

Heart Failure Treatments

Past & Present

Background

Background

Chronic heart failure

- Drugs
- Mechanical
- Electrical

Background

Chronic heart failure

- Drugs
- Mechanical
- Electrical

Sudden cardiac death

- Amiodarone
- Implantable Cardioverter-Defibrillator

Heart Failure



Big Problem

Prevalence over 65y = 4%

5 year mortality = 50%

Clasificación

Clasificación

Clasificación

Systolic Vs Diastolic

Clasification

Systolic Vs Diastolic

Right Vs Left

Clasification

Systolic Vs Diastolic

Right Vs Left

Forward Vs Backward

Clasification

Systolic Vs Diastolic

Right Vs Left

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High output Vs Low output

Clasification

Systolic Vs Diastolic

Right Vs Left

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High output Vs Low output

Acute Vs Chronic

Causes

Ischaemic Heart Disease	40%
Dilated Cardiomyopathy	35%
Hypertension	15%

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Dilated Cardiomyopathy	35%
Hypertension	15%

- Undilated cardiomyopathy
- Valvular
- Cor pulmonale
- Congenital
- Alcohol and drugs
- Arrhythmia

Heart Failure

- Ventricular remodelling
- High filling volumes
- Fluid & salt retention
- Hypotension & under perfusion
- High circulating catecholamines
- Redirection of cardiac output
- High levels of ADH
- High levels and resistance to natriuretic peptides
- Arrhythmia

