Cập nhật điều trị suy tim 2019

PGS TS BS Hồ Huỳnh Quang Trí

Viện Tim – Đại học Y Dược TP Hồ Chí Minh

2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

Table 3.1 Definition of heart failure with preserved (HFpEF), mid-range (HFmrEF) and reduced ejection fraction (HFrEF)

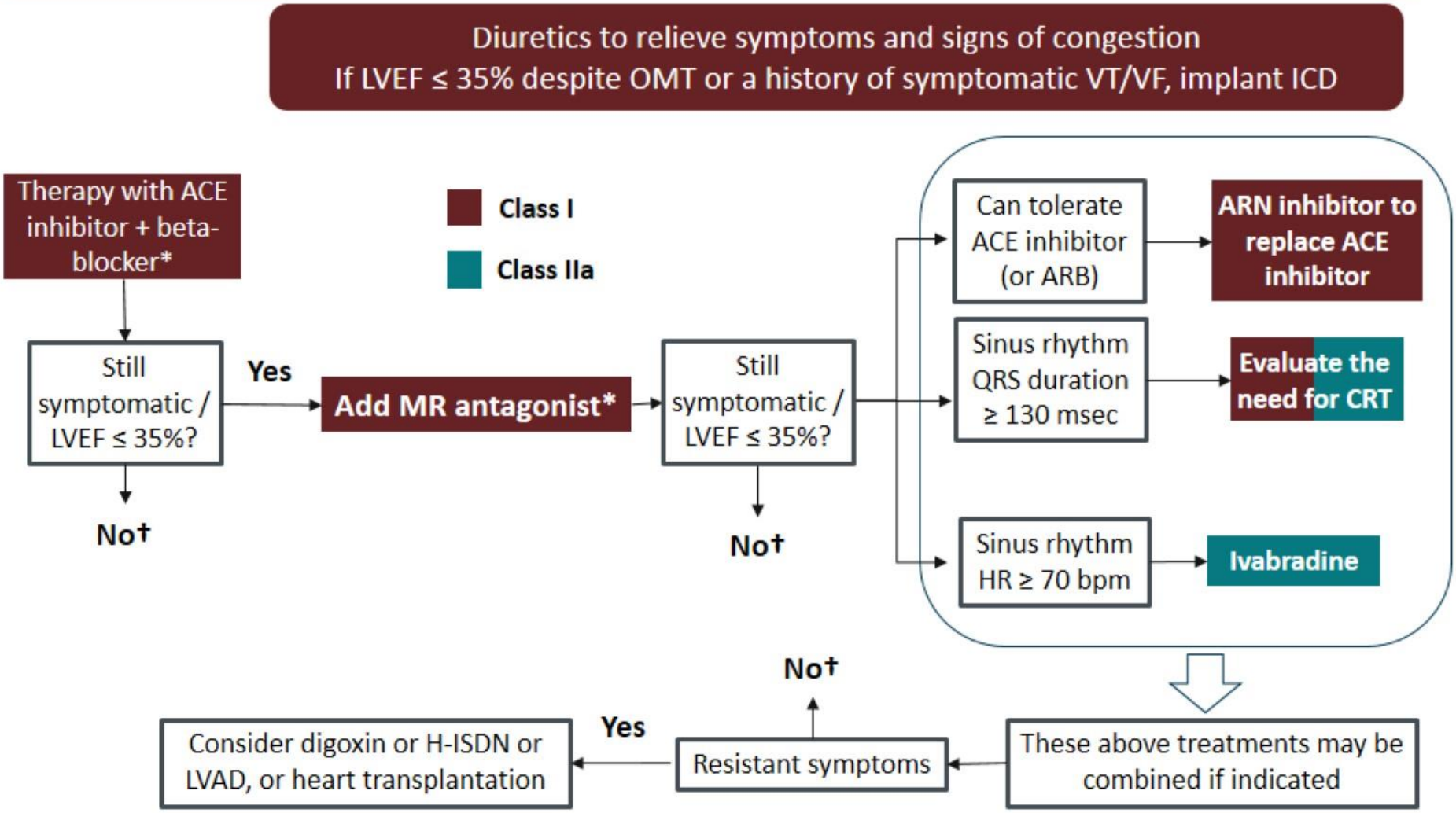
Type of HF		HFrEF	HFmrEF	HFpEF
CRITERIA	1	Symptoms ± Signs[a]	Symptoms ± Signs[a]	Symptoms ± Signs[a]
	2	LVEF <40%	LVEF 40–49%	LVEF ≥50%
	3	–	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).	1. Elevated levels of natriuretic peptides[b]; 2. At least one additional criterion: a. relevant structural heart disease (LVH and/or LAE), b. diastolic dysfunction (for details see Section 4.3.2).

BNP = B-type natriuretic peptide; HF = heart failure; HFmrEF = heart failure with mid-range ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction; LAE = left atrial enlargement; LVEF = left ventricular ejection fraction; LVH = left ventricular hypertrophy; NT-proBNP = N-terminal pro-B type natriuretic peptide.

[a]Signs may not be present in the early stages of HF (especially in HFpEF) and in patients treated with diuretics.

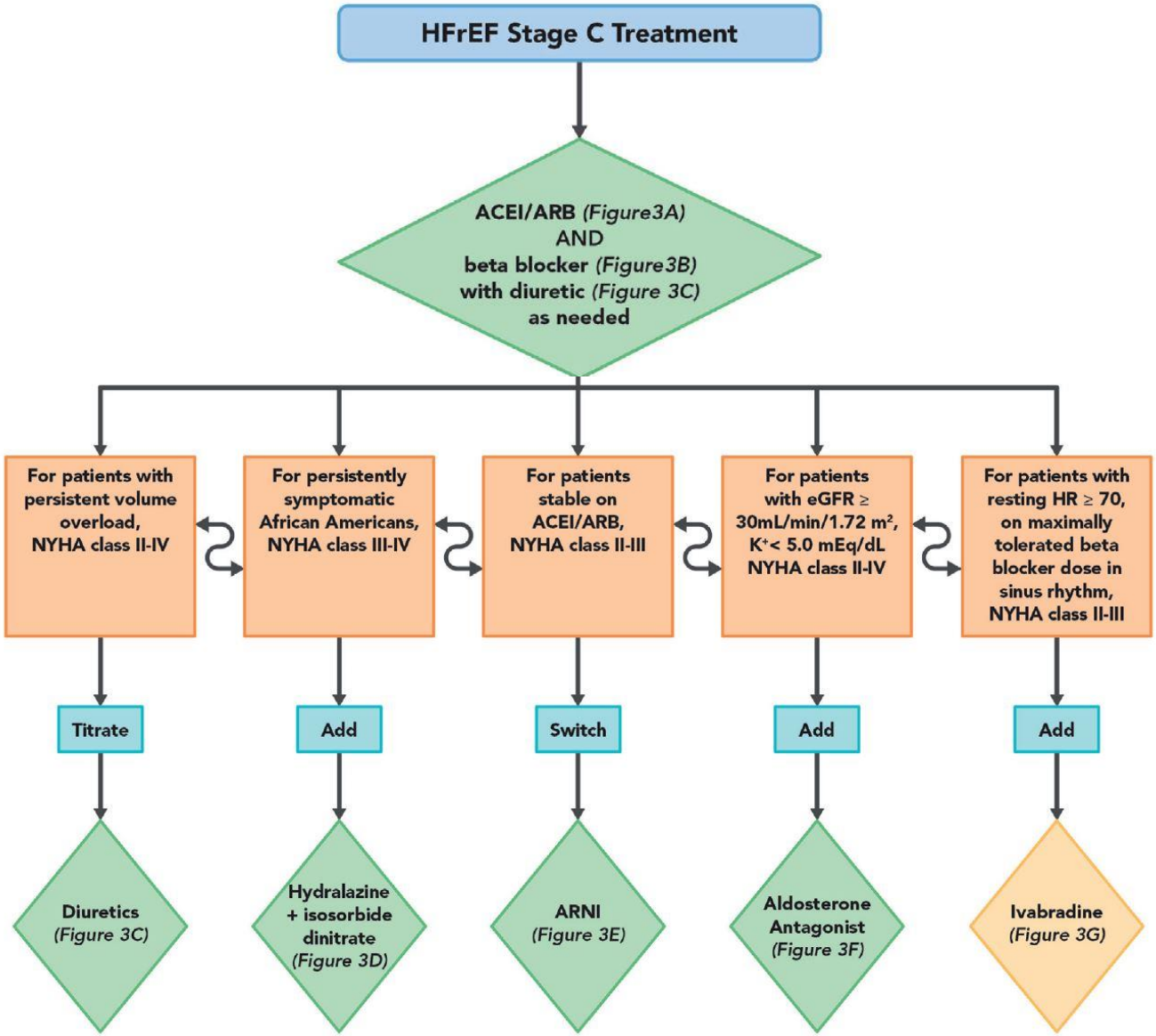
[b]BNP>35 pg/ml and/or NT-proBNP>125 pg/mL.

ESC Guidelines for HF: Patient With HFrEF



*Up-titrate to maximum tolerated evidence-based doses; †No further action required, Consider reduction diuretic dose.
Ponikowski P, et al. *Eur Heart J*. 2016;18:891-975.

2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment



2017 ACC Expert Consensus Decision Pathway for Optimization of Heart Failure Treatment

Ten Pathways and Principles to Guide Optimal Therapy:

- Principle 1: Target doses are associated with best outcomes.
- Principle 3: Optimal SNS modulation with target doses of beta-blockers appears to have the best effect on HFrEF outcomes (CV mortality, pump failure mortality, and SCD).
- Principle 6: Primary prevention device therapy and CRT should only be considered after consistent use of optimal doses of all medications for 3 to 6 months.
- Principle 7: Symptomatic congestion should be treated with diuretics irrespective of other therapies.
- Principle 9: Tolerability and side effects in part depend on how and when therapy is prescribed.

