ĐIỀU TRỊ SUY TIM 2016: TẦM QUAN TRỌNG CỦA THUỐC CHẸN BETA THẾ HỆ MỚI

PGS. TS. Phạm Nguyễn Vinh
Đại học Y khoa Phạm Ngọc Thạch
Đại học Y khoa Tân Tạo
Bệnh viện Tim Tâm Đức
Viện Tim Tp. HCM

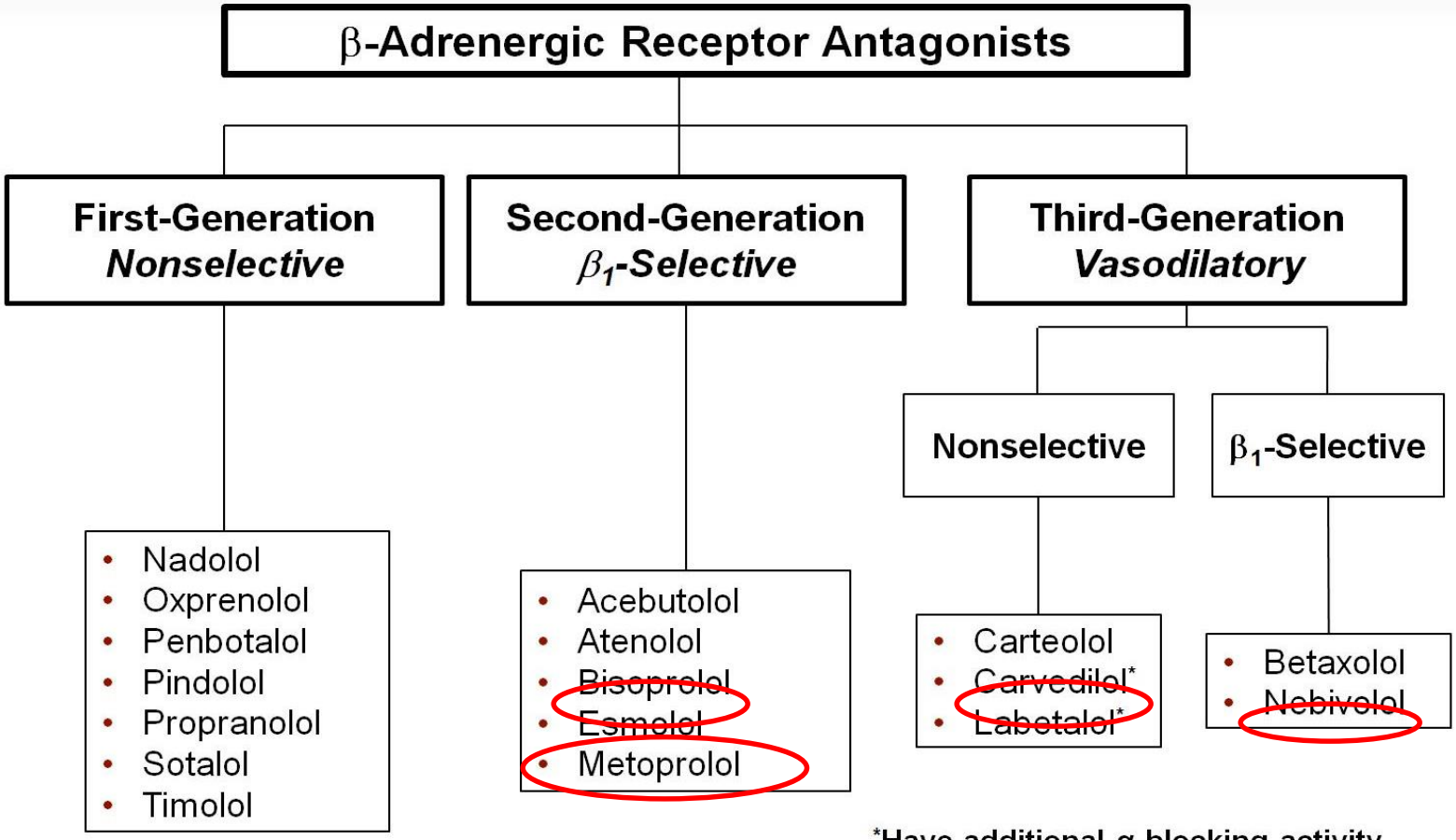
Các vấn đề về sử dụng chẹn beta trong suy tim

- Thuốc thiết yếu: giúp kéo dài đời sống b/n
- Lựa chọn và phương thức sử dụng
- Tại sao thất bại/ một số b/n suy tim

Sự phát minh ra thuốc chẹn beta giao cảm được coi như một cuộc cách mạng trong Y học (Tim mạch)

