Diagnosis and Treatment of Heart Failure

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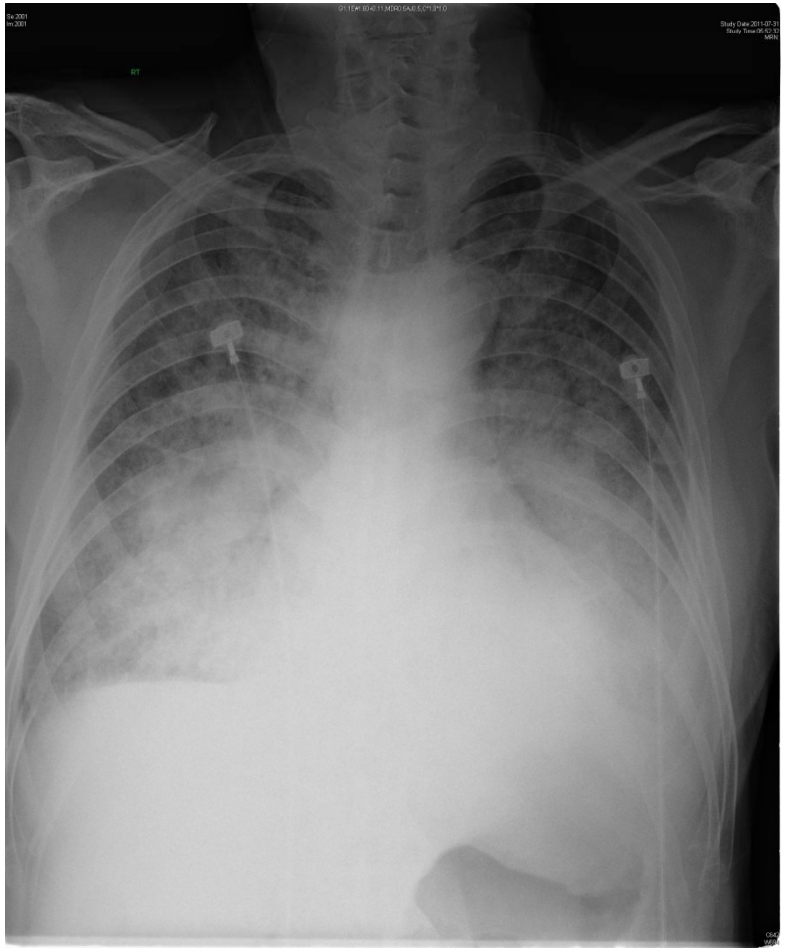
Case Summary

- 63세 남자
- 1 개월 전 계단 오르면 숨이 차다.
- 4 시간 전 가슴이 답답하고 심하게 숨이 차다.
  → 지방의료원 NTG response (+)
- Transferred to SMC ER
  - BP 159/82 HR 110/min RR 37/min
  - Chest PA at ER : O2 sat 83%
  -
  - POCT
    - cTnI 0.05 ng/ml (0-0.78)
    - CK-MB 2.50 ng/ml (0-4.3)
    - Myoglobin 315 ng/ml (0-107)
    - BNP 456 pg/ml (5-100)
  - NT-proBNP 1116 pg/ml (0-194)



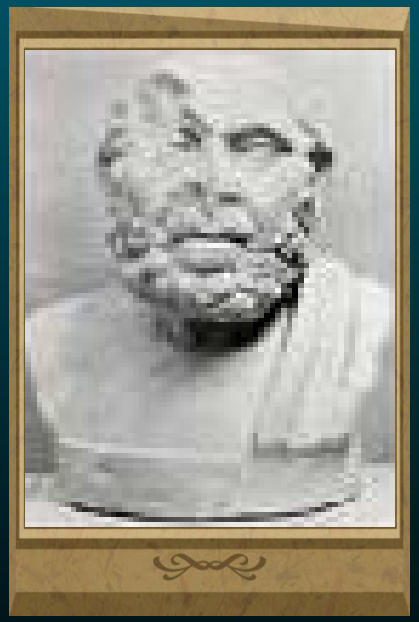
Contents

1. 심부전의 진단
   - Role of Natriuretic peptides

2. 급성 심부전 환자의 치료
   - Type of Acute HF
   - Volume status and Diuretics
   - Blood pressure and Inotropics
   - Beta blocker issues in acute HF
   - Guideline for chronic HF

Hippocrates

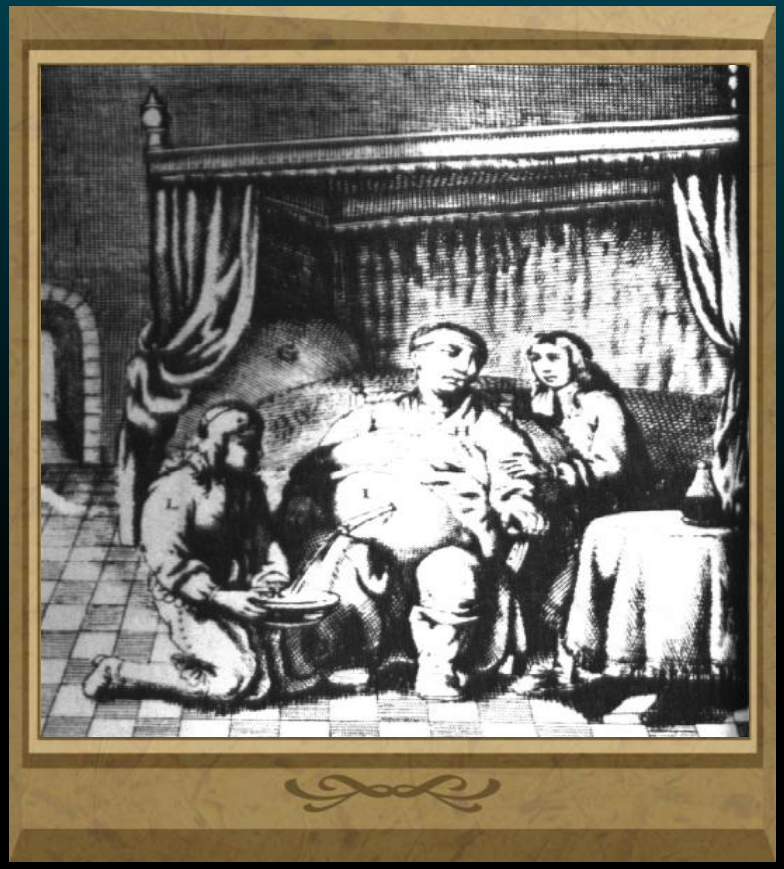
(460-370 BC)

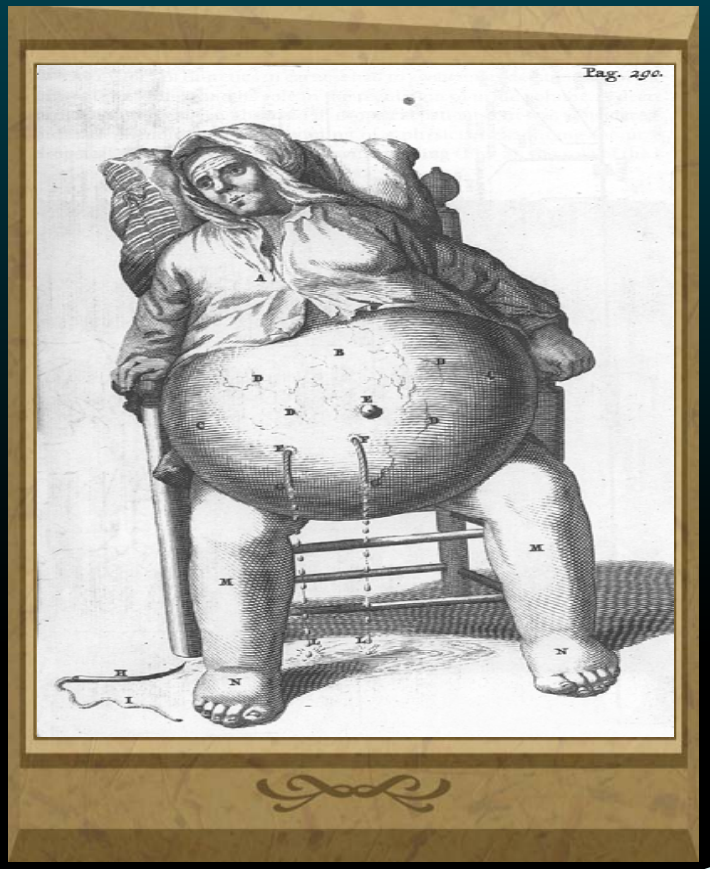


"Dropsy is usually produced when the patient remains for a long time with impurities of the body following a long illness. The flesh is consumed and becomes water… the abdomen fills with water, the feet and legs swell, the shoulders, clavicles, chest and thighs melts away."

{Affections XXII}

Hydropsy or “Dropsy”





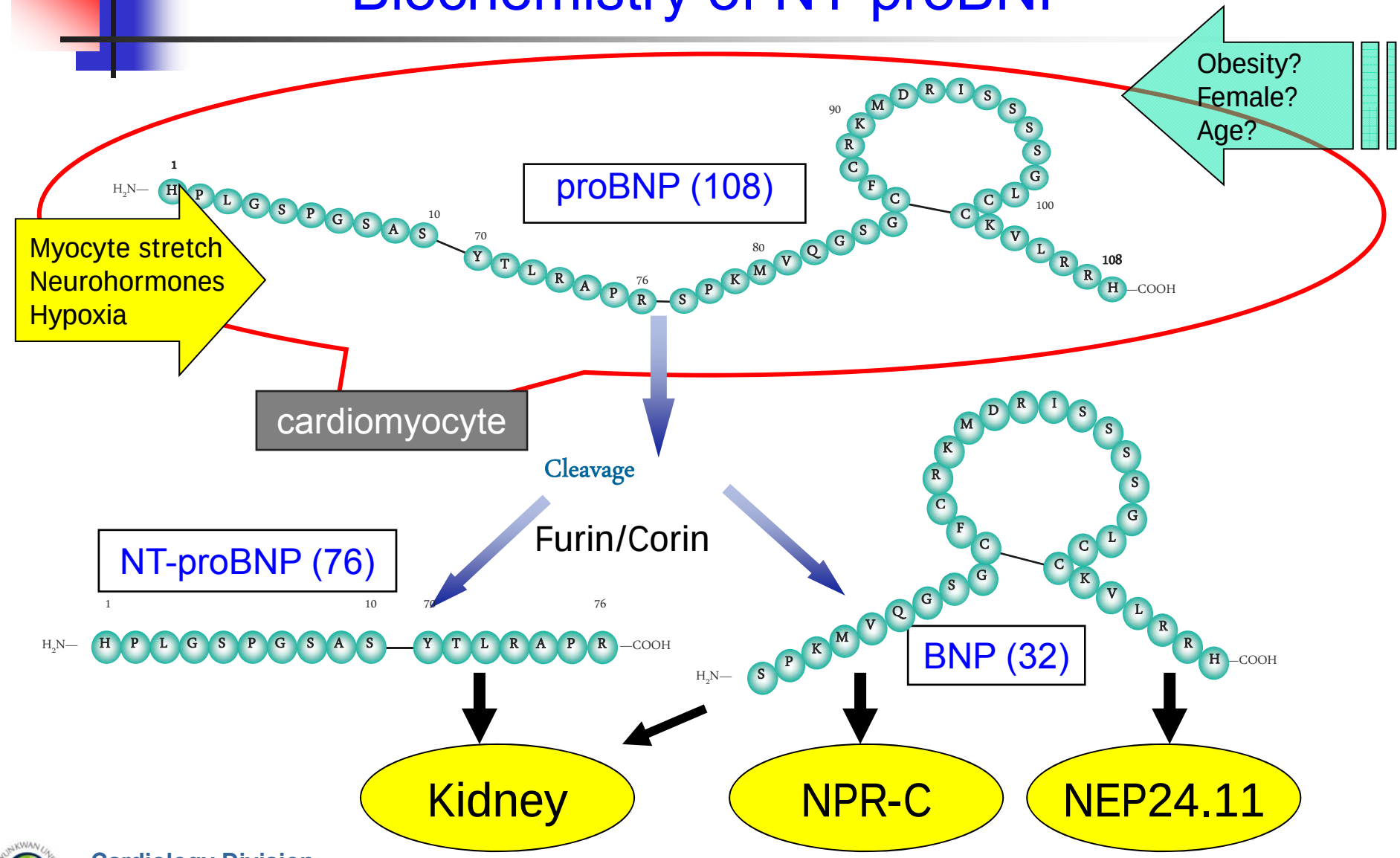
Generalized swelling due to accumulation of excess water

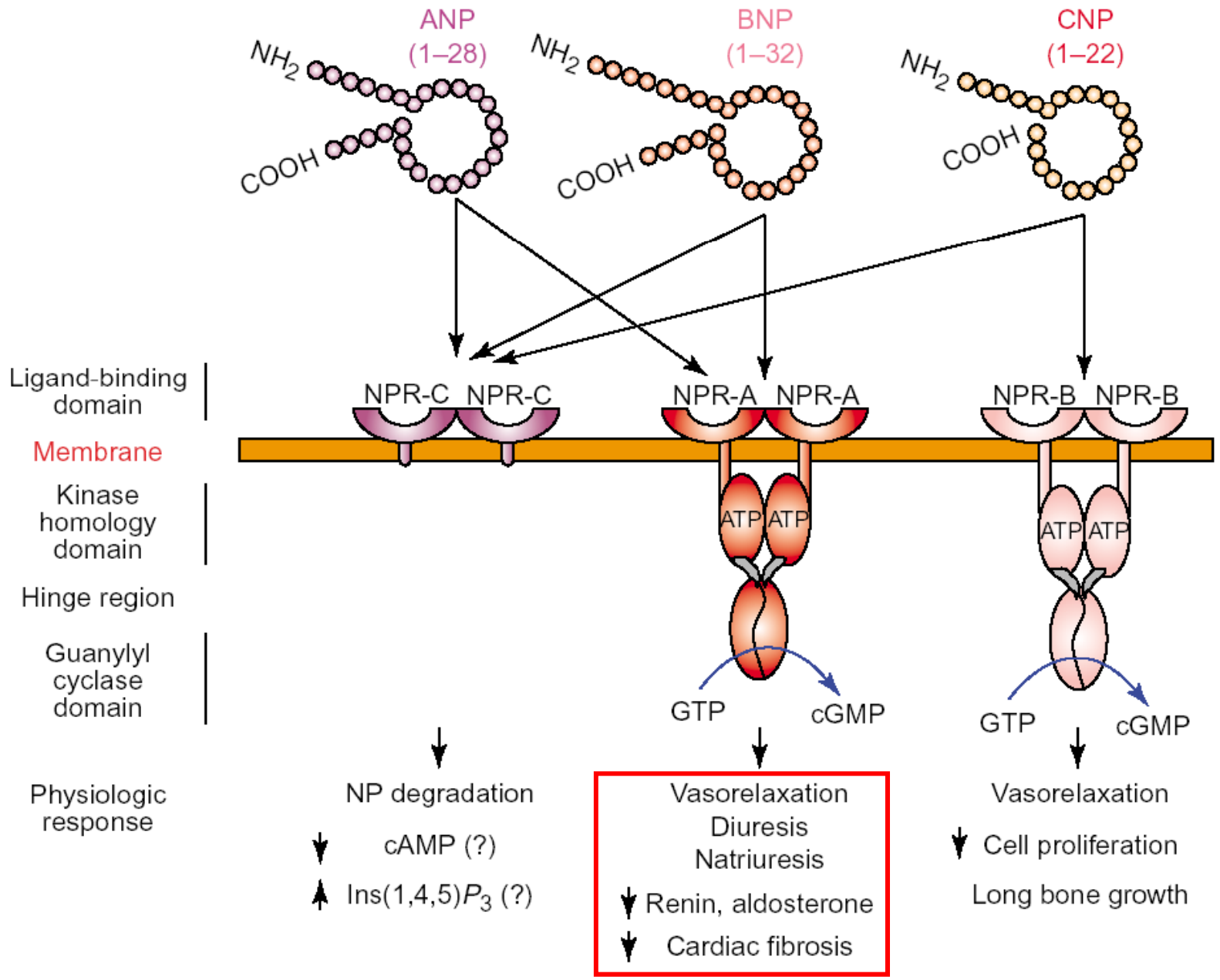
Biomarkers in Heart Failure

Mechanism	Biomarkers
Inflammation	C-reactive protein. Tumor necrosis factor α, Fas (APO-1) Interleukins 1, 6, and 18
Oxidative stress	Oxidized low-density lipoproteins, Myeloperoxidase Urinary biopyrrins, Urinary and plasma isoprostanes Plasma malondialdehyde
EC matrix remodellng	Matrix metalloproteinases(MMP), issue inhibitors of metalloproteinases(TIMP) Collagen propeptides: Propeptide procollagen type I & procollagen type III
Neurohormones	Norepinephrine, Renin, Angiotensin II, Aldosterone Arginine vasopressin, Endothelin
Myocardial injury	Cardiac-specific troponins I and T, Myosin light-chain kinase I Heart-type fatty-acid protein, Creatine kinase MB fraction
Myocyte stress	**Brain natriuretic peptide,** N-terminal pro–brain natriuretic peptide Midregional fragment of proadrenomedullin, ST2
New Biomarkers	Chromogranin, Galectin 3, Osteoprotegerin, Adiponectin Growth differentiation factor 15

Braunwald. N Engl J Med 2008;358:2148-59.

Natriuretic peptides:
Biochemistry of NT-proBNP



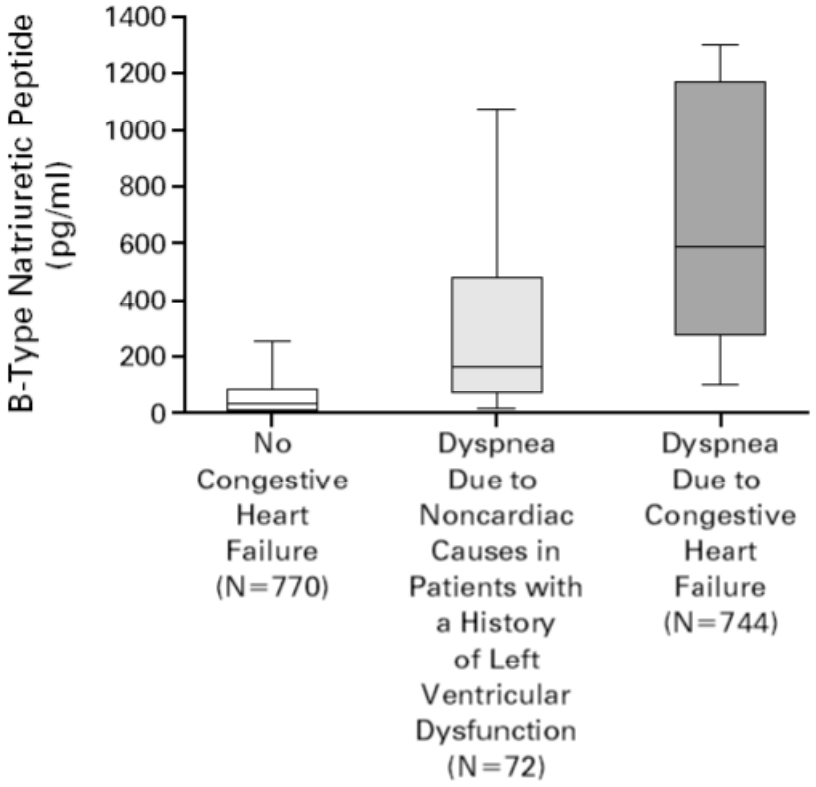


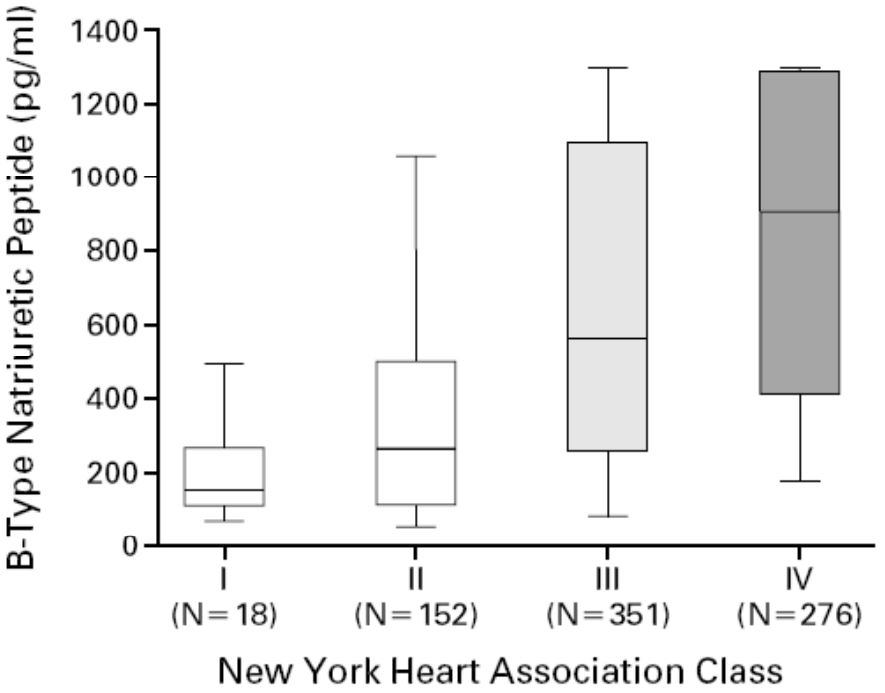
Trends Endocrinol Metab 2003 4:411

The New England
Journal of Medicine

VOLUME 347 JULY 18, 2002 NUMBER 3

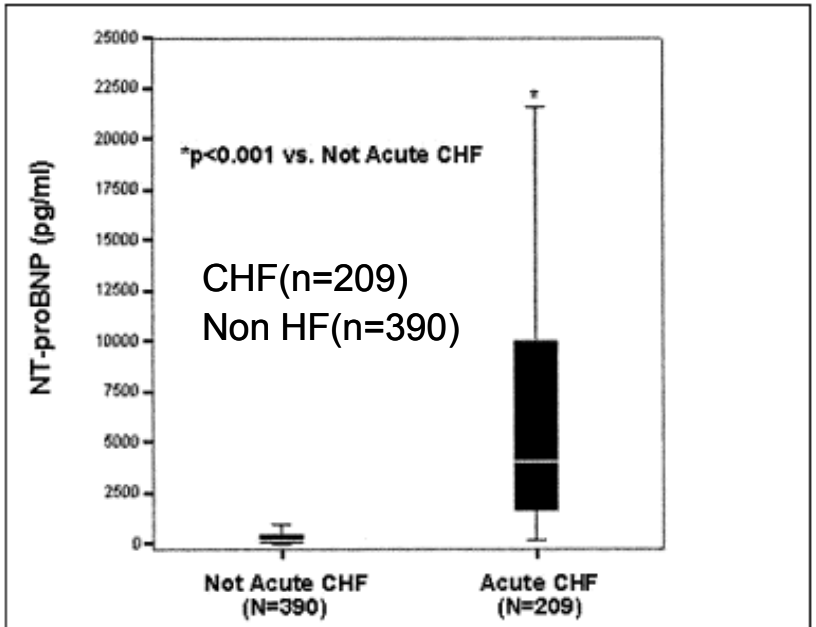
RAPID MEASUREMENT OF B-TYPE NATRIURETIC PEPTIDE IN THE EMERGENCY DIAGNOSIS OF HEART FAILURE