Nghiên cứu PIONEER-HF

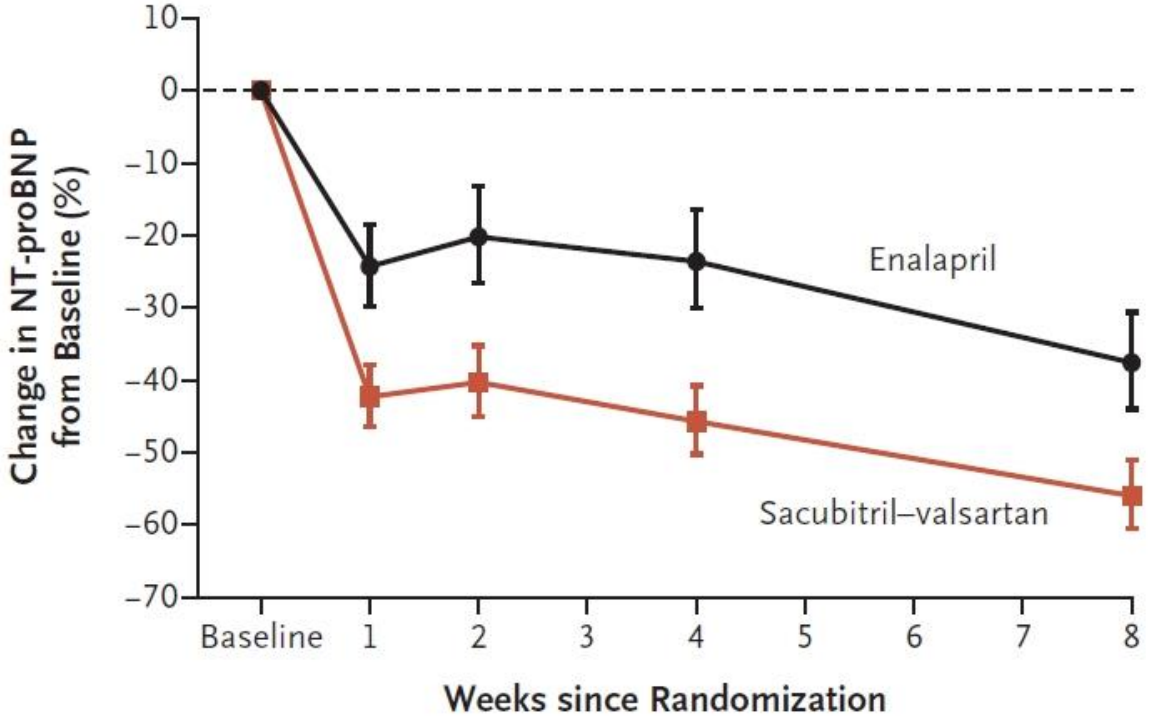
- TNLS phân nhóm ngẫu nhiên, mù đôi, đa trung tâm.
- Đối tượng: 881 bệnh nhân suy tim với EF ≤40% mới nhập viện vì đợt mất bù cấp, có huyết động đã ổn định:
  - HA tâm thu ≥100 mmHg
  - không phải tăng liều lợi tiểu tiêm TM
  - không phải dùng thuốc dãn mạch đường TM

  (trong 6 giờ trước)
  - không phải dùng thuốc tăng co bóp đường TM

  (trong 24 giờ trước)
- Loại trừ: eGFR <30 ml/min/1,73m^2, K^+ >5,2 mmol/L, tiền sử h/c MVC hoặc đột quị/TIA hoặc tái tưới máu ĐMV/ĐM cảnh 1 tháng trước, phụ nữ có thai hoặc đang cho con bú.
- Can thiệp: Sacubitril/valsartan hoặc enalapril.

Velazquez EJ et al. N Engl J Med 2018. DOI:10.1056/NEJMoa1812851.

Kết quả PIONEER-HF: Thay đổi NT-proBNP



No. at Risk					
Enalapril	394	359	351	350	348
Sacubitril–valsartan	397	355	363	365	349

Ratio of change with sacubitril/valsartan vs enalapril: 0,71 (95% CI 0,63 to 0,81; P < 0,001).

Tái nhập viện vì suy tim: RR sacubitril/valsartan vs enalapril 0,56 (0,37 - 0,84)

Velazquez EJ et al. N Engl J Med 2018. DOI:10.1056/NEJMoa1812851.

Use of Sacubitril/Valsartan: 2019 ESC Clinical Practice Update

2019 ESC Clinical Practice Update

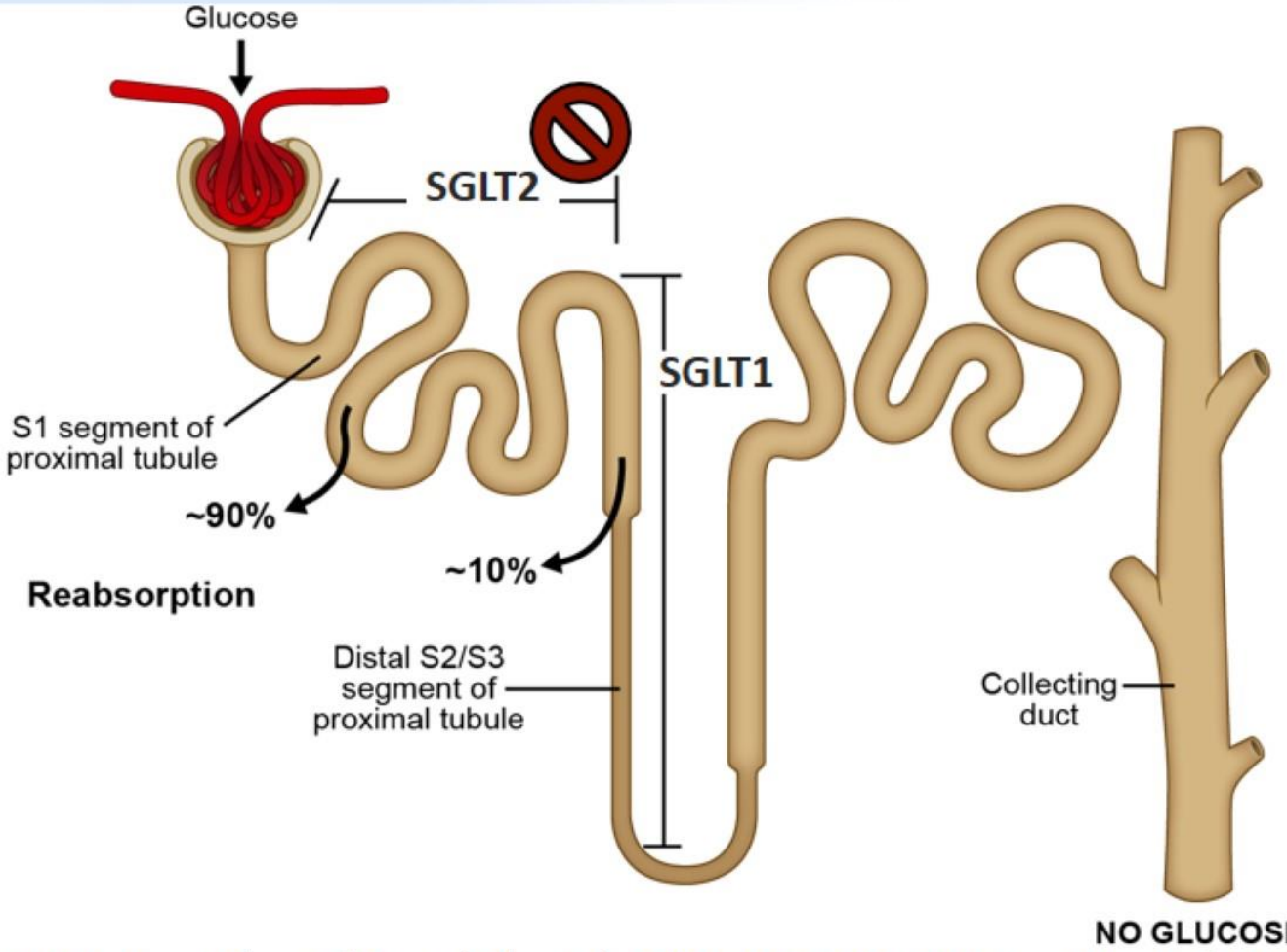
Sacubitril/valsartan is recommended as a replacement for an ACEI to further reduce the risk of HHF and death in ambulatory patients with HFrEF who remain symptomatic despite optimal treatment with an ACEI, BB, and MRA

Initiation of sacubitril/valsartan rather than an ACEI or an ARB may be considered for patients hospitalized with new-onset HF or decompensated HF to reduce the short-term risk of AEs and to simplify management

Seferovic PM, et al. *Eur J Heart Fail*. 2019 May 26 [Epub ahead of print]