Ventricular Volumes

normal



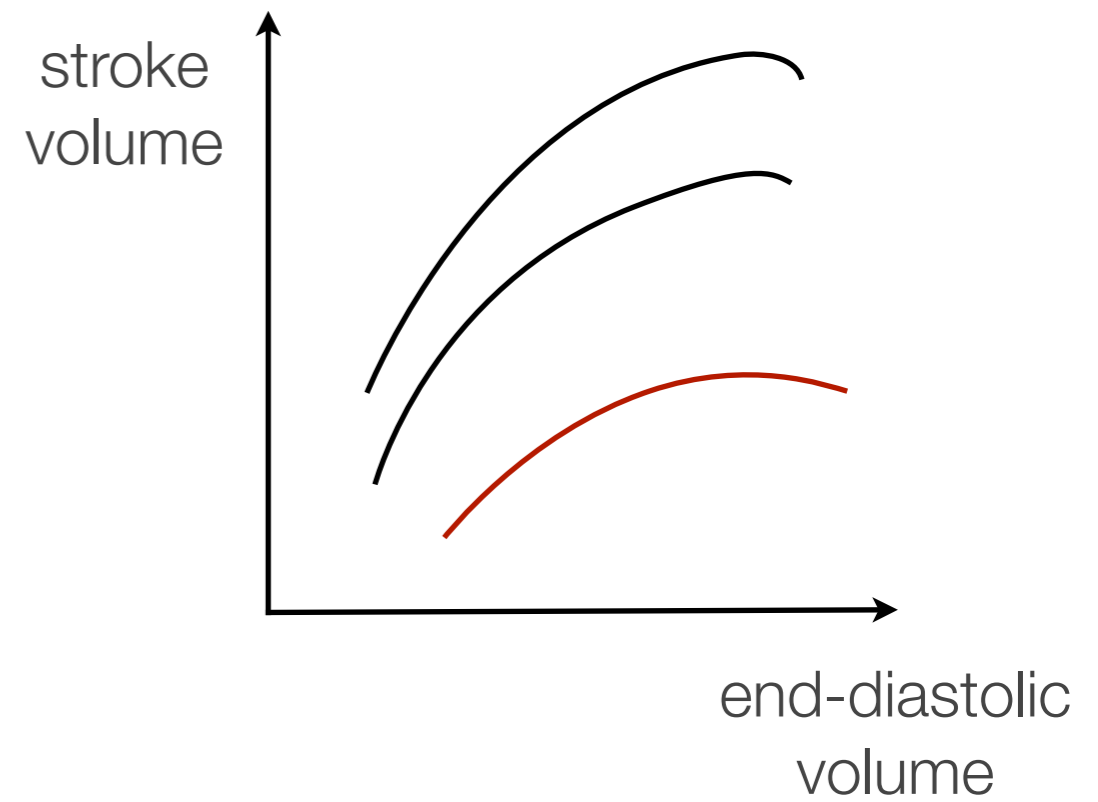
LVEF: 65%

Ventricular Volumes

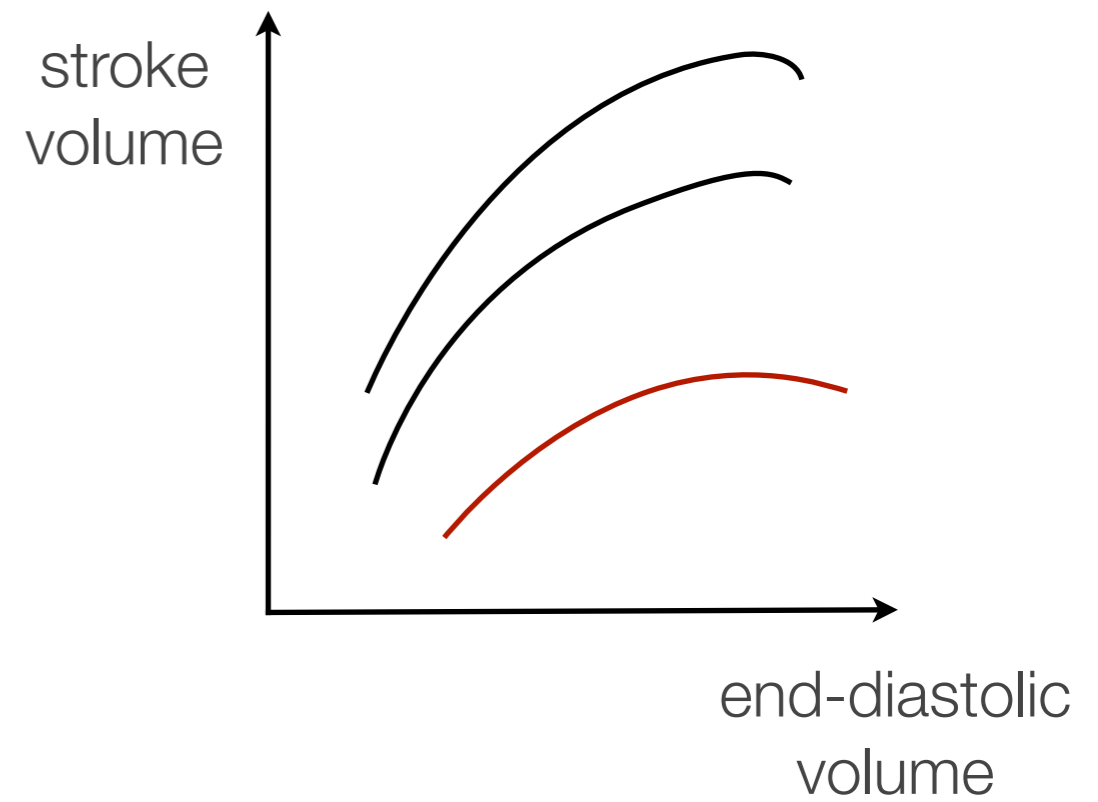
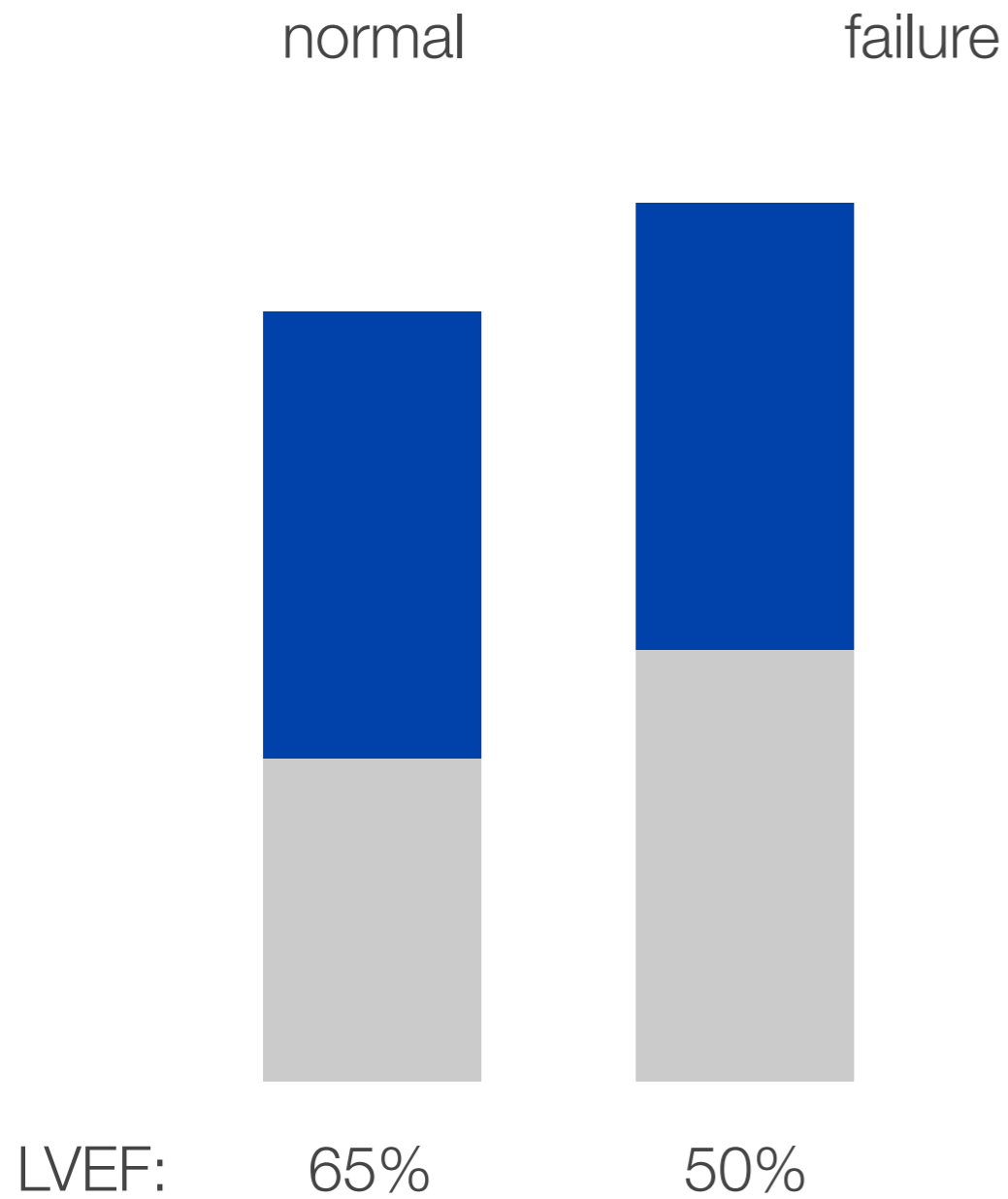
normal



