Management of congestive heart failure with reduced ejection fraction

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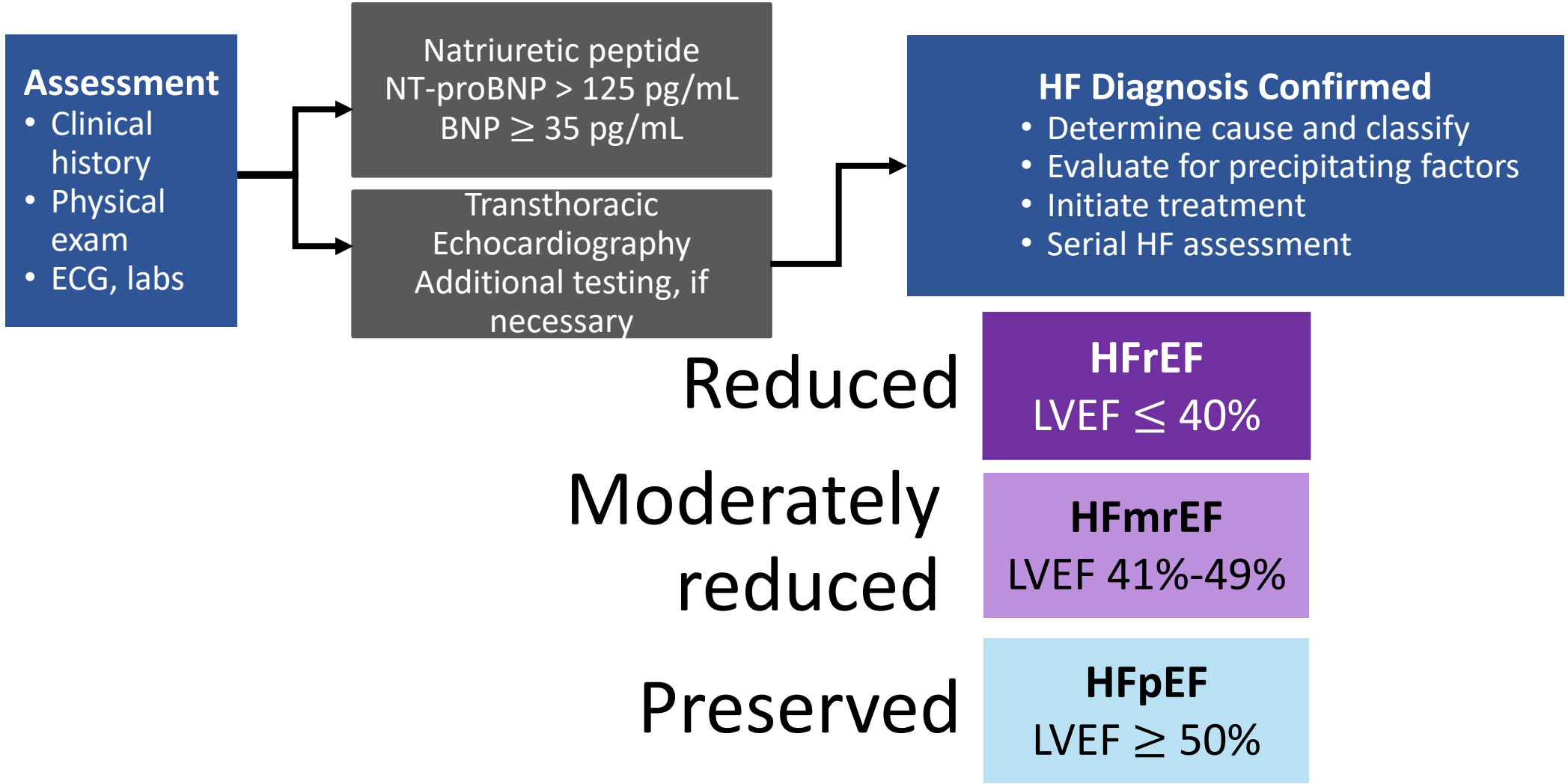
Duke University

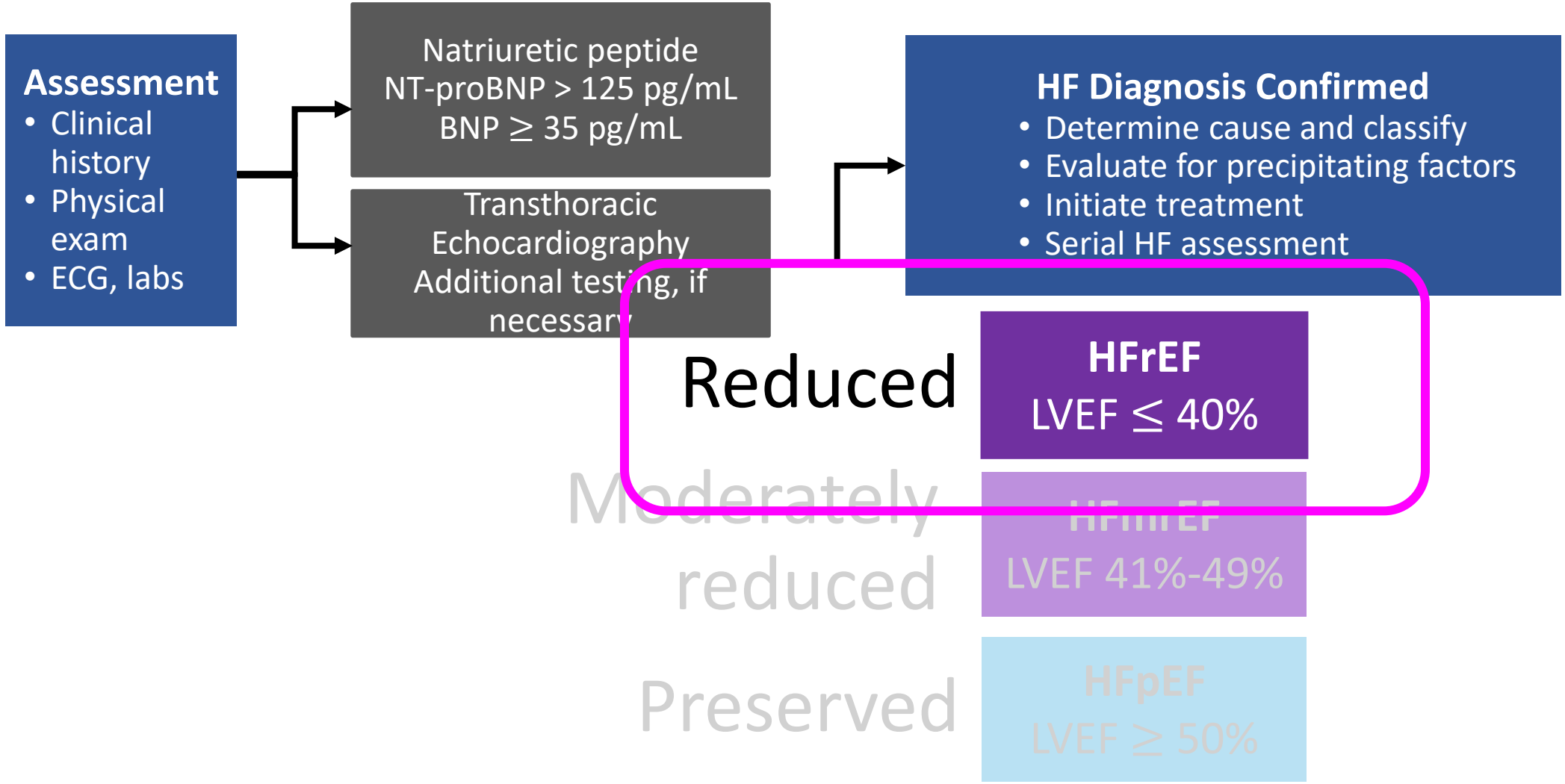
Disclosures

- None

Heart failure with reduced ejection fraction

- **Definitions**
- Medical therapy
- Referral
  - Revascularization
  - Implantable cardiac defibrillators (ICD) cardiac resynchronization therapy (CRT)


Assessment
• Clinical history
• Physical exam
• ECG, labs
Natriuretic peptide
NT-proBNP > 125 pg/mL
BNP ≥ 35 pg/mL
Transthoracic Echocardiography
Additional testing, if necessary
HF Diagnosis Confirmed
• Determine cause and classify
• Evaluate for precipitating factors
• Initiate treatment
• Serial HF assessment
Reduced
HFrEF
LVEF ≤ 40%
Moderately reduced
HFmrEF
LVEF 41%-49%
Preserved
HFpEF
LVEF ≥ 50%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Heart failure with reduced ejection fraction

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CS 68 y.o. man

68-year-old man previously ran a commercial cleaning business

Diabetes - hemoglobin A 1 of 10.5 to 8.5 with metformin.

Progressive shortness of breath walking up 1 flight of stairs. Leg swelling.

