Advanced Imaging in Heart Failure

Robert J. Donovan, MD
Advanced Heart Failure/Transplant Cardiology Fellow (PGY-7)
University of Virginia Health System
Division of Cardiovascular Medicine

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Disclosures

I have no personal or professional financial relationship or interest with any proprietary entity producing healthcare goods and/or services.

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Objectives

1. Examine the epidemiologic impact of heart failure both in the United States and worldwide

2. Detail the fundamental role of echocardiography in the diagnosis/management of heart failure and the limitations of this modality

3. Explore new techniques in echocardiography for the quantification of left and right ventricular function/size

4. Overview of the ever-expanding role of cardiac MRI in heart failure diagnosis and management

5. Explore the current and future role specialized nuclear medical imaging in the diagnosis of infiltrative cardiomyopathies, particularly amyloid heart disease

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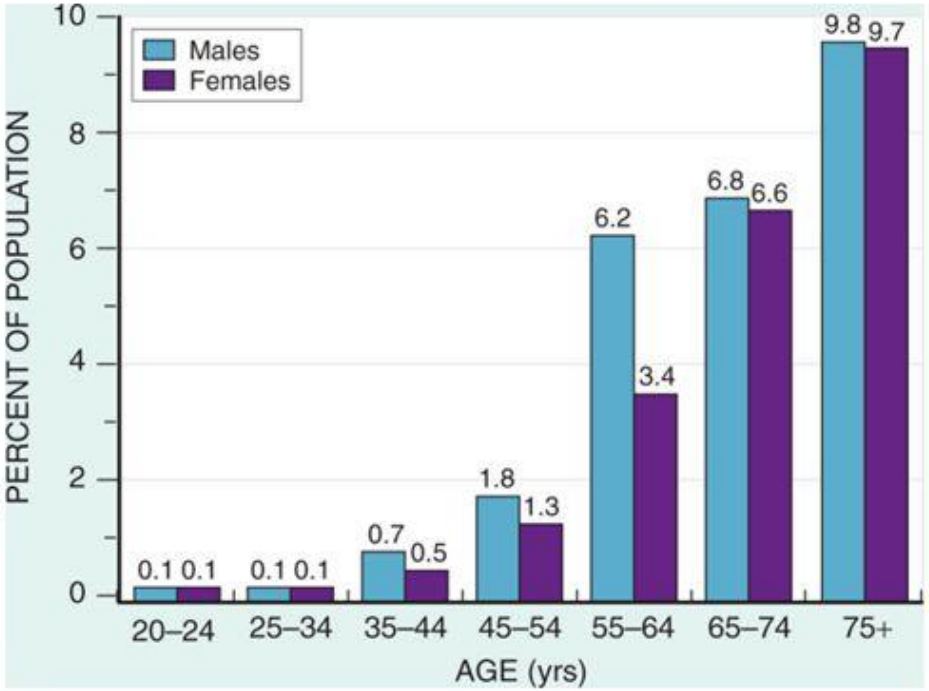
Heart Failure Is a Big Problem

- Prevalence: >5,000,000
- Incidence: >650,000 new cases/year in the US
- Most common discharge diagnosis
- Most common cause of readmission < 60 days
- Cost: > 34.8 billion annualy



Allen et al., *Cardiovascular Disease*. 2012.

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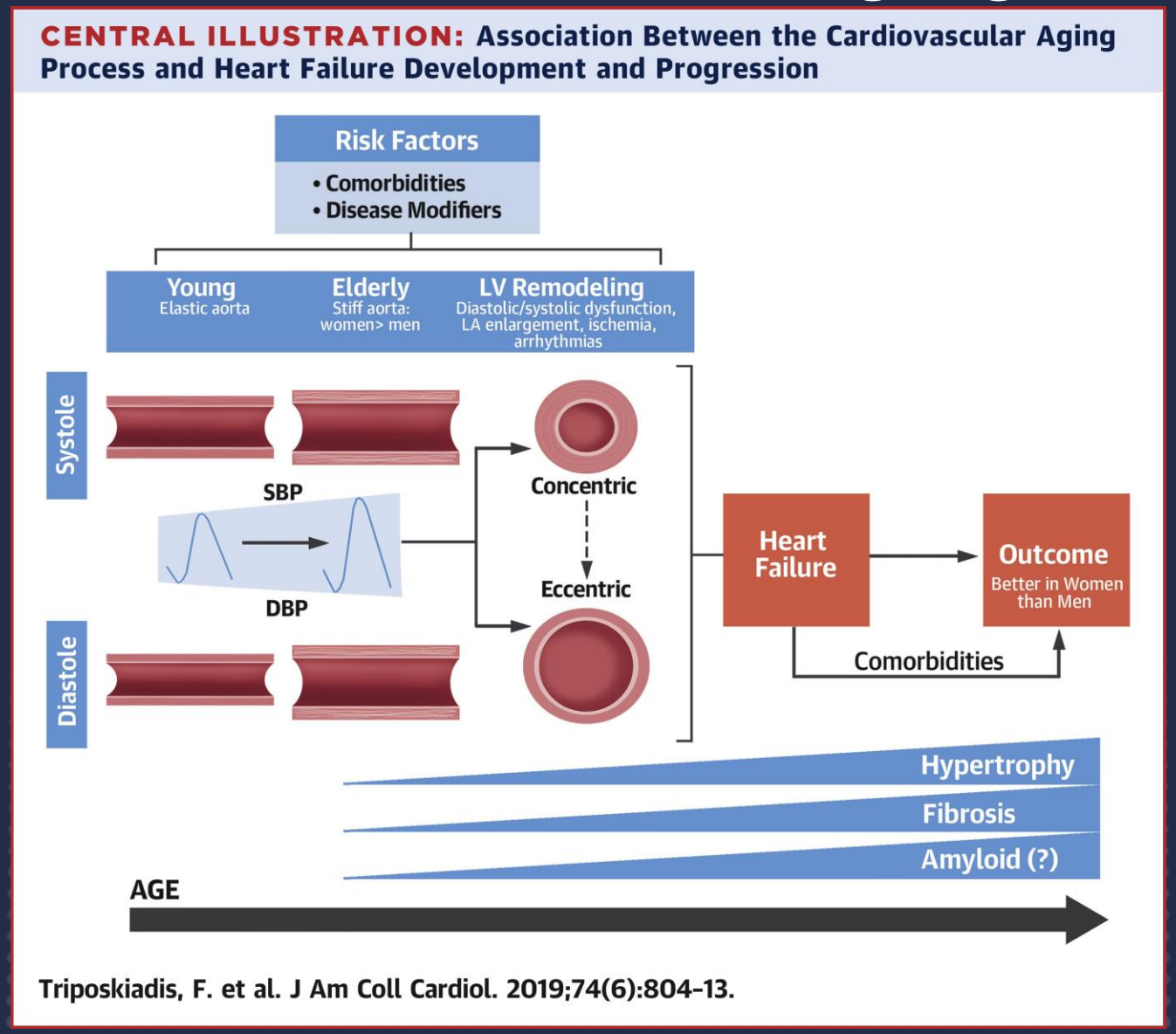
Heart Failure and Aging



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Definitions

HFrEF = heart failure with *reduced* ejection fraction (<40%)

HFpEF = heart failure with *preserved* ejection fraction (>50%)

HFmrEF = heart failure with *mid-range* ejection fraction (40-49%)

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Heart Failure Guidelines

Table 6. ACC/AHA Heart Failure Performance Measures Inpatient Data Collection Flowsheet

ACC/AHA Heart Failure Performance Measures Inpatient Data Collection Flowsheet			
1. Left ventricular systolic (LVS) function assessment		**YES**	**NO**
LV1.	Was an assessment of left ventricular systolic (LVS) function made in diagnosed HF patients, LVS documented as assessed before arrival, during hospitalization, or planned for after discharge?	○ (go to **LV2**)	○ (go to **4**)
LV2.	☐ Quantitative EF:_____%: _____ Qualitatively assessed as (circle one): Normal Mildly Depressed Moderately Depressed Severely Depressed		
2. ACE inhibitor or ARB therapy for left ventricular systolic dysfunction ("ACE/ARB") at discharge		**YES**	**NO**
ACE/ARB1.	Was ejection fraction <40% or with moderately or severely depressed left ventricular systolic function?	○	○ (go to **3**)
ACE/ARB2.	Was ACE inhibitor prescribed upon discharge?	○ (go to **3**)	○ (go to **ACE/ARB3**)
ACE/ARB3.	Was ARB prescribed upon discharge?	○ (go to **3**)	○ (go to **ACE/ARB4**)
ACE/ARB4.	Reasons documented by physician, nurse practitioner, or physician assistant for not prescribing ACE inhibitor and ARB?	○	○
3. Anticoagulant use for heart failure and atrial fibrillation ("ACU")		**YES**	**NO**
ACU1.	Chronic or recurrent atrial fibrillation documented?	○ (go to **ACU2**)	○ (go to **4**)
ACU2.	If yes, was warfarin prescribed?	○ (go to **4**)	○ (go to **ACU3**)
ACU3.	Reasons documented by physician, nurse practitioner, or physician assistant for not prescribing warfarin?	○	○ (go to **4**)
4. Discharge instructions ("PE")		**YES**	**NO**
PE1.	Patient discharged with complete written discharge instructions, as documented in the medical record?	○	○ (go to **5**)
5. Adult smoking cessation advice/counseling ("SC")		**YES**	**NO**
SC1.	Adult patient who smokes cigarettes given smoking cessation counseling/advice?	○	○

This flowsheet is intended for prospective data collection only. It is not designed to meet the reporting requirements of organizations, such as the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) or the Centers for Medicare and Medicaid Services (CMS).

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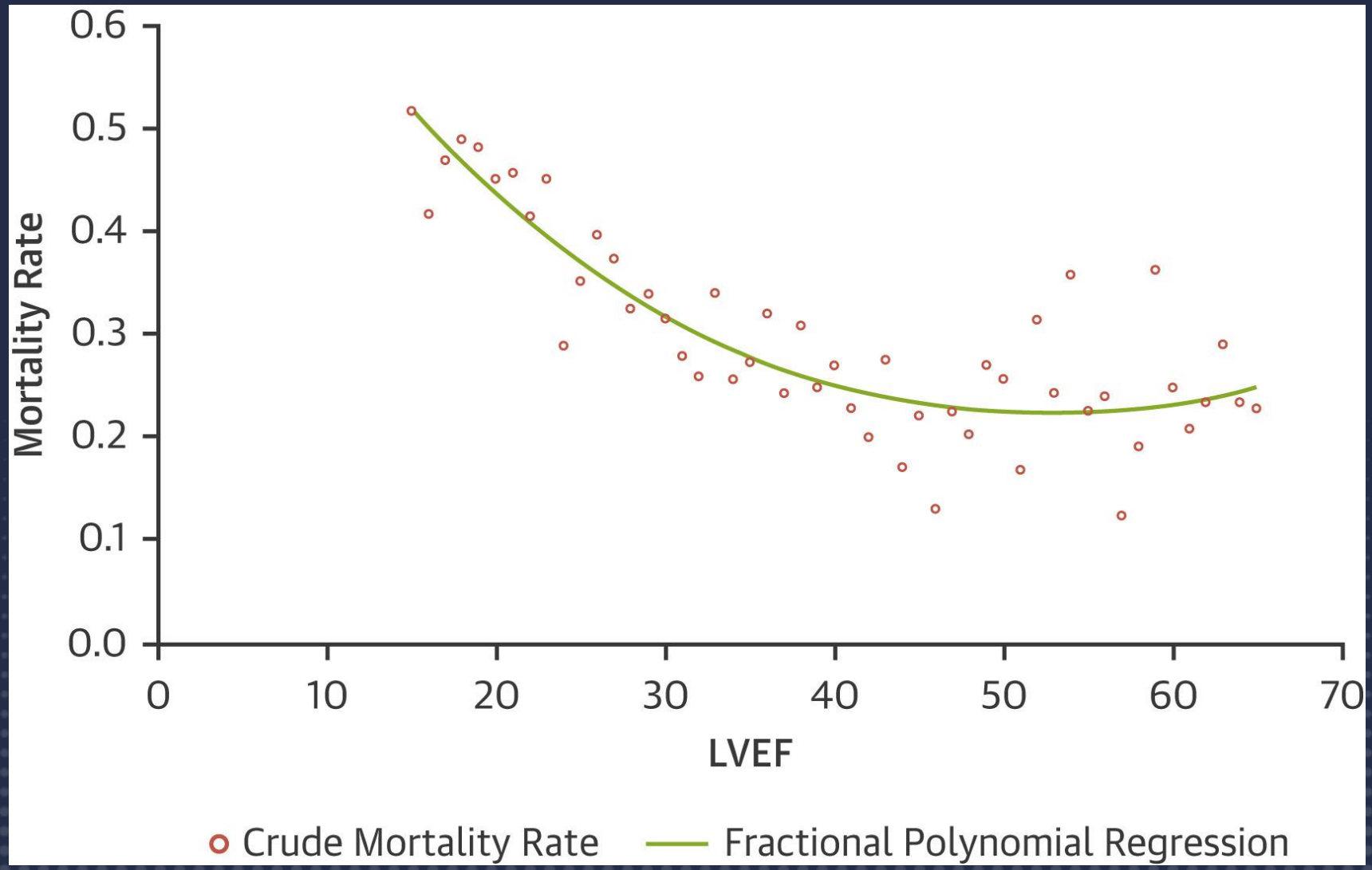
Robert O. Bonow. Circulation. ACC/AHA Clinical Performance Measures for Adults With Chronic Heart Failure, Volume: 112, Issue: 12, Pages: 1853-1887, DOI:

Prognostic Value of LV Ejection Fraction



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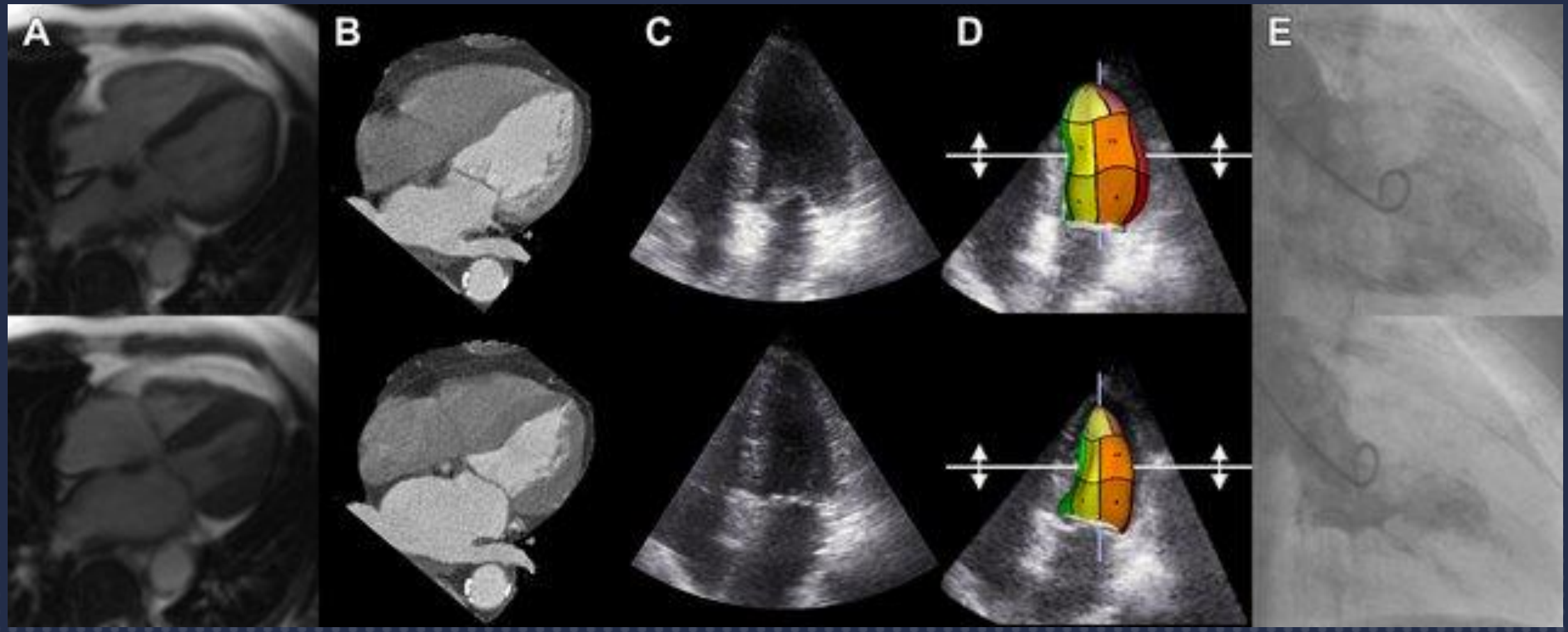
J.P. Curtis, S.I. Sokol, Y. Wang, *et al.* **The association of left ventricular ejection fraction, mortality, and cause of death in stable outpatients with heart failure**. J Am Coll Cardiol, 42 (2003), pp. 736-742

Modalities for LV EF Estimation



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J Am Coll Cardiol 2012;59:1897-1907

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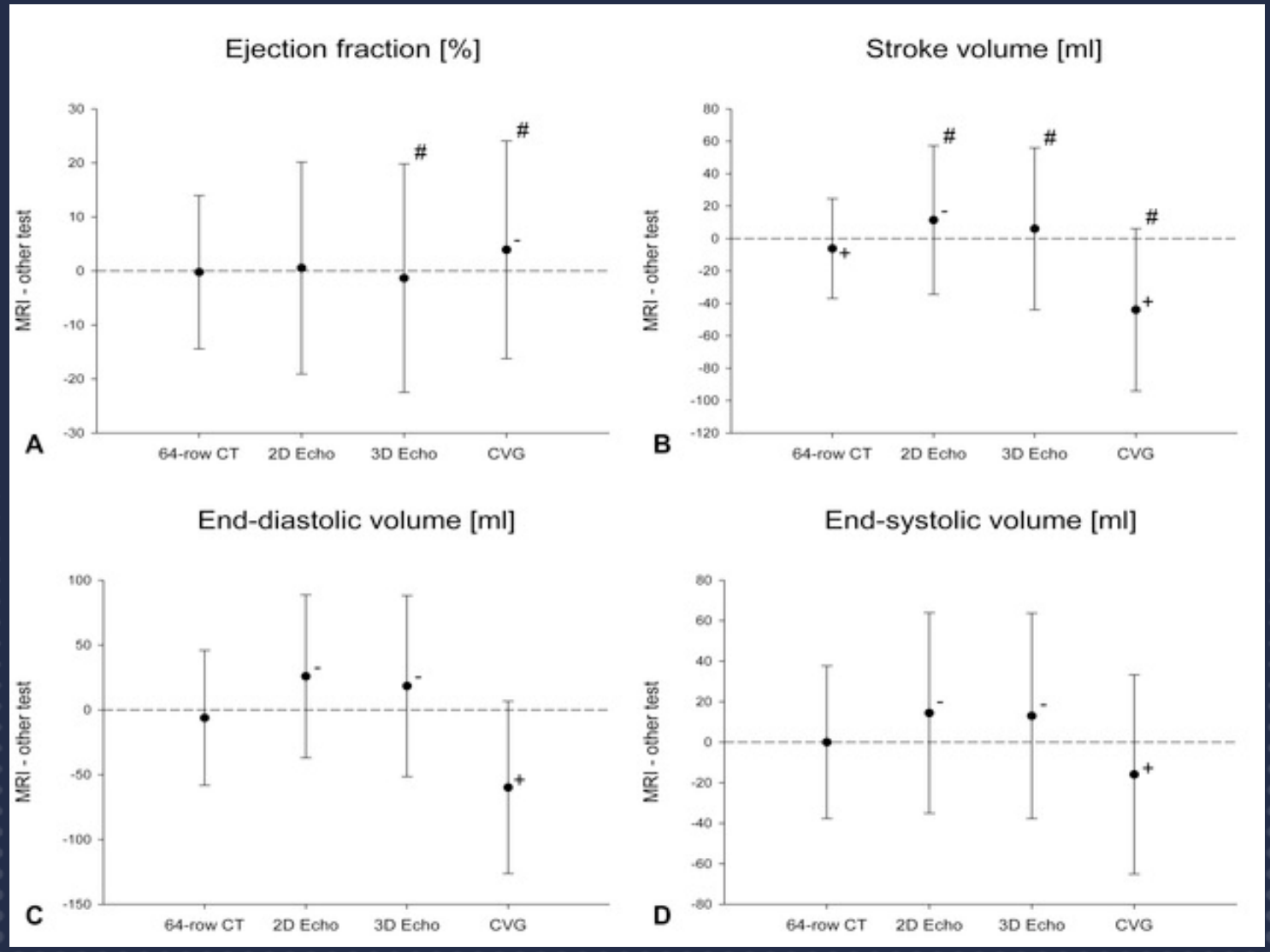