Black (UK) Giải thưởng Nobel 1960

Các thế hệ thuốc chẹn beta giao cảm

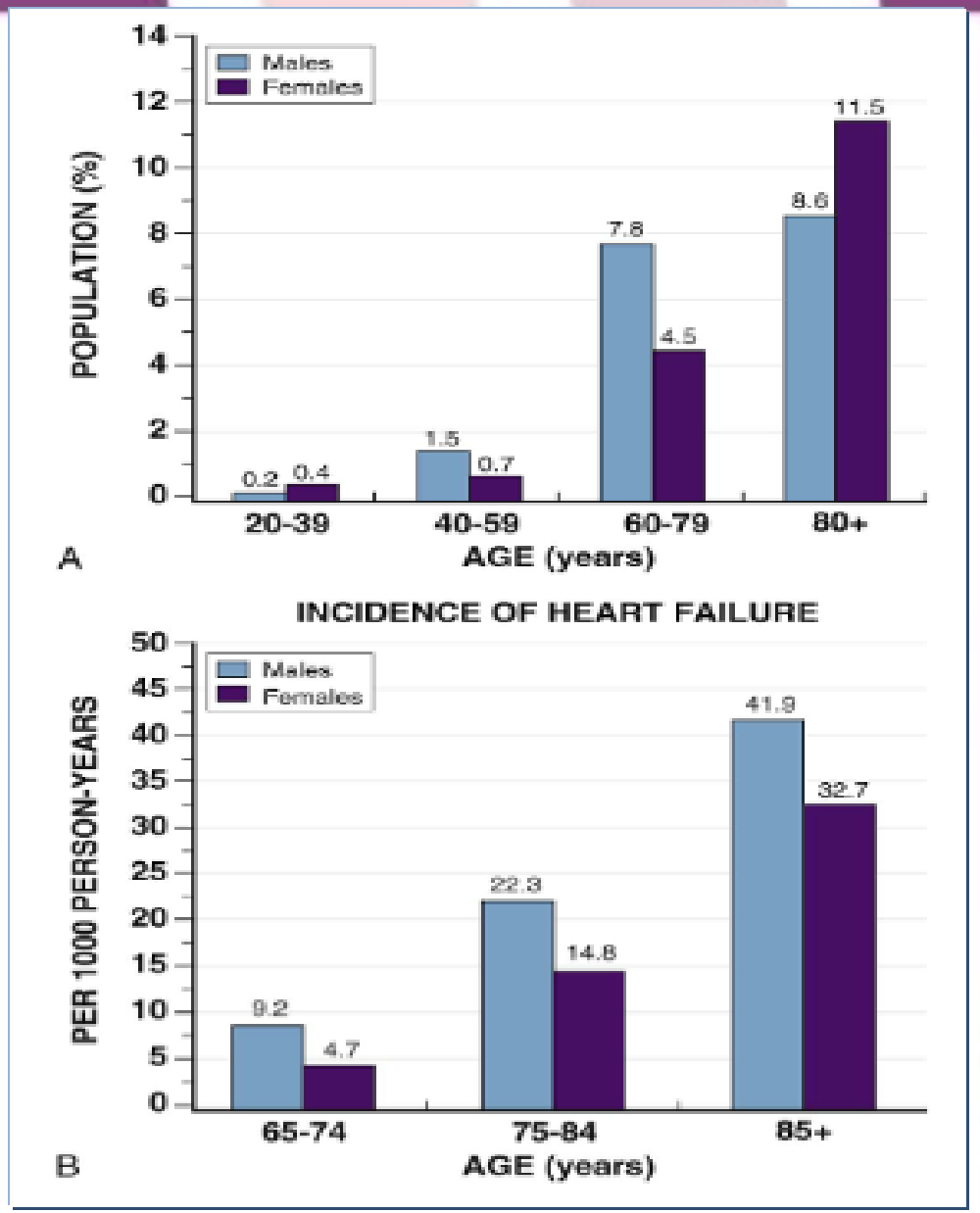


Manrique C, et al. *J Clin Hypertens*. 2009;11:369-375.[1]

Pham Nguyen Vinh

Tần suất suy tim

- **Thế giới: 23 triệu người lớn**
- **Hoa Kỳ:**
  - 5.1 triệu người ≥ 20 tuổi
  - Năm 2030: tần suất tăng 25%



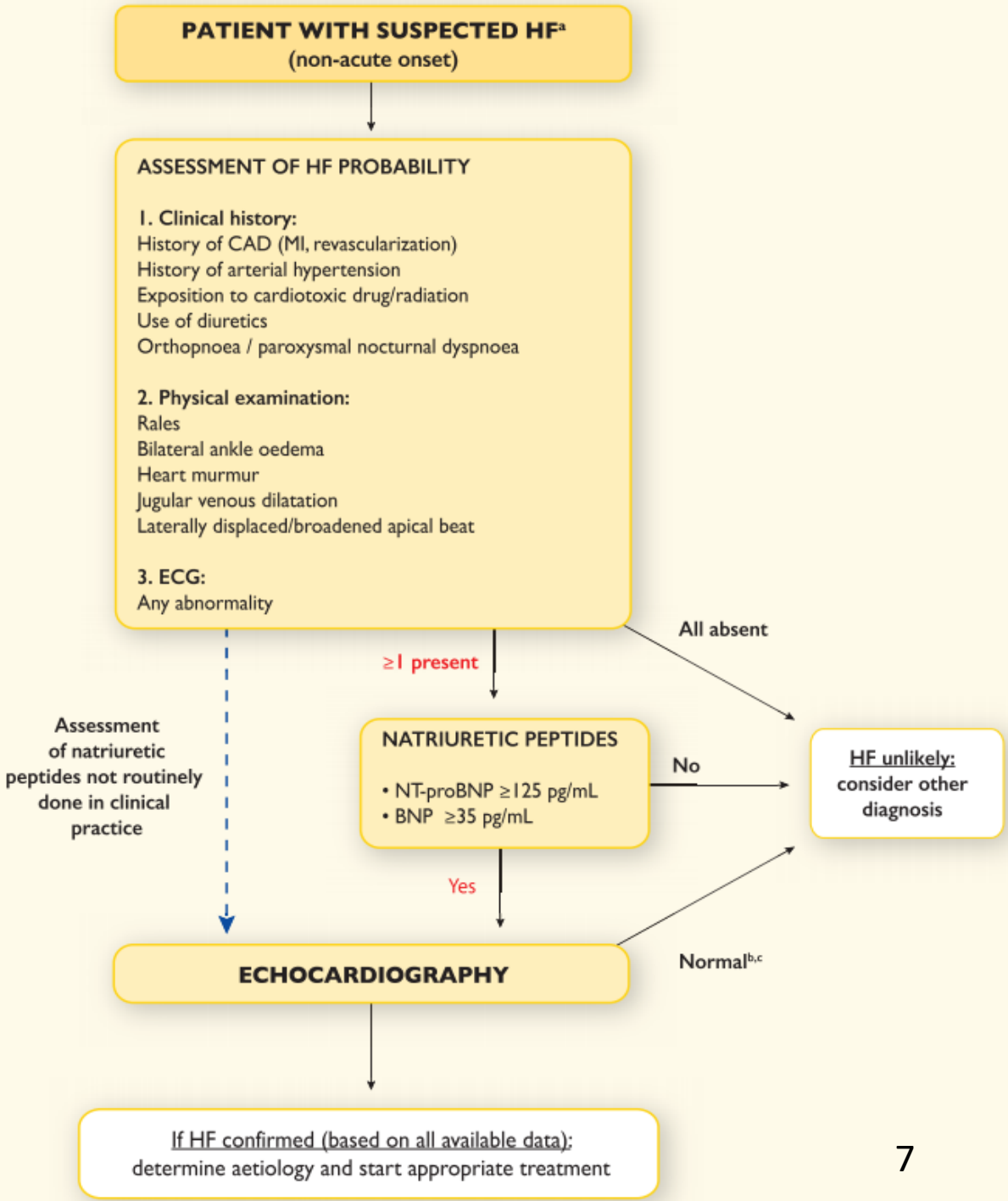
TL: Mann LD. In Braunwald's Heart Disease, 2015, 10th ed, Elsevier- Saunders, p 512-540

Định nghĩa suy tim

- **Suy tim là một hội chứng lâm sàng phức tạp do tổn thương cấu trúc hoặc chức năng đổ đầy thất hoặc tống máu.**
- **Biểu hiện lâm sàng chính của suy tim là mệt và khó thở.**

TL: Yancy CW et al. 2013 ACCF/AHA Guideline for the Mangement of Heart Failure.
DOI: 10.1016/j.jacc.2013.05.019

Quy trình chẩn đoán suy tim



TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Pham Nguyen Vinh

Tiêu chuẩn chẩn đoán suy tim PXTM bảo tồn

1. Có triệu chứng cơ năng và/hoặc thực thể của suy tim
2. PXTM bảo tồn (LVEF ≥ 50%)
3. Tăng Natriuretic Peptide (BNP > 35 pg/ml và/hoặc NT-proBNP > 125 pg/ml)
4. Chứng cứ biến đổi cấu trúc và chức năng của suy tim

