

Heart Failure Treatments

Past & Present

Background

Background

Chronic heart failure

- Drugs
- Mechanical
- Electrical

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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

Forward Vs Backward

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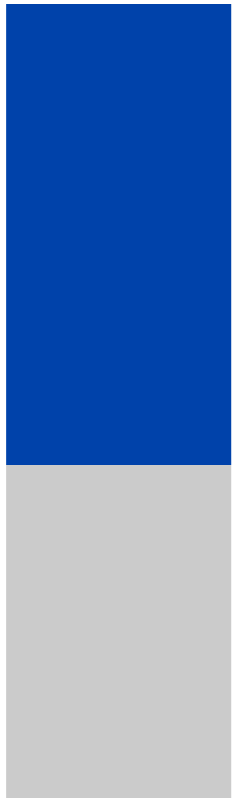
- Undilated cardiomyopathy
- Valvular
- Cor pulmonale
- Congenital
- Alcohol and drugs
- Arrhythmia

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



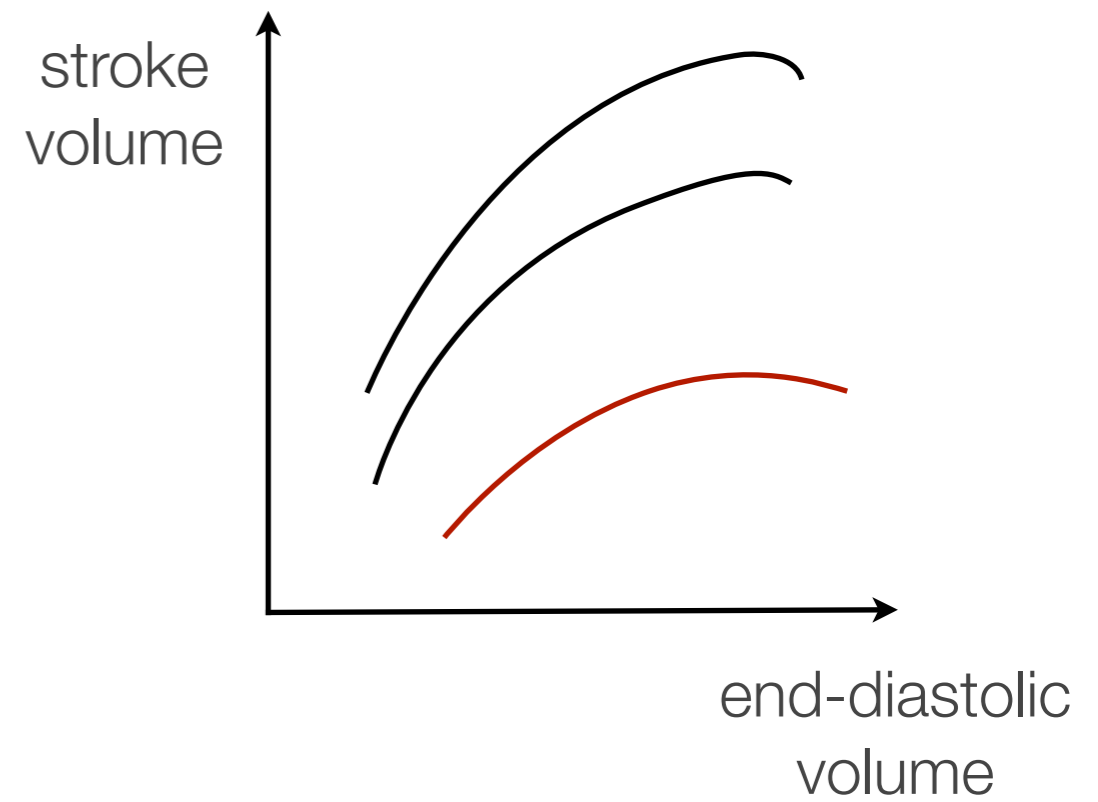
LVEF: 65%

Ventricular Volumes

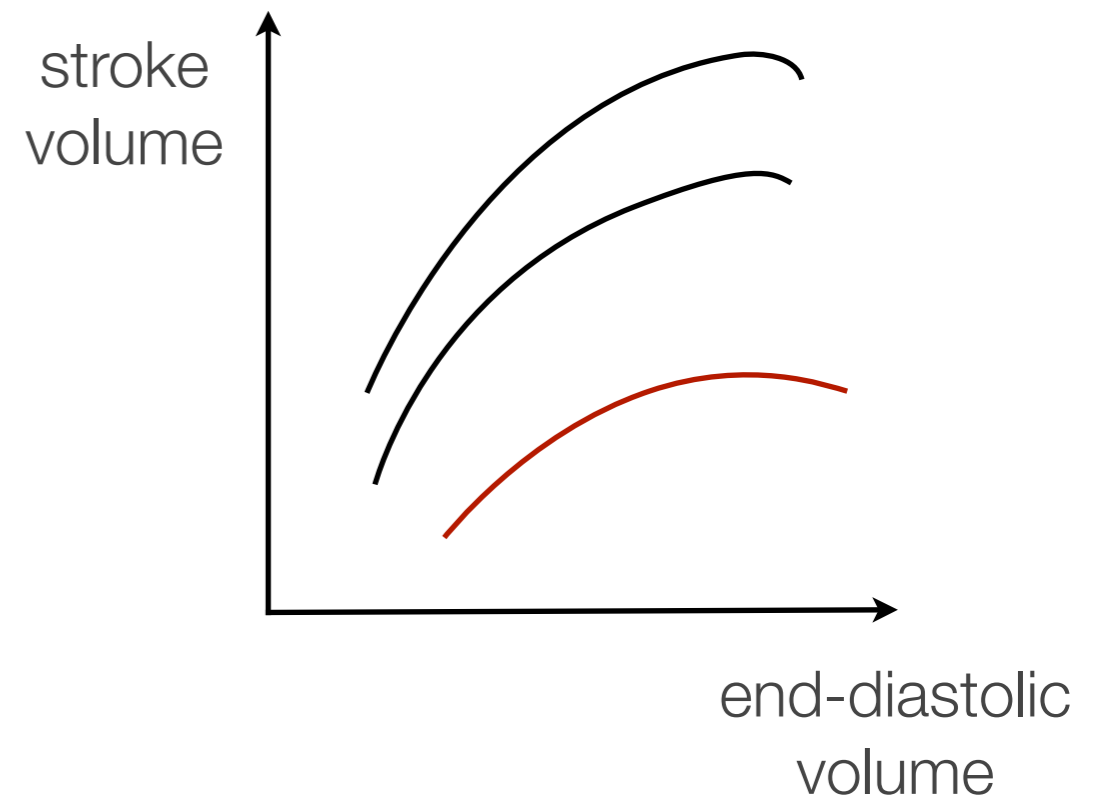
normal



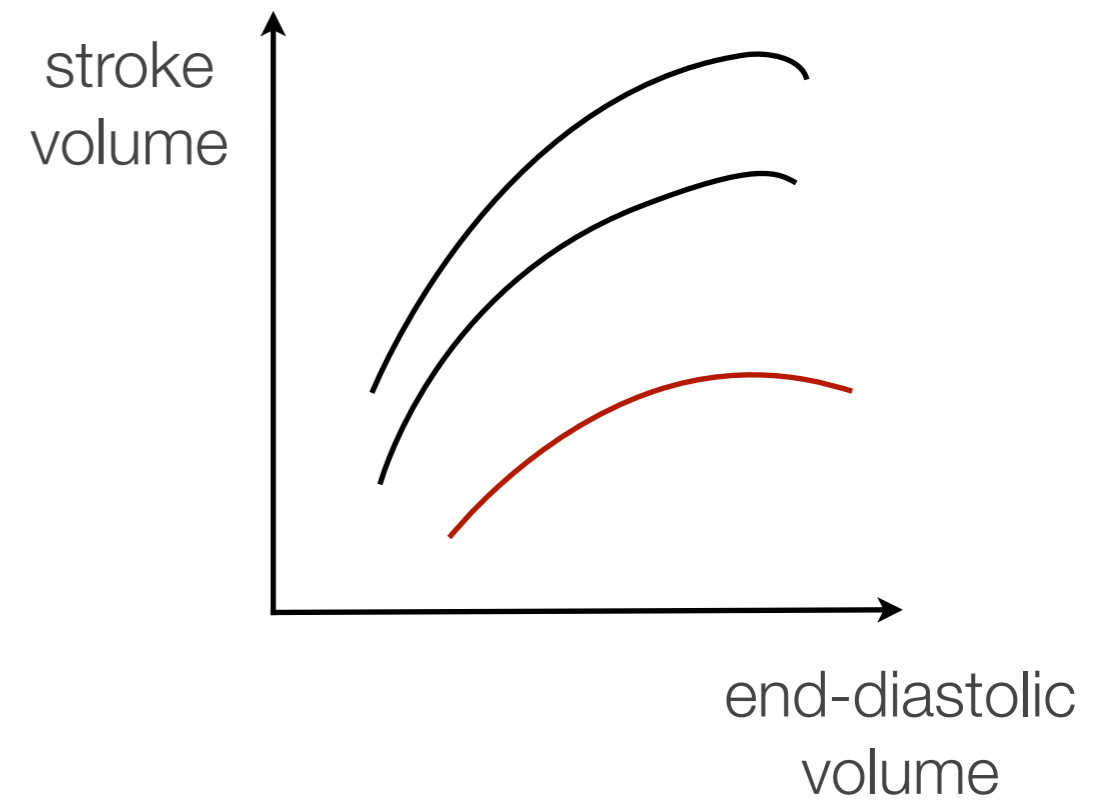
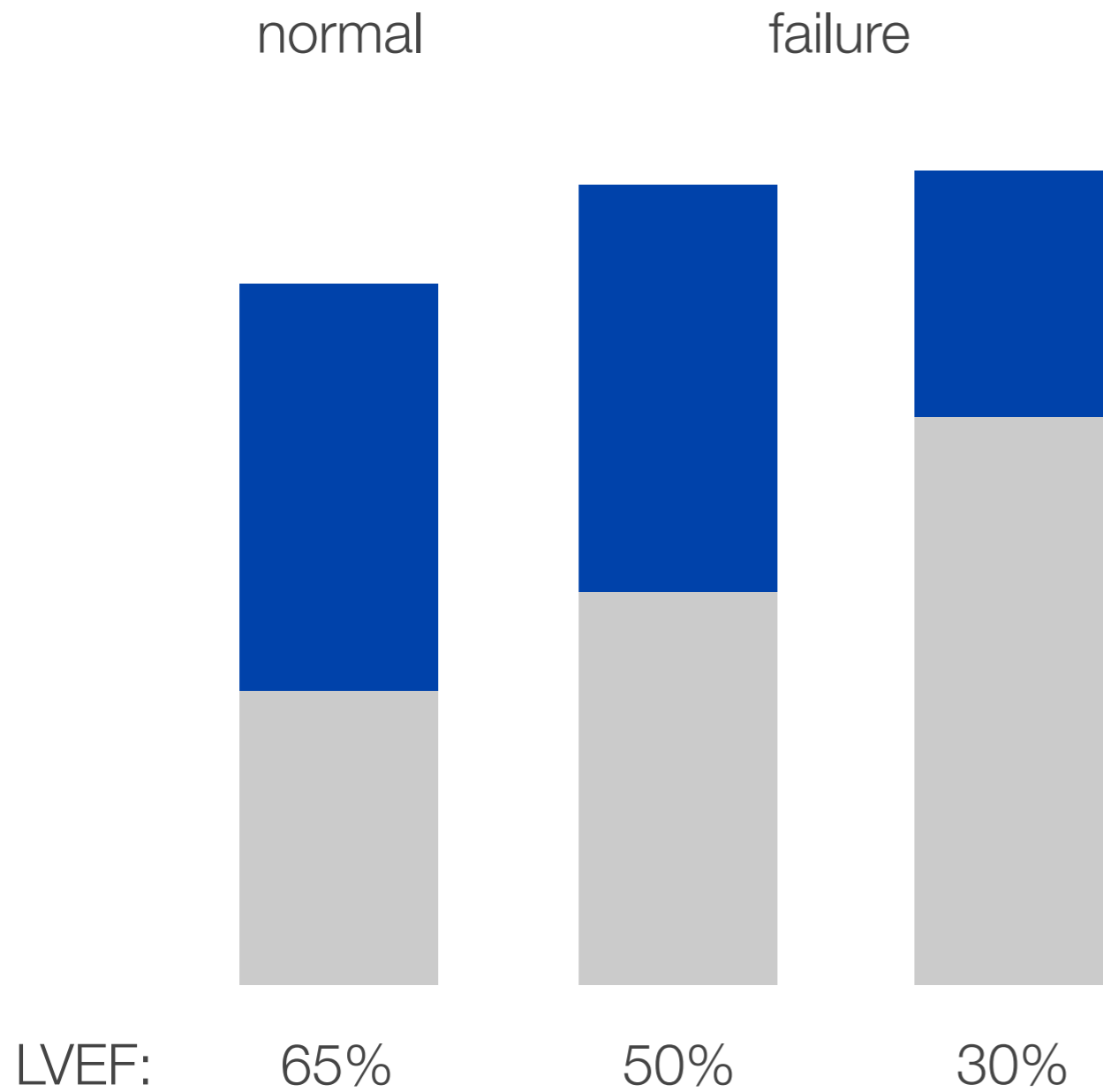
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Ventricular Volumes



