**Disclosures**

- Edwards – speaker on Sapien3 valves (TAVR)

**Stages A-D and NYHA Classes I-IV**

- **Stage A**: High risk but without structural disease or symptoms of HF
- **Stage B**: Structural heart disease without signs/symptoms of HF
- **Stage C**: Structural heart disease with signs/symptoms of HF
- **Stage D**: Refractory HF requiring advanced therapies

- **Class I**: No limitation
- **Class II**: Slight limitation of physical activity; okay at rest but symptoms with normal activity
- **Class III**: Marked limitation; okay at rest but less than ordinary activity causes symptoms
- **Class IV**: Symptoms at rest
2017 updates

- Several updates to 2013 CHF guidelines
  - Evaluation of patient biomarkers (BNP, NT-proBNP)
  - Treatment updates for Stage C in HF with reduced ejection fraction (HFrEF) and HF with preserved ejection fraction (HFpEF)
  - Management of comorbidities in HF: anemia, HTN, sleep disorders

Biomarkers for prevention, diagnosis and prognosis

- Natriuretic peptides (BNP, NT-proBNP) can be used to establish presence and severity of HF
  - Values and cutpoints should not be used interchangeably
  - BNP is substrate of neprilysin (but not NT-proBNP)
  - Angiotensin Receptor Neprilysin Inhibitor (ARNI) increases BNP levels but not NT-proBNP
  - Sacubitril/ARNI showed reduced NT-proBNP levels and associated improved outcomes
Biomarkers for prevention, diagnosis and prognosis

- Use of biomarkers especially helpful when cause of dyspnea is unclear:
  - Can be elevated from cardiac (HF, ACS, AFib) & non-cardiac causes (AKI, G1, chronic heart failure)
  - Obesity associated with lower peptide concentrations reducing diagnostic utility
- Insufficient recommendations related to natriuretic peptide-guided Rx or serial measurements of BNP or NT-proBNP levels for purpose of reducing hospitalization or deaths

Biomarkers - updates

- Prevention:
  - Patients at risk of developing HF, natriuretic peptide marker-based screening followed by team-based care, including a cardiologist optimizing GDMT, can be useful to prevent the development of LV dysfunction (systolic or diastolic) or new HF — Class IIa recommendation
  - New data suggest screening and early intervention may prevent HF

Biomarker update

- Prognosis:
  - Measurement of baseline levels of natriuretic peptide biomarkers and/or cardiac troponin on admission to the hospital is useful to establish a prognosis in acutely decompensated HF — Class I recommendation
  - Current recommendation emphasizes the admission levels that are useful
  - During HF hospitalization, a predischarge natriuretic peptide level can be useful to establish a post-discharge prognosis — Class IIa recommendation
  - Pre-discharge natriuretic peptide biomarker levels and the relative change in levels during hospital treatment are strong predictors of the risk of death or HF readmission
  - Patients who do not have decrease in levels have worse outcomes
  - Prognostic value or absolute change does not imply necessity for serial or repeated biomarkers during hospitalisation
Biomarkers Update - summary

- **Class I recommendation:**
  - BNP or NT-proBNP level at time of admission for both diagnosis and prognosis

- **Class IIa recommendations:**
  - BNP or NT-proBNP screening in patients at risk for developing HF to implement early intervention
  - Pre-discharge BNP or NT-proBNP useful to establish post-discharge prognosis

Treatment for Stage C HFREF

- Recommendations for Renin-Angiotensin system with ACE-I, ARB or ARNI
  - Use of ACE-I, ARB or ARNI in conjunction with evidence-based beta blockers and aldosterone antagonists in selected patients is recommended for chronic HFREF patients to reduce morbidity and mortality. **Class I recommendation**
  - ACE-I previously shown to have class benefit in reducing morbidity and mortality in HF pt’s
  - ARBs shown to be an acceptable alternative to ACE-I intolerant pt’s to reduce M&M in HF pt’s
  - ARNI – combined ARB and nephrilysin inhibitor (enzyme that degrades natriuretic peptides, bradykinin, and other vasoactive peptides).

Angiotensin receptor blocker-Nephrilysin Inhibitor (ARNI)

- Randomized trial compared sacubitril/valsartan with enalapril
  - Significant reduction (~20%) in composite endpoint of CV death or HF hospitalization
  - Benefit similar for both death and HF hospitalization
  - Consistent across subgroups
  - ARNI associated with hypotension, AI, and angioedema
ARNI

- Patient's w/ chronic symptomatic HF r NYHA class II or III who tolerate ACE-I or ARB → replacement by ARNI is recommended to further reduce morbidity and mortality → Class I recommendation
- ARNI approved in 3 doses → target dose 97/103 mg BID in the trial
- Initiate and titrate based on BP response, renal function, electrolytes
- ARNI should not be administered concomitantly with ACE-I or within 36 hours of last dose of ACE-I or in pt's with history of angioedema → Class III recommendation
- Previous study of a neprilysin inhibitor combined with ACE-I was terminated because of unacceptable incidence of angioedema and significant morbidity → both break down bradykinin which can directly or indirectly cause angioedema

