triglycerides [>150 mg/dL, nonfasting], elevated blood pressure, elevated glucose, and low HDL-C [<40 mg/dL in men; <50 mg/dL in women] are factors; a tally of 3 makes the diagnosis)
- **Chronic kidney disease** (eGFR 15–59 mL/min/1.73 m^2 with or without albuminuria; not treated with dialysis or kidney transplantation)
- **Chronic inflammatory conditions**, such as psoriasis, RA, lupus, or HIV/AIDS
- **History of premature menopause (before age 40 y) and history of pregnancy-associated conditions that increase later ASCVD risk, such as preeclampsia**
- **High-risk race/ethnicity** (e.g., South Asian ancestry)
- **Lipids/biomarkers**: associated with increased ASCVD risk
  - Persistently elevated* primary hypertriglyceridemia (≥175 mg/dL, nonfasting)
  - If measured:
    - **Elevated high-sensitivity C-reactive protein** (≥2.0 mg/L)
    - **Elevated Lp(a)**: A relative indication for its measurement is family history of premature ASCVD. An Lp(a) ≥50 mg/dL or ≥125 nmol/L constitutes a risk-enhancing factor, especially at higher levels of Lp(a).
    - **Elevated apoB** (≥130 mg/dL): A relative indication for its measurement would be triglyceride ≥200 mg/dL. A level ≥130 mg/dL corresponds to an LDL-C >160 mg/dL and constitutes a risk-enhancing factor
    - **ABI** (<0.9)

J Am Coll Cardiol 2019. DOI:10.1016/j.jacc.2019.03.010

Cholesterol: Coronary Artery Calcium Scoring

- Low radiation 1mSv multidetector-row CT scan to assess calcium burden in arteries but not functional information
  - Mammogram 0.5 mSv, CXR 0.05 mSv, chest CT 10 mSv
  - Less than background radiation per year (3mSv)
  - Average Nuclear stress test 4-10 mSv
- About $200 and 5-10-year warranty
- Grading:
  - 0 Agatston units – No identifiable disease
  - 1 to 99 Agatston units – Mild disease
  - 100 to 399 Agatston units – Moderate disease
  - ≥400 Agatston units – Severe disease
- Caveat: CAC does not detect or grade stenosis of arteries
- Caveat: CAC of 0 does not mean there is no plaque.



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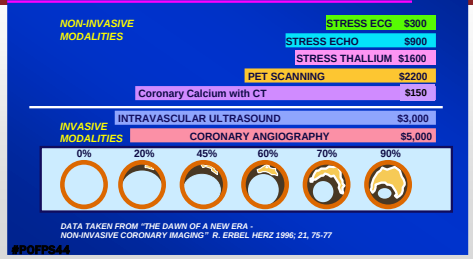
DIAGNOSTIC SENSITIVITY



DATA TAKEN FROM "THE DAWN OF A NEW ERA - NON-INVASIVE CORONARY IMAGING" R. ERBEL HERZ 1996; 21, 75-77

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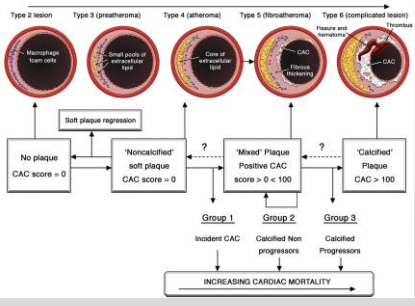
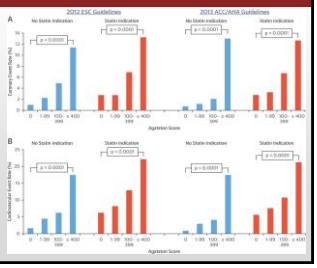


#POFPS44 American College of Cardiology Foundation John W. McEvoy et al. JACC 2010;56:1613-1622 JACC

Cholesterol: Coronary Artery Calcium Score

- Use of CAC has been validated in multiple population-based cohorts and metanalysis including MESA, HNR and Rotterdam Study. FHS
- Risk scoring calculators: MESA Risk Score
- CAC score progression on serial CAC studies at least 5 years apart can further predict risk
- CAC score helps re-classify intermediate and borderline risk patients based on MESA cohort into low or high risk and determine the benefit of starting statin therapy.