Pham Nguyen Vinh

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Khảo sát di truyền bệnh nhân suy tim

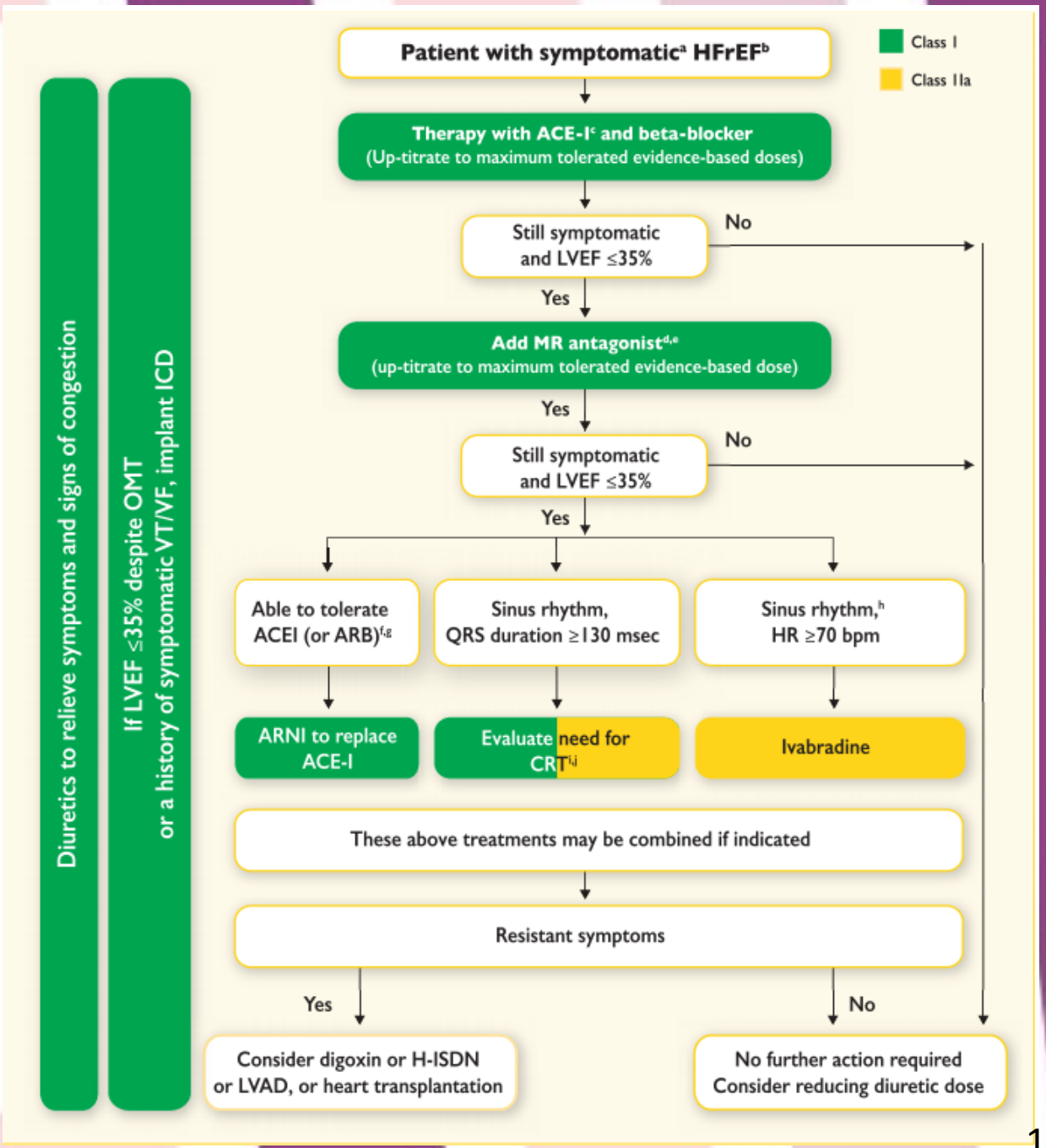
- **BCT phì đại (HCM)**
- **BCT dãn nở (DCM)**
- **Loạn sản thất phải gây loạn nhịp (ARVC)**
- **BCT hạn chế**
- **BCT không lên chặt (non-compaction cardiomyopathies)**
  - HCM: 20 gens, 1400 neutations đã xác định
  - DCM: 50% vô căn/ 1/3 nhóm vô căn do di truyền 50 gens đã xác định
  - ARVC: 10 gens đã xác định

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Mục tiêu điều trị suy tim

- Giảm tử vong
- Giảm nhập viện
- Cải thiện triệu chứng cơ năng, chất lượng cuộc sống

Quy trình điều trị suy tim có t/c cơ năng kèm PXTM giảm



TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Pham Nguyen Vinh

Các thuốc được chứng minh kéo dài đời sống/ST PXTM giảm

	Starting dose (mg)	Target dose (mg)
ACE-I		
Captopril[a]	6.25 *t.i.d.*	50 *t.i.d.*
Enalapril	2.5 *b.i.d.*	20 *b.i.d.*
Lisinopril[b]	2.5–5.0 *o.d.*	20–35 *o.d.*
Ramipril	2.5 *o.d.*	10 *o.d.*
Trandolapril[a]	0.5 *o.d.*	4 *o.d.*
Beta-blockers		
Bisoprolol	1.25 *o.d.*	10 *o.d.*
Carvedilol	3.125 *b.i.d.*	25 *b.i.d.*[d]
Metoprolol succinate (CR/XL)	12.5–25 *o.d.*	200 *o.d.*
Nebivolol[c]	1.25 *o.d.*	10 *o.d.*
ARBs		
Candesartan	4–8 *o.d.*	32 *o.d.*
Valsartan	40 *b.i.d.*	160 *b.i.d.*
Losartan[b,c]	50 *o.d.*	150 *o.d.*
MRAs		
Eplerenone	25 *o.d.*	50 *o.d.*
Spironolactone	25 *o.d.*	50 *o.d.*
ARNI		
Sacubitril/valsartan	49/51 *b.i.d.*	97/103 *b.i.d.*
If-channel blocker		
Ivabradine	5 *b.i.d.*	7.5 *b.i.d.*

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ARNI = angiotensin receptor neprilysin inhibitor; b.i.d. = bis in die (twice daily); MRA = mineralocorticoid receptor antagonist; o.d. = omne in die (once daily); t.i.d. = ter in die (three times a day).

[a]Indicates an ACE-I where the dosing target is derived from post-myocardial infarction trials.

[b]Indicates drugs where a higher dose has been shown to reduce morbidity/mortality compared with a lower dose of the same drug, but there is no substantive randomized, placebo-controlled trial and the optimum dose is uncertain.

[c]Indicates a treatment not shown to reduce cardiovascular or all-cause mortality in patients with heart failure (or shown to be non-inferior to a treatment that does).

