Updates in Congestive Heart Failure

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1/28/2018

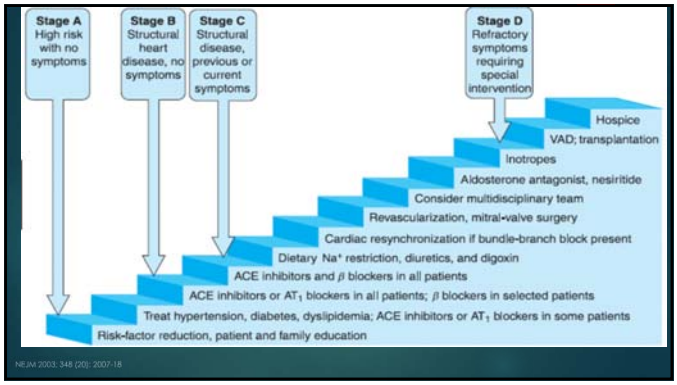
Disclosures

- 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 Blocker Neprilysin Inhibitor (ARNI) increases BNP levels but not NT-proBNP
    - Studies w/ 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, OSA, sepsis, burns)
  - Obesity associated with lower peptide concentrations reducing diagnostic sensitivity
- 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:
  - Patient's 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 onset HF → **Class IIa recommendation**
    - ***New data suggest screening and early intervention may prevent HF***

Biomarkers 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 relative change does not imply necessity for serial or repeated biomarkers during hospitalization*

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 patient's 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 OR ARBS OR ARNIs 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 clear benefit in reducing morbidity and mortality in HF pt's
    - ARBs shown to be accepted alternative to ACE-I intolerant pt's to reduce M&M in HF pt's
    - **ARNI -> combined ARB and neprilysin inhibitor (enzyme that degrades natriuretic peptides, bradykinin, and other vasoactive peptides).**

Angiotensin receptor blocker-Nepirlysin 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, AKI and angioedema

ARNI

- Patient's w/ chronic symptomatic HFrEF 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, other meds
- 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 HFrEF (LVEF<35%) who are receiving goal directed medical therapy (GDMT) including a maximally 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* ARNIs in conjunction with evidence based beta blockers and aldosterone antagonists for pt's w/ HFrEF
  - Pt's with chronic NYHA class II-III HFrEF who tolerate ACE-I or ARBs 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 still 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 HF*p*EF

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

Treatment for Stage C HF*p*EF - Updates

- Appropriately selected HF*p*EF pt's (LVEF>45%, elevated BNP levels or HF admission within 1 year, GFR>30mL/min, Cr<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 pt's with HF*p*EF
    - Small, non-statistically significant difference in composite endpoint (HR 0.89) although HF hospitalization was significantly reduced (HR 0.83)

Treatment for Stage C HF*p*EF - Updates

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

Treatment of HF*p*EF - Summary

- **Class IIb** – Use of aldosterone antagonist for select patient's to reduce HF hospitalizations
- **Class III –** Routine use of nitrates or phosphodiesterase-5 inhibitors (e.g. sildenafil) in HF*p*EF pt's is ineffective

Comorbidities in HF

- Anemia
  - Patient's with NYHA class II–III HF and iron deficiency anemia, IV iron replacement might be reasonable to improve functional status and quality of life → **Class IIb recommendation**
    - Anemia independently associated with HF disease severity and Iron deficiency associated with reduced exercise capacity
    - Studies have shown improvement in surrogate endpoints (i.e. quality of life, NT-proBNP, and LVEF) but none have been able to shown reductions in morbidity or mortality
    - Improvements in 6 minute walk tests, functional status
    - Uncertain evidence for oral iron repletion in HF pt's 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 strokes

Comorbidities in HF

- Hypertension
  - Patients at increased risk (Stage A HF) should have optimal BP less than 130/80 mmHg → **Class I**
  - Patients with HF*r*EF should be prescribed GDMT to attain SBP <130 mmHg → **Class I**
  - Patients with HF*p*EF with persistent HTN after adequate diuresis/volume control should be prescribed GDMT titrated to attain SBP<130mmHg →**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 HFrEF and central sleep apnea, adaptive servo-ventilation causes harm → **Class III**

Comorbidities in HF - Summary

- **Class I:**
  - Patient's at increased risk (Stage A HF) with HTN, patient's w/ HFrEF with HTN and patients with HFpEF 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 NYHA class II-III HF and 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 HFrEF patients with central sleep apnea

Thank you