Cardiovascular Disease and the Geriatric Patient: Diagnosis and Treatment

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The Aging Cardiovascular System

Cardiovascular Changes Associated with Aging
- Increased arterial and myocardial stiffness
- Decreased beta adrenergic responsiveness
- Decreased baro-receptor responsiveness
- Impaired endothelial function
- Sinus node dysfunction
- Net effect is marked reduction in CV reserve

Effect of Aging on Vascular Structure
- Increased calcium, collagen & collagen cross-links
- Increased intima-medial thickness
- Increased vessel diameter
- Decreased elastin
- Increased systolic BP and pulse pressure
- Increased vascular stiffness indices and pulse wave velocity
- Net effect is increase in afterload

Results of Aging Ventricle and Vasculature

- Reduced augmentation of coronary flow
- Increased late afterload
- Widened Pulse Pressure

(Am J Cardiol 2003;92:554-561)
Effect of Aging on CV Conduction System

- Increased elastic tissue and collagen
- Marked decrease SA node pacemaker cells
- Calcification of cardiac skeleton
- Slowed conduction in AV node and proximal His-Purkinje system
- Conduction abnormalities amplified by hypertension, CAD and amyloid infiltration

ECG Changes with Aging

- Modest increase in PR and QT interval
- Left shift in QRS axis
- Increased prevalence of RBBB
- Flattening of the ST segment
- Decreased T-wave amplitude
- No significant change in resting heart rate but marked reduction in HR variability

What do these changes mean for CV therapies in older adults?

“High Risk-High Reward”

Prevention - Lipids

Statin Therapy in Older Adults

- Meta-Analysis of Data from 8 trials for Primary Prevention in High Risk Older Adults
- 24,674 Patients
- Average age 73, Mean follow-up of 3.5 years
- Significant 39.4% RRR for MI, 23.8% RRR for stroke. No differences in deaths, CV deaths, or cancer cases
- Therefore statin therapy for primary prevention in older adults reduces morbidity, although not mortality in the short term


PCSK9 Inhibitors
Cardiac Ischemia, ACS, and STEMI in Older Adults

Treatment of Chronic Stable Angina in Older Adults
- Newer appropriate use criteria updates reduce indications for interventions
- PCI has yet to be shown to reduce CV events in patients with stable disease
- It may improve symptoms in the short term but long term outcomes are equal to that of guideline based medical therapy (GBMT)
- Current symptomatic indications for PCI:
  - 1 or more vessels with significant stenoses and unacceptable anginal despite GBMT (β-blocker + nitrate)
  - 1 or more vessels with significant stenoses and unacceptable anginal in patients who cannot follow GBMT
  - Previous CABG in similar situation to #1 above

Anti-Platelet Therapy - Acute Coronary Syndrome (ACS)

Aspirin
- Generally recommended indefinitely after PCI
- Risk reduction is equivalent with doses of ASA above and below 100 mg, but doses greater than 100 mg have increased bleeding risk
- OASIS-7: Compared low dose (75-100mg) to high dose (300-325mg) ASA post stenting in ACS patients and found no differences in 30 day outcomes (also double dose clopidogrel for 7 days post stenting vs. usual dosing)
- Take home point - Generally doses of < 100mg of ASA are reasonable for use for both primary prevention in low bleed risk patients and secondary prevention in patients with established coronary artery disease

Comparison of Oral P2Y12 Inhibitors

Current Recommendations

- 2014 ACC/AHA Guidelines for NSTEMI
  - Clopidogrel loading or ticagrelor loading followed by maintenance dosing (I)
  - Ticagrelor favored over clopidogrel (IIa)
- Older Patients:
  - Same GBMT as younger patients with early invasive strategy as appropriate (Class Ia)
  - Tailor pharmacotherapy with appropriate weight and renal clearance adjustments
  - Management decisions should be patient-centered and consider preference/goals, comorbidities, functional and cognitive status, and life expectancy (II)
  - Bivalirudin, rather than IIB/IIIa inhibitor+heparin, is reasonable in older patients given similar efficacy but less bleeding (IIa)

Aspirin
- The main medications
- Issues in Older Adults
- Unique uses of new anti-platelets and side effects