[d]A maximum dose of 50 mg twice daily can be administered to patients weighing over 85 kg.

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Pham Nguyen Vinh

Liều lượng lợi tiểu thường dùng/ suy tim

Diuretics	Initial dose (mg)		Usual daily dose (mg)	
Loop diuretics[a]				
Furosemide	20–40		40–240	
Bumetanide	0.5–1.0		1–5	
Torasemide	5–10		10–20	
Thiazides[b]				
Bendroflumethiazide	2.5		2.5–10	
Hydrochlorothiazide	25		12.5–100	
Metolazone	2.5		2.5–10	
Indapamide[c]	2.5		2.5–5	
Potassium-sparing diuretics[d]				
	+ACE-I/ ARB	-ACE-I/ ARB	+ACE-I/ ARB	-ACE-I/ ARB
Spironolactone/ eplerenone	12.5–25	50	50	100–200
Amiloride	2.5	5	5–10	10–20
Triamterene	25	50	100	200

ACE-I = angiontensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker.
[a]Oral or intravenous; dose might need to be adjusted according to volume status/ weight; excessive doses may cause renal impairment and ototoxicity.
[b]Do not use thiazides if estimated glomerular filtration rate < 30 mL/min/1.73 m^2, except when prescribed synergistically with loop diuretics.
[c]Indapamide is a non-thiazide sulfonamide.
[d]A mineralocorticoid antagonist (MRA) i.e. spironolactone/eplerenone is always preferred. Amiloride and triamterene should not be combined with an MRA.

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Pham Nguyen Vinh

Các thuốc khác được sử dụng điều trị suy tim PXTM giảm kèm NYHA II- IV (1)

Recommendations	Class [a]	Level [b]	Ref [c]
Diuretics			
Diuretics are recommended in order to improve symptoms and exercise capacity in patients with signs and/or symptoms of congestion.	I	B	178, 179
Diuretics should be considered to reduce the risk of HF hospitalization in patients with signs and/or symptoms of congestion.	IIa	B	178, 179
Angiotensin receptor neprilysin inhibitor			
Sacubitril/valsartan is recommended as a replacement for an ACE-I to further reduce the risk of HF hospitalization and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACE-I, a beta-blocker and an MRA[d]	I	B	162

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Các thuốc khác được sử dụng điều trị suy tim PXTM giảm kèm NYHA II- IV (2)

If-channel inhibitor			
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm despite treatment with an evidence-based dose of beta-blocker (or maximum tolerated dose below that), ACE-I (or ARB), and an MRA (or ARB).	IIa	B	180
Ivabradine should be considered to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients with LVEF ≤35%, in sinus rhythm and a resting heart rate ≥70 bpm who are unable to tolerate or have contra-indications for a beta-blocker. Patients should also receive an ACE-I (or ARB) and an MRA (or ARB).	IIa	C	181
ARB			
An ARB is recommended to reduce the risk of HF hospitalization and cardiovascular death in symptomatic patients unable to tolerate an ACE-I (patients should also receive a beta-blocker and an MRA).	I	B	182
An ARB may be considered to reduce the risk of HF hospitalization and death in patients who are symptomatic despite treatment with a beta-blocker who are unable to tolerate an MRA.	IIb	C	-

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Pham Nguyen Vinh

Các thuốc khác được sử dụng điều trị suy tim PXTM giảm kèm NYHA II- IV (3)

Recommendations	Class [a]	Level [b]	Ref [c]
Hydralazine and isosorbide dinitrate			
Hydralazine and isosorbide dinitrate should be considered in self-identified black patients with LVEF ≤35% or with an LVEF <45% combined with a dilated LV in NYHA Class III–IV despite treatment with an ACE-I a beta-blocker and an MRA to reduce the risk of HF hospitalization and death.	IIa	B	183
Hydralazine and isosorbide dinitrate may be considered in symptomatic patients with HFrEF who can tolerate neither an ACE-I nor an ARB (or they are contra-indicated) to reduce the risk of death.	IIb	B	184
Other treatments with less-certain benefits			
Digoxin			
Digoxin may be considered in symptomatic patients in sinus rhythm despite treatment with an ACE-I (or ARB), a beta-blocker and an MRA, to reduce the risk of hospitalization (both all-cause and HF-hospitalizations).	IIb	B	185
N-3 PUFA			
An n-3 PUFA[e] preparation may be considered in symptomatic HF patients to reduce the risk of cardiovascular hospitalization and cardiovascular death.	IIb	B	186

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; BNP = B-type natriuretic peptide; bpm = beats per minute; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal pro-B type natriuretic peptide; NYHA = New York Heart Association; PUFA = polyunsaturated fatty acid. OMT = optimal medical therapy (for HFrEF this mostly comprises an ACEI or sacubitril/valsartan, a beta-blocker and an MRA).

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

[d]Patient should have elevated natriuretic peptides (plasma BNP ≥150 pg/mL or plasma NT-proBNP ≥600 pg/mL, or if HF hospitalization within the last 12 months, plasma BNP ≥100 pg/mL or plasma NT-proBNP ≥400 pg/mL) and able to tolerate enalapril 10 mg *b.i.d.*

[e]Applies only to preparation studied in cited trial.

Pham Nguyen Vinh

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Các thuốc có thể làm nặng suy tim PXTM giảm kèm NYHA II- IV

Recommendations	Class [a]	Level [b]	Ref [c]
Thiazolidinediones (glitazones) are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	A	209, 210
NSAIDs or COX-2 inhibitors are not recommended in patients with HF, as they increase the risk of HF worsening and HF hospitalization.	III	B	211–213
Diltiazem or verapamil are not recommended in patients with HFrEF, as they increase the risk of HF worsening and HF hospitalization.	III	C	214
The addition of an ARB (or renin inhibitor) to the combination of an ACE-I and an MRA is not recommended in patients with HF, because of the increased risk of renal dysfunction and hyperkalaemia.	III	C	

ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; COX-2 inhibitor = cyclooxygenase-2 inhibitor; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; MRA = mineralocorticoid receptor antagonist; NSAIDs = non-steroidal anti-inflammatory drugs.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations

Pham Nguyen Vinh

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Điều trị bằng máy phá rung cấy được (ICD)

Recommendations	Class [a]	Level [b]	Ref [c]
Secondary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status.	I	A	223–226
Primary prevention An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA Class II–III), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than one year with good functional status, and they have:			
• IHD (unless they have had an MI in the prior 40 days – see below).	I	A	149, 156, 227
• DCM.	I	B	156, 157, 227
ICD implantation is not recommended within 40 days of an MI as implantation at this time does not improve prognosis.	III	A	158, 228
ICD therapy is not recommended in patients in NYHA Class IV with severe symptoms refractory to pharmacological therapy unless they are candidates for CRT, a ventricular assist device, or cardiac transplantation.	III	C	229–233
Patients should be carefully evaluated by an experienced cardiologist before generator replacement, because management goals and the patient's needs and clinical status may have changed.	IIa	B	234–238
A wearable ICD may be considered for patients with HF who are at risk of sudden cardiac death for a limited period or as a bridge to an implanted device.	IIb	C	239–241