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

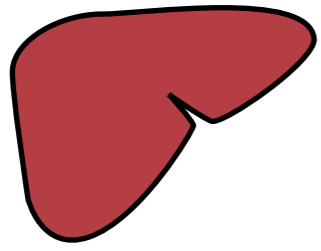
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Mechanical

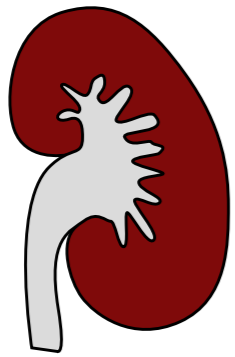
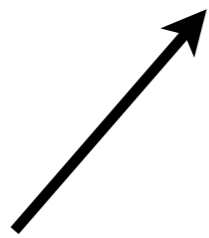
- Biventricular pacing
- Intra aortic balloon pump
- Intra aortic propeller pump
- Left ventricular assist devices

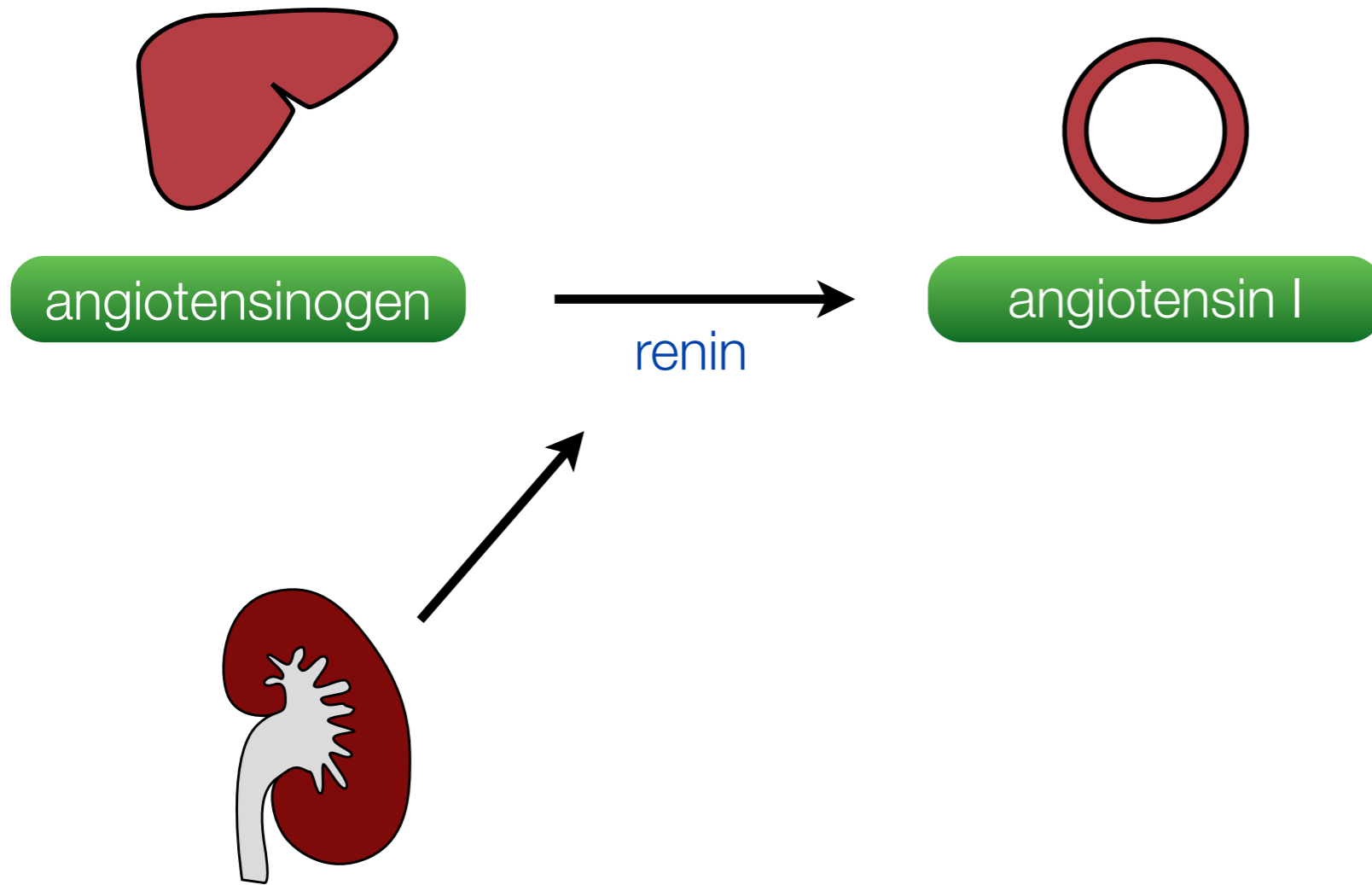


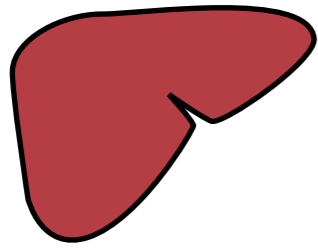


angiotensinogen

renin



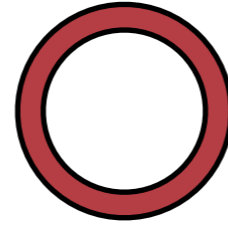




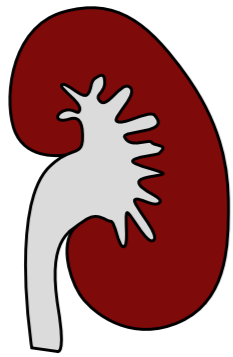
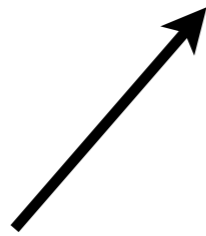
angiotensinogen