State of art review
Philip Greenland et al. JACC 2018;72:434-447

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Table 6. Selected Examples of Candidates for Coronary Artery Calcium Measurement Who Might Benefit From Knowing Their Coronary Artery Calcium Score Is Zero

Coronary Artery Calcium Measurement Candidates Who Might Benefit from Knowing Their Coronary Artery Calcium Score Is Zero
• Patients reluctant to initiate statin who wish to understand their risk and potential for benefit more precisely • Patients concerned about need to reinstitute statin therapy after discontinuation for statin-associated symptoms • Older patients (men 55–80 y of age; women 60–80 y of age) with low burden of risk factors (S4.3-53) who question whether they would benefit from statin therapy • Middle-aged adults (40–55 y of age) with PCE-calculated 10-year risk of ASCVD 5% to <7.5% with factors that increase their ASCVD risk, although they are in a borderline risk group.

Caveats: If patient is at intermediate risk and if a risk decision is uncertain and a coronary artery calcium score is obtained, it is reasonable to withhold statin therapy unless higher-risk conditions, such as cigarette smoking, family history of premature ASCVD, or diabetes mellitus, are present and to reassess coronary artery calcium score in 5 to 10 years. Moreover, if coronary artery calcium scoring is recommended, it should be performed in facilities that have current technology and expertise to deliver the lowest radiation possible.

ASCVD indicates atherosclerotic cardiovascular disease; LDL-C, low-density lipoprotein cholesterol; and PCE, pooled cohort equations.

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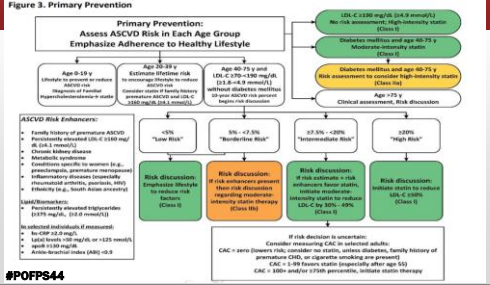
Arnett et al.
2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease

Figure 3. Primary Prevention



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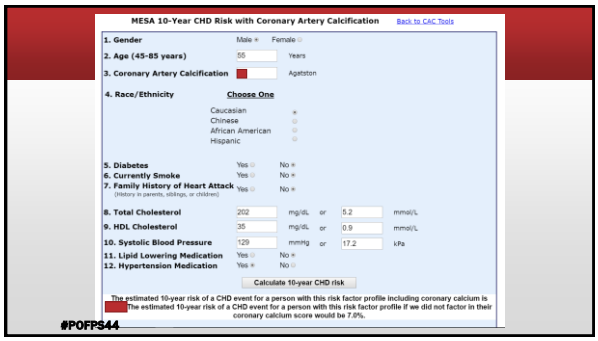

Patients Not At Goal: Non-Statin Lipid Lowering

- Intermediate-risk adults who need aggressive LDL-C lowering and in whom cannot tolerate high intensity, it is reasonable to add a non-statin drug (ezetimibe or bile acid sequestrant) to a moderate-intensity statin
  - Ezetimibe (Zetia) – cholesterol absorption inhibitor. SHARP trial showed 17% reduction in CV death zetia + simva
- 20 -75 yo with LDL-C >190 who achieve < 50% reduction in LDL-C on max tolerated statin LDL-C >100 ezetimibe therapy is reasonable
- 30-75 yo with heterozygous FH LDL-C >100 while on max tolerated statin and ezetimibe therapy, adding PCSK9 inhibitor may be considered (IIb)
- 40-75 yo with baseline LDL-C >220 on max statin and zetia and LDL-C >130 adding PCSK9 inhibitor may be considered (IIb)

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Cholesterol: PCSK9 inhibitors