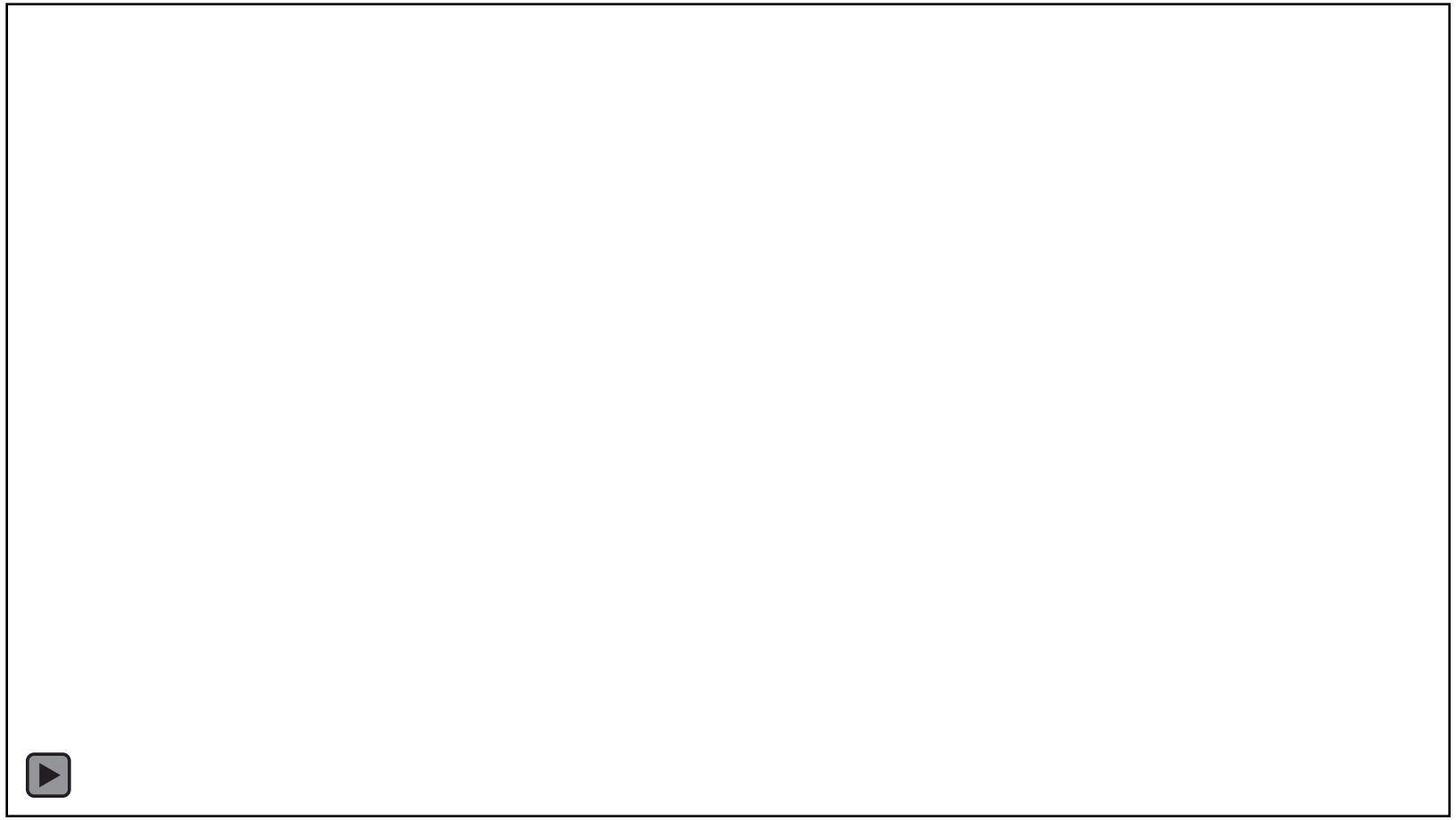
Echocardiogram - a mildly dilated left ventricle with ejection fraction in the 30% range. During echo heart rate was above 100.

Denies any chest pain

Father died of a myocardial infarction at 69. No family history of heart failure.

BP running 130-150 /85-97 range, on lisinopril

CS 68 y.o. man



CS 68 y.o. man

- Pro B-type Natriuretic Peptide 1290 pg/mL
- Na 139, K 4.9, creatinine 1.0

CS

ID:001956882

Male

Room:Exam Room 132
Loc:300

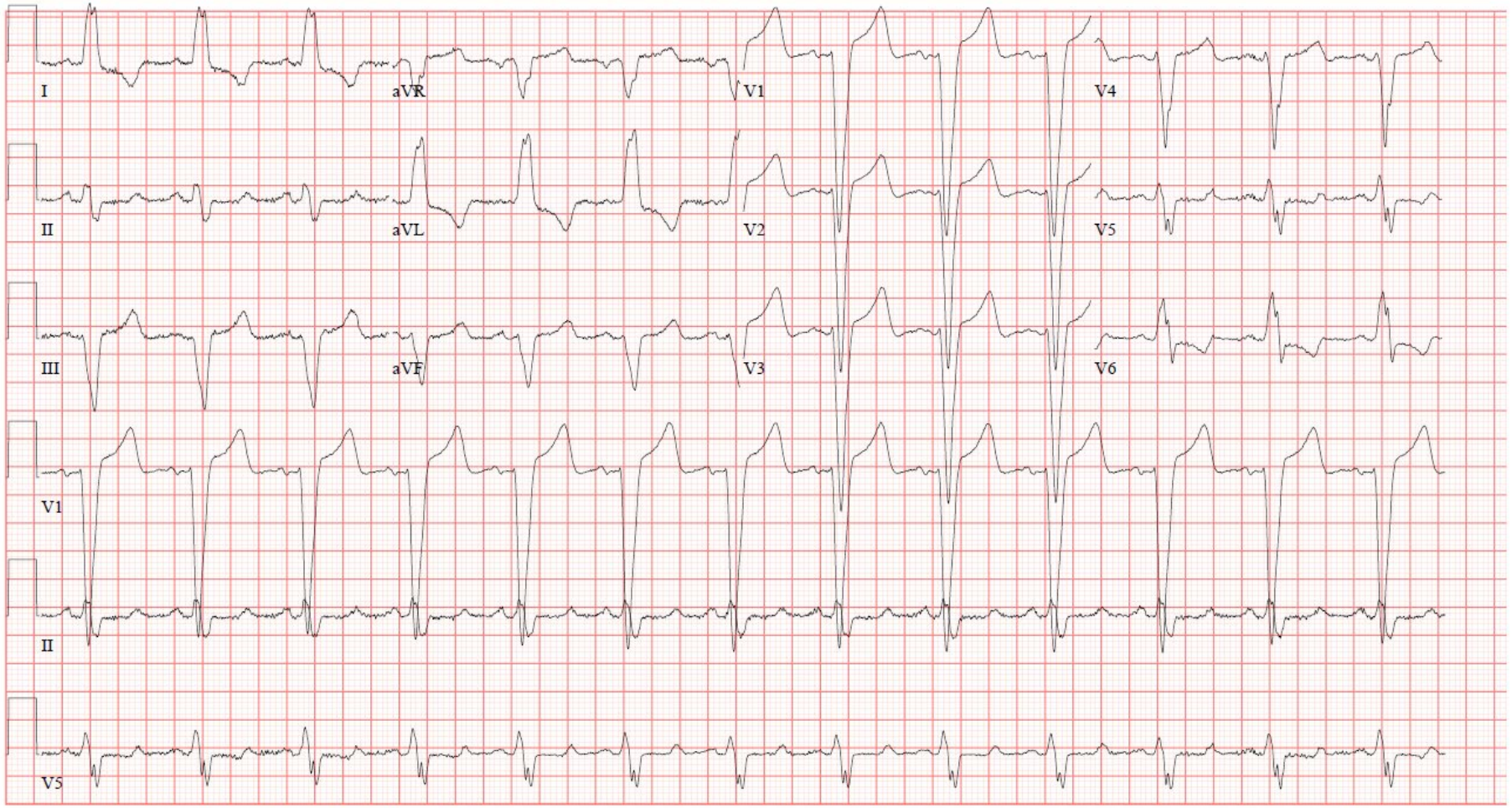
Vent. rate	78	BPM
QRS duration	162	ms
P-R-T axes	59 -33	141

Normal sinus rhythm
Left axis deviation
Left bundle branch block
Abnormal ECG
No previous ECGs available
Confirmed by JOLLIS MD, JA

Technician:TAMMY CASE
Test ind:

Referred by: John Rouchard

Confirmed By: JAMES JOLLIS MD



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Page 1 of '

LBBB
QRS duration 162 ms

CS 68 y.o. man

- Started Sacubitril / Valsartan 49 mg / 51 mg after holding lisinopril for 3 days.

