COPD
Common disease associated with HF

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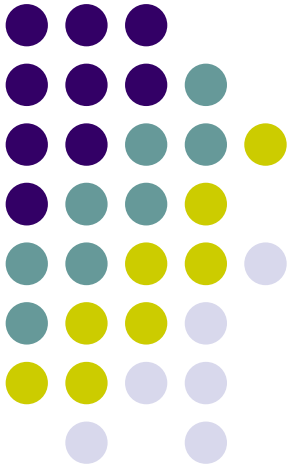
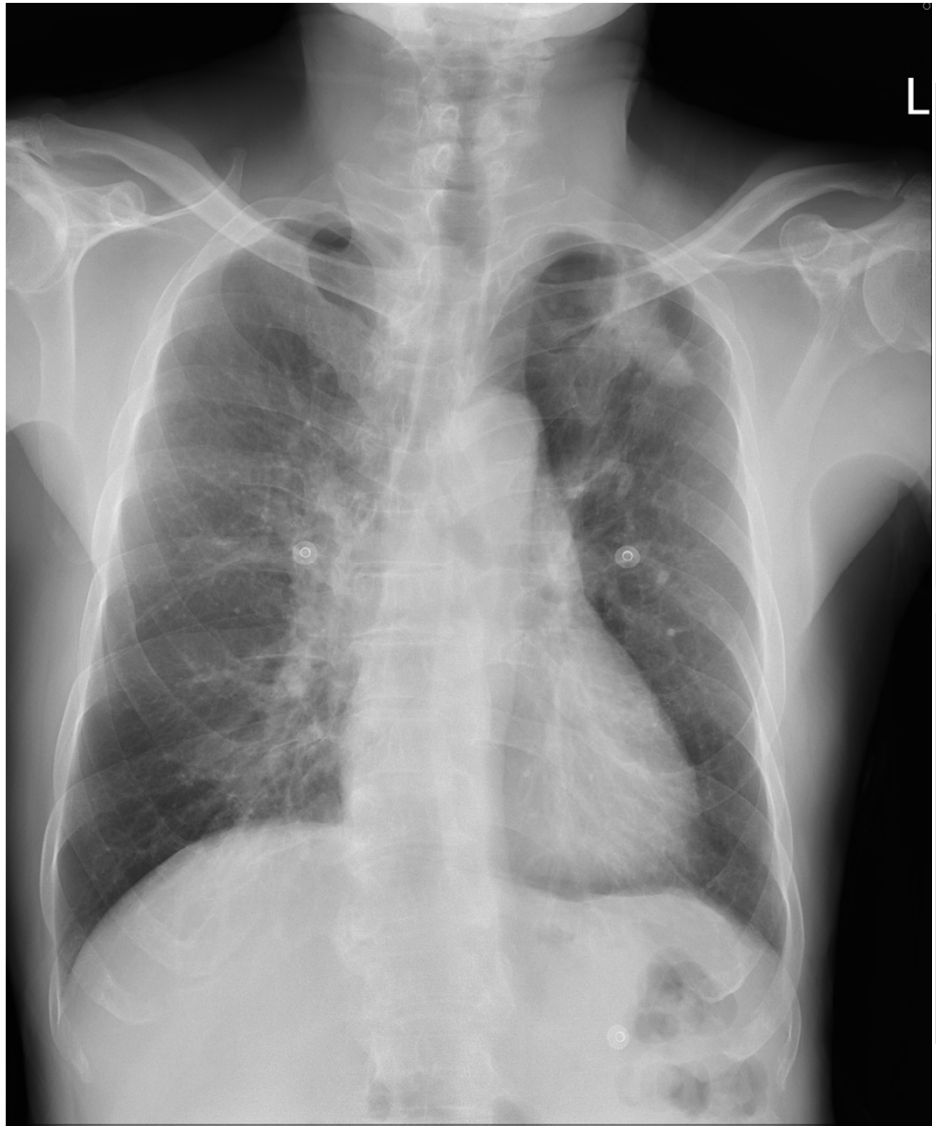
양 동 헌

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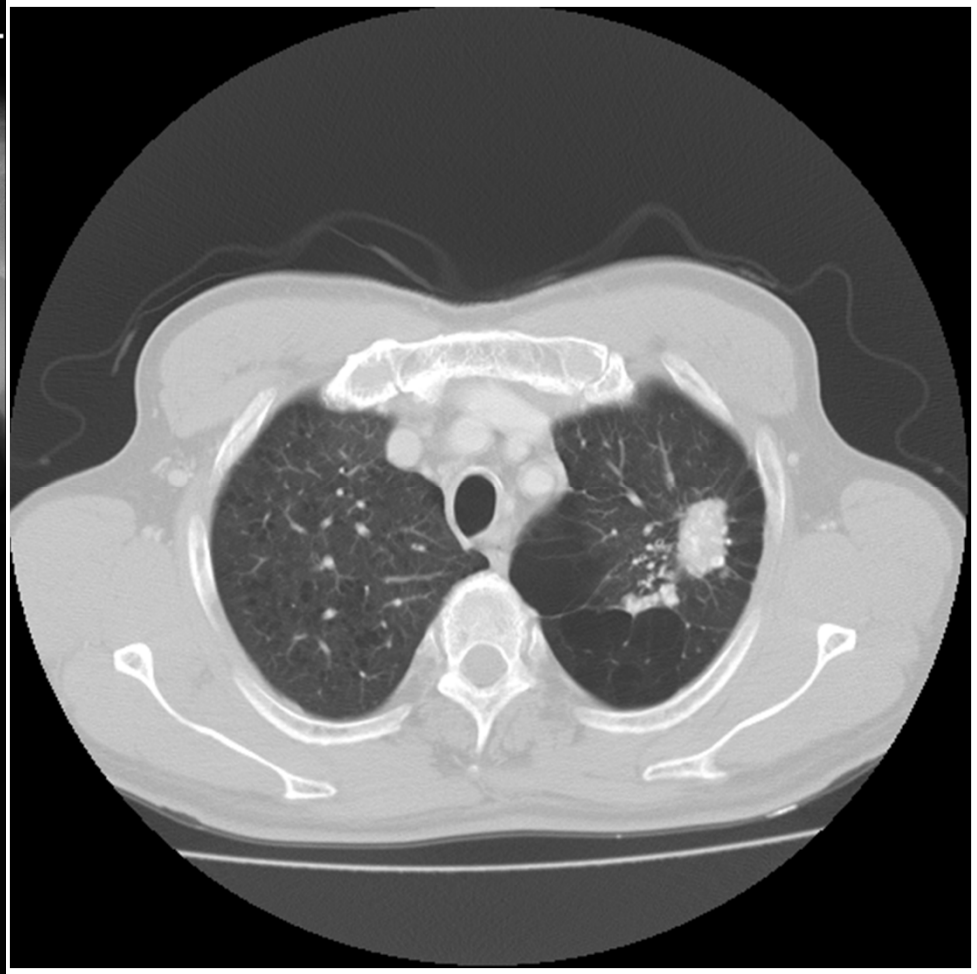
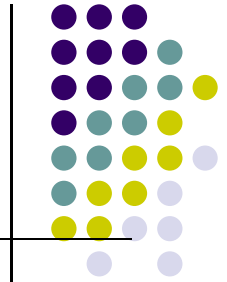


호흡기 내과 vs 순환기 내과

Sliding doors concept



Male patient, age 70y, with DOE

Depending on whether the patient first sees:

Pulmonologist

procalcitonin
Chest x-ray / CT
PFT

Bronchodilator
antibiotics

Cardiologist

BNP/NTproBNP
ECG
Echocardiography

HF treatment

Sliding doors concept

Male patient, age

Depending on whether

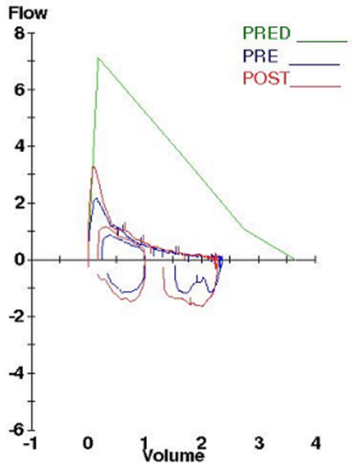
Pulmonologist

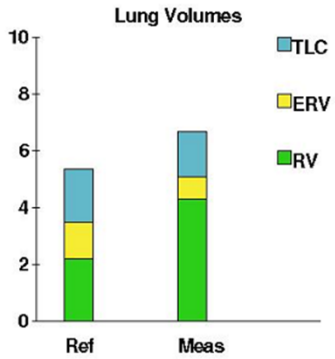
CRP 46.5mg/L
PCT 9.4ng/L

procalcitonin
Chest x-ray / CT
PFT

Bronchodilator
antibiotics

Spirometry		Ref	Pre	% Ref	Post	% Ref	%Chg
FVC	Liters	3.65	2.37	65	2.29	63	-3
FEV1	Liters	2.51	0.96	38	1.00	40	3
FEV1/FVC	%	70	41		44		
FEF25-75%	L/sec	2.46	0.31	13	0.36	15	17
FEF75-85%	L/sec	0.47	0.13	28	0.14	29	2
FEF25%	L/sec		1.04		0.89		-15
FEF50%	L/sec	3.29	0.37	11	0.39	12	7
FEF75%	L/sec	1.08	0.18	17	0.17	15	-10
FEF200-1200	L/sec	5.85	0.68	12	0.69	12	1
PEF	L/sec	7.11	2.16	30	3.31	47	53
FET25-75%	Sec	0.54	3.84	711	3.17	587	-17
FET100%	Sec		11.31		13.28		17
FEF/FIF50			0.42		0.26		-38