- PCSK9 inhibitors (proprotein convertase subtilisin/kexin type 9)
  - Monoclonal antibody that binds to PCSK9. PCSK9 binds to LDL receptors that are responsible for binding and degrading circulating LDL. PCSK9 inhibition leads to less LDLR degradation and more LDL receptors, thus LDL is lowered in the blood.
- FOURIER (evolocumab/Repatha) 2017
  - Population: Established CVD (MI, stroke, PAD) on statin. 70% were high intensity. Avg LDL 92. age 62.
  - Outcomes: 12.6% vs 14.6% in MACE, hospitalization for UA or PCI (NNT 67). PAD was significantly lower. Absolute reduction in LDL was 56mg/dL. No serious events. No benefit in CV and all-cause mortality. May have been underpowered
- ODYSSEY OUTCOMES (Alirocumab/Praluent) 2019
  - Population: ACS 1- 12 months prior on high statin; LDL > 70
  - Outcomes: 9.5% vs 11.1% MACE. cardiovascular death: 2.9% vs.4.2%, all-cause mortality: 3.5% vs. 4.1%. LDL average of 40
  - Higher baseline LDL had more reduction in primary outcome: lower is better
  - Patients in this trial were sicker than patients in FOURIER
  - PCSK9 is more cost effective in patient's LDL > 100
- Overall, the price of PCSK9 inhibitors limits patient access. With the new update and studies like ODYSSEY, hopefully access with become easier
  - More research to assess cost effectiveness is warranted

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D - Diabetes

- Diabetes is prevalent disease and is a major risk factor for ASCVD.
- Diabetic control maintained by a heart-healthy nutritional plan to improve glucose.
  - DASH, Mediterranean diet, vegetarian/vegan diet and calorie restriction with limits on simple carbohydrates
- Weight loss, exercise (>150 minutes moderate) and improve other ASCVD risk factors
- Metformin (IIa) should be first line therapy and SGLT-2 inhibitors or GLP1R agonists are reasonable to use along with lifestyle modifications (IIb)

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Diabetes: SGLT2 inhibitors

- In SGLT2 inhibitors – have been shown to help patients with CV disease, HF and renal disease
  - **EMPA-REG OUTCOME** (Empagliflozin; Jardiance) 2015
    - Population: 7000 diabetics a1c 7-10%. > 18yo. 47% had CAD
    - Results: MACE reduction was 10.5% vs 12.1% in CAD pt. Less HF 2.7% vs 4.1%. **All cause mortality** 5.7% vs 8.3%
  - **CANVAS** (Canagliflozin; Invokana) 2017
    - Population: 11000 diabetics a1c 7-10.5%, 65% had CAD. >30 yo.
    - Results: MACE reduction 26.9 vs 31.5 per 1000 pt y. **Less progression of renal failure and hospitalization for HF**. More amputations
  - **DECLARE-TIMI 58** (Dapagliflozin; Farxiga) 2019
    - Population: 17,000 diabetics a1c 6.5-12%, CAD or risk for CAD, HF and PAD. > 40yo.
    - Results: **Reduction in HF hospitalization and CV death** (4.9 vs 5.8%), and renal failure progression (4.3% vs. 5.6%)
    - All-cause mortality was noninferior. Amputations (1.4 vs 1.3%)
    - HFeEF population was only 4% of total
- Low risk populations not studied. However high risk, secondary prevention had benefit. HF reduction
- Starting these mediations should be weighted against increased risk of PVD, leg amputations, osteoporosis

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Diabetes: GLP1R agonists

- Major adverse cardiac events (MACE): non-fatal stroke, non-fatal MI, and cardiovascular death
- Those that were non-inferior but did not show MACE or hospitalization reduction
  - EXSCEL (exenatide), ELIXA (Lixisenatide)
- Those that did show reduction in MACE
  - SUSTAIN-6 2016 (semaglutide; Ozempic) – 6.6% vs 8.9% had reduced MACE. Driven by Less strokes.
  - REWIND 2019 (dulaglutide; Trulicity) - 12% vs 13.4% less MACE. Driven by less strokes
  - LEADER 2016 (liraglutide; Victoza) - 13% vs 14.9% had reduced MACE. Pt had one risk factor, MI, CVA or renal failure
- All-cause mortality did not differ between these medications.

