ISMRM | Iranian CHAPTER
1st Annual Meeting
24-26 August 2022

MRI and Sudden Cardiac Death Risk Stratification