SGLT2 Inhibitors

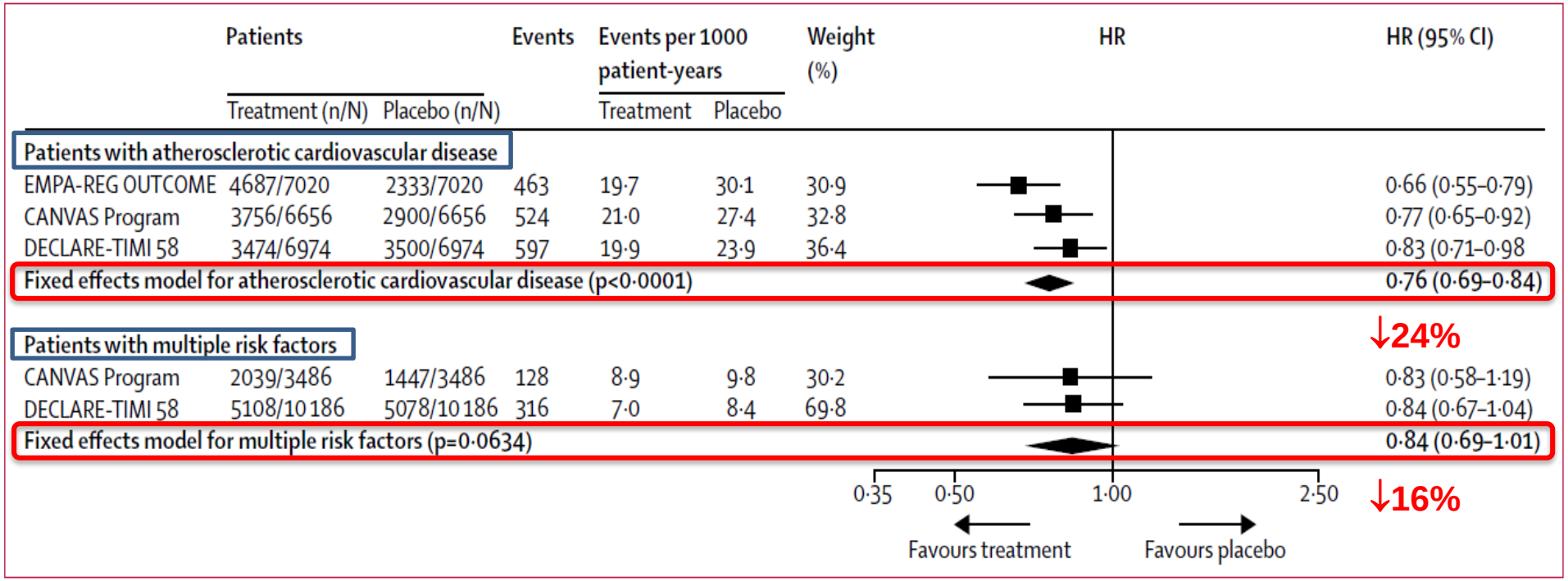
Canagliflozin, Dapaglifozin, Empagliflozin



Wright EM. *Am J Physiol Renal Physiol*. 2001;280:F10-F18; Lee YJ, et al. *Kidney Int Suppl*. 2007;106:S27-S35; Han S, et al. *Diabetes*. 2008;57:1723-1729.

Phân tích gộp kết quả của 3 TNLS với thuốc SGLT2i

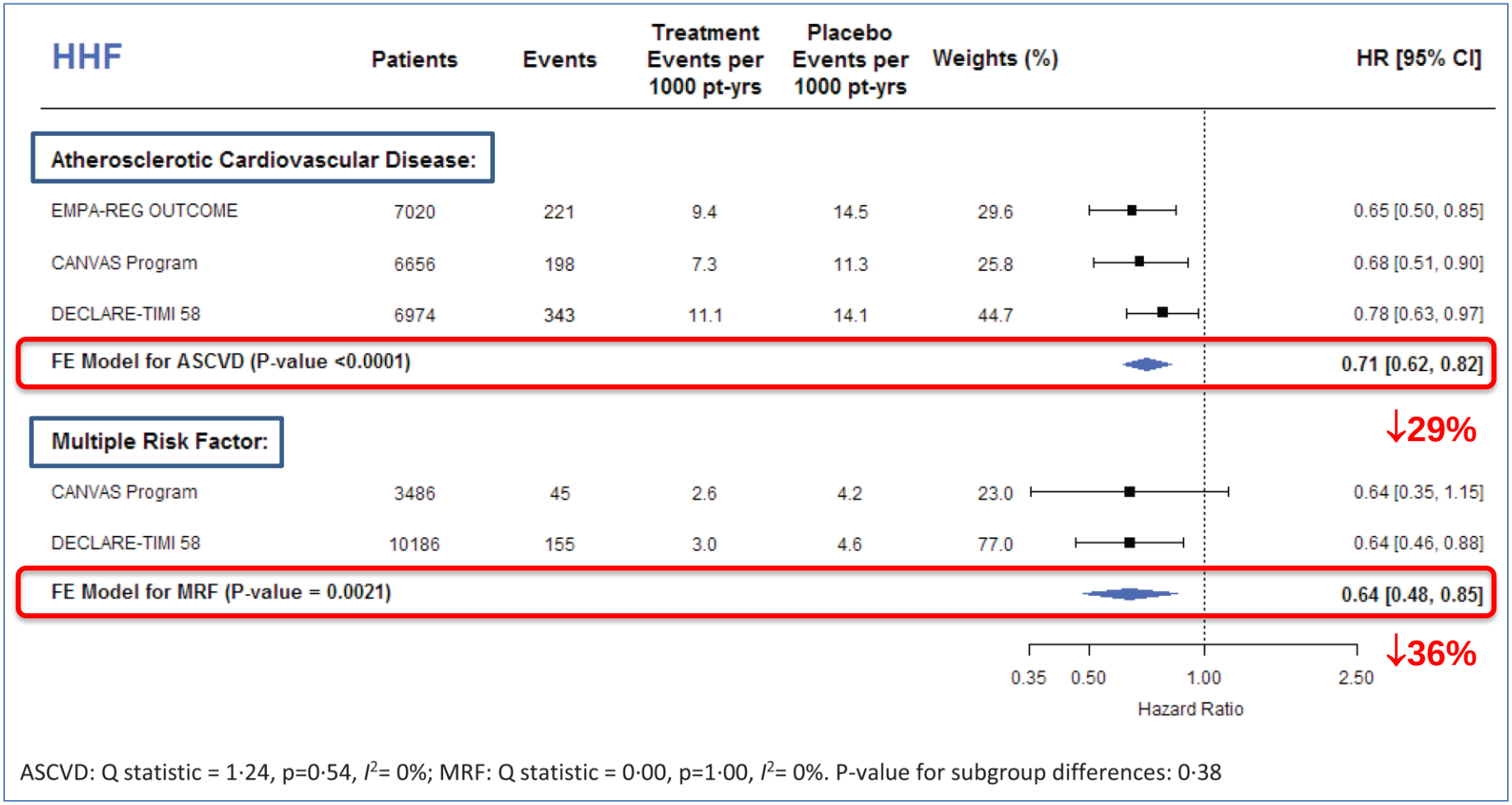
Nhập viện vì suy tim /chết do nguyên nhân tim mạch



Zelniker TA, et al. www.thelancet.com. Published online November 10, 2018. http://dx.doi.org/10.1016/S0140-6736(18)32590-X.

Phân tích gộp kết quả của 3 TNLS với thuốc SGLT2i

Nhập viện vì suy tim



ASCVD: Q statistic = 1·24, p=0·54, I^2= 0%; MRF: Q statistic = 0·00, p=1·00, I^2= 0%. P-value for subgroup differences: 0·38

Zelniker TA, Wiviott SD…Sabatine MA, Lancet 2018.

Cơ chế ngăn ngừa suy tim mới mắc/tăng nặng của thuốc ức chế SGLT2

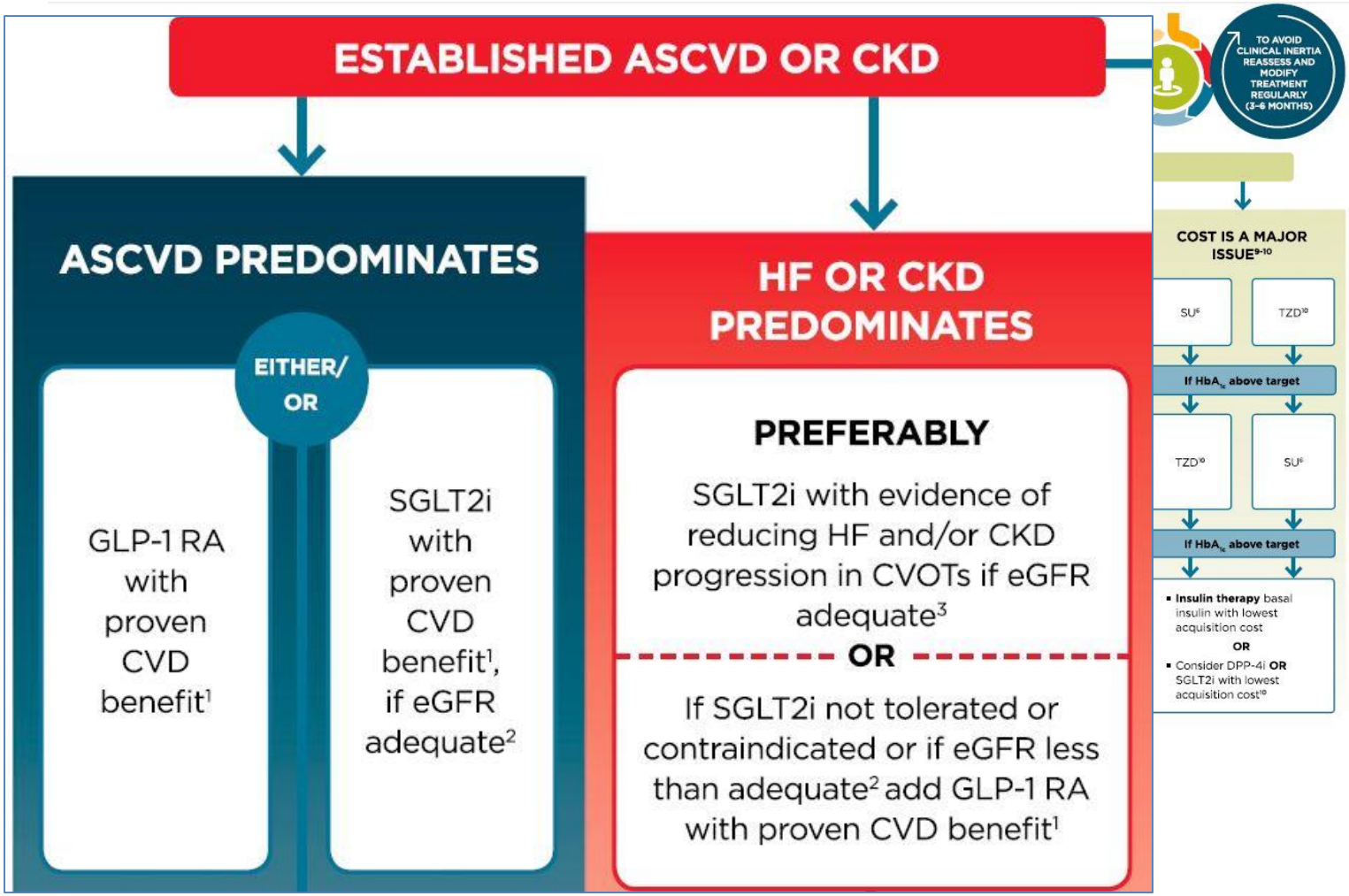
- Bài niệu, ↑thải Na & nước ở thận → ↓thể tích tuần hoàn, ↓tiền tải của tim (tác dụng giống thuốc lợi tiểu).
- ↓hoạt tính hệ RAA (↑lượng Na đến *macula densa*).
- ↓huyết áp → ↓hậu tải của tim.
- ↓nhu cầu dùng các thuốc hạ đường huyết uống có tác dụng giữ nước, gây tăng cân (TZD).
- Cải thiện chuyển hóa trong tế bào cơ tim (↑oxy hóa glucose, ↓sử dụng axít béo tự do để sinh năng lượng).