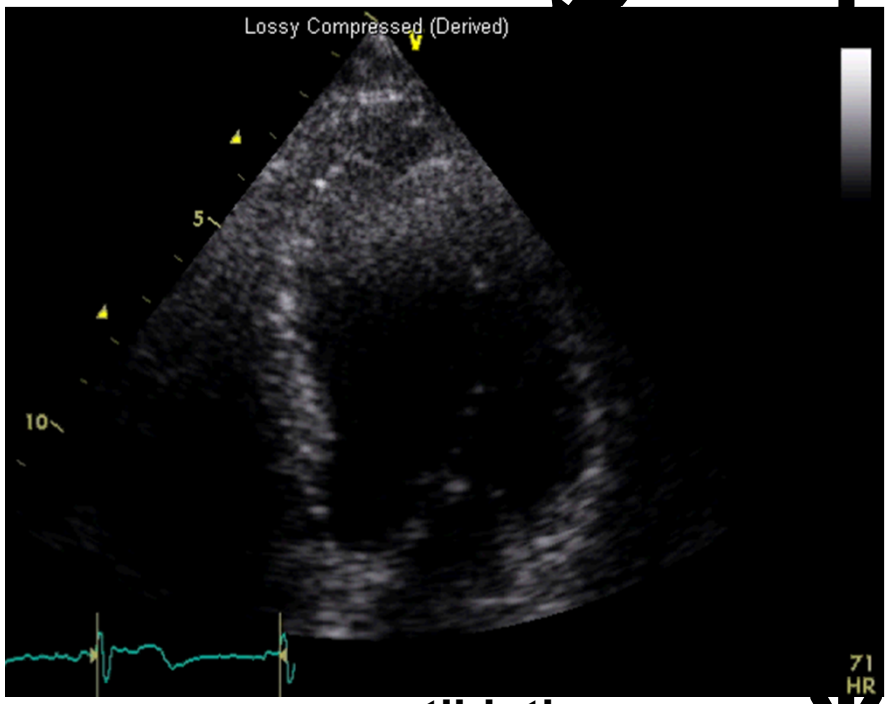




Sliding doors concept

Male patient, age 70y, with DOE

Depending on whether the patient first sees:



antibiotics

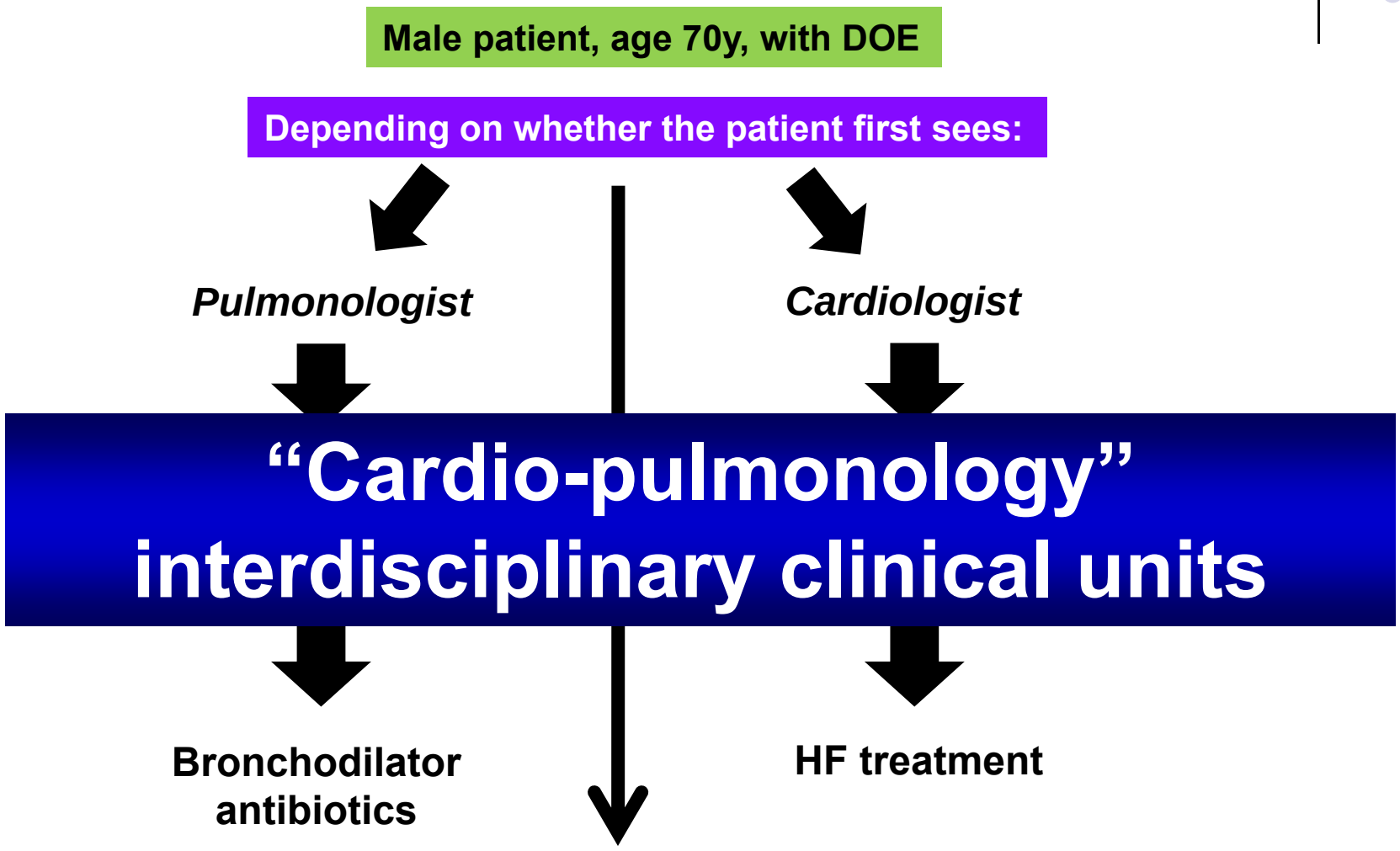
Cardiologist

NTproBNP 1347pg/mL
TnI 0.13ng/mL

BNP/NTproBNP
ECG
Echocardiography

HF treatment

Sliding doors concept



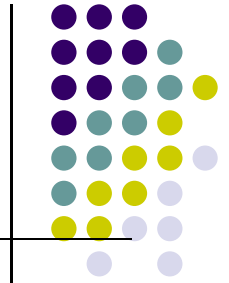
COPD and HF

- Prevalence
  - COPD : 14 million Americans
  - CHF : 5 million
- Tobacco as a common risk factor
  - Coexistance of COPD and HF
- COPD in patients with CHF
  - The one that most delays the diagnosis of CHF
  - Cause of nonadherence to therapeutic guidelines, especially beta-blockade

Comorbidity in HF

Variable	1988-1994 (n = 581)	1999-2002 (n = 280)	2003-2008 (n = 534)	Change, 1988-2008 (95% CI)	*P* Value
MI	58.8 (3.3)	46.5 (3.3)	47.7 (3.1)	−11.2 (−20.3-−2.0)	.02
Angina	NA[b]	38.7 (3.8)	26.9 (2.7)	−11.9 (−12.1-−2.6)[c]	.01[c]
Stroke	17.6 (2.1)	16.6 (2.6)	19.4 (2.4)	1.8 (−4.8-8.4)	.59
Diabetes[a]	24.7 (2.7)	29.3 (2.9)	38.3 (2.3)	13.6 (6.4-20.7)	<.001
Blood pressure (BP)					
Hypertension[a]	67.8 (2.5)	71.2 (3.7)	73.3 (2.2)	5.5 (−1.1-12.1)	.10
Systolic BP (mm Hg)	141.7 (1.1)	131.7 (1.8)	130.6 (1.3)	−11.2 (−14.5-−7.8)	<.001
Diastolic BP (mm Hg)	73.1 (1.1)	66.9 (1.5)	65.9 (0.7)	−7.2 (−9.9-−4.5)	<.001
Cholesterol					
Hypercholesterolemia[a]	41.3 (3.0)	49.3 (3.9)	53.5 (2.8)	12.2 (5.0-19.4)	.001
LDL cholesterol[d] (mg/dL)	139.2 (3.1)	116.7 (5.1)	105.3 (4.6)	−33.9 (−44.9-−22.8)	<.001
HDL cholesterol <40 mg/dL	35.1 (2.9)	34.0 (3.8)	25.8 (2.2)	−9.2 (−16.6-−1.8)	.02
Obesity					
Obesity[a]	32.8 (2.5)	40.3 (4.7)	46.8 (2.5)	13.9 (7.5-20.4)	<.001
BMI (kg/m^2)	28.3 (0.3)	30.0 (0.8)	31.1 (0.4)	2.8 (1.8-3.7)	<.001
Waist circumference (cm)					
Women	95.9 (1.2)	102.6 (1.9)	105.5 (1.2)	9.6 (6.1-12.1)	<.001
Men	102.0 (1.0)	105.1 (1.2)	109.2 (1.4)	7.2 (3.7-10.7)	<.001
High-risk waist circumference[a]	57.6 (3.4)	73.0 (2.9)	75.7 (2.7)	18.0 (8.5-27.6)	<.001
Kidney function					
Kidney disease[a]	34.7 (2.9)	41.2 (3.6)	45.9 (2.1)	11.2 (4.2-18.3)	.002
Creatinine (mg/dL)	1.10 (0.06)	1.29 (0.09)	1.23 (0.04)	0.13 (0.00-0.26)	.06
Creatinine >2 mg/dL	4.6 (1.8)	6.9 (1.8)	7.4 (1.0)	2.8 (−1.2-6.7)	.17
Anemia[a]	15.3 (2.7)	15.0 (1.8)	22.2 (2.7)	6.9 (−0.6-14.5)	.07
Asthma	18.0 (2.5)	16.8 (2.7)	24.6 (1.9)	6.6 (0.3-12.9)	.04
Arthritis	60.4 (2.9)	68.5 (3.3)	62.0 (2.4)	1.6 (−5.4-8.6)	.65
COPD	26.2 (2.8)	26.8 (2.9)	30.9 (2.3)	4.8 (−2.5-12.1)	.20
Cancer	21.5 (2.5)	29.3 (2.8)	24.4 (2.0)	2.9 (−3.6-9.4)	.38
Thyroid disease	9.9 (1.5)	15.2 (2.8)	22.9 (1.9)	13.0 (8.3-17.7)	.001
Osteoporosis	4.9 (1.2)	13.6 (3.1)	16.4 (2.5)	11.5 (5.9-17.1)	.001

COPD in HF



- Prevalence of COPD in HF
  - North American : 11 – 52%
  - European cohorts : 9 – 41%

  - Population age, sex
  - Risk factors : smoking
  - Urban vs Rural area
  - Awareness
    - 219 patients with both HF and COPD
      - 82% echocardiography vs 36% PFT