<table>
<thead>
<tr>
<th>Comparison of Oral P2Y12 Inhibitors</th>
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<td></td>
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<tr>
<td>Pro-Drug</td>
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<tr>
<td>Loading Dose</td>
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<tr>
<td>Maintenance Dose</td>
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<tr>
<td>Frequency of Dose</td>
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<tr>
<td>Onset of Action</td>
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<td>Offset of Action</td>
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<tr>
<td>Individual Variability</td>
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<tr>
<td>CYP-450 Activation</td>
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<tr>
<td>Inev P2Y12 Inhibition</td>
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<tr>
<td>Relative Potency</td>
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<tr>
<td>Mean Plt inhibition</td>
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<tr>
<td>Time to Peak Inhibition</td>
</tr>
<tr>
<td>Half-life</td>
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<tr>
<td>Days to hold pre-CABG</td>
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</tbody>
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Adapted from Bhatias et al JAMA 2013

**Clopidogrel**

- Currently still your best bet for most patients over the ages ≥ 75, weight < 60 kg, or with previous stroke
- Requires 2 CYP dependent steps- particularly uses CYP2C19 and CYP3A4.
  - Atorvastatin use CYP3A4, Omeprazole uses CYP2C19. These do not appear to be “class” effects
- Bottom line is that there is no consistent evidence of clinical significance to these interactions, but it may prompt you to alter therapy for specific patients.
- Current recommendations not to switch, but if needed use pantoprazole or ranitidine instead of omeprazole and rosuvastatin instead of simvastatin.

Bates et al, J Am Coll Cardiol 2011 p 1251

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**Ticagrelor and Older Adults**

- PLATO Trial- 18,624 ACS patients for ticagrelor vs. clopidogrel
  - Reduced 12 month CV risk and all cause mortality without increase in bleed risk or stent thrombosis
  - Benefit seen in age over 65 group and trend remained for those over 75.
  - Increased incidence of dyspnea (13.8 vs. 7.8%) from adenosine receptor activation that dissipates over about 1 week. Also increase in ventricular pauses of greater than 3 seconds but not requiring specific treatment and disappear after 30 days based on Holter data.
  - Not to be given with more than 100 mg of ASA.
  - Increases uric acid levels in some patients
  - Issues: reversibility, BID dosing, significant conduction defects or bradycardia

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**Prasugrel and Older Adults**

- Less inter-individual variability than clopidogrel
- Current dosing not recommended for individuals who weigh less than 60 kg and age ≥ 75 years (no benefit shown in these group)
- 10 mg dose reduced adverse CV events overall with ACS but there are key patients who should NOT get this drug
  - TRITON TIMI-38: 9.9% vs. 12.1% event rate (HR 0.81 (0.73-0.90)), NNT 45 vs. clopidogrel.
  - Increased bleeding risk in those with previous stroke/TIA, age ≥ 75, and wt < 60 kg made it higher risk in stroke/TIA pts and neutralized the benefit in those over 75 or under 60 kg.
- GENERATIONS - prasugrel 5 mg/day in adults age ≥ 75 – slightly better inhibition of platelet aggregation vs. clopidogrel 75 mg/day, fewer poor responders than clopidogrel, similar bleeding profile.

J Am Coll Cardiol 2013 p577

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**Recommended Durations of Therapy for DAPT**

- According to all major RCTs, DAPT should be continued for 12 months if at all possible for patients presenting with ACS
- Meta-analyses indicate prolonged DAPT (> 12 months) has no clinical benefit and may increase risk of bleeding but recent data suggests longer therapy with clopidogrel and ticagrelor in those who tolerate it well may be beneficial out to 3 years.
- Minimal time periods for non-ACS patients depend on stent type:
  - Bare metal: 1 month, ideally for 12 months
  - Drug Eluting: Ideally for 12 months if patient is not high risk for bleeding

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**Anti-Platelet Therapy with Oral Anticoagulation**

- “Triple Therapy” with OAC, ASA, and a P2Y₁₂ inhibitor at least doubles the bleeding risk (4-6% with DAPT to 10-14% with TAPT)
- Potentially get away with OAC + clopidogrel and do away with ASA, but not common practice in the US
  - WOEST trial: 573 stable patients undergoing PCI who required OAC and DAPT randomized to Warfarin + Clopidogrel vs. Warfarin alone: Found significantly lower bleeding in those on clopidogrel alone than triple therapy as well as reduced mortality in the dual group.