Nonischemic Causes of HF

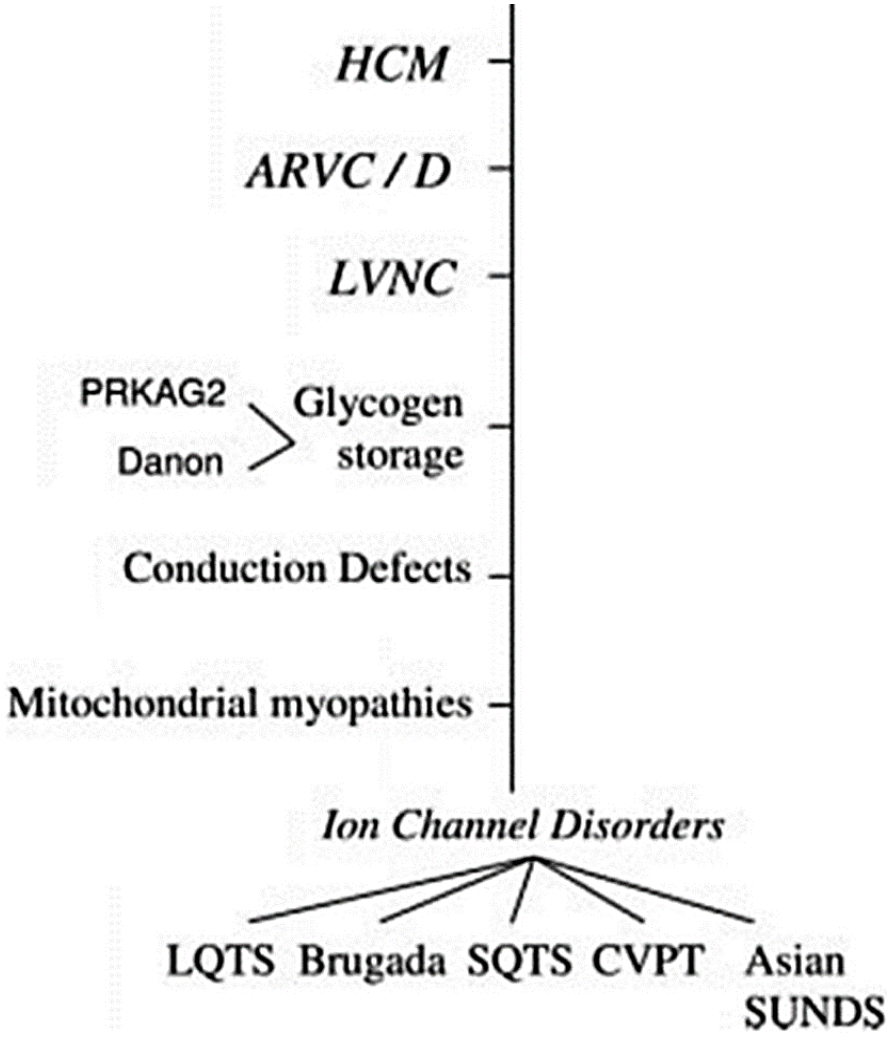
- Chemotherapy and other cardiotoxic medications
- Rheumatologic or autoimmune
- Endocrine or metabolic (thyroid, acromegaly, pheochromocytoma, diabetes, obesity)
- Familial cardiomyopathy or inherited and genetic heart disease
- Heart rhythm–related (e.g., tachycardia-mediated, PVCs, RV pacing)
- Hypertension
- Infiltrative cardiac disease (e.g., amyloid, sarcoid, hemochromatosis)
- Myocarditis (infectious, toxin or medication, immunological, hypersensitivity)
- Peripartum cardiomyopathy
- Stress cardiomyopathy (Takotsubo)
- Substance abuse (e.g., alcohol, cocaine, methamphetamine)

Lab studies

COR	LOE
1	C-EO

Laboratory evaluation should include CBC, UA, electrolytes, BUN / creatinine, glucose, lipid profile, liver function tests, iron studies, and TSH

Genetic cardiomyopathies



Family history – 3 generations

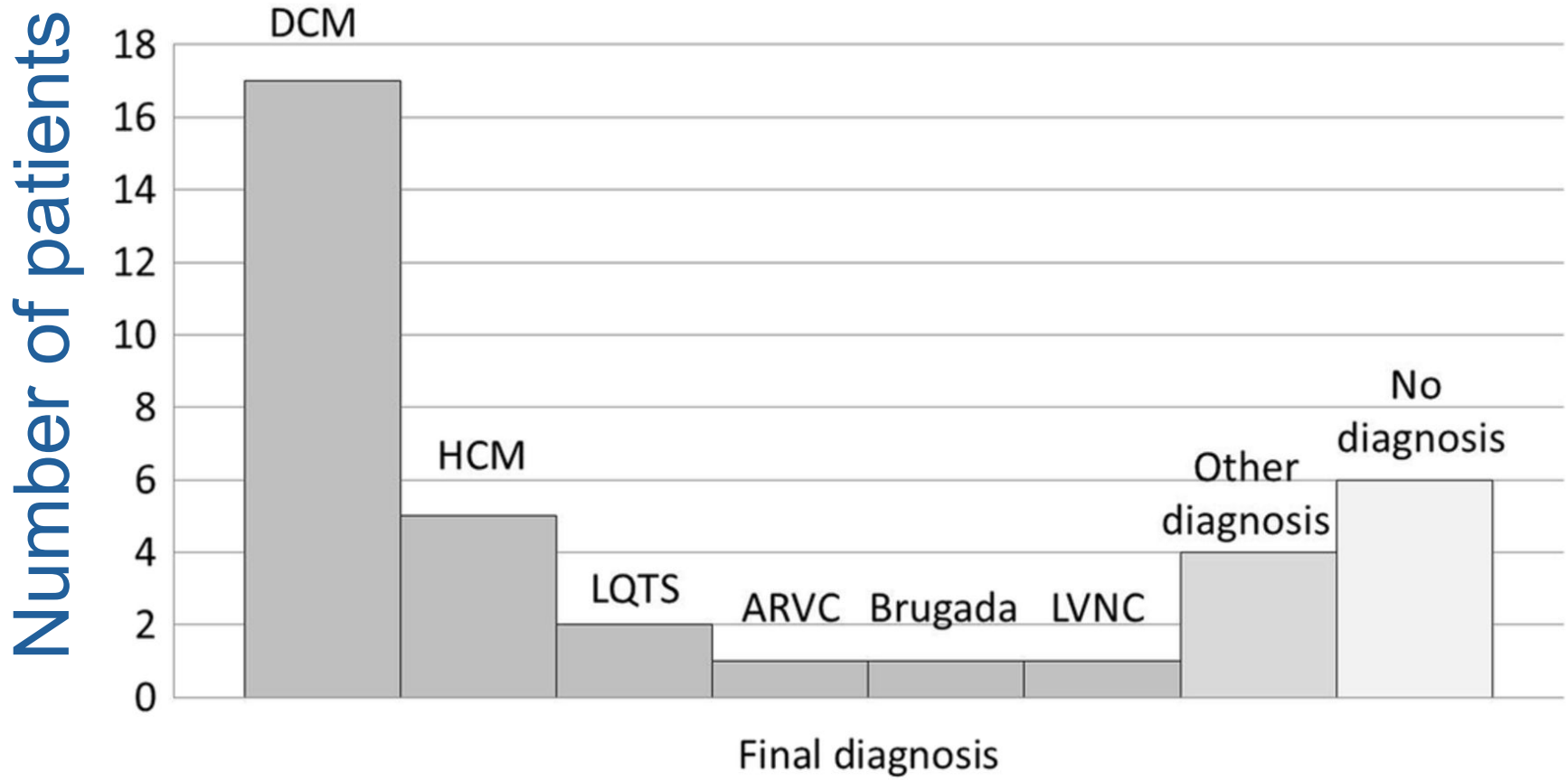
COR	LOE
1	B-NR

In patients with cardiomyopathy, a 3-generation family history should be obtained or updated when assessing the cause of the cardiomyopathy to identify possible inherited disease

syncope, young sudden death and cardiac disease

Family history – 3 generations

Diagnosis at hospital discharge



37 patients

HCM - hypertrophic cardiomyopathy;

LQTS - long QT syndrome;

ARVC - arrhythmogenic right ventricular cardiomyopathy

Brugada syndrome;

LVNC - left ventricular non-compaction

Kathryn Waddell-Smith, et al.Inpatient detection of cardiac-inherited disease: the impact of improving family history taking. Open Heart. 2016;3:e000329.

Heart failure with reduced ejection fraction

- Definitions
- **Medical therapy**
- Referral
  - Revascularization
  - Implantable cardiac defibrillators (ICD) cardiac resynchronization therapy (CRT)

Guideline directed medical therapy (GDMT)
4 medication classes

COR	LOE	Recommendations
1	A	In patients with HFrEF and NYHA class II to III symptoms, the use of **ARNi** is recommended to reduce morbidity and mortality
1	A	In patients with previous or current symptoms of chronic HFrEF, the use of **ACEi** is beneficial to reduce morbidity and mortality when the use of ARNi is not feasible
1	B - R	In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, **replacement by an ARNi** is recommended to further reduce morbidity and mortality
1	A	In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 **beta blockers** proven to reduce mortality is recommended to reduce mortality and hospitalizations
1	A	In patients with HFrEF and NYHA class II to IV symptoms, an **MRA** is recommended to reduce morbidity and mortality, if eGFR >30 mL/min/ 1.73 m2 and serum potassium is <5.0 mEq/L
1	A	In patients with symptomatic chronic HFrEF, **SGLT2i** are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes

Heidenreich PA, *et al. 2022 AHA/ACC/HFSA Guideline for Heart Failure. Circulation, JACC, J Card Fail* 2022

Beta blockers

In patients with HFrEF, with current or previous symptoms, use of 1 of the 3 beta blockers proven to reduce mortality (bisoprolol, carvedilol, sustained-release metoprolol succinate) is recommended to reduce mortality and hospitalizations.