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Primary Prevention: Aspirin

- Aspirin is no longer recommended based on presence of ASCVD risk alone.
  - Now based on ASCVD risk + risk enhancing factors, and weighed against bleeding risk
- It is REASONABLE to start aspirin in patients 40-70yo when:
  - High ASCVD risk
  - At least moderate CAC and LOW risk of bleeding (IIb)
  - A patient-clinician tailored approach: strong family history of premature MI, inability to achieve lipid, BP or glucose targets
- Aspirin is no longer recommended for moderate risk or age >70 if risk outweighs protective benefit (III)
- There is no role for aspirin in colorectal cancer prevention
- Risk factors for bleeding
  - History of previous GI bleeding or PUD or bleeding at other sites, age >70 years, thrombocytopenia, coagulopathy, CKD, and concurrent use of other medications that increase bleeding risk, such as NSAIDs, steroids, direct oral anticoagulants, and warfarin

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Primary Prevention: Aspirin

- US Physicians' Health Study 1995 and Women's health study 2004
  - 44% relative reduction in CV death but no decrease in overall mortality with aspirin 325mg daily use in primary prevention
  - Aspirin increases risk of bleeding, PUD and hemorrhagic strokes
  - Note: In 1996, Statins were not widely used for primary prevention.
- **ARRIVE** 2018
  - Population: non-diabetics >55 with 3 risk factors (HTN, tob, FHX, HLD) with intermediate risk
  - Results: 4.3% vs 4.5% in MACE, or UA. GIB 0.97% vs 0.46% Event rates were lower than expected from FHS.
- **ASCEND** 2018
  - Population: Controlled (A1c <8) diabetics (high risk)
  - Results: ASA had 1.1% (91 at 7.4 pt y) absolute reduction in serious events but had 0.9% (112 at 7.4 patient/year) increase in major bleeding. Asa did not reduce incidence of GI related cancer.
- **ASPREE** 2018
  - Population: Patients, >70yo; 11% diabetics, mean age 74. excluded: dementia, CVD, high bleed risk or chronic condition limiting life to < 5 years
  - Results: 21.5 vs 21.2 events per 1000 person-years of Disability-free survival (all cause mortality, dementia, or persistent physical disability). More major hemorrhage was noted in ASA group 8.6 vs 6.2 events per 1000 person/years.

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Atrial fibrillation Guidelines: What's new since 2014

- CHADS2VASC score updates:
  - Female sex alone no longer counts as a point if it is the only risk factor present
  - Aspirin is no longer recommended for CHADS2VASC score of 0.
  - Anticoagulation is recommended for AF patients with CHADS2VASC of 2 for men, and 3 for women
  - Anticoagulation is reasonable for patients with CHADS2VASC of 1 for men and 2 for women
    - Diabetes, HTN, age > 65 are greater risk for CVA then being Female or having vascular disease
- Anticoagulation:
  - Direct oral anticoagulants (DOAC) is preferable to Vitamin K antagonists
  - Valvular atrial fibrillation is defined as moderate-severe mitral stenosis, or mechanical heart valve
    - These patients should receive Warfarin only for anticoagulation
  - For patients with ESRD, apixaban is reasonable alternative to warfarin (IIb)
  - For patients on dabigatran, idarucizumab is the reversal agent (I)
  - For patients on rivaroxaban and apixaban, Andexanet Alfa is the reversal agent (IIa)

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Atrial fibrillation Guidelines: What's new since 2014

- Devices for atrial fibrillation
  - Left atrial appendage occlusion (Watchman) device may be considered for patients with contraindications to long-term anticoagulation (IIb)
    - PROTECT AF and PREVAIL showed less hemorrhagic strokes but equal ischemic strokes
  - AF catheter ablation may be reasonable in symptomatic patients with HF with reduced EF to reduce mortality and HF hospitalizations (IIb)
    - CASTLE-AF
  - In patients with cryptogenic strokes in whom external ambulatory monitoring is inconclusive, implantation of a cardiac loop monitor is reasonable (IIa)

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Atrial fibrillation: Apple heart study