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**Anti-Plt Therapy and Non-Cardiac Surgery Post Stenting**

- Combination of pro-thrombotic post-operative state and discontinuation of anti-platelet therapy is a bad combination
- I always insist on continuing the aspirin.
- No approved “bridging” strategies
- Do you need to continue the P2Y₁₂ inhibitor?
  - Bare Metal Stent: Can hold after 6 weeks
  - DES: Would not hold until 12 months of therapy
Recommendations for the duration of triple therapy in patients with atrial fibrillation and a coronary stent (BMS or DES) with moderate/high stroke risk (CHADS2 ≥1).


Non-ST Elevation ACS in the Elderly (NSTEACS)


NSTEACS in Older Adults

- Epidemiological Points
  - Age is a powerful predictor for events following ACS – risk of in-hospital death increased by 70% for every 10 yrs of age.
  - While they are higher risk patients, they tend to undergo invasive evaluation at low rates than younger patients.
  - Limited randomized trial data for those ages 75 and over.
  - Registry/community patient have a significantly higher co-morbidities (e.g. renal dysfunction, CHF, stroke) burden than trial patients with increasing age, increasing their overall risk.
  - Little inclusion of frailty and functional status into risk modeling or prediction for suggesting therapeutic paths.

NSTEACS in Older Adults- Early Invasive vs. Conservative Management

- "High Risk-High Reward" - Older patients tend to derive the greatest benefit from intervention, but at a cost of increased bleeding (about 300% increase).

NSTEACS and Medications

- Antiplatelet therapy choices as previously discussed.
- No clear age-specific data favoring any of the anticoagulants although potentially less bleeding and greater benefit with bivalirudin or fondaparinux.
- Medications:
  - Oral b-blockers with 1st 24 hours unless contraindication, can give IV if LV ejection fraction is normal.
  - Initiate high intensity statins (Atorvastatin 40-80mg/day rosuvastatin 20 mg/day).
  - ACE Inhibitors if LV ejection fraction < 40%, hypertension, diabetes, or stable CKD.
  - ARB if ACE intolerant.
  - Aldosterone antagonist for same as for ACE inhibitors (unless potassium > 5, Cr > 2.5 in men or 2.0 in women).
Early Invasive vs. Conservative Management

Similar epidemiology and presentation issues as NSTEACS
- Age is associated with delayed presentation and reperfusion
- LBBB makes up a significantly larger portion of STEMI presentation as age increases, up to nearly 34% of STEMI by age 85 and up.

STEMI in the Older Patient

- Action Registry GWTG data- 30,188 patients with STEMI (79.7% < 75, 14.2% 75-84, 6.1% ≥ 85)
- 42% of oldest old (age ≥ 85) cited as having a contraindication to reperfusion, but only 10% with absolute/relative contraindication with patient preference the most cited. Less likely to be reperfused even if eligible
- Benefits of reperfusion seen in those < 75 years. No benefit seen for oldest old- likely due to pt selection issues, age-related time delays (in diagnosis, examining comorbidities, etc..), and competing risks

STEMI in the Older Patient

- Choosing Reperfusion Therapy
  - PCI > Fibrinolysis. Fibrinolysis can be done if there are no contraindications. Age over 75 is not a contraindication but may give less benefit.
  - PCI+Fibrinolysis within 3 hours. PCI+Fibrinolysis 6-12 hours out.
  - PCI for shock, heart failure
- PCI benefit in this population is reduced reinfarction and need for target vessel revascularization. Mortality data not as convincing but in the same direction
- Dose-adjusting anticoagulant medications is very important
- B-blockers and statins have greater benefits in older patients with STEMI. ACEI has benefits. IV b-blocker are no longer used in acute STEMI

CABG in the Older Adult

- Electrolytes have a higher incidence of:
- Left main disease
- Multi-vessel disease
- LV dysfunction
- Re-operation as an indication for surgery
- Concomitant heart valve disease
- Additional co-morbidities
- Frailty
- Operative mortality age ≥ 80 (5-8% non urgent, 11% urgent), 13% at age ≥ 90
- Longer lengths of stay than patients < 50 years old and discharge to home about 50% of the time
Atrial Fibrillation