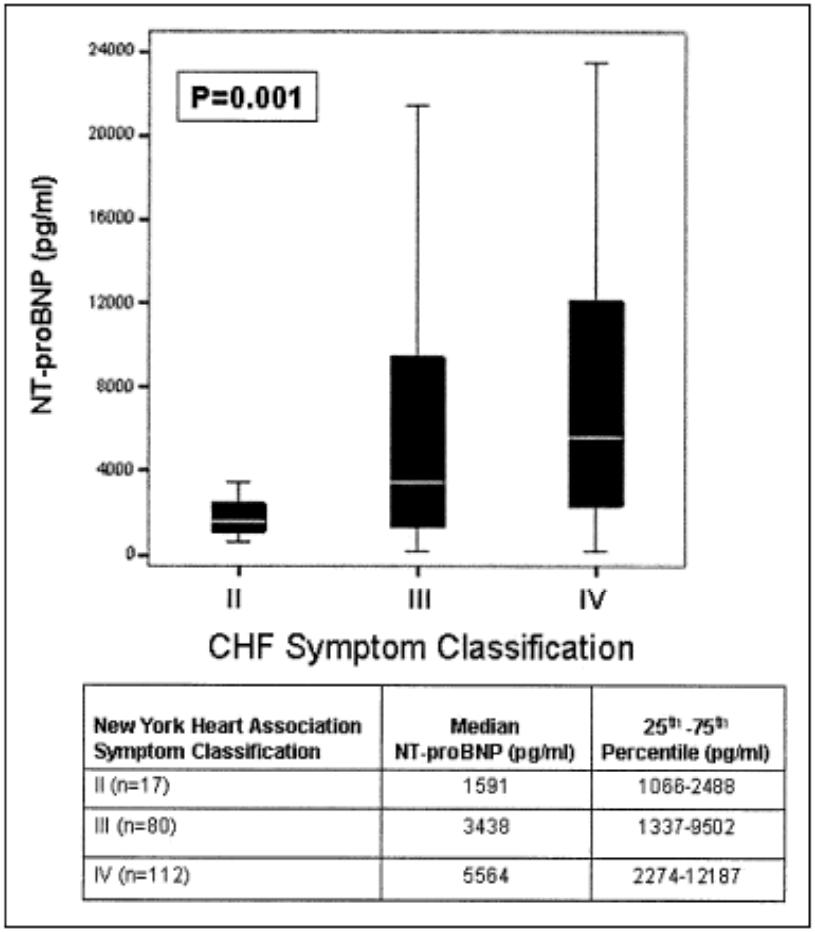
Maisel et al. N Engl J Med 2002;347:161-7

The N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department (PRIDE) Study



Diagnostic Category	Median NT-proBNP (pg/ml)	25th-75th Percentile (pg/ml)
Acute CHF (N=209)	4054	1675-10028
Not Acute CHF (N=390)	131	46-433
in patients with prior CHF (N=35)	1175	462-2590
in patients without prior CHF (N=355)	114	42-340

FIGURE 2. Median NT-proBNP levels among patients who had acute CHF (n = 209) and those who did not (n = 390; p <0.001 for difference). Boxes, interquartile ranges; whiskers

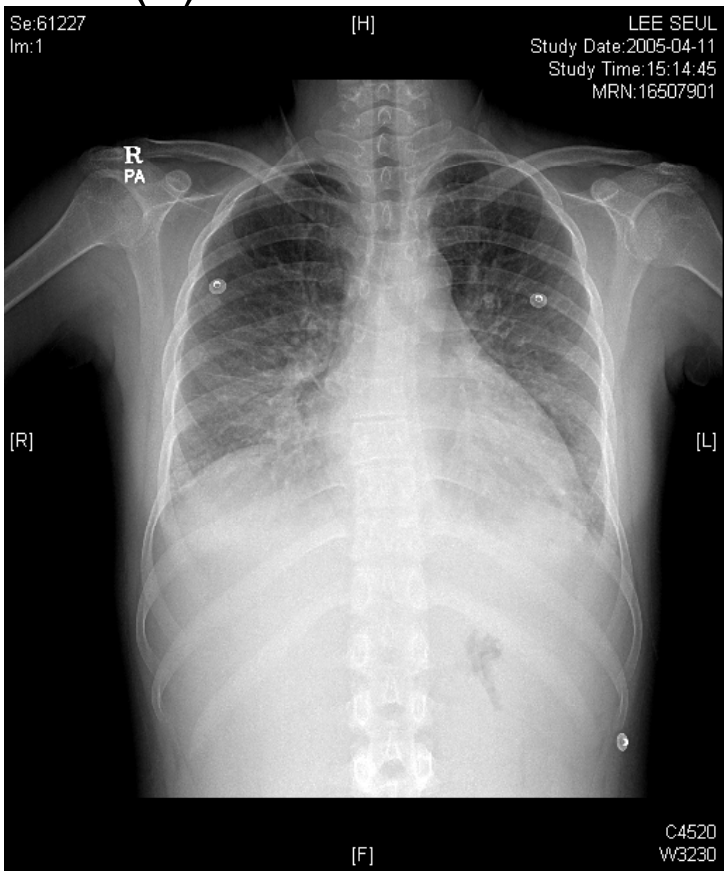


New York Heart Association Symptom Classification	Median NT-proBNP (pg/ml)	25th-75th Percentile (pg/ml)
II (n=17)	1591	1066-2488
III (n=80)	3438	1337-9502
IV (n=112)	5564	2274-12187

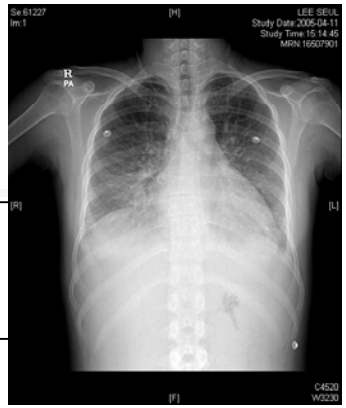
Januzzi Jr et al AM J Cardiol 2005;95:948

Case Summary – initial presentation

- 47세 여자
- Dyspnea at rest and orthopnea for 7 days
- 2주전, cough and sputum (+) / 일주일 전 DOE (+)
- 타병원 심초음파상:
  - diffuse hypokinesia, EF 23%
- 본원 응급실로 transferred
  - BP 169/103 mmHg
  - CK-MB/cTnI 4.02/0.28
  - NT-proBNP 18782 pg/ml



Diagnosis of Acute HF



Suspected Acute Heart Failure
Assess Symptoms & signs

Heart disease?
ECG/BNP/X-ray?

Normal → NT-proBNP 18782 pg/ml

Consider other diagnosis

Abnormal

Evaluate cardiac function by
Echocardiography/other imaging

Normal

Abnormal

LVID s/d 56/61 EF 17%
RVSP 60 mmHg

HEART FAILURE, assess by Echocardiography

Selected tests (angio, hemodynamically monitoring, PAC)

Characterize type and severity

Diagnosis of HF by natriuretic peptides

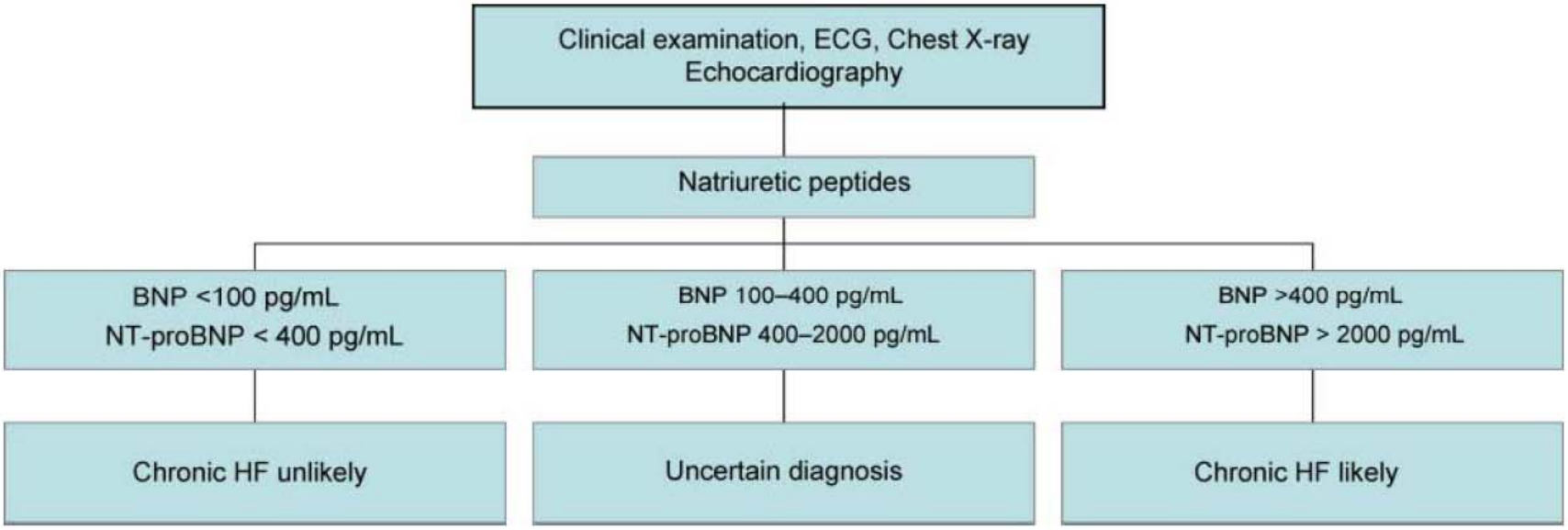


Figure 1 Flow chart for the diagnosis of HF with natriuretic peptides in untreated patients with symptoms suggestive of HF.

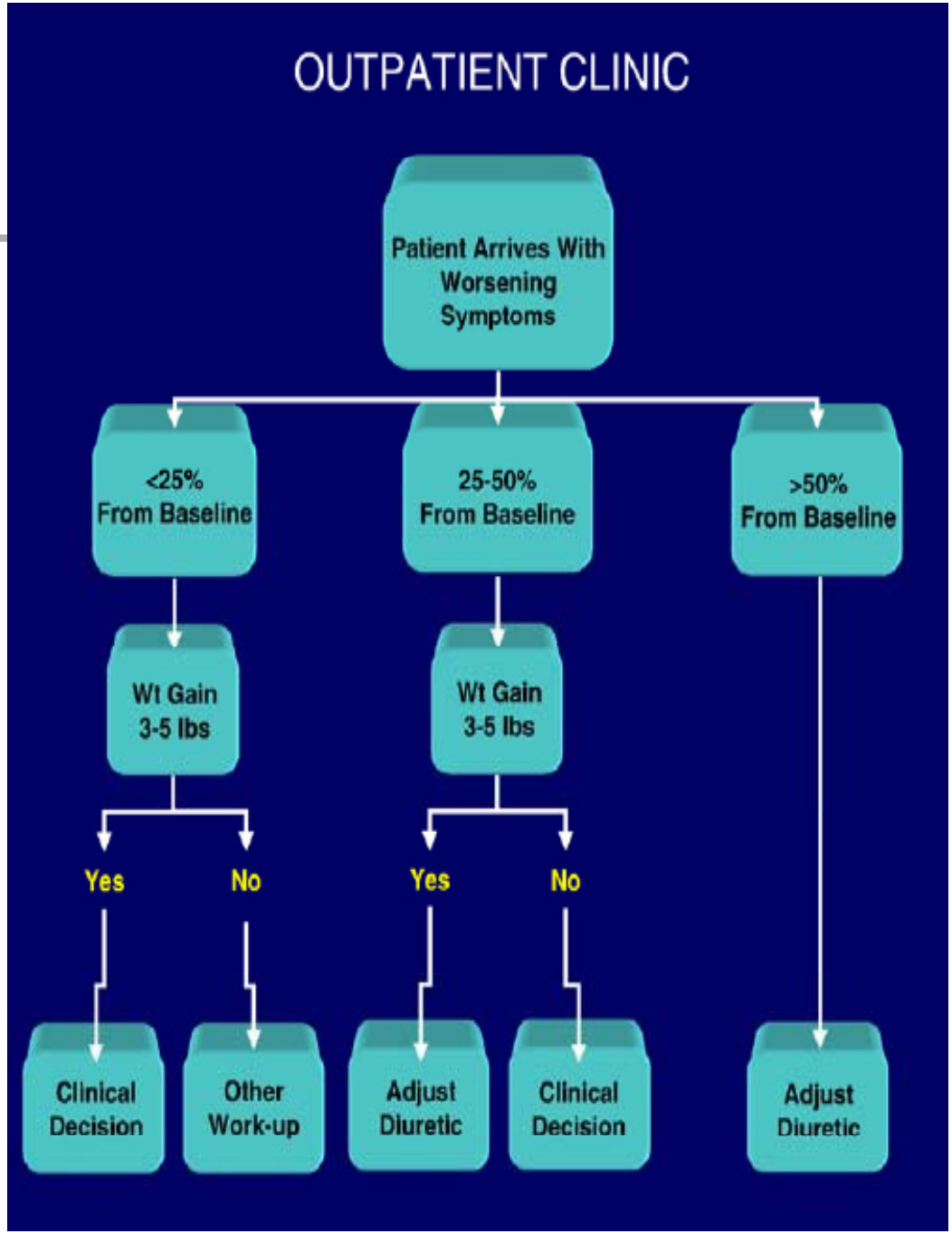
ESC Guideline for HF. Eur Heart J 2008;29:2388

Roles of NP's in other heart disease

Disease	Roles of NP
Obesity	• Decreased in higher BMIs, related to reduced synthesis and secretion • NT-proBNP cut-off point (>1000pg/ml) is equal to all BMIs
In general population	• Noncardiac source of NP: age, gender, obesity, renal function • Screening for LV structural abnormality: LVH or dysfunction • Risk stratification for CV death/events with CRP
Acute Coronary Syndrome	• Increase in ACS but not useful for diagnosis of ACS • Independent predictor of death and HF • NT-proBNP > 1000 ng/ml need intervention
Valvular Heart Disease	• Elevated in all VHD and related to severity and NYHA FC • Reversed after valve replacement • Prognostic factors in AS and AR
Pulmonary Thromboembolism	• Elevated both LV dysfunction and in isolated or chronic RV volume overload • Related to severity of RV dysfunction • Predict clinical course in acute PTE (NT proBNP >600 pg/ml) / PAH (>1400)
Congenital Heart Disease	• Elevated at birth, decreased in the first days of life • Elevated & correlate with disease severity in volume/pressure overload (>300) • Predict prognosis/outcome in D-CMP and

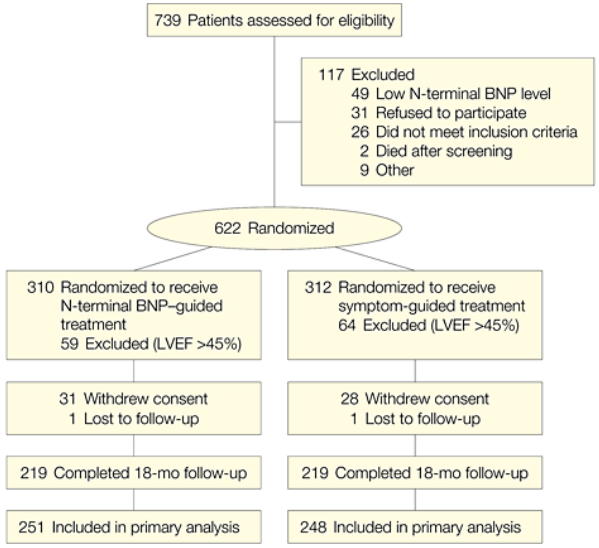
Januzzi et al. NT-proBNP as a biomarker in Cardiovascular Disease. 2008

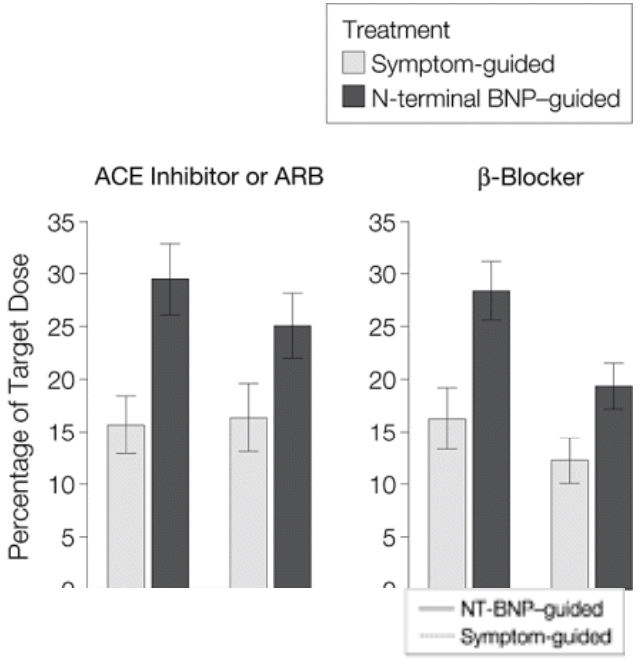
Algorithms for NP outpatient management

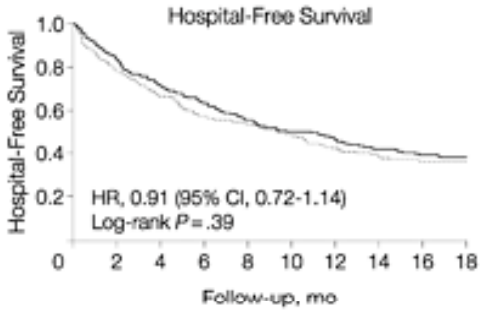


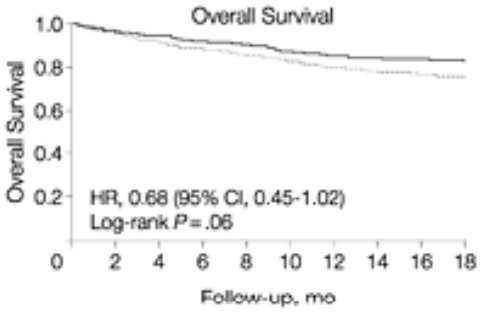
Maisel et al. Eur J HF 2008;10:824

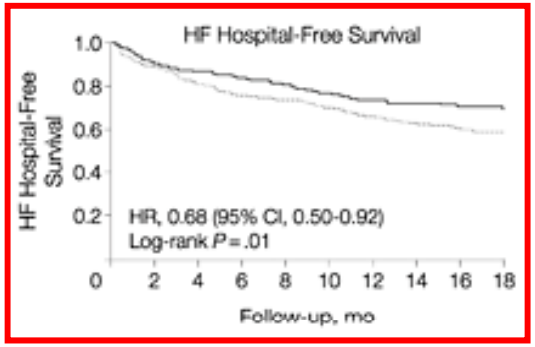
BNP-Guided vs Symptom-Guided Heart Failure Therapy; The Trial of Intensified vs Standard Medical Therapy in Elderly Patients With Congestive Heart Failure (TIME-CHF) Randomized Trial