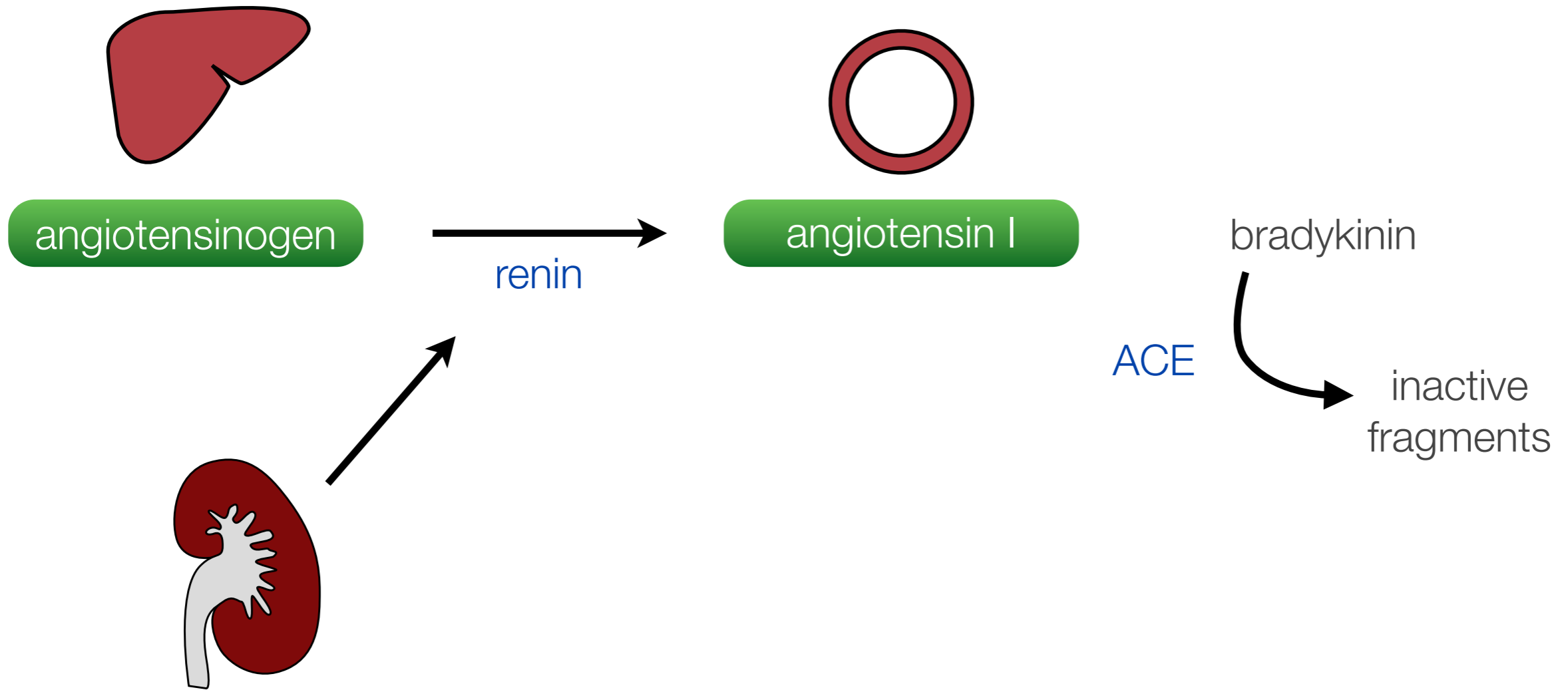
renin

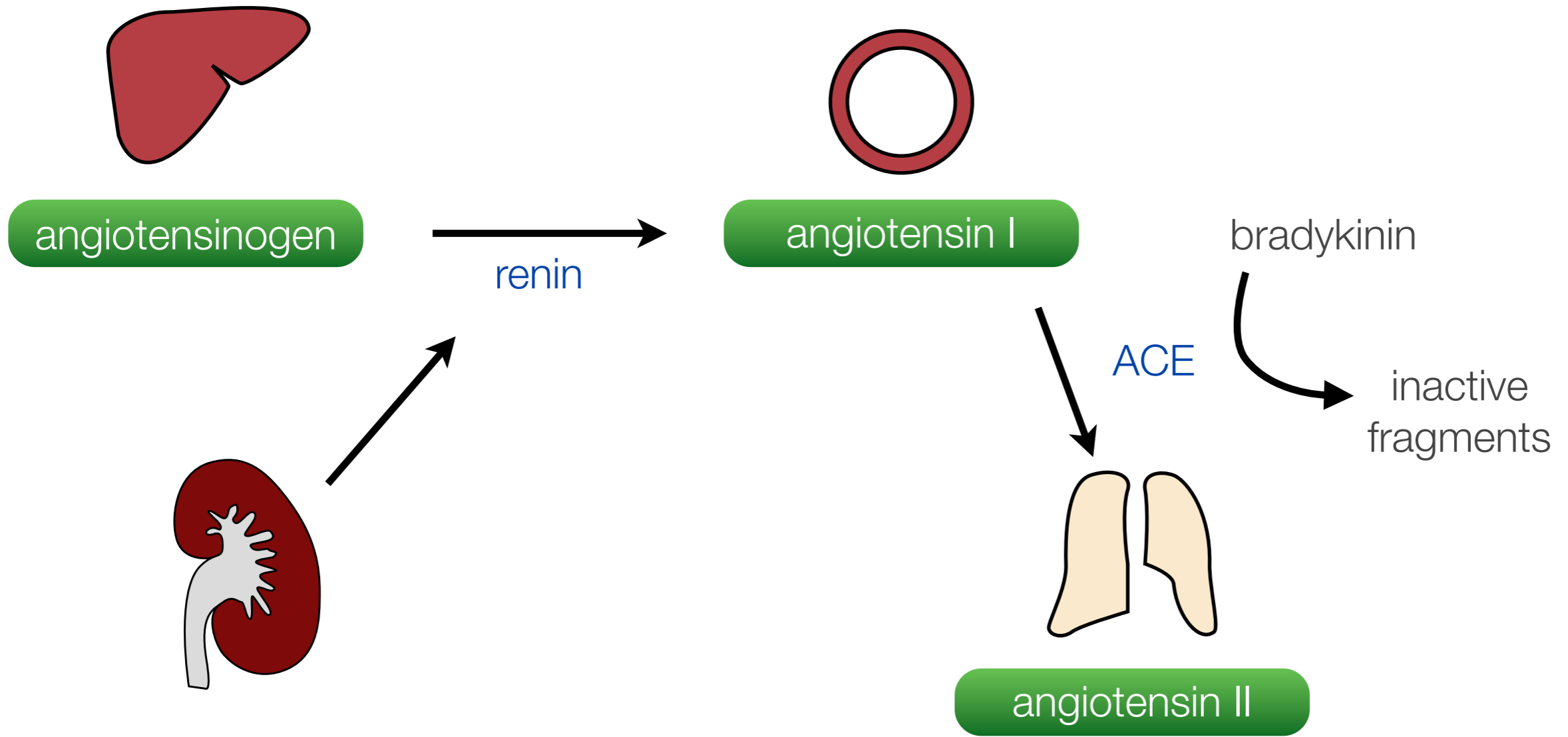


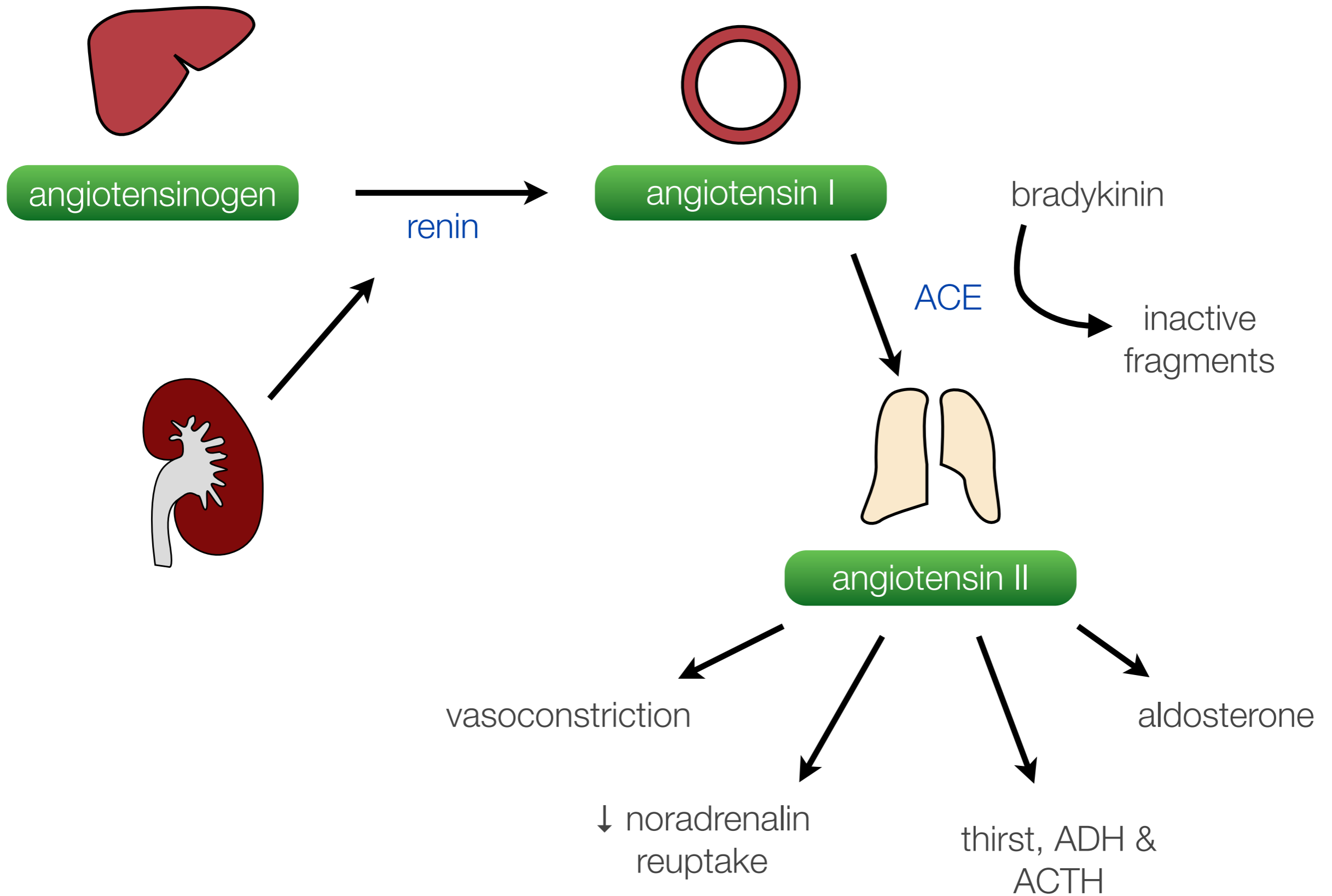
angiotensin I



ACE



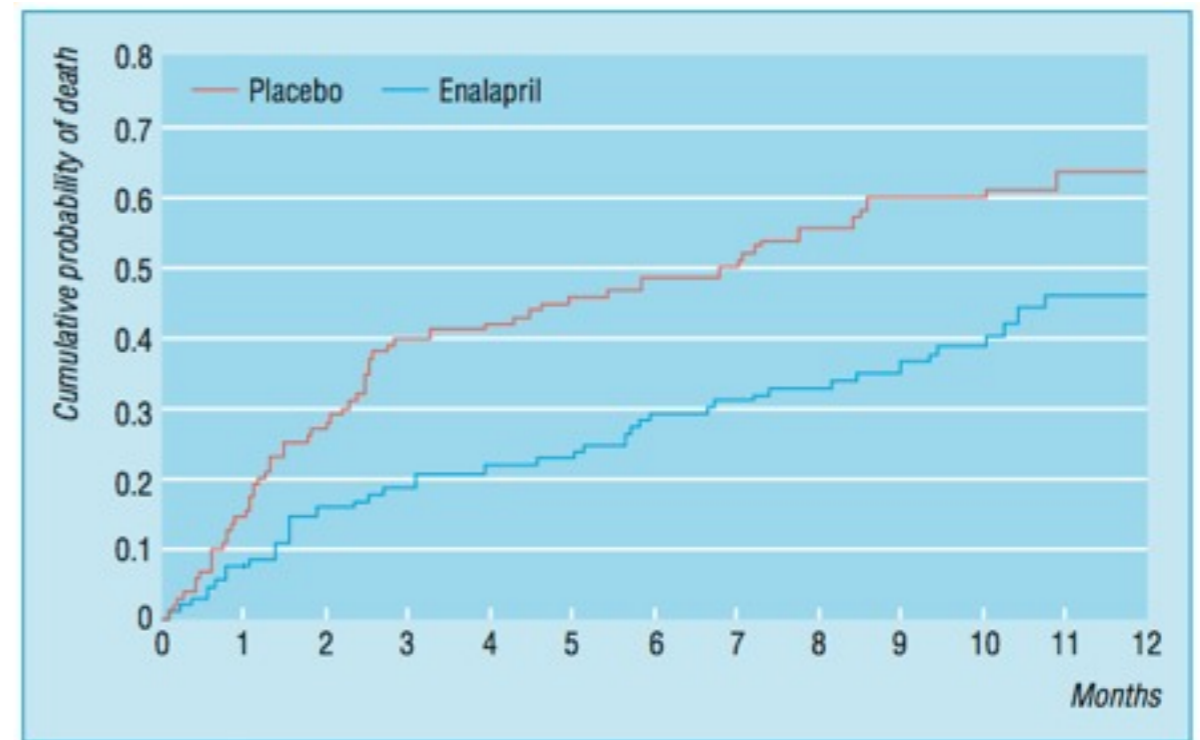