Sattar N et al. Diabetologia 2016;59:1333-1339.

9. Pharmacologic Approaches to Glycemic Treatment: *Standards of Medical Care in Diabetes—2019*

American Diabetes Association

Diabetes Care 2019;42(Suppl. 1):S90–S102 | https://doi.org/10.2337/dc19-S009



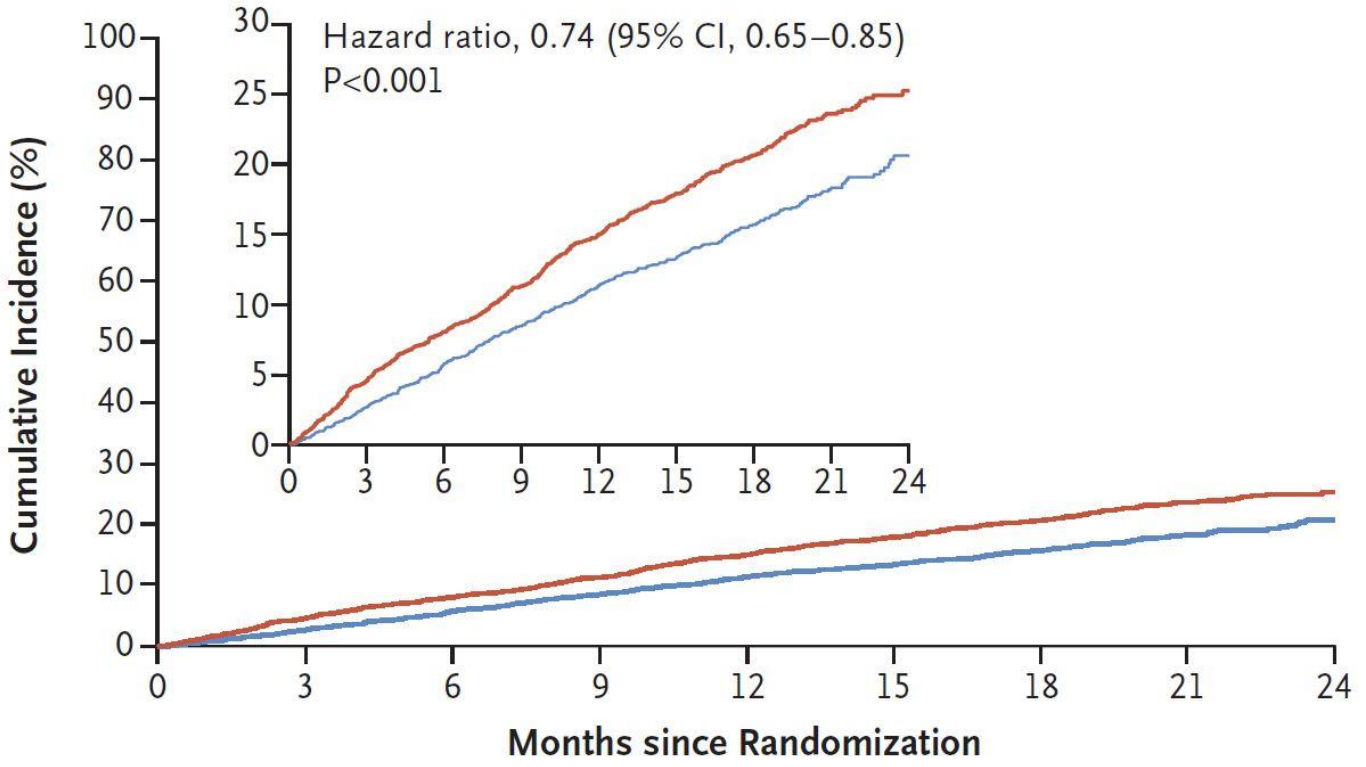
Nghiên cứu DAPA-HF

(Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure)

- TNLS phân nhóm ngẫu nhiên, mù đôi.
- Đối tượng: 4744 bệnh nhân suy tim mạn NYHA II-IV có PSTM ≤40% (42% có đái tháo đường).
- Can thiệp: Dapagliflozin 10 mg/ngày hoặc placebo trên nền điều trị chuẩn.
- Theo dõi trung bị 18,2 tháng.
- TCĐG chính: Suy tim tăng nặng (nhập viện hoặc khám cấp cứu & sau đó phải dùng thuốc TM điều trị suy tim) hoặc chết do nguyên nhân tim mạch.

McMurray JJV et al. N Engl J Med 2019. DOI:10.1056/NEJMoa1911303.

Kết quả DAPA-HF:
Suy tim tăng nặng /chết do nguyên nhân tim mạch



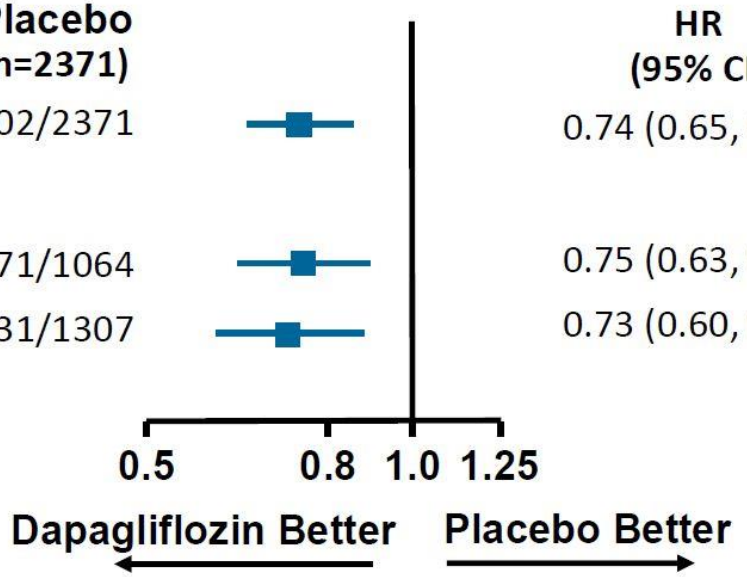
No. at Risk									
Placebo	2371	2258	2163	2075	1917	1478	1096	593	210
Dapagliflozin	2373	2305	2221	2147	2002	1560	1146	612	210

McMurray JJV et al. N Engl J Med 2019. DOI:10.1056/NEJMoa1911303.

Kết quả DAPA-HF

No diabetes/diabetes subgroup: Primary endpoint

	Dapagliflozin (n=2373)	Placebo (n=2371)	HR (95% CI)
All patients	386/2373	502/2371	0.74 (0.65, 0.85)
Type 2 diabetes at baseline*			
Yes	215/1075	271/1064	0.75 (0.63, 0.90)
No	171/1298	231/1307	0.73 (0.60, 0.88)



*Defined as history of type 2 diabetes or HbA1c ≥6.5% at **both** enrollment and randomization visits.

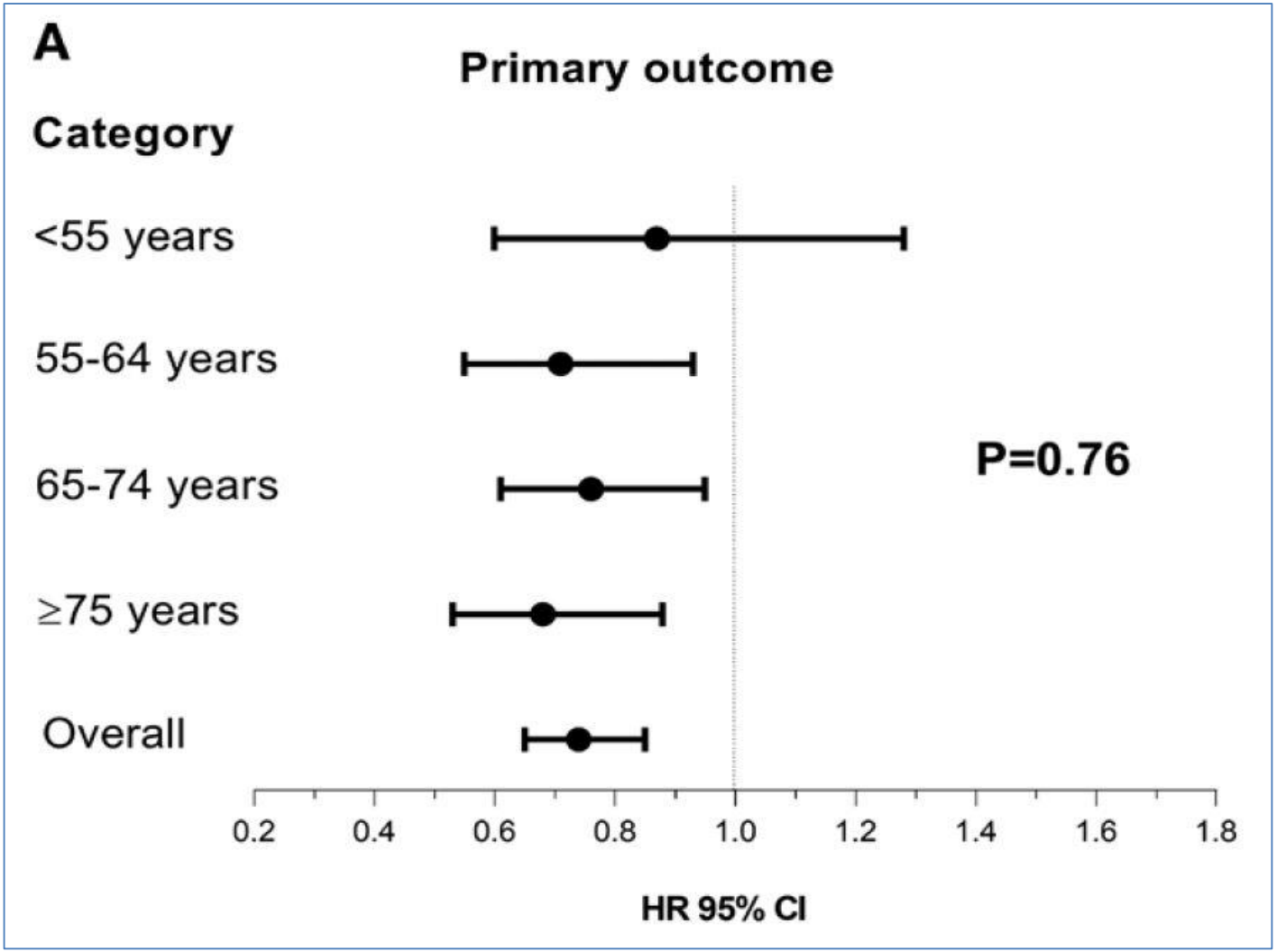
McMurray JJV et al. N Engl J Med 2019. DOI:10.1056/NEJMoa1911303.