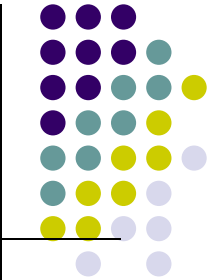
Risk of HF in COPD

- **Prevalence of CHF in pt with COPD: 20-30%**

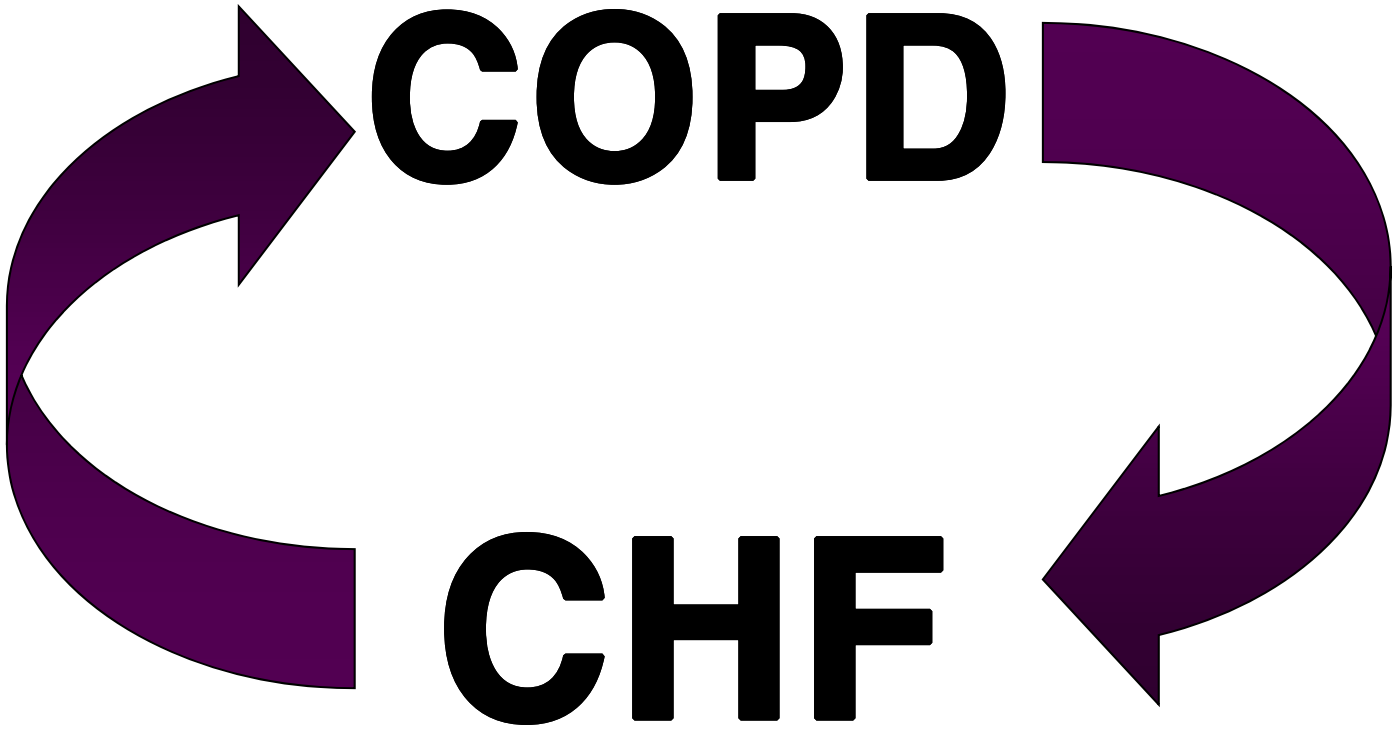
TABLE 6. Risk ratios of incidence of hospitalization and mortality due to cardiovascular causes,* Saskatchewan COPD study, 1998–2001

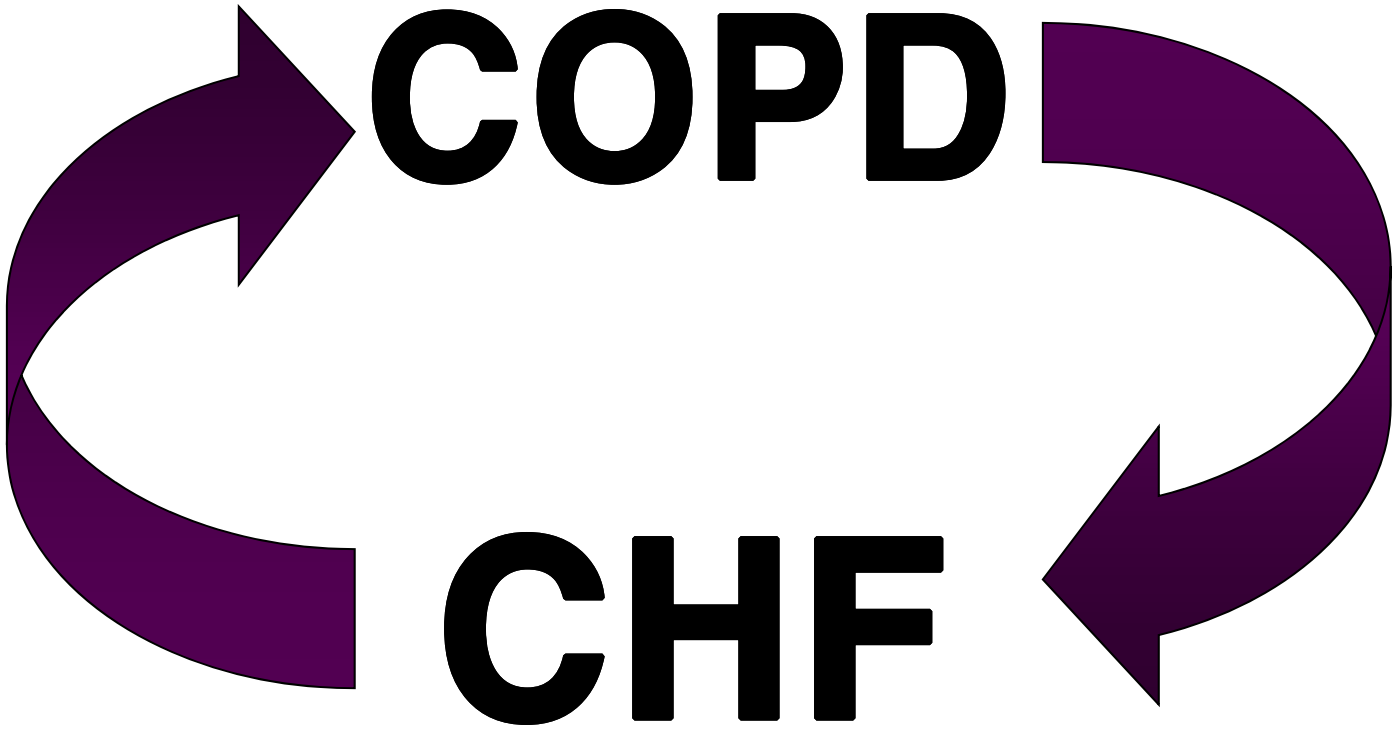
	COPD patients (n = 11,493)	Matched controls (n = 22,986)		
	Event /1000 person-years	Event/1000 person-years	Risk ratio (95% CI)	Adjusted risk ratio (95% CI)†
Cause of hospitalization				
Arrhythmia	16.44	8.18	2.01 (1.68, 2.41)	1.67 (1.27, 2.22)
Angina	6.02	2.34	2.57 (1.87, 3.53)	2.08 (1.52, 2.86)
Acute myocardial infarction	10.86	6.56	1.66 (1.34, 2.05)	1.49 (0.71, 3.13)
Congestive heart failure	31.96	6.10	5.24 (4.42, 6.20)	3.45 (2.78, 4.17)
Stroke	12.44	9.77	1.27 (1.05, 1.54)	1.23 (0.68, 2.22)
Pulmonary embolism	1.72	0.31	5.52 (2.64, 11.51)	4.76 (0.79, 25.00)
Any cardiovascular hospitalization	109.50	44.66	2.45 (2.27, 2.65)	2.17 (2.00, 2.33)
Any Hospitalization	598.36	221.23	2.70 (2.60, 2.82)	2.50 (2.38, 2.63)
Underlying cause of death				
Arrhythmia	1.94	0.69	2.81 (1.59, 4.98)	N/A
Acute myocardial infarction	5.89	3.90	1.51 (1.14, 2.01)	N/A
Congestive heart failure	4.10	1.00	4.09 (2.64, 6.33)	N/A
Stroke	4.17	3.37	1.24 (0.90, 1.71)	N/A
Pulmonary embolism	0.33	0.15	2.23 (0.60, 8.23)	N/A
Any cardiovascular mortality	31.89	15.39	2.07 (1.82, 2.36)	N/A
Any mortality	106.58	37.79	2.82 (2.61, 3.05)	N/A

COPD as a CVD risk



- COPD is an independent risk factor of mortality and CV comorbidity in HF
  - FEV1 : good predictor of CV mortality as serum cholesterol
- Smoking
- CRP 증가 (2.18-2.74 배)
  - role in pathogenesis of atherosclerosis
- LV systolic dysfunction


COPD
CHF


COPD
CHF

COPD 환자에서 심부전 진단

- **Diagnostic Difficulties**
  - **similar in symptoms and physical findings**

1. CXR:

less sensitive

CT ratio is adversely affected by hyperinflated lung

LV dilatation is masked by RV enlargement

Pulmonary congestion (even pulmonary edema) can be present in COPD

2. EKG abnormality: overlap with those seen in HF

3. BNP/pro-BNP: helpful

4. Echo / Cardiac MRI

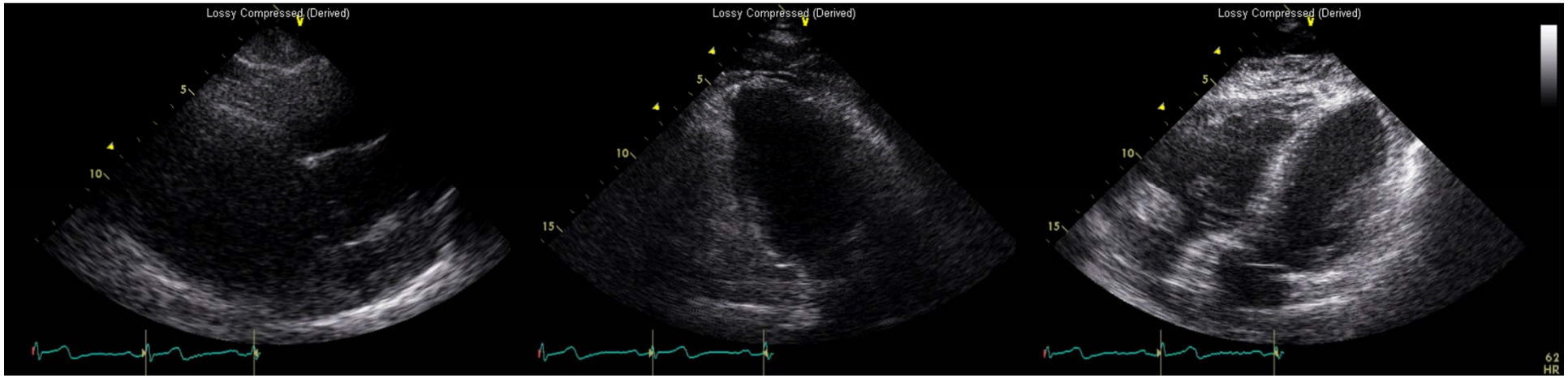
Diagnostic Difficulties

- **Chest X-ray**
  - **Chest hyperinflation → cardiothoracic ratio↓**
  - **Pulmonary vascular remodelling and radiolucent lung fields mask the typical alveolar shadowing of pulmonary edema.**
  - **pulmonary congestion (even pulmonary edema) can be present in COPD**
  - **LV dilatation is masked by RV enlargement**
  - **Emphysematous vascular bed loss**