Angiotensin Converting Enzyme Inhibitors

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%
- Moderate quality evidence to show angiotensin II blockers are as effective as ACEi.

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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 \uparrow
 - \uparrow delivery of Na to distal tubule
 - \uparrow vagal tone



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Cardiac Glycosides

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

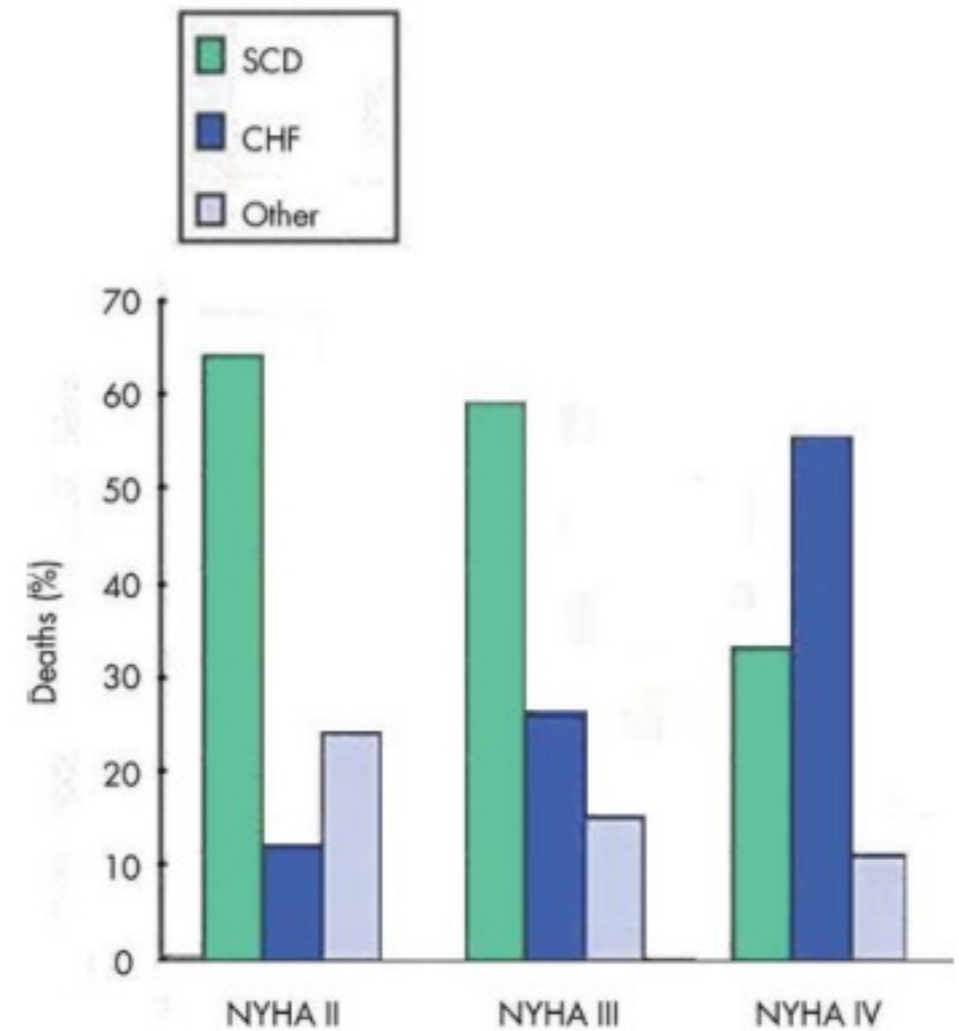
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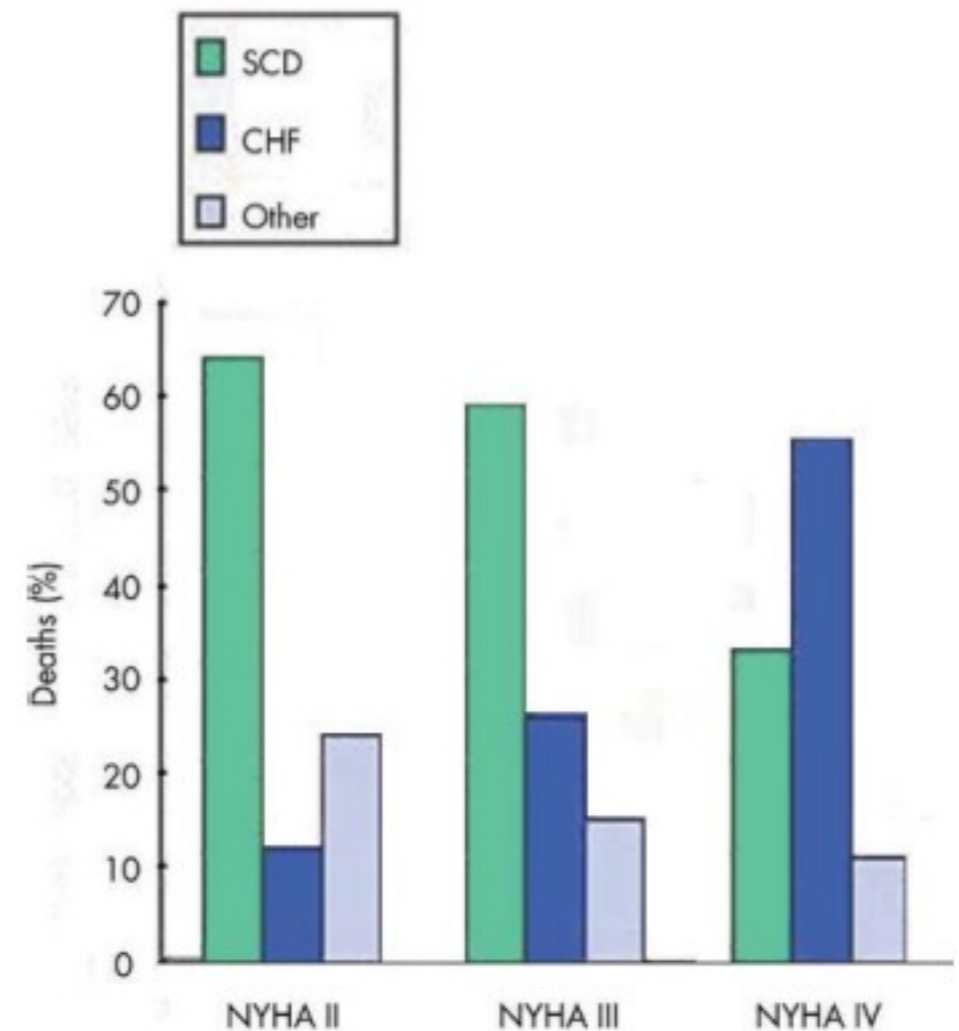