No. at risk

NT-BNP–Guided	251	201	170	147	128	115	105	94	88	81
Symptom-Guided	248	184	152	129	120	108	94	86	78	75

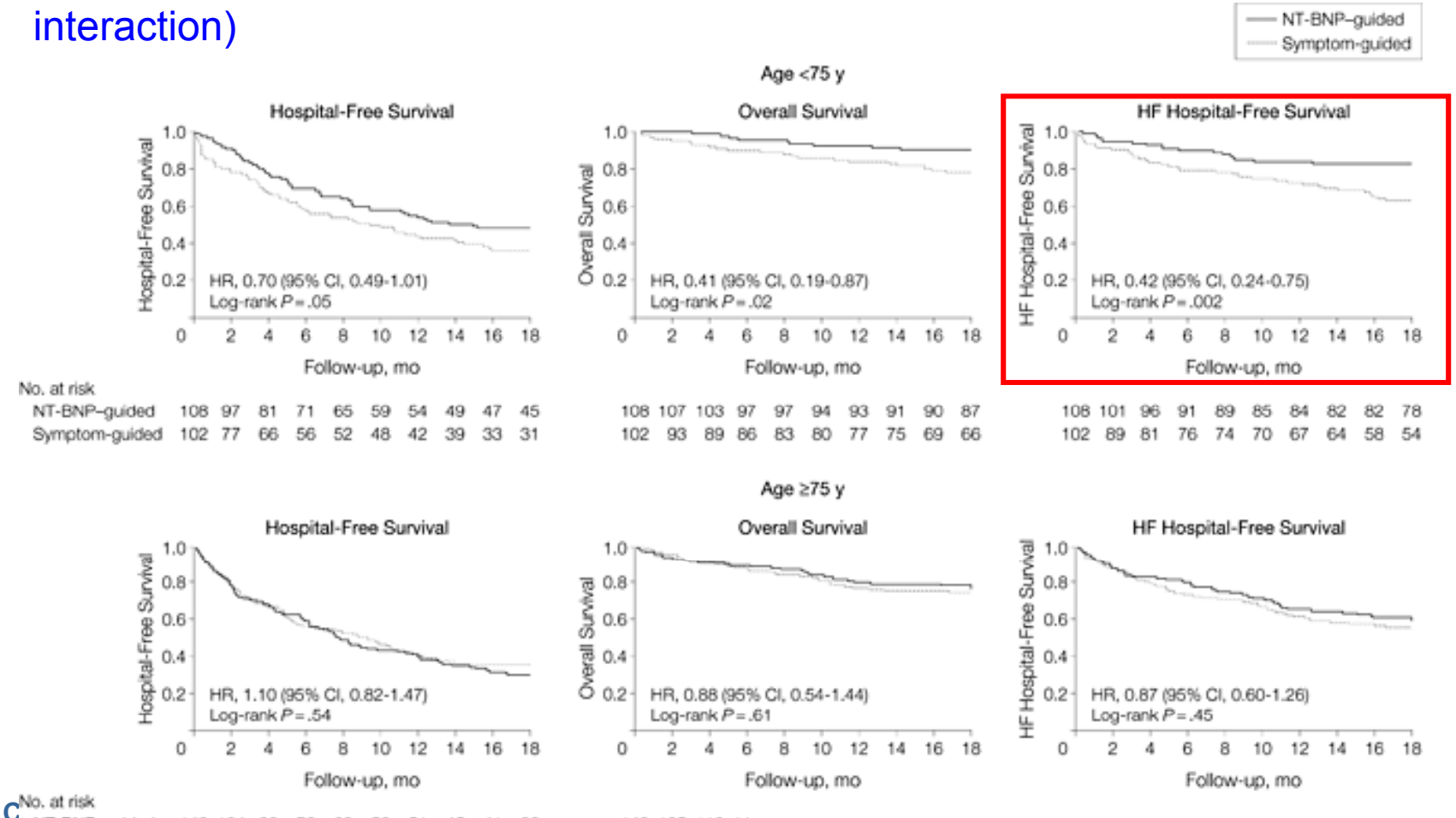
	251	232	219	210	207	200	193	190	189	179
	248	224	206	197	189	182	173	167	161	153

	251	218	203	193	185	176	168	163	160	151
	248	209	182	169	164	155	144	135	127	119

Pfisterer, M. et al. JAMA 2009;301:383-392

Treatment Effects on Main Outcomes in Younger Compared With Older Patients

Heart failure therapy guided by N-terminal BNP improved outcomes in patients **aged 60 to 75 years** but not in those aged 75 years or older (P < .02 for interaction)



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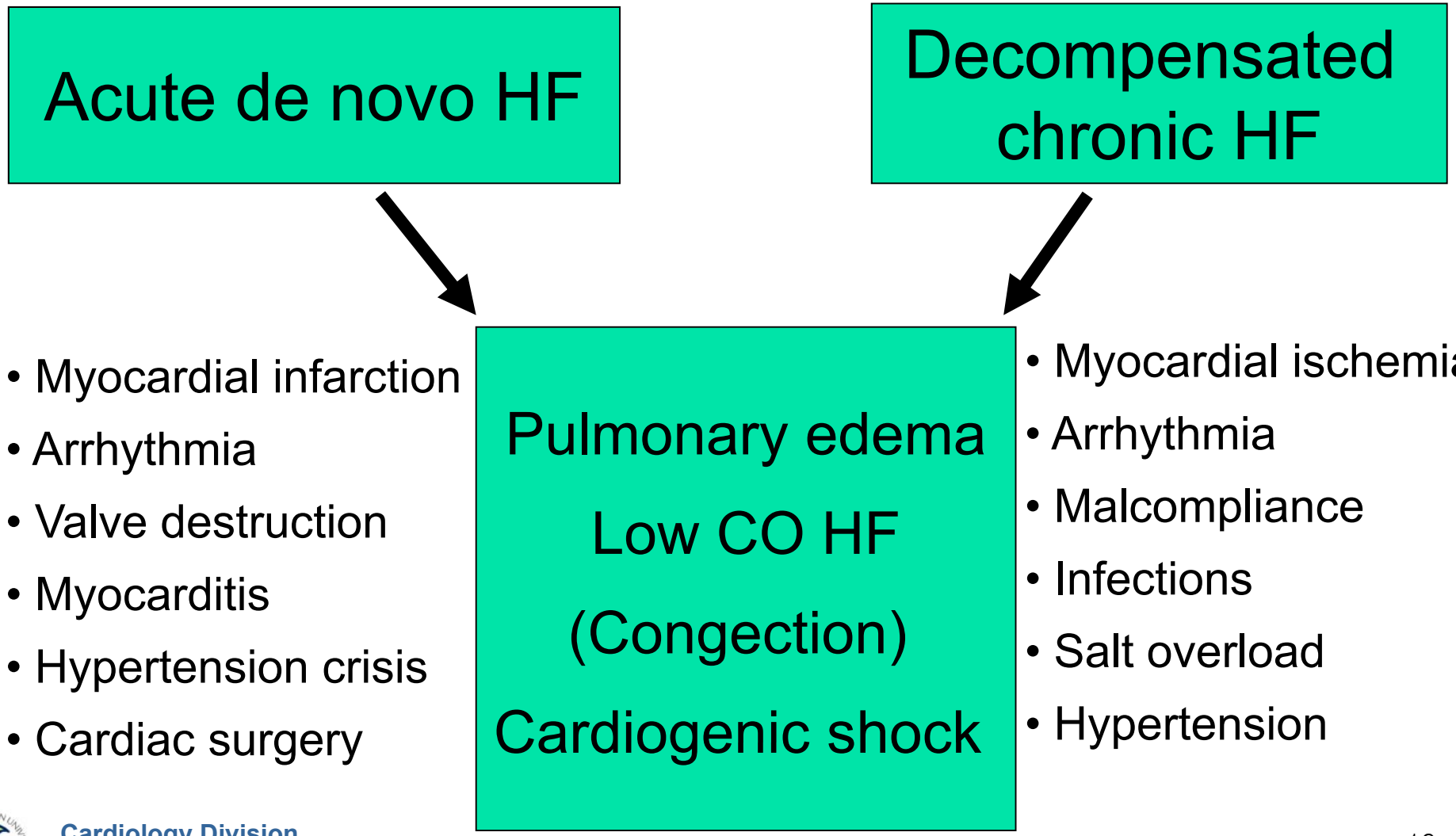
Types and causes of AHF



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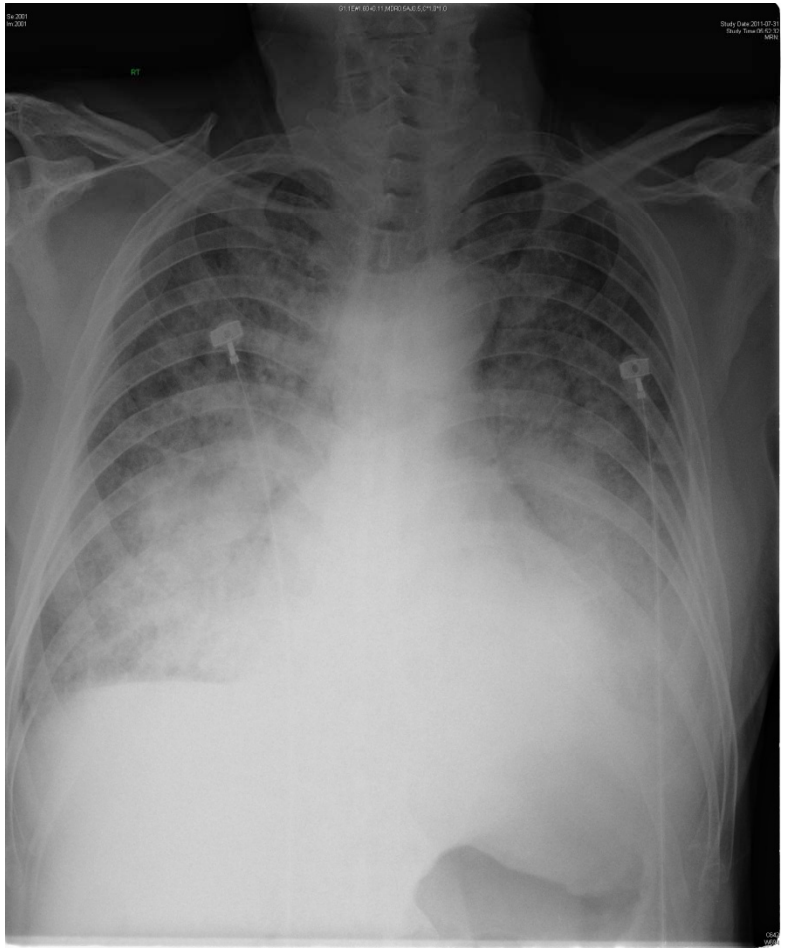
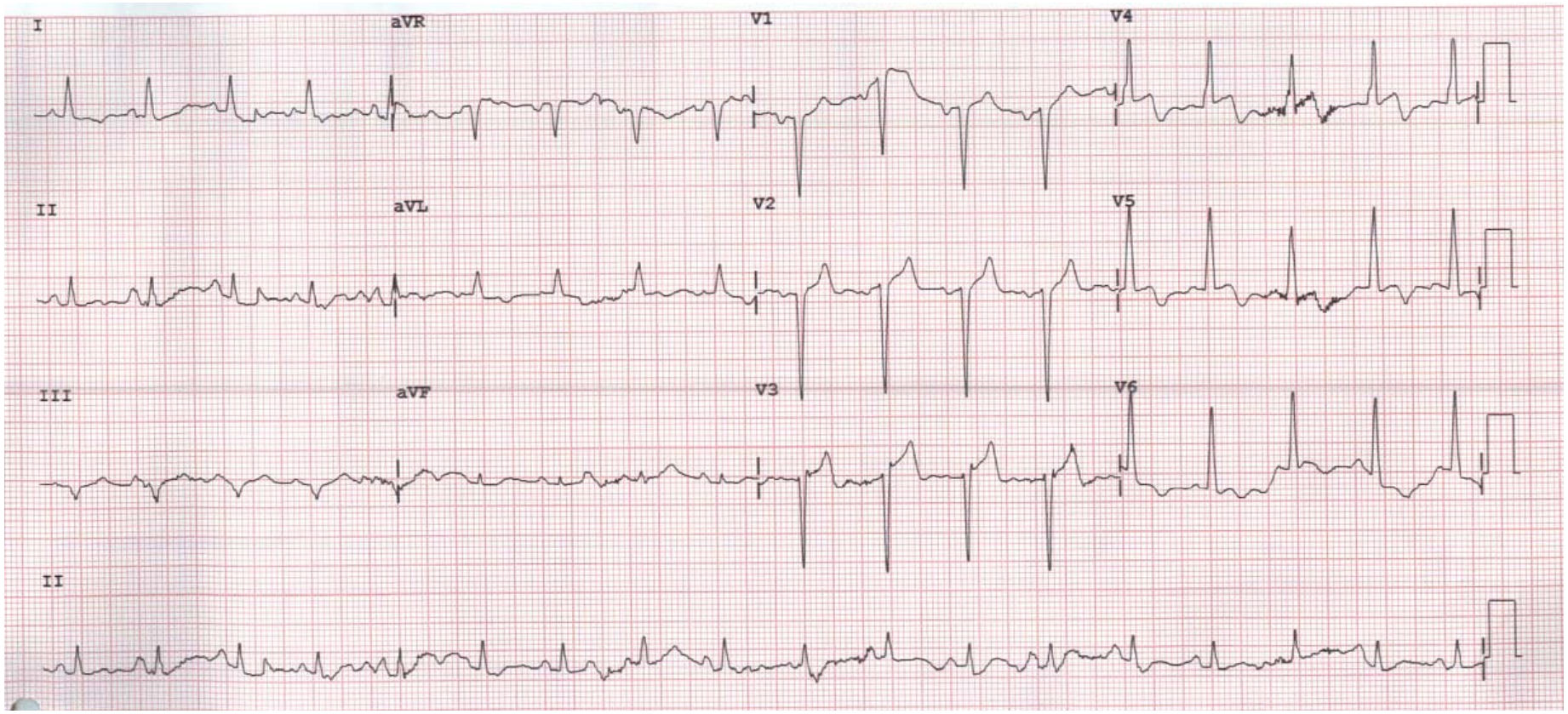
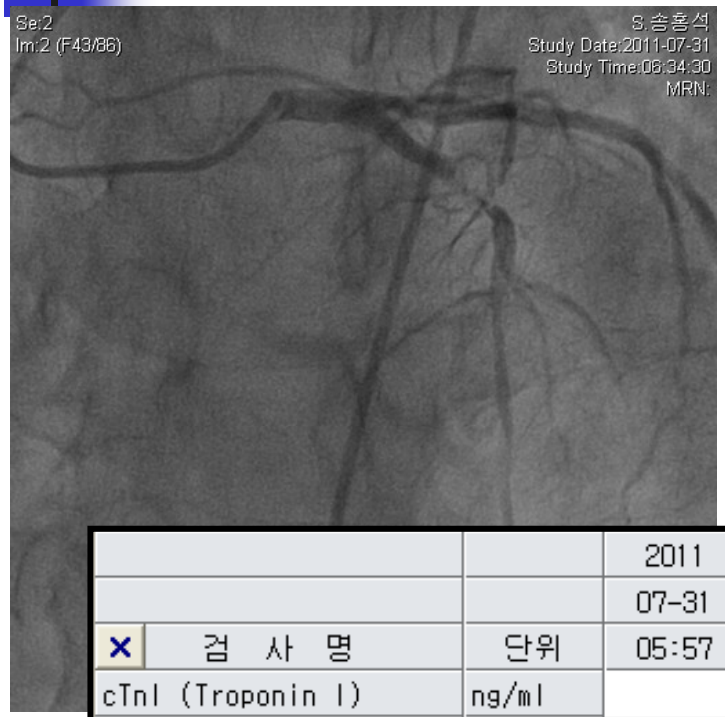
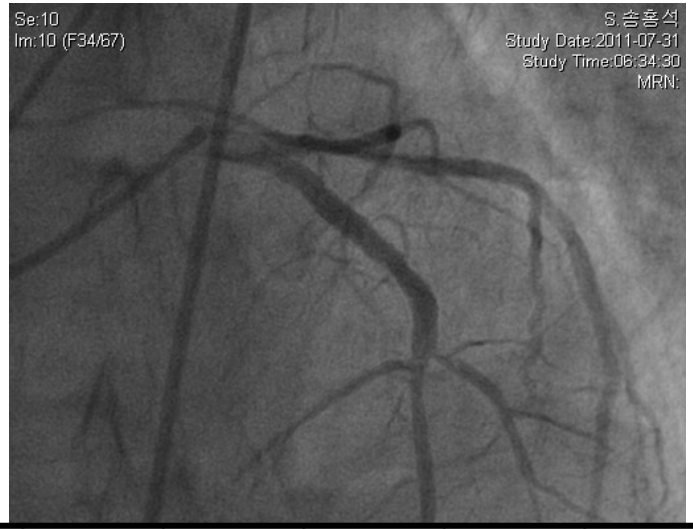


ECG



CAG





		2011	2011	2011	2011	2011	2011	2011	2011
		07-31	07-31	07-31	07-31	07-31	07-31	08-01	08-02
검 사 명	단위	05:57	06:00	06:00	08:54	15:24	22:37	05:08	04:46
cTnI (Troponin I)	ng/ml			0.100	▲6.430	▲52.190	▲33.982	▲19.419	
CK-MB	ng/ml			2.50	▲29.68	▲98.48	▲69.63	▲36.68	▲5.09
NT-proBNP(N-Terminal pr	pg/mL		▲1116						
cTnI,POCT(Troponin I)	ng/mL	0.05							
Myoglobin,POCT	ng/mL	▲315							
CK-MB,POCT	ng/mL	2.9							
BNP, POCT	pg/mℓ	▲456							