    → upper lobe venous diversion, mimicking HF

Diagnostic Difficulties

- Echocardiography
  - poor acoustic windows
  - unsatisfactory in 10.4% of patients with COPD
  - 35% in patients with severe COPD
  - Contrast echo

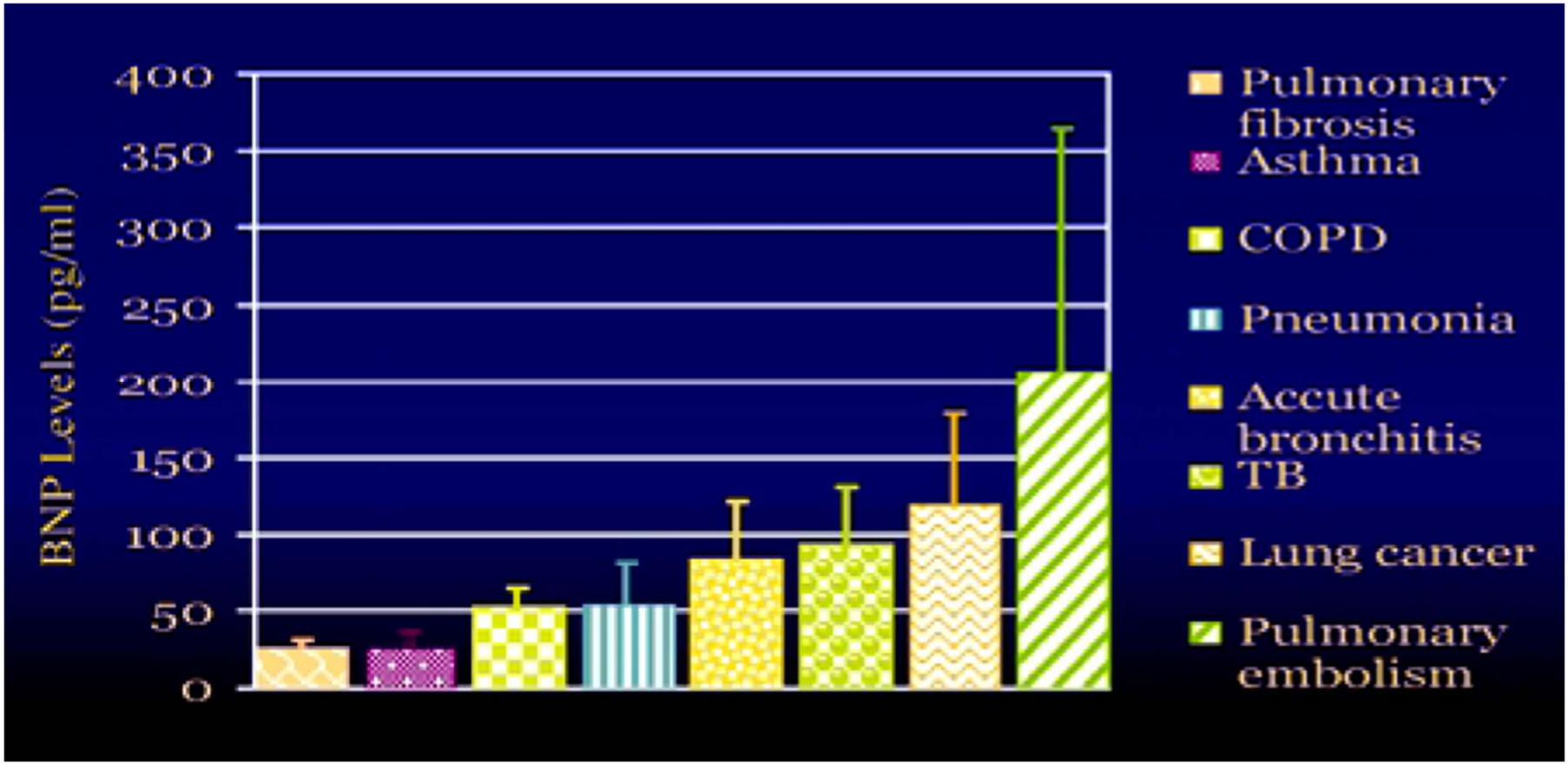


Diagnostic Difficulties

- Cardiac MRI
  - standard for measuring LV volumes and ejection fraction
  - precise quantification of RV volumes, function, and transvalvular flow,
  - Difficulties in breathing holding