Kết quả DAPA-HF

	Dapagliflozin (n = 2373)	Placebo (n = 2371)	HR (95% CI)	P
TCĐG chính	16,3%	21,2%	0,74 (0,65-0,85)	< 0,001
Nhập viện vì suy tim	9,7%	13,4%	0,70 (0,59-0,83)	
Tử vong tim mạch	9,6%	11,5%	0,82 (0,69-0,98)	
Tử vong mọi nguyên nhân	11,6%	13,9%	0,83 (0,71-0,97)	

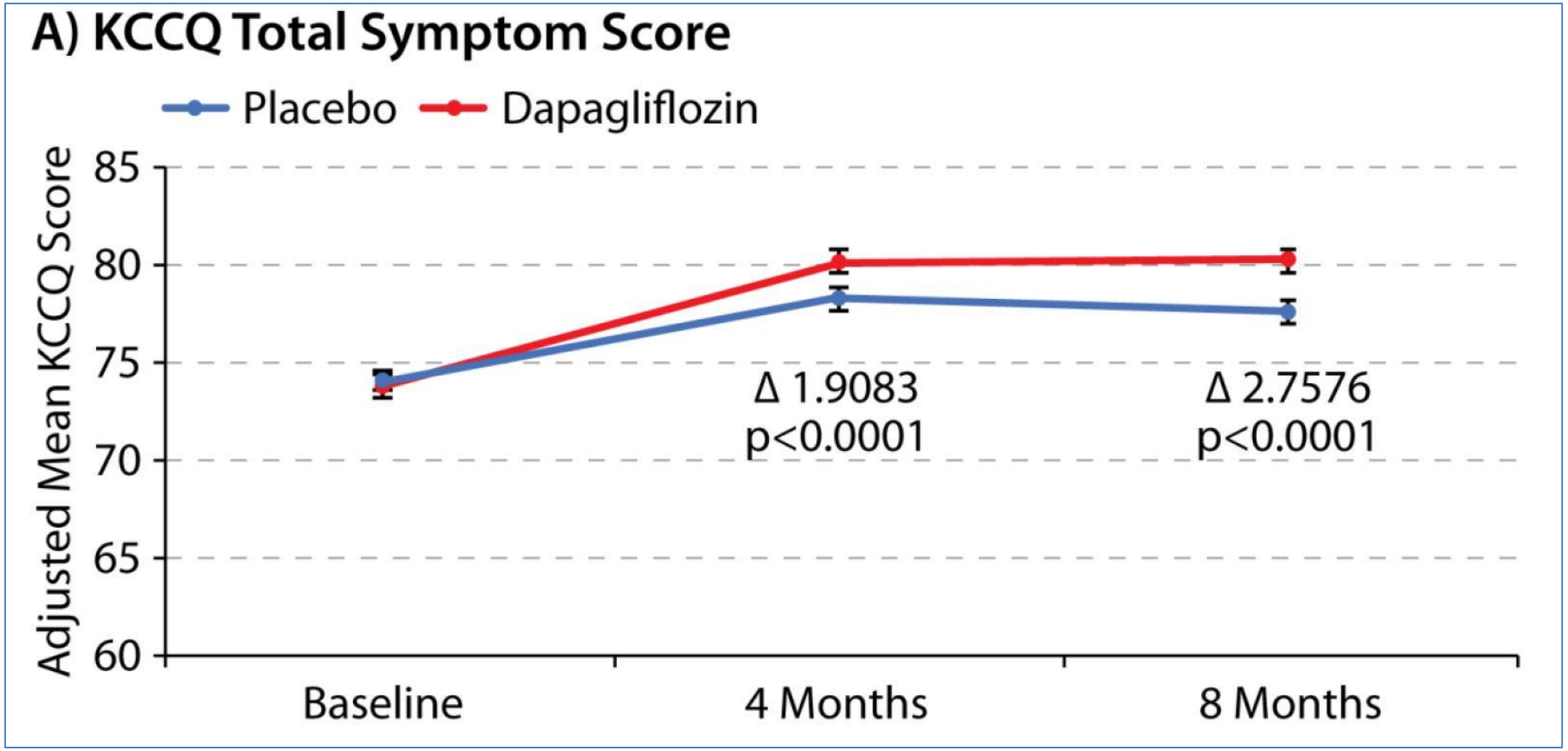
McMurray JJV et al. N Engl J Med 2019. DOI:10.1056/NEJMoa1911303.

Kết quả DAPA-HF



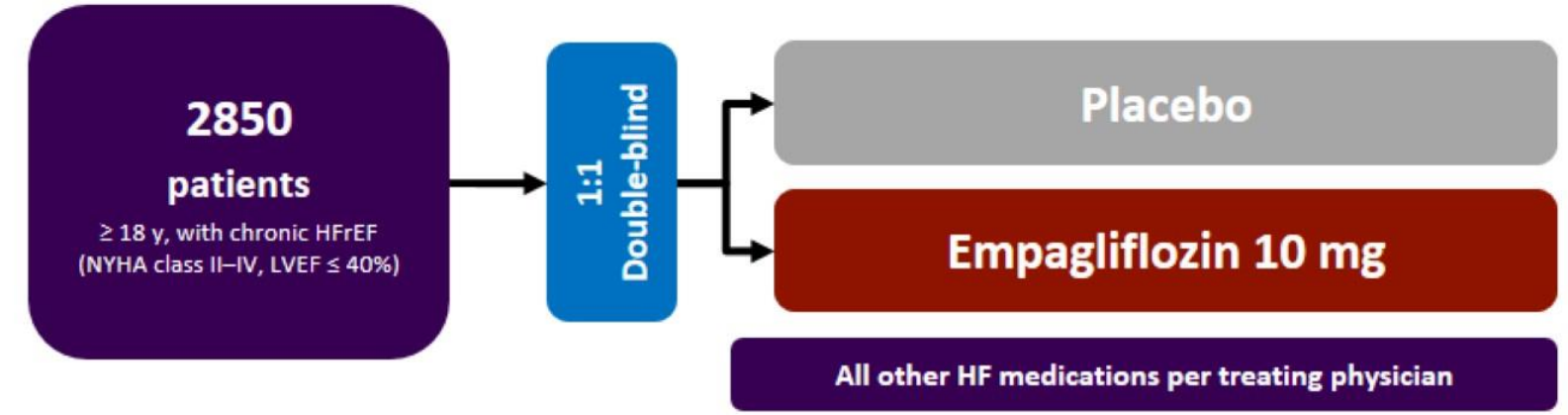
Martinez FA et al. Circulation 2019. DOI:10.1161/CIRCULATIONAHA.119.044133.

Kết quả DAPA-HF



Kosiborod M et al. Circulation 2019. DOI:10.1161/CIRCULATIONAHA.119.044138.

EMPEROR-Reduced: Empagliflozin Outcome Trial in Patients With Chronic HFrEF



Primary endpoint:

- Time to first event of: CV death **or** hospitalization for HF

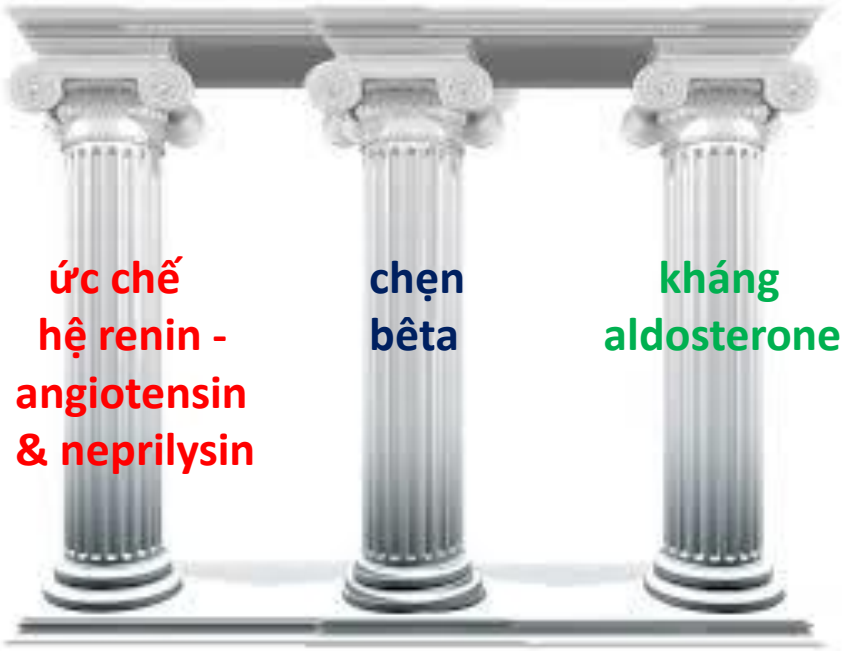
Secondary endpoints:

- Occurrence of adjudicated hHF
- Change from baseline in eGFR
- Time to occurrence of sustained reduction in eGFR
- Time to occurrence of all-cause mortality
- Time to onset of T2D
- Change from baseline in KCCQ

ClinicalTrials.gov. NCT03057977.

