

Heart Failure in Women

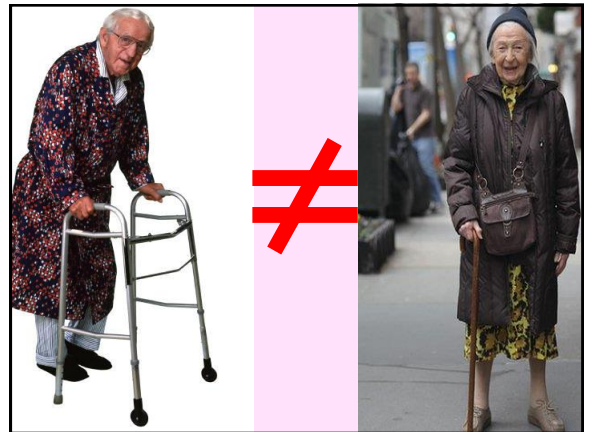
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Disclosure

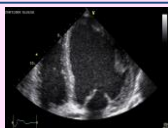
Professor Sindone has received honoraria, speaker fees, consultancy fees, is a member of advisory boards or has appeared on expert panels for:

Alphapharm, Aspen, Astra Zeneca, Bayer, Biotronik, Boehringer Ingelheim, Bristol Myer Squibb, CSL, HealthEd, Menarini, Merck Sharp and Dohm, Mylan, Novartis, Otsuka, Pfizer, Roche, Sanofi, Servier, Vifor

(Sorry if I forgot anyone)...



HF = Symptoms + Structural heart disease



HF with reduced EF
HFREF
“Systolic HF”



HF with preserved EF
HFPEF
“Diastolic HF”



HF due to valvular
heart disease

Evaluation of Heart Failure

- Patients with signs and symptoms of heart failure require:
- ECG
- CXR
- Serum NT-proBNP
- Echocardiogram

CXR

Cardiomegaly
Pulmonary congestion



Echocardiogram



- Left ventricular function
 - Systolic and diastolic function
- Atrial size
- Assess valves
 - Stenosis or regurgitation
- Right heart size and systolic function
 - Pulmonary hypertension

We Are in a Heart Failure Epidemic

Hospital Discharges for HF, 1979–2003: 174% Increase



Adapted from Thom T et al. Circulation. 2006;113:e85–e151.

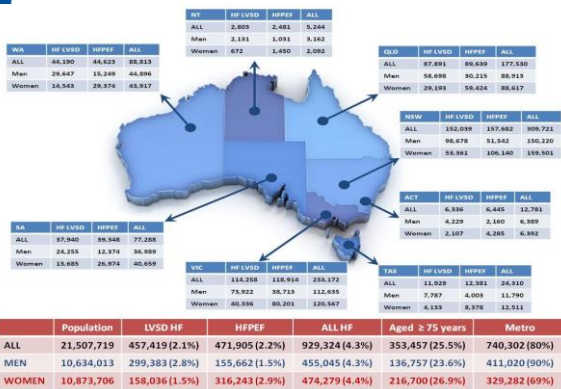
ADHERE-AP ADHERE-US* AUS

Number	10,171	17,382	909
Period	01/06 – 12/08	04/05 – 03/06	01/06-08/06
Age (mean/median)	67/66	75/-	74/77
Female	43%	51%	42%
LVEF assessed	50%	62%	48%
LVEF <40%	51%	54%	53%

* Refers to last 12 months of ADHERE-Core module

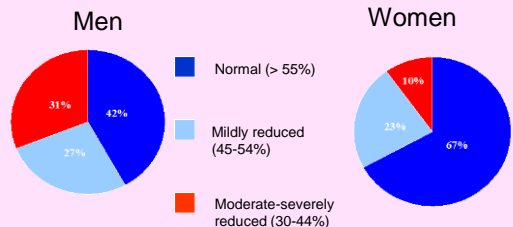
Adapted from Atherton JJ et al. J CardiacFail 2012;18:82

Population Prevalence



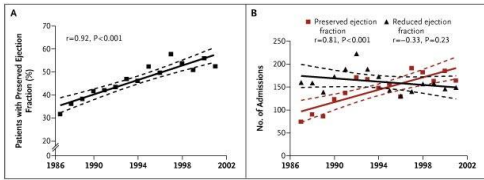
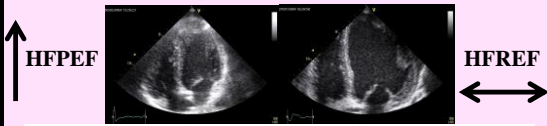
Gender differences in LV function

Cardiovascular Health Study (NHLBI)