Adapted from MERIT-HF Study Group.
Lancet 1999;353:2001-7.

Sudden Cardiac Death

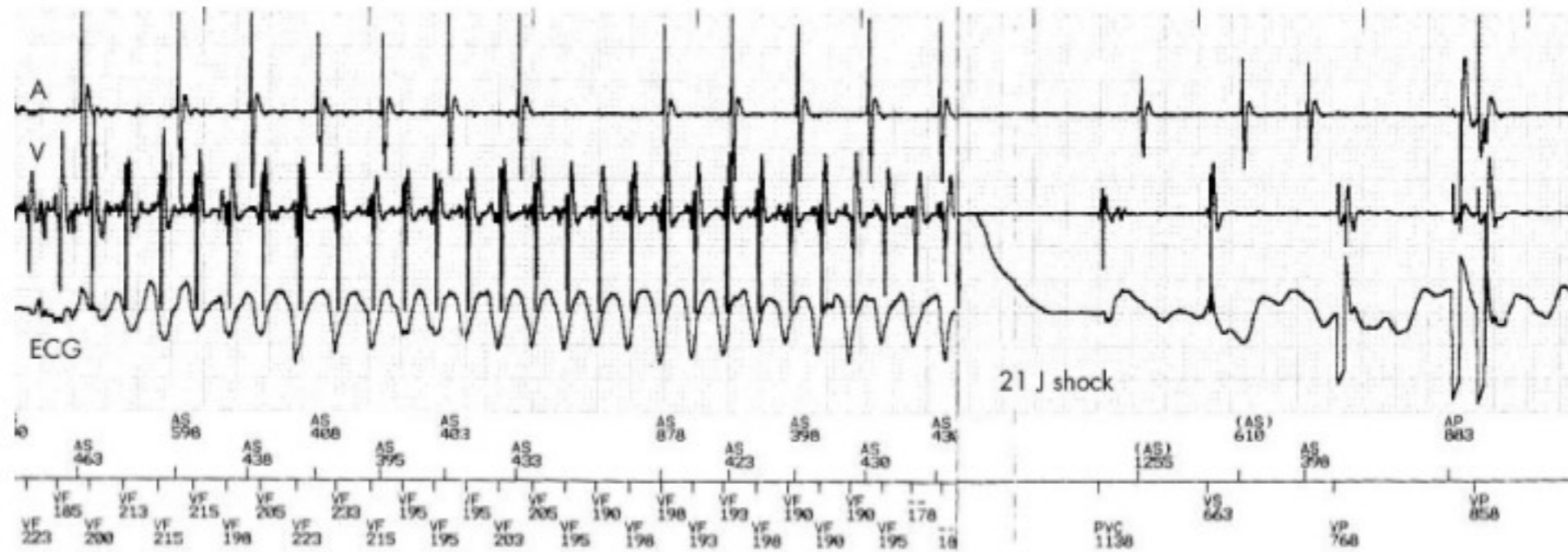
Sudden Cardiac Death accounts for 50% of patients with an impaired left ventricular ejection fraction.

- 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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- Irrespective of QRS
- Ischaemic & non ischaemic heart failure

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