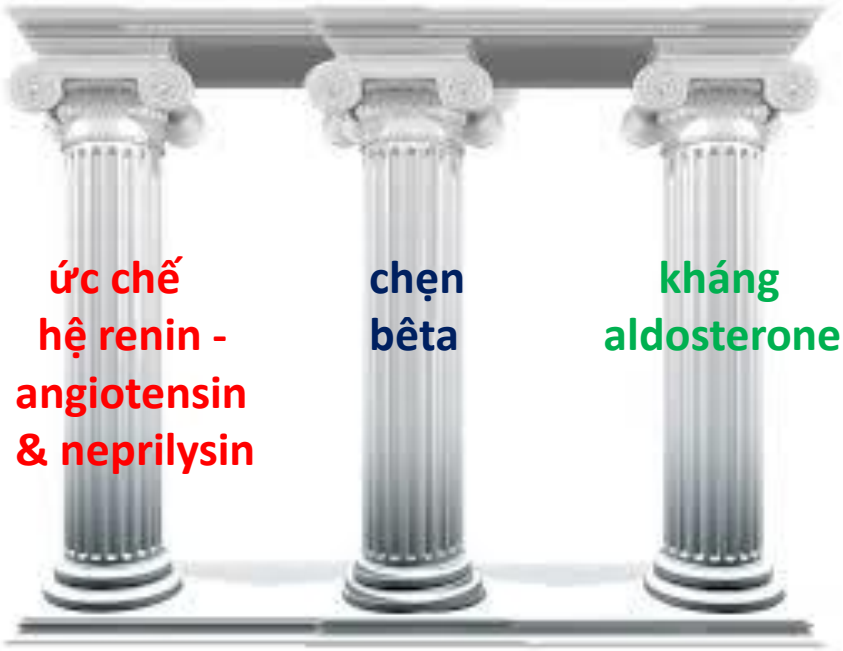
Điều trị suy tim mạn với PSTM giảm bằng thuốc

Hiện tại



Điều trị suy tim mạn với PSTM giảm bằng thuốc

Hiện tại → Triển vọng tương lai



Điều trị suy tim mạn với PSTM bảo tồn (HFpEF) hoặc PSTM trong khoảng giữa (HFmrEF) – ESC 2016

Recommendations	Class [a]	Level [b]	Ref [c]
it is recommended to screen patients with HFpEF or HFmrEF for both cardiovascular and non-cardiovascular comorbidities, which, if present, should be treated provided safe and effective interventions exist to improve symptoms, well-being and/or prognosis.	I	C	
Diuretics are recommended in congested patients with HFpEF or HFmrEF in order to alleviate symptoms and signs.	I	B	178, 179

[a]Class of recommendation.
[b]Level of evidence.
[c]Reference(s) supporting recommendations.

Điều trị suy tim mạn với PSTM bảo tồn
Nghiên cứu PARAGON-HF

- TNLS phân nhóm ngẫu nhiên, đa trung tâm.
- Đối tượng: 4822 bệnh nhân suy tim NYHA II-IV, EF ≥ 45%, có bệnh tim cấu trúc và ↑NT-proBNP.
- Can thiệp: Sacubitril/valsartan (200 mg x 2/ngày) hoặc valsartan (160 mg x 2/ngày).
- Theo dõi trung vị 35 tháng.
- TCĐG chính: Nhập viện vì suy tim hoặc chết do nguyên nhân tim mạch.

Solomon SD et al. N Engl J Med 2019. DOI:10.1056/NEJMoa1908655.

Điều trị suy tim mạn với PSTM bảo tồn
Nghiên cứu PARAGON-HF

	Sacubitril-Valsartan (n = 2407)	Valsartan (n = 2389)	RR (95% CI)
Nhập viện vì suy tim /chết do NN tim mạch	12,8/100 BN-năm	14,6/100 BN-năm	0,87 (0,75-1,01)
Chết do NN tim mạch	8,5%	8,9%	0,95 (0,79-1,16)
Tử vong mọi NN	14,2%	14,6%	0,97 (0,84-1,13)

Solomon SD et al. N Engl J Med 2019. DOI:10.1056/NEJMoa1908655.

Clinical practice update on heart failure 2019

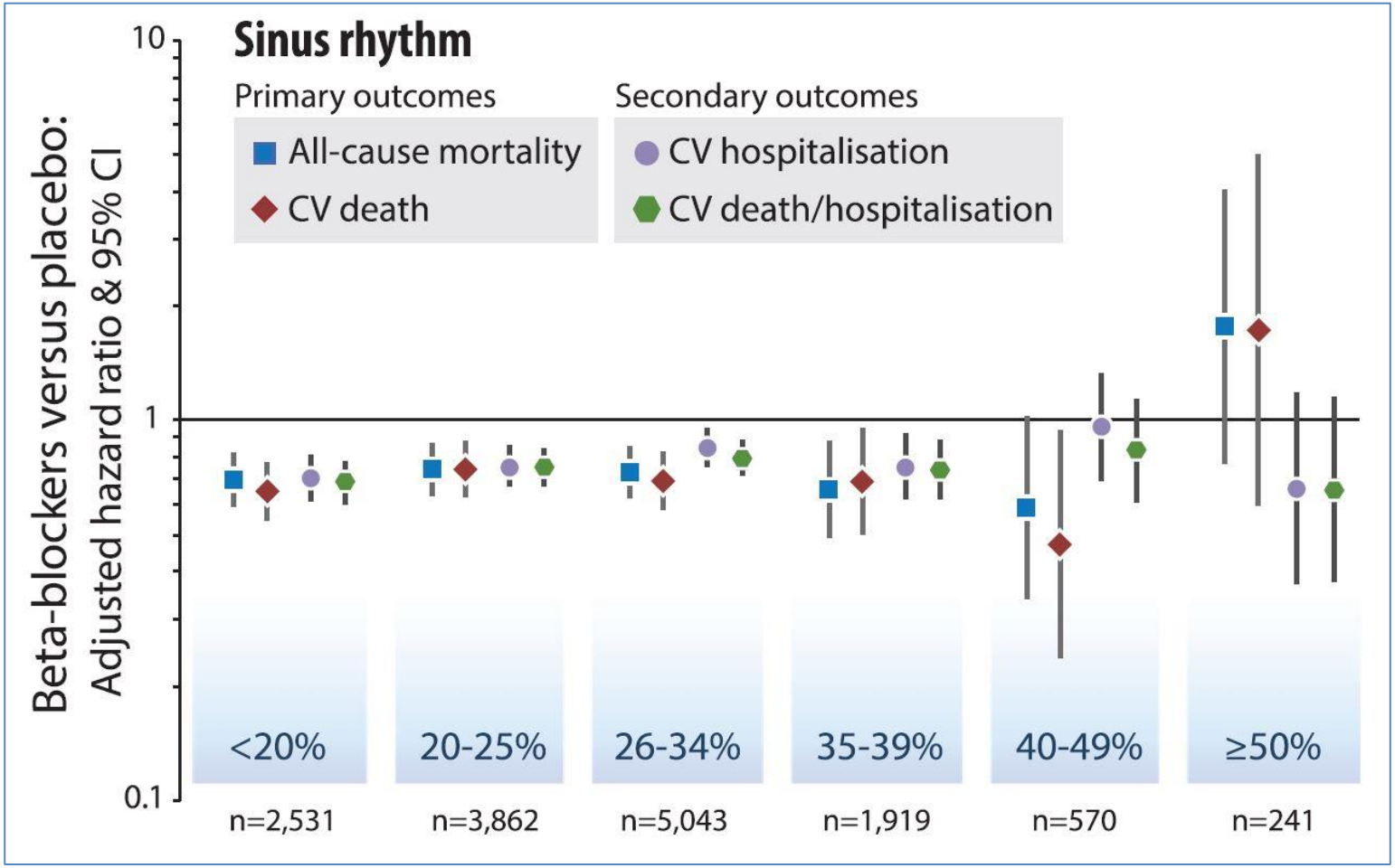
An expert consensus meeting report of the Heart Failure Association of the European Society of Cardiology

Pharmacotherapy in HFmrEF:

- **A beta-blocker** *may be considered* for ambulatory patients with symptomatic HFmrEF in sinus rhythm in order to reduce the risk of all-cause and CV death.
- **Candesartan** *may be considered* for ambulatory patients with symptomatic HFmrEF in order to reduce the risk of HF hospitalization and CV death (CHARM programme post-hoc analysis).
- **Spironolactone** *may be considered* for ambulatory patients with symptomatic HFmrEF without contraindications in order to reduce the risk of CV death and HF hospitalization (TOPCAT post-hoc analysis).