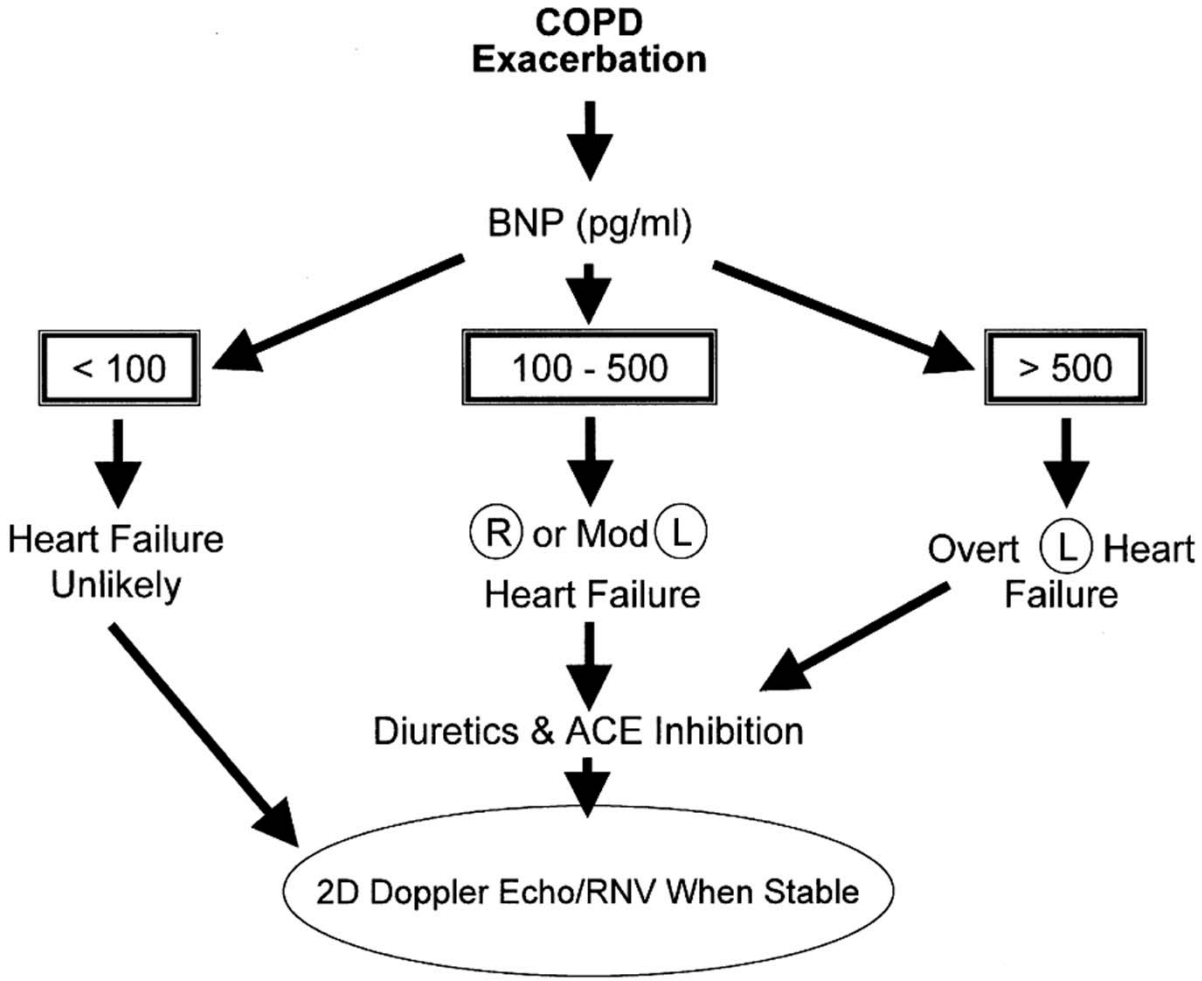
Diagnostic Difficulties

- **Natriuretic peptides**

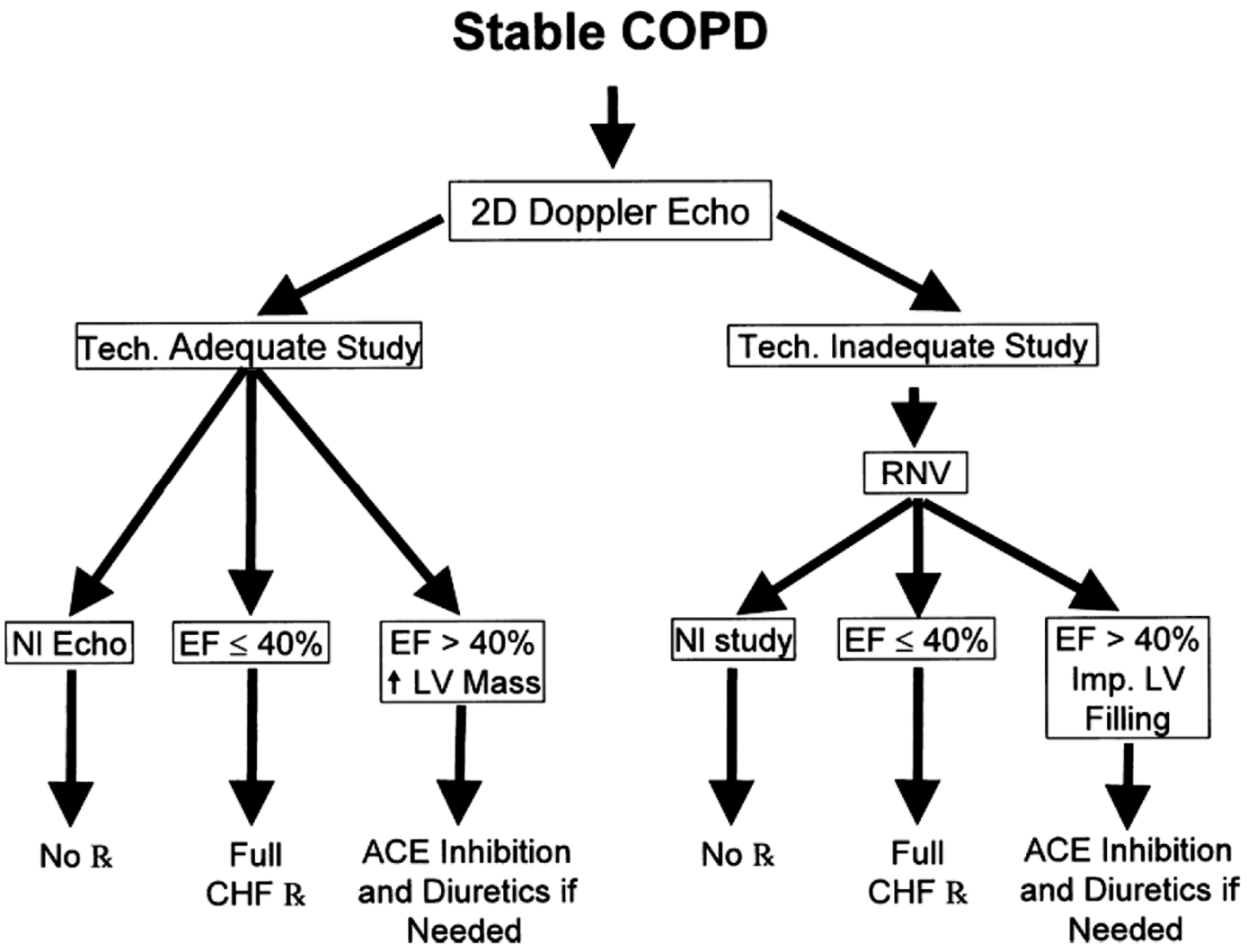


Diagnostic Difficulties

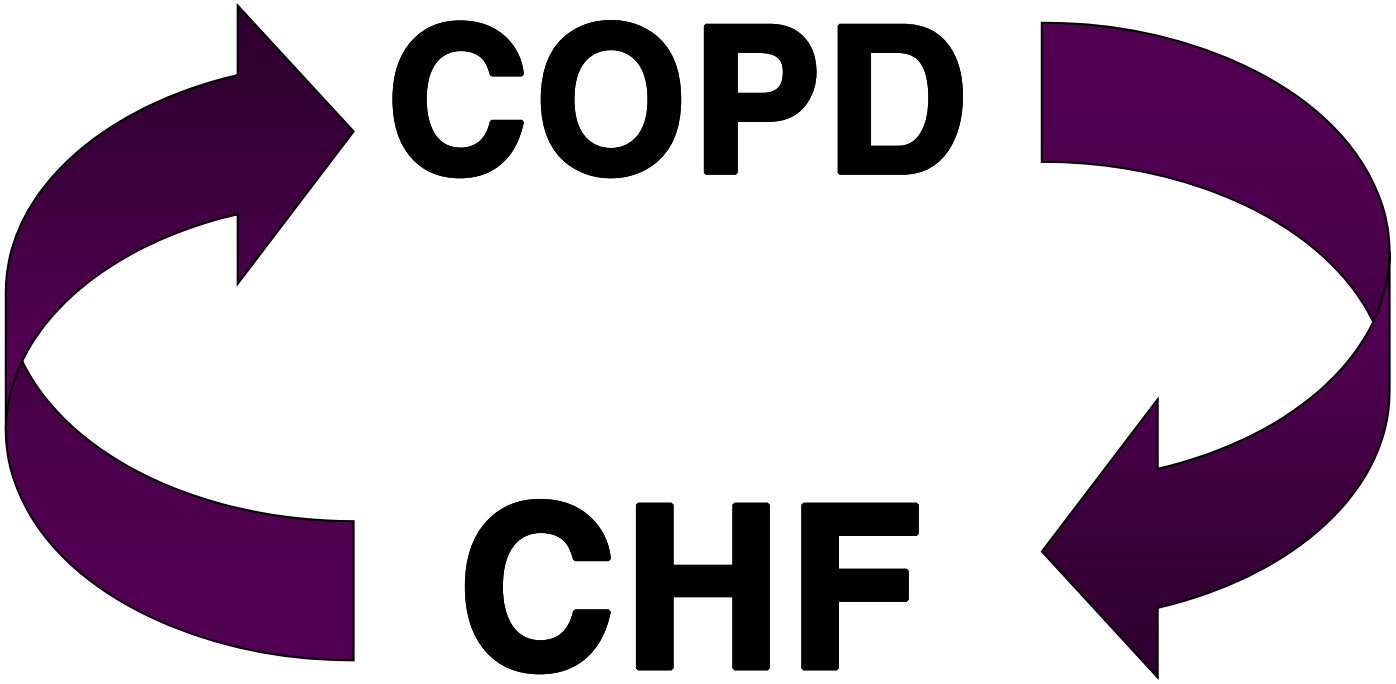
- **Natriuretic peptides**



HF in stable COPD

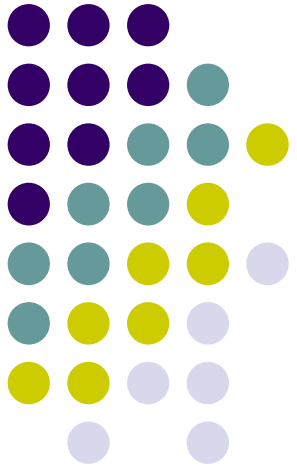


Therapeutic implications



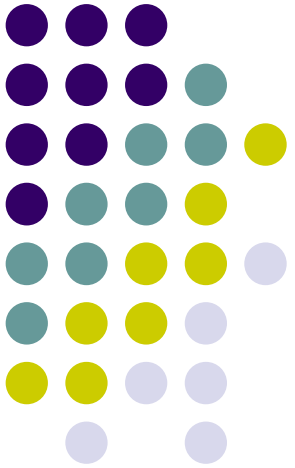
Therapeutic implications

- Pulmonary medication influencing cardiac function
- CV medication influencing pulmonary function



Pulmonary medication influencing cardiac function

1. β2 receptor agonist
2. Anticholinergics



β2-receptor agonist

- β2 agonist - not highly selective

  → activation of β1-receptor in myocardial tissue

  → down regulation of β1-receptor

  increase myocardial O_2 consumption

  endogenous catecholamine production

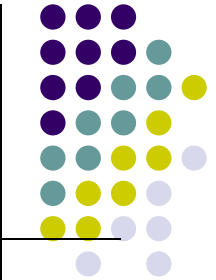
Table 3—*Risk of All-Cause Death Within 1 Year of Entry Associated With Inhaled β-Agonist Use

Average No. of Canisters Filled per Month	Dead (n = 259)	Alive (n = 1,270)	Unadjusted RR (95% CI)	Adjusted RR (95% CI)
0	185	981	Referent	Referent
1	17	100	0.9 (0.5–1.5)	0.9 (0.5–1.6)
2	28	111	1.3 (0.9–2.1)	1.4 (0.9–2.2)
≥ 3	29	78	2.0 (1.3–3.1)	2.0 (1.3–3.2)

*Adjusted for age, ACE inhibitor use, β-blocker use, diabetes, acute myocardial ischemia, cardiovascular disease, hypertension, and alcohol abuse.

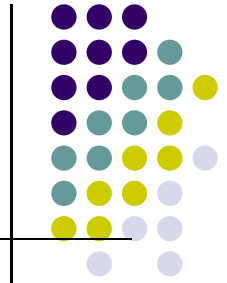
See Table 1 for expansion of abbreviation.

beta2-receptor agonist



- inhalation of long acting β2-R agonist
  - more quickly removed from myocardial beta-receptor
  - potential deleterious cardiac effects less likely

Anticholinergics



- Reduce acetylcholine release over short period
- Potentially exert (adverse) cardiac effects - atropine