CAD = coronary artery disease; CRT = cardiac resynchronization therapy; DCM = dilated cardiomyopathy; HF = heart failure; ICD = implantable cardioverter-defibrillator; IHD = ischaemic heart disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NYHA = New York Heart Association, OMT = optimal medical therapy.
[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Pham Nguyen Vinh

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Điều trị tái đồng bộ tim (CRT)

Recommendations	Class [a]	Level [b]	Ref [c]
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	A	261–272
CRT should be considered for symptomatic patients with HF in sinus rhythm with a QRS duration ≥150 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIa	B	261–272
CRT is recommended for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	I	B	266, 273
CRT may be considered for symptomatic patients with HF in sinus rhythm with a QRS duration of 130–149 msec and non-LBBB QRS morphology and with LVEF ≤35% despite OMT in order to improve symptoms and reduce morbidity and mortality.	IIb	B	266, 273
CRT rather than RV pacing is recommended for patients with HFrEF regardless of NYHA class who have an indication for ventricular pacing and high degree AV block in order to reduce morbidity. This includes patients with AF (see Section 10.1).	I	A	274–277
CRT should be considered for patients with LVEF ≤35% in NYHA Class III–IV[d] despite OMT in order to improve symptoms and reduce morbidity and mortality, if they are in AF and have a QRS duration ≥130 msec provided a strategy to ensure bi-ventricular capture is in place or the patient is expected to return to sinus rhythm.	IIa	B	275, 278–281
Patients with HFrEF who have received a conventional pacemaker or an ICD and subsequently develop worsening HF despite OMT and who have a high proportion of RV pacing may be considered for upgrade to CRT. This does not apply to patients with stable HF.	IIb	B	282
CRT is contra-indicated in patients with a QRS duration < 130 msec.	III	A	266, 283–285

AF = atrial fibrillation; AV = atrio-ventricular; CRT = cardiac resynchronization therapy; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; ICD = implantable cardioverter-defibrillator; LBBB = left bundle branch block; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association; OMT = optimal medical therapy; QRS = Q, R and S waves (combination of three of the graphical deflections); RV = right ventricular.

[a]Class of recommendation.

[b]Level of evidence.

[c]Reference(s) supporting recommendations.

[d]Use judgement for patients with end-stage HF who might be managed conservatively rather than with treatments to improve symptoms or prognosis.

Pham Nguyen Vinh

TL: Ponikowski P. 2016 ESC Guideline for the diagnosis and treatment of acute and chronic heart failure. Eur. H. J, May 20, 2016

Chẹn bêta/ suy tim tâm thu

(Loại I, MCC: A)

- **Tất cả bệnh nhân có PXTM ≤ 40%, NYHA II →IV**
- **Đã được dùng liều đầy đủ UCMC hoặc chẹn thụ thể AG II ± đối kháng aldoslerone**
- **Lâm sàng đang ổn định**
- **Không bị:**
  - Suyễn
  - Blốc NT II,III, hội chứng suy nút xoang, nhịp xoang chậm (< 50/phút)

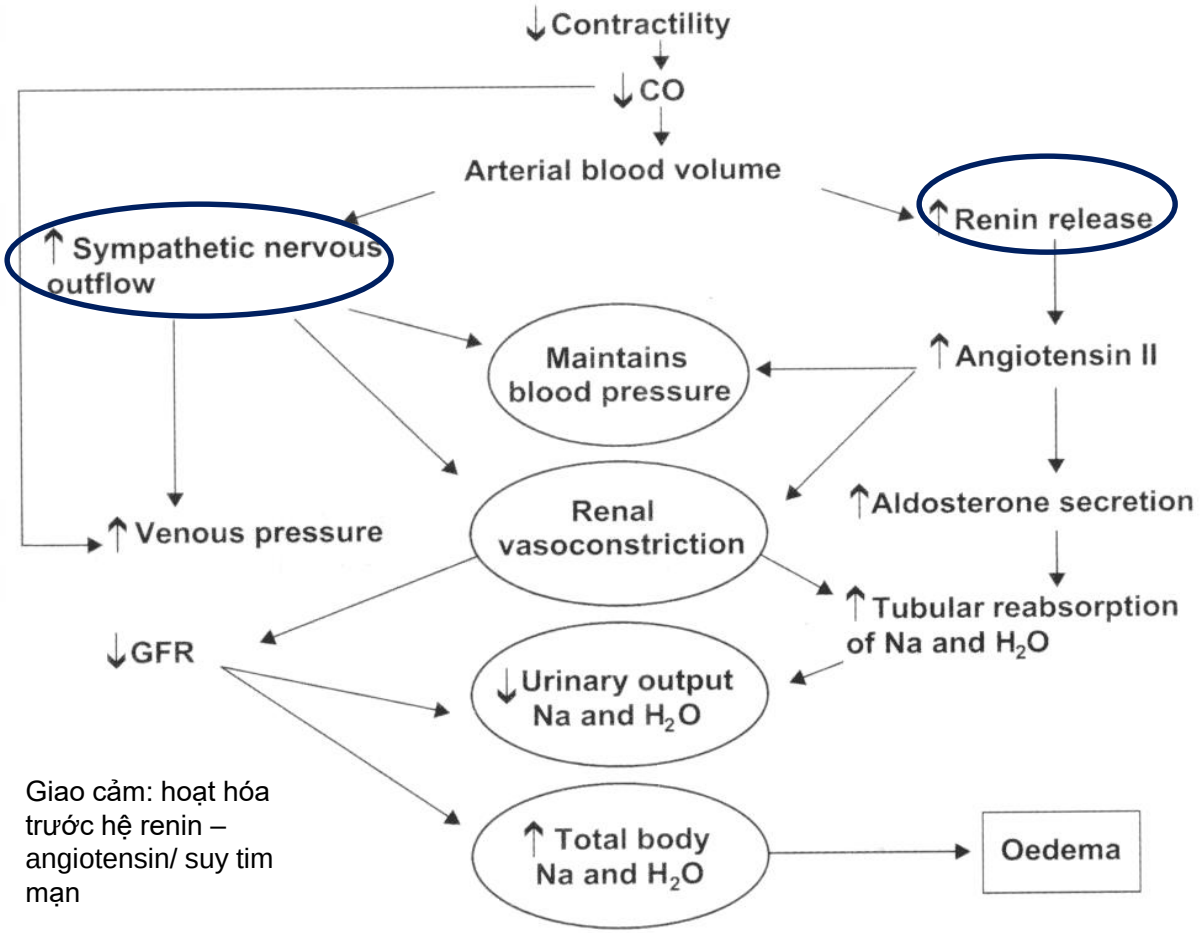
Các nghiên cứu chứng minh hiệu quả của chẹn bêta / suy tim tâm thu