Ivabradine

- Ivabradine can be beneficial to reduce HF hospitalization for pt's with symptomatic (NYHA class II-III) but stable chronic HF r LVEF<35% who are on goal directed medical therapy (GDMT) including maximal tolerated dose of beta blocker and who are in sinus rhythm with a HR>70 bpm at rest → Class IIa recommendation
- Ivabradine inhibits channel in the SA node to reduce HR
- RCT showed ivabradine reduced composite endpoint of CV death or HF hospitalization → driven mostly by reduction in HF hospitalization
- Target of ivabradine is HR slowing → important to titrate to maximally tolerated doses of beta blocker therapy before considering ivabradine

Treatment of Stage C HFrEF - Summary

- Class I: Use of ACE-I OR ARBs OR ARNI in conjuction with evidence based beta blockers and aldosterone antagonist for pts w/ HFrEF
- Pt's with chronic NYHA class IV HF who tolerate ACE-I or ARNI are recommended to change to ARNI to further reduce morbidity and mortality

- Class IIa:
  - Ivabradine can be beneficial to reduce HF hospitalization for pt's w/ stable chronic HFrEF who are on maximally tolerated beta blocker dose and do have sinus rhythm with resting HR>70 bpm

- Class III:
  - ARNI should not be administered concomitantly with ACE-I within 36 hours of last dose.
  - ARNI should not be given to patients with history of angioedema
Treatment for Stage C HFpEF

- Most treatment revolves around adequate control of BP to prevent morbidity and diuretics to relieve symptoms of hypervolemia.

Treatment for Stage C HFpEF - Updates

- Appropriately selected HFpEF pts (LVEF>45%, elevated BNP, elevated HF admission within 1 year, GFR>90mL/min, C<2.5mg/dL, K<5.0), aldosterone receptor antagonists might be considered to reduce hospitalizations → Class IIb recommendation
  - TOPCAT trial: spironolactone on combined endpoint of death, aborted cardiac death, and HF hospitalization in pts with HFpEF
    - Small, non-statistically significant difference in composite endpoint (HR 0.89) although HF hospitalization was significantly reduced (HR 0.83)

- Routine use of nitrates or phosphodiesterase-5 inhibitors to increase activity or quality of life in pts with HFpEF is ineffective → Class III recommendation
  - Nitrates reduce pulmonary congestion and improve exercise intolerance for pts with HFpEF but showed no benefit in HFpEF pts (NEAT-HFpEF trial)
  - Phosphodiesterase-5 inhibition with sildenafil in the RELAX trial showed no improvement in oxygen consumption or exercise tolerance
Treatment of HFpEF - Summary

- **Class IIb** - Use of aldosterone antagonist for select patients to reduce HF hospitalizations.
- **Class III** - Routine use of nitrates or phosphodiesterase-5 inhibitors (e.g. sildenafil) in HFpEF pts is ineffective.

Comorbidities in HF

- **Anemia**
  - Patients with NYHA class II-III and iron deficiency anemia, where anemia cannot be reversed may be reasonable to improve functional status and quality of life.
  - Class IIb recommendation.
  - Anemia associated with HF disease severity and iron deficiency may have a direct effect on left ventricular ejection fraction.
  - Studies have shown improvement in surrogate endpoints (e.g., quality of life, NT-proBNP, and LVEF), but none have been able to show reductions in morbidity or mortality.
  - Improvements in 6-minute walk tests, functional status.
  - Uncertain evidence for the use of repletion in HF pts with anemia.
  - Erythropoietin-stimulating agents should not be used - Class III.
    - The largest randomized trial using darboetin alfa did not show benefit but rather showed potential for harm with increased risk of thromboembolic events and non-significant increase in fatal/non-fatal stroke.

Comorbidities in HF

- **Hypertension**
  - Patients at increased risk (Stage A HF) should have optimal BP less than 130/80 mmHg - Class I.
  - Patients with HFpEF should be prescribed GDMT to attain SBP <130 mmHg - Class I.
  - Patients with HFpEF with persistent HTN after adequate diuretic/volume control should be prescribed GDMT started to attain SBP <130 mmHg - Class I.
Comorbidities in HF

- **Sleep disorders**
  - Patients with NYHA class II–IV HF and suspicion of sleep disordered breathing or excessive daytime somnolence should undergo a formal sleep study → Class IIa
  - Patients with CV disease and OSA → CPAP may be reasonable to improve sleep quality and daytime somnolence → Class IIb
  - Patients with NYHA class II–IV HF and central sleep apnea, adaptive servo-ventilation causes harm → Class III

Comorbidities in HF - Summary

- **Class I:**
  - Patients at increased risk (Stage A HF) with HTN, patients with HF r EF with HTN and patients with HF p EF and persistent HTN despite diuresis should be prescribed GDMT to attain SBP<130 mmHg.

- **Class IIa:**
  - NYHA class II–IV HF pt's with suspicion for sleep apnea should undergo a formal sleep study.

- **Class IIb:**
  - CPAP may be reasonable in pt's with CV disease and OSA.
  - IV iron replacement might be reasonable to improve quality of life and functional status in pt's with iron deficiency anemia.

- **Class III:**
  - Erythropoietin stimulating agents should not be used in HF pt’s with anemia.
  - Adaptive servo-ventilation should not be used in NYHA class II–IV HF patients with central sleep apnea.

Thank you