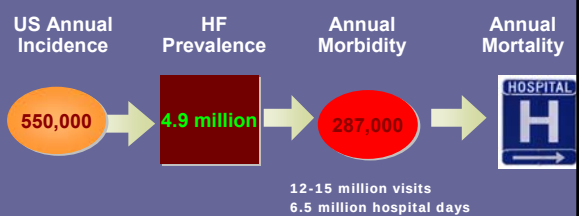
Heart Failure Review

Heart Failure

- Final common pathway for many cardiovascular diseases whose natural history results in symptomatic or asymptomatic left ventricular dysfunction
- Cardinal manifestations of heart failure include dyspnea, fatigue and fluid retention
- Risk of death is 5-10% annually in patients with mild symptoms and increases to as high as 30-40% annually in patients with advanced disease

Why is it so important?



12-15 million visits
6.5 million hospital days

HF management cost $ 27.9 billion in 2005

*AHA. *Heart and Stroke Statistics – 2005 Update.*

Causes of HF:
Anything that affects the pumping efficiency

Systolic HF – Most common HF (70%), due to contractile failure of myocardium or inability to empty ventricles, EF<40%.
- CAD and Ischemic Cardiomyopathy
- Hypertension
- Diabetes
- Thyroid Disorders

Diastolic HF – Inability to fill or to relax, contractility can be normal or increased. (Think Frank-Starling)
- CAD
- Valve Disease
- Hypertrophic Cardiomyopathy.
- Systemic Hypertension
- Constrictive Pericarditis

NYHA Classification of heart failure

- Class I: No limitation of physical activity
- Class II: Slight limitation of physical activity
- Class III: Marked limitation of physical activity
- Class IV: Unable to carry out physical activity without discomfort

New classification of heart failure

- Stage A: Asymptomatic with no heart damage but have risk factors for heart failure
- Stage B: Asymptomatic but have signs of structural heart damage
- Stage C: Have symptoms and heart damage
- Stage D: Endstage disease

ACC/AHA guidelines, 2001

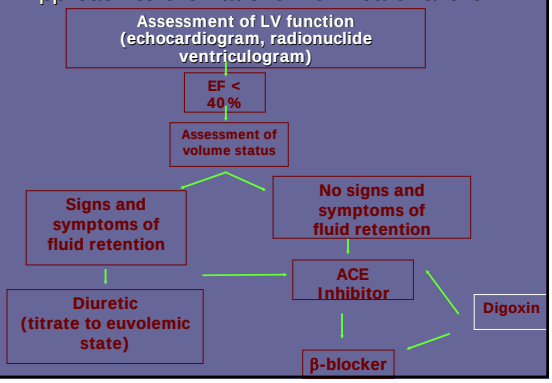
Factors aggravating heart failure

- Myocardial ischemia or infarct
- Dietary sodium excess
- Excess fluid intake
- Medication noncompliance
- Arrhythmias
- Intercurrent illness (eg infection)
- Conditions associated with increased metabolic demand (eg pregnancy, thyrotoxicosis, excessive physical activity)
- Administration of drug with negative inotropic properties or fluid retaining properties (e. NSAIDs, corticosteroids)
- Alcohol

Goals of treatment

- To improve symptoms and quality of life
- To decrease likelihood of disease progression
- To reduce the risk of death and need for hospitalisation

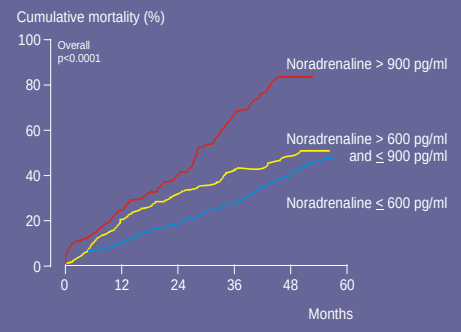
Approach to the Patient with Heart Failure



Compensatory changes in heart failure

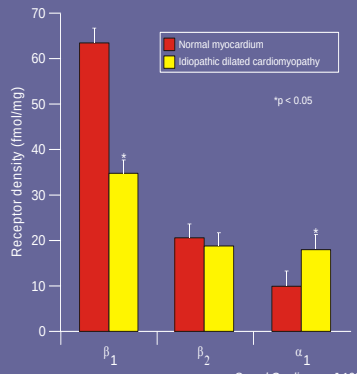
- Activation of SNS
- Activation of RAS
- Increased heart rate
- Release of ADH
- Release of atrial natriuretic peptide
- Chamber enlargement
- Myocardial hypertrophy

Relation between plasma noradrenaline and mortality in patients with heart failure