- Prospective, single arm. 420,000 self enrolled patients
  - Inclusion criteria: No hx of AF, not on anticoagulants and required to already have apple watch
  - 6% of patients were over 65 years old
- Goals:
  - Characterize concordance of pulse irregularity notification of episodes from device and simultaneously recorded ambulatory ECG
  - To estimate rate of initial contact with health care provider within 3 months after notification
- Methods:
  - Apple app used opportunistic sampling algorithm, which continuously checks rhythm for AF on a Tachogram generated from the watch. Once notified, patients contacted study doctor via video consultation. Then patient wore ECG patch and AF was correlated to watch with ECG patch.
- Results:
  - AF detected on 34% of those who wore patch. Mostly age >65.
  - PPV 71% for tachogram and 84% for notification
- Smart devices may be utilized more in future for AF/arrythmia detection
  - Future studies needed

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Heart failure

- Despite 30 years of advances in HF, it remains a leading cause of morbidity and mortality in the USA.
  - Heart failure costs the nation an estimated **$30.7 billion** each year according to the CDC
- Traditional therapies: beta blocker, angiotensin-converting enzyme inhibitors, aldosterone receptor antagonist
  - Although medications such as Ivabradine have been shown to improve survival, its use is only indicated for a small number of total HF patients
- Outpatient initiation of medications is more difficult to perform then Inpatient initiation of medications
- Entresto (Sacubitril–Valsartan): neprilysin inhibitor
  - PARADIGM-HF 2014
    - Population: stable outpatients 36 hr washout from ACE-I. EF 30%
    - Results: CV mortality and HF hospitalization 21.8% vs 26.5%, NNT 21
  - PIONEER-HF 2019
    - Goal: assess safety of hospital initiation of stable acutely decompensated HF
    - Population: 1-10 days from presentation with stable SBP > 100 for 6 hours and no changes to diuretics. EF < 40; pro/BNP > 400/1600. 36-hour washout. CrCl >30
    - Outcomes: 46% vs 25% reduction in BNP. Other: All cause death and HF rehospitalization 9.2% vs 15.2%. Not powered for HF rehospitalization.

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Cardio Oncology

- Advances in cancer treatment has led to longer life prognosis after diagnosis: there are about 13.7 million cancer survivors and increasing
- Chemotherapy-induced cardiotoxicity
  - Anthracyclines: Doxorubicin, daunorubicin, idarubicin, epirubicin
  - Monocloncal antibodies: trastuzumab (Herceptin)
- Radiation therapy
  - Structural damage: Valve, coronaries and pericardium
- Prevention, monitoring and follow up is key for cancer patients and survivors
- Multidisciplinary approach to care of patient

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Cardio Oncology

- Doxorubicin
  - Commonly used for leukemias and cancers of breast, uterus, ovary, lung
  - Thought to be dose dependent toxicity (200mg/m2)
  - Causes reduction in LVEF
- Trastuzumab (Herceptin – HER2 inhibitor)
  - Causes reduction in LVEF
  - Non-dose dependent
  - Effects are likely reversable

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Cardio Oncology

- Reduction in LVEF is a sign of cardio-toxicity but indicates late damage: Cancer therapeutics related cardiac dysfunction (CTRCD)
- Early Initiation of cardioprotective drugs is key to prevent myocardial changes and preserve heart function
  - ACEI and beta blockers
- But what if we can detect subclinical changes before EF decline?
- Echo
  - LV EF estimation
  - Tissue doppler, diastology
  - Myocardial strain
- Biomarkers: tropnonins, BNP

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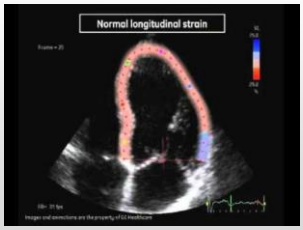
Moycardial Strain