Case Summary – initial presentation

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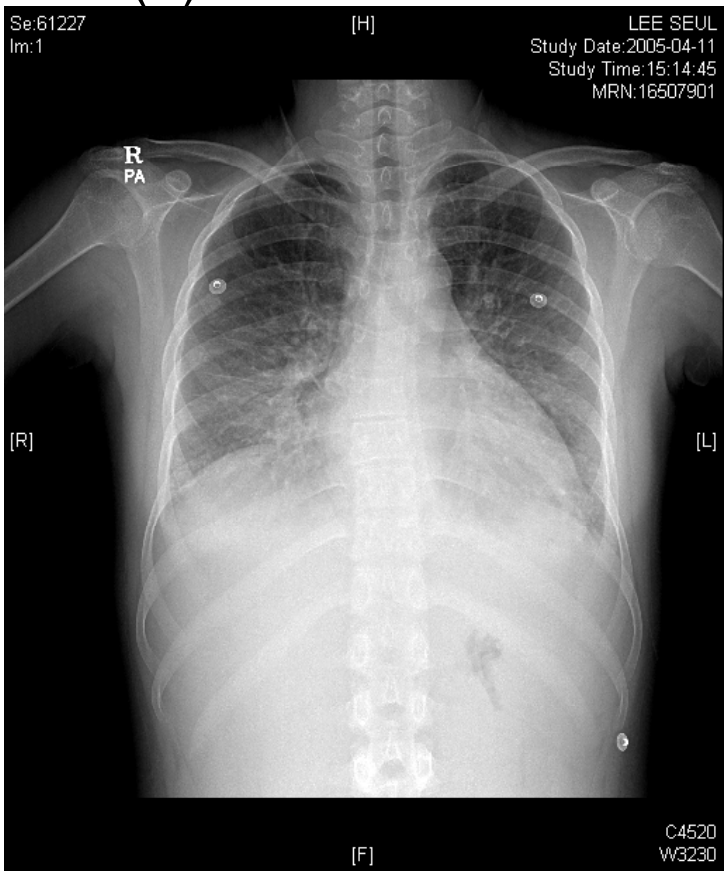
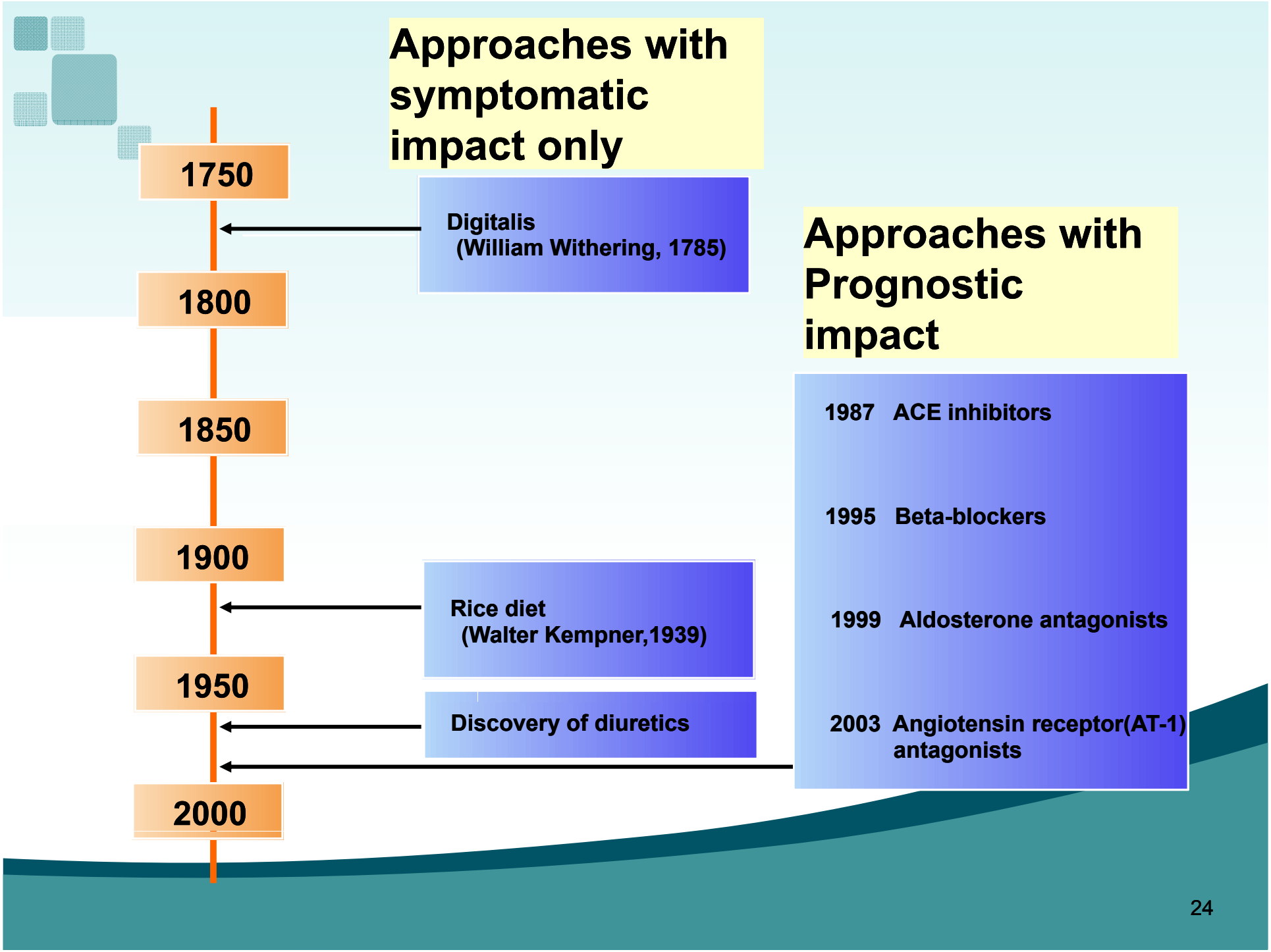



Approaches with symptomatic impact only
1750
1800
1850
1900
1950
2000
Digitalis
(William Withering, 1785)
Rice diet
(Walter Kempner,1939)
Discovery of diuretics
Approaches with Prognostic impact
1987 ACE inhibitors
1995 Beta-blockers
1999 Aldosterone antagonists
2003 Angiotensin receptor(AT-1) antagonists

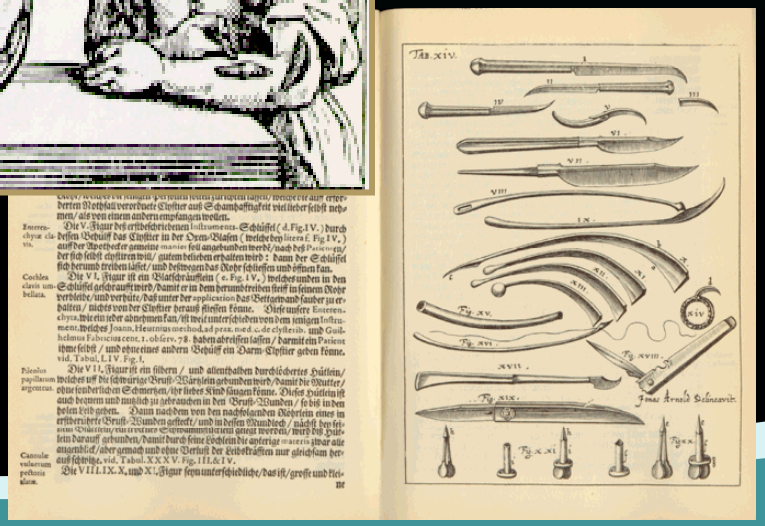
Blood letting

doctors' treatment of choice in 1780.

Ventura HO & Mehra MR. *J Card Fail*. 2005;11:247-52.

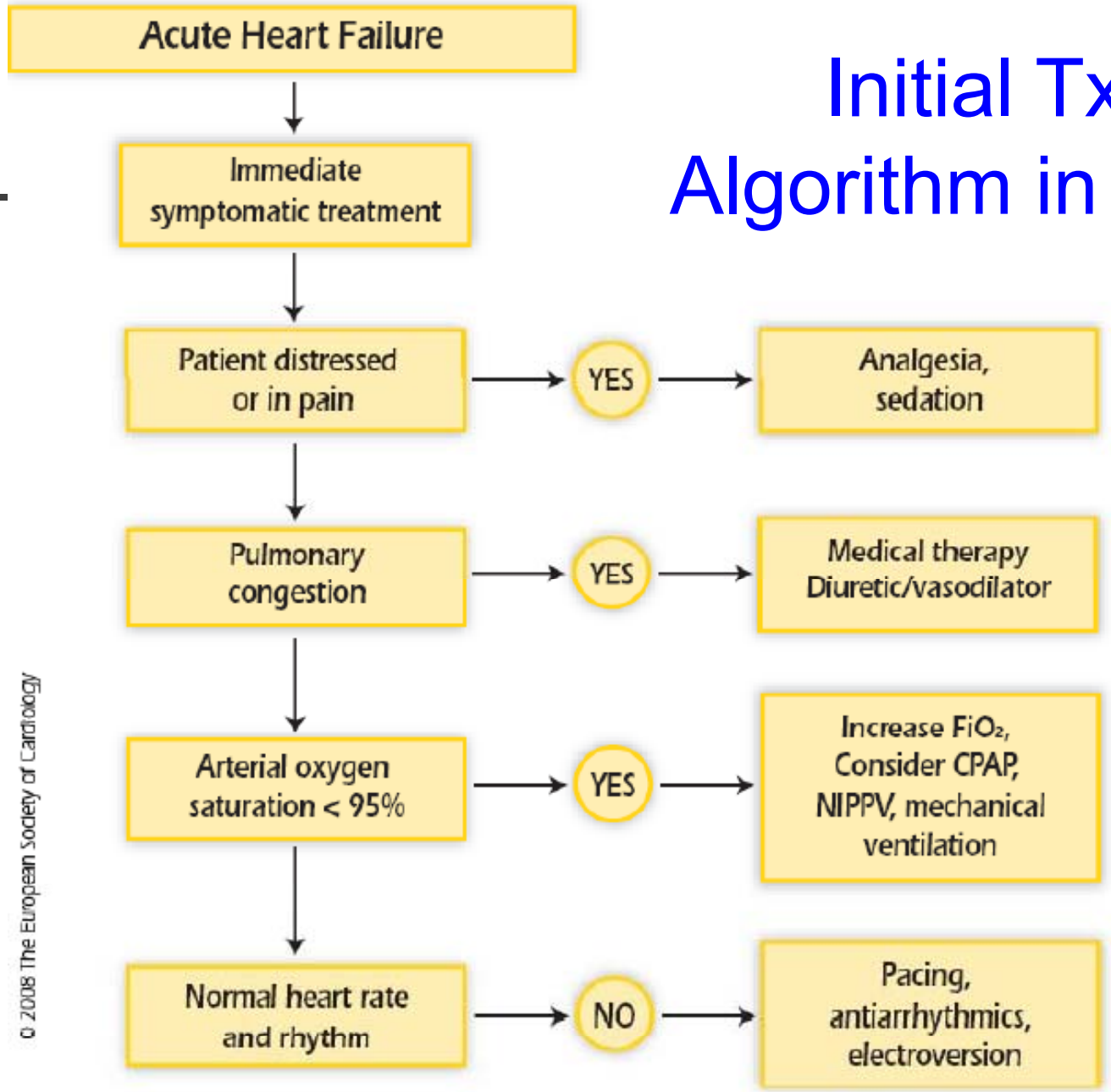
Bloodletting

"It is the least equivocal of remedies: its good effects, when properly administered, are, in most cases, so immediate and striking...
In short, bloodletting is a remedy which, when judiciously employed, it is hardly possible to estimate too highly."



Ventura HO & Mehra MR. *J Card Fail*. 2005;11:247-52.

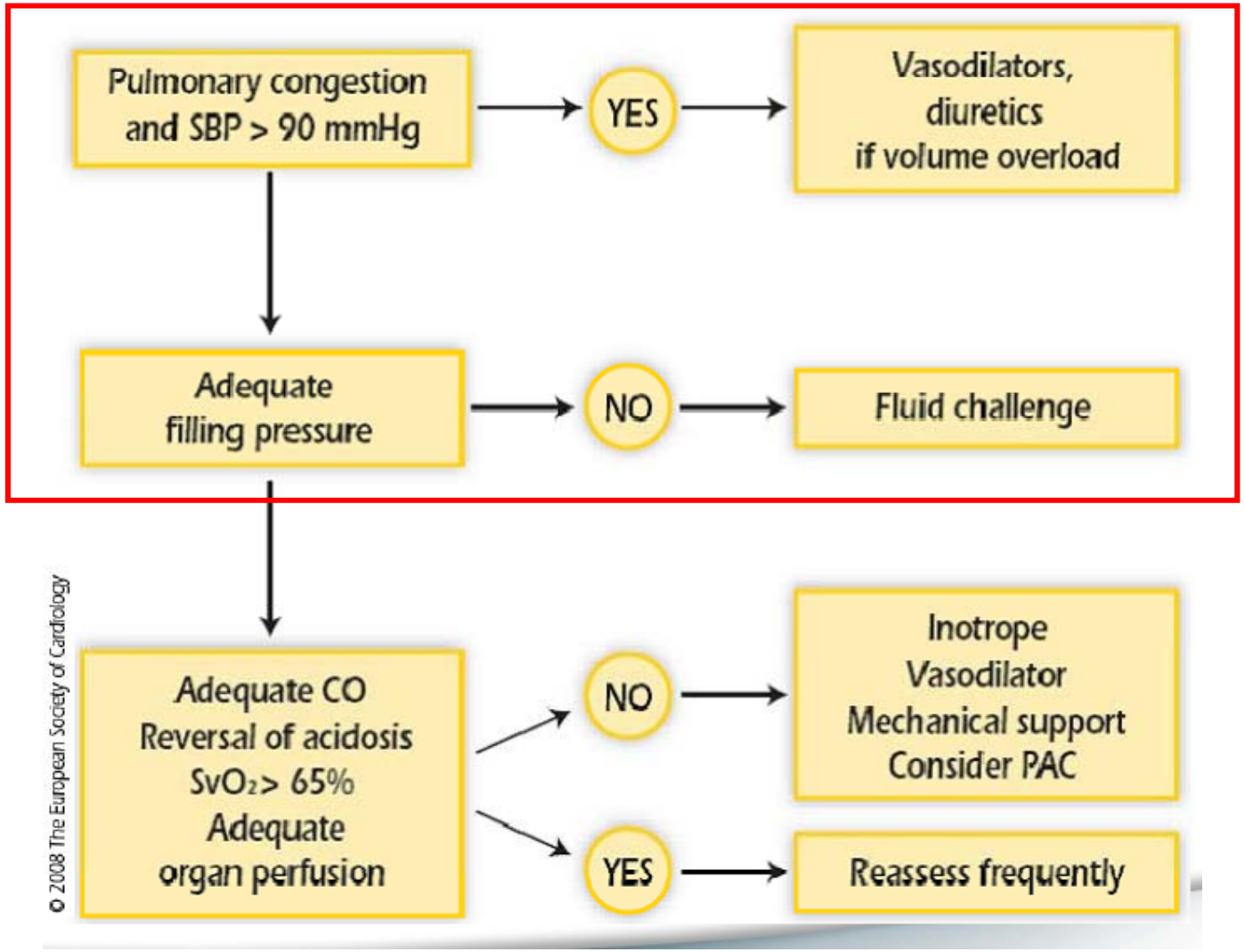
Initial Tx Algorithm in AHF



Treatment goals in management of HF

- To reduce mortality
  - All cause mortality
  - Cardiovascular mortality
- To reduce morbidity
  - Rehospitalization
  - Hospitalization due to HF
- To improve Quality of life

Treatment strategy in AHF (LV filling pressure)



Diuretics in AHF

- Patients admitted with HF and with evidence of significant fluid overload should be treated with **intravenous loop diuretics.**
- Therapy should begin in the emergency department or outpatient clinic without delay, as early intervention may be associated with better outcomes for patients hospitalized with decompensated HF. *(Level of Evidence: B)*
- *If patients are already* receiving loop diuretic therapy**, the initial intravenous dose should equal or exceed their chronic oral daily dose.** Urine output and signs and symptoms of congestion should be serially assessed, and diuretic dose should be titrated accordingly to relieve symptoms and to reduce extracellular fluid volume excess. *(Level of Evidence: C)*
- **When diuresis is inadequate** to relieve congestion, as evidenced by clinical evaluation, the diuretic regimen should be intensified using either:

  a. higher doses of loop diuretics;

  b. addition of a second diuretic (such as metolazone, spironolactone or intravenous chlorothiazide); or

  c. continuous infusion of a loop diuretic. *(Level of Evidence: C)*

Diuretic Strategies in Patients with Acute Decompensated Heart Failure

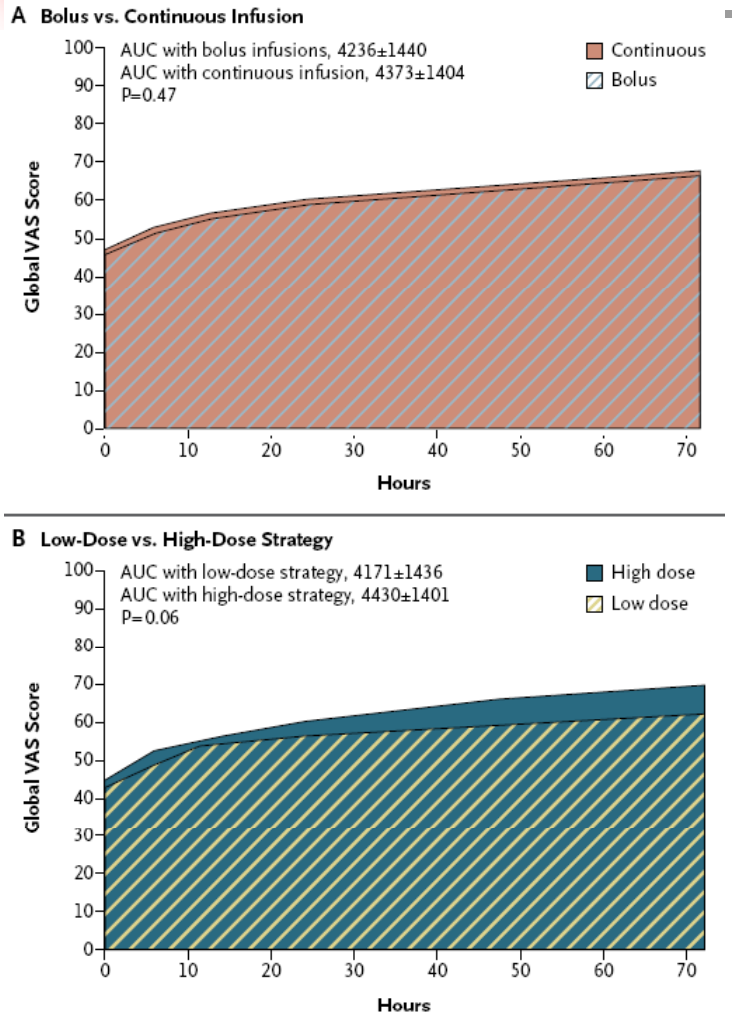


Fig. 1. Patients' Global Assessment of Symptoms during the 72-Hour Study-Treatment Period.

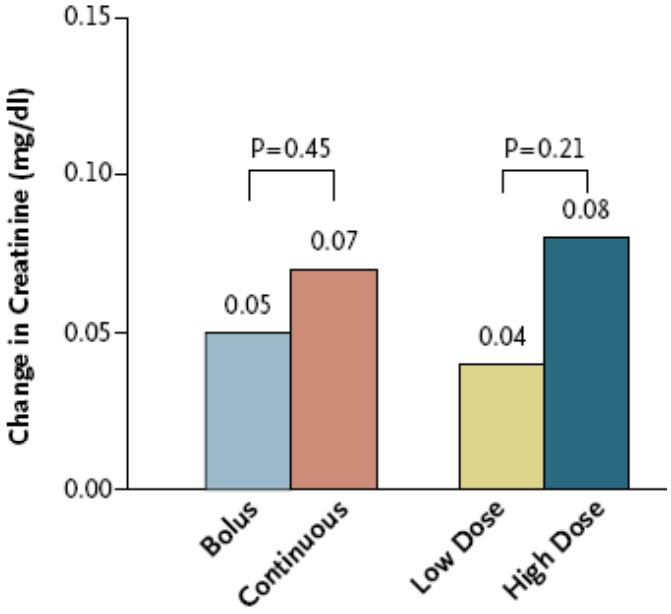


Fig. 2. Mean Change in Serum Creatinine Level.

Among patients with acute decompensated heart failure, there were no significant differences in patients' global assessment of symptoms or in the change in renal function when diuretic therapy was administered by bolus as compared with continuous infusion or at a high dose as compared with a low dose.

DOSE trial. N Engl J Med 2011;364:797-805.