NEJM 1984; 311: 819-823

Receptor densities in human left ventricular myocardium



Scand Cardiovasc J 1998; Suppl 47:45-55

Carvedilol in Heart Failure

- Effective receptor-blockade approach to heart failure
- Negative inotropic effect counteracted by vasodilation
- Provides anti-proliferative, anti-arrhythmic activity and inhibition of apoptosis
- Prevents renin secretion

Drugs of Today 1998; 34 (Suppl B): 1-23

US Multicenter Program

	Placebo (n=398)	Carvedilol (n=696)	% Risk Reduction
All-cause mortality	31 (7.8%)	22 (3.2%)	65%
Death due to progressive heart failure	13 (3.3%)	5 (0.7%)	
Sudden death	15 (3.8%)	12 (1.7%)	
Risk of hospitalization for cardiovascular reasons	78 (19.6%)	78 (14.1%)	27%
Combined risk of mortality & hospitalization	98 (25%)	110 (16%)	38%

NEJM 1996; 334:1349-1355

ANZ Multicentre Heart Failure Trial

	Placebo (n=208)	Carvedilol (n=207)	% Risk Reduction
All-cause mortality	26 (12.5%)	20 (10%)	24%
Risk of hospitalization for cardiovascular reasons	84 (40%)	64 (31%)	28%
Combined risk of mortality & hospitalization	97 (47%)	74 (36%)	29%

Lancet 1997; 349: 375-380.

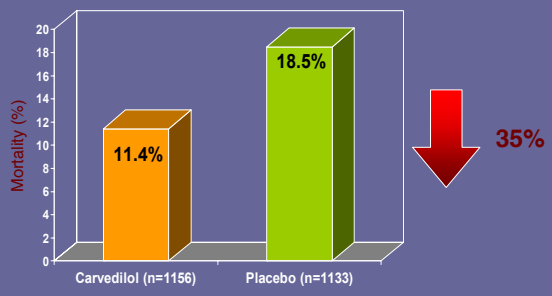
Effect of carvedilol on progression of congestive heart failure

Endpoint	All randomized patients	
	Placebo (n=134)	Carvedilol (n=232)
Primary endpoint	28 (21%)	25 (11%)*
Death due to CHF	4 (3%)	0 (0%)
Hospitalization due to worsening CHF	8 (6%)	9 (4%)
Increase in CHF medication	16 (12%)	16 (7%)

* Placebo vs. carvedilol, p = 0.008

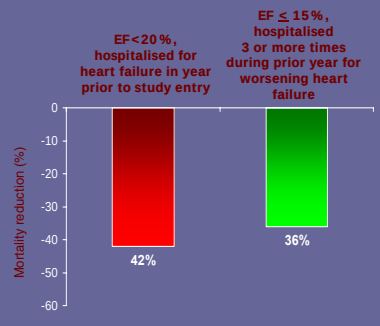
Drugs of Today 1998; 34 (Suppl B): 1-23.

COPERNICUS: Effect on Mortality



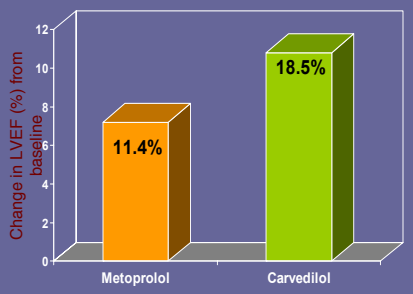
22nd Congress of European Society of Cardiology, August 2000

COPERNICUS: Mortality reduction in special patient groups with carvedilol



22nd Congress of European Society of Cardiology, August 2000

Carvedilol vs. Metoprolol



Circulation 2000; 102: 546-551

Dosage guidelines for Carvedilol in heart failure

Patient selection
- Stable on background medications (diuretics, digoxin and/or ACE inhibitors)
- Not in a fluid-overload state
- Not hypotensive

3.125 mg bid → 2 weeks → Doubled every 2 weeks → Max dose 25 mg bid (<85 kg); 50 mg bid (>85 kg)

Before dose increase
Evaluate for
- Worsening heart failure
- Vasodilation
- Bradycardia

After each new dose initiation
- Observe for signs of dizziness or light headedness for one hour

Management of Complications

Transient worsening of heart failure (e.g. increasing dyspnea, decreasing exercise capacity)

- Increase dose of diuretic and/or ACE inhibitor
- If necessary, reduce carvedilol dose and/or prolong titration interval
- Search for other possible causes (e.g. thyroid malfunction, infection, non-compliant drug intake, excessive liquid intake, etc.)