J Am Coll Cardiol 2012;59:1897-1907

Limitations of LV EF by Echocardiography

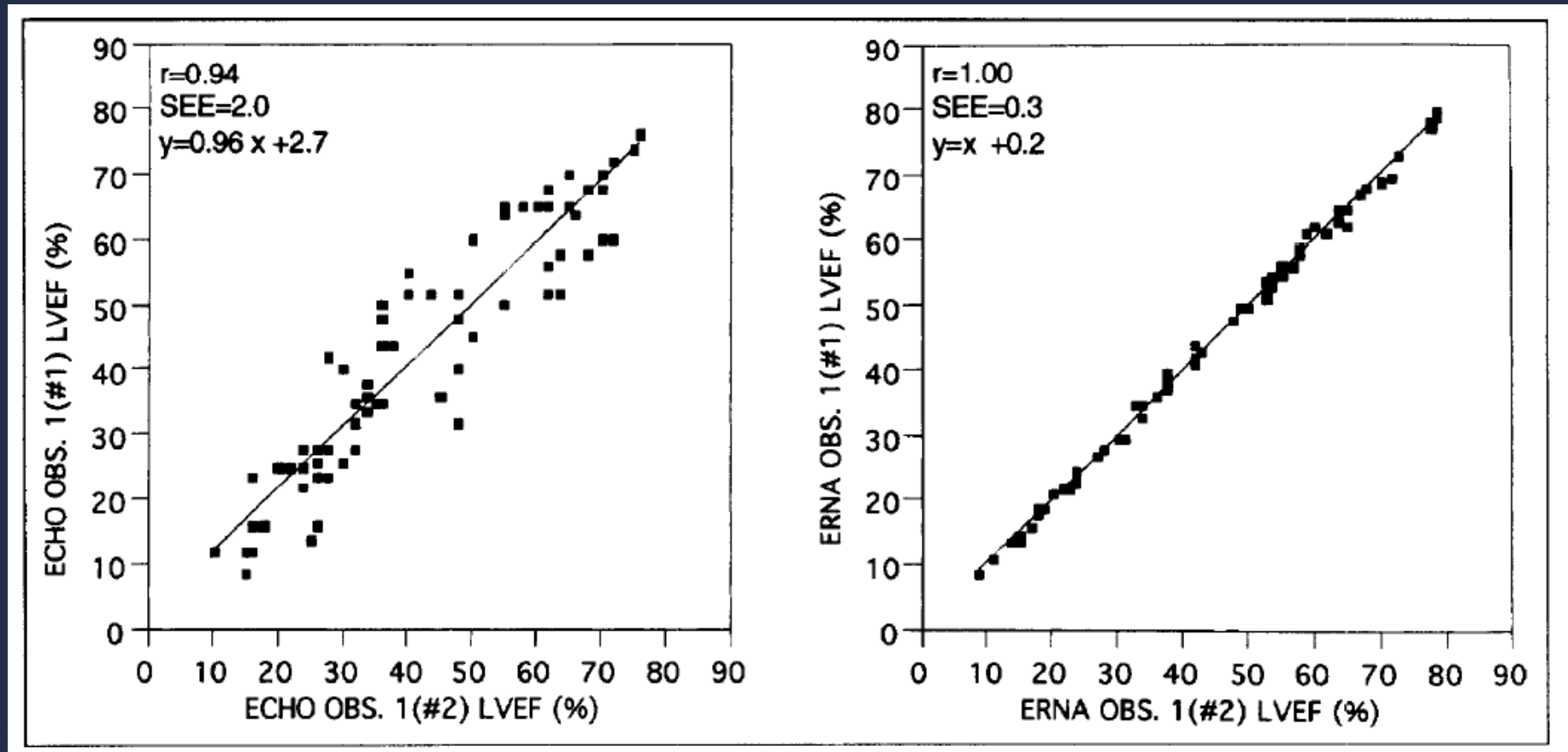

FIGURE 3. Intraobserver variability. Correlation between the first and the second assessment of left ventricular ejection fraction (LVEF) by echocardiographer #1 *(left)*, and between the first and the second assessment of LVEF by nuclear technologist #1 *(right)*. Mean intraobserver variability is 2% for equilibrium radionuclide angiography (ERNA) and 15.3% for 2-dimensional echocardiography (ECHO). OBS. = observer.

Comparison and reproducibility of visual echocardiographic and quantitative radionuclide left ventricular ejection fractions. Uvan Royen N, Jaffe CC, Krumholz HM, Johnson KM, Lynch PJ, Natale D, Atkinson P, Deman P, Wackers FJ. Am J Cardiol. 1996;77(10):843.

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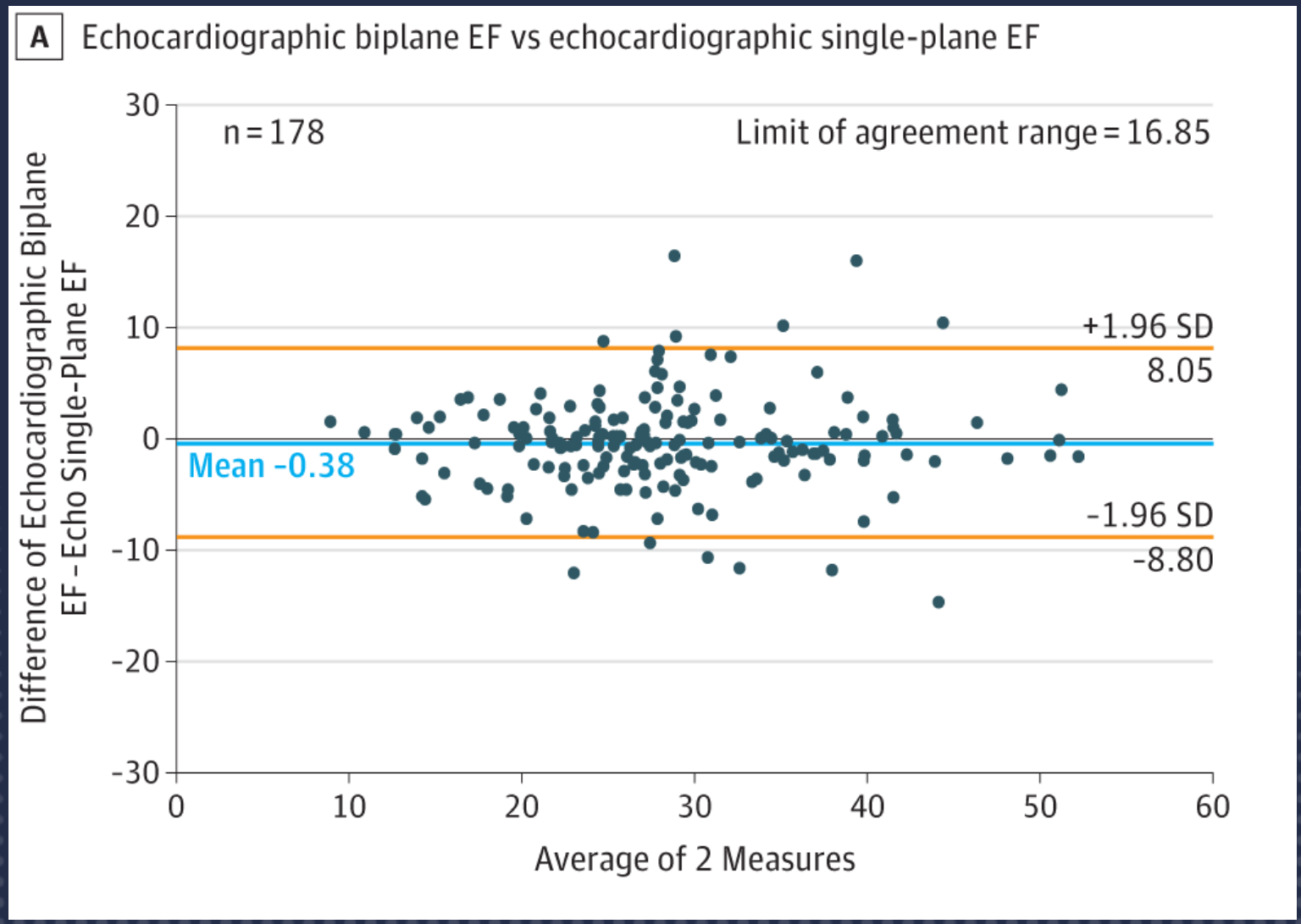

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Pellikka, et al. **Variability in Ejection Fraction Measured By Echocardiography, Gated Single-Photon Emission Computed Tomography, and Cardiac Magnetic Resonance in Patients With Coronary Artery Disease and Left Ventricular Dysfunction.** JAMA Netw Open. 2018;1(4):

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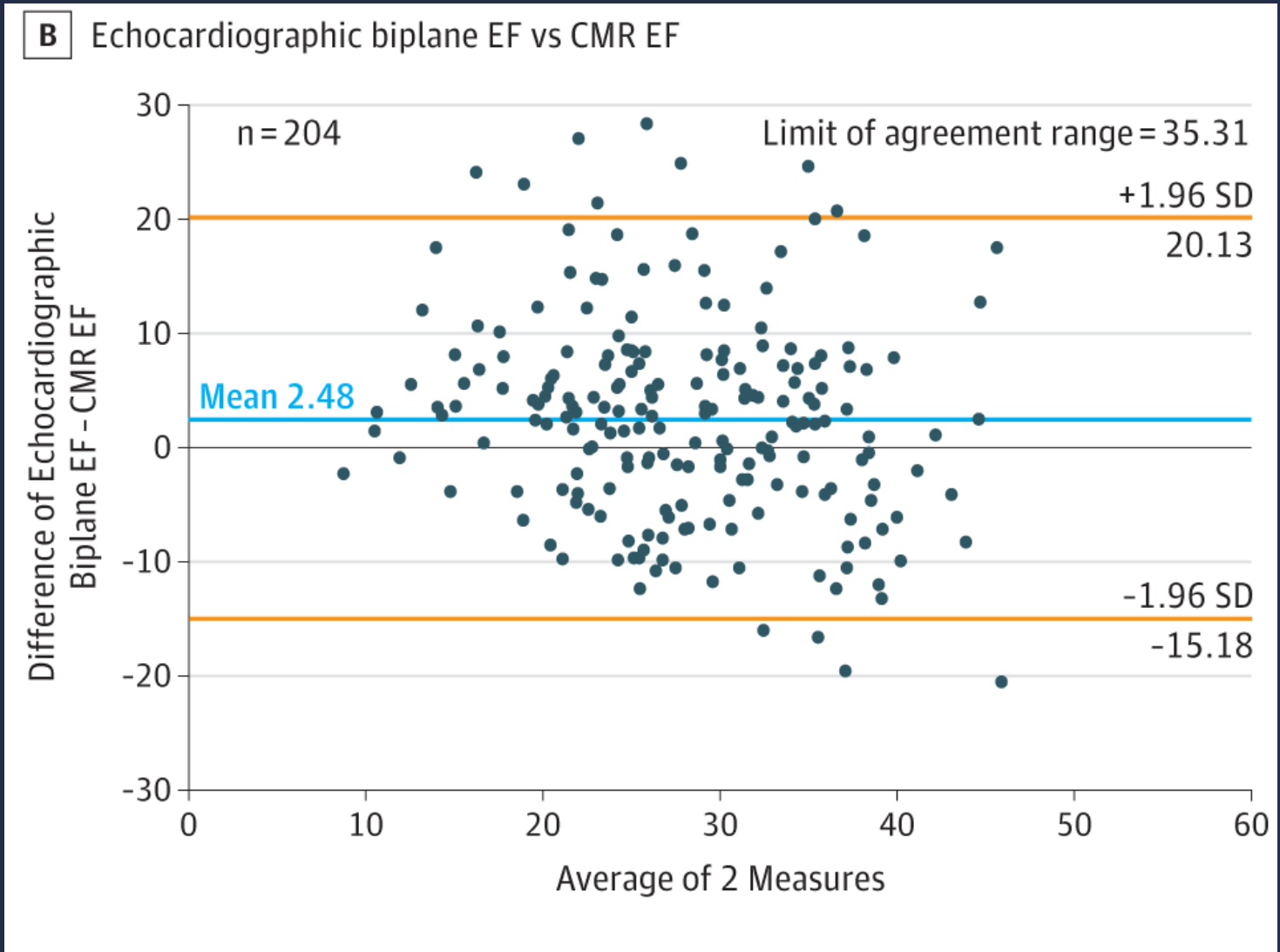

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Advances in Echocardiography in Heart Failure

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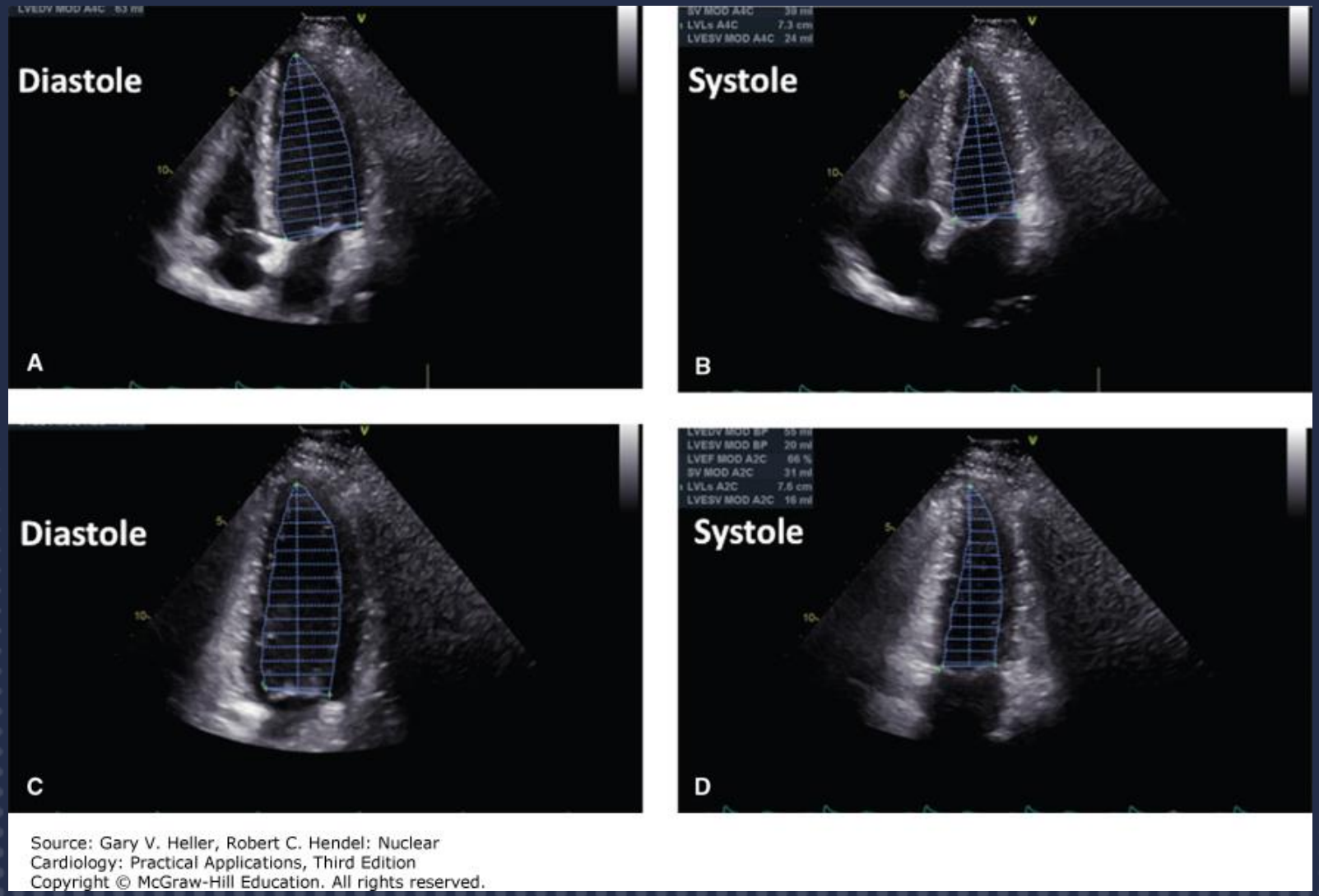
Biplane Simpson's Method



Source: Gary V. Heller, Robert C. Hendel: Nuclear Cardiology: Practical Applications, Third Edition

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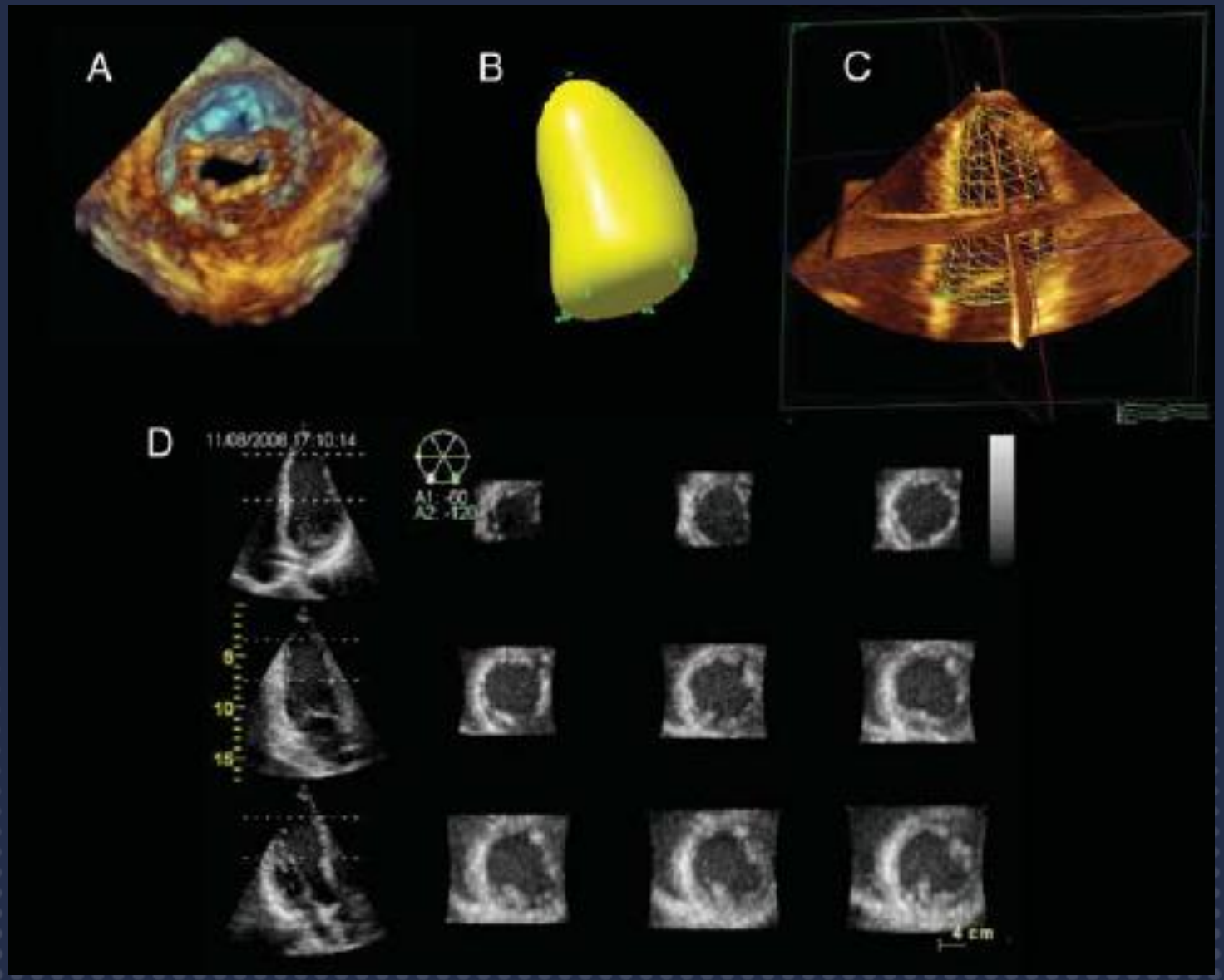
3-D Volumetric Assessment



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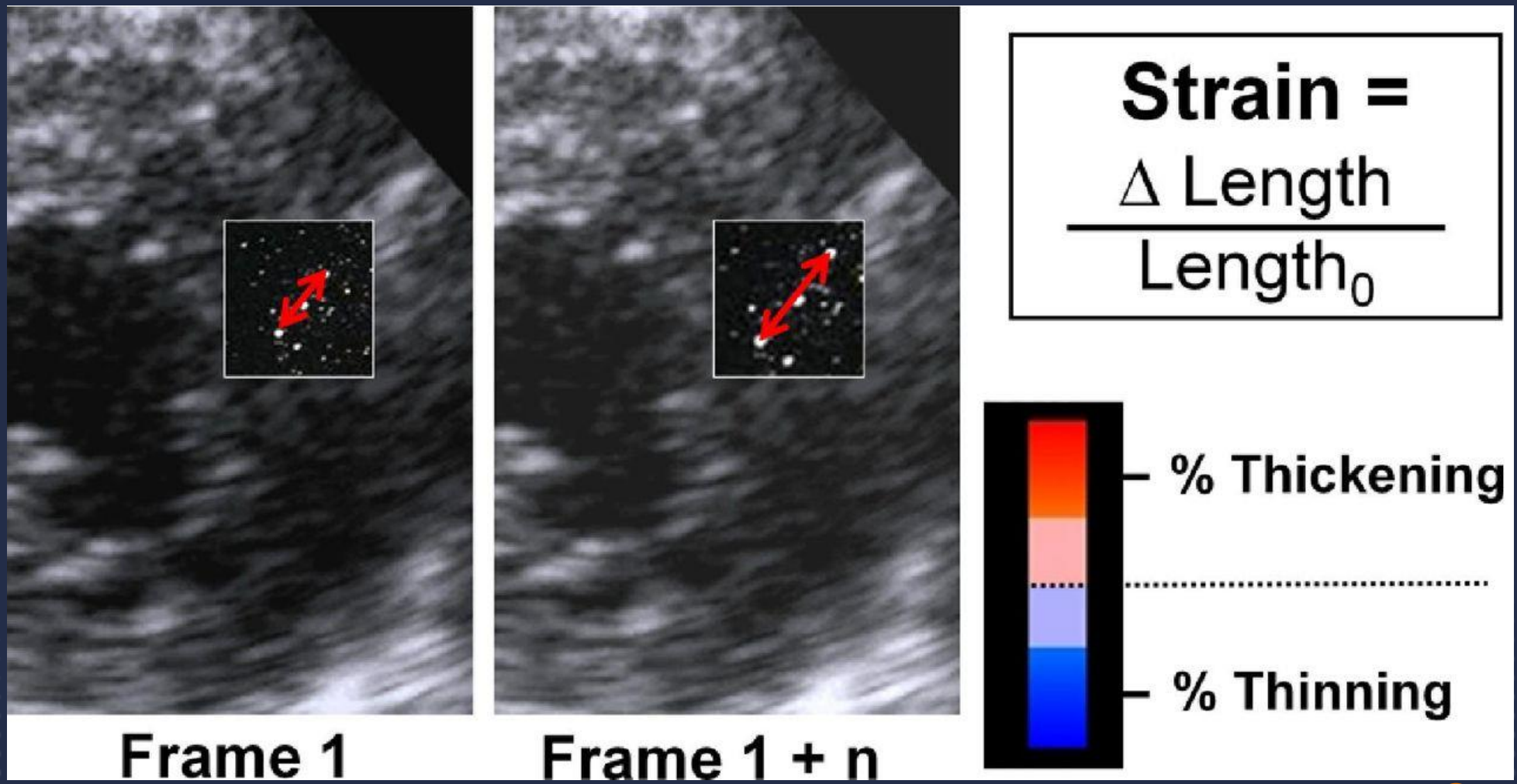
Speckle-Tracking Echocardiograph (Strain)