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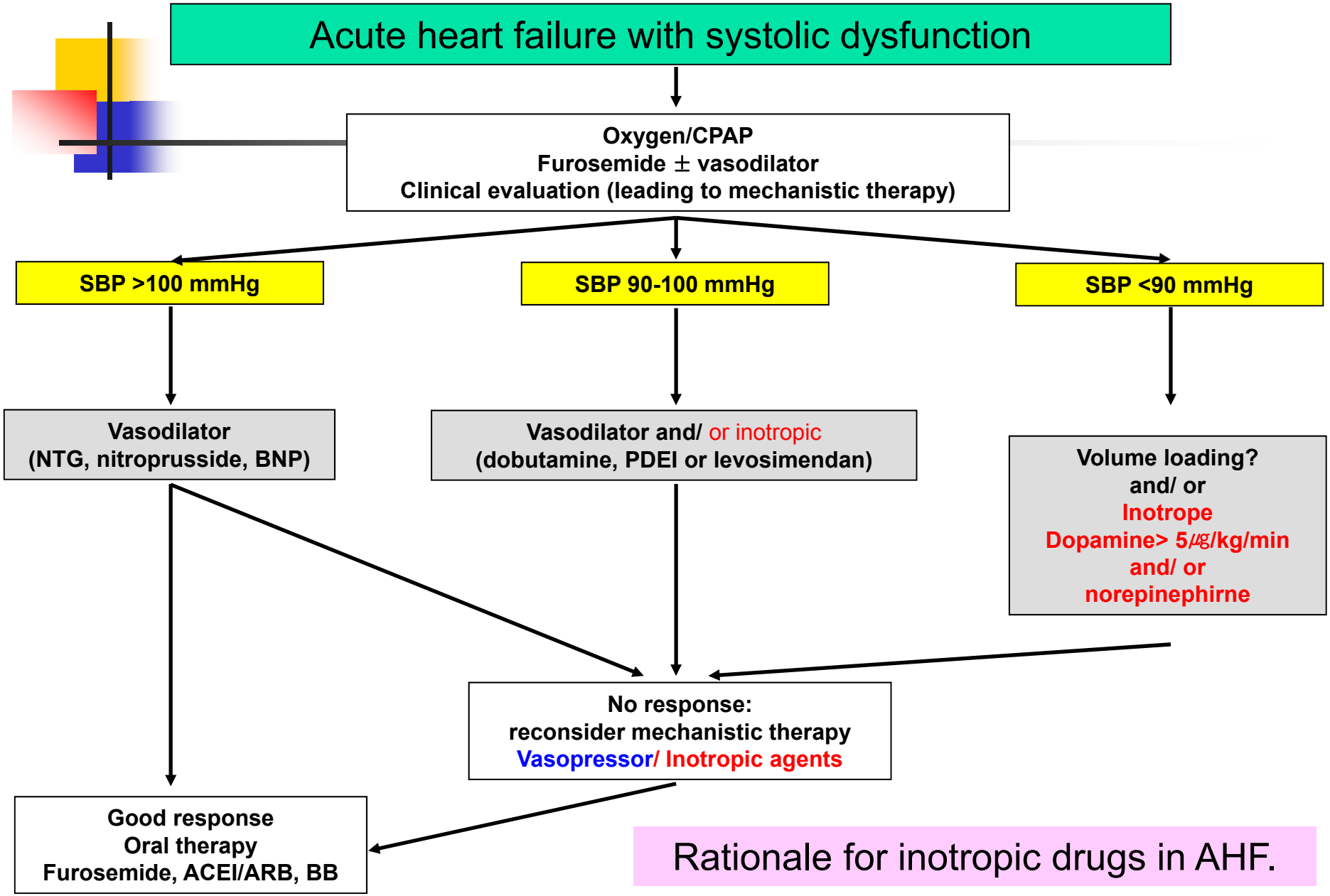
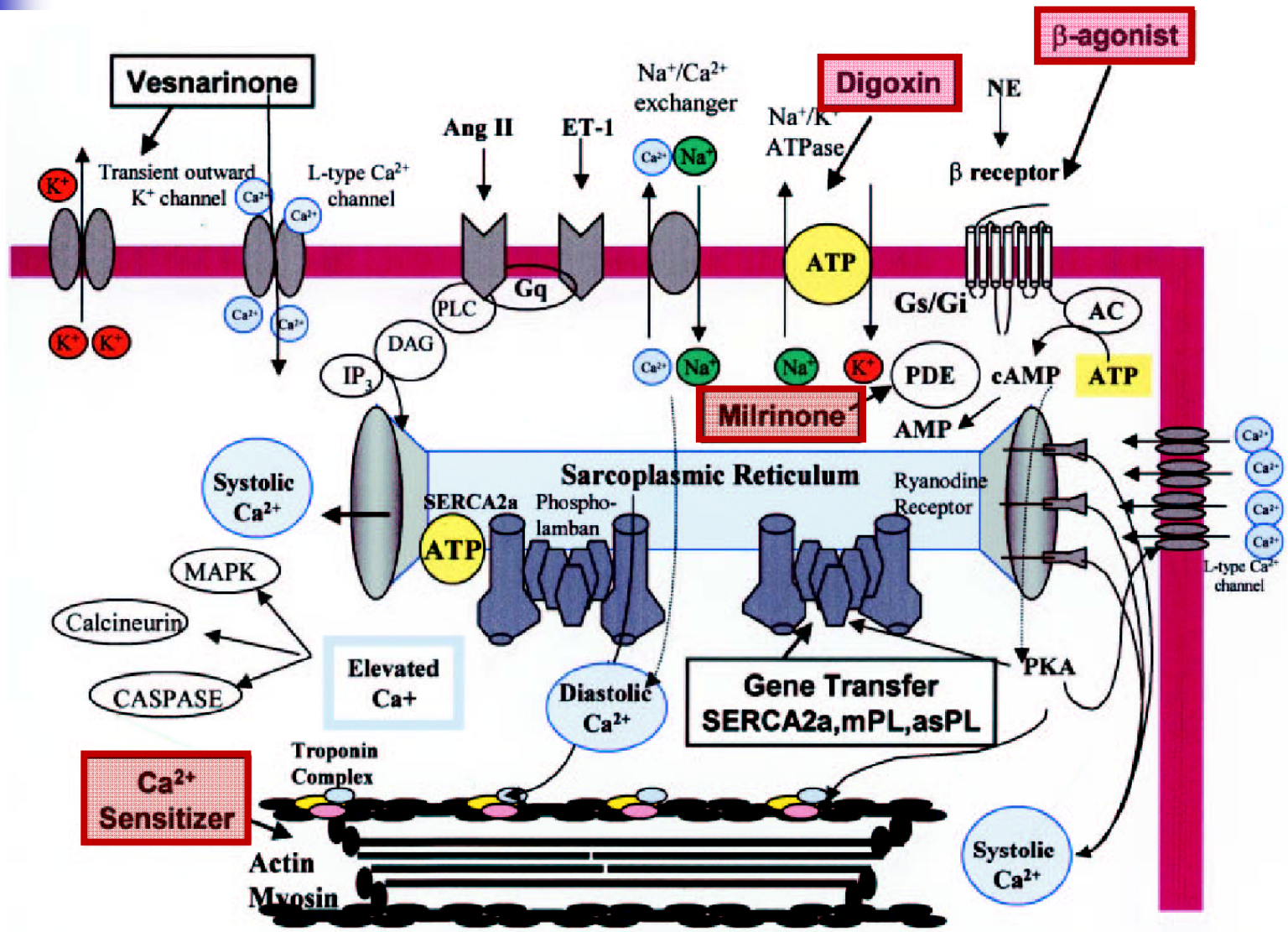


Rationale for inotropic drugs in AHF.

Effects of inotropic therapy on intracellular calcium handling in cardiac myocytes



Circulation. 2003;108:492-497

Inotropic Agents

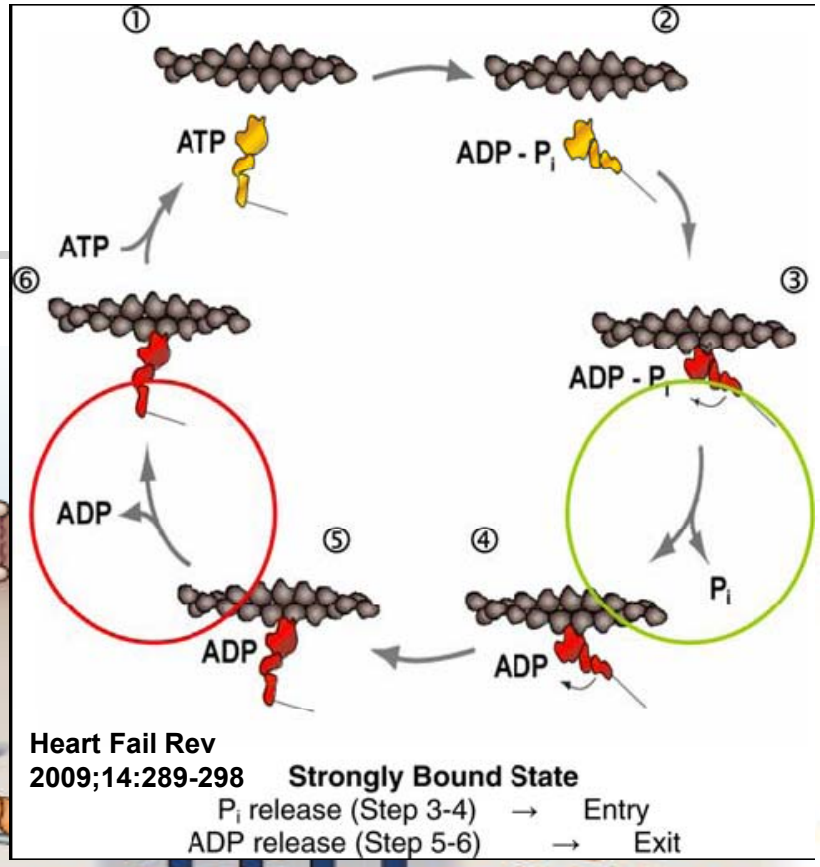
- Indication:
  - In the presence of peripheral hypoperfusion (hypotension, decreased renal function)
  - With or without congestion or pulm edema refractory to diuretics or vasodilator
  - Class IIa, level C
- Potentially harmful
  - ↑O2 demand, ↑calcium loading, arrhythmia
- ? Risk-benefit ratio

Inotropic Agents

	Bolus	Infusion rate
Dobutamine	No	2 to 20 µg/kg/min (ß+)
Dopamine	No	< 3 µg/kg/min: renal effect (δ+) 3 - 5 µg/kg/min: inotropic (ß+) > 5 µg/kg/min: (ß+), vasopressor (α+)
Milrinone	25 - 75 µg/kg over 10 - 20 min	0.375 - 0.75 µg/kg/min
Enoximone	0.25 - 0.75 mg/kg	1.25 - 7.5 µg/kg/min
Levosimendan*	12 µg/kg over 10 min (optional)**	0.1 µg/kg/min which can be decreased to 0.05 or increased to 0.2 µg/kg/min
Norepinephrine	No	0,2 - 1,0 µg/kg/min
Epinephrine	Bolus: 1 mg can be given i.v. during resuscitation, repeated every 3 - 5 min	0.05 - 0.5 µg/kg/min

Myosin Activator

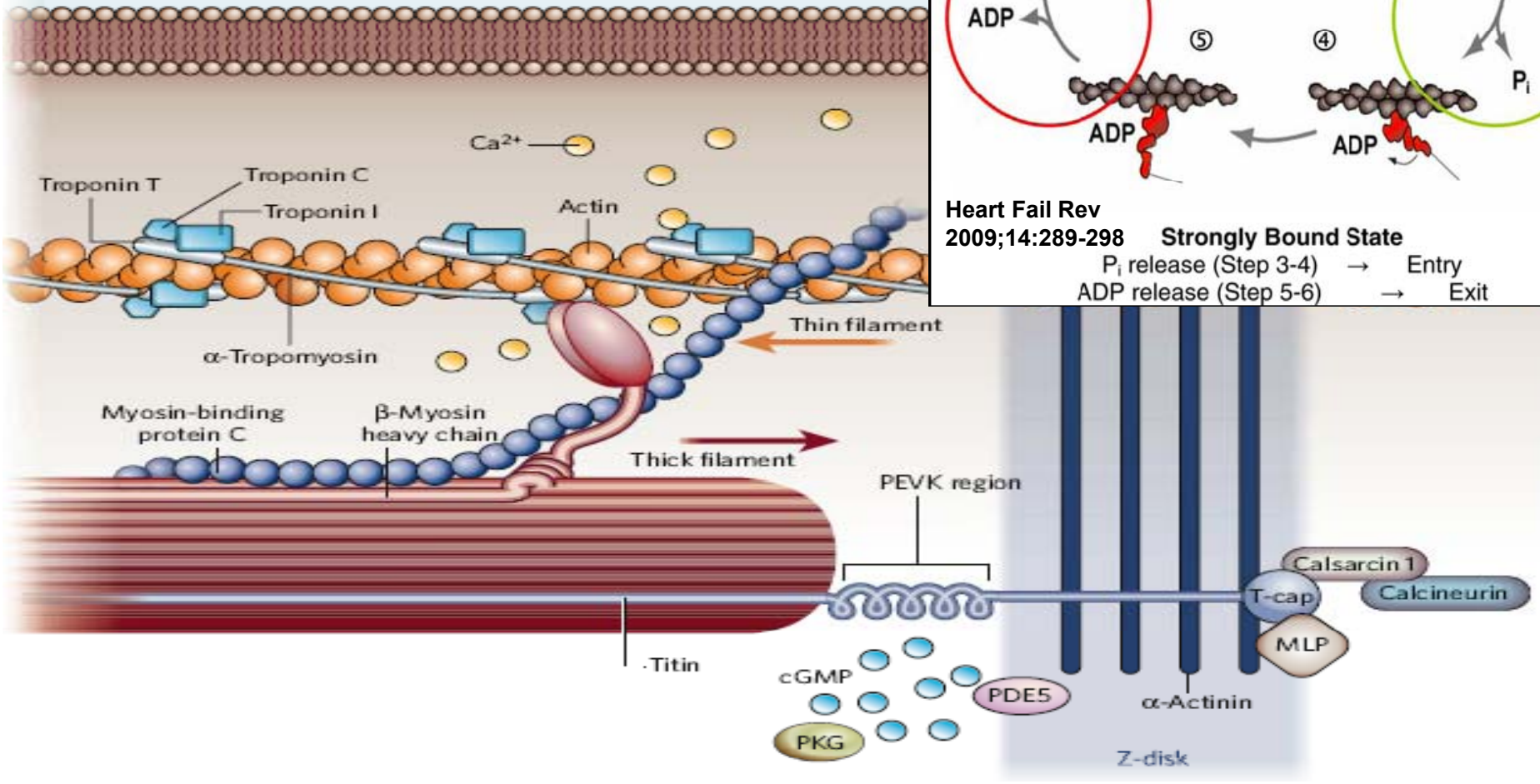
a new class of cardiac enhancers that stimulate cardiac contractility without causing intracellular calcium overload or increasing myocardial oxygen demand.



Heart Fail Rev 2009;14:289-298 **Strongly Bound State**

P_i release (Step 3-4) → Entry

ADP release (Step 5-6) → Exit



Omecamtiv mecarbil (CK-1827452)

- resulting in **improvement of cardiac contractility without alterations of intracellular calcium concentration.**

- In anesthetized rats, CK-452 (0.25-2.5 mg/kg/h) significantly **increases fractional shortening without significant changes in HR and BP**

- In a dog model of heart failure induced by MI combined with rapid ventricular pacing, CK-1827452 (0.5 mg/kg bolus, then 0.5 mg/kg/min for 6-8 h)
  → significantly increases LV systolic function by lengthening LV systolic ejection time without affecting the velocity of cardiac contraction, myocardial oxygen consumption, arterial blood pressure, coronary blood flow or diastolic function

CV and Heamatol Dis-Drug Targets 2009:9:193-205

Ongoing studies of Omecamtiv

- Absence of phase III clinical trials and the lack of long-term safety data, at the present time,
- Three ongoing phase II randomized, double blind, placebo controlled trials analyze the pharmacokinetics, efficacy and safety
  - of intravenous and oral CK-1827452 in patients with ischemic cardiomyopathy (NCT00682565),
  - of intravenous CK-1827452 in patients with stable heart failure (NCT00624442 and NCT00748579).

CV and Heamatol Dis-Drug Targets 2009:9:193-205

Inadequate consensus in AHF

- Which vasodilator is most efficacious?
- Which inotrope is most efficacious?
- The role of NIV in AHF?
- Management of beta-blocker in Acute decompensation?

* NIV: non-invasive ventilation without E-tube

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   - Beta blocker issues in acute HF
   - Guideline for chronic HF

First β-blocker trial in heart failure

British Heart Journal, 1975 37,1022-1036

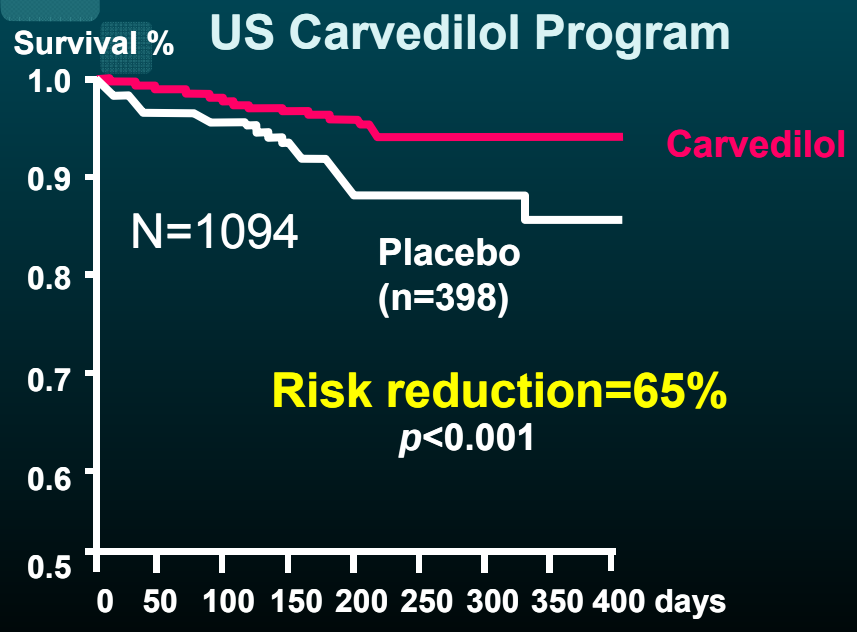
Effect of chronic beta-adrenergic receptor blockade in congestive cardiomyopathy

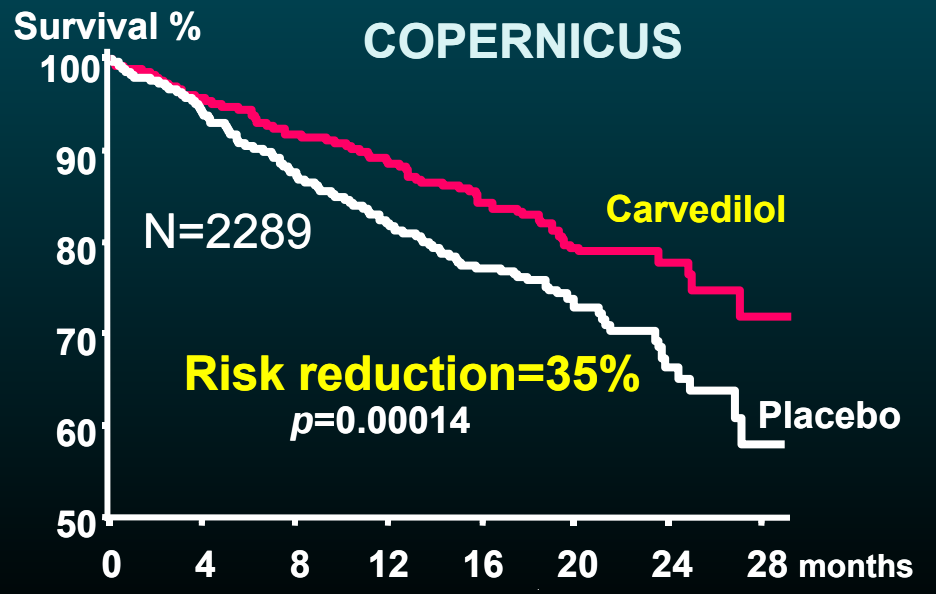
F.Waagstein, A. Hjalmarson, E. Varnauskas, and I. Wallentin

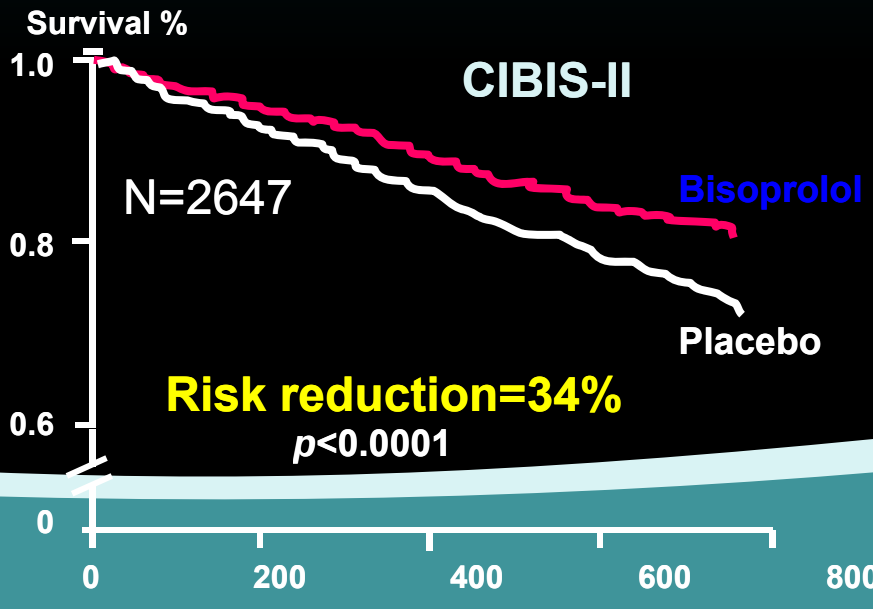
From the Department of Medicine I, Division of Cardioloyg and Department of Clinical Physiology, Sahlgren's Hospital, University of Goteborg, Sweden

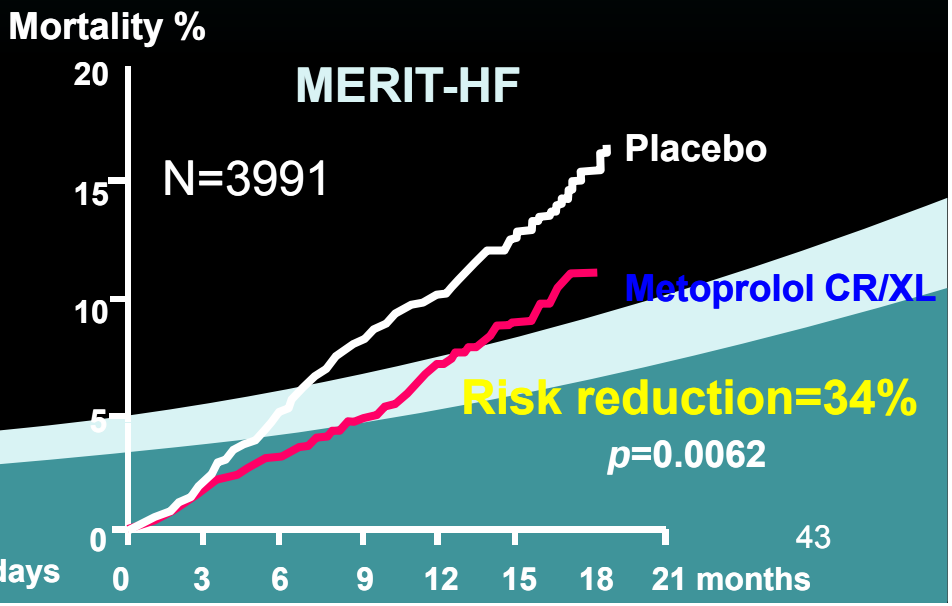
Adrenergic beta-blocking agents were given to 7 patients with advanced congestive cardiomyopathy who had tachycardia at rest (98±13 beats/min). The patients were on beta-adrenergic receptor blockads for 2 to 12months (average 5.4months). One patient was given alprenolol 50mg twice daily and the other patients were given practolol 50 to 400 mg twice daily. Virus infection had occurred in 6 of the patients before the onset of symptoms of cardiac disease. All patients were in a steady state or were progressively deteriorating at the start of beta-adrenergic receptor blockade. Conventional treatment with digitalis and diuretics was unaltered or reduced during treatment with beta-blocking agents. An improvement was seen in their chinical condition shortly after administration of the drugs. Continued treatment resulted in an increase in physical working capacity and a reduction of heart size. Noninvasive investigations including phonocardiogram, carotid pulse curve, apex cardiogram, and echo-cardiogram showed improved ventricular function in all cases. The present study indicates that advenergic beta-blocking agents can improve heart function in at least some patients with congestive cardiomyopathy. Furthermore, it is suggested that increased catecholamine activity may be an important factor for the develop-ment of this disease, as has been shown in animal experiments.