- **CIBIS II (bisoprolol), COPERNICUS (carvedilol), MERIT- HF (metoprolol CR/XL)**
- **SENIORS (nebivolol)**
- **COMET (carvedilol)**

Pham Nguyen Vinh

Khía cạnh sinh lý bệnh của sử dụng chẹn bêta trong điều trị suy tim mạn

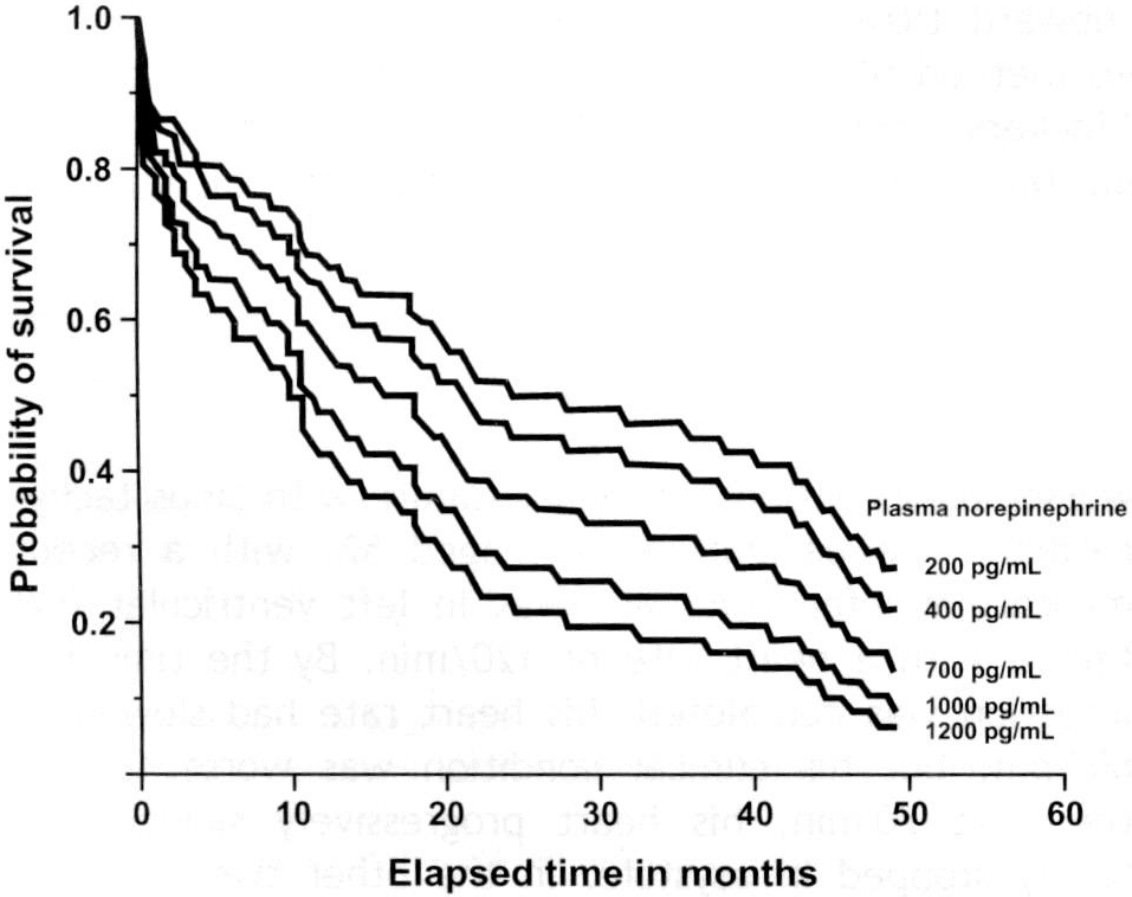
Hậu quả thần kinh nội tiết của suy tim mạn



Giao cảm: hoạt hóa trước hệ renin – angiotensin/ suy tim mạn

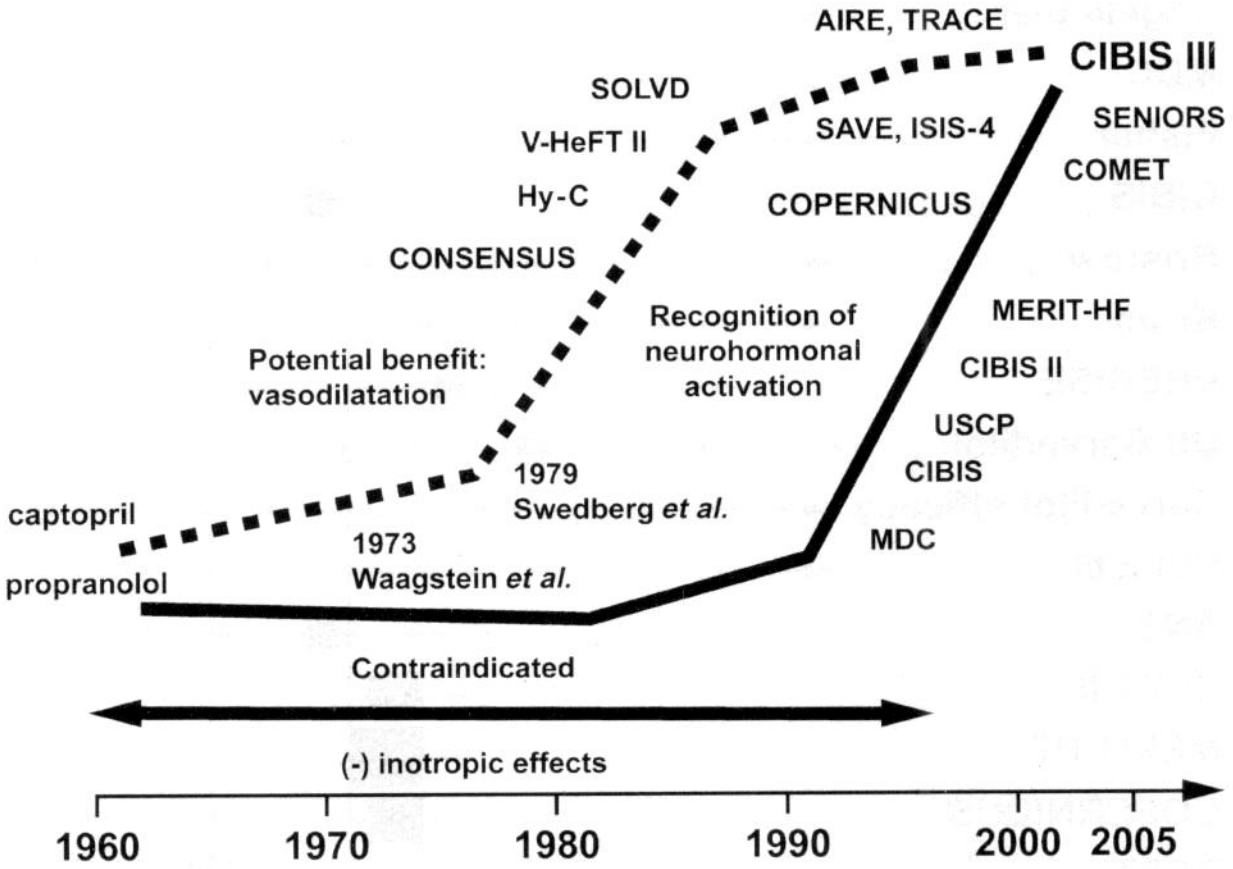
TL: Silke B. Beta-blokade in CHF: pathological considerations. Eur. H. J (2006); 8 (Suppl C): C13 – C18