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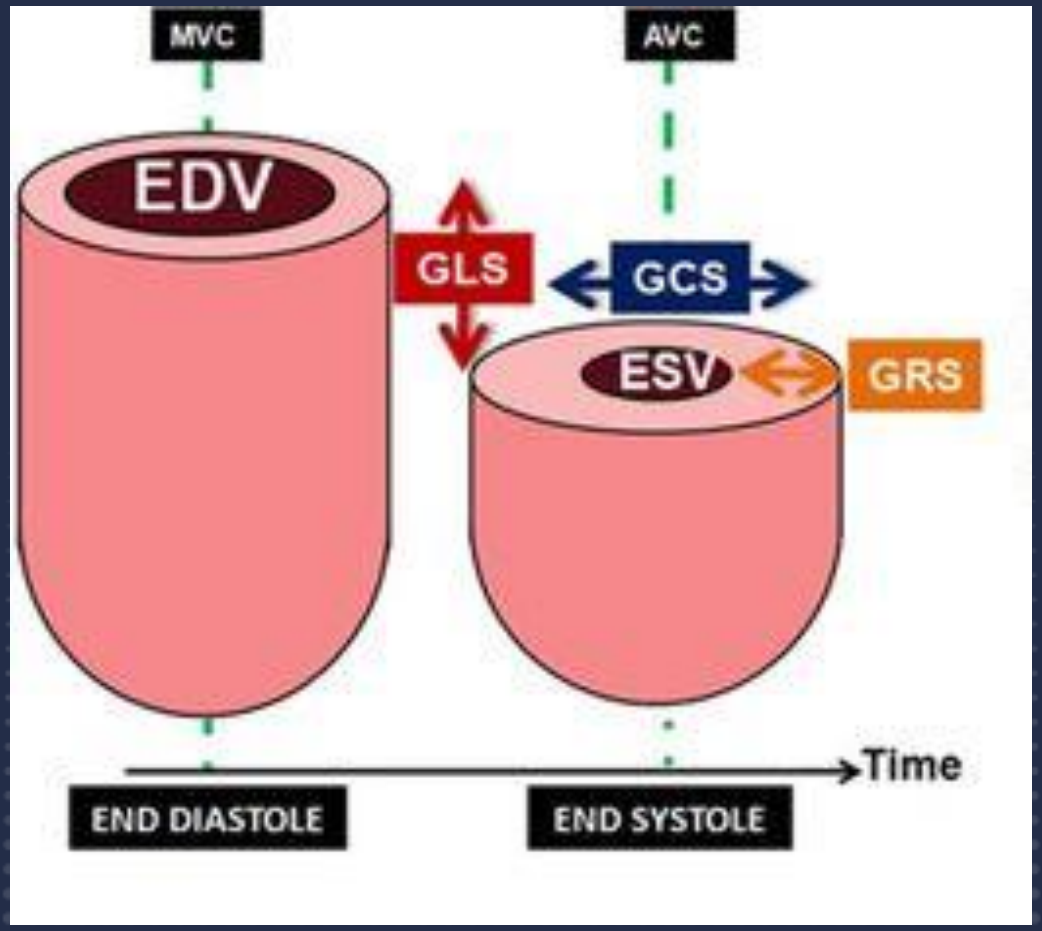

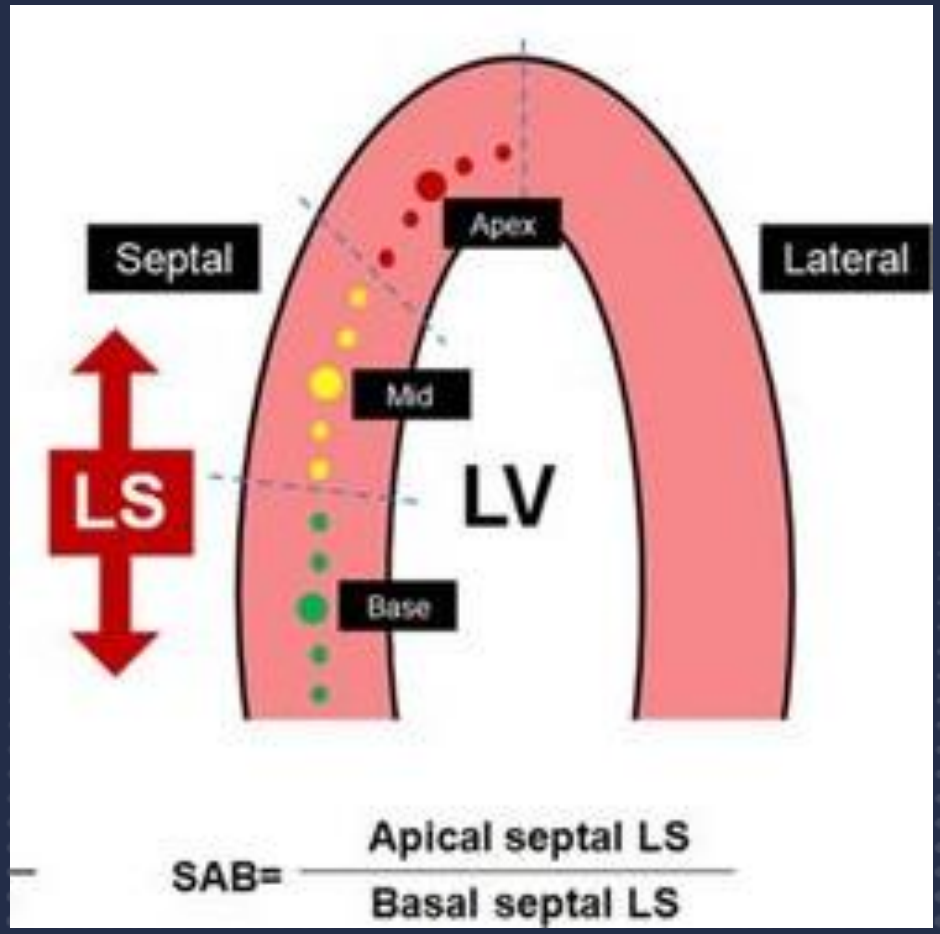

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Efstathios D. Pagourelias. Circulation: Cardiovascular Imaging. Echo Parameters for Differential Diagnosis in Cardiac Amyloidosis, Volume: 10, Issue: 3

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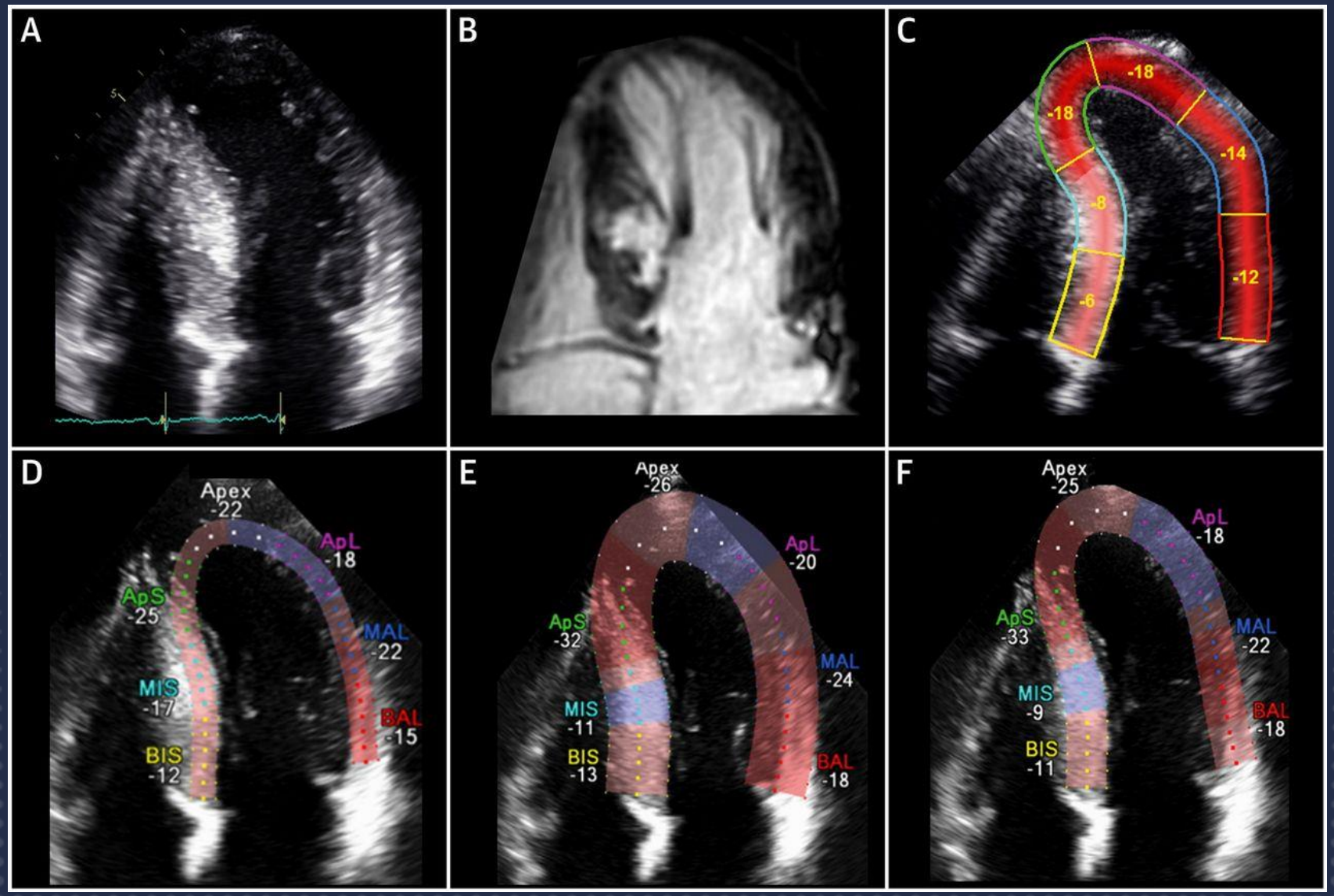

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Patrick Collier et al. JACC 2017;69:1043-1056

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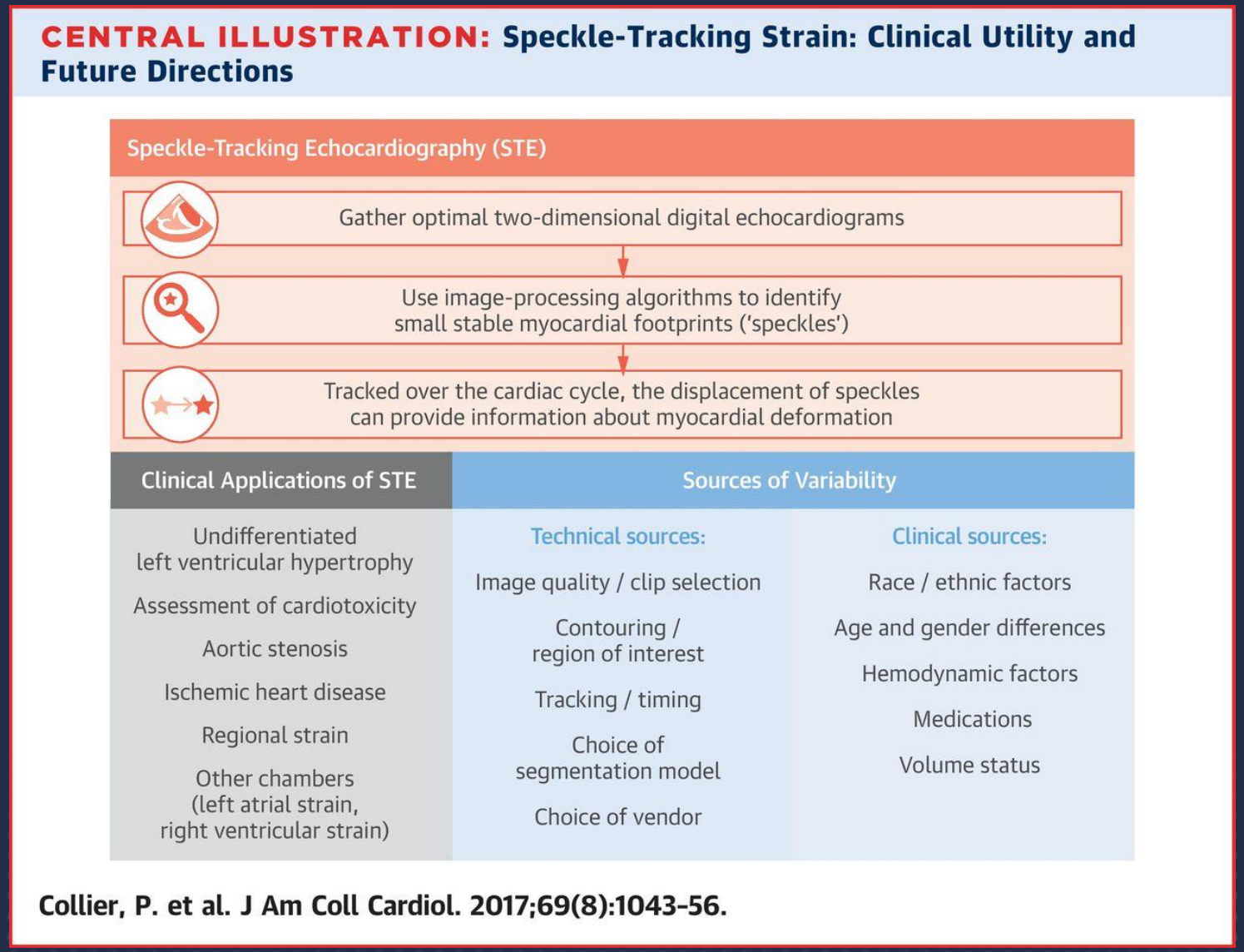

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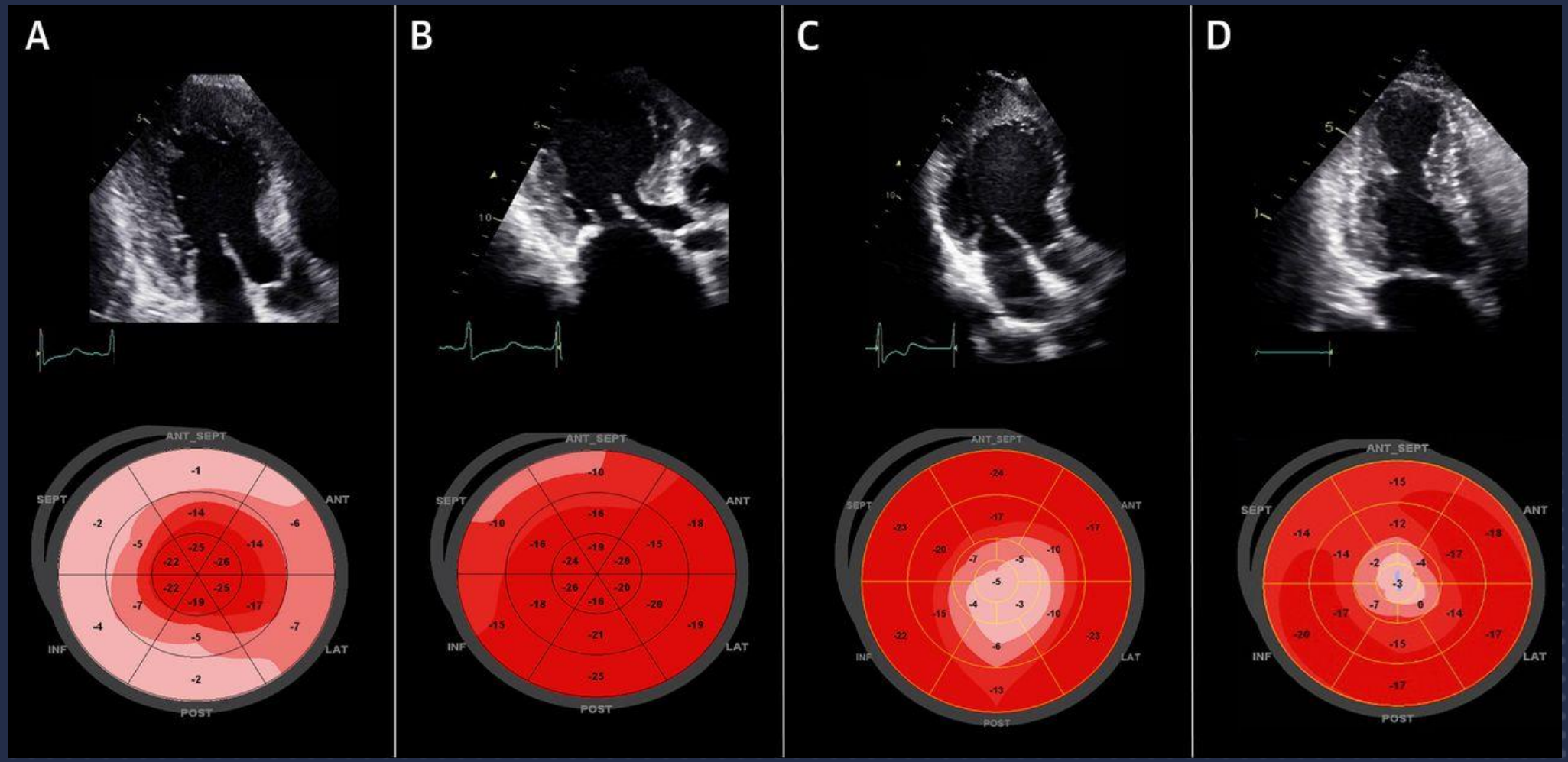

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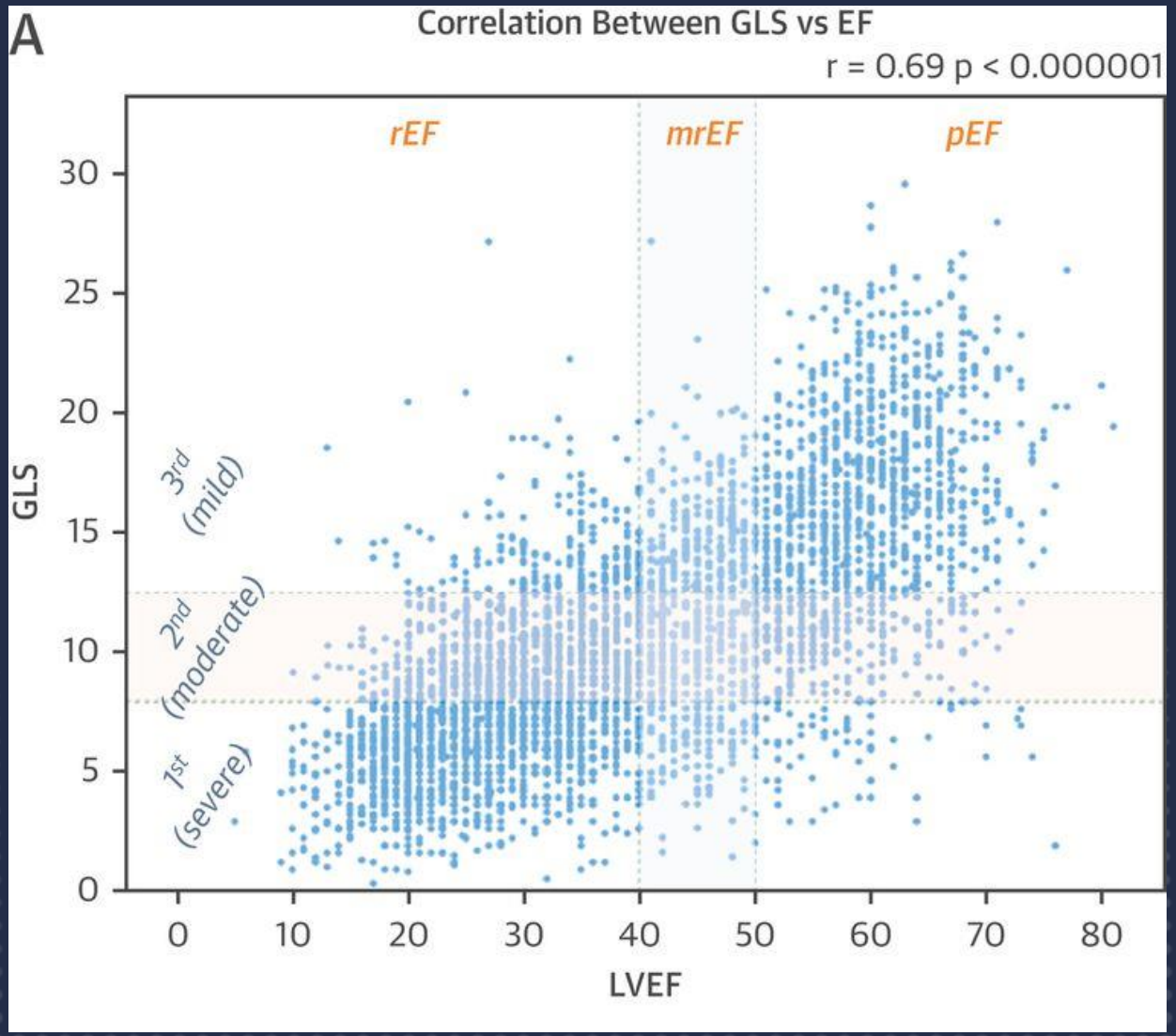
Strain Echocardiography in Heart Failure