MERIT-HF

- 3991 pts.
- NYHA II-IV, EF <= 40%
- Stabil on ACE/ARB/hydral.
- Metoprolol succinate

  12·5 - 25 QD
- Target dose 200 mg / 8 weeks

  Mean dose 159 mg,

  13% stopped

Lancet 1999; 353: 2001–07.

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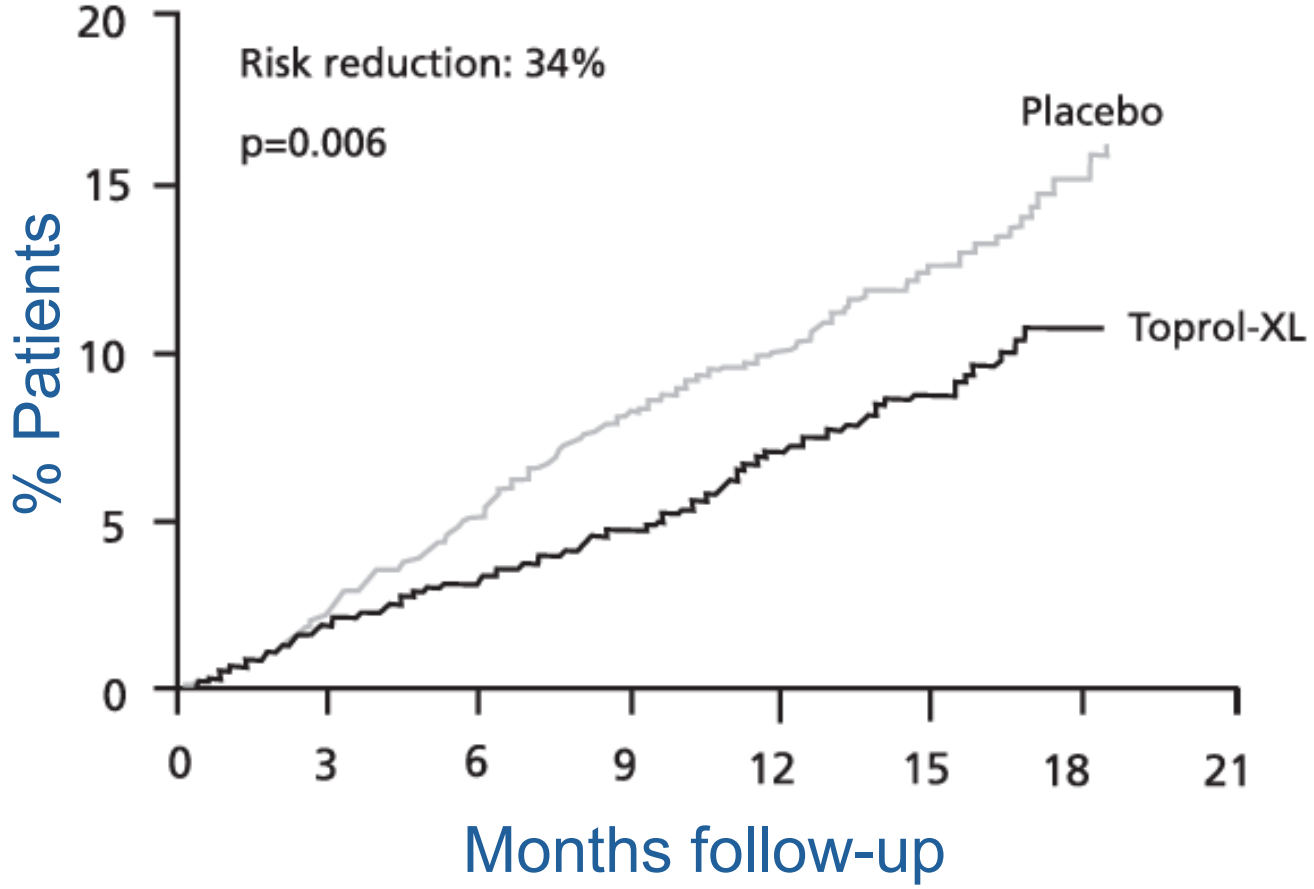
All-cause mortality



Lancet 1999; 353: 2001–07.

Beta blockers

Bisoprolol	1.25 mg once daily	10 mg once daily
Carvedilol	3.125 mg twice daily	25–50 mg twice daily
Carvedilol CR	10 mg once daily	80 mg once daily
Metoprolol succinate extended release (metoprolol CR/XL)	12.5–25 mg once daily	200 mg once daily

Beta blockers

Select initial dose of beta-blocker

Consider increasing dose every 2 weeks until maximum tolerated dose is achieved.

Monitor pulse, BP, and for signs of congestion.

2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction JACC 2024;83:1444-1488.

MRA
Mineralocorticoid Receptor Antagonists

COR	LOE
1	A

In patients with HFrEF and NYHA class II to IV symptoms, an MRA (spironolactone or eplerenone) is recommended to reduce morbidity and mortality,
if eGFR is >30 mL/min/1.73 m2 and serum potassiumis <5.0 mEq/L.

Eplerenone in Patients with Systolic Heart Failure and Mild Symptoms EMPHASIS-HF

- 2737 pts.
- NYHA II, EF <= 35%
- K+ < 5.0 mmol/l
- GFR >30 ml/min/1.7 BSA
- Treated w/ ACE/ARB/ β-blocker
- Eplerenone 25 QOD-QD
- Target dose 25-50 mg

  Mean dose 39 mg,

  16% stopped

N Engl J Med 2011;364:11-21.

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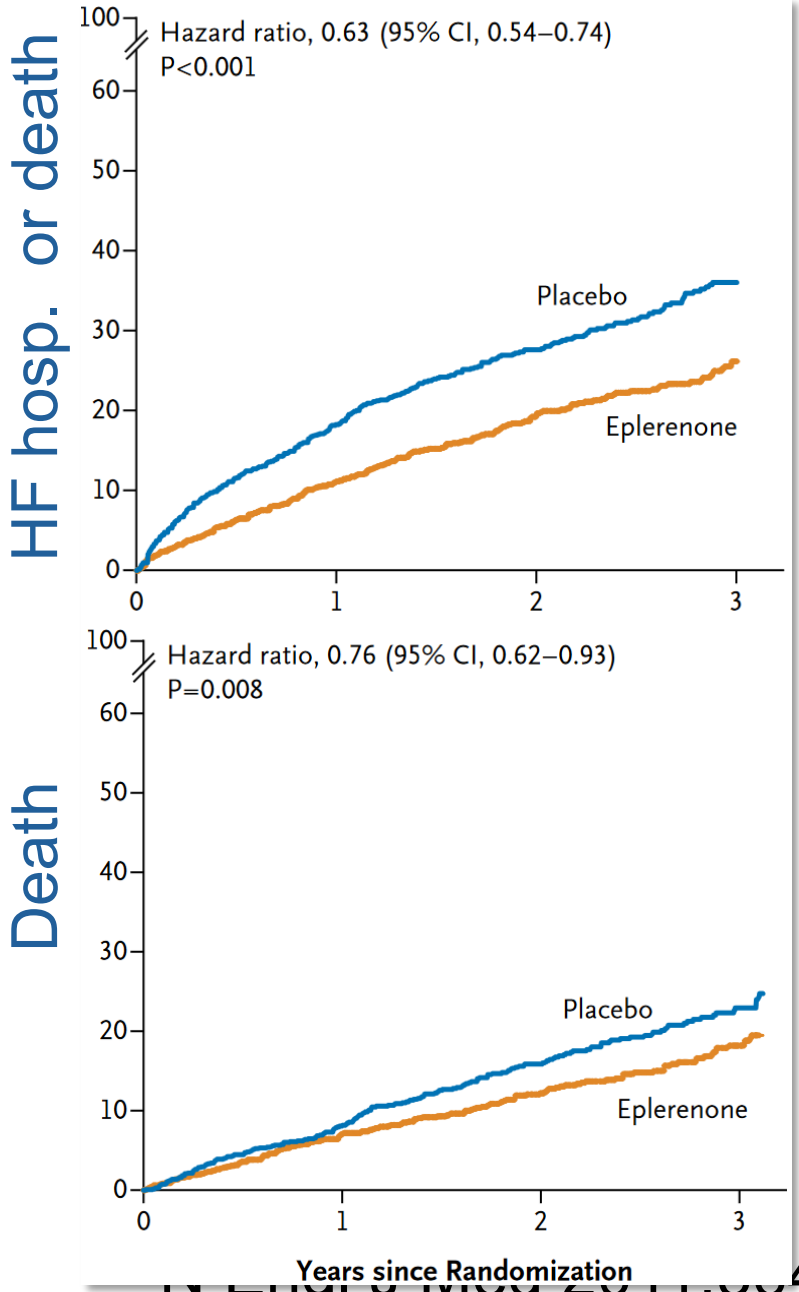

N Engl J Med 2011;364:11-21.