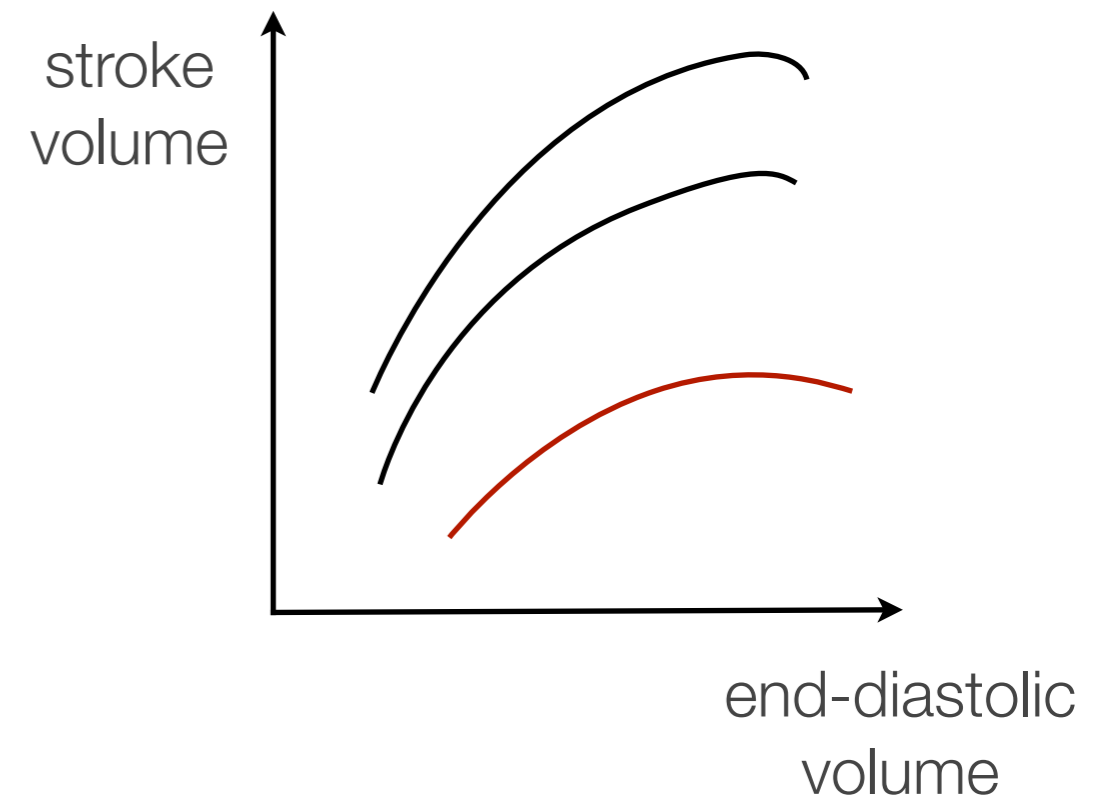
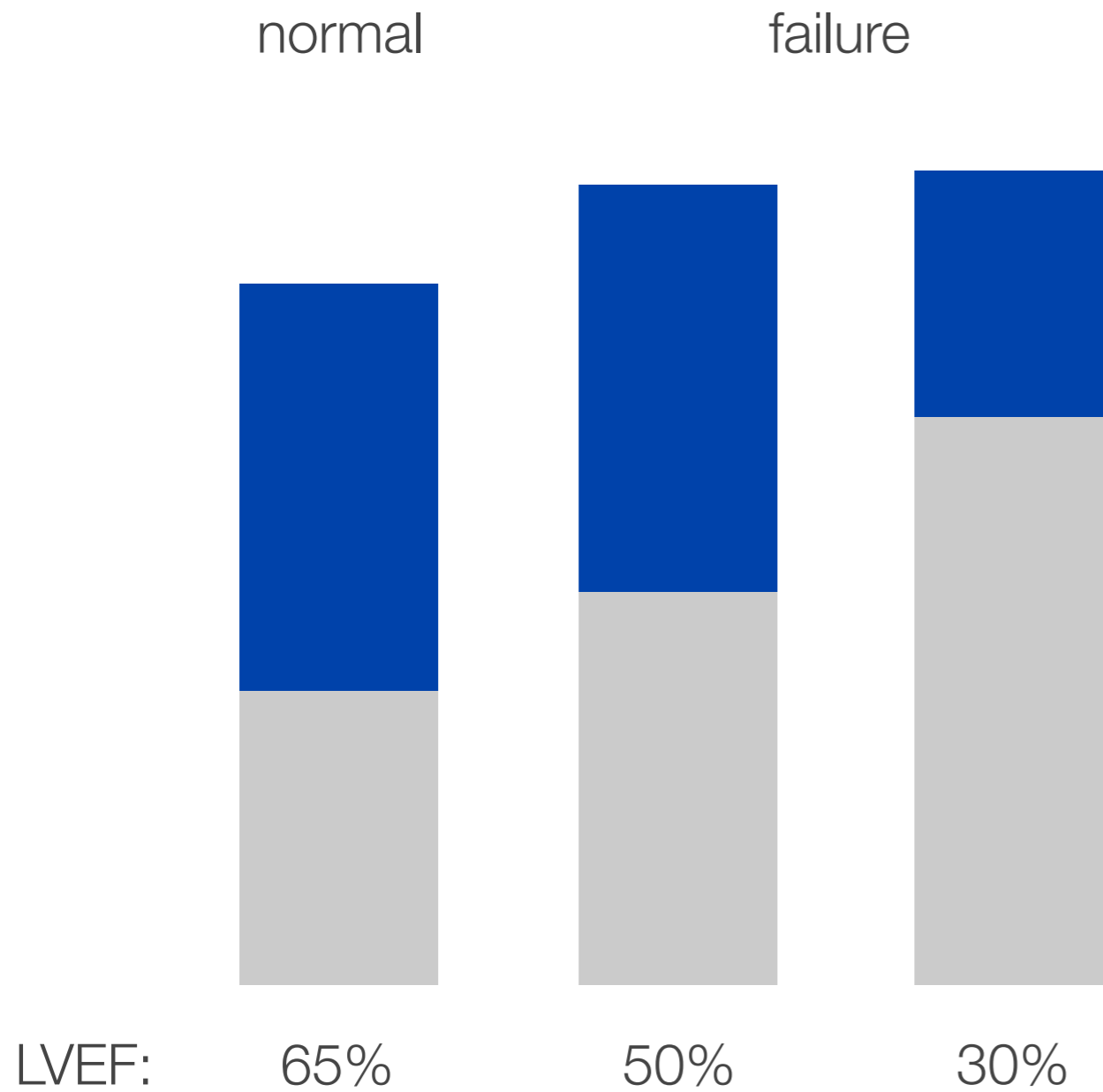
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Ventricular Volumes



Ventricular Volumes



Treatment Options

Chronic Heart Failure

Underlying Problem

- Stop smoking
- Stop drinking
- Loose weight
- Exercise
- Diabetic control
- Blood pressure control
- Statins
- Valvuloplasty
- Revascularisation

Drugs

Drugs

- ACE inhibitors
- Angiotensin II receptor antagonists
- Beta blockers
- Aldosterone inhibitors
- Loop diuretics
- Cardiac glycosides
- Non glycoside inotropes
- Anti-arrhythmics
- Anticoagulation

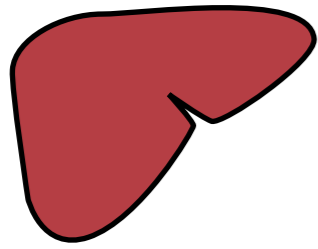
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Mechanical

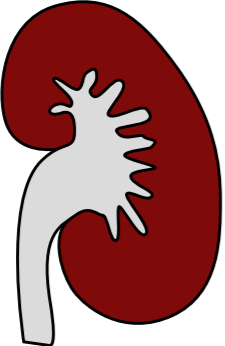
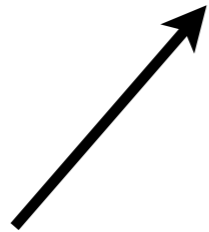
- Biventricular pacing
- Intra aortic balloon pump
- Intra aortic propeller pump
- Left ventricular assist devices