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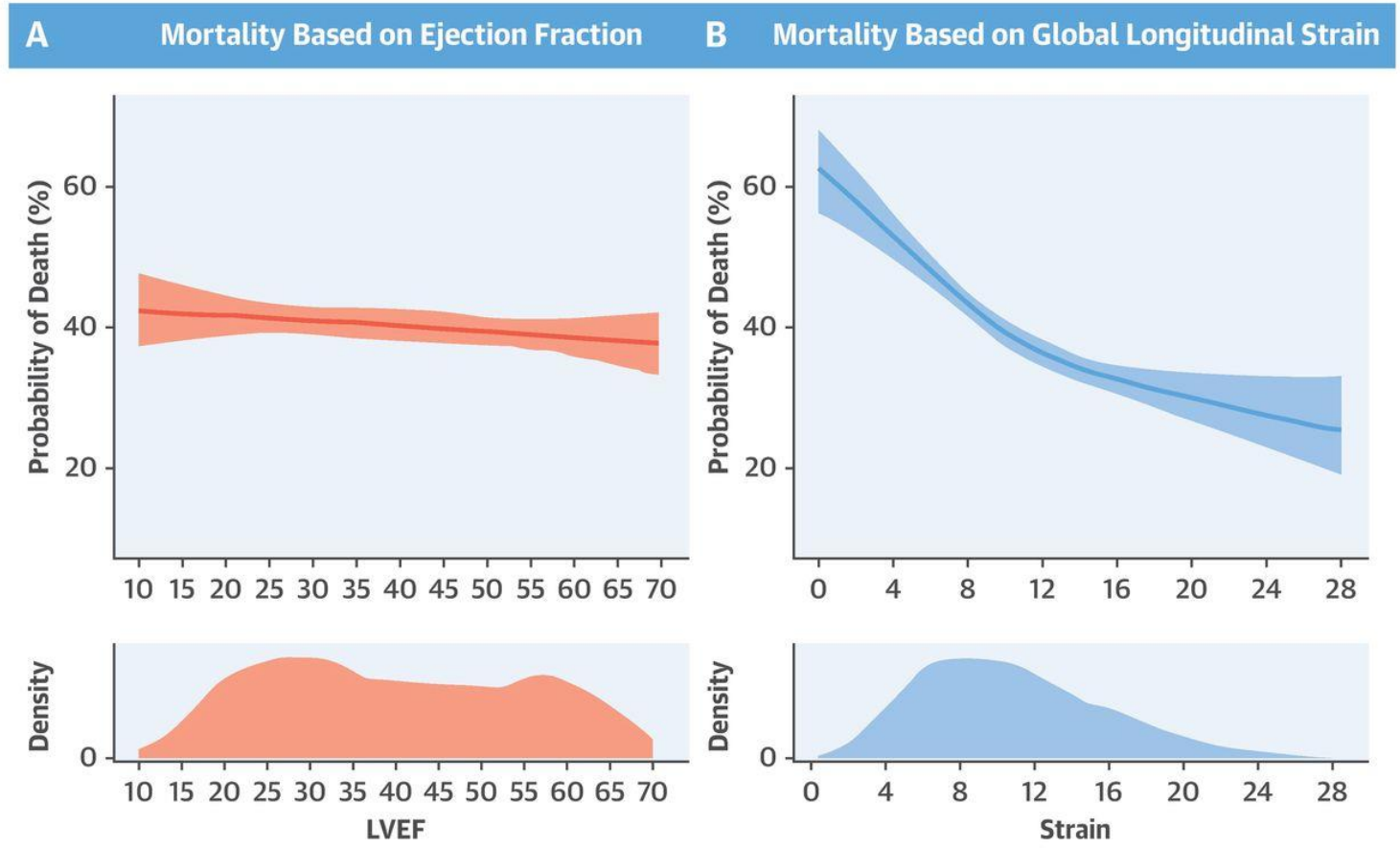
Jin Joo Park et al. JACC 2018;71:1947-1957

Strain Echocardiography in Heart Failure

CENTRAL ILLUSTRATION: Prognostic Value of Strain in Acute Heart Failure: Probability Plot for 5-Year All-Cause Mortality



Park, J.J. et al. J Am Coll Cardiol. 2018;71(18):1947-57.

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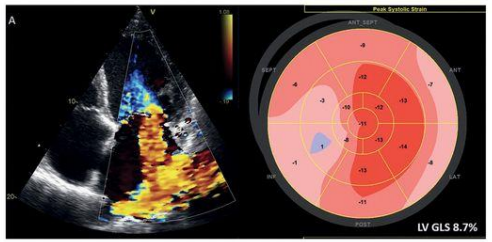
Jin Joo Park et al. JACC 2018;71:1947-1957

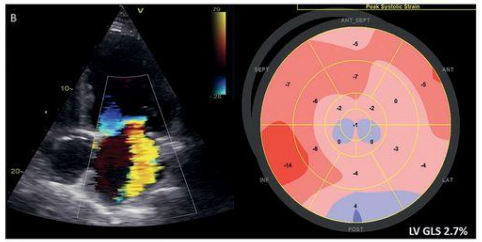
Strain Echocardiography in Heart Failure

CENTRAL ILLUSTRATION: Association of Left Ventricular Global Longitudinal Strain and All-Cause Mortality in Patients With Significant Secondary Mitral Regurgitation

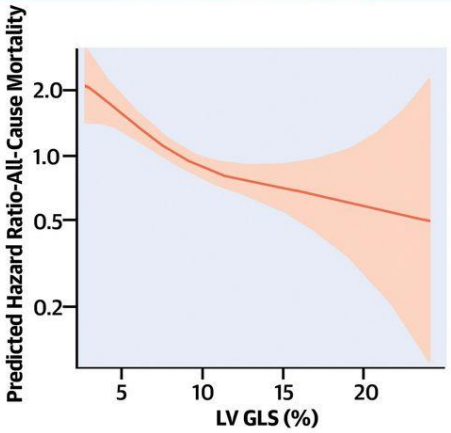
A Patient With Severe Mitral Regurgitation, LVEF 21% and LV Global Longitudinal Strain >7%



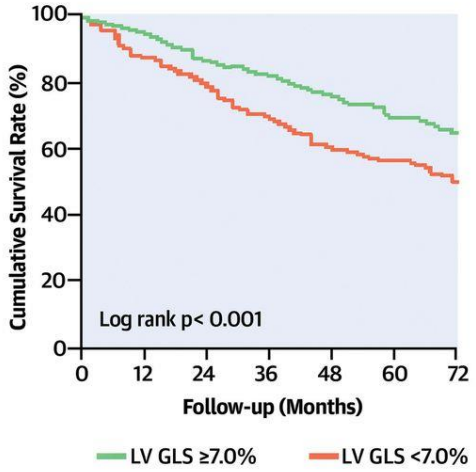
B Patient With Severe Mitral Regurgitation, LVEF 20% and LV Global Longitudinal Strain <7%



C Association Between LV Global Longitudinal Strain and All-Cause Mortality



D Survival Analysis



Namazi, F. et al. J Am Coll Cardiol. 2020;75(7):750-8.

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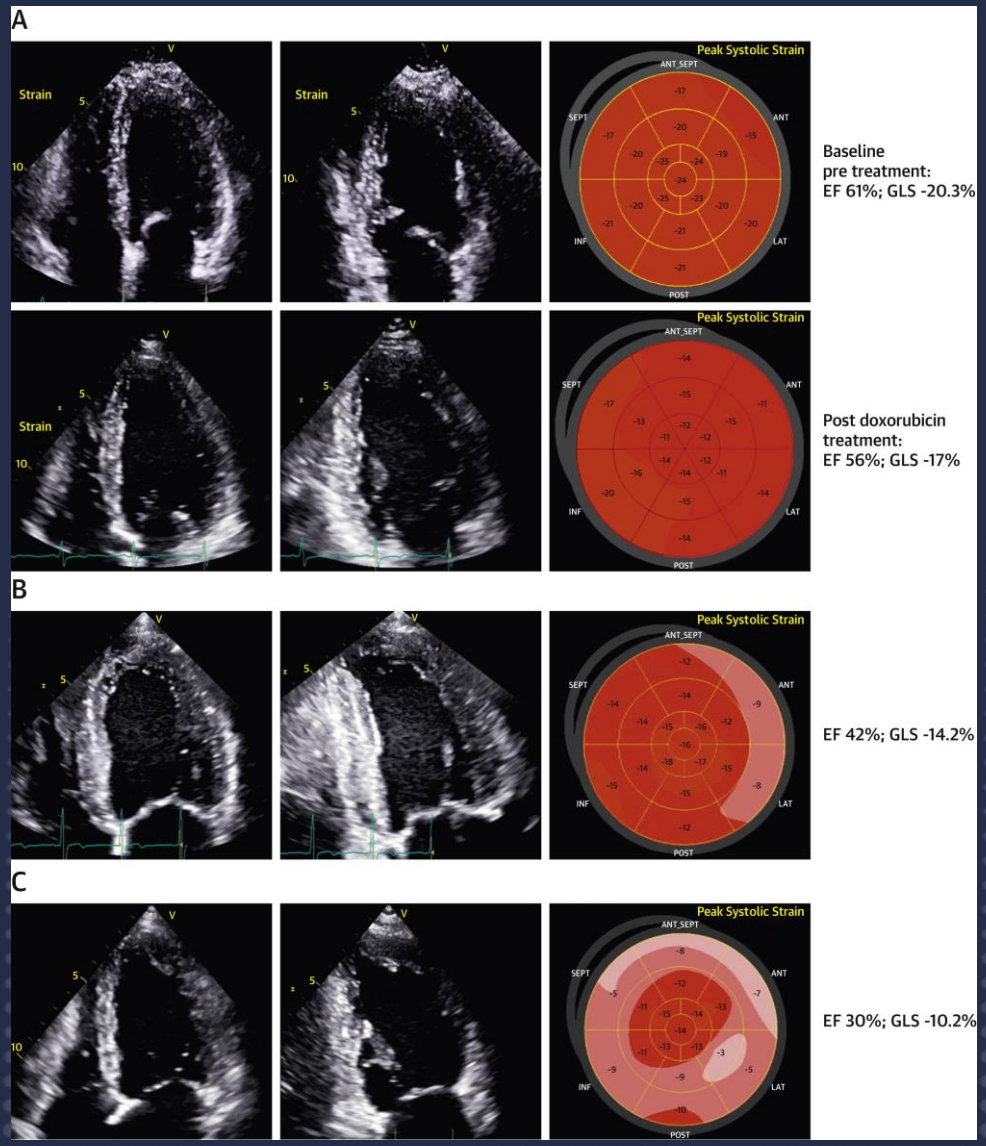
Strain Echocardiography in Cardio-Oncology



Jennifer Liu et al. JIMG 2018;11:1122-1131

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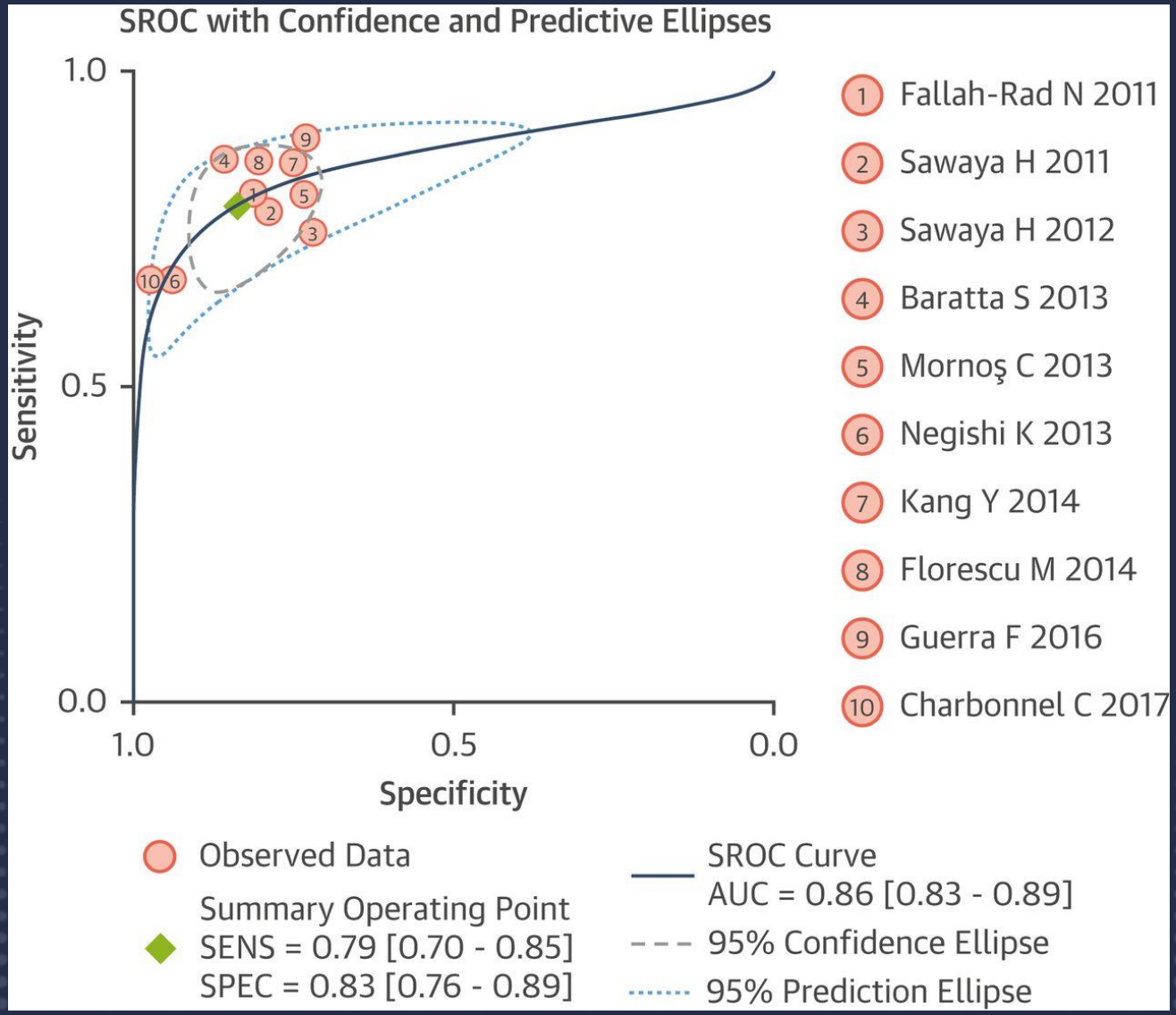

Myocardial Strain Imaging by Echocardiography for the Prediction of Cardiotoxicity in Chemotherapy-Treated Patients A Meta-Analysis. Lu Ye, Zhi-gang Yang, Joseph B. Selvanayagam, Hong Luo, Tai-zhu Yang, Rebecca Perry, Kai-yue Diao, Shan Huang, Meng-xi Yang, Pan Yang, Ya Jin and Ying-kun Guo. JACC: Cardiovascular Imaging. November 2019

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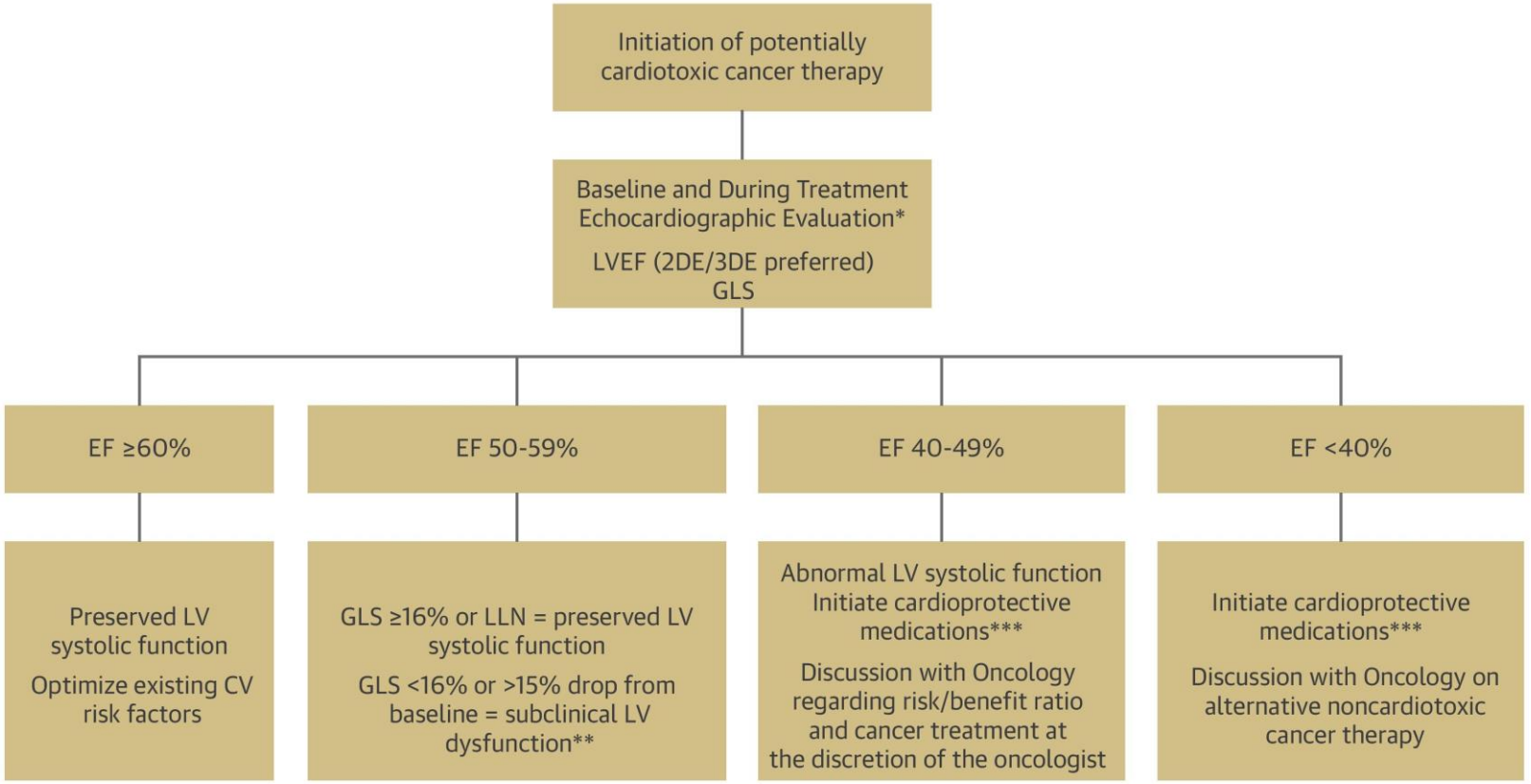
Strain Echocardiography in Cardio-Oncology

CENTRAL ILLUSTRATION: Echocardiography-Guided Clinical Decision Making



Liu, J. et al. J Am Coll Cardiol Img. 2018;11(8):1122-31.