MRA
Mineralocorticoid Receptor Antagonists

Mineralocorticoid receptor antagonists		
Spironolactone	12.5–25 mg once daily	25–50 mg once daily
Eplerenone	25 mg once daily	50 mg once daily

Careful monitoring at initiation and closely monitored thereafter to minimize risk of hyperkalemia and renal insufficiency

MRA
Mineralocorticoid Receptor Antagonists

Select initial dose of mineralocorticoid antagonist

↓

Consider increasing dose every 2 weeks until maximum tolerated dose is achieved.

Monitor potassium and creatinine 7 days after initiation / titration.

Then check monthly for 3 months,
every 3 months for a year

2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction JACC 2024;83:1444-1488.

ARNi
Angiotensin receptor/neprilysin inhibitor

COR	LOE
1	A

In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality

ARNi
Angiotensin receptor/neprilysin inhibitor

COR	LOE
1	A
1	B-R

In patients with HFrEF and NYHA class II to III symptoms, the use of ARNi is recommended to reduce morbidity and mortality

In patients with chronic symptomatic HFrEF NYHA class II or III who tolerate an ACEi or ARB, replacement by an ARNi is recommended to further reduce morbidity and mortality

Angiotensin–Neprilysin Inhibition versus Enalapril in Heart Failure PARADIGM-HF

- 8442 pts.
- NYHA II-IV, EF <= 40%
- 4 weeks before ACE/ARB,

  β-blocker
- K+ < 5.5 mmol/l
- GFR >30 ml/min/1.7 BSA
- Sacubitril / Valsartan BID vs

  Enalapril 10 BID
- 17%/19% stopped

N Engl J Med 2014;371:993-1004.

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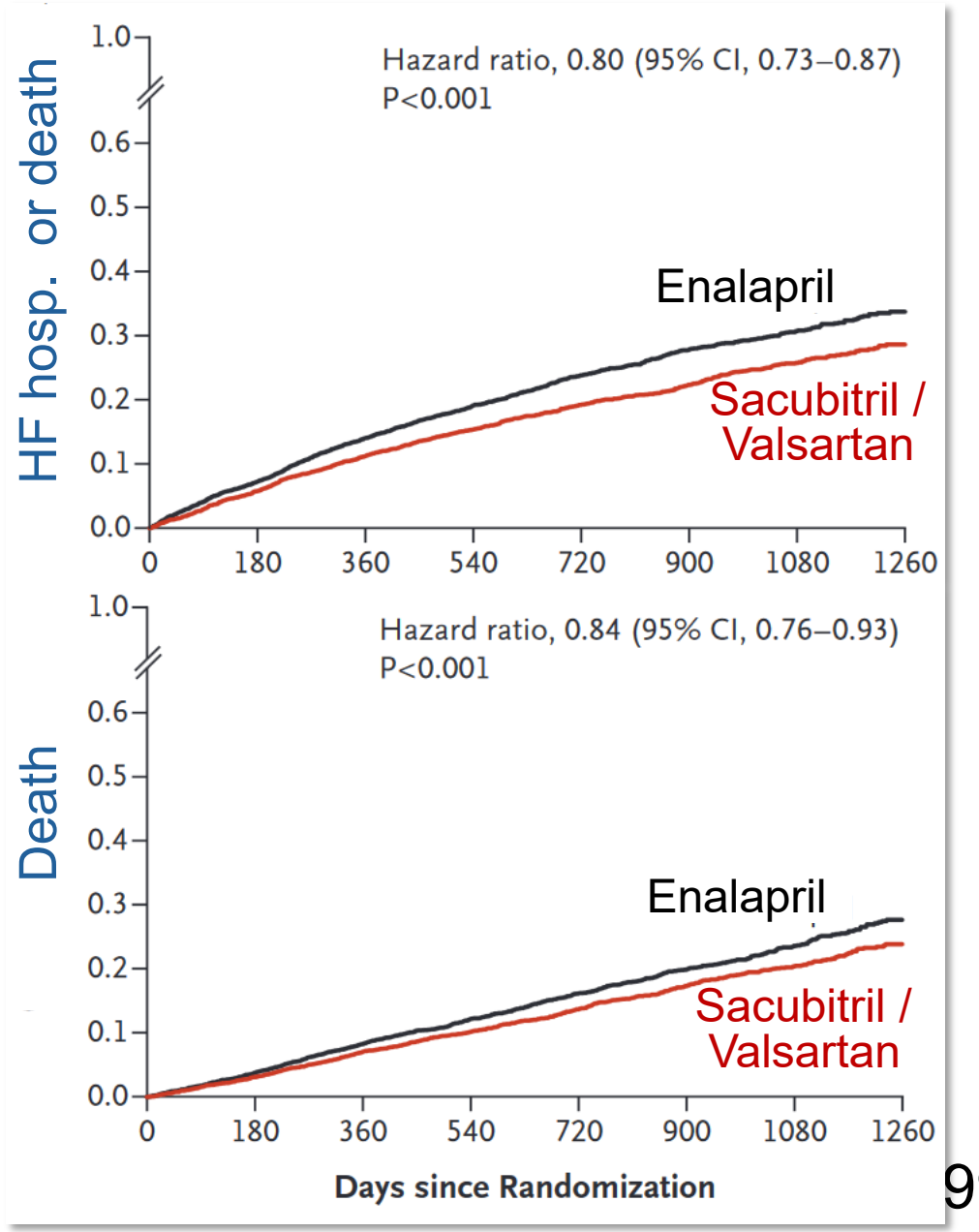

993-1004.

ARNi
Angiotensin receptor/neprilysin inhibitor

ARNi		
Sacubitril-valsartan	24 mg / 26 mg 49 mg / 51 mg twice daily	97 mg / 103 mg twice daily

ARNi
Angiotensin receptor/neprilysin inhibitor

Ensure off ACEi 36 hours before initiation

Select starting dose:
<= 10 mg enalapril daily or
<= 160 mg valsartan daily or equivalent

<u>24/46 mg twice daily</u>

> 10 mg enalapril daily or
> 160 mg valsartan daily or equivalent

<u>49/51 mg twice daily</u>

In 1-2 weeks, assess tolerability

If possible, increase dose stepwise to target of 97/103 twice daily

Monitor BP, electrolytes, kidney function

2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction JACC 2024;83:1444-1488.

ARNi
Angiotensin receptor/neprilysin inhibitor

COR
1
1

“In patients with previous or current symptoms of chronic HFrEF, in whom ARNi is not feasible, treatment with an ACEi or ARB provides high economic value”

SGLT2i
Sodium-Glucose Cotransporter 2 Inhibitors

In patients with symptomatic chronic HFrEF, SGLT2i are recommended to reduce hospitalization for HF and cardiovascular mortality, irrespective of the presence of type 2 diabetes.

Dapagliflozin in Patients with Heart Failure and Reduced Ejection Fraction DAPA-HF

- 4744 pts.
- NYHA II-IV, EF <= 40%
- eGFR >=30 ml/min/1.73 BSA
- Dapagliflozin 10 mg daily

- Diabetes 45%
- Black 5%

  (North America 14%)

N Engl J Med 2019;381:1995-2008.