- Risk Stratification for Stroke and Bleeding- CHADS_2-Vasc – HAS BLED
- New Agents- dabigatran, rivaroxaban, apixaban, edoxaban
- Rate vs. Rhythm Control

Risk Stratification

- CHADS_2
  - Not all ‘0’s’ were low risk- still a 1.9%/yr risk of stroke calculating to a 10 year cumulative risk of near 20%
- Female Sex, Age 65-74, and prevalent vascular disease (MI, PVD, aortic plaque) all showed independent predictive value for stroke in AF but not included in this score

CHA2DS2-VASc

- Congestive Heart Failure - 1 point
- Hypertension - 1 point
- Age 75 and over 2 points
- Diabetes 1 Point
- Stroke/TIA/TE event 2 points
- Vascular Disease (e.g prior MI) 1 point
- Age 64-74 years 1 point
- Female sex 1 point

Score ≥ 2 indicates need from anticoagulation. Score of 1 is choice between OAC and anti-platelet therapy. Better defines truly low risk compared to old score

ATRIA Stroke Risk

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Points Without Prior Stroke</th>
<th>Points With Prior Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≥ 85</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>75–84</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>65–74</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>&lt;65</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>CHF</td>
<td>1</td>
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<tr>
<td>Hypertension</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>eGFR &lt;45 or ESRD</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

Scoring: 0-2-Low Risk, 3-4 Moderate Risk, 6-15- High Risk

OAC Bleeding Risk

- Generally overestimated by providers
- Has lead to clear evidence of under use of OAC, particularly in those at highest risk
- Despite increase in bleed risk with increasing age, data from 12 trials suggests that the benefit of OAC for stroke prophylaxis in AF increases with age while anti-platelet therapy’s impact decreases with age. Risk of serious bleed on warfarin was low and bleed risk equivalent to aspirin.
- Multiple scores have been proposed but are not user friendly or need values not often not available at the time the decision for OAC must be made
- The need to better quantify the bleeding risk at the bedside as a well is clear.

HAS BLED

| Risk Factor                                      | 1 point
|--------------------------------------------------|----------------------|
| Hypertension (SBP > 160) -                      | 1 point each
| Abnormal Liver/Renal Func.                     | 1 point
| Cr ≥ 2, Dialysis, Renal Txp                     | 1 point
| Nonrenal or BMI 2-3X normal in association with AST/ALT/AP > 3 X normal |
| Stroke                                           | 1 point
| Bleeding tendency/predisposition                | 1 point
| History of bleeding or anemia                   | 1 point
| Labile INRs (if on warfarin)                    | 1 points
| Time in therapeutic range (TTR) < 60%           | 1 points
| Elderly (Age ≥ 65)                              | 1 point
| Drugs or Alcohol                                | 1 point each
| - on aspirin or NSAIDS that need to be continued or excess alcohol intake |

Score ≥ 3 indicates high bleeding risk.
HAS BLED

- Has Been Validated in Multiple Populations, both trial data and real world
- Works as well or better than prior scores but is easier to apply
- Good to help evaluate both therapeutic initiation of OAC and to determine whether it is still reasonable over time
- Use has helped show us the balance of risk/benefit between OAC use for stroke prevention and bleed risk

Net Clinical Benefit of OAC

- Based on Dutch Cohort Data (130,000 patients)
- Risk-Benefit still favors OAC with warfarin with HAS-BLED ≥ 3 with CHA₂DS₂-VASc ≥ 2 or CHADS₂ ≥ 1. Only pair with Risk > Benefit is when CHA₂DS₂-VASc=0 and HAS BLED ≥ 3. Aspirin had no benefit in any strata.
- Interestingly, newer agents (dabigatran, rivaroxaban, and apixaban) may have expanded benefit into the CHA₂DS₂-VASc = 1 group even when HAS BLED indicates high risk. With warfarin, there is no net benefit with CHA₂DS₂-VASc = 1.

Olesen et al Thromb Haemost. 2011; 106: 739–749

New Oral Anticoagulants

Cumulative Hazard Rates for the Primary Outcome of Stroke or Systemic Embolism, According to Treatment Group.