Tương quan giữa nồng độ norepinephrine huyết tương với sống còn/ 106 b/n suy tim nặng vừa đến nặng



TL: Cohn JN et al. N Engl J Med 1984; 311: 819 - 823

Trình tự các nghiên cứu đặt nền móng cho sử dụng chẹn bêta/ suy tim mạn



TL: Funck-Brentano C. Beta-blokade in CHF: from contraindication to indication. Eur. H. J (2006) – 8 (Suppl C): C19 – C27

Cách sử dụng chẹn bêta/ suy tim tâm thu

- **Khởi đầu liều thấp**
  - Bisoprolol 1,25 mg/ngày; carvedilol 3.125 – 6.25 2 lần/ngày; metoprolol CR/XL 12.5- 25 mg/ngày; nebivolol 1.25 mg/ngày
  - Bắt đầu trước xuất hiện
- **Tăng liều mỗi 2-4 tuần hoặc lâu hơn**
- **Liều mục tiêu: bisoprolol 10 mg/ngày, carvedilol 25-50 mg 2 lần/ngày, metoprolol CR/XL 200 mg/ngày; nebivolol 10 mg/ngày**

Phương thức sử dụng thích hợp chẹn bêta/ suy tim mạn nặng

- Các nghiên cứu CHF –CIBIS II, MERIT-HF, COPERNICUS: liều khởi đầu rất thấp
- Bí quyết sử dụng thành công chẹn bêta/ suy tim mạn: “start low and go slow”

Hiệu quả cao của chẹn bêta/ suy tim mạn: tại sao còn ít sử dụng

- **Nghiên cứu IMPROVEMENT*, nghiên cứu EURO HEART FAILURE SURVEY (EURO – HF)****
  - Chỉ 34 – 37%b/n suy tim mạn được sử dụng chẹn bêta.
  - B/n > 75 tuổi: < 20% được dùng chẹn bêta

TL: Cleland JG et al. Lancet 2002; 360: 1631 – 1639*

*** Komajda M et al. Eur Heart J 2003; 24: 464 - 474*

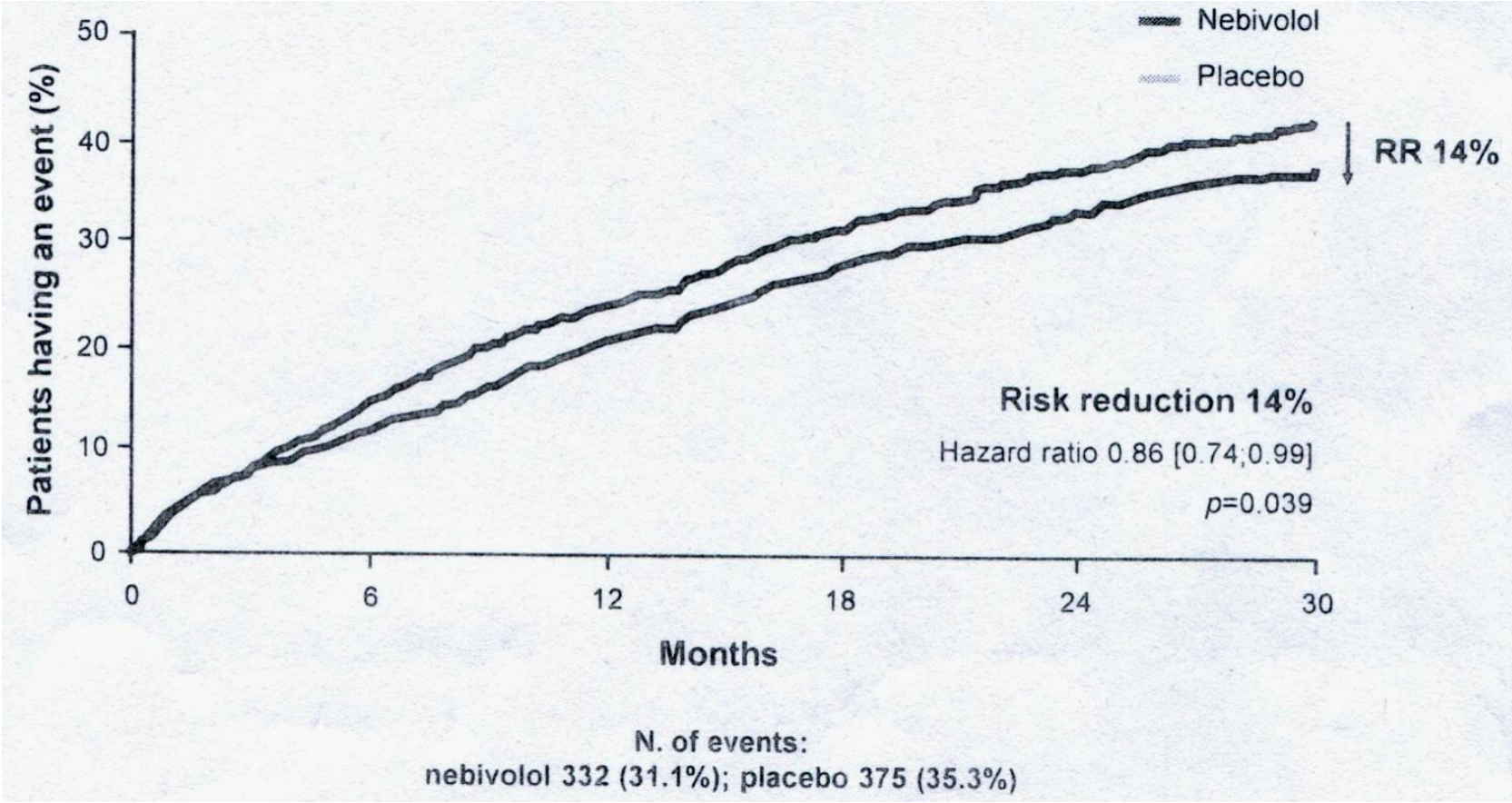
Nghiên cứu SENIORS

- Nghiên cứu hiệu quả của Nebivolol trên bệnh nhân cao tuổi bị suy tim
- Mù đôi, đa trung tâm, có so sánh với placebo, quốc tế
- 2135 b/n: tuổi trung bình 76.1
- PXTM ≤ 35%
- Theo dõi: trung bình 21 tháng