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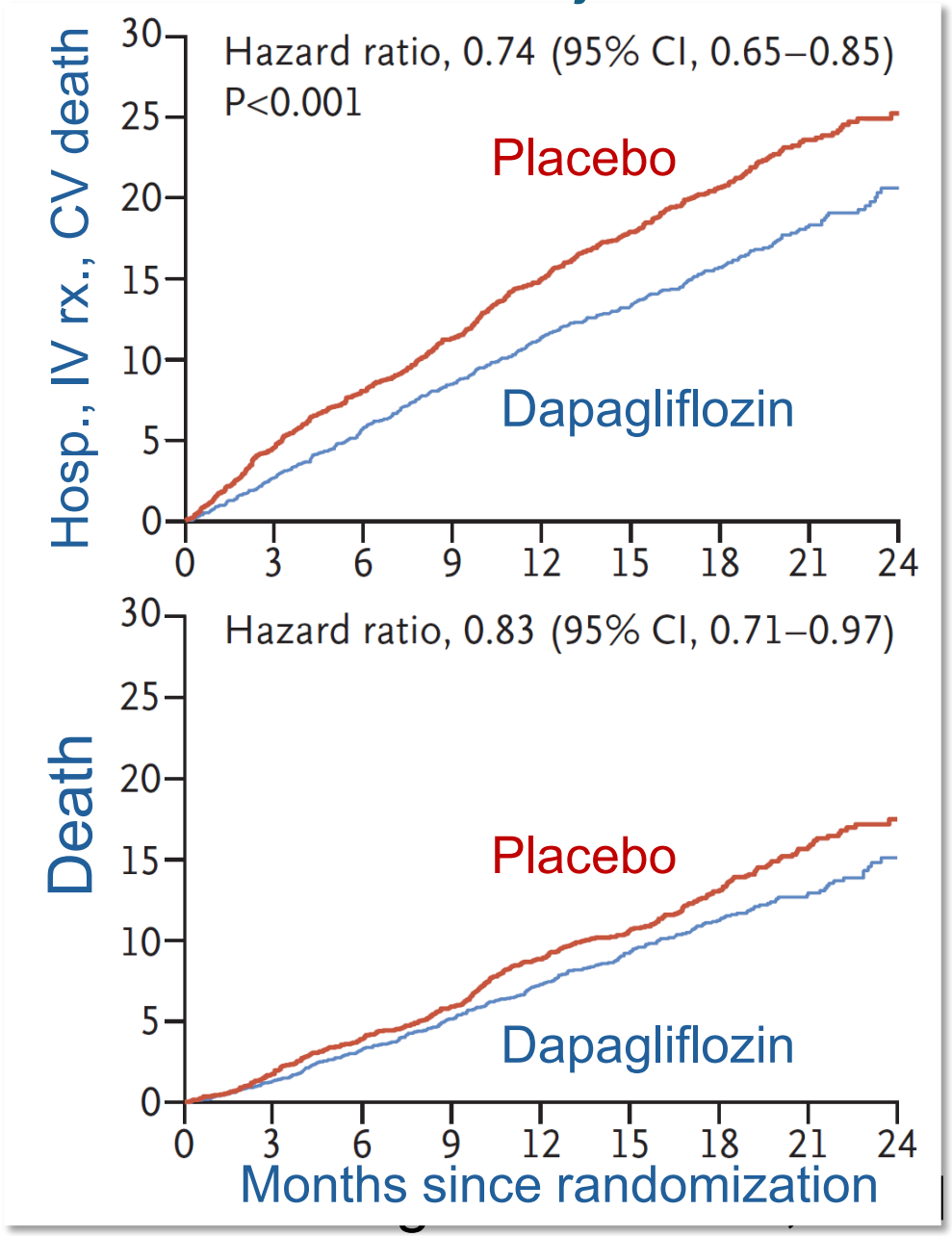


995-2008.

SGLT2i
Sodium-Glucose Cotransporter 2 Inhibitors

SGLT inhibitors		
Dapagliflozin	10 mg daily	10 mg daily
Empagliflozin	10 mg daily	10 mg daily
Sotagliflozin	200 mg daily	400 mg daily

SGLT2i
Sodium-Glucose Cotransporter 2 Inhibitors

Select dapagliflozin, empagliflozin, or sotagliflozin

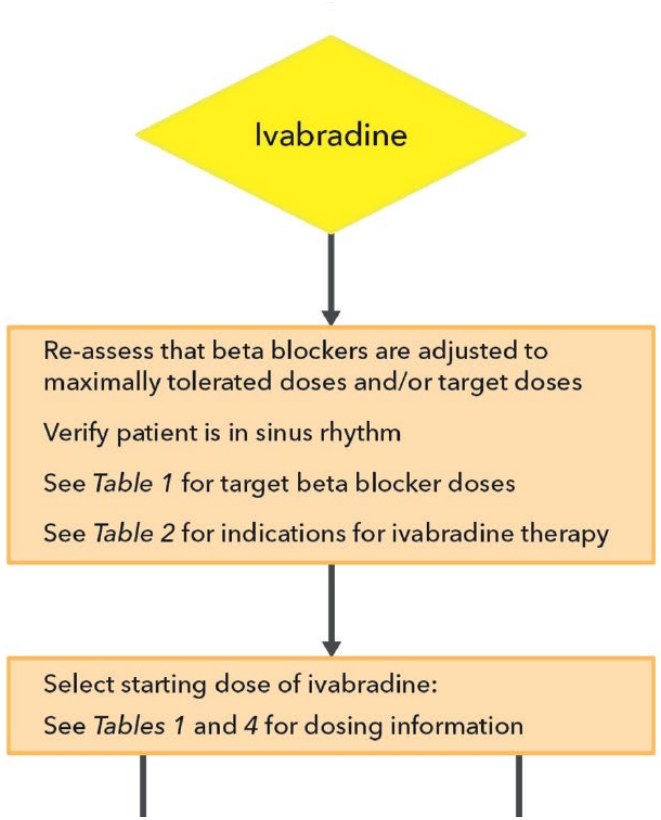
↓

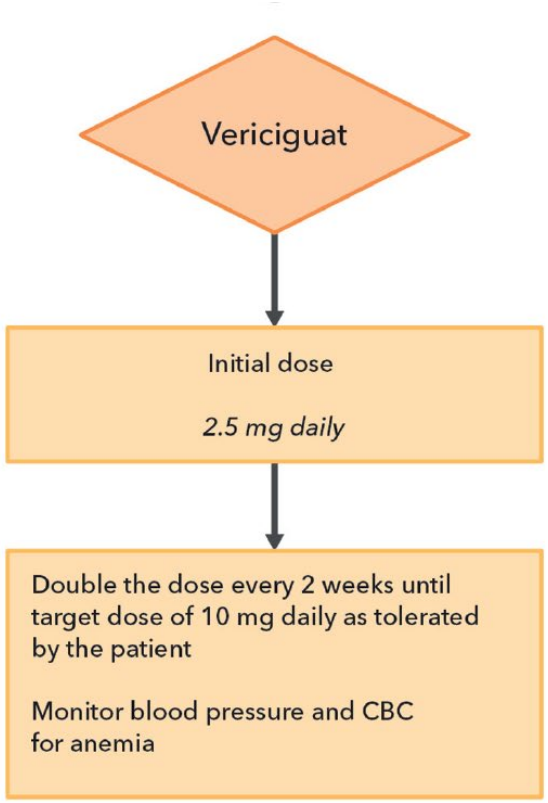
Before initiation, ensure
eGFR >= 25mL/min/1.73 m^2 for dapagliflozin or sotagliflozin
eGFR >= 20mL/min/1.73 m^2 for empagliflozin

2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction JACC 2024;83:1444-1488.

Ivabradine

- LVEF <= 35%
- On maximum tolerated dose of beta-blocker
- Sinus rhythm with a resting heart rate $70 beats/min
- NYHA functional class II or III HF





Vericiguat

- HFrEF (LVEF <45%)
- On maximum tolerated GDMT
- Worsening HF symptoms

Loop diuretics

COR	LOE
1	B-NR

Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to improve symptoms and reduce morbidity

Loop diuretics

COR	LOE
1	B-NR

Patients with HF admitted with evidence of significant fluid overload should be promptly treated with intravenous loop diuretics to improve symptoms and reduce morbidity

1	B-NR

For patients requiring diuretic treatment during hospitalization for HF, the discharge regimen should include a plan for adjustment of diuretics to decrease rehospitalizations

Loop diuretics

Loop diuretics		
Bumetanide	0.5–1.0 mg once or twice	10 mg
Furosemide	20–40 mg once or twice	600 mg
Torsemide	10–20 mg once	200 mg

CS 68 y.o. man

- 2 weeks later

  Dyspnea improved, still present with marked exertion

  Pro B-type Natriuretic Peptide fell from 1290 to 269 pg/mL

  Na 139, K 4.3, creatinine 1.0

  Advance sacubitril, add eplerenone,

Heart failure with reduced ejection fraction

- Definitions
- Medical therapy
- **Referral**
  - Revascularization
  - Implantable cardiac defibrillators (ICD) cardiac resynchronization therapy (CRT)

Revascularization for CAD

COR	LOE
1	B-NR

Selected patients with HF, reduced EF (EF <=35%), and suitable coronary anatomy, surgical revascularization plus GDMT is beneficial to improve symptoms, cardiovascular hospitalizations, and long-term all-cause mortality

CABG Improves Outcomes in Patients With Ischemic Cardiomyopathy STICH Trial

- 1,212 pts.
- EF <= 35%
- Suitable vessel targets for bypass surgery
- CABG

- NYHA II-IV – 89%

J Am Coll Cardiol HF 2019;7:878–87.