Am J Cardiol 2001; 87: 413

Secular Trends in the Prevalence of HF



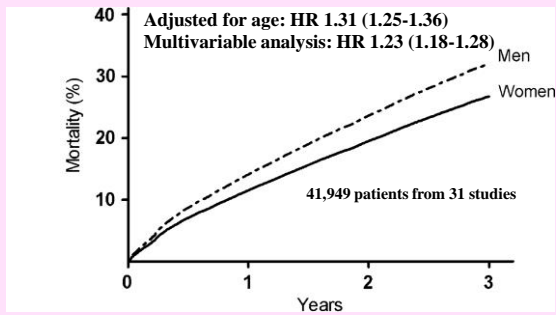
Owan TE et al. NEJM 2006;355:251

MAGGIC Meta-Analysis

N = 41,949	Men	Women	P value
Age (years)	66	71	<0.001
Hypertension	40%	50%	<0.001
Myocardial infarction	51%	33%	<0.001
Diabetes	20%	22%	<0.001
Atrial fibrillation	23%	25%	<0.001
HFPEF (LVEF \geq 50%)	18%	37%	<0.001

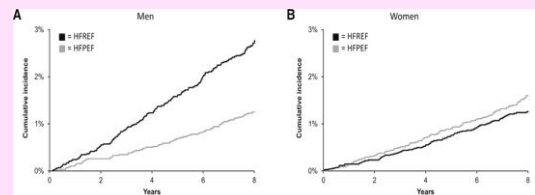
Martinez-Selles M et al. Eur J HF 2012;14:473-9

HF: All-cause mortality adjusted for age



Martinez-Selles M et al. Eur J Heart Fail 2012;14:473-479

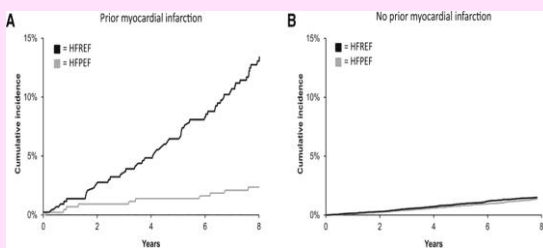
Incident HFPEF (LVEF >45%) vs. HFREF in men and women



- 457 incident HF cases with documented LVEF in 6,340 individuals over 7.7 yrs.
- Incident rates for HFPEF in men and women and HFREF in women similar.
- Incident rate of HFREF in men higher (P=0.0003).

Ho J E et al. Circ Heart Fail. 2013;6:279-286

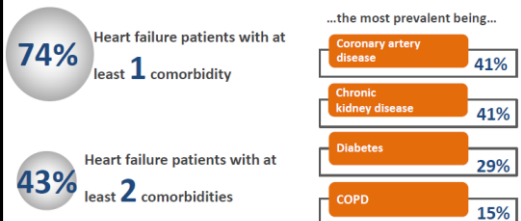
Incident HFPEF (LVEF >45%) vs. HFREF by history of MI



- 457 incident HF cases with documented LVEF in 6,340 individuals over 7.7 yrs.
- Incident rate of HFREF higher if prior MI (P=0.0003).

Ho J E et al. Circ Heart Fail. 2013;6:279-286

Main challenges: multimorbidity



The number of comorbidities increases with the severity of heart failure and limits the use of standard therapy.

van Doornen-VI et al. Eur J Heart Fail. 2014;16:103-111

Heart Failure in the Elderly

- Women
- Hypertension
- Atrial fibrillation
- Obesity
- Iron deficiency
- Diabetes mellitus
- Coronary artery disease



Average Aged Care Patient

- More than 80 years of age
- Symptom improvement is the primary goal
- Rationalising treatment medications important
- Survival is sometimes less of an issue
- Revascularisation usually not an issue

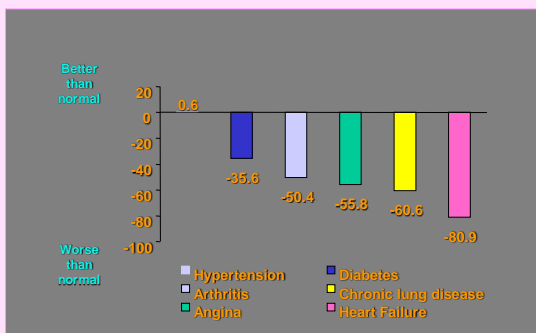
Issues for the Elderly Patient's Physician

- Postural hypotension
- Low BP due to endstage heart failure
- Renal impairment
- Conduction disease
- Polypharmacy
- Multiple pathologies

Problems Treating Elderly Patients

- Multifactorial dyspnoea
 - LV dysfunction
 - CAL & asthma
 - Kyphosis
 - Basal atelectasis
 - Pneumonia
 - Anaemia
 - Decreased strength and mobility

Quality of Life in Chronic Heart Failure



Stewart AL et al JAMA 1989

Heart Failure Symptoms

- F – Fatigue, tiredness
- A – Activities difficult
- C – Congestion, cough
- E – Edema (swollen ankles, legs)
- S – Shortness of breath

Heart Failure Symptoms in Women

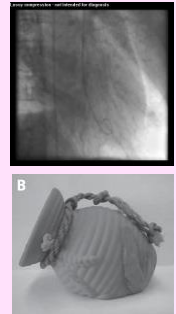
- F – Fatigue, forgetfulness
- A – Apathy, anxiety
- C – Cough, concentration poor
- E – Edema, exercise intolerance
- S – Severe shortness of breath

Heart failure presentations that are more common in women

	% Female	Prevalence
Peripartum cardiomyopathy	All	Rare
Takotsubo cardiomyopathy	>80-90%	Uncommon
Chemotherapy-related	?	Uncommon
HF with preserved EF (HFPEF)	≈60%	Common

Takotsubo Cardiomyopathy

- >80-90% women
- Often post-menopausal
- Precipitated by stressful event
- 1-2% of MI presentations
- Usually no significant CAD
- LV function recovers <4 weeks
- May recur

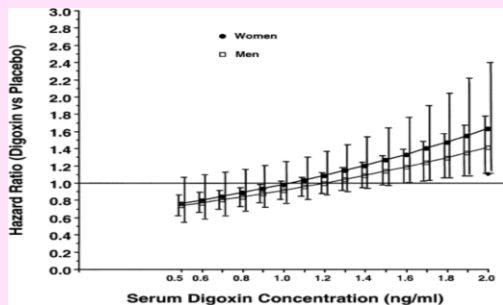


Systolic HF: Placebo-controlled RCT's

	Significant effect men	Significant effect women	No significant interaction
ACE inhibitors	✓	-	✓
Beta blockers	✓	✓	✓
MR antagonists	✓	✓	✓
ARB's	✓	✓	✓
Hydral/ Nitrates	✓	✓	✓
Ivabradine	✓	✓	✓
Digoxin	-	✗	✗
CRT	✓	✓	✓
ICD	✓	-	✓

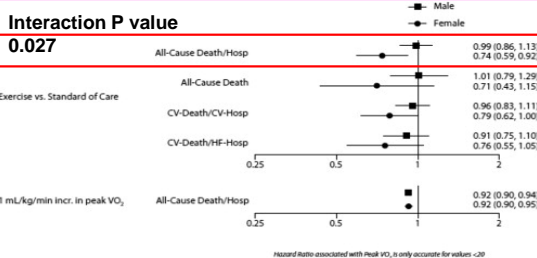
DIG study

Relationship of Serum Digoxin Concentration to Mortality HR



Adams KF et al. J Am Coll Cardiol. 2005;46:497

HF-ACTION Exercise Benefit vs. Gender



Pina IL et al. JACC Heart failure 2014;2:180

Major placebo-controlled RCT's of drug therapy in CHF

Drug class	HFREF major RCT's	HFPEF major RCT's	
ACEi	CONSENSUS SOLVD-T	Positive Positive	PEP-CHF Neutral
Beta blockers	CIBIS-II MERIT-HF COPERNICUS BEST	Positive Positive Positive Neutral	
ARB	CHARM-Alternative CHARM-Added Val-HeFT	Positive Positive Positive	CHARM-Preserved I-Preserve Neutral Neutral
MRA	RALES EMPHASIS	Positive Positive	TOPCAT Neutral
Ivabradine	SHIFT	Positive	
n3-PUFA	GISSI-HF	Positive	

HFPEF Management

- Diuretics to treat congestion
- Manage cardiovascular risk factors (hypertension, obesity, diabetes)
- Control ventricular rate in AF
- Consider underlying ischaemic heart disease

Avoid Drugs Which Worsen Heart Failure

Calcium Channel Blockers (peripherally and centrally acting agents)	NSAID's (including COX II antagonists)
Tricyclic Anti-Depressants	Type I Anti-Histamines
Type I Anti-arrhythmic agents (eg Flecainide, Disopyramide, Quinidine)	Macrolide Antibiotics
Corticosteroids	Moxonidine
Glitazones	TNF-α Antagonists
Tyrosine Kinase Inhibitors	Herceptin

Ex-DHF

64 HFPEF patients (65 yrs)

- NYHA 2-3
- LVEF $\geq 50\%$
- Diast dysfunction ≥ 1
- Sinus rhythm
- Additional RF

Prim EP (Peak VO_2) 3 mths:

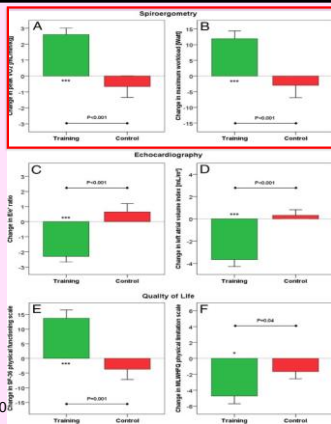
- Ex: 16.1 to 18.7 mL/min/kg
- Co: 16.7 to 16.0 mL/min/kg
- P < 0.001

E/E' decreased

LA volume decreased

Symptoms/ QOL improved

Edelmann F et al.
J Am Coll Cardiol 2011;58:1780



Heart Failure in Women

- Age-adjusted incident HF lower in women (less HFREF)
- Overall HF prevalence is similar in women and men due to longer female life expectancy.
- Specific presentations occur more often in women including Takotsubo cardiomyopathy and HFPEF.
- HFREF treatments have similar effects in men/ women.
- HFPEF prevalence is increasing but treatment options are limited to fluid management and treating CV risk factors.
- Women respond well to exercise training, which also improves quality of life in HFPEF.