Betablockers in HF: all-cause mortality

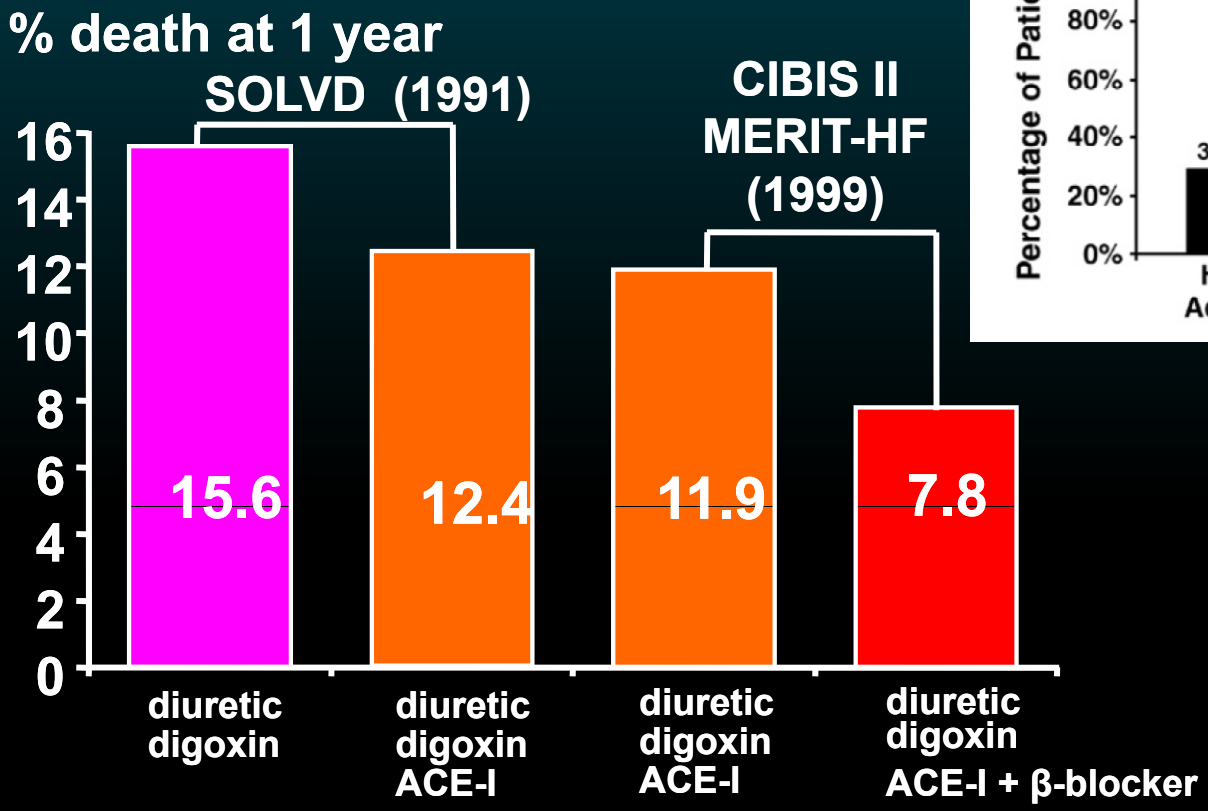






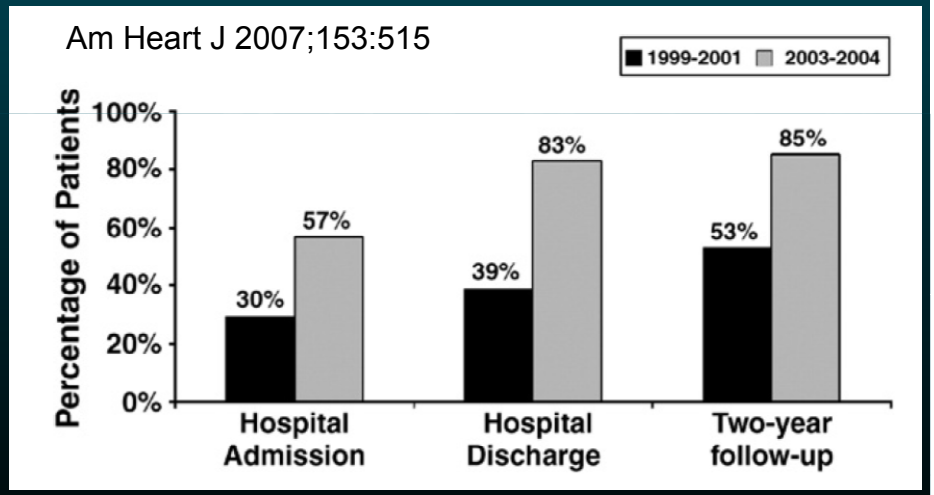


Mortality Benefit of Beta-blockers and ACE-inhibitors in HF trials



McMurray Heart 1999

Am Heart J 2007;153:515

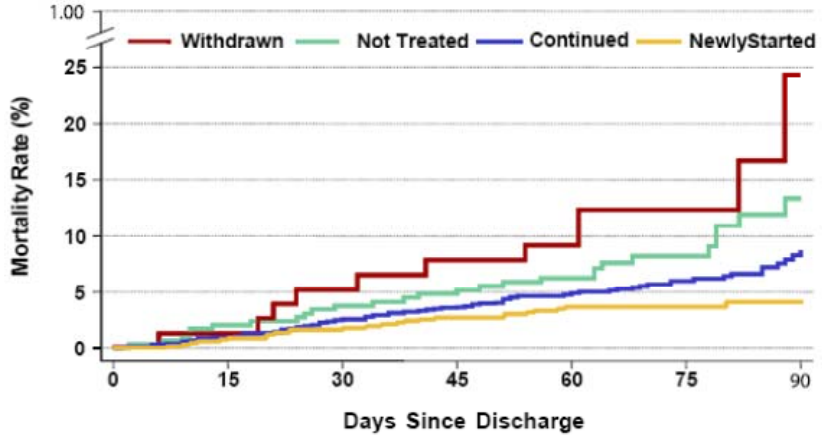


β-blockers in AHF

- Initiate BB Tx in acute de novo HF
  - Who is eligible for BB therapy ?
  - When should be initiated?
  - Which BB is better?
- BB Tx in acute decompensated HF
  - Should we discontinue/reduce BB dose?
  - When can we re-institute?

Influence of Beta-Blocker Continuation or Withdrawal on Outcomes in Patients Hospitalized With Heart Failure

Findings From the OPTIMIZE-HF Program



Patients at risk:

Withdrawn	79	77	73	68	66	26	10
Not Treated	303	275	269	262	242	114	51
Continued	1350	1303	1268	1236	1123	536	224
NewlyStarted	632	609	591	575	531	274	110

Among 2,373 patients eligible for beta-blockers at discharge, there were 1,350 (56.9%) who were receiving beta-blockers before admission and continued on therapy, 632 (26.6%) newly started, 79 (3.3%) in which therapy was withdrawn, and 303 (12.8%) eligible but not treated. Continuation of beta-blockers was associated with a significantly lower risk and propensity adjusted post-discharge death (hazard ratio [HR]: 0.60; 95% confidence interval [CI]: 0.37 to 0.99, p = 0.044) and death/rehospitalization (odds ratio: 0.69; 95% CI: 0.52 to 0.92, p = 0.012) compared with no beta-blocker. In contrast, withdrawal of beta-blocker was associated with a substantially higher adjusted risk for mortality compared with those continued on beta-blockers (HR: 2.3; 95% CI: 1.2 to 4.6, p = 0.013), but with similar risk as HF patients eligible but not treated with beta-blockers.

The continuation of beta-blocker therapy in patients hospitalized with decompensated HF is associated with lower post-discharge mortality risk and improved treatment rates. In contrast, withdrawal of beta-blocker therapy is associated with worse risk and propensity-adjusted mortality. (Organized Program To Initiate Lifesaving Treatment In Hospitalized Patients With Heart Failure [OPTIMIZE-HF]; NCT00344513) (J Am Coll Cardiol 2008; 52:190–9)

B-CONVINCED:

Beta-blocker CONtinuation Vs. INterruption in patients with Congestive heart failure hospitalized for a decompensation episode

In a randomized, controlled, open labelled, non-inferiority trial, we compared beta-blockade continuation vs. discontinuation during ADHF in patients with LVEF below 40% previously receiving stable beta-blocker therapy.

169 patients were included, among which 147 were evaluable. Mean age was 72+12 years, 65% were males.

After 3 days, 92.8% of patients pursuing beta-blockade improved for both dyspnoea and general well-being according to a physician blinded for therapy vs. 92.3% of patients stopping beta-blocker.

Similar findings were obtained at 8 days and when evaluation was made by the patient.

Plasma BNP at Day 3, length of hospital stay, re-hospitalization rate, and death rate after 3 months were also similar.

Beta-blocker therapy at 3 months was given to 90% of patients vs. 76% (P , 0.05)

In conclusion, during ADHF, continuation of beta-blocker therapy is not associated with delayed or lesser improvement,

but with a higher rate of chronic prescription of beta-blocker therapy after 3 months, the benefit of which is well established.

European Heart Journal 2009;30:2186–2192

BETA -BLOCKERS in ADHF

- In patients admitted due to worsening HF, a reduction in β-blocker is necessary.
- In severe situations, temporary discontinuation can be considered.
- Low-dose therapy should be re-instituted and up-titrated as soon as the patients clinical situation permits, preferably prior to discharge.

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The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Systolic Heart Failure

John J.V. McMurray, M.D.

This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.*

A 74-year-old man with a history of hypertension and myocardial infarction that occurred 5 years previously presents with breathlessness on exertion. His current medications include a statin and aspirin. On examination, his pulse is 76 beats per minute and regular, and his blood pressure is 121/74 mm Hg. There is jugular venous distention, lateral displacement of the apex beat, and edema in his lower limbs. The lung examination is normal. An echocardiogram shows left ventricular dilatation, globally reduced contractility, and an ejection fraction of 33%. How should his case be managed?

N Engl J Med 2010;362:228-38.

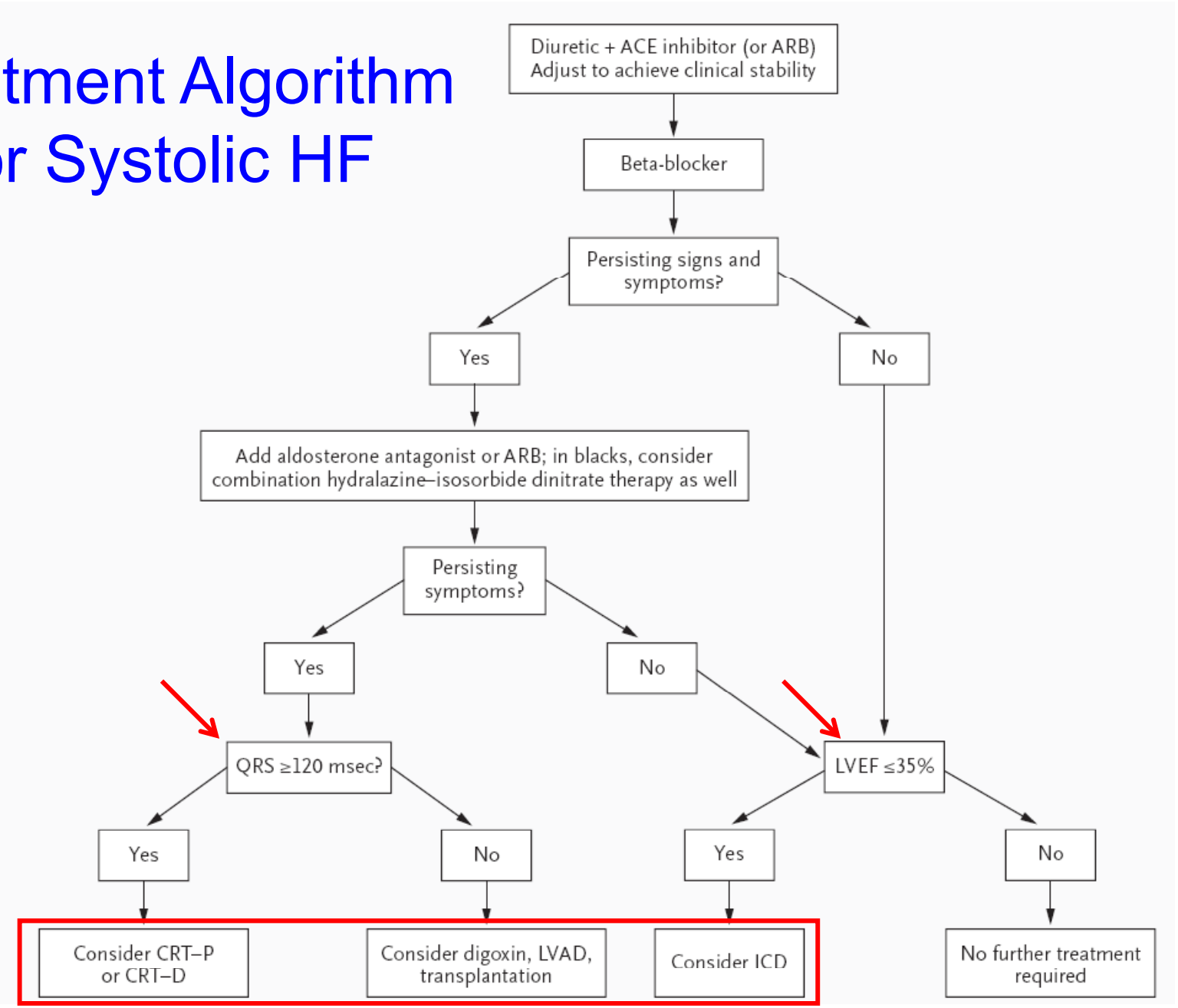
심부전의 단계적 치료 원칙
ACC/AHA Guideline of HF 2009

Stage A	Stage B	Stage C	Stage D
At high risk for HF w/o structural HD or Sx. of HF	Structural HD w/o Sx. of HF	Structural HD with prior or current Sx. of HF	Refractory HF Requiring specialized interventions
- HT, Atherosclerosis - obesity,DM, metabolic - Using cardiotoxins - FHx of CM	- previous MI - LV systolic dysftn - asymptomatic VHD	- known structural HD - SOB, fatigue - exercise intolerance	marked Sx. despite maximal medical Tx. 입원 및 특수 치료가 필요한 경우
- 고혈압 치료 - 금연, 운동, 금주 - 고지혈증 치료 - ACEI / ARB	- As stage A - ACEI / ARB - 베타차단제 - *ICD in case*	- As stage A,B - ACEI/Diuretics/BB - in case Digitalis ARB CRT / ICD Aldosterone blocker Hydralazine/nitrate - *ICD/CRT*	- As stage A, B,C - *Mechanical AD* - *심장이식* - IV inotropics - Hospice care

Prevention of deterioration of myocardial function

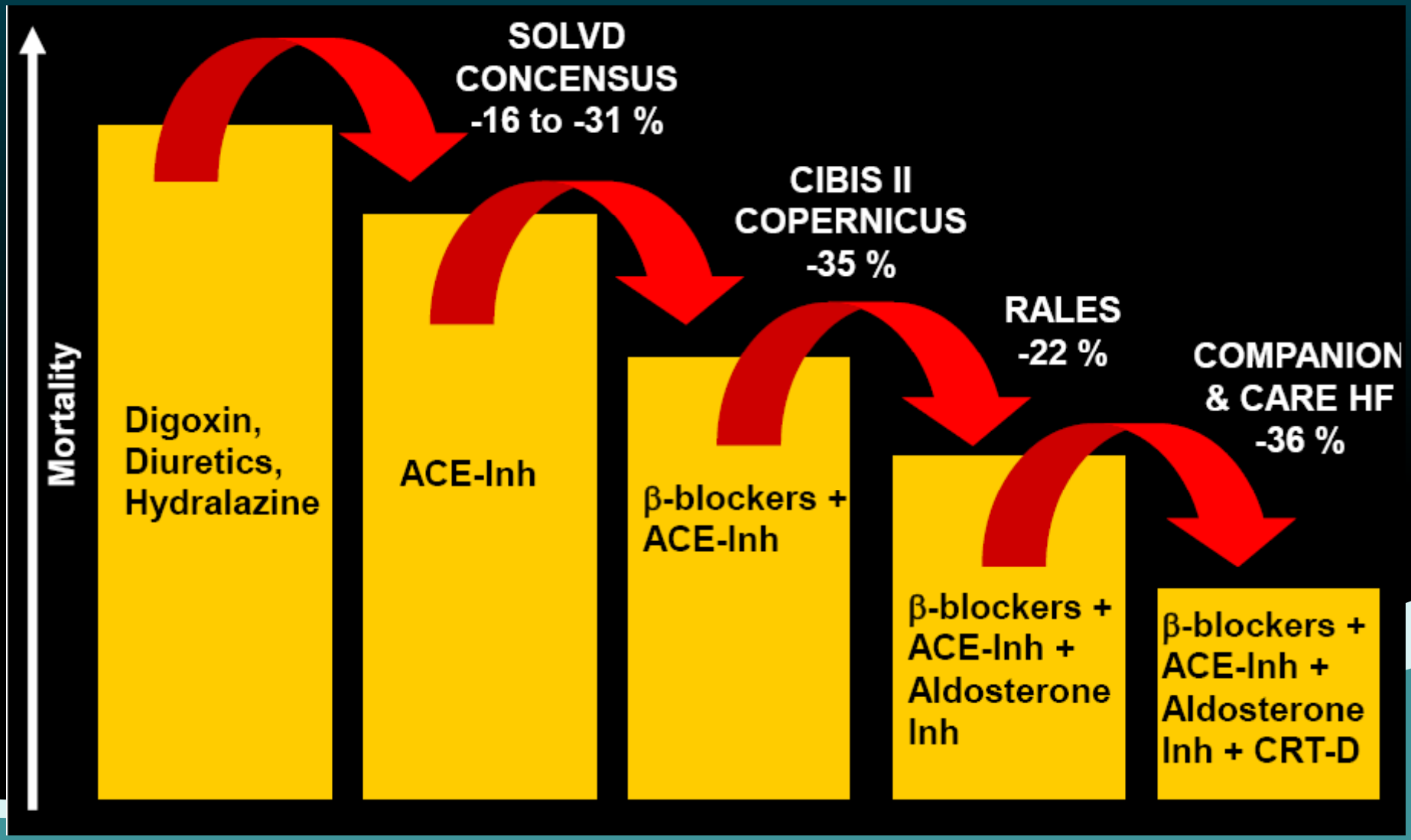
1) Angiotensin-converting enzyme inhibitor (ACEI)
2) Angiotensin receptor (AT1R) antagonist
3) Aldosterone antagonist
4) β–adrenoreceptor blocker
5) Vasodilator in African-American
6) HR reduction: SHIFT trial