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Cardiac MRI

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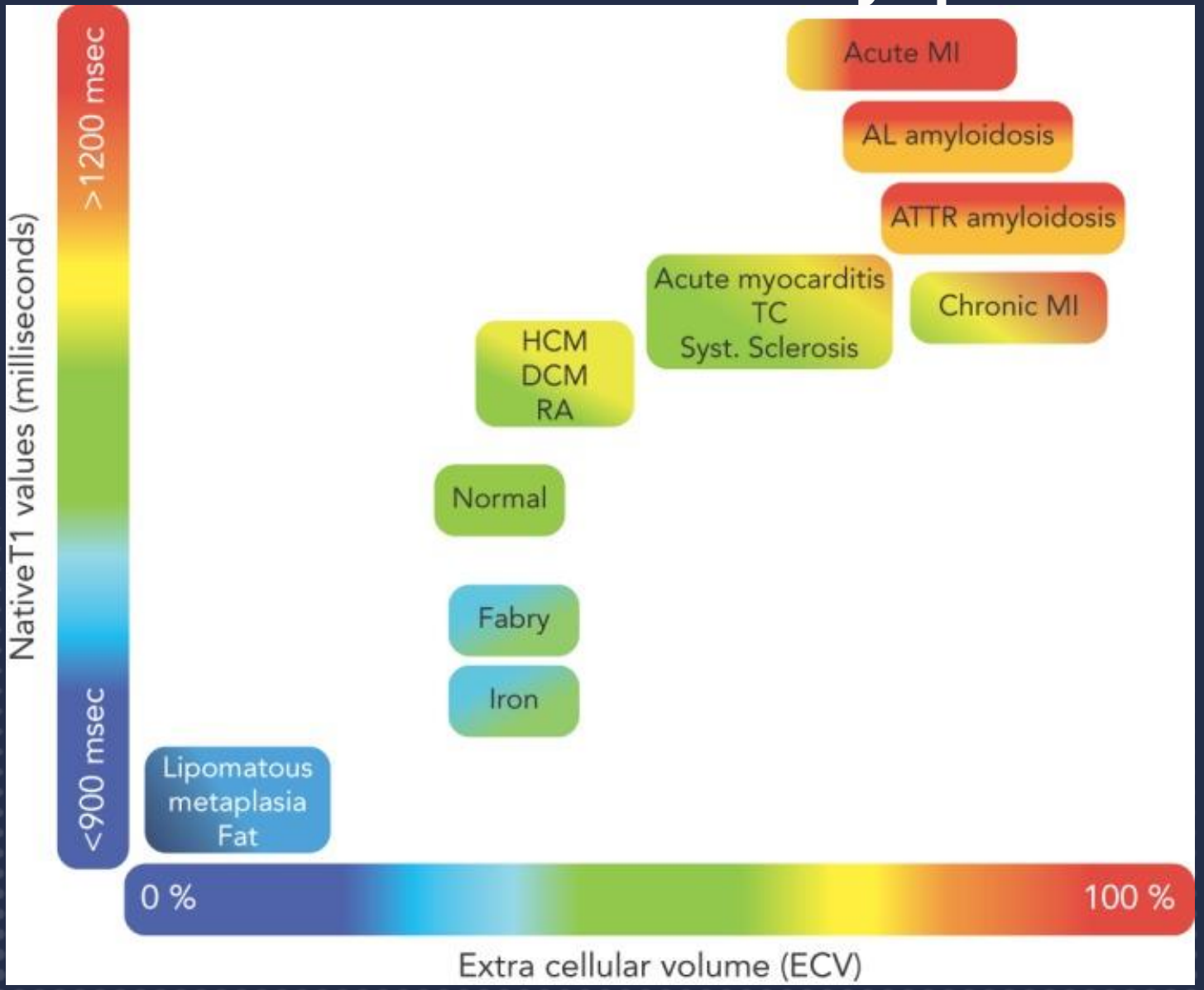
LGE Patterns in Cardiomyopathies



The Prognostic Role of Tissue Characterisation using Cardiovascular Magnetic Resonance in Heart Failure. Robert D Adam, James Shambrook, Andrew S Flett. Card Fail Rev. 2017 Nov; 3(2): 86–96.

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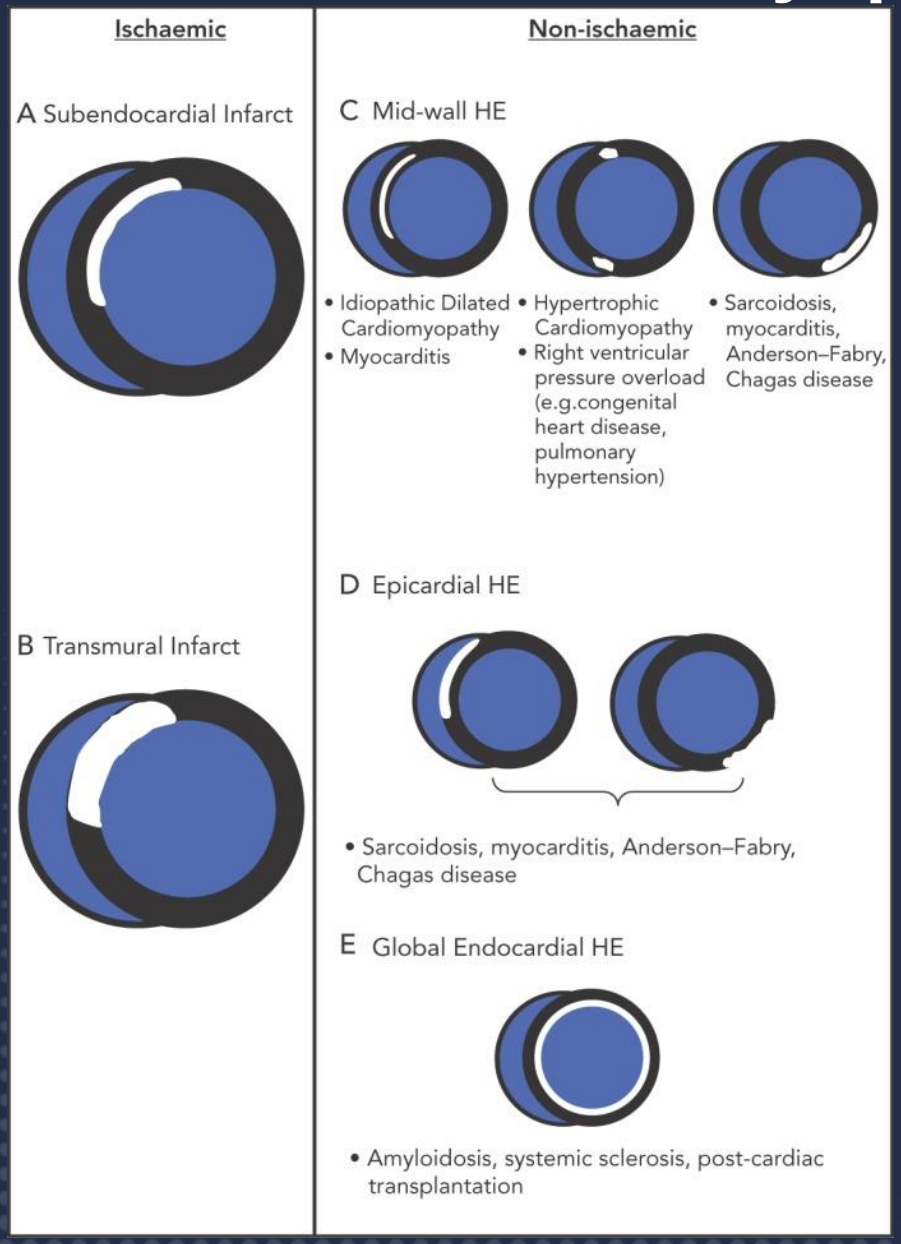

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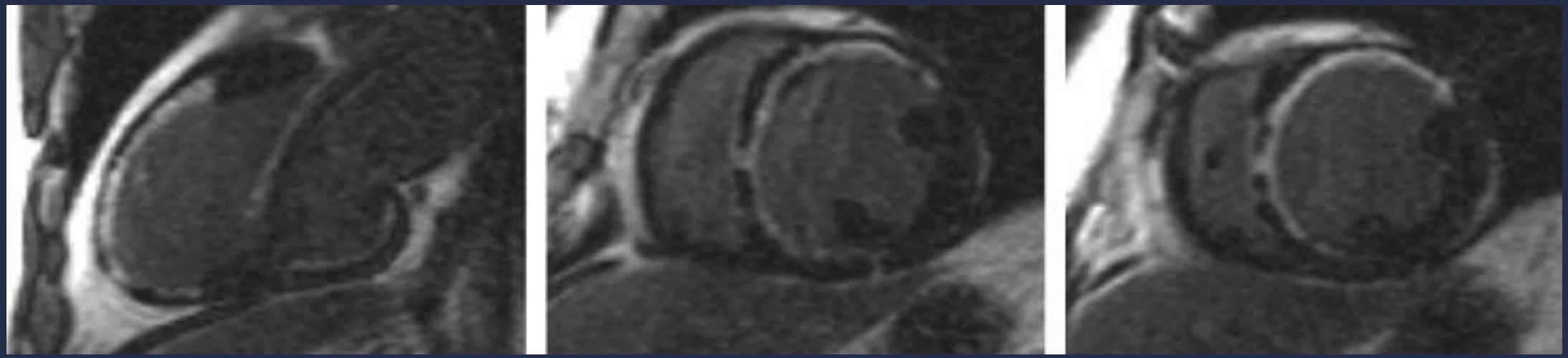
LGE in Ischemic Cardiomyopathy



The Role of Cardiovascular Magnetic Resonance Imaging in Heart Failure. Mark A Peterzan, Oliver J Rider, Lisa J Anderson. Card Fail Rev. 2016 Nov; 2(2): 115–122.

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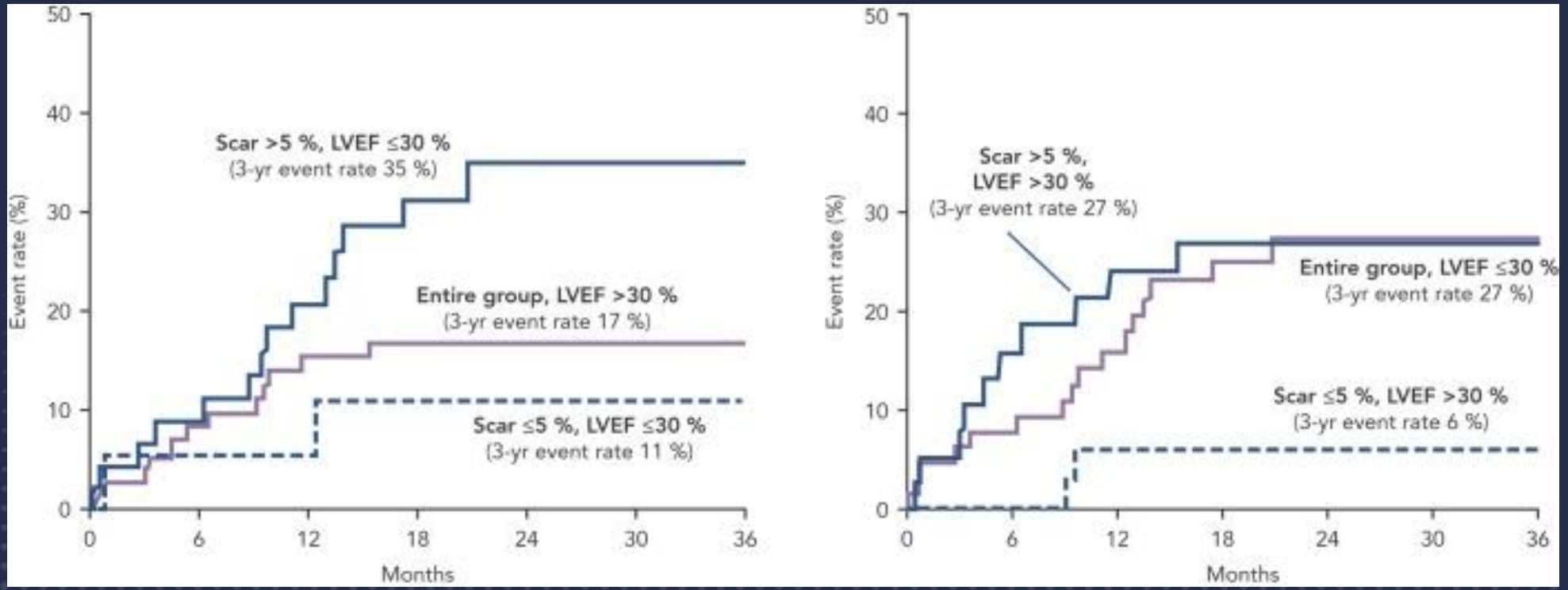
LGE in Ischemic Cardiomyopathy



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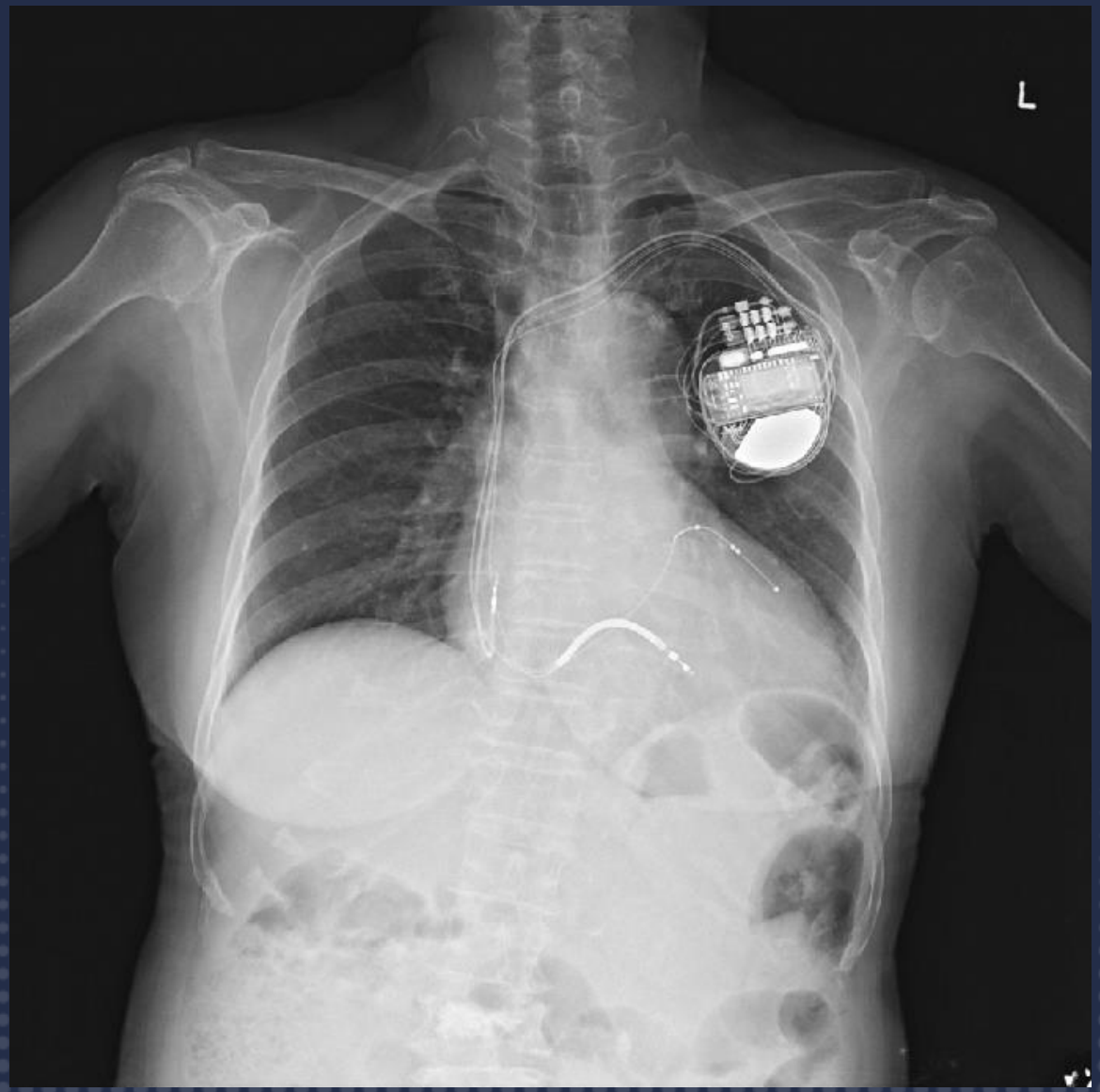
LGE and CRRT Therapy



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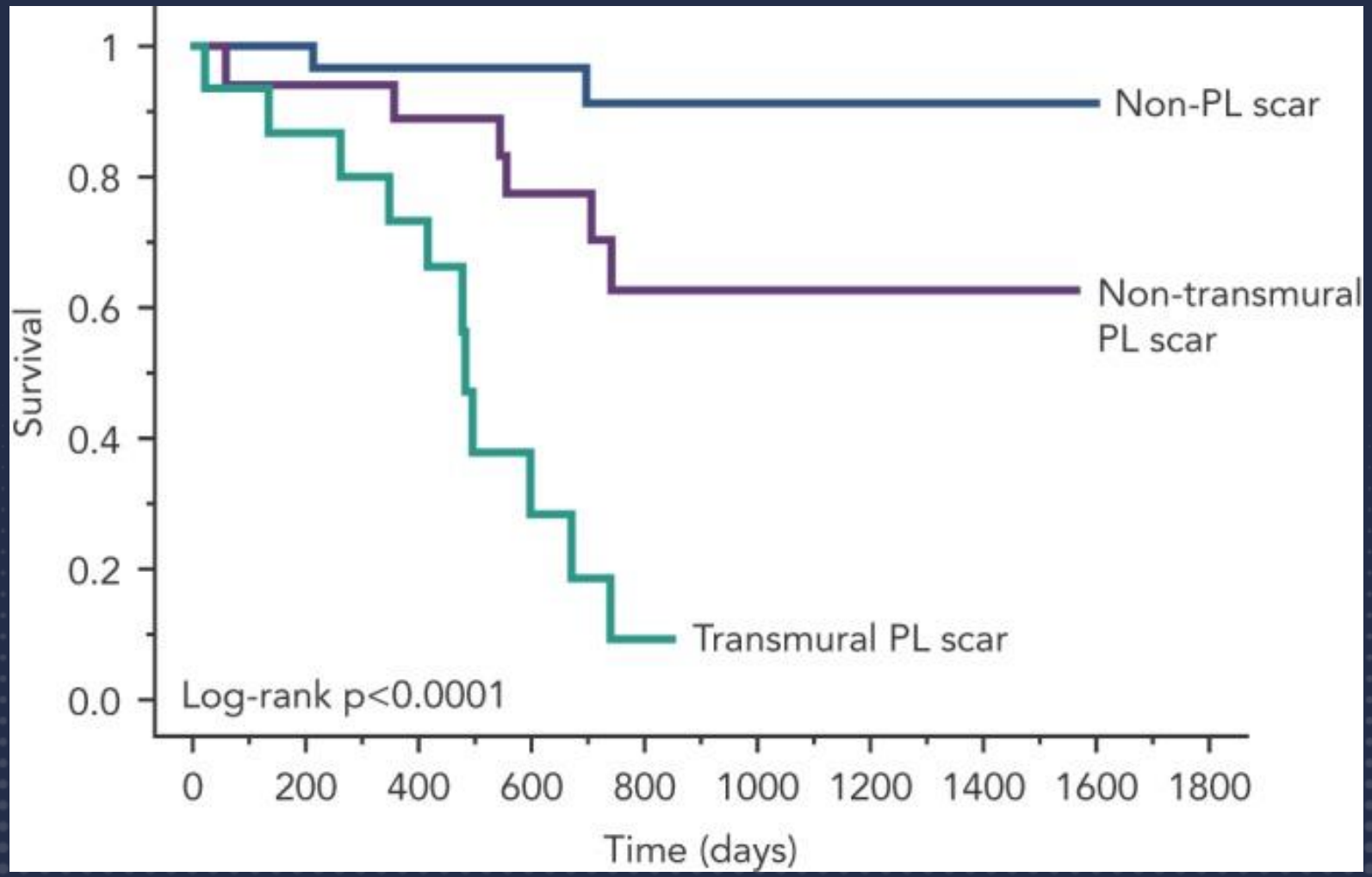
LGE and CRRT Therapy



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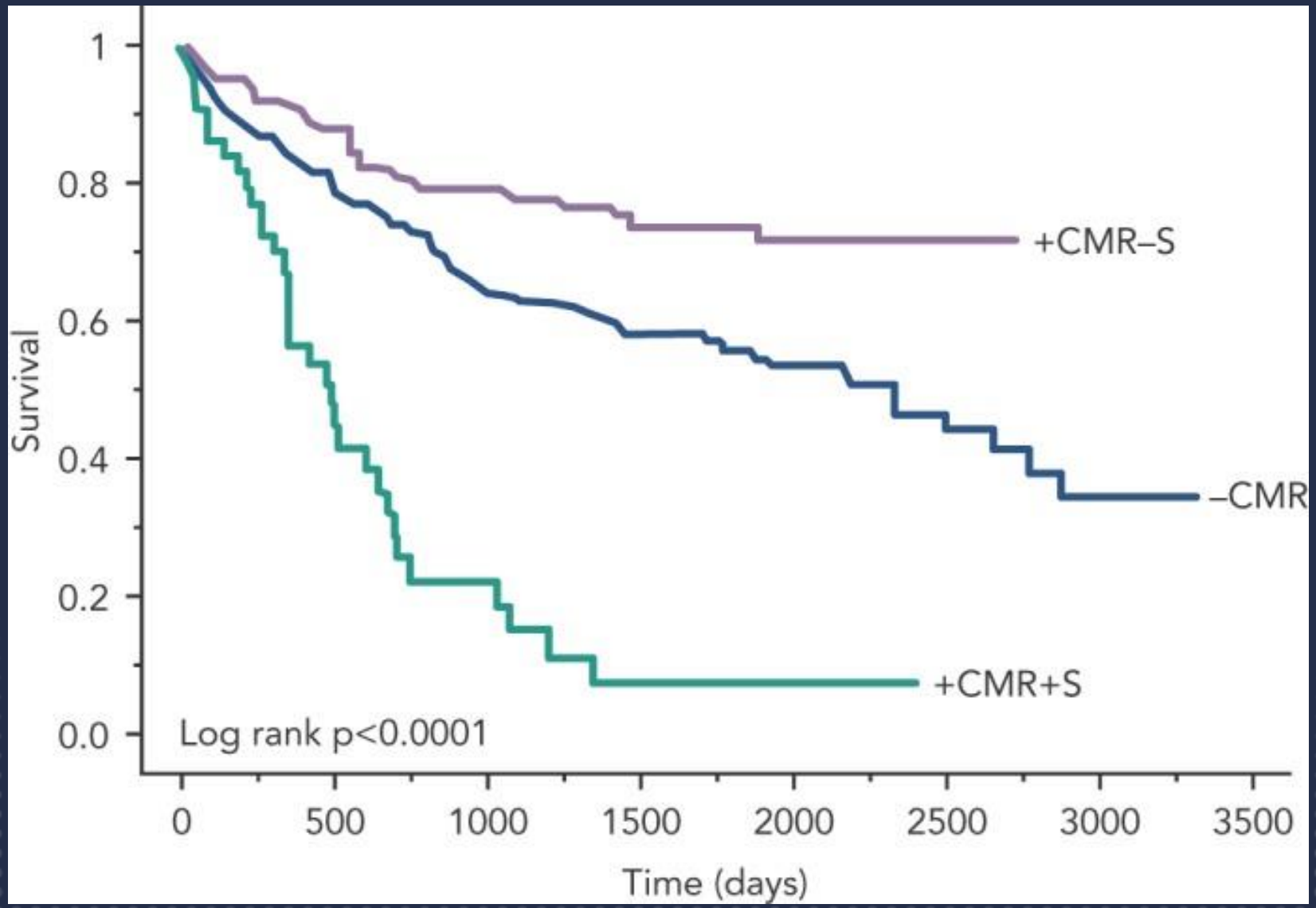