Vasodilatory Symptoms (dizziness, light headedness, symptomatic hypotension)

- Decrease diuretic dose and, if necessary, ACE inhibitor dose
- If the cessation of both is not successful, reduce carvedilol dose and/or prolong titration interval

Management of Complications *(Contd.)*

Bradycardia (Pulse rate below 55 beats/min)

- Check and eventually reduce digitalis dose
- If necessary, reduce carvedilol dose and/or prolong titration interval
- Withdraw carvedilol only in the event that hemodynamics are affected

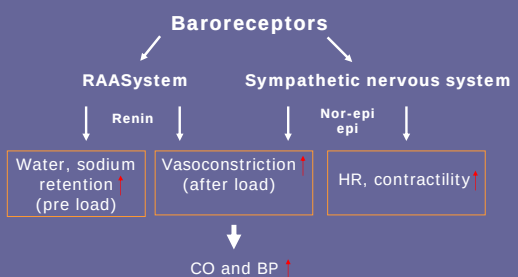
Symptoms of Bronchial obstruction

- Search for other possible causes (e.g., concurrent infection, subacute pulmonary edema)
- Reduce dose of, or withdraw, carvedilol only after possible causes for symptoms have been ruled out

A pause to think and digest ...

Body's Compensatory Response

Neurohormonal Response



ACE Inhibitors: physiologic benefits

Arteriovenous Vasodilatation

- ↓ pulmonary arterial diastolic pressure
- ↓ pulmonary capillary wedge pressure
- ↓ left ventricular end-diastolic pressure
- ↓ systemic vascular resistance
- ↓ systemic blood pressure
- ↓ maximal oxygen uptake (MVO_2)

ACE Inhibitors: physiologic benefits

- ↑ LV function and cardiac output
- ↑ renal, coronary, cerebral blood flow
- No change in heart rate or myocardial contractility
- no neurohormonal activation
- resultant diuresis and natriuresis

ACE Inhibitors: clinical benefits

- Increases exercise capacity
- improves functional class
- attenuation of LV remodeling post MI
- decrease in the progression of chronic HF
- decreased hospitalization
- enhanced quality of life
- improved survival

Asymptomatic Patients

Enalapril

SOLVD Prevention Trial

EF < 35 %
↓ HF progression, ↓ hospitalization

Captopril

SAVE, GISSI-3, ISIS-4

Post MI, EF < 40 %
↓ overall mortality, ↓ re-infarction
↓ hospitalization, ↓ HF progression

Symptomatic Patients

Hydralazine + Isosorbide dinitrate

VHeFT-I

↓ mortality, improved functional class
as compared with use of digoxin and diuretics

VHeFT-II

proved less effective than enalapril

Guidelines to ACE Inhibitor Therapy

- Contraindications
  - Renal artery stenosis
  - Renal insufficiency (relative)
  - Hyperkalemia
  - Arterial hypotension
  - Cough
  - Angioedema
- Alternatives
  - Hydralazine + ISDN, AT-II inhibitor

Guidelines to ACE Inhibitor Therapy

- **All patients with symptomatic heart failure and those in functional class I with significantly reduced left ventricular function should be treated with an ACE inhibitor, unless contraindicated or not tolerated**
- **ACE inhibitors should be continued indefinitely**
- **It is important to titrate to the dosage regimen used in the clinical trials ... in the absence of symptoms or adverse effects on end-organ perfusion**
- **In very severe heart failure, hydralazine and nitrates added to ACE inhibitor therapy can further improve cardiac output**

Diuretics

- Indicated in patients with symptoms of heart failure who have evidence of fluid retention
- Enhance response to other drugs in heart failure such as beta-blockers and ACE inhibitors
- Therapy initiated with low doses followed by increments in dosage until urine output increases and weight decreases by 0.5-1kg daily

Digoxin

- Enhances LV function, normalizes baroreceptor-mediated reflexes and increases cardiac output at rest and during exercise
- Recommended to improve clinical status of patients with heart failure due to LV dysfunction and should be used in conjunction with diuretics, ACE inhibitors and beta-blockers
- Also recommended in patients with heart failure who have atrial fibrillation
- Digoxin initiated and maintained at a dose of 0.25 mg daily
- Adverse effects include cardiac arrhythmias, GI symptoms and neurological complaints (eg. visual disturbances, confusion)

Summary of drug treatment for CHF

Asymptomatic LV dysfunction	Mild to moderate CHF	Mod to severe CHF
ACE Inhibitor Beta blocker	Digoxin Diuretics ACE Inhibitor Beta blocker	Digoxin Diuretics ACE inhibitor Beta blocker Spironolactone

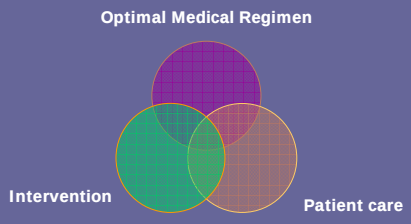
Any questions?