Flather MD, et al. Eur Heart J 2005; 26: 215-25

Pham Nguyen Vinh

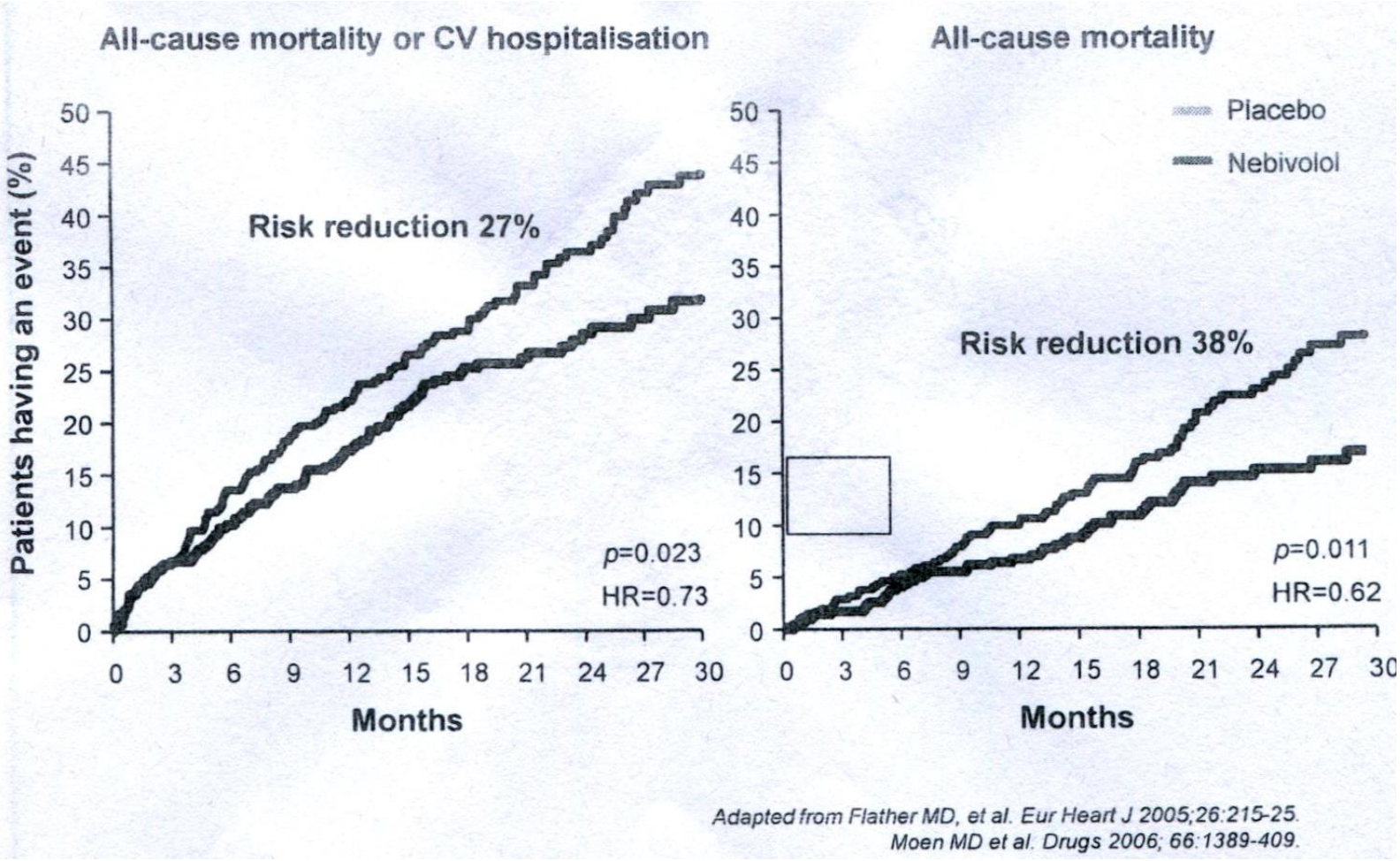
Kết quả n/c SENIORS: tử vong mọi nguyên nhân hoặc nhập viện do tim mạch



Flather MD, et al. Eur Heart J 2005; 26: 215-25

Pham Nguyen Vinh

Kết quả phân tích dưới nhóm (b/n < 75.2 tuổi và PXTM ≤ 35%)



Adapted from Flather MD, et al. Eur Heart J 2005;26:215-25.
Moen MD et al. Drugs 2006; 66:1389-409.

Khuyến cáo kiểm soát tần số thất/ b/n rung nhĩ suy tim NYHA II-IV

Khuyến cáo	Loại	MCC
Bước 1: chẹn beta		
Hàng đầu vì có thêm ưu điểm giảm tử vong và nhập viện vì suy tim	I	A
Biện pháp khác của bước I		
Digoxin nếu b/n không dùng được chẹn beta	II	B
Amiodarone nếu b/n không dùng được chẹn beta hay digoxin	IIb	C
Hủy nút nhĩ thất kèm tạo nhịp, nếu b/n không dùng được cả 3 thuốc	IIIb	C
Bước 2: Digoxin		
Digoxin giúp kiểm soát tần số thất ở b/n kiểm soát bằng chẹn beta không đủ	II	B

- TL: McMurray JJV et al. Euro. H. Journal (2012); 33: 1787-1847

Pham Nguyen Vinh

Hiệu quả điều trị thuốc GĐC của suy tim tâm thu dựa trên các nghiên cứu phân phối ngẫu nhiên

GDMT	RR Reduction in Mortality (%)	NNT for Mortality Reduction (Standardized to 36 mo)	RR Reduction in HF Hospitalizations (%)
ACE inhibitor or ARB	17	26	31
Beta blocker	34	9	41
Aldosterone antagonist	30	6	35
Hydralazine/nitrate	43	7	33

ACE indicates angiotensin-converting enzyme; ARB, angiotensin-receptor blocker; GDMT, guideline-directed medical therapy; HF, heart failure; HF*r*EF, heart failure with reduced ejection fraction; NNT, number needed to treat; RCTs, randomized controlled trials; and RR, relative risk.
Adapted with permission from Fonarow et al (483).

TL: Yancy CW et al. 2013 ACCF/AHA Guideline for the Mangement of Heart Failure. DOI: 10.1016/j.jacc.2013.05.019

Kết luận

- **Hai khuyến cáo cập nhật của ACC/AHA và ESC:**
  - Mục tiêu hàng đầu điều trị suy tim: tăng sống còn
  - Thuốc mới:
    - Ivabradine
    - Valsartan + sacubitril (Entresto*)
  - Chẹn beta giúp kéo dài đời sống+++ (NNT=9)
- **Sinh lý bệnh và nghiên cứu: chẹn beta thế hệ mới hiệu quả cao trong suy tim mạn PXTM giảm**

Pham Nguyen Vinh