Treatment Algorithm for Systolic HF



N Engl J Med 2010; 362:228-238

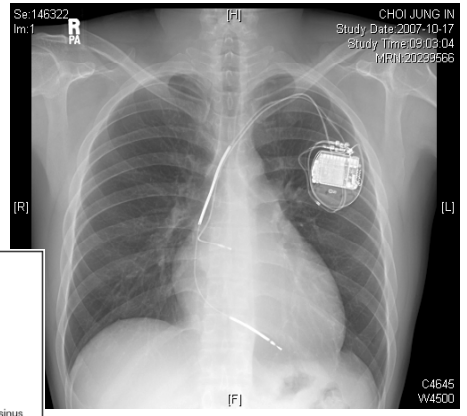
Progression of HF Mx; Add-on Tx

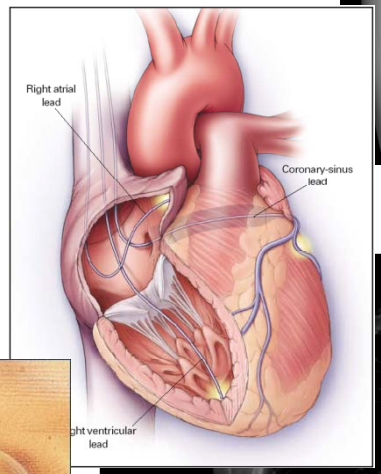


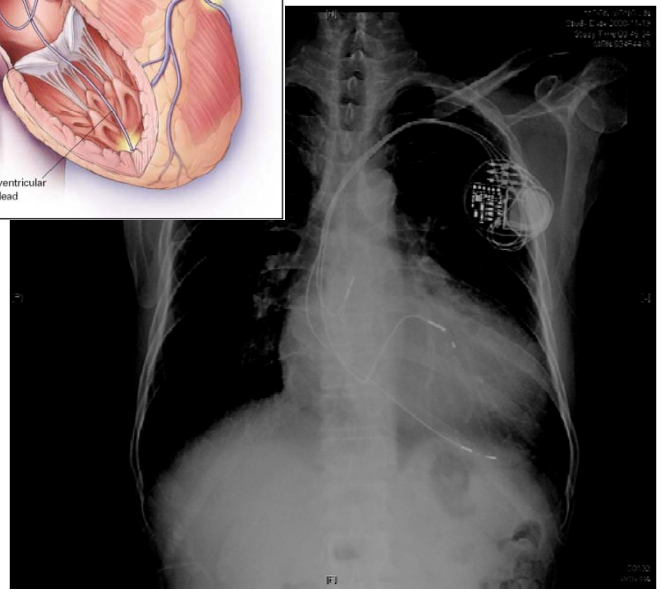
JACC 2005:46;2199-2203

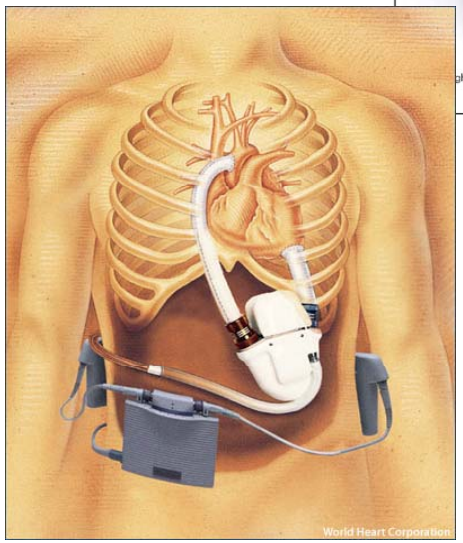
Device Therapy for HF

- Implantable Cardioverter-Defibrillator (ICD)
  - Prevention of SCD
- Cardiac Resynchronization Therapy (CRT)
  - Anti-remodeling therapy
- Ventricular Assist Device (LAD)
  - Reduce mortality
  - Anti-remodeling therapy
- HF monitoring
  - Reduce mortality
  - Reduce morbidity









ICD/CRT Indications: Who has benefit?

	ICD	CRT
Indications	1) primary prevention; EF<35%, NYHA FC II-III 2) 2nd prevention; Survivals from Vf or sustained V-tac regardless LVEF	1) QRS ≥120msec with NYHA FC III-IV, EF ≤35% 2) EF ≤30%, NYHA FC I-II, QRS ≥130 msec
Undefined		1) NYHA I-II with Narrow QRS (<120msec) 2) Atrial fibrillation
Uncertainty	1) LVAD survival at 2 year after implantation 2) STICH trial : CABG with ventricular reconstruction-no benefit 3) CRT-D: no benefit in non-LBBB (MADIT-CRT)	

N Engl J Med 2010; 362:228-238

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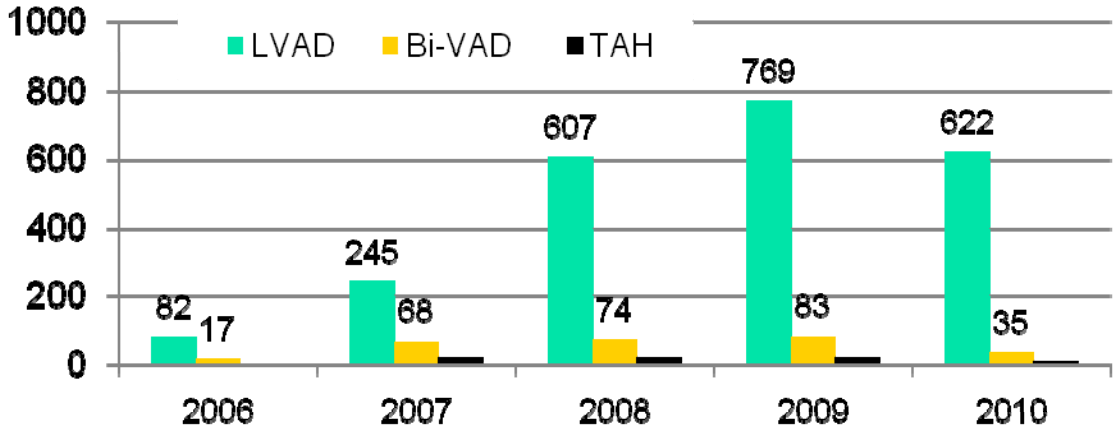
Advance Heart Failure

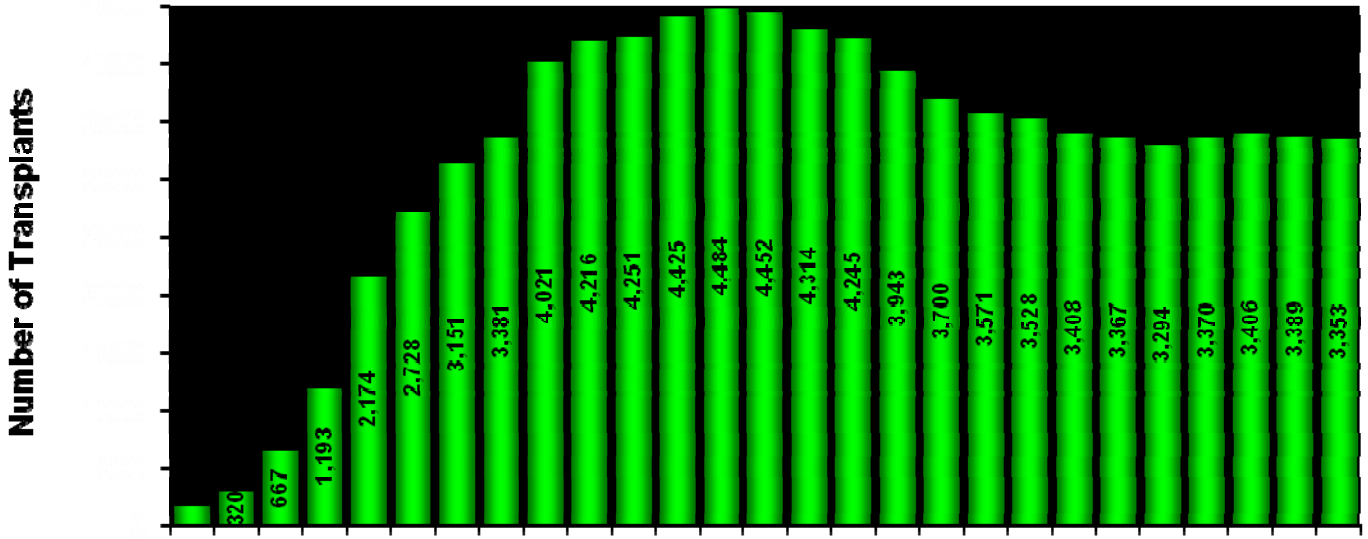
INTERMACS level	Status	Time Frame
1	Critical cardiogenic shock	Hours
2	Progressive decline	Days to week
3	Stable but inotrope dependent	Weeks
4	Recurrent advanced HF	Weeks to few months if baseline restored
5	Exertion intolerant	Weeks to months
6	Exertion limited	Months, if nutrition and activity maintained
7	Advanced NYHA class III	

INETERMACS : Interagency Registry for Mechanical Assist Devices, 2006

MCS as destination therapy



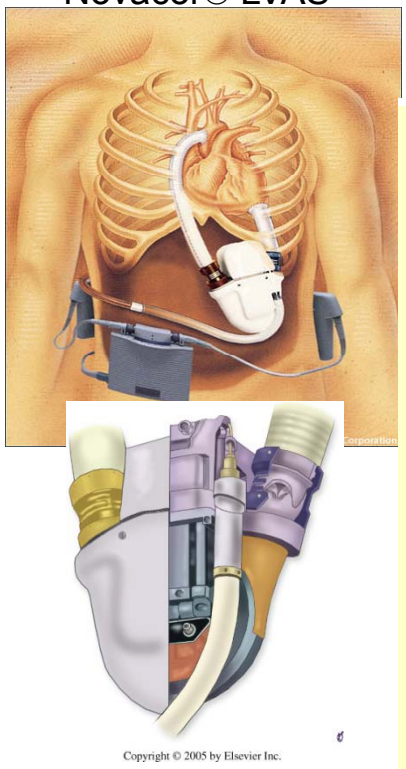
3rd annual report of INTERMACS
J Heart Lung Transpl 2011;30:115-23



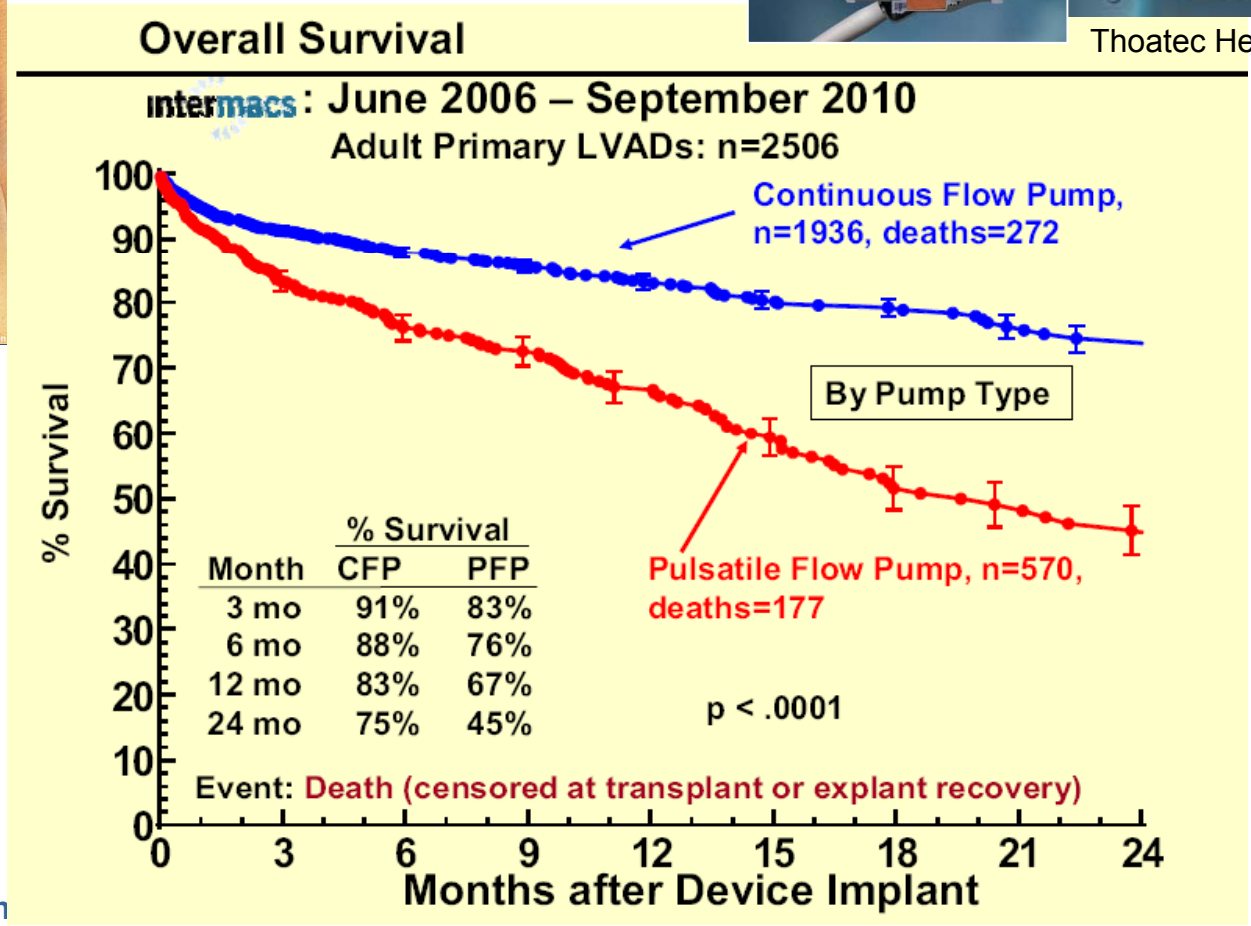
J Heart Lung Transpl 2010 ; 29: 1083-1141