Comparison of Oral P2Y₁₂ Inhibitors

<table>
<thead>
<tr>
<th>Trial</th>
<th>Inhibits</th>
<th>Maintenance Dose</th>
<th>Frequency of Dose</th>
<th>Clearance</th>
</tr>
</thead>
<tbody>
<tr>
<td>RE-LY</td>
<td>IIa</td>
<td>150 mg</td>
<td>BID</td>
<td>Renal</td>
</tr>
<tr>
<td>ARISTOTLE</td>
<td>Xa</td>
<td>5 mg</td>
<td>BID</td>
<td>25% Renal, 55% Liver (CYP3A4)</td>
</tr>
<tr>
<td>ROCKET-AF</td>
<td>Xa</td>
<td>20 mg</td>
<td>qDay</td>
<td>36% Renal, 50% Liver/metabolism</td>
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<tr>
<td>ENGAGE-AF</td>
<td>Xa</td>
<td>60 mg</td>
<td>qDay</td>
<td>50% Renal, 50% Liver/metabolism</td>
</tr>
<tr>
<td>TIMI-48</td>
<td>Xa</td>
<td></td>
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Dabigatran

- 150 mg/BID dose superior in stroke/embolism prevention with equivalent bleeding risk to warfarin
- Always check serum Cr before starting and periodically with use
- Reduce dose to 75 mg BID for CrCl 15-30 mL/min
- Reduce dose to 75 mg BID for CrCl 30-50 mL/min if on a strong P-glycoprotein inhibitors (dronaderone, ketoconazole)
- Do not use if CrCl < 30 and patient requires amiodarone, verapamil, erythromycin
- Must be used within 4 months of opening the bottle

Rivaroxaban

- Superior to warfarin in stroke/systemic embolus prevention. Lower rate of hemorrhagic strokes than warfarin
- Check baseline and periodic Cr to see if dose adjustments are needed
- Reduce dose to 15 mg qDay for CrCl 30-50 mL/min. Not for use if CrCl < 15 mL/min
- Do not give with strong CYP 3A4 inhibitors
Apixaban
- Dose reduction to 2.5 mg BID if age > 80, Cr > 1.5, or body weight < 60 kg.
- Superior to warfarin for prevention of ischemic stroke and reduced hemorrhagic stroke risk/conversion
- Similar drug interaction concerns as rivaroxaban and dabigatran. It uses CYP3A4 for metabolism and binds P-glycoprotein
- Best overall profile for safety and efficacy, particularly in older adults

Doxaxaban
- Dose reduction to ½ dose if CrCl 15-50, or body weight < 60 kg or use P-glycoprotein inhibitors (verapamil, quinidine, dronaderone, ketoconazole)
- Less efficacy if CrCl > 95 mL/min
- Minimal CYP3A4 interaction

Issues: New Agents vs. Warfarin
- Switching to newer
  - Desiratran and Apixaban: INR closer to 2.0
  - Rivaroxaban: Start with INR > 3
- Switching back to warfarin
  - Desiratran: Start warfarin 3 days before stopping if normal CrCl
  - Rivaroxaban: Can affect INR. Begin LMWH or IV heparin before stopping at the time the next aspirin dose would be given.
- Reversibility: Rivaroxaban and apixaban (and probably edoxaban) appear to respond to prothrombin concentrate concentrate. Desiratran can be discontinued and now has an approved reversal agent (Andexanet alfa should inhibit all 4 Factor Xa decoy- ANNEXA-A and R showed efficacy for rivaroxaban and apixaban rapid reversal within 2-3 h of administration. FDA approved)
- Short ½ life- issues of adherence. Also no simple monitoring assay available for efficacy of new agents
- “Time in Therapeutic Range” for Warfarin
  - The more stable a patient is maintained in the therapeutic range on coumadin, the less advantage for the newer agents.  TTR in ARISTOTLE was 62.2%  In RE-LY, advantage of dabigatran for stroke begins to disappear about 65.5% TTR.
  - If someone TTR is < 60%, a new agent would certainly be a consideration but where the cut point is at this point is unclear.

Atrial Fibrillation Rate/Rhythm Control Strategies
- RACE II: 614 subjects (average age 68, 65% male) with permanent AF assigned to lenient (resting HR < 110 bpm) vs. strict rate control (resting HR < 80 bpm). Most with normal LVEF.
- Composite Outcome: CV death, HF hospitalization, stroke, systemic embolism, bleeding, life threatening arrhythmia
- 97.7% of lenient group achieved target HR, 67% of strict group.