- Until now, no adverse effect on cardiac function

CV medication influencing pulmonary function

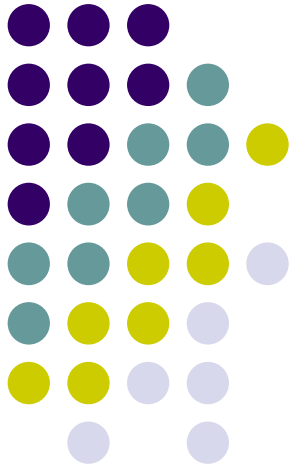
β-blocking agent

ACE inhibitor / ARB

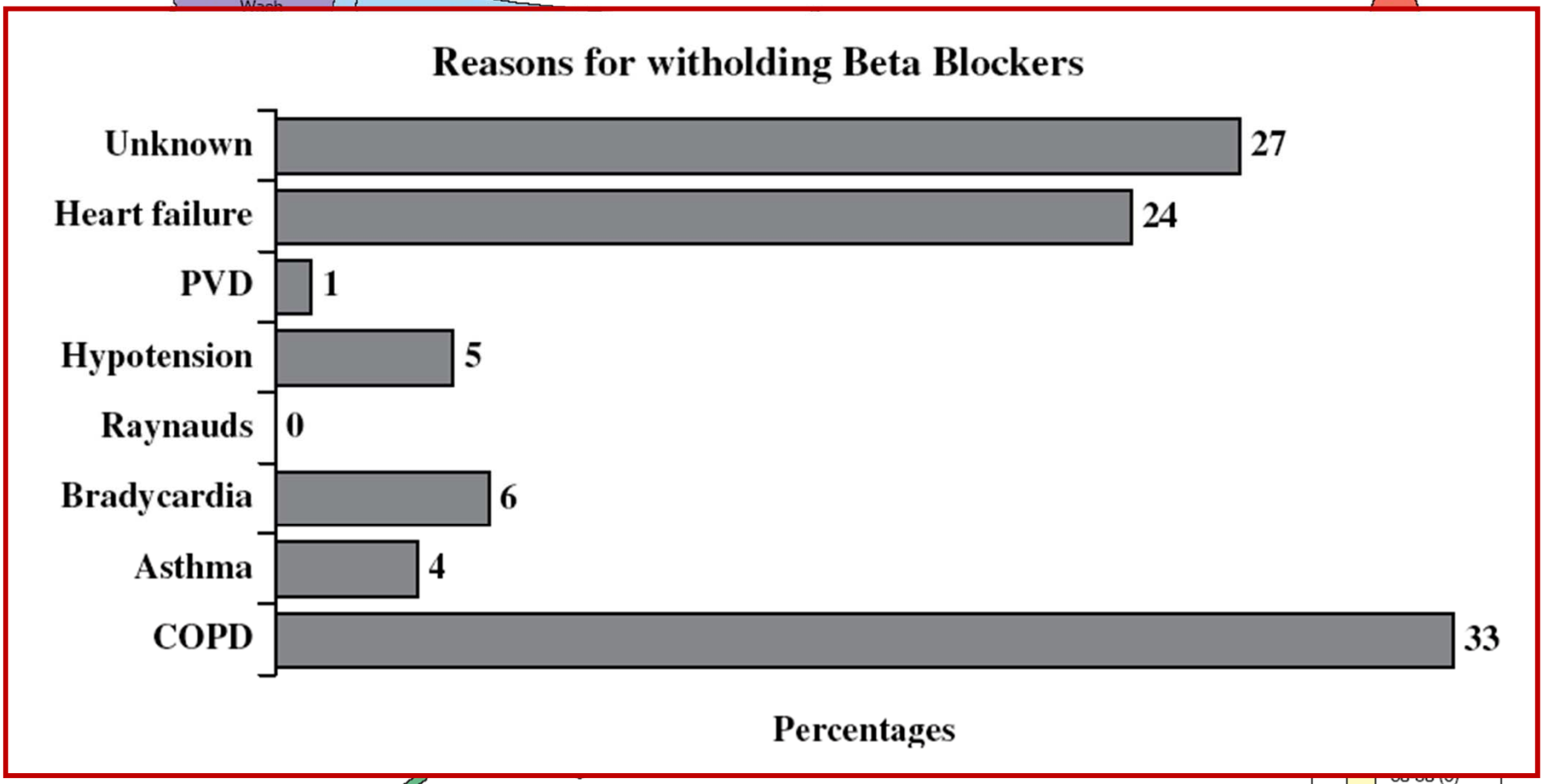
Aldosterone antagonist

Digitalis

Diuretics

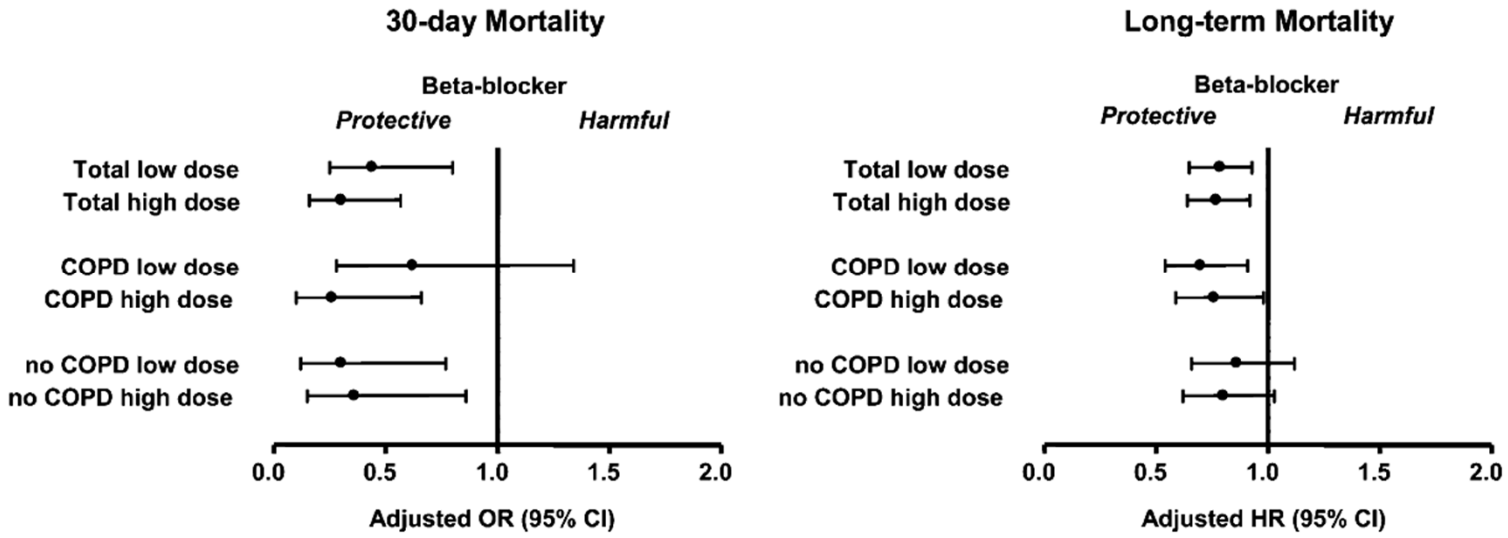


Underused beta-blocker



β-blocking agent

- **Selective β1 blockade**
  - Respiratory symptoms and FEV1 are not significantly worsened by selective β1 blockade in COPD patients
  - does not attenuate β2 receptor agonist-induced bronchodilatation



β-Blockers May Reduce Mortality and Risk of Exacerbations in Patients With Chronic Obstructive Pulmonary Disease

Frans H. Rutten, MD, PhD; Nicolaas P. A. Zuithoff, MSc; Eelko Hak, MSc, PhD; Diederick E. Grobbee, MD, PhD; Arno W. Hoes, MD, PhD

Table 4. Crude and Adjusted Hazard Ratios (HRs) for Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) According to β-Blocker Use in 2230 Patients With a Diagnosis of COPD[a]

Variable	HR (95% Confidence Interval)		
	Any β-Blocker	Cardioselective β-Blocker	Nonselective β-Blocker
Unadjusted (crude)	0.73 (0.63-0.83)	0.75 (0.65-0.87)	0.72 (0.57-0.90)
Covariates included in the Cox model to calculate adjusted HRs +			
Age	0.71 (0.62-0.82)	0.74 (0.64-0.86)	0.71 (0.56-0.89)
Sex	0.71 (0.62-0.81)	0.74 (0.64-0.85)	0.70 (0.56-0.89)
Current or former smoker	0.70 (0.61-0.80)	0.73 (0.63-0.84)	0.71 (0.56-0.89)
Diabetes, hypertension, cardiovascular diseases	0.63 (0.54-0.74)	0.68 (0.58-0.80)	0.66 (0.52-0.84)
Cardiovascular drugs other than β-blocker	0.58 (0.50-0.68)	0.64 (0.54-0.75)	0.66 (0.52-0.84)
Pulmonary drugs	0.67 (0.57-0.79)	0.72 (0.61-0.85)	0.72 (0.56-0.91)
Referral to a pulmonologist	0.71 (0.60-0.83)	0.78 (0.66-0.92)	0.74 (0.58-0.94)
Adjusted with propensity score[b]	0.64 (0.55-0.75)	0.68 (0.58-0.80)	0.70 (0.56-0.89)

[a] Adjusted HRs based on the Cox proportional hazards model were calculated step by step after adjustment for age, sex, current or former smoking, diabetes, hypertension, cardiovascular diseases, cardiovascular drugs other than the one under study, use of pulmonary inhalation drugs, and referral to a pulmonologist. Cardiovascular drugs include β-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, aldosterone antagonists, digoxin, loop and thiazide diuretics, nitrates, aspirin, vitamin K antagonists, and calcium channel blockers. Pulmonary drugs include inhalers of β_2-agonists, anticholinergic agents, corticosteroids, and oral xanthine derivates.

[b] Adjusted HRs of β-blocker use are conditional on the propensity score (based on covariates related to prescription of β-blockers).

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QUARTERLY FOCUS ISSUE: HEART FAILURE

Clinical Research

Differences Between Beta-Blockers in Patients With Chronic Heart Failure and Chronic Obstructive Pulmonary Disease

A Randomized Crossover Trial

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Switching between β1-selective beta-blockers and the nonselective beta-blocker carvedilol is well tolerated but results in demonstrable changes in airway function, most marked in patients with COPD. Switching from β1-selective beta-blockers to carvedilol causes short-term reduction of central augmented pressure and N-terminal pro-hormone brain natriuretic peptide. (Comparison of Nonselective and Beta1-Selective Beta-Blockers on Respiratory and Arterial Function and Cardiac Chamber Dynamics in Patients With Chronic Stable Congestive Cardiac Failure; Australian New Zealand Clinical Trials Registry, ACTRN12605000504617) (J Am Coll Cardiol 2010; 55:1780–7) © 2010 by the American College of Cardiology Foundation