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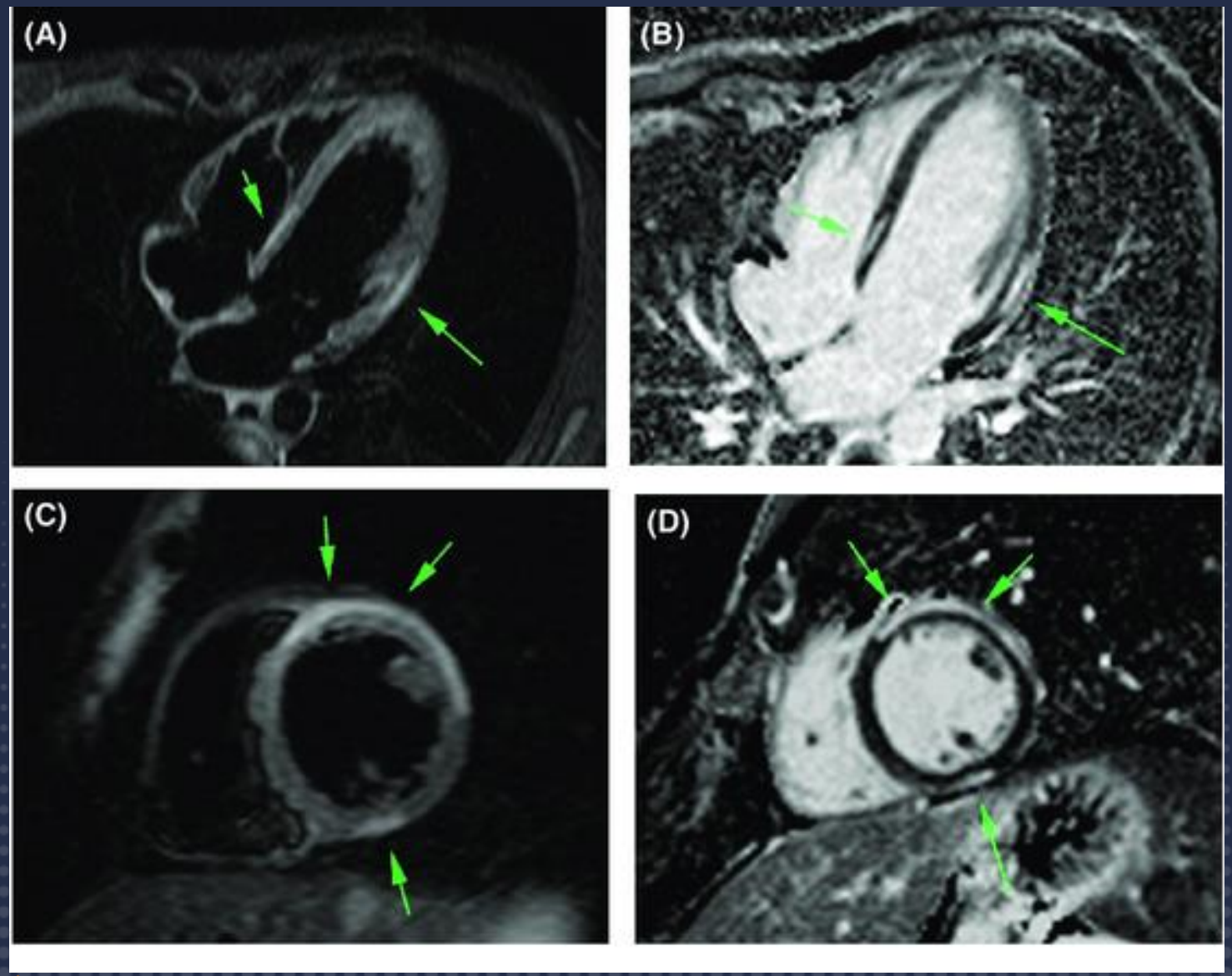
LGE Patterns in NICM



European Cardiology Review, 2016;11(1):20–4

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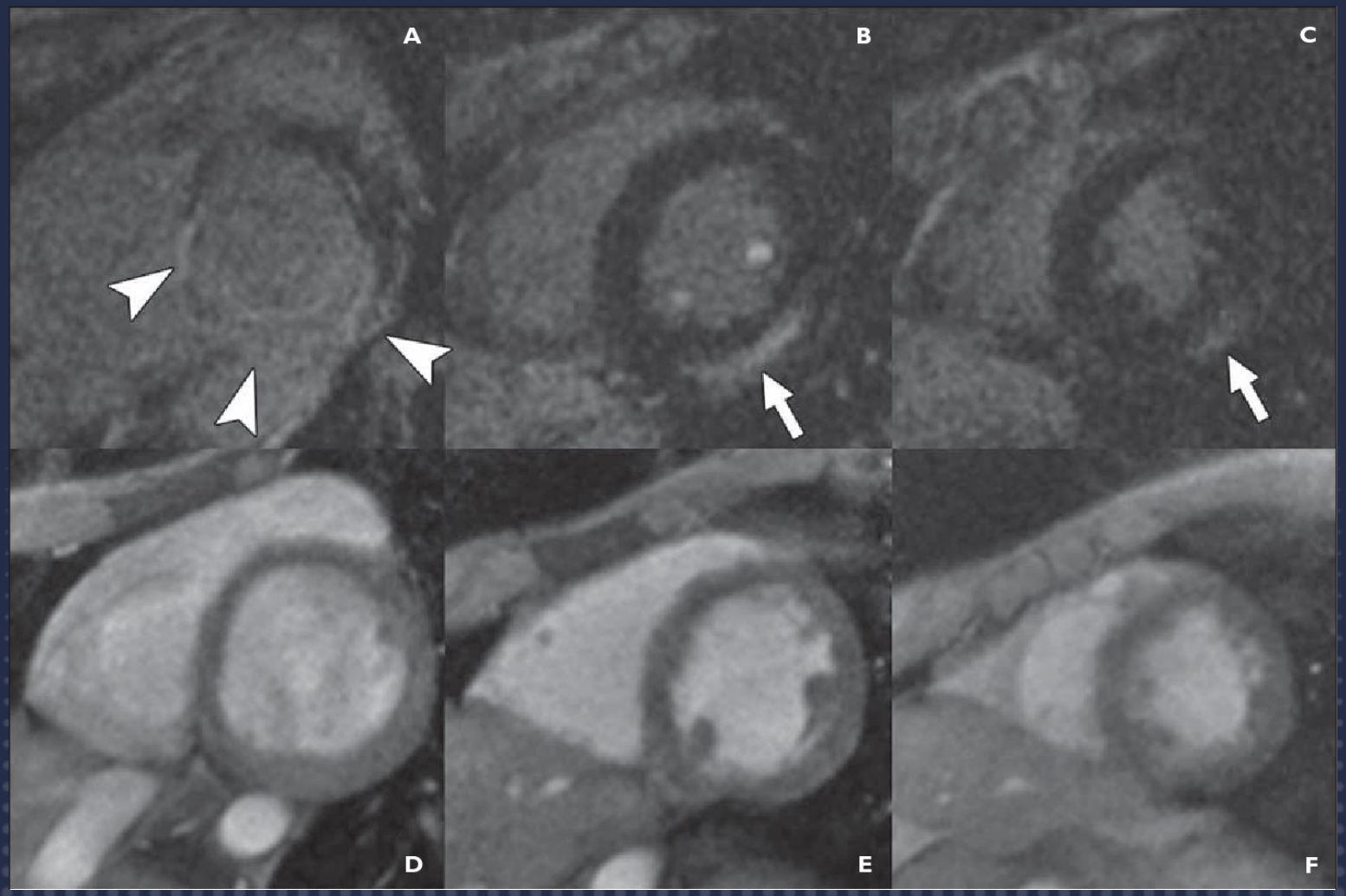
LGE Patterns in NICM



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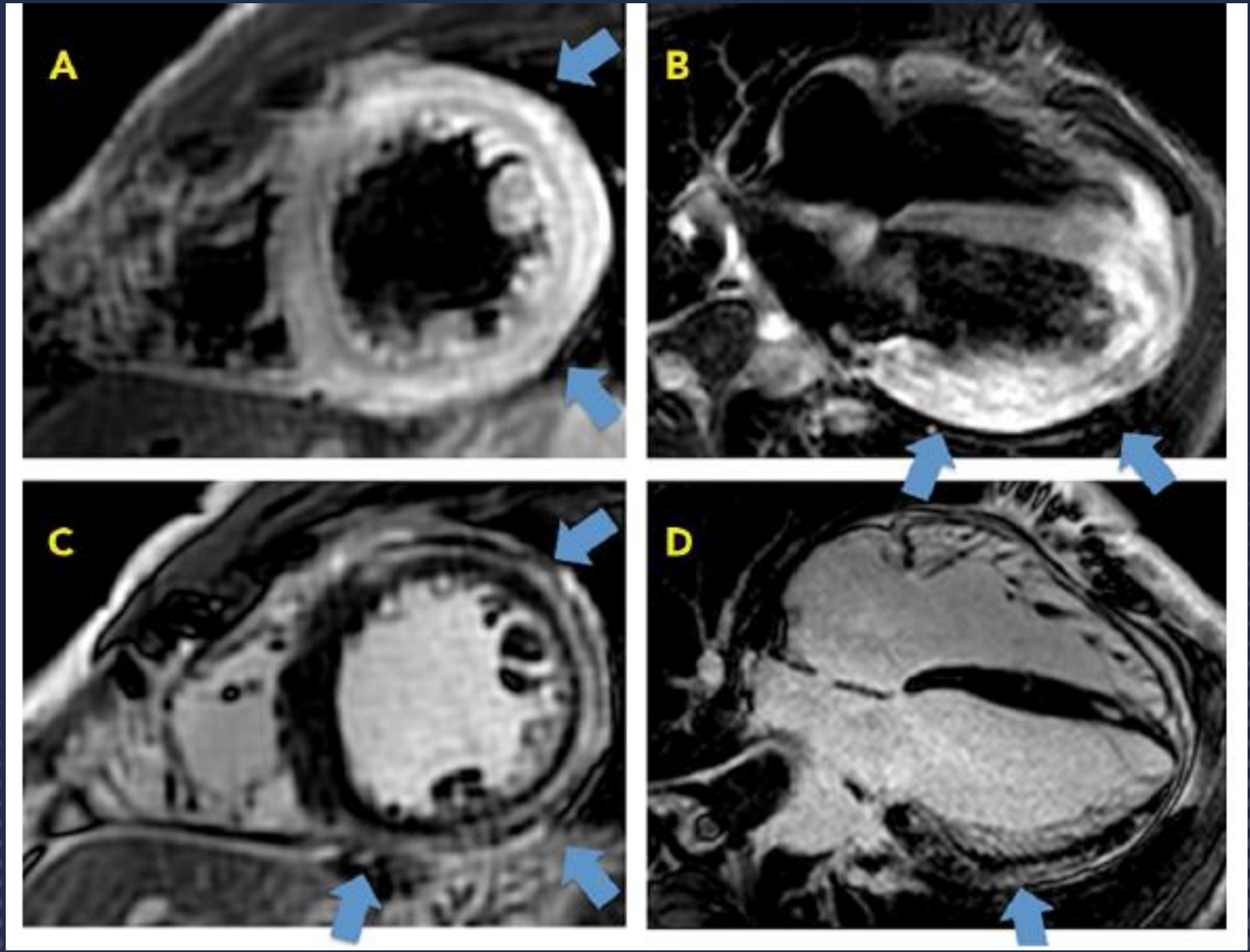

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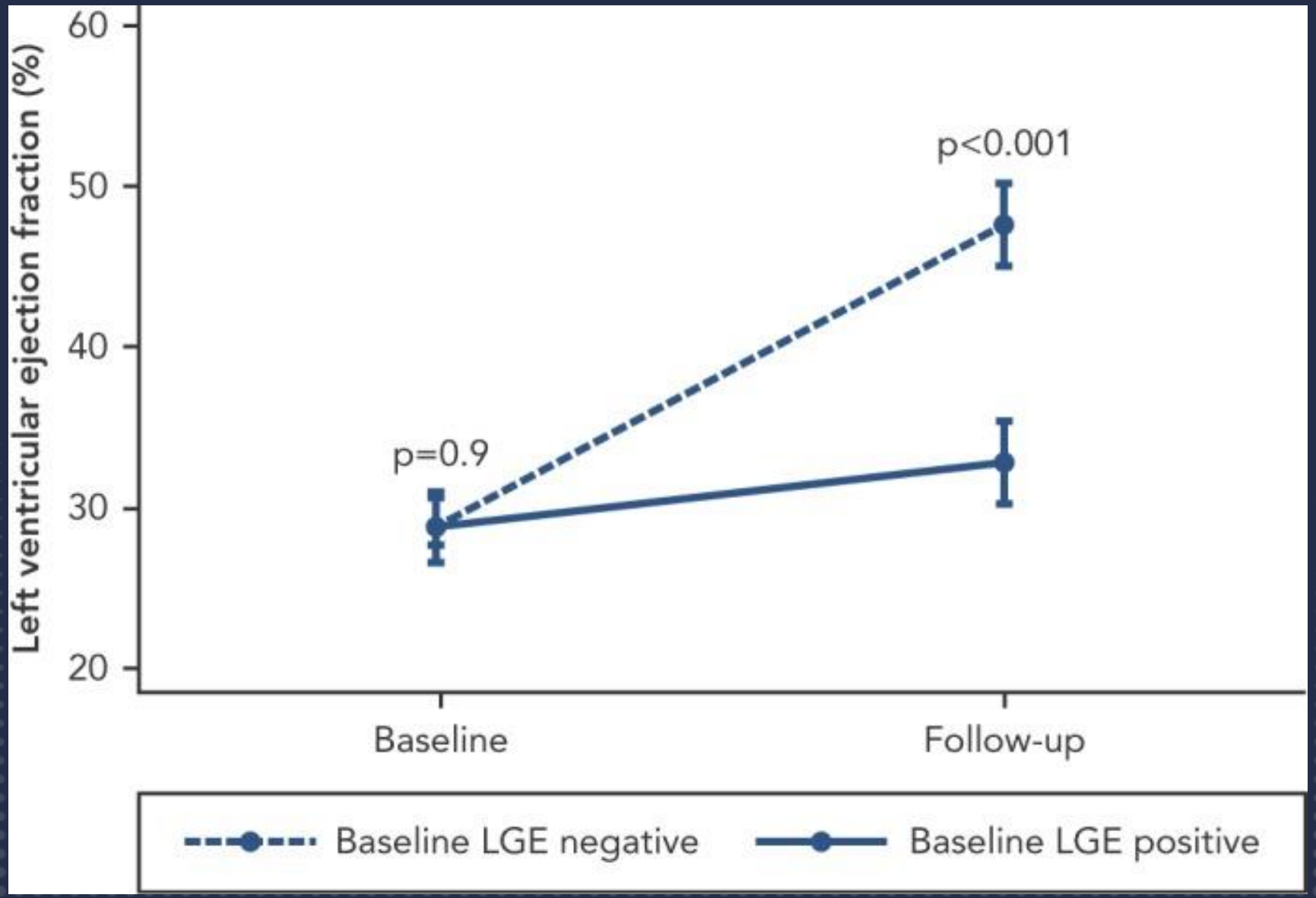

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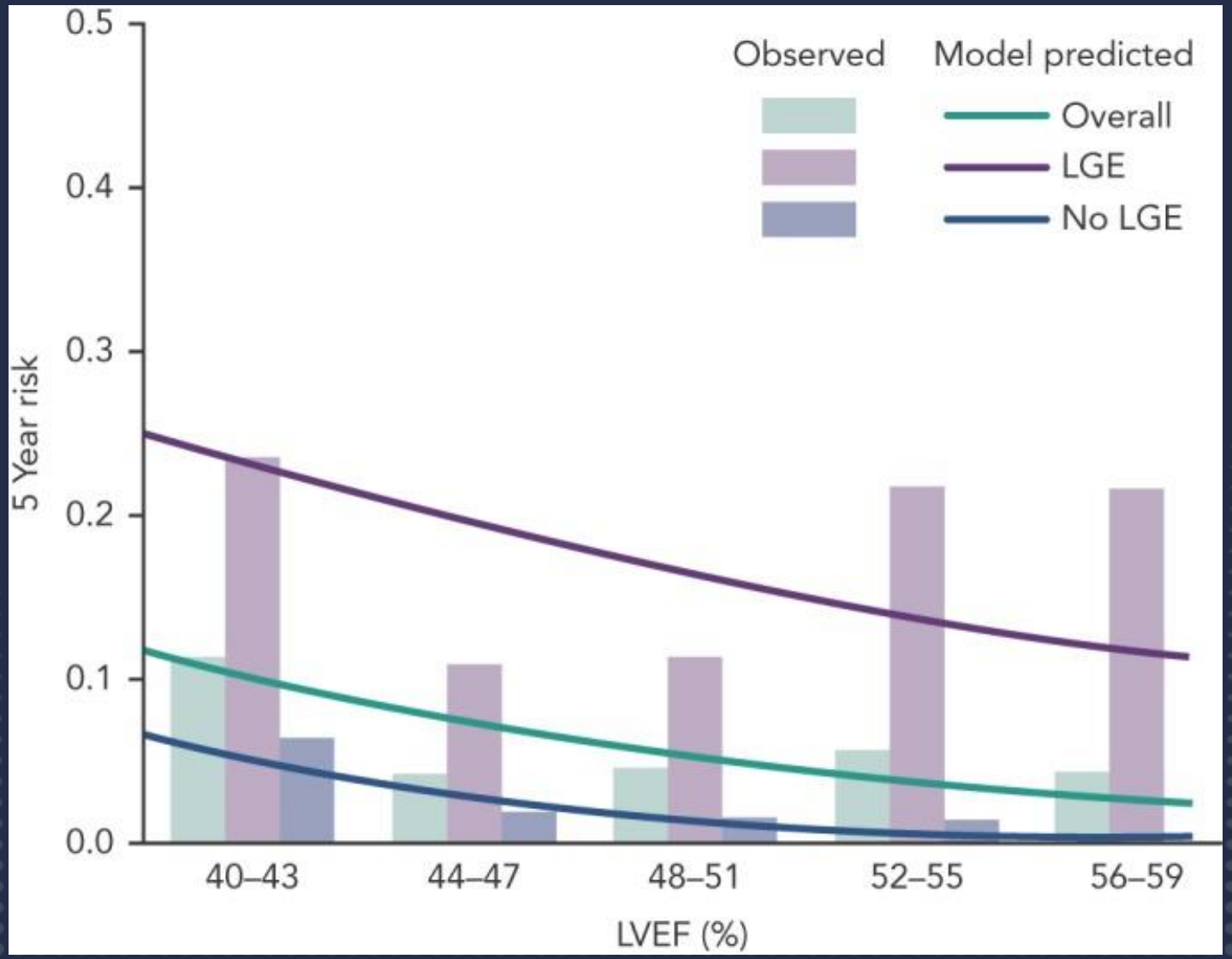

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Imaging for Amyloid Heart Disease