Biventricular Pacing in Older Adults
- Class I indication for CRT in patients with systolic heart failure.
- LVEF ≤ 35%, Sinus rhythm, LBBB with QRS duration ≥ 150 ms, NYHA Class II, III, ambulatory IV
- If QRS duration is > 150 but not LBBB
- In atrial fibrillation where V-pacing can be done nearly 100% of the time
- LVEF ≤ 35% and demand for ventricular pacing will be > 40%
- NOT indicated (Class III) for patients whose comorbidities/frailty limit survival with good functional capacity to less than 1 year.

Biventricular Pacing in Older Adults
- Average age approximately 73 years
- Patients with high-degree AV block and an indication for pacing
- LVEF 50% or less: Average LVEF of about 43% in the pacemaker group
- Primary outcome: combined time to death from any cause, an urgent care visit for heart failure that required intravenous therapy, or a 15% or more increase in LVE/SVI
Primary ICD and Older Adults

- 2013 Appropriate Use Criteria
- Appropriate
  - Non-Ischemic Cardiomyopathy
    - LVEF ≤ 35% on guideline based therapy for at least 3 months (< 3 months in NSVT and inducible VT)
  - Ischemic Disease (> 40 days out from MI)
    - LVEF ≤ 35%, NYHA Class I,II,III, ambulatory IV
      - Ideally with EF still ≤ 35% after 3 months of guideline based medical therapy or if inducible VT by EPS in patients on less than 3 months of therapy with NSVT
      - LVEF 36-40%, asymptomatic NSVT, EP study with inducible sustained VT/VF.

Issues with Comorbidities

- Rarely indicated if life expectancy is < 1 year due to cardiac or other co-morbidities
- Rarely indicated in those unable to provide informed consent without a health care proxy.
- Rarely indicated in patients with psychiatric illness that may be aggravated by device or preclude follow-up

Risk Stratification for Primary ICD

- Age > 70
- BUN > 26 mg/dl
- QRS Duration > 120 ms
- Atrial Fibrillation
- NYHA Class > II
- Very High Risk (BUN ≥ 50, Cr ≥ 2.5)

Goldenberg J Am Coll Cardiol 2008 p 288

Heart Failure

- Diagnostic and Management Principals
  - Use of Biomarkers
  - HFrEF and HFpEF

Heart Failure- HFrEF and HFpEF

Poor Outcomes with HFrEF or HFpEF

Roger V L Circulation Research 2012;113:646-659

Trends in HFpEF and HFrEF prevalence

Heart Failure

- Diagnostic Testing
  - 12 lead ECG
  - CBC, Chem 7, Mg, Ca, TSH
  - Screening test for hemochromatosis, HIV, amyloidosis, rheumatological disease, or pheochromocytoma based on clinical suspicion
- Biomarkers
  - NT-Pro-BNP/BNP for supporting HF diagnosis if uncertain or to establish prognosis
  - Cardiac Troponin: aids with prognosis (in patient setting)

Heart Failure – Use of Biomarkers in the Older Patient

- BNP and N-Terminal proBNP:
  - Derived from the ventricles and released related to wall stress- pro-BNP is cleaved into active BNP (1/2 life 20 min) and inactive NT-proBNP (½ life 120 min). NT-proBNP cleared by the kidney.
  - Both are predictive of increased risk in older patients with ACS. Serial BNP appear useful in management at least in systolic heart failure.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Effect on BNP</th>
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<tbody>
<tr>
<td>Diminished Renal function</td>
<td>Increase</td>
</tr>
<tr>
<td>Reduced Lean Body Mass</td>
<td>Increase</td>
</tr>
<tr>
<td>Reduced Androgens</td>
<td>Increase</td>
</tr>
<tr>
<td>Anemia</td>
<td>Increase</td>
</tr>
</tbody>
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Serial BNP and Hospitalization

Heart Failure – Use of Biomarkers in the Older Patient

- TIME-CHF-499 systolic HF patient age ≥ 60 years (average age ~77 years with hospitalization in the last year and NT-proBNP > 2x normal).
  - Symptom guided management vs. NT-proBNP guided management
  - Although the primary outcome of hospitalization free survival was not significantly improved, HF free hospitalization was improved- 34% reduction and mortality shows a strong trend toward improvement in the biomarker-guided are (32% RRR, P=0.06)
  - Biomarker arm was also cost-effective dominant