Myocardial strain

Used to describe elastic properties of cardiac muscle

Strain (ε) = $\frac{L_f - L_0}{L_0}$

-20%

- Circumferential, radial and longitudinal strain
- Longitudinal strain is the most reproducible
  - Normal global longitudinal strain is about -18% to -20%

https://youtu.be/Lx2DXkGwkm4

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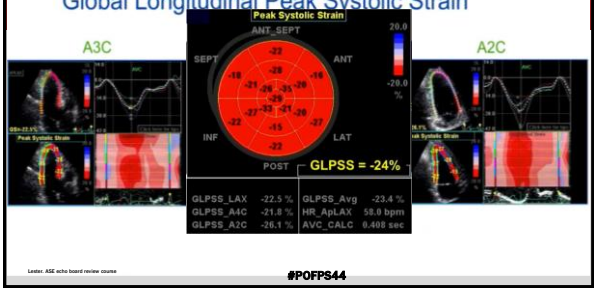
Global Longitudinal Peak Systolic Strain



Lester. ASE echo board review course

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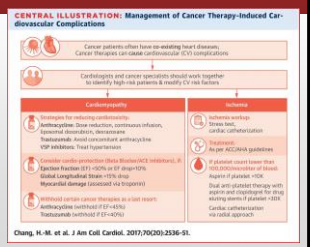
Cardio Oncology

- Echo every 3 months during chemo
- CTRCD present if decrease in LVEF > 10% to a value to < 53%
  - Initiate ACEI and beta blockers
- Relative percent reduction if GLS < 8% from baseline is not meaningful however > 15% change from baseline is abnormal
  - Subclinical LV dysfunction
  - Consultation to cardio-oncology
  - May initiate cardioprotective therapies
  - Monitoring and continuation of chemotherapy may be modified
  - Ongoing trials to determine the best approach to this knowledge
- Strain can be used in detection of other disease processes
  - Amyloidosis and sarcoidosis
  - HCM and athletes' heart
  - Cardiac dyssyncrony



2017 American College of Cardiology Foundation

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Hui-Ming Chang et al. JACC 2017;70:2536-2551

Summary

- Aspirin should no longer be used for primary prevention unless patient is high risk and risk of bleeding has been weight against benefits
  - When considering aspirin for primary prevention, consider a statin
- Coronary artery calcium score is a cost-effective way that is helpful to reclassify risk in borderline and intermediate risk patients for primary prevention
- PCSK9 inhibitor trials demonstrated "the lower the LDL the better" especially in high risk populations
- Consider SGLT2i and GLP1R agonists for mortality benefit for diabetic patients with established CAD and HFrEF
- DOAC are now preferred agents for anticoagulation
- Initiation of Entresto before hospital discharge may help long term outcomes and overall mortality due to heart failure.
- Patients undergoing cancer treatment with cardiotoxic chemotherapies should have baseline echo with strain with serial follow up to detect subclinical myocardial dysfunction

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References

- **Journal of the American College of Cardiology** Nov 2017, 70 (20) 2536-2551; DOI: 10.1016/j.jacc.2017.09.1096
- Uptodate
- **Journal of the American College of Cardiology** Mar 2019, 26029; DOI:10.1016/j.jacc.2019.03.010
- **Journal of the American College of Cardiology** May 2018, 71 (19) e127-e248; DOI: 10.1016/j.jacc.2017.11.006
- **Hui-Ming Chang et al. JACC 2017;70:2536-2551**
- Lester. ASE echo board review course
- youtu.be/Lx20XkGwkm4
- **Journal of the American College of Cardiology** Jan 2019, 25873; DOI:10.1016/j.jacc.2019.01.011
- **NCHS, National Vital Statistics System, Mortality.**
- **State of art review; Philip Greenland et al. JACC 2018;72:434-447**
- https://www.cdc.gov/dhdsp/data_statistics/fact_sheets/fs_heart_failure.htm
- **John W. McEvoy et al. JACC 2010;56:1613-1622**
- www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx
- *J Am Coll Cardiol 2019. DOI:10.1016/j.jacc.2019.03.010*
- "The Dawn of a New Era-Noninvasive Coronary Imaging" R. Erbel Herz 1996:21, 75-77
- **John W. McEvoy et al. JACC 2010;56:1613-1622**
- www.acc.org/latest-in-cardiology/clinical-trials
  - Apple heart study
  - ASPREE, ARRIVE, ASCEND
  - PIONEER-HF, PARADIGM-HF
  - SUSTAIN-6, REWIND, LEADER
  - ODYSSEY, FOURIER
  - EMPA-REG, CANVAS, DECLARE-TIMI-58

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