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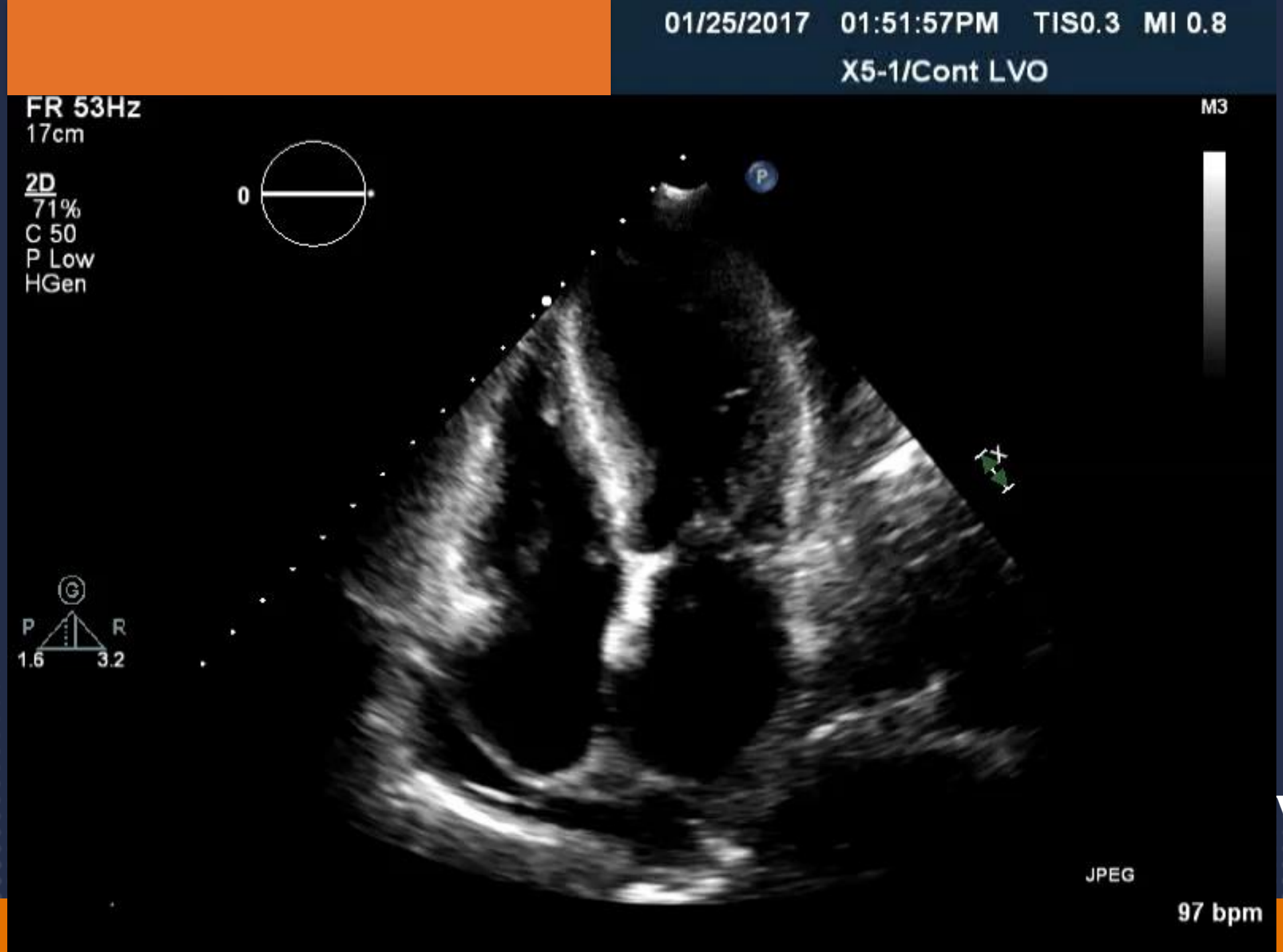
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X5-1/Cont LVO
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17cm
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P Low
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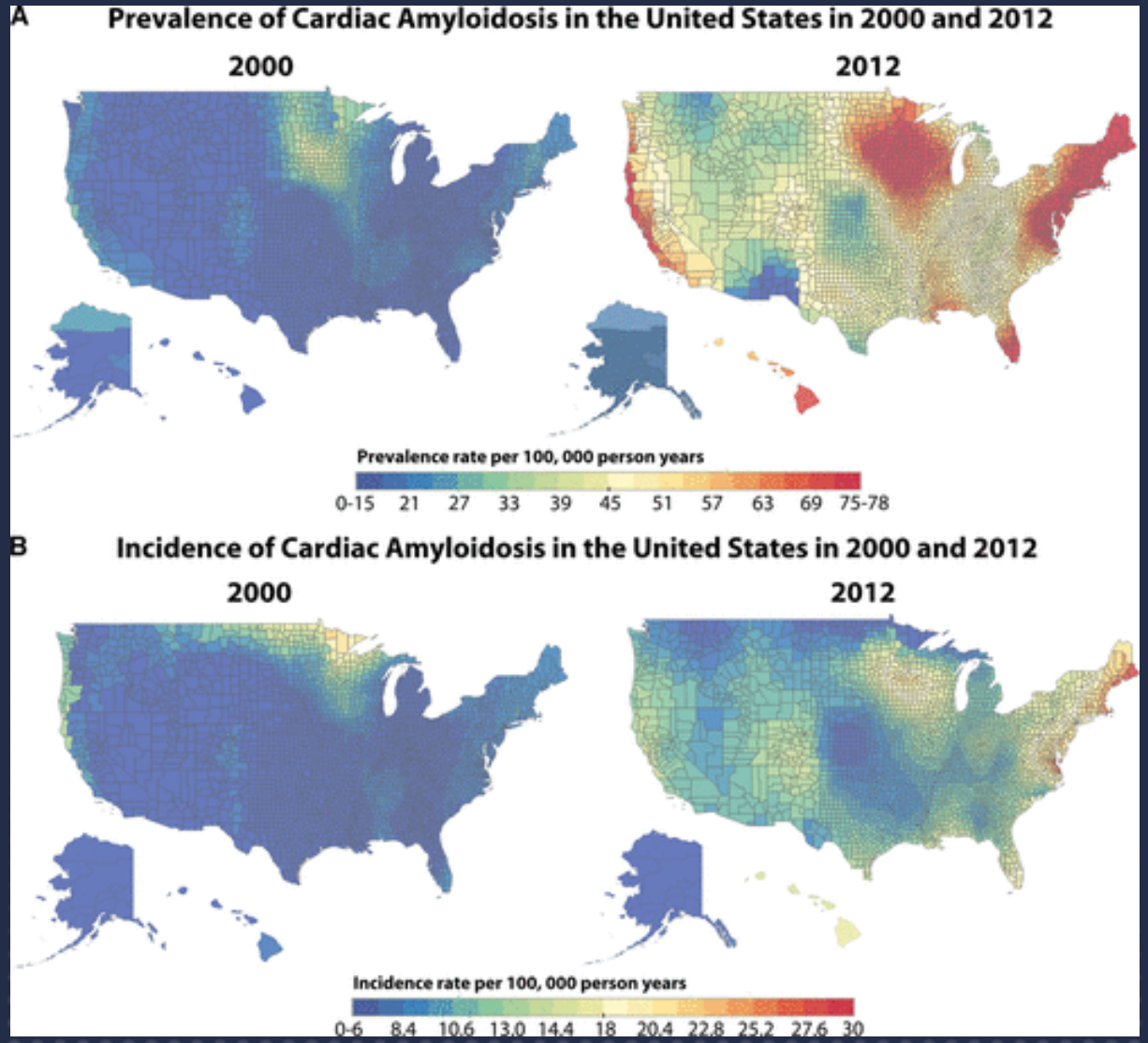
Cardiac Amyloidosis



Lauren G. Gilstrap. Circulation: Heart Failure. Epidemiology of Cardiac Amyloidosis–Associated Heart Failure Hospitalizations Among Fee-for-Service Medicare Beneficiaries in the United States, Volume: 12, Issue: 6, DOI:

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Cardiac Amyloidosis

Amyloid Type	Systemic Amyloidosis		Transthyretin (TTR) Amyloidosis	
Subtype	**AL**	**AA**	**ATTRm**	**ATTRwt**
Protein Deposited	Light chain	Amyloid A	Mutated TTR protein	wt TTR monomers
Disease Etiology	Plasma cell dyscrasia with ↑ light chains	Systemic autoimmune or infections	Familial mutation of TTR	Common in elderly aged > 75 years
Specific Features	Kidney, heart and liver affected	Renal dysfunction	V122I common in African Americans	Carpal tunnel; Male dominance
Median Survival	1-3 years	11 years	2 years	4-6 years
Prognostic Factors	Cardiac function, BNP, troponin	Serum AA levels, renal function	Duration, HR>70/min, ↓LVEF	BNP, uric acid, ↓LVEF, ↑ Wall Thickness
Therapy	Chemotherapy ± Stem cell transplant	Treat underlying conditions	Liver ± heart Tx ?siRNA or ASO ?Tafamidis or Diflunisal	?siRNA or ASO ?Tafamidis or Diflunisal

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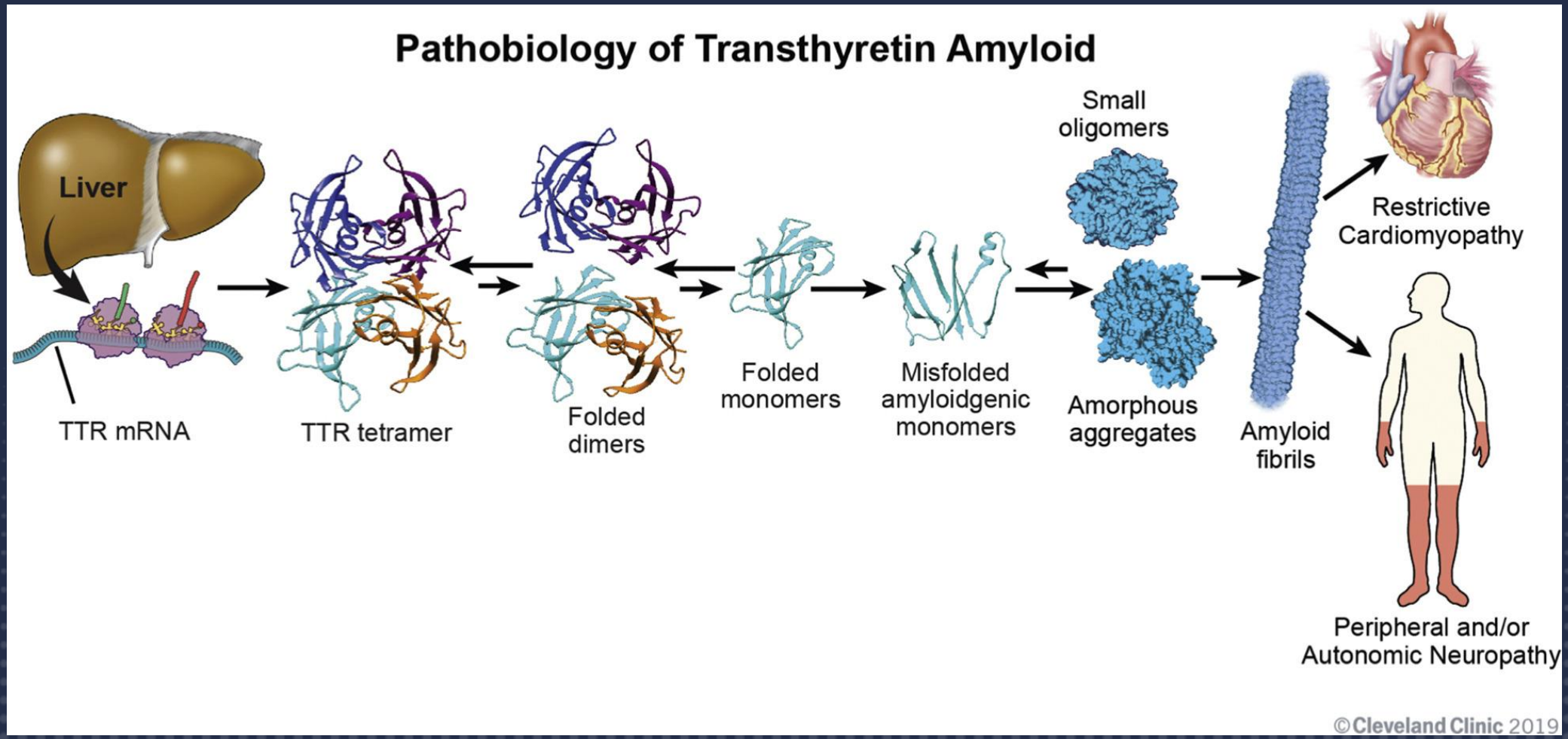
ATTR Cardiac Amyloidosis



Frederick L. Ruberg, Martha Grogan, Mazen Hanna, Jeffery W. Kelly, Mathew S. Maurer, Transthyretin Amyloid Cardiomyopathy: JACC State-of-the-Art Review,Journal of the American College of Cardiology, Volume 73, Issue 22,2019,Pages 2872-2891,

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ATTR Cardiac Amyloidosis

	Hereditary (hATTR-CM)	Wild-Type (wtATTR-CM)
Age of onset	Variable (30–80 yrs) dependent on the mutation	Average 75 yrs, usually >60 yrs
TTR genotype	Abnormal, single nucleotide mutation	Normal
Heritability	Autosomal dominant (50% chance of passage to offspring)	Not known to be heritable
Predominant countries of origin	Val122Ile: U.S., U.K., Western Africa Thr60Ala (Appalachian mutation): U.S., U.K. (predominately Northern part of Republic of Ireland) Val30Met: Sweden, Portugal, Japan Leu111Met: Denmark Ile68Leu: Italy	No known geographic disparities
Prevalence	Val122Ile genotype: 3.4% of African Americans Thr60Ala genotype: ~1% of Northern part of Republic of Ireland	Up to 25% with wtATTR deposits at autopsy 13% in hospitalized HFpEF with wall thickness >12 mm 6%–16% of patients undergoing AVR possibly 1%–3% >75 yrs of age
Median survival after diagnosis without treatment	~2.5 yrs* (Val122Ile)	~3.5 yrs*

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ATTR-Amyloidosis

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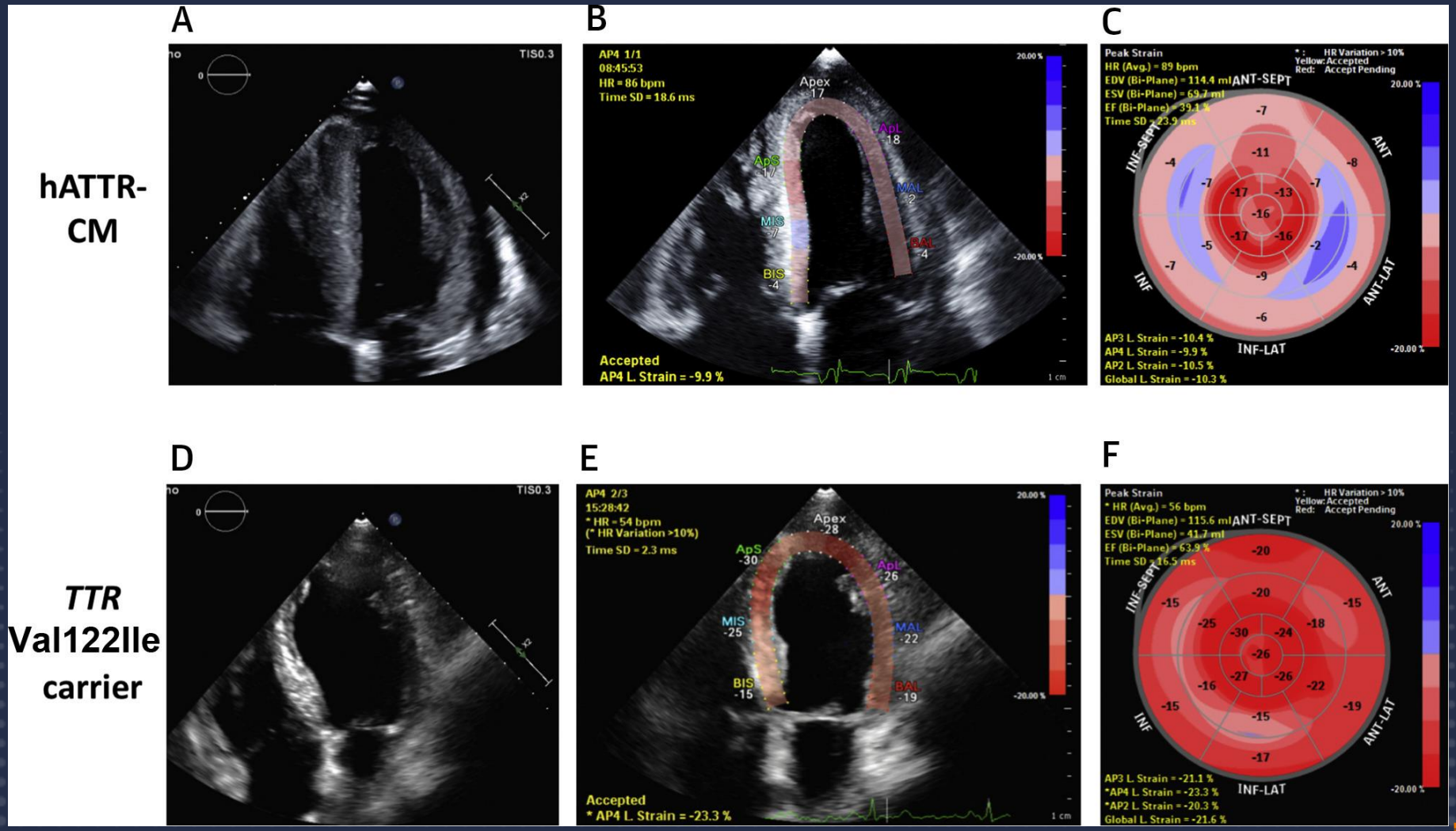
Echocardiography for ATTR-Amyloidosis



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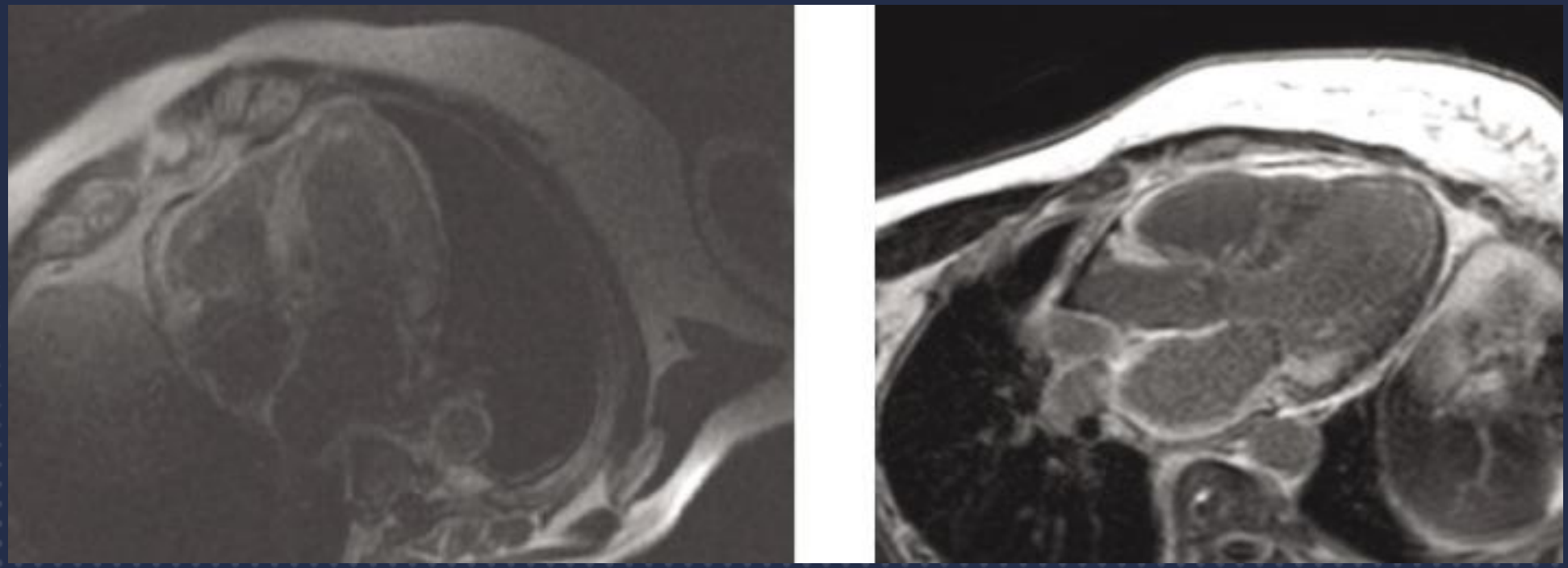
cMRI for ATTR-Amyloidosis



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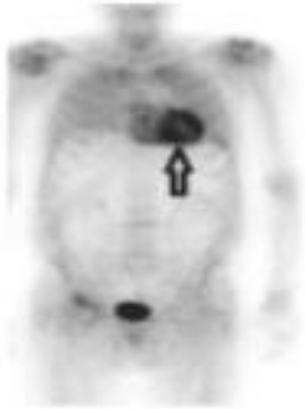
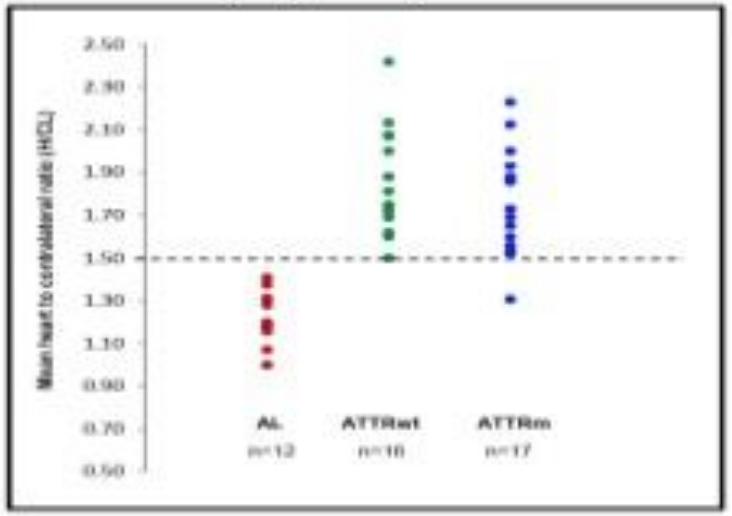
The Role of Cardiovascular Magnetic Resonance Imaging in Heart Failure Mark A Peterzan, Oliver J Rider, Lisa J Anderson Card Fail Rev. 2016 Nov; 2(2): 115–122.