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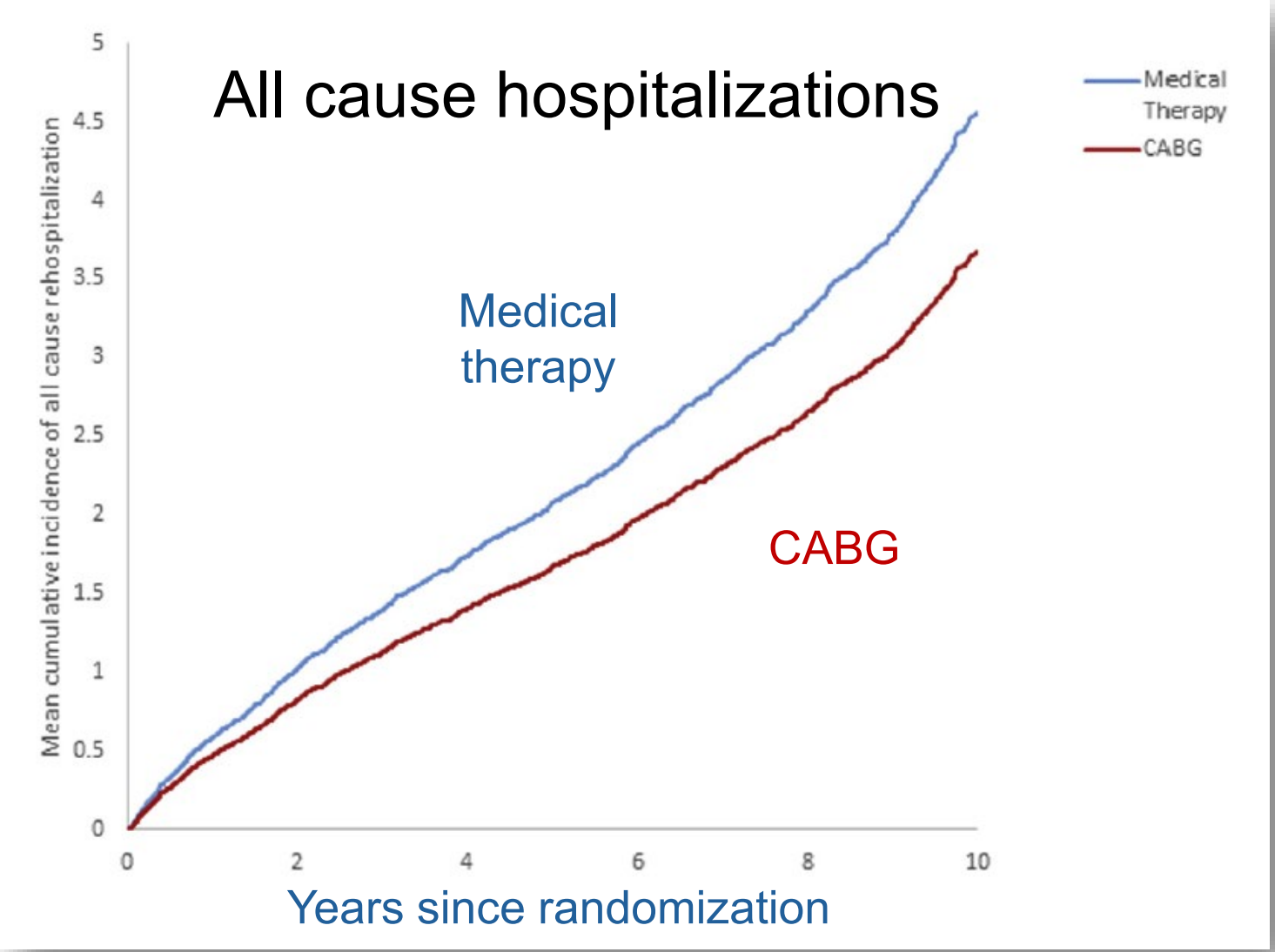


J Am Coll Cardiol HF 2019;7:878–87.

CS 68 y.o. man

- Cor angio

  50% mid LAD, 70% small CM1

- Right heart cath.

  RA 5, PA 35/13, PCWP 13,

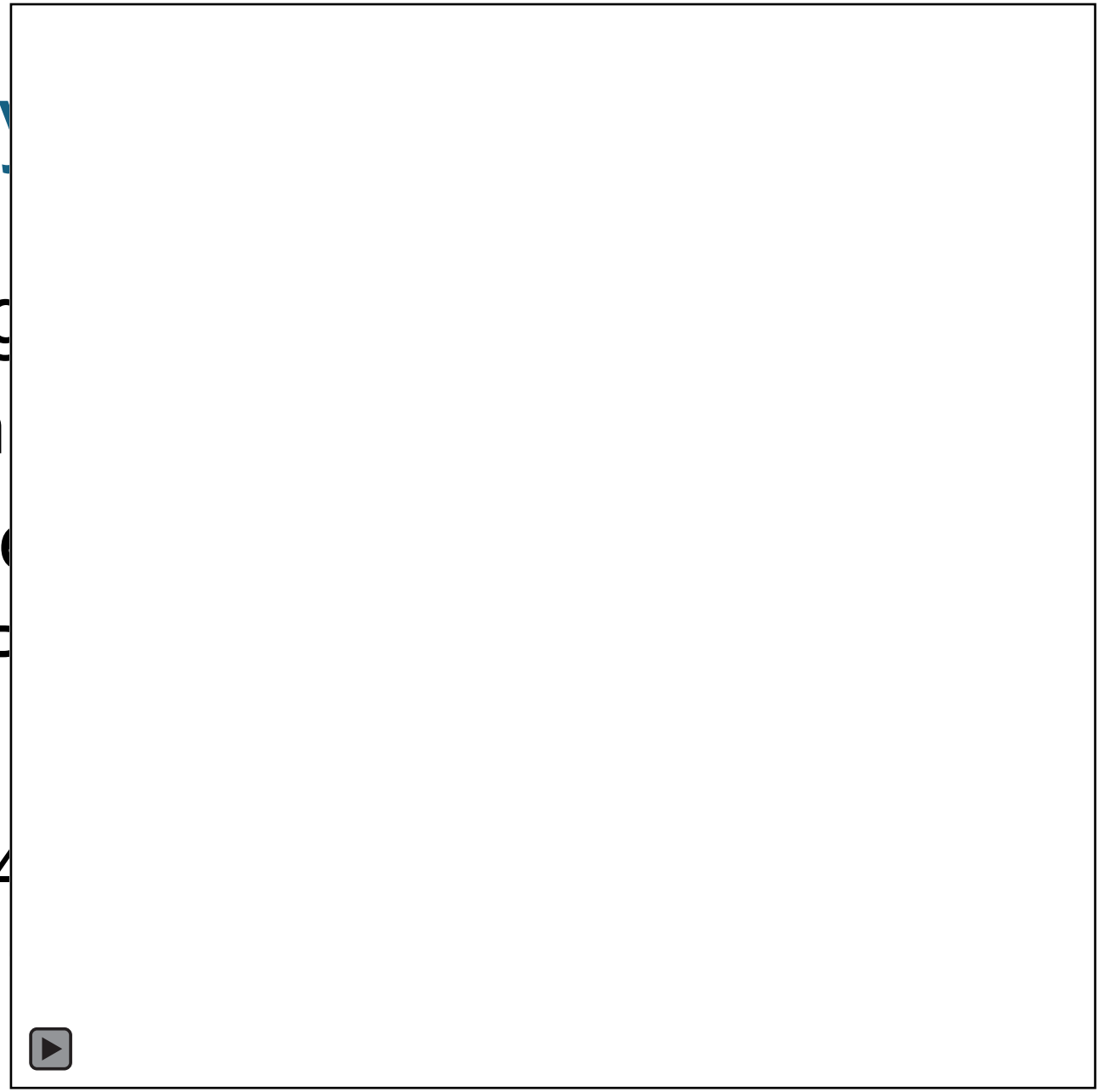
  CI 2.2

  SVR 1400, PVR 114

  MVO2 70%

CS 68 y

- Cor ang
  - 50% m
- Right h
  - RA 5, P
  - CI 2.2
  - SVR 14
  - MVO2



Implantable cardiac defibrillators (ICD) cardiac resynchronization therapy (CRT)

COR	LOE
1	A
1	B-R
1	B-R

Nonischemic cardiomyopathy or ischemic heart disease at least 40 days post-MI, LVEF <=35%, NYHA class II or III symptoms on chronic GDMT, expectation of meaningful survival for >1 year, ICD therapy is recommended for primary prevention of SCD to reduce total mortality

40 days post-MI, LVEF <=30%, NYHA class I symptoms while receiving GDMT, expectation of meaningful survival for >1 year, ICD therapy is recommended for primary prevention of SCD to reduce total mortality

LVEF <=35%, sinus rhythm, left bundle branch block (LBBB) with a QRS duration >=150 ms, NYHA class II, III, or ambulatory IV symptoms on GDMT, CRT is indicated to reduce total mortality, reduce hospitalizations, and improve symptoms and QOL

Cardiac-Resynchronization Therapy for Mild-to-Moderate Heart Failure
Resynchronization–Defibrillation for Ambulatory Heart Failure Trial (RAFT)

- 1798 pts.
- NYHA II-III, EF <= 30%
- QRS duration of 120 msec
- ICD alone vs ICD plus CRT
- NYHA II-IV – 89%