HF Clinical Evaluation

Objectives:

1. Reveal the root cause of the HF:
   - Ischemic Heart Disease
   - Hypertension
   - Infections (e.g., viral myocarditis, Chagas' disease)
   - Toxins (e.g., alcohol or cytotoxic drugs)
   - Valvular Disease
   - Prolonged Arrhythmias
   - Idiopathic Cardiomyopathy
2. Assess cardiac dysfunction
3. Assess functional capacity

Multi-dimensional Approach



Assess HF severity

1. History assessment:
   - Previous MI, Cardiomyopathy
   - Atrial Fibrillation, other rhythm disturbances
   - EF – LV function
   - Minnesota Living With Heart failure Questionnaire
2. QRS duration
3. Six-minute walk test
4. Brain Natriuretic Peptide (BNP) blood test
5. Peak VO_2
6. ECHO

ECHO – important diagnostic tool

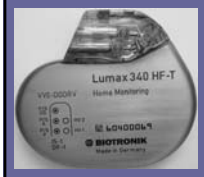
- **2-D ECHO** - to assess:
  - LV size
  - Ejection Fraction
  - Valvular status (regurgitation, stenosis)
- **Stress ECHO** - to assess:
  - the occurrence of new wall motion abnormalities with exercise

Challenge for Drug Therapy

- Drug therapy is considered the gold standard for treatment of HF
- HF patients are prescribed an average of six medications
- Only 10% patients are fully compliant
- 1/3 of patients never refill their prescriptions

Stand by for a really important message …

Cardiac Resynchronization Therapy



Indicated for the treatment of CHF:

- Optimal Drug Therapy
- IVCD >120ms **(implies v. dyssynchrony)**
- LVEF < 35%
- NYHA Class III or IV (not all IVs qualify)

Studies have indicated improvement in quality of life, functional capacity, and reversal of ventricular remodeling.

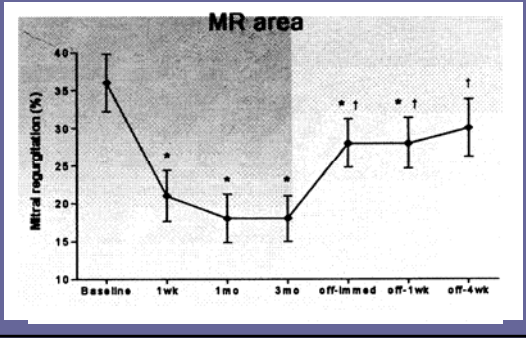
(Meta study showed improvement in mortality)

"Remodeling"

- Ventricular remodeling = worsening HF
- Reverse ventricular remodeling suggests:
  - ↓ overall size of the heart – primarily LV
  - conduction delays are improved
  - ↓ Mitral valve regurgitation
  - improved LV contraction dynamics
  - therefore ↑ CO and ↓ HF symptoms

Does CRT really work?

Yes – look at what happened … CRT on for three months, then off for 4 weeks!



New Directions in HF therapy

- Work is now in identifying "responder" to resynchronization therapy - CRT
  - (1/3 don't respond)
- Identification of mechanical dyssynchrony
  - (wide QRS inadequate)
- Echo enhancement of tissue doppler flow

Need For Better Selection Criteria

- QRS duration: **has been an inclusion criteria in all major trials**
  - mechanical dyssynchrony may be absent in approx 30% of pts with HF & BBB
  - present in 40-50% of pts with a normal QRS.[1-3]
- Since LV contractility is not dependent on QRS width, pt selection with something like Tissue Velocity Imaging (TVI) measuring contractility of myocardial fibers in a longitudinal plane would be a better measure of dyssynchrony than a wide QRS[4]
- Identify lagging segments for optimal LV placement !

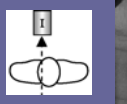
1. Fauchier L, et al. Am J Cardiology 2003; 92:341-344
2. Yu CM, et al. Heart 2003; 89:54-60
3. Burri H, Lerch R. PACE 2006; 3:474-479.
4. Hayes et. al. Resynchronization & Defibrillation for Heart Failure. P151-54

Lead Placement

- 233 patients with NYHA Class III-IV and EF <35%
  - Group 1: LV lead in anterior or anterolateral branches (66 pts.)
  - Group 2: LV lead in lateral or posterolateral branches (167 pts.)
- LVEF by echo did NOT improve significantly in Group 1
  - Pre-LVEF = 18% vs. Post-LVEF = 20%
- LVEF by echo DID improve significantly in Group 2
  - Pre-LVEF = 19% vs. Post-LVEF = 27%
- Conclusion:
  - Placement of CS lead in lateral and posterolateral branches is associated with significant improvement in LV function as a measure of post-implant LVEF.