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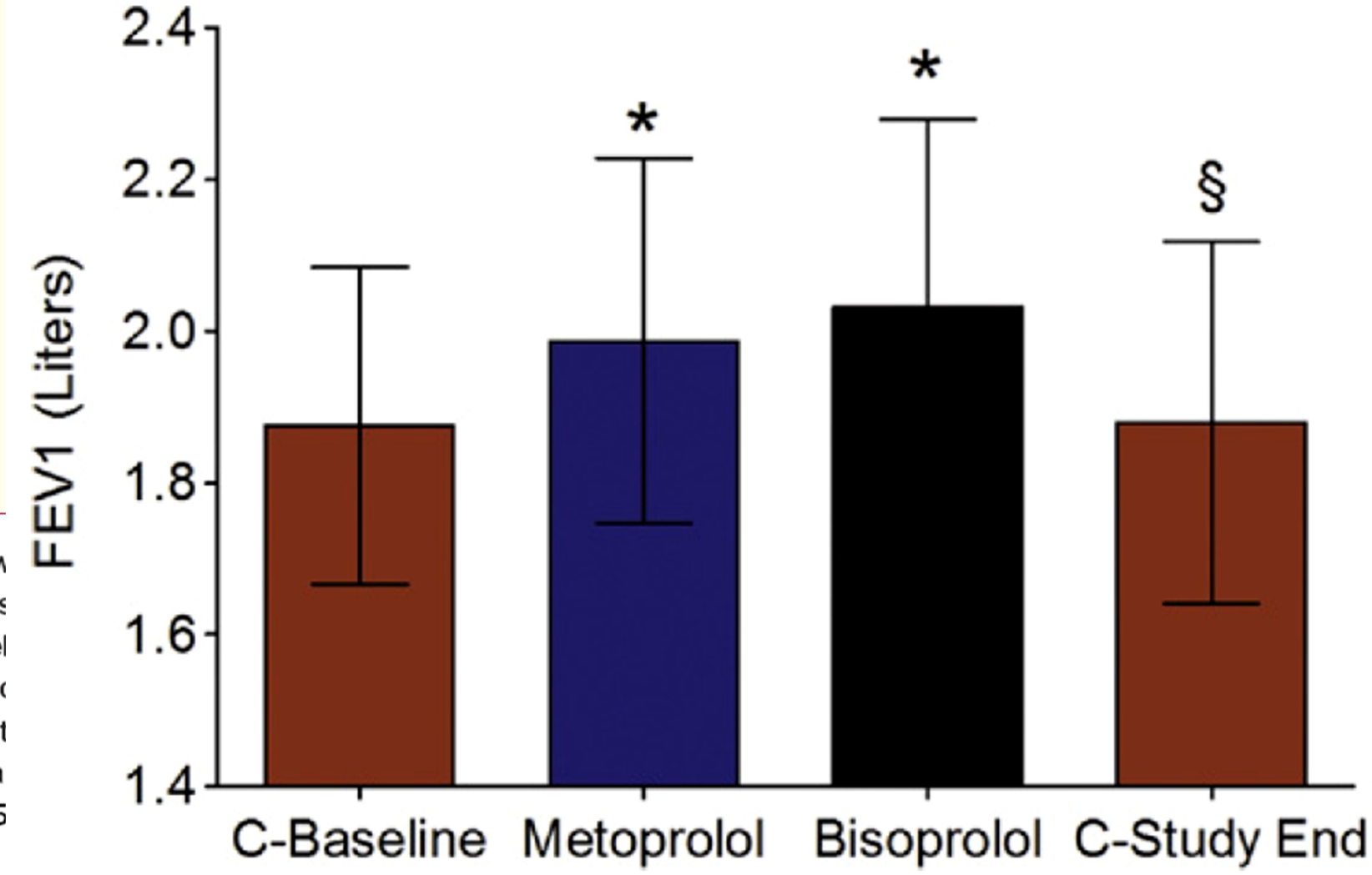
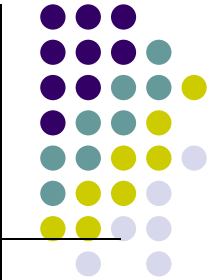
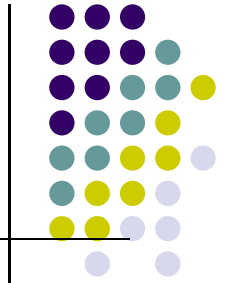


Recommendation



- all CHF + stable COPD without reversible airway obstruction
  - Selective or nonselective beta-blocker
- CHF + COPD with reversible airway obstruction
  - Selective β1-blocker
  - Nonselective β-blocker : no safety data
- COPD exacerbation
  - avoid β-blocker until safety data are available

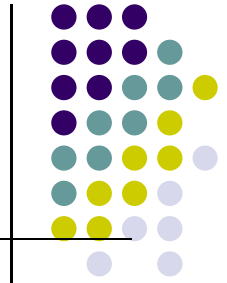
ACE inhibitor & ARB



- Angiotensin-II : potent pulmonary airway constrictor
- ACE inhibitor
  - ↓ pulmonary inflammation
  - ↓ pulmonary vascular constriction
  - ameliorate the alveolar membrane gas conductance abnormality

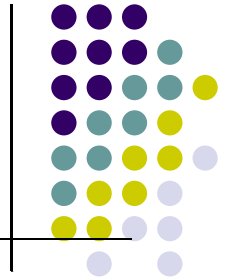
  ⇒ benefit in treating pt with COPD

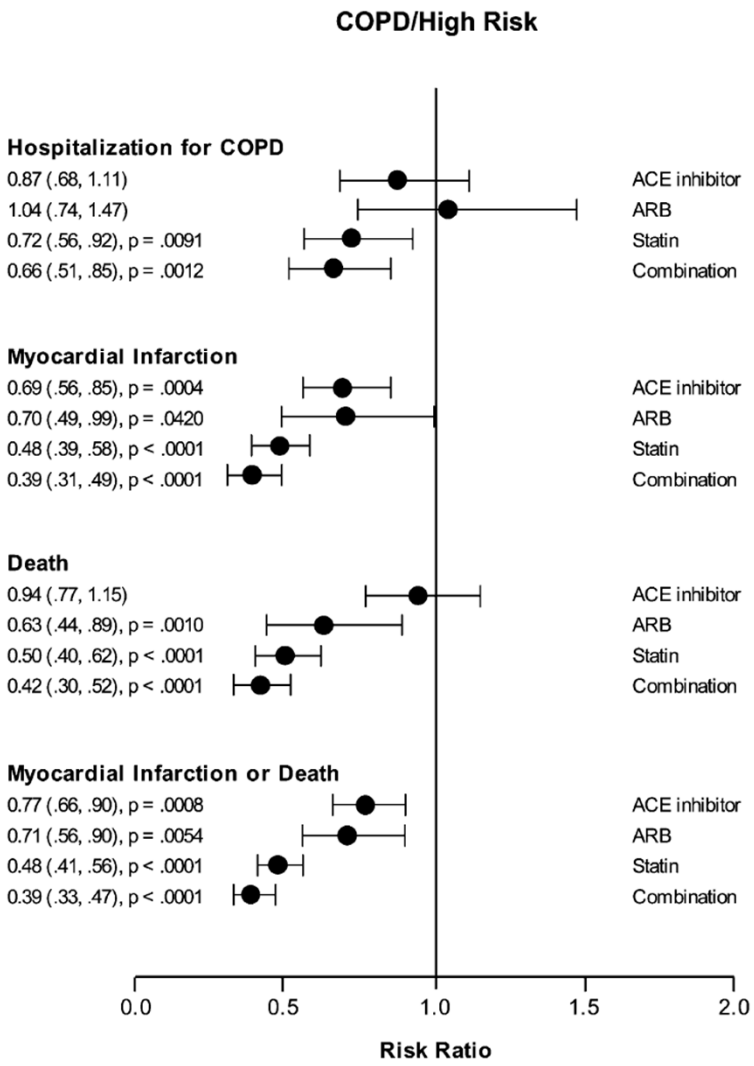
Statin

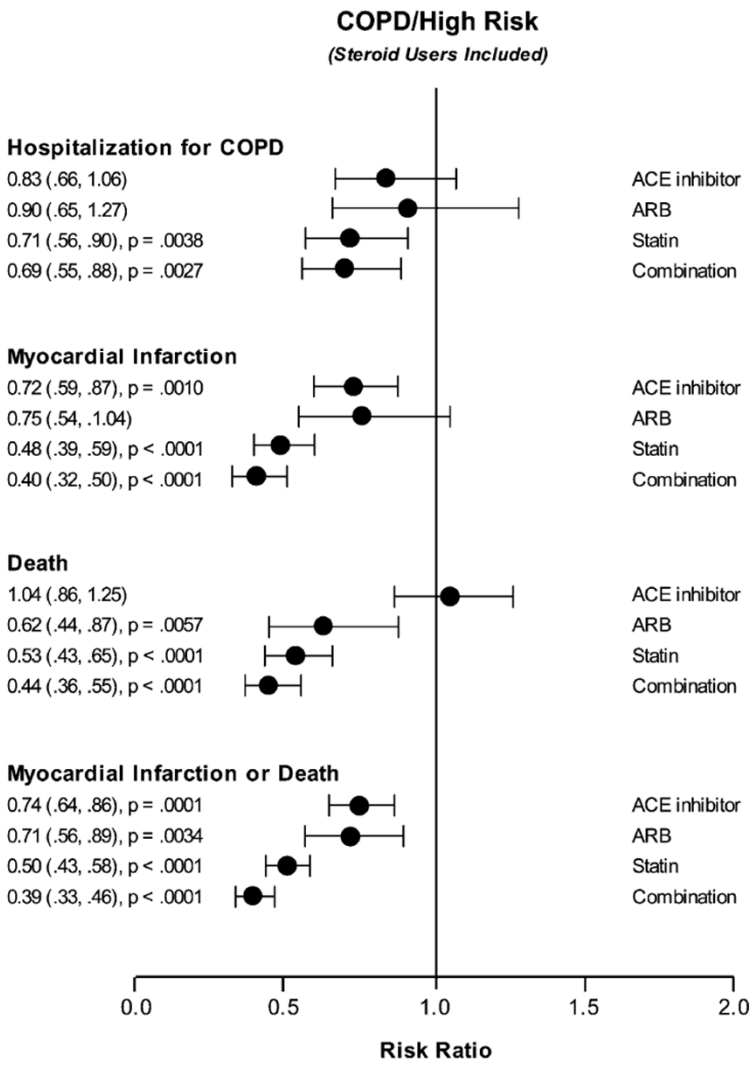


- **Inhibit development of emphysema, inflammation, pulmonary hypetension**
  - **pleiotrophic effect**
  - **anti-inflammatory action**

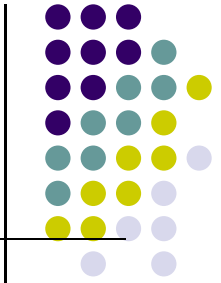
ACEI/ARB and Statin





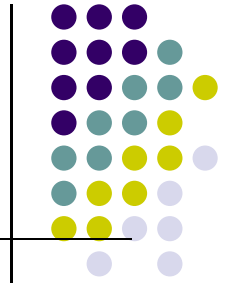


Diuretics & Digitalis



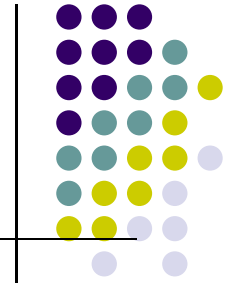
- high dose diuretics
  - acid-base disturbance → metabolic alkalosis
  - blunt respiratory derive
- Normal dosage of diuretics
  - No influence on pulmonary function
- Digitalis
  - Pulmonary vasoconstriction → reduce lung fx