Medical Therapy for HFrEF

<table>
<thead>
<tr>
<th>Drug</th>
<th>Symptoms</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-blockers</td>
<td>improved</td>
<td>decreased</td>
</tr>
<tr>
<td>ACE-I inhibitors</td>
<td>improved</td>
<td>decreased</td>
</tr>
<tr>
<td>ARB’s</td>
<td>improved</td>
<td>decreased</td>
</tr>
<tr>
<td>Aldosterone Anta.</td>
<td>improved</td>
<td>decreased (GFR &gt; 30, K &lt; 5)</td>
</tr>
<tr>
<td>Isordil/hydralazine</td>
<td>improved</td>
<td>decreased</td>
</tr>
<tr>
<td>Digoxin</td>
<td>improved</td>
<td>reduce hospitalizations</td>
</tr>
<tr>
<td>Diuretics</td>
<td>improved</td>
<td>?</td>
</tr>
</tbody>
</table>

NOTE: Statins are not here: Not indicated for HF treatment alone
Helpful Non-Pharmacological Interventions for HFrEF

Treatments
- CPAP for OSA: Improved LVEF, reduced SNS activation, increase walking distance
- Exercise Training: possible reduction in mortality
- Cardiac Rehab: increased_fn, QOL, reduced mortality

Effect of Aging on Diastolic Function
- Decrease in elastic properties of heart and great vessels (SBP, myocardial stiffness)
- Decrease in rate of ventricular filling
- Increase in cardiac fibrosis
- Decline in active relaxation
- Decrease in beta receptor density
- Decline in peripheral vasodilatory capacity

Medical Therapy for HFpEF
- Control Heart Rate and Blood Pressure (β-blockers/ACEI/ARBs)
- Diuretics for Volume symptoms
- ARBs may reduce hospitalizations in HFpEF

NOTE: Statins are not here: Not indicated for HF treatment alone

Aortic Stenosis and Older Adults
- Roles of Echocardiography
- Decision for TAVR vs. AVR: risk stratification,

Aortic Stenosis and Older Adults- CV Health Study

Transaortic Valve Replacement (TAVR)

TAVR for High Risk Patients with Severe Aortic Stenosis

- Latest Models Based on Published Data Suggest:
  - Prevalence of severe AS in patients ages ≥ 75: 12.4%
  - 75.6% of these are symptomatic
  - 40.3% of these do not undergo surgery
  - Currently nearly 300,000 of these patients are TAVR eligible
  - Nearly 27,000 patients become TAVR eligible annually

TAVR PARTNERS Trial Patient Selection

- 2 Cohorts
  - Cohort 1 (358 patients): Patients considered surgical candidates but with high surgical risk (STS Score indicating ≥10% risk of death, other co-morbidities suggesting ≥15% risk of death at 30 days)
  - Cohort 2 (348 TAVR, 351 SAVR): Patients not considered surgical candidates due to “coexisting conditions that would be associated with a predicted probability of 50% or more of either death by 30 days after surgery or a serious irreversible condition.”
  - Excluded LVEF < 20%, significant CAD requiring revascularization, moderate to severe MR, recent TIA/Stroke, renal insufficiency

TAVR- PARTNERS Trial – Cohort 2- Ave Age 83 years

- TAVR PARTNERS Cohort 2
  - Ave Age 83 years
  - NYHA Class
  - P=0.08, P=0.001, P=0.001

TAVR PARTNERS Cohort 2

- NYHA
  - Dead
  - I
  - II
  - III
  - IV

- Percentage of Patients
  - Baseline
  - 30 Days
  - 6 Months
  - 1 Year
TAVR PARTNERS Cohort 2

- Primary and secondary outcomes at 30 days were similar but some key differences in other outcomes
- Stroke risk 5.1% for TAVR vs. 2.4% SAVR at 1 year (P=0.07)
- Increase risk of vascular complications (11% vs.3.2%) for TAVR
- Lower risk of bleeding (11.0% vs. 3.2%) and new onset Afib (19.5% vs. 9.3%)

Thanks!