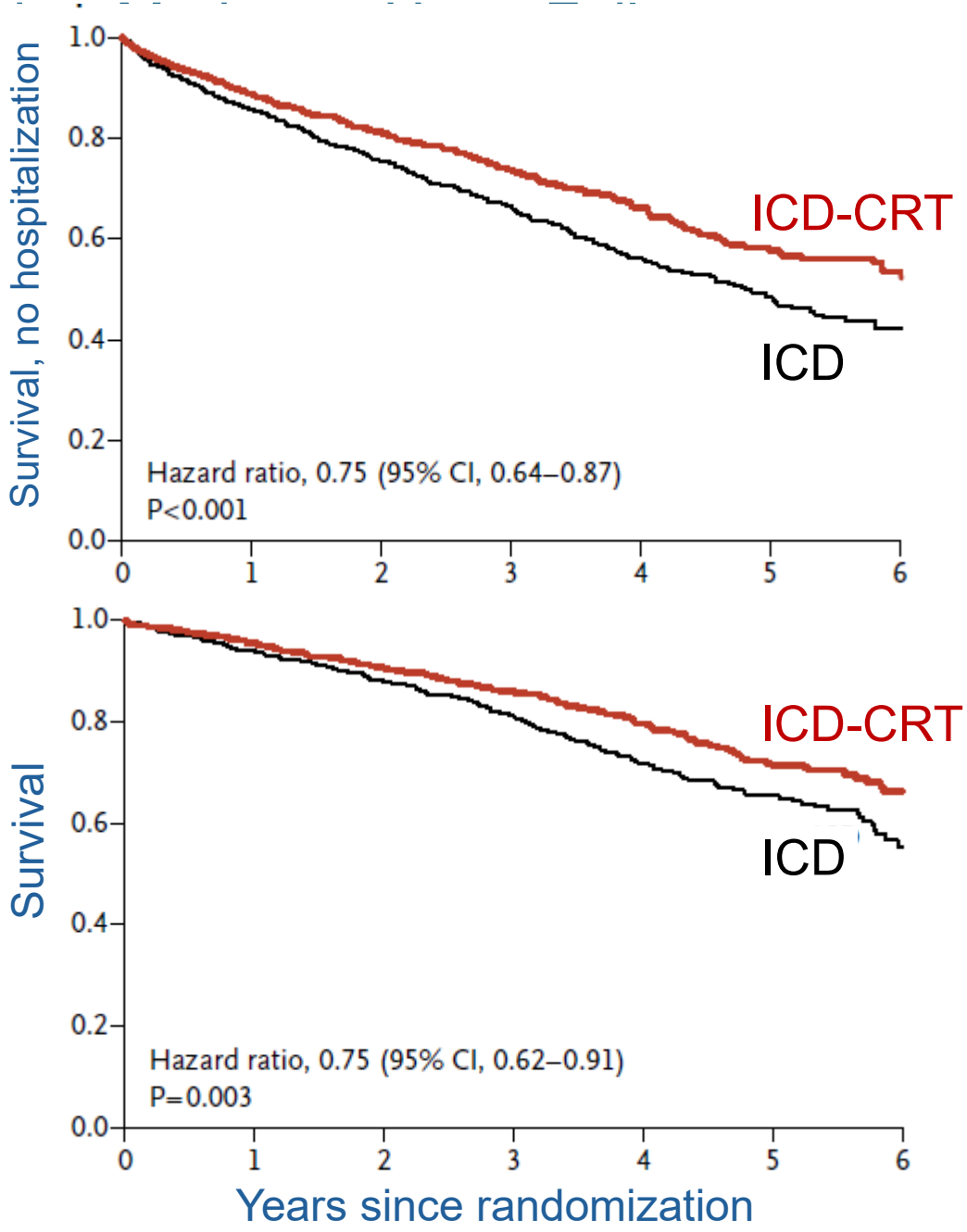
- Mean QRS 158 msec

N Engl J Med 2010;363:2385-95.

Cardiac-Resynchronization Therapy for
Resynchronization–Defibrillation for Ambulatory

- 1798 pts.
- NYHA II-III, EF <= 30%
- QRS duration of 120 msec
- ICD alone vs ICD plus CRT
- NYHA II-IV – 89%

- Mean QRS 158 msec



CS

ID:001956882 MISSION HOSPITAL-ACAASH ROUTINE RECORD

Male

Room:Exam Room 132
Loc:300

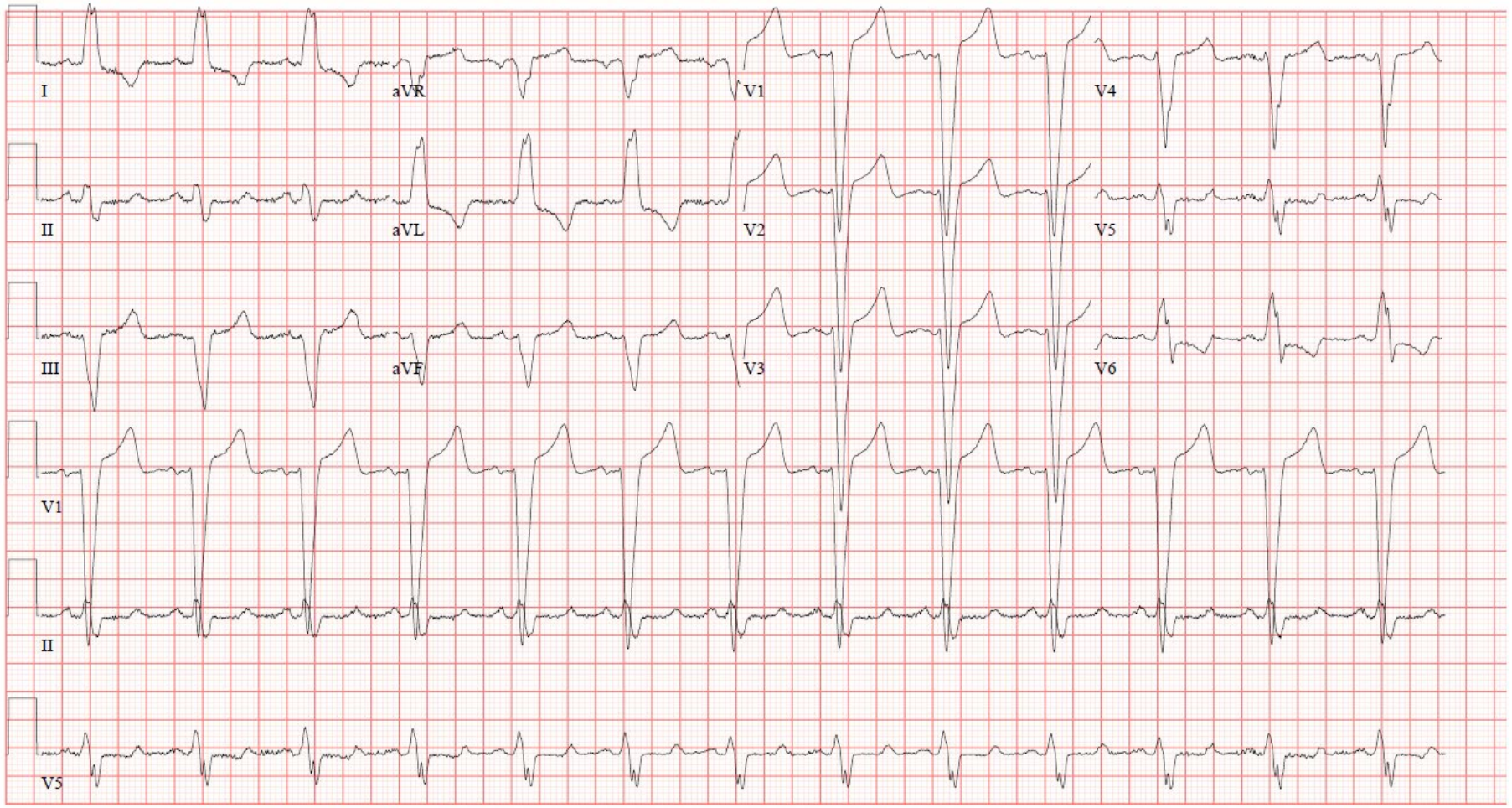
Vent. rate	78		BPM
QRS duration	162		ms
P-R-T axes	59	-33	141

Normal sinus rhythm
Left axis deviation
Left bundle branch block
Abnormal ECG
No previous ECGs available
Confirmed by JOLLIS MD, JA

Technician:TAMMY CASE
Test ind:

Referred by: John Rouchard

Confirmed By: JAMES JOLLIS MD



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CS 68 y.o. man

- Continued follow up
  - Add metoprolol, SGLT2 inhibitor
  - EP consult
    - CRT-P vs CRT-D when GDMT optimal
    - Repeat echocardiogram - if LVEF is less than 30% then CRT-D

Conclusion

- For patients with reduced ejection fraction heart failure (ejection fraction <= 40%) and heart failure symptoms, there are 4 medications associated with improved survival and fewer hospitalizations
    1. Beta blockers
    2. Mineralocorticoid receptor antagonists
    3. Angiotensin receptor/neprilysin inhibitor
    4. Sodium-Glucose Cotransporter 2 Inhibitors

Conclusion

- Patients with reduced ejection fraction and multi-vessel coronary artery disease benefit from coronary revascularization regardless of response to medical therapy.

Conclusion

- Patients who remain symptomatic with reduced ejection fraction despite application of these therapies should be considered for:

1. Cardiac resynchronization therapy and defibrillator (QRS duration > 120.
2. Edge-to-edge mitral valve clipping – next talk.