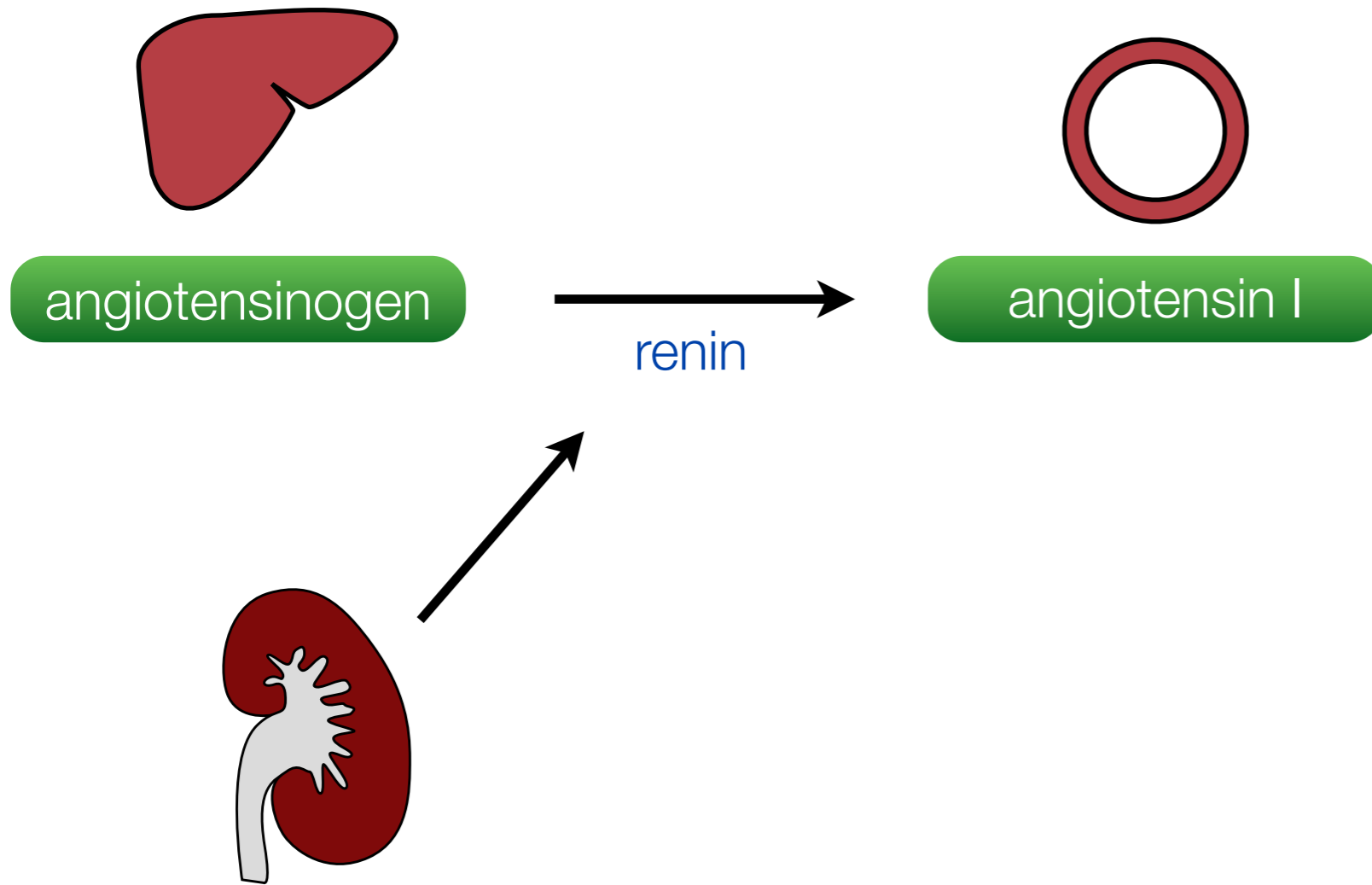


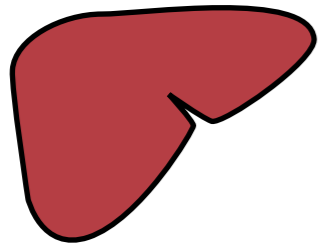


angiotensinogen

renin



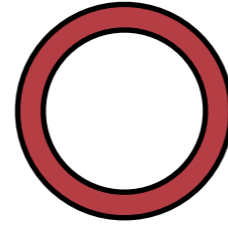




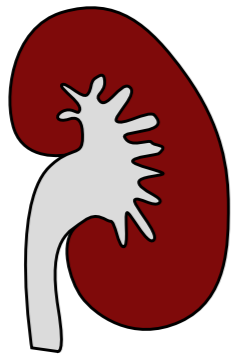
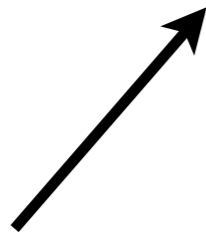
angiotensinogen