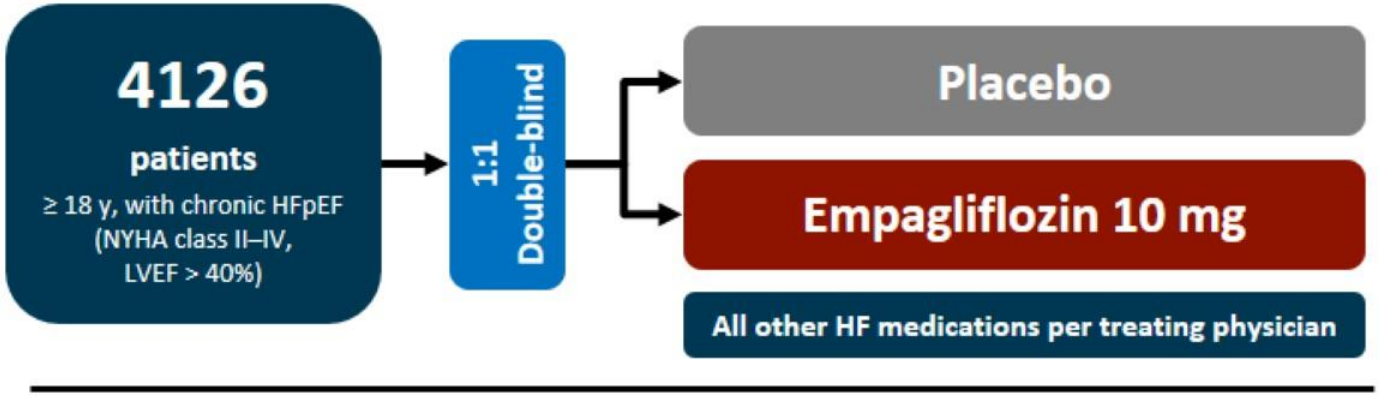
Lợi ích của thuốc chẹn β tùy theo PSTM

Phân tích gộp số liệu 11 TNLS (17 312 bệnh nhân suy tim)



Cleland JGF et al. Eur Heart J 2018;39:26-35.

EMPEROR-Preserved: Empagliflozin Outcome Trial in Patients With Chronic HFpEF



Primary endpoint:

- Time to first event of: CV death **OR** hospitalization for HF

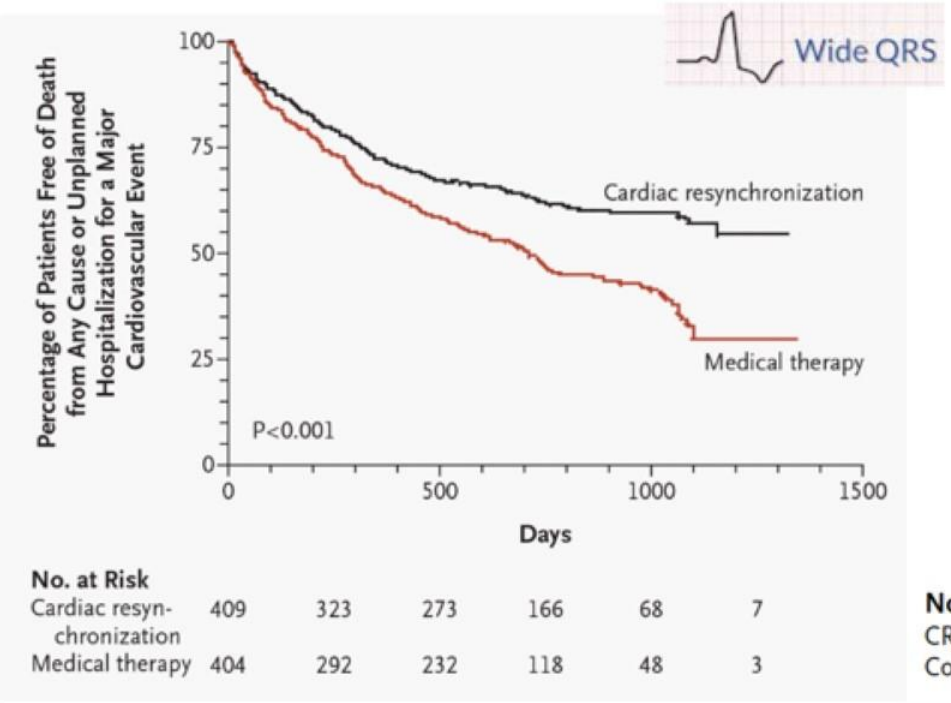
Secondary endpoints:

- Occurrence of adjudicated hHF
- Change from baseline in eGFR
- Time to occurrence of sustained reduction in eGFR
- Time to occurrence of all-cause mortality
- Time to onset of T2D
- Change from baseline in KCCQ

ClinicalTrials.gov. NCT03057951.

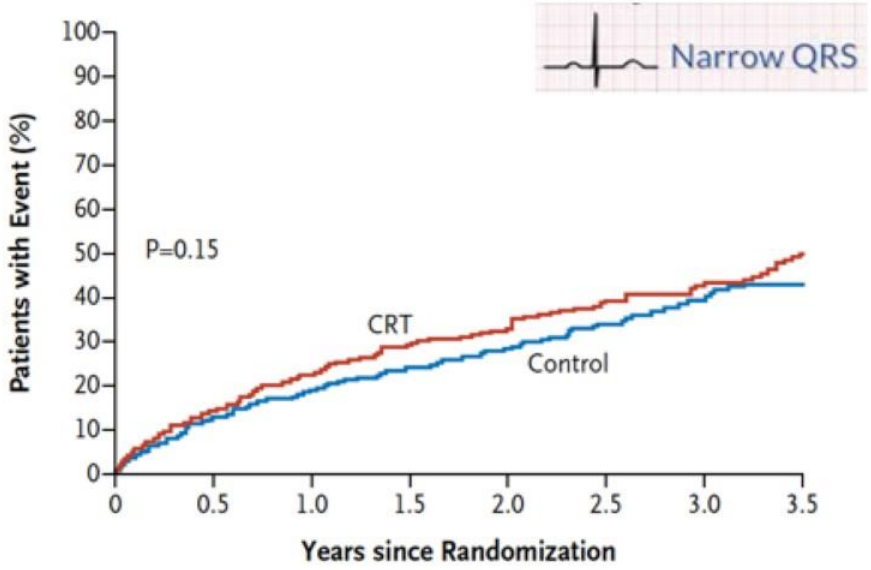
CRT: Life Saving Therapy in Wide QRS

CARE-HF



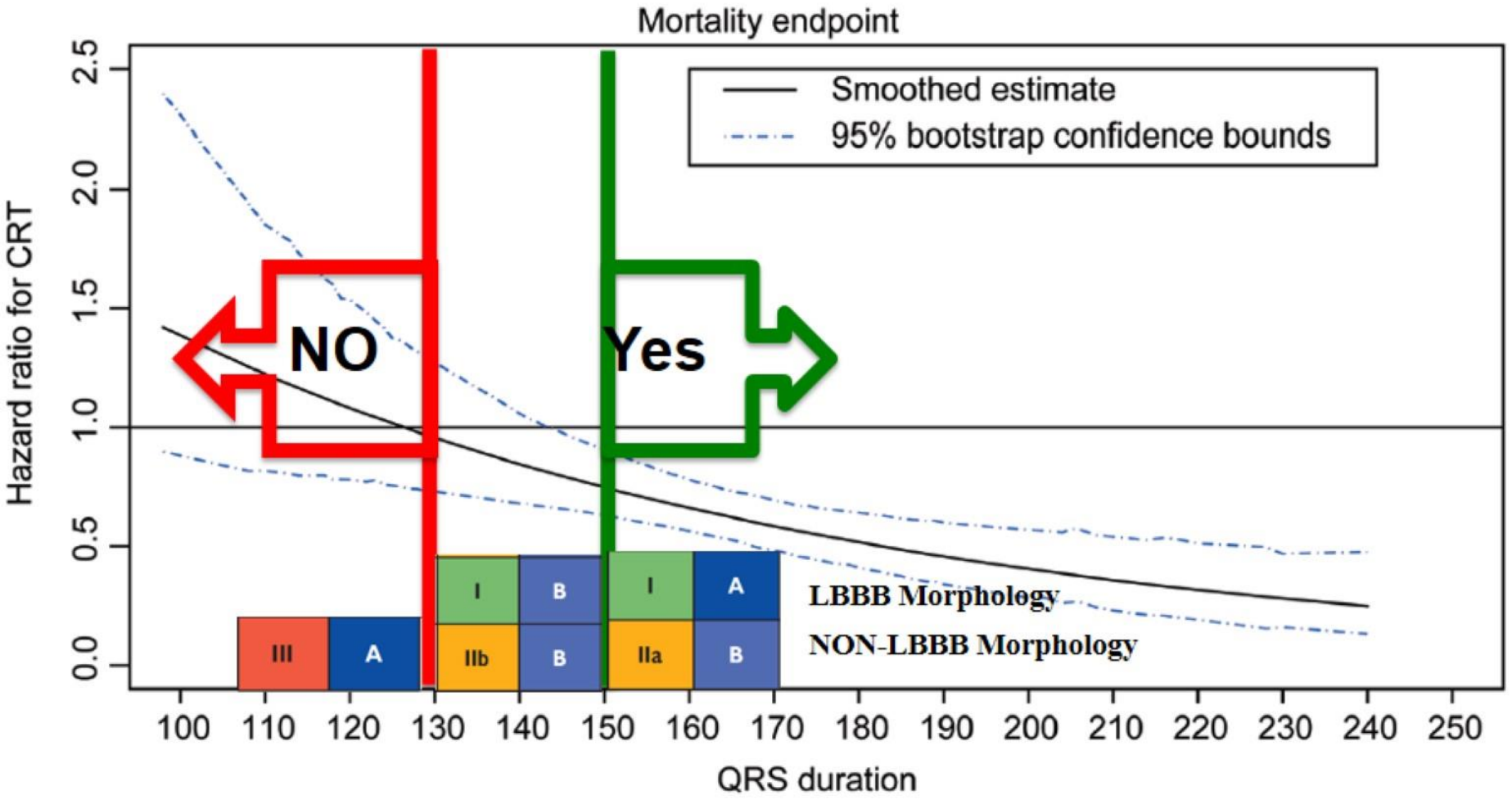
No. at Risk						
Cardiac resynchronization	409	323	273	166	68	7
Medical therapy	404	292	232	118	48	3

EchoCRT



No. at Risk								
CRT	404	297	223	155	103	65	42	19
Control	405	302	236	166	119	71	44	15

ESC Guidelines: The DOs and DON'Ts of CRT



Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

Recommendations for CRT Therapy in HF

Recommendations*	Class†	Level‡
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 to improve symptoms and reduce morbidity and mortality.	I	A
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 to improve symptoms and reduce morbidity and mortality.	IIa	B
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 to improve symptoms and reduce morbidity and mortality.	I	B

*Please see published guidelines for full list. †Class of Recommendation. ‡Level of Evidence.
Ponikowski P, et al. *Eur Heart J.* 2016;18:891-975.