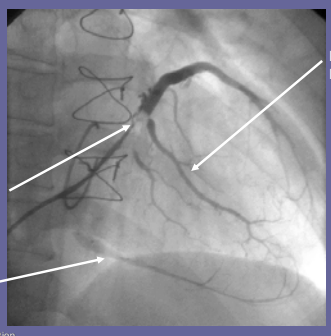
Rossillo, Antonio, M.D., et al. "Impact of Coronary Sinus Lead Position on Biventricular Pacing: Mortality and Echocardiographic Evaluation During Long-Term Follow-Up." Journal of Card. Elect. 15;10:1120 – Oct. 2004.

Venogram



AP

Balloon

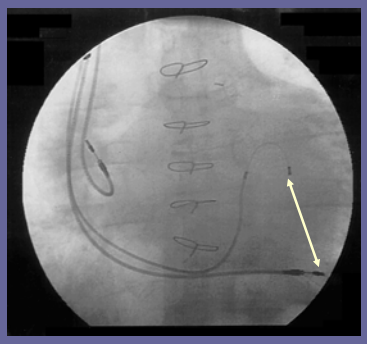


Postero-Lateral/ Lateral veins

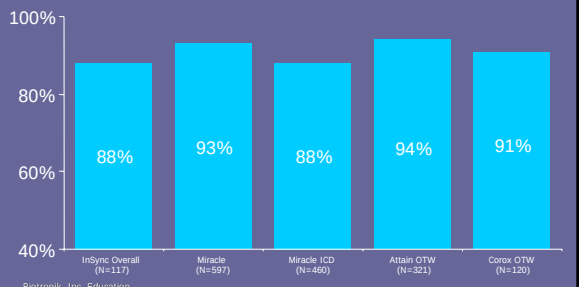
Middle Cardiac Vein

Good Anatomical Distance

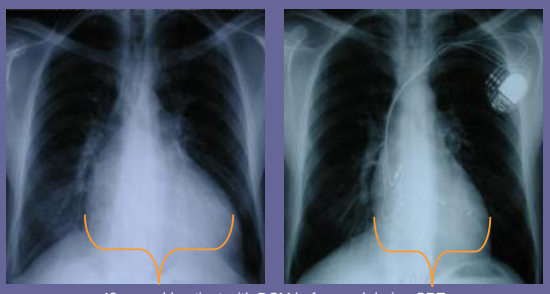
- LV lead in lateral or postero-lateral position
- RV lead in apex or at septum
- Good distance between the leads tips



LV Systems - Implantation Success



As a Reward for the Effort: Successful Bi-ventricular Therapy

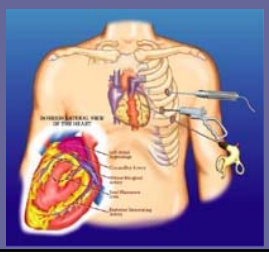


42 year old patient with DCM before and during CRT

When LV placement fails ... then what ?

- **... call the surgeon ...**

go for epicardial lead placement (via laparoscopy)



Heart Failure Concepts

- CRT represents an important new therapy for patients with Class III/IV heart failure, low ejection fraction and a wide QRS
- CRT has the potential to improve symptoms and functional status, reduce ventricular remodeling and improve survival.
- CRT with a defibrillator (CRT-D) provides added protection against sudden death in heart failure.

CASE STUDIES

Case I

- 74 year old male, 2 previous hospitalizations for CHF over a 4 month period, known ischemic CM, EF 20-25%.
- EKG: LBBB.
- Meds: B. Blockers, ACEI, Diuretics, Digoxin, spironolactone.

Case 1 (contd.)

- Treatment: BiV Icd placed in 2007.
- Have followed for 3 years, no hospitalizations for CHF.
- Benefits to Pt: able to work in yard daily, builds Bbq's.
- Has gone from Class IV to Class II, no change in EF, MR Improved.

Case II

- 65 year old female, multiple hospitalizations for CHF over 1 year period, EF 20%, 3+MR.
- Biv Icd placed in 2009.
- Benefits: EF inc. to 30%, MR 1-2+, no hospitalizations for CHF, fully functional.