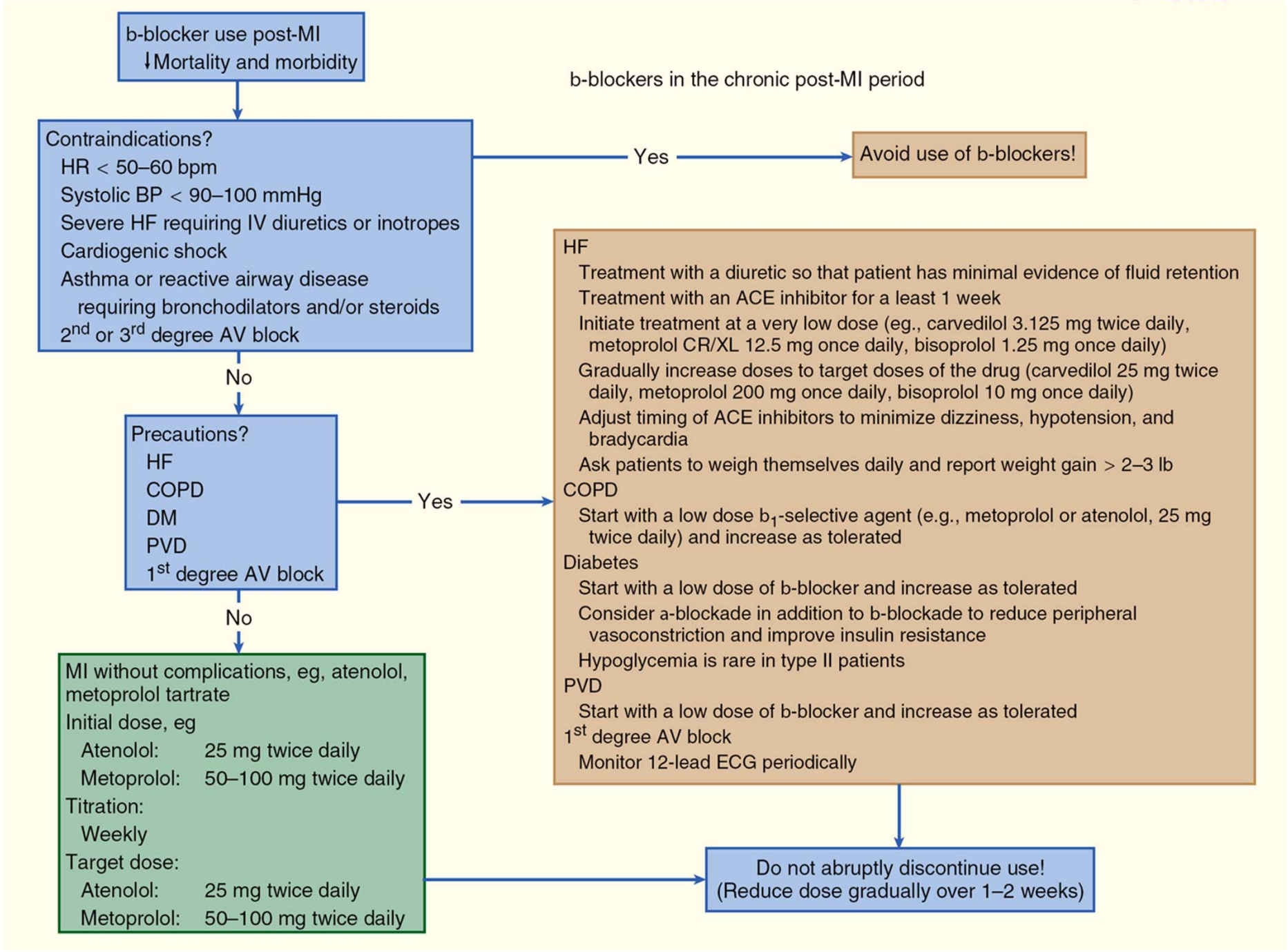
Summary

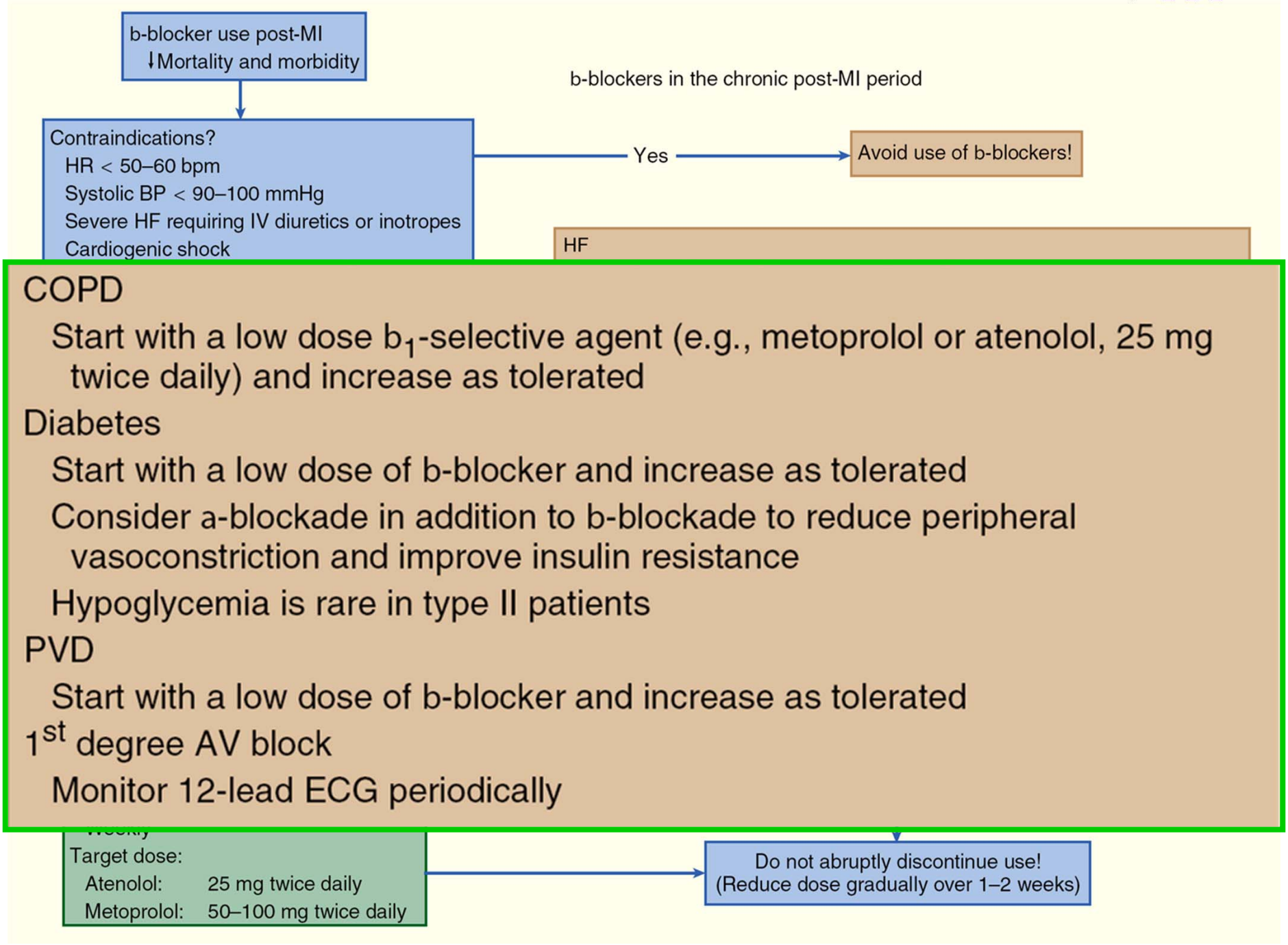


- COPD in patients with HF is not uncommon.
- Early and appropriate diagnosis
- Proper management
  - Selective and/or nonselective β-blocker
  - ACEI / ARB
  - Statin
  - Proper bronchodilator
    - Anticholinergic
    - inhalation of long acting β2-R agonist

경청해 주셔서 감사합니다.




b-blocker use post-MI
↓Mortality and morbidity
b-blockers in the chronic post-MI period
Contraindications?
HR < 50–60 bpm
Systolic BP < 90–100 mmHg
Severe HF requiring IV diuretics or inotropes
Cardiogenic shock
Asthma or reactive airway disease requiring bronchodilators and/or steroids
2nd or 3rd degree AV block
Yes
Avoid use of b-blockers!
No
Precautions?
HF
COPD
DM
PVD
1st degree AV block
Yes
No
HF
Treatment with a diuretic so that patient has minimal evidence of fluid retention
Treatment with an ACE inhibitor for a least 1 week
Initiate treatment at a very low dose (eg., carvedilol 3.125 mg twice daily, metoprolol CR/XL 12.5 mg once daily, bisoprolol 1.25 mg once daily)
Gradually increase doses to target doses of the drug (carvedilol 25 mg twice daily, metoprolol 200 mg once daily, bisoprolol 10 mg once daily)
Adjust timing of ACE inhibitors to minimize dizziness, hypotension, and bradycardia
Ask patients to weigh themselves daily and report weight gain > 2–3 lb
COPD
Start with a low dose b1-selective agent (e.g., metoprolol or atenolol, 25 mg twice daily) and increase as tolerated
Diabetes
Start with a low dose of b-blocker and increase as tolerated
Consider a-blockade in addition to b-blockade to reduce peripheral vasoconstriction and improve insulin resistance
Hypoglycemia is rare in type II patients
PVD
Start with a low dose of b-blocker and increase as tolerated
1st degree AV block
Monitor 12-lead ECG periodically
MI without complications, eg, atenolol, metoprolol tartrate
Initial dose, eg
Atenolol: 25 mg twice daily
Metoprolol: 50–100 mg twice daily
Titration:
Weekly
Target dose:
Atenolol: 25 mg twice daily
Metoprolol: 50–100 mg twice daily
Do not abruptly discontinue use!
(Reduce dose gradually over 1–2 weeks)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Sliding doors concept