Ventricular Assist Device

Novacor® LVAS

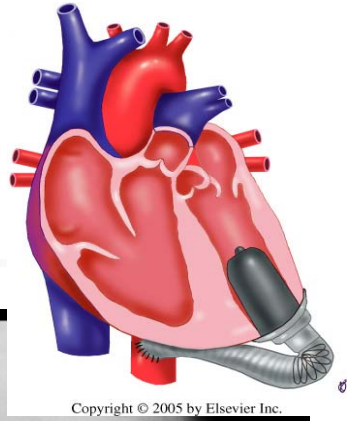


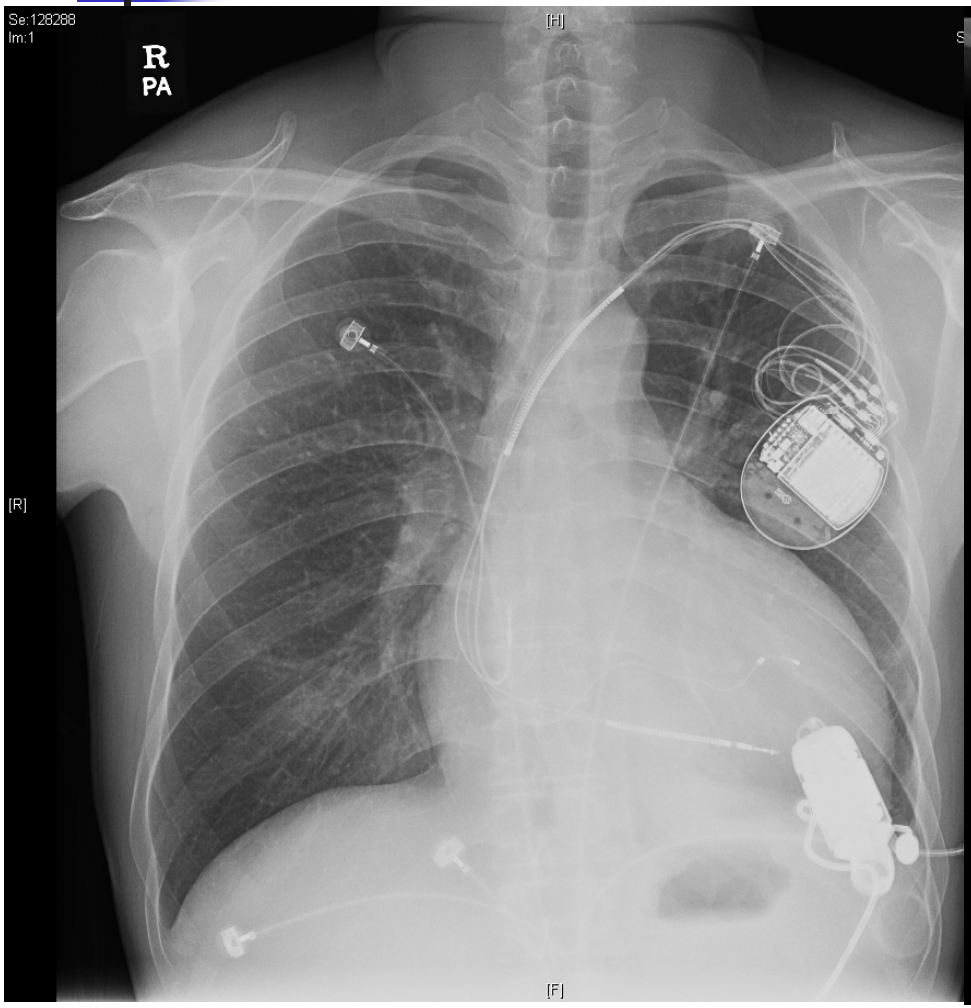
Thoatec Heartmate II

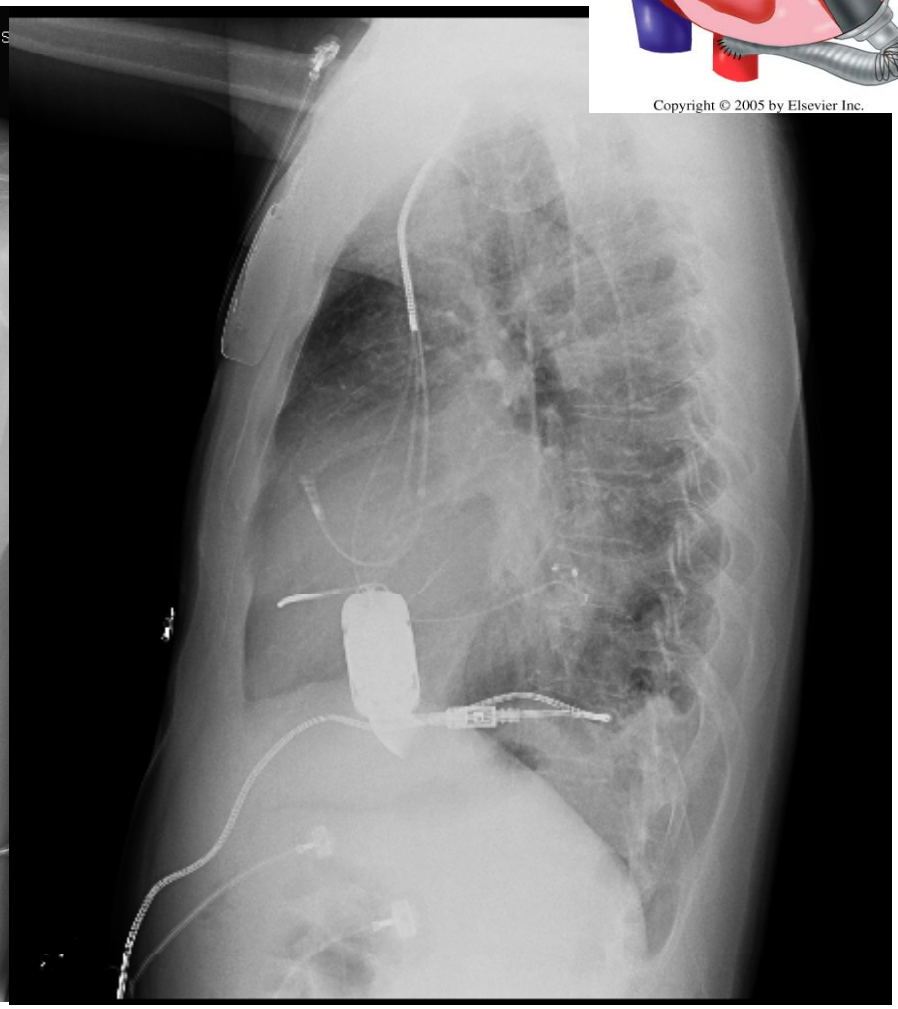


3rd annual report of INTERMACS. J Heart Lung Transpl 2011;30:115-23

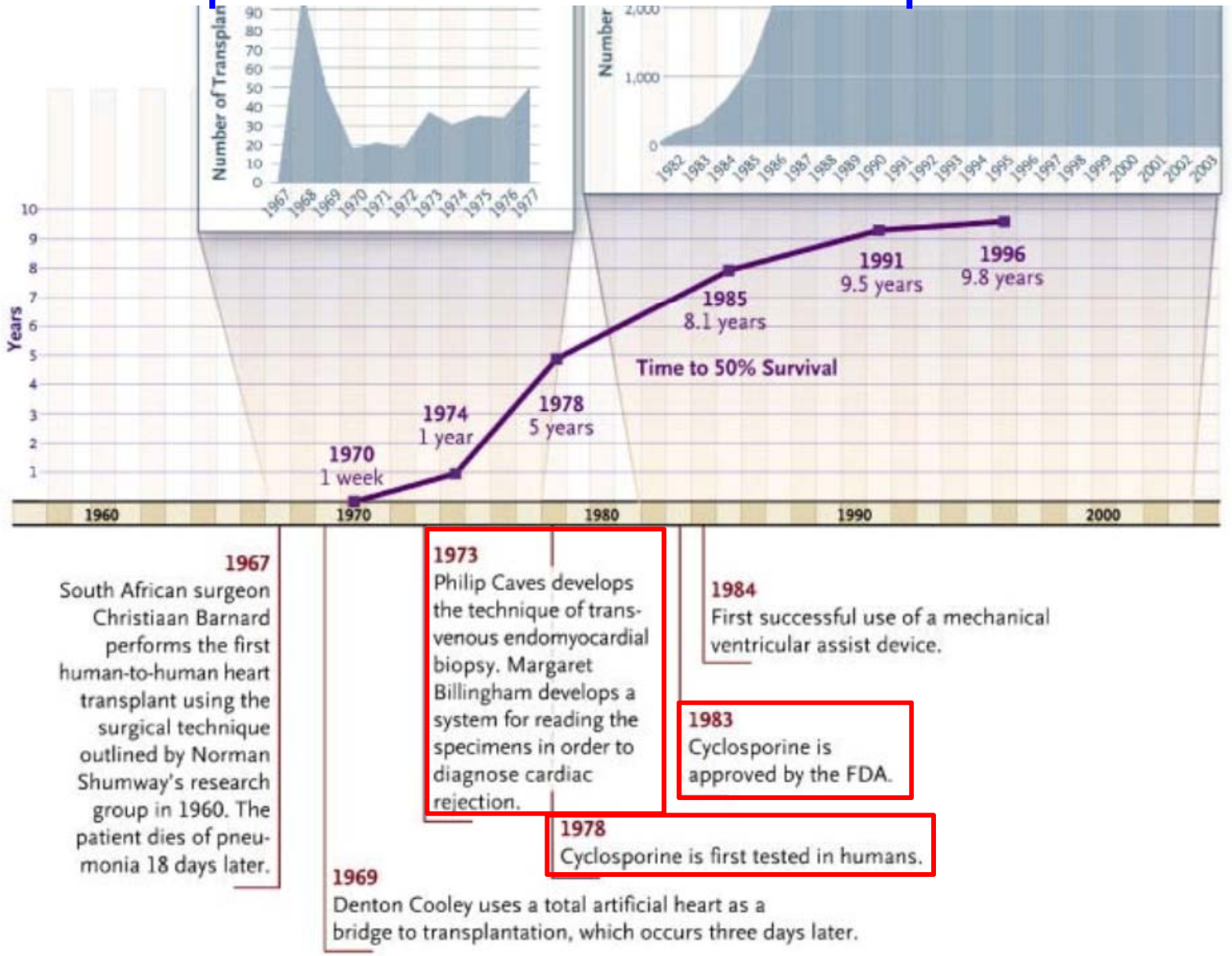
Jarvik 2000 axial flow pump





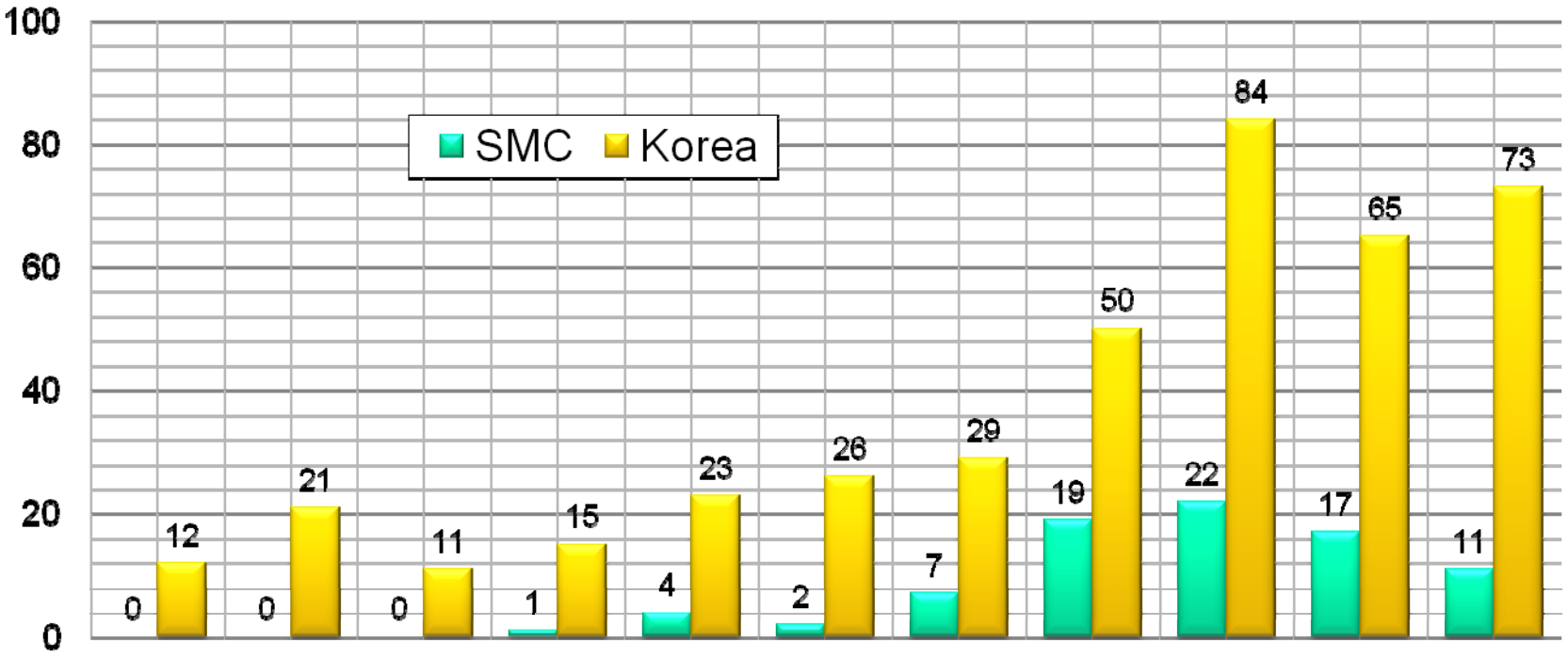


Development of Cardiac Transplantation



Hunt SA, et al. NEJM 2006;355:231-235.

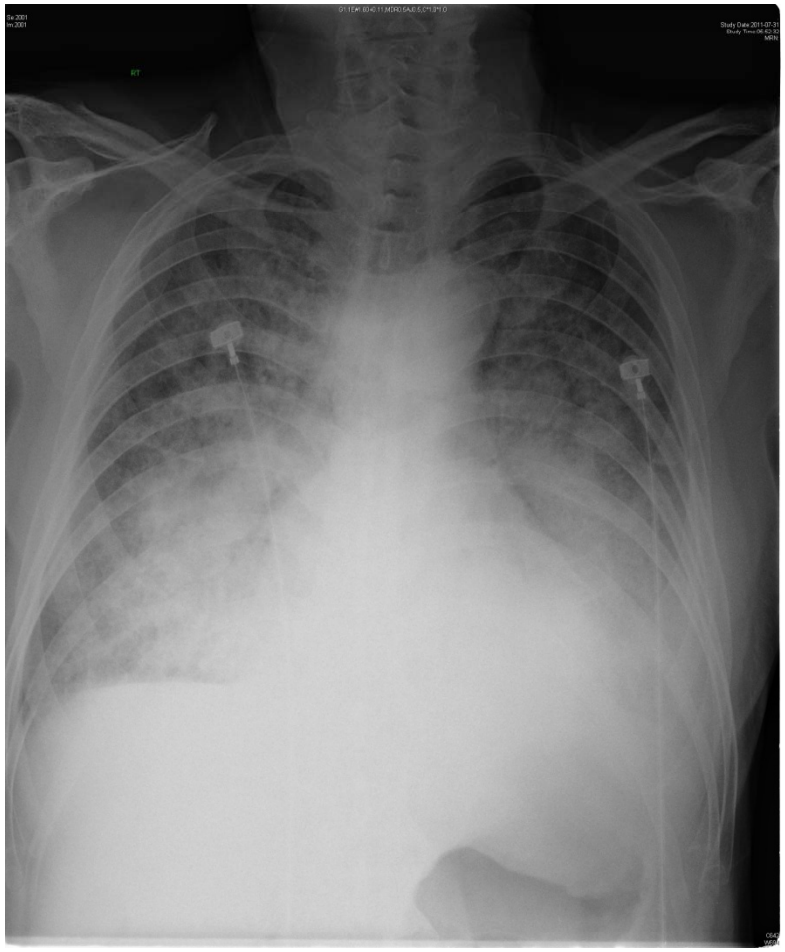
국내 심장 이식 현황

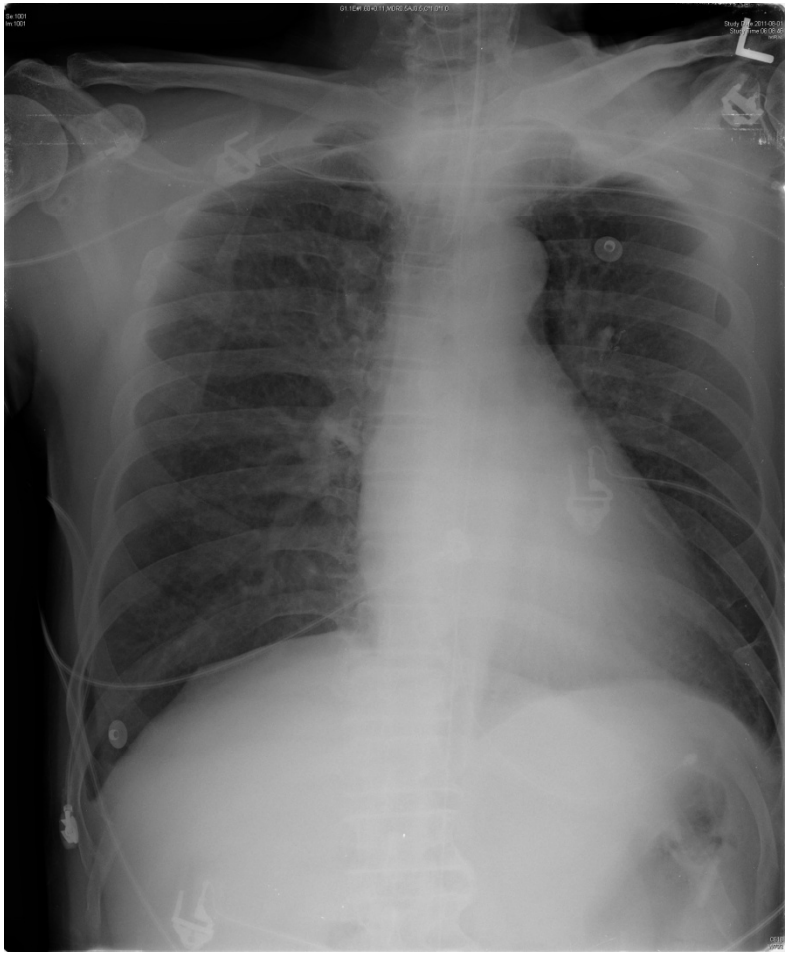


	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010
대기자	70	62	71	81	81	93	91	99	127	138	202


Thanks for
your attention

Case Summary (Hosp # 27392961)





Controversies in AHF Tx

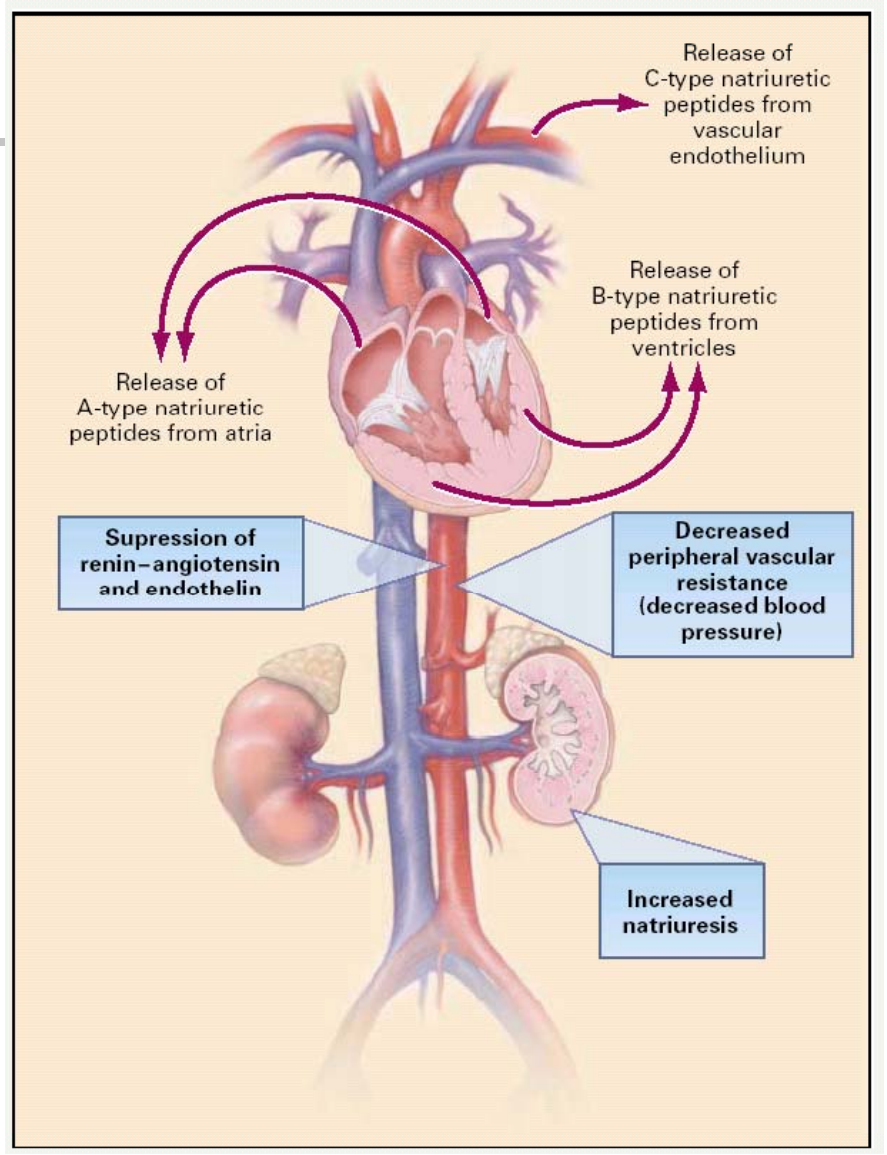
Need for objective, quantitative, reliable and reproducible measure of clinical outcome improvement.

- Mortality in hospital / 30 / 60 days
- Symptoms / QOL / Dyspnea scores
- Hospitalization indexes

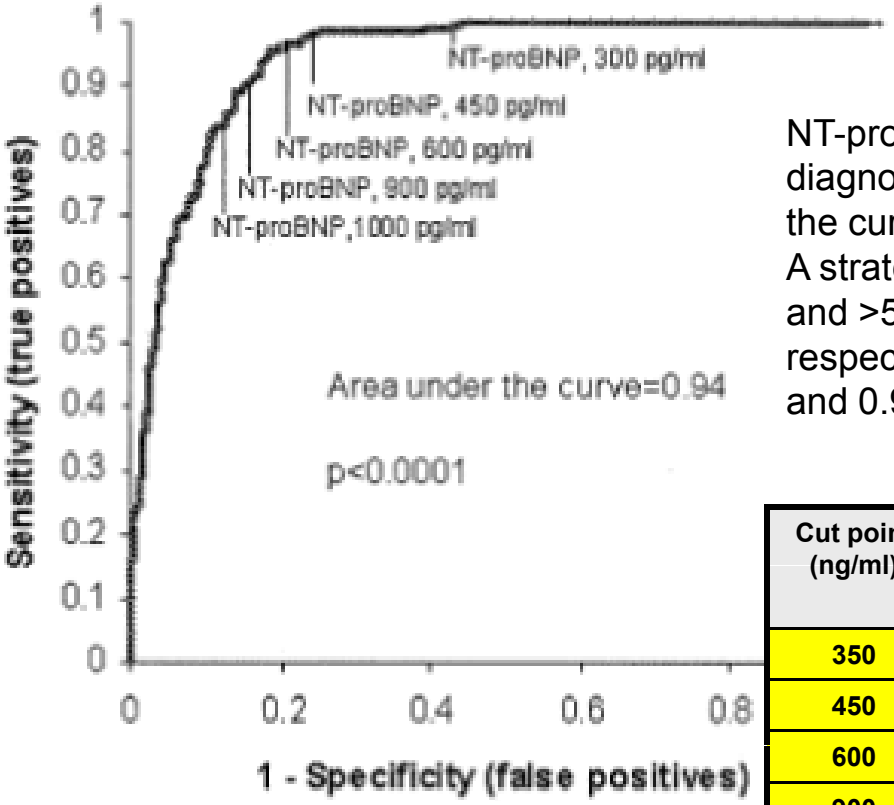
→ NO AGREEMENT

Physiologic Effect

- Natriuresis
- Vasodilatation
- Inhibition of RAA axis
- Inhibition of sympathetic nerve activity



The N-Terminal Pro-BNP Investigation of Dyspnea in the Emergency Department (PRIDE) Study



NT-proBNP was highly sensitive and specific for the diagnosis of acute CHF, with a highly significant area under the curve.

A strategy of partitioning patients in age categories of <50 and >50 years (with cu-tpoints of 450 and 900 pg/ml, respectively) was optimal, with areas under the curve of 0.98 and 0.93, respectively (p <0.0001 for the 2 categories).

Cut point (ng/ml)	Sensitivity (%)	Specificity (%)	Positive predictive value(%)	Negative predictive value(%)	Accuracy (%)
350	99	68	62	99	79
450	98	76	68	99	83
600	96	81	73	97	86
900	90	85	76	94	87
1000	87	86	78	91	87

Januzzi Jr et al AM J Cardiol 2005;95:948

Clinical Data of Omecamtiv mecarbil

- **A phase IIa double-blind**, randomized, placebo-controlled Study evaluated the safety and tolerability of CK-1827452
  - intravenous infusion in 28 patients
  - with LVEF <40% + ACEI or ARB + BB ± diuretics

- CK-1827452 significantly increased systolic ejection time and fractional shortening at plasma concentrations greater than 100 ng/mL,
- Increased stroke volume at concentrations greater than 200 ng/mL
- cardiac output at greater than 300 ng/mL.
- At plasma levels greater than 400 ng/mL, increases in stroke volume and cardiac output appeared to plateau in association with a concentration-dependent decline in heart rate.

- Statistically significant correlation concentration dependence was observed for increases in systolic ejection time, stroke volume, fractional shortening and ejection fraction and for decreases in heart rate and LV end systolic volume.

CV and Heamatol Dis-Drug Targets 2009:9:193-205