2018 ACC/AHA/HRS Guideline on the Evaluation and Management of Patients with Bradycardia and Cardiac Conduction Delay

IIa	B-R[SR]	4. In patients with atrioventricular block who have an indication for permanent pacing with a LVEF between 36% and 50% and are expected to require ventricular pacing more than 40% of the time, it is reasonable to choose pacing methods that maintain physiologic ventricular activation (e.g., cardiac resynchronization therapy [CRT] or His bundle pacing) over right ventricular pacing (S6.4.4.1-7, S6.4.4.1-11–S6.4.4.1-19).

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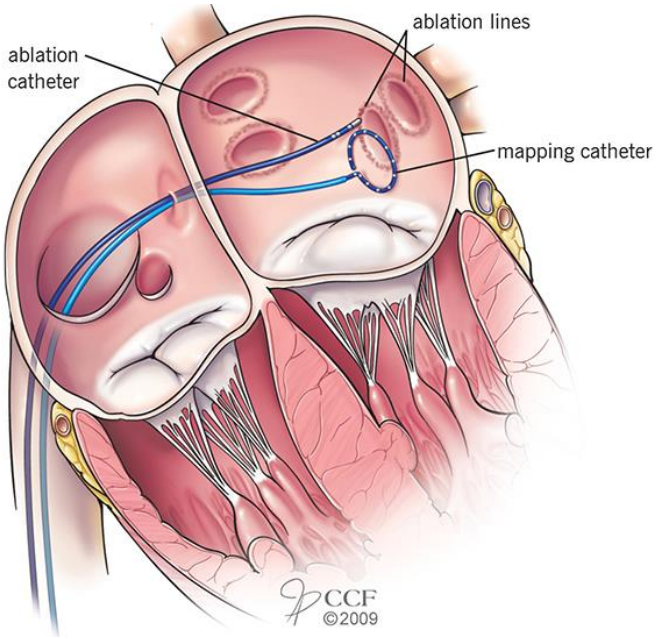
Atrial fibrillation ablation:

- **Pulmonary vein ablation** of patients with HF and symptomatic paroxysmal AF *may be considered*, if paroxysms cause troublesome symptoms despite implementation of guideline-recommended pharmacological and device therapy.



Nghiên cứu CASTLE-AF

(Catheter Ablation versus Standard conventional Treatment in patients with Left ventricular dysfunction and Atrial Fibrillation)

- TNLS phân nhóm ngẫu nhiên, đa trung tâm.
- Đối tượng: 363 bệnh nhân rung nhĩ kịch phát hoặc dai dẳng có triệu chứng, suy tim NYHA II-IV, LVEF ≤ 35%, không dung nạp ≥ 1 thuốc CLN hoặc không muốn dùng thuốc CLN.
- Can thiệp: Triệt phá rung nhĩ bằng ca-tê-te (cô lập các tĩnh mạch phổi) hoặc điều trị qui ước.
- Theo dõi trung vị 37,8 tháng.
- Kết quả: Triệt phá rung nhĩ bằng ca-tê-te giảm

  38% (P = 0,007) tử vong mọi nguyên nhân/nhập viện vì suy tim↑

  47% (P = 0,011) tử vong mọi nguyên nhân

Marrouche NF et al. N Engl J Med 2018;378:417-427.

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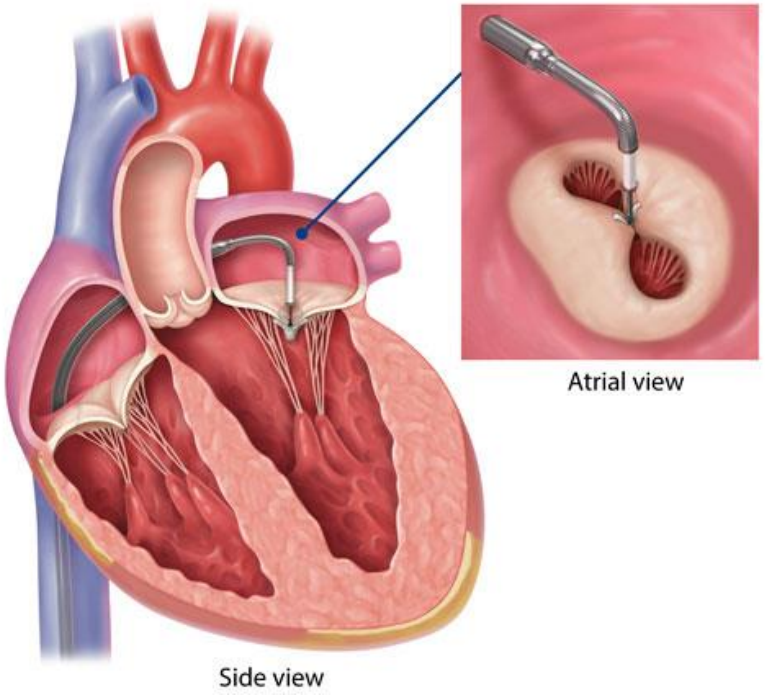
Mitraclip:

- Referral of patients with HF and secondary (i.e. functional) mitral regurgitation to a multidisciplinary HF team that will decide on management *is recommended.*
- Reduction in mitral regurgitation using a **Mitraclip device** *may be considered* for patients with HFrEF who fulfill the COAPT selection criteria.



Nghiên cứu COAPT

(Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation)

- TNLS phân nhóm ngẫu nhiên, đa trung tâm (Hoa Kỳ & Canada).
- Đối tượng: 614 bệnh nhân hở van 2 lá thứ phát (từ vừa-nặng đến nặng), có PSTM 20-50% và triệu chứng suy tim NYHA II-IV dù đã được điều trị nội khoa tối ưu.
- Can thiệp: Sửa van 2 lá qua đường ca-tê-te bằng MitraClip hoặc điều trị nội khoa đơn thuần (nhóm chứng).
- Kết quả: Sửa van 2 lá bằng MitraClip giảm

  47% ($P < 0,001$) nhập viện vì suy tim sau 24 tháng

  38% ($P < 0,001$) tử vong do mọi nguyên nhân sau 24 tháng

Stone GW et al. N Engl J Med 2018. DOI:10.1056/NEJMoa1806640.

COAPT selection criteria

Exclusion criteria (all must be absent)

1. Untreated clinically significant coronary artery disease requiring revascularization
2. CABG, PCI, or TAVR within the prior 30 days
3. Aortic or tricuspid valve disease requiring surgery or transcatheter intervention
4. COPD requiring continuous home oxygen therapy or chronic outpatient oral steroid use
5. Cerebrovascular accident within prior 30 days
6. Severe symptomatic carotid stenosis (>70% by ultrasound)
7. Carotid surgery or stenting within prior 30 days
8. ACC/AHA Stage D heart failure
9. Presence of any of the following: estimated PASP >70 mmHg assessed by site based on echocardiography or right heart catheterization, unless active vasodilator therapy in the cath lab is able to reduce PVR to <3 Wood Units or between 3 and 4.5 Wood Units with v wave less than twice the mean of PCWP
10. Hypertrophic cardiomyopathy, restrictive cardiomyopathy, constrictive pericarditis, or any other structural heart disease causing heart failure other than dilated cardiomyopathy of either ischaemic or non-ischaemic aetiology
11. Infiltrative cardiomyopathies (e.g. amyloidosis, haemochromatosis, sarcoidosis)
12. Haemodynamic instability requiring inotropic support or mechanical heart assistance
13. Physical evidence of right-sided congestive heart failure with echocardiographic evidence of moderate or severe right ventricular dysfunction
14. Implant of CRT or CRT-D within the last 30 days
15. Mitral valve orifice area <4.0 cm^2 by site-assessed transthoracic echocardiography
16. Leaflet anatomy which may preclude MitraClip implantation, proper MitraClip positioning on the leaflets, or sufficient reduction in mitral regurgitation by the MitraClip
17. Haemodynamic instability defined as systolic pressure <90 mmHg with or without afterload reduction, cardiogenic shock, or the need for inotropic support or intra-aortic balloon pump or other haemodynamic support device
18. Need for emergent or urgent surgery for any reason or any planned cardiac surgery within the next 12 months
19. Life expectancy <12 months due to non-cardiac conditions
20. Modified Rankin Scale ≥4 disability
21. Status 1 heart transplant or prior orthotopic heart transplantation
22. Prior mitral valve leaflet surgery or any currently implanted prosthetic mitral valve, or any prior transcatheter mitral valve procedure
23. Echocardiographic evidence of intracardiac mass, thrombus, or vegetation
24. Active endocarditis or active rheumatic heart disease or leaflets degenerated from rheumatic disease (i.e. non-compliant, perforated)
25. Active infections requiring current antibiotic therapy
26. Transoesophageal echocardiography is contraindicated or high risk
27. Known hypersensitivity or contraindication to procedural medications which cannot be adequately managed medically
28. Pregnant or planning pregnancy within the next 12 months
29. Currently participating in an investigational drug or another device study that has not reached its primary endpoint
30. Subject belongs to a vulnerable population or has any disorder that compromises his/her ability to give written informed consent and/or to comply with study procedures

Cảm ơn sự chú ý của quý đồng nghiệp