Tc-99m PYP Scan for ATTR-Amyloidosis

NUCLEAR IMAGING: SELECTIVE FOR TTR

- Tc-99m Bone avid compounds
  - Pyrophosphate (PYP) and DPD
  - May preferentially identify TTR amyloid cardiomyopathy





Rapezzi *Eur J Nuc Med Mol Imag* 2011, *JACC Img* 2011: Banypersad, *JAHA* 2012
Bokhari *Circ CV Imaging* 2013: Longhi JACC Img 2014

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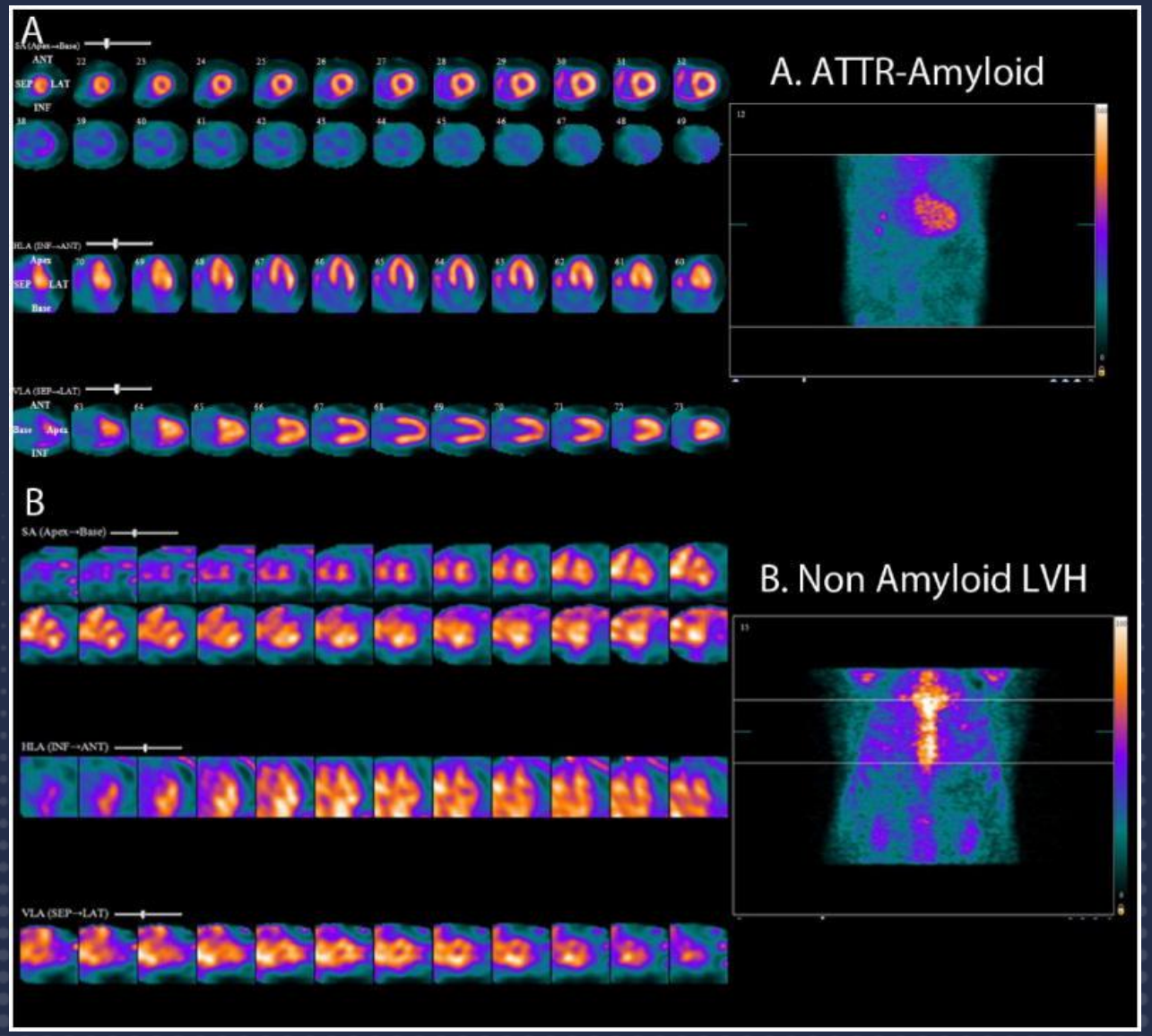
Tc-99m PYP Scan for ATTR-Amyloidosis



Nuclear imaging modalities for cardiac amyloidosis. Adam Castaño, MD,[b] and Mathew S. Maurer, MD[b]. J Nucl Cardiol. 2014 Feb; 21(1): 175–184.

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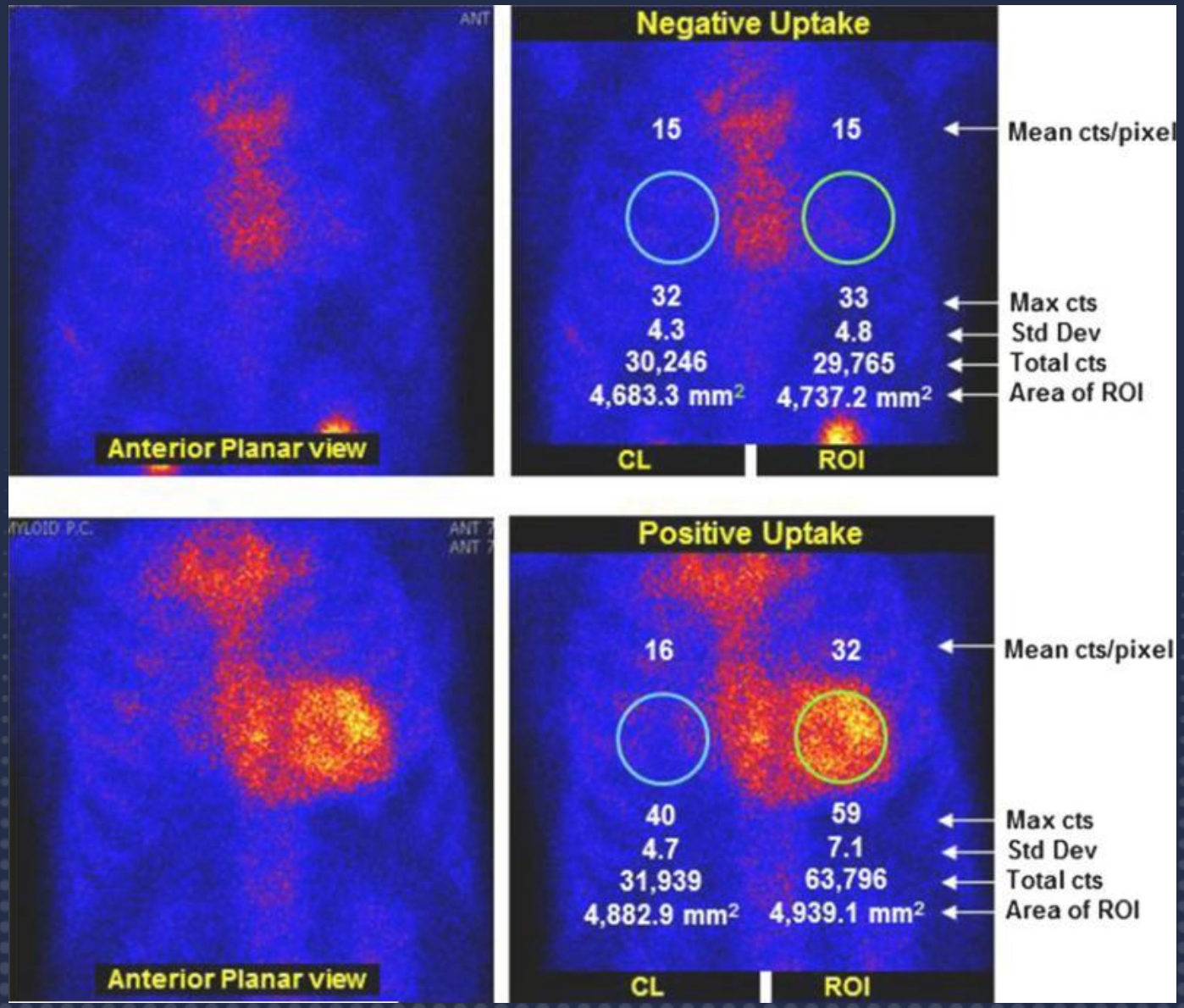

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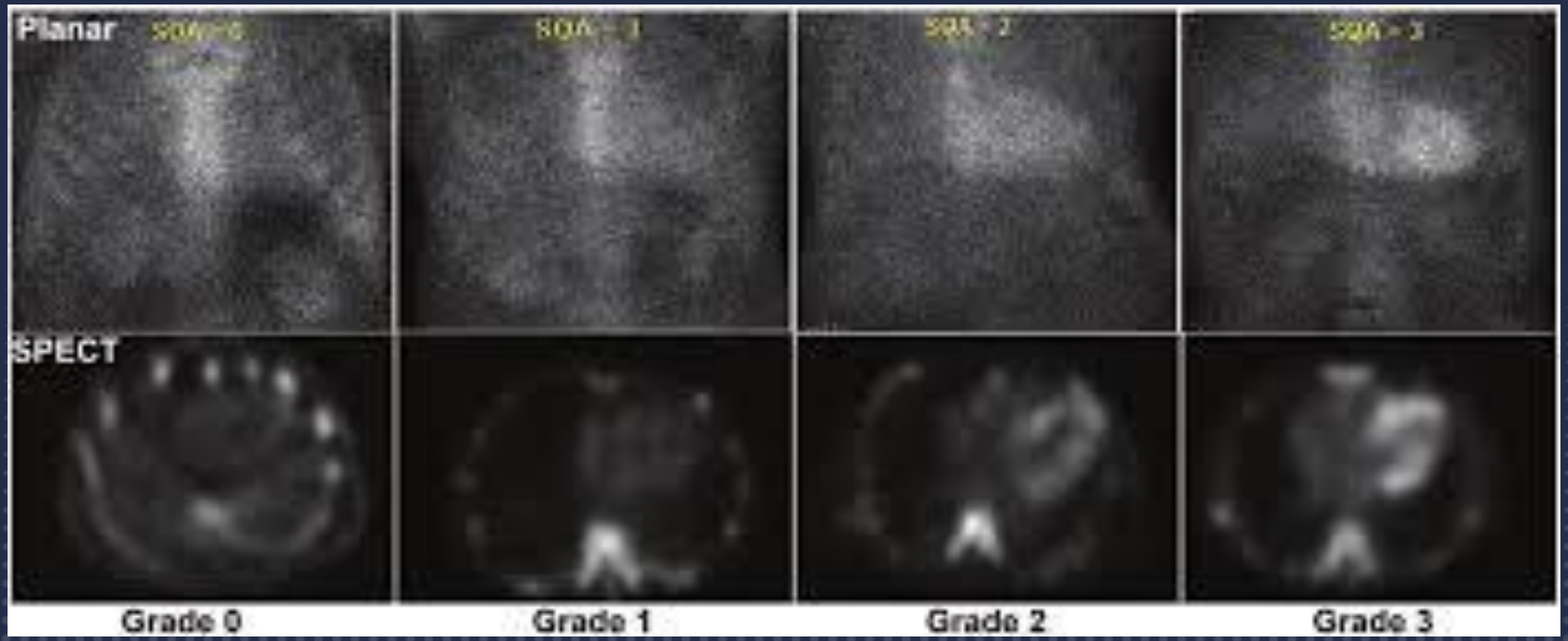
ASNC Grading System



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Tafamidis Treatment for Patients with Transthyretin Amyloid Cardiomyopathy

Mathew S. Maurer, M.D., Jeffrey H. Schwartz, Ph.D., Balarama Gundapaneni, M.S., Perry M. Elliott, M.D., Giampaolo Merlini, M.D., Ph.D., Marcia Waddington-Cruz, M.D., Arnt V. Kristen, M.D., Martha Grogan, M.D., Ronald Witteles, M.D., Thibaud Damy, M.D., Ph.D., Brian M. Drachman, M.D., Sanjiv J. Shah, M.D., Mazen Hanna, M.D., Daniel P. Judge, M.D., Alexandra I. Barsdorf, Ph.D., Peter Huber, R.Ph., Terrell A. Patterson, Ph.D., Steven Riley, Pharm.D., Ph.D., Jennifer Schumacher, Ph.D., Michelle Stewart, Ph.D., Marla B. Sultan, M.D., M.B.A., and Claudio Rapezzi, M.D., for the ATTR-ACT Study Investigators*

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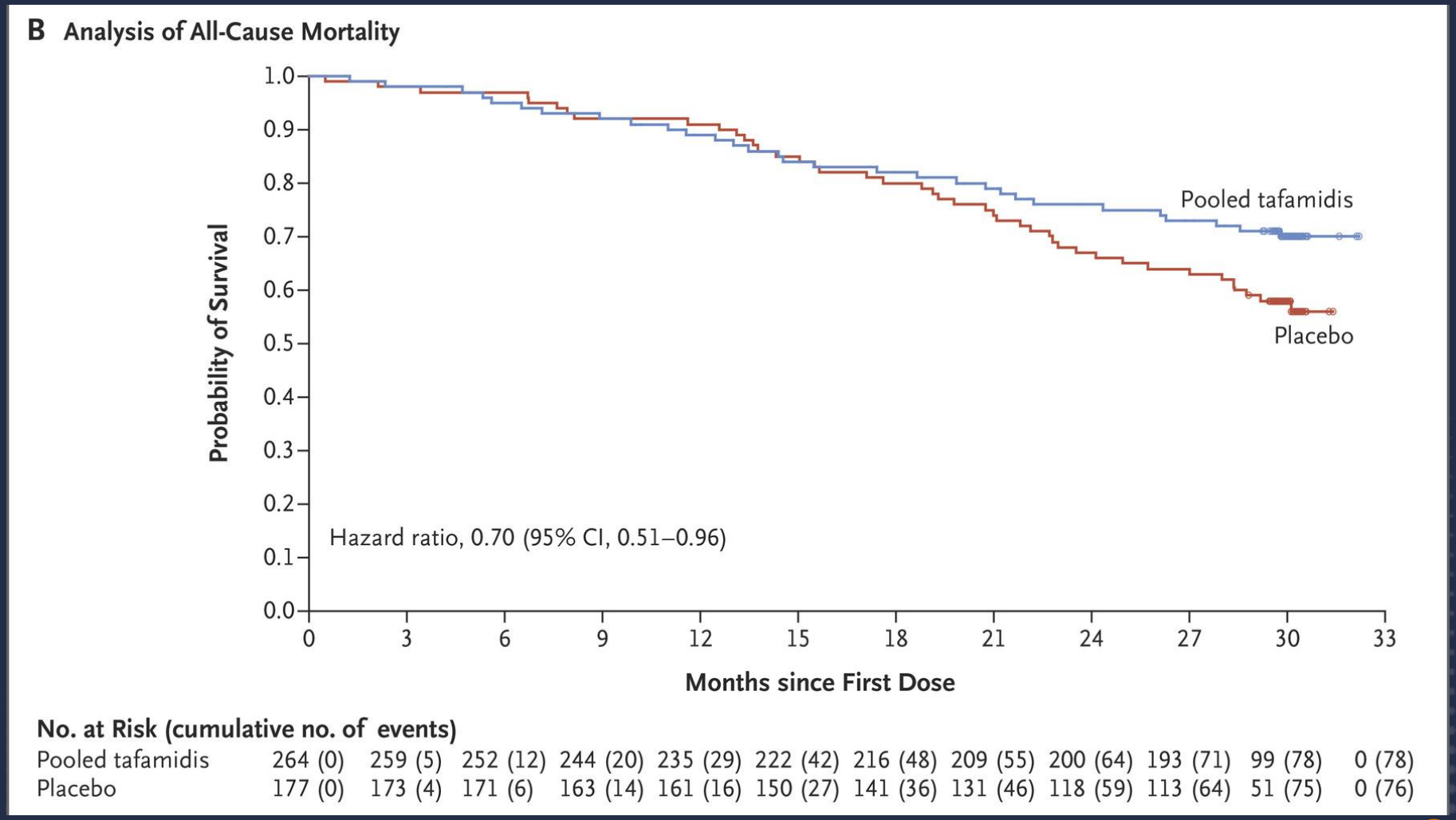
ATTR-ACT Trial



No. at Risk (cumulative no. of events)

Pooled tafamidis	264 (0)	259 (5)	252 (12)	244 (20)	235 (29)	222 (42)	216 (48)	209 (55)	200 (64)	193 (71)	99 (78)	0 (78)
Placebo	177 (0)	173 (4)	171 (6)	163 (14)	161 (16)	150 (27)	141 (36)	131 (46)	118 (59)	113 (64)	51 (75)	0 (76)

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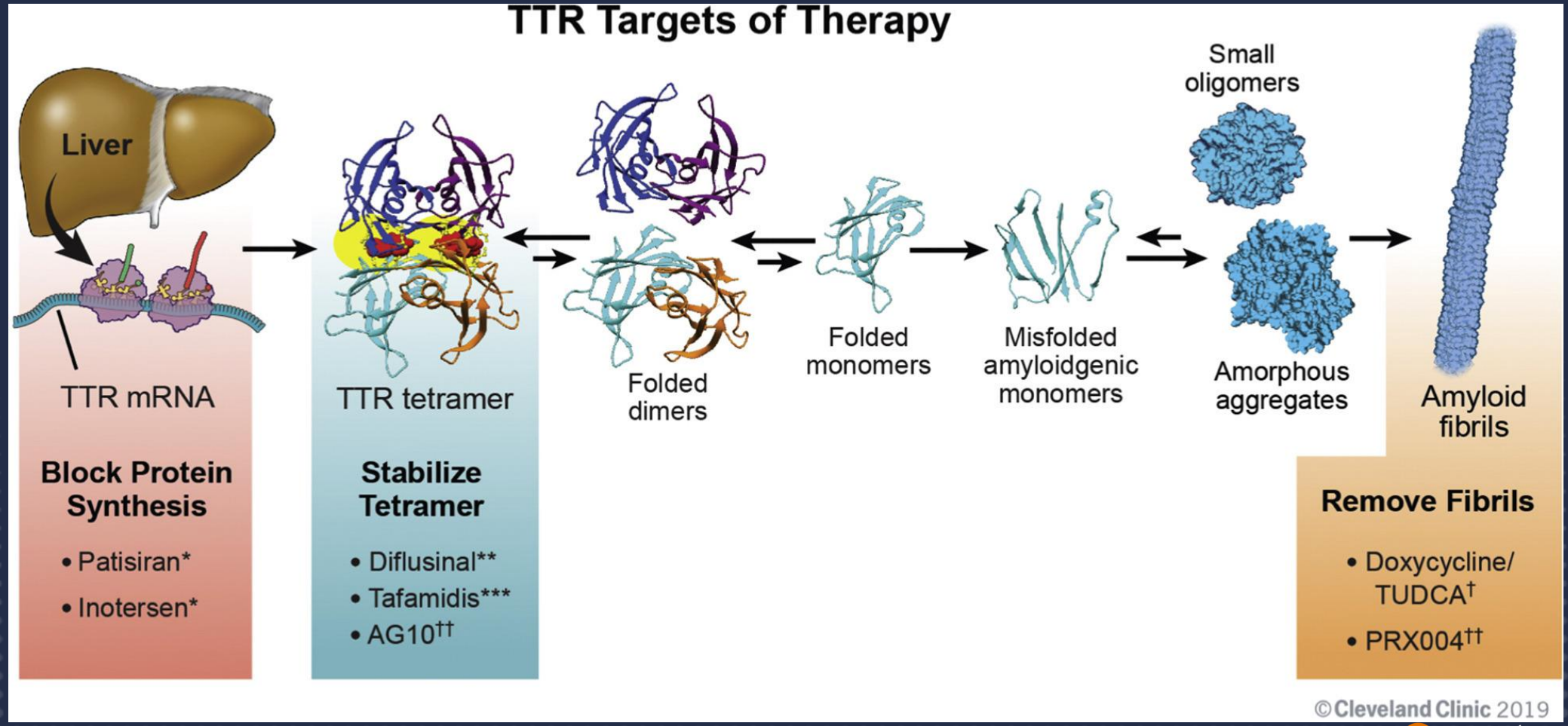
ATTR-Amyloidosis Therapeutic Targets



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Conclusions

- Heart Failure is a growing epidemic with high morbidity and mortality that will only increase in prevalence as our population ages
- Non-invasive evaluation of left ventricular function has strong prognostic significance, but can be fraught with error and misrepresentation
- Newer techniques for quantifying left ventricular function, including strain echocardiography, offer new opportunities to detect heart disease prior to clinical events
- cMRI is not only a powerful tool for quantifying chamber size/function, but its ability to characterize myocardial tissue has expanded our diagnostic repertoire
- Novel imaging techniques and increased disease recognition, along with new medical therapies, have changed the landscape in amyloid heart disease

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Questions and Comments

Thank You

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