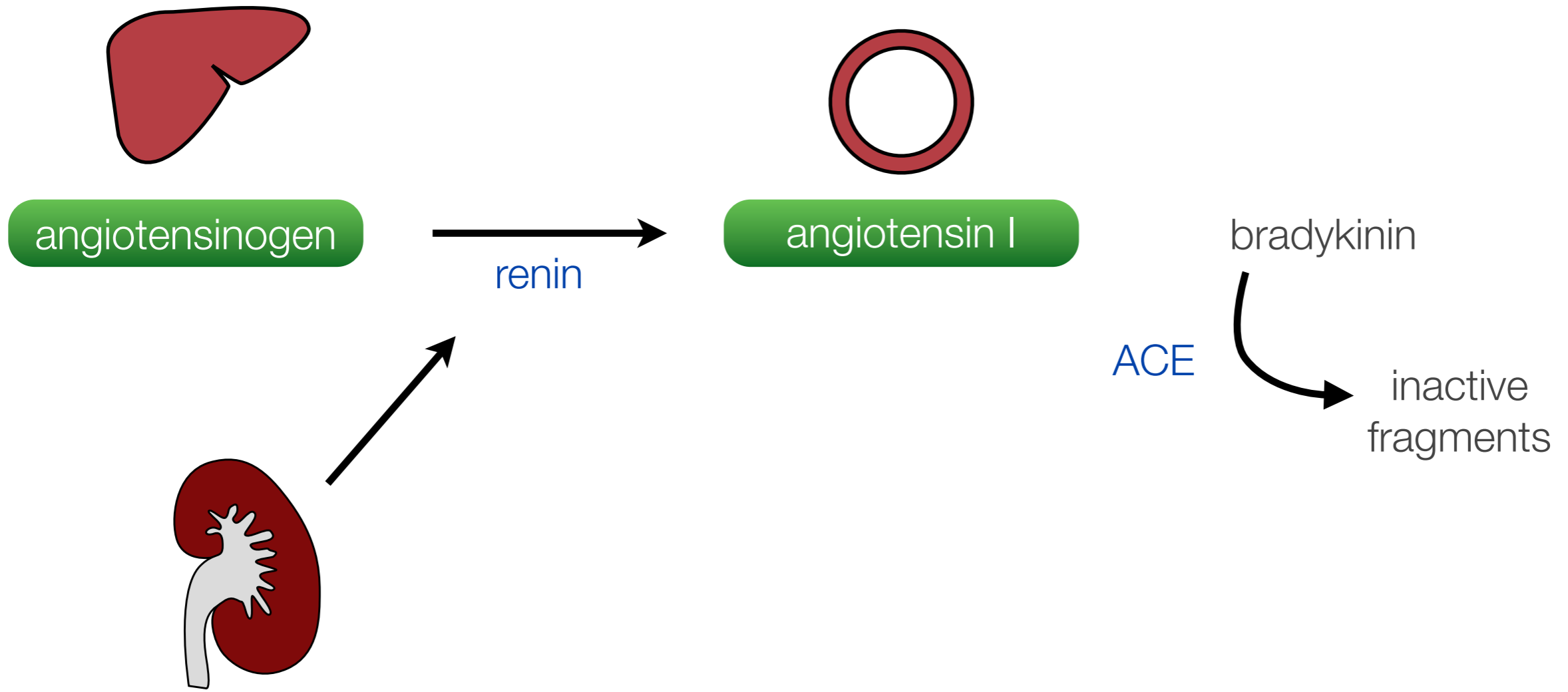
renin

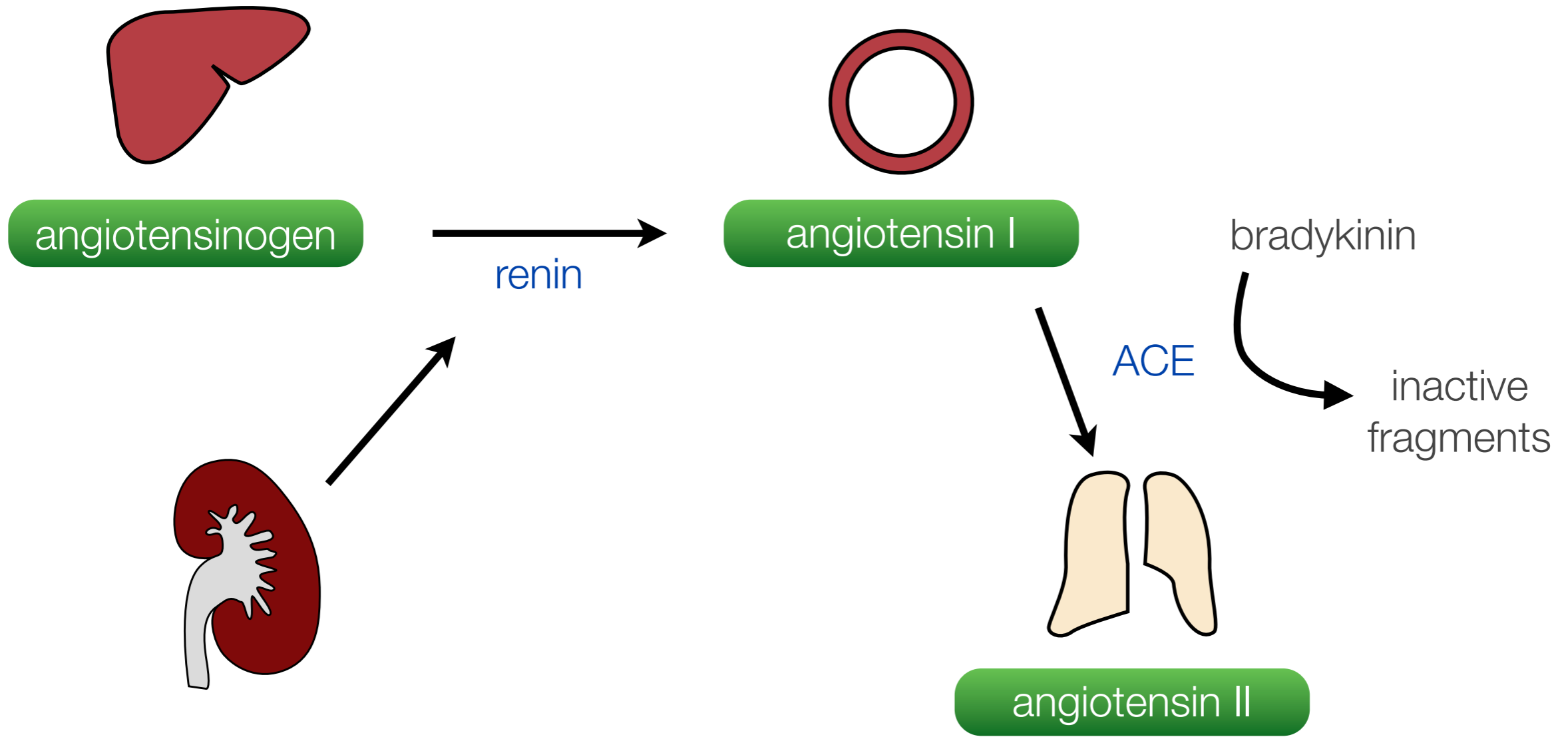


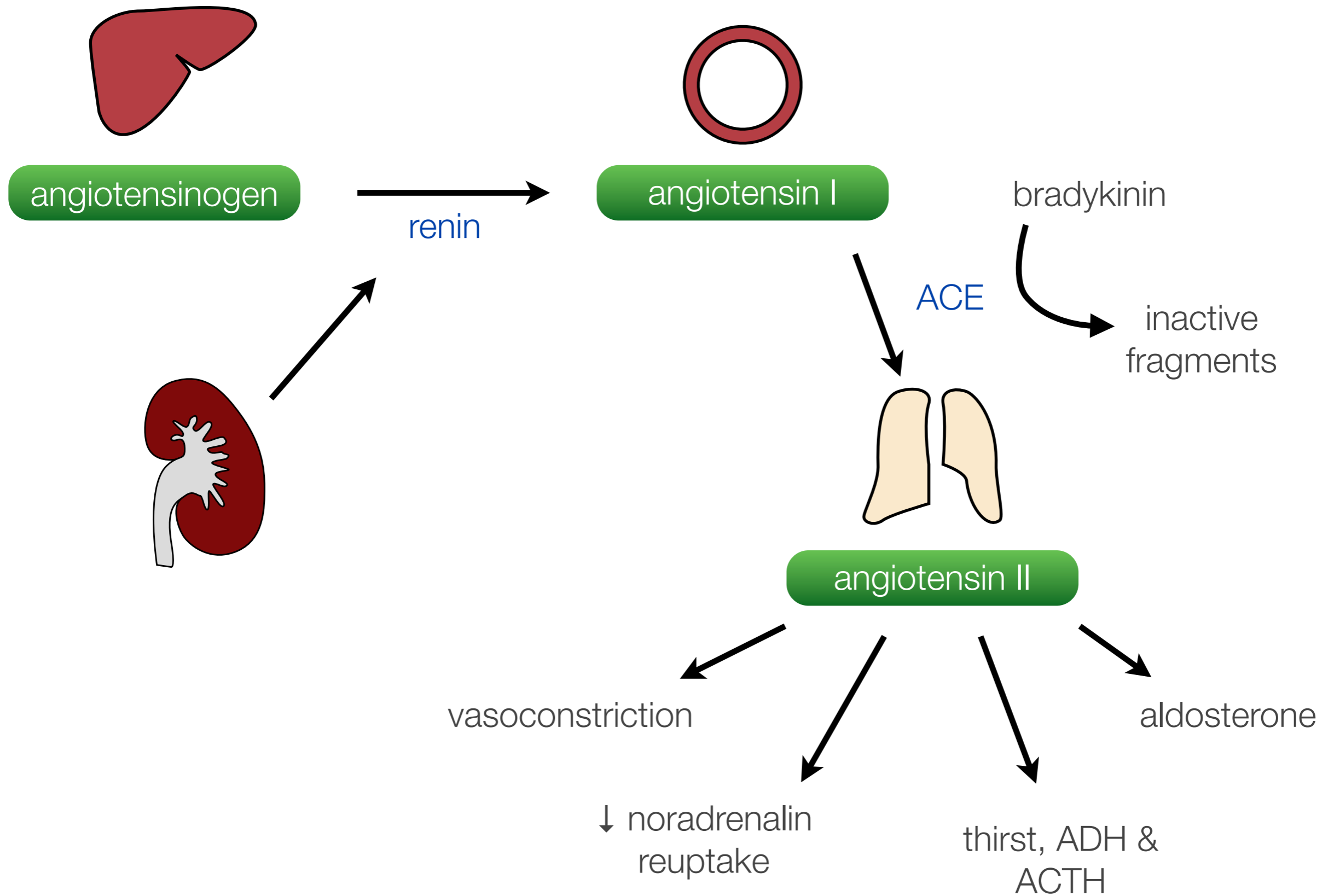
angiotensin I



ACE



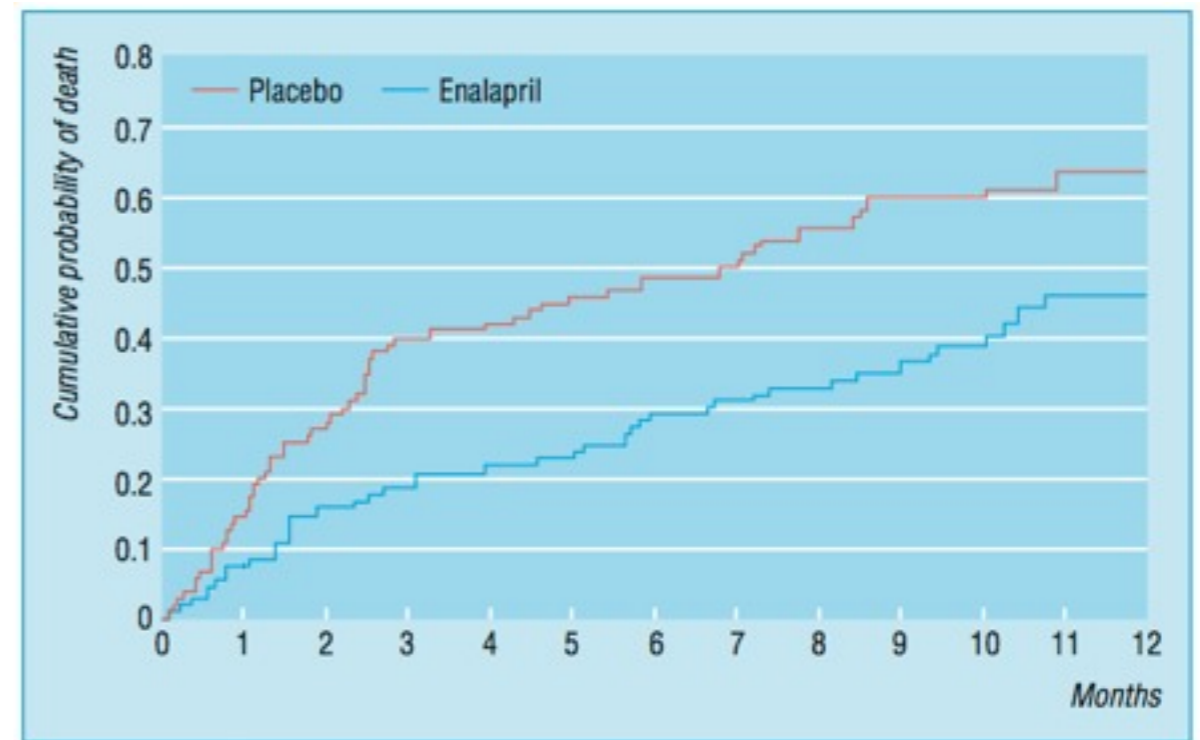




Angiotensin Converting Enzyme Inhibitors

CONSENSUS-I

- NYHA class IV
- 40mg enalapril Vs. placebo
- 40% risk reduction of death
- reduced hospitalisation
- less need for diuretics
- Biggest benefit in advanced disease



Angiotensin Converting Enzyme Inhibitors

SOLVD, SAVE, AIRE & TRACE

- mild-moderate symptoms + LVEF < 30%
- various agents
- n = 7105
- 23% risk reduction - death (95%CI 12% - 23%, p=0.001)
- 35% risk reduction - combined death & admission for HF (95%CI 12% - 23%, p=0.001)

Angiotensin II Receptor Antagonists

- ACE inhibitors prevent breakdown of bradykinin, which causes cough in 10%
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AIIRB Vs Placebo

- 22 RCT - meta-analysis
- NYHA class I - IV
- n = 38,080
- follow up 2.7 years
- Odds Ratio on all cause mortality = 0.83 (95%CI 0.69 - 1.00)

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AIIRB Vs ACEi

- 8 RCT - meta-analysis
- NYHA class I - IV
- n = 5,201
- follow up 2.7 years
- Odds Ratio on all cause mortality = 1.06 (95%CI 0.90 - 1.26)

Beta Blockers

CIBIS-II

- NYHA class III - IV, LVEF < 35%
- adjuvant to ACEi
- n = 2,600
- follow up 2.7 years
- Risk Reduction all cause mortality = 34% (p < 0.0001)

Beta Blockers

CIBIS-II

- NYHA class III - IV, LVEF < 35%
- adjuvant to ACEi
- n = 2,600
- follow up 2.7 years
- Risk Reduction all cause mortality = 34% (p < 0.0001)

MERIT-HF

- NYHA class I - II
- n = 3,988
- similar mortality benefit

Beta Blockers - Meta-analysis

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Mild to Moderate

- NYHA class I - II
- adjuvant to ACEi
- n = 10,315
- Death 8% Vs 13%
- OR 0.64 (CI 0.53 - 0.79)

Beta Blockers - Meta-analysis

Mild to Moderate

- NYHA class I - II
- adjuvant to ACEi
- n = 10,315
- Death 8% Vs 13%
- OR 0.64 (CI 0.53 - 0.79)

Severe

- NYHA class IV
- adjuvant to ACEi + diuretics
- n = 635
- Death 18% Vs 25%
- RR 0.71 (CI 0.52 - 0.96)

Aldosterone Receptor Antagonists

Aldosterone Receptor Antagonists

1 RCT - Spironolactone

- NYHA class III - IV
- adjuvant to ACEi + β B
- n = 1,663
- 2 year follow up
- Death 35% Vs 46%
- ARR 11% (CI 7% - 16%)
- RR 0.75 (CI 0.66 - 0.85)

Aldosterone Receptor Antagonists

1 RCT - Spironolactone

- NYHA class III - IV
- adjuvant to ACEi + β B
- n = 1,663
- 2 year follow up
- Death 35% Vs 46%
- ARR 11% (CI 7% - 16%)
- RR 0.75 (CI 0.66 - 0.85)

NOTES

- Risk of hyperkalaemia with ACEi
- Gynaecomastia / breast pain 10%
- Eplerenone

Cardiac Glycosides



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- Digoxin inhibits Na/K ATPase
 - Intracellular Ca↑
 - ↑ delivery of Na to distal tubule
 - ↑ vagal tone



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Cardiac Glycosides

- Digoxin inhibits Na/K ATPase
 - Intracellular Ca^{\uparrow}
 - \uparrow delivery of Na to distal tubule
 - \uparrow vagal tone
- Toxicity
 - renal failure (try digitoxin)
 - hypothyroidism
 - elderly
 - diuretics



Digoxin

Meta-analysis

- NYHA class I - IV
- sinus rhythm
- n = 7,896
- Follow up 36 months
- Death - no difference
- Hospitalisation OR 0.68
(CI 0.61 - 0.75)

Drugs to be avoided

- Inotropes
- Calcium channel blockers
- Class 1 antiarrhythmics

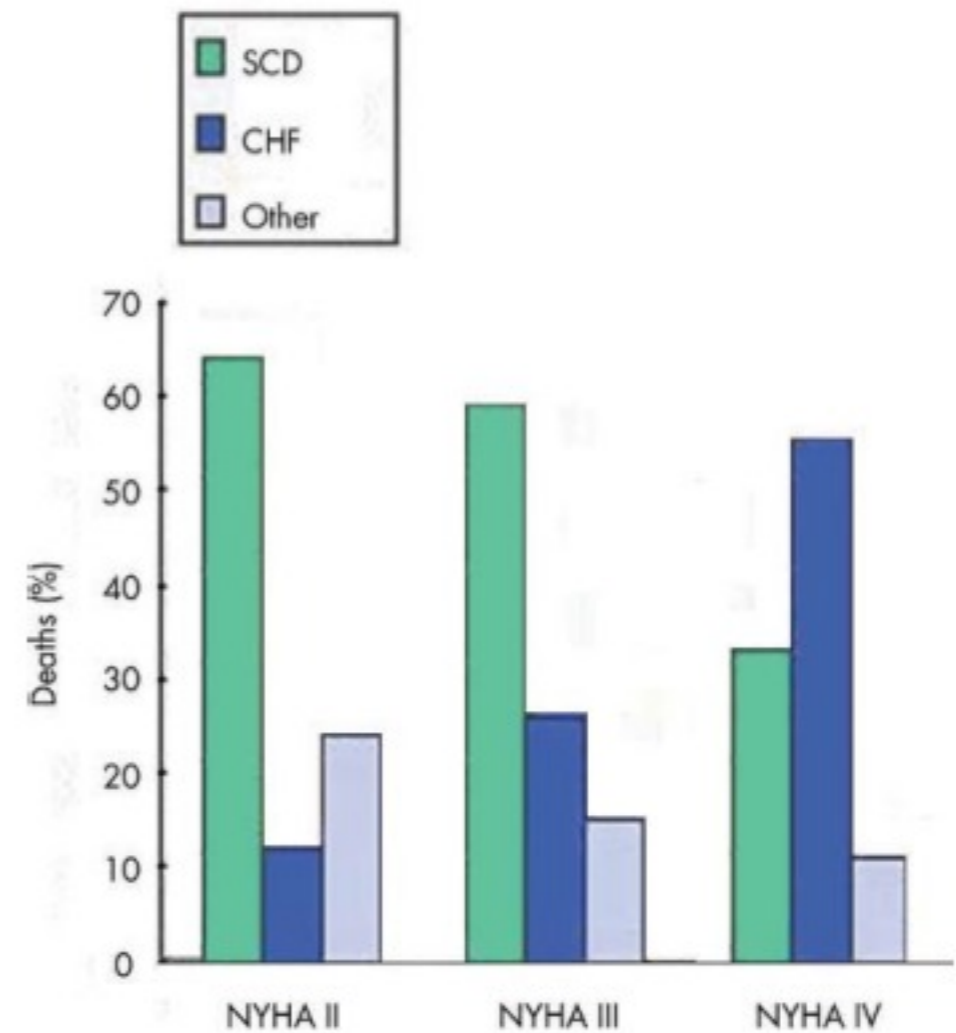
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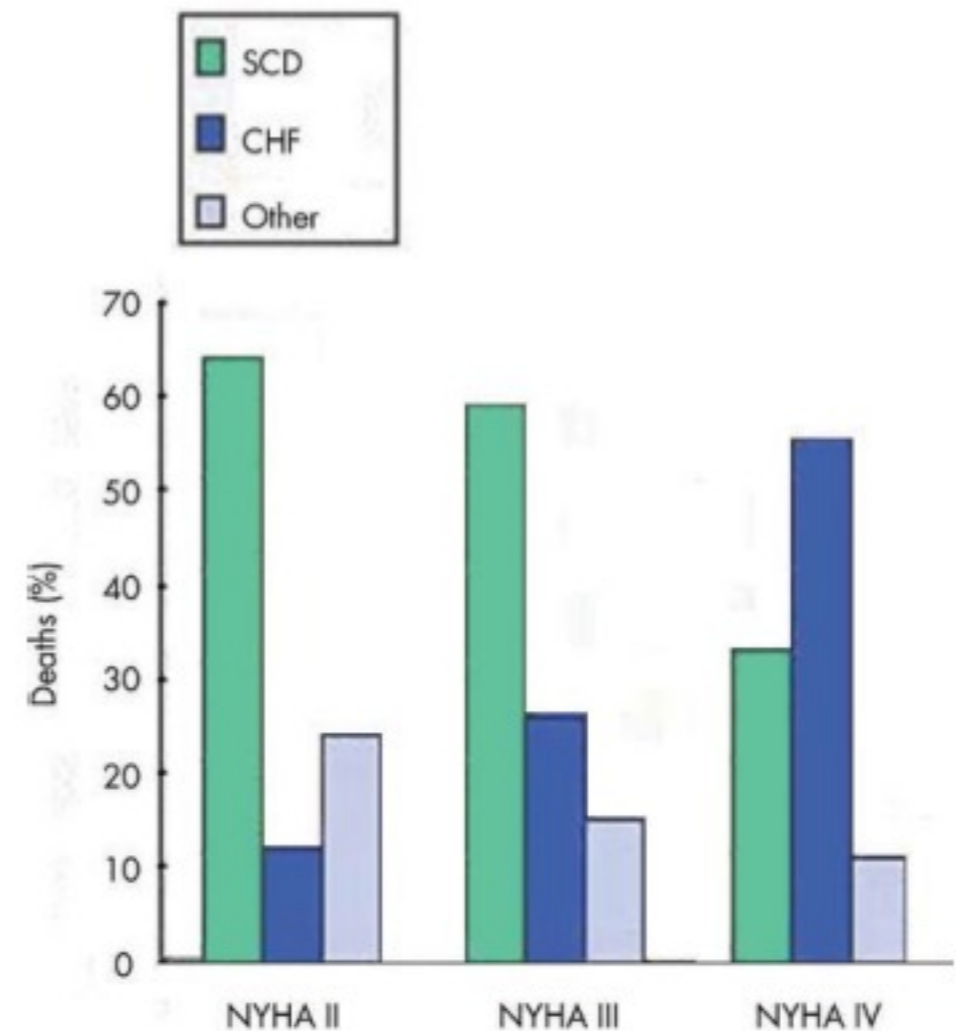


Adapted from MERIT-HF Study Group.
Lancet 1999;353:2001-7.

Sudden Cardiac Death

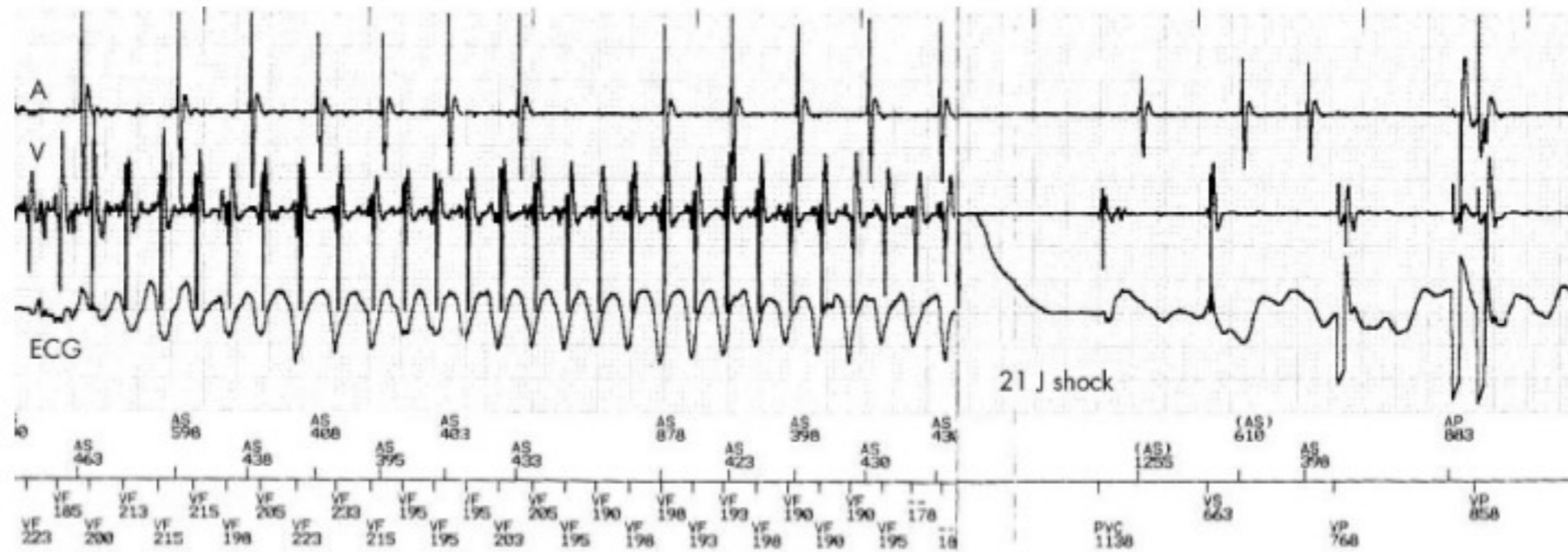
Sudden Cardiac Death accounts for 50% of patients with an impaired left ventricular ejection fraction.

- Amiodarone
- Implantable Cardioverter-Defibrillator (ICD)



Adapted from MERIT-HF Study Group.
Lancet 1999;353:2001-7.

Implantable Cardioverter-Defibrillator (ICD)



ICD Randomised Controlled Trials

	Cohorts	n	Criteria	QRS	LVEF
MADIT II	ICD v. med	1232	post MI		< 30%
COMPANION	CRT v. CRT-D v. Med	1520		> 120ms	< 35%
DEFINITE	ICD v. Med	458	non IHD	evidence of arrhythmia	< 36%
SCD-HeFT	ICD v. Med v. ICD + amiodarone	2521	non IHD		< 35%

ICD Pooled Results

- Irrespective of QRS
- Ischaemic & non ischaemic heart failure

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Relative Risk	0.74
95% CI	0.67 - 0.83
p	0.00001
Absolute Risk Reduction	7.9
NNT	13

Treatment Options

Acute Decompensated Heart Failure

Summary of Benefit

	Symptoms	Mortality	SCD
Duuretics	↓↓↓	↔	↔
ACE inhibitors	↓↓	↓↓	(↓)
Angiotensin II antagonists	↓↓	↓↓	↔
Beta blockers	↓	↓	↓↓
Glycosides	↓	↔	↔
Aldosterone antagonists	↓	↓	↔
ICD (primary prevention)	?↑	↓↓	↓↓↓

Relative Impact On Survival

	RR	NNT
ICD (primary prevention)	7.9%	13
ACE inhibitor / Angiotensin II receptor antagonist	6.1%	16
Beta blockers	4.4%	23
Aldosterone antagonists (severe disease & in addition to ACEi & β B)	11%	9

Alternative Strategy

- Fluid resuscitation
- Antibiotics



Questions

Key Points

- ACE inhibitors/ Angiotensin II receptor antagonists and Beta Blockers are proven to slow progression through NYHA grades and increase survival.
- Aldosterone antagonists confer worthwhile additional benefit
CAUTION: Hyperkalaemia.
- Digoxin might keep you out of hospital but doesn't make you live longer
- ICD for anyone with an ejection fraction $< 35\%$
- No evidence for any treatment in diastolic heart failure
- Inotropes (except digoxin), Ca channel blockers and Class I anti-arrhythmic increase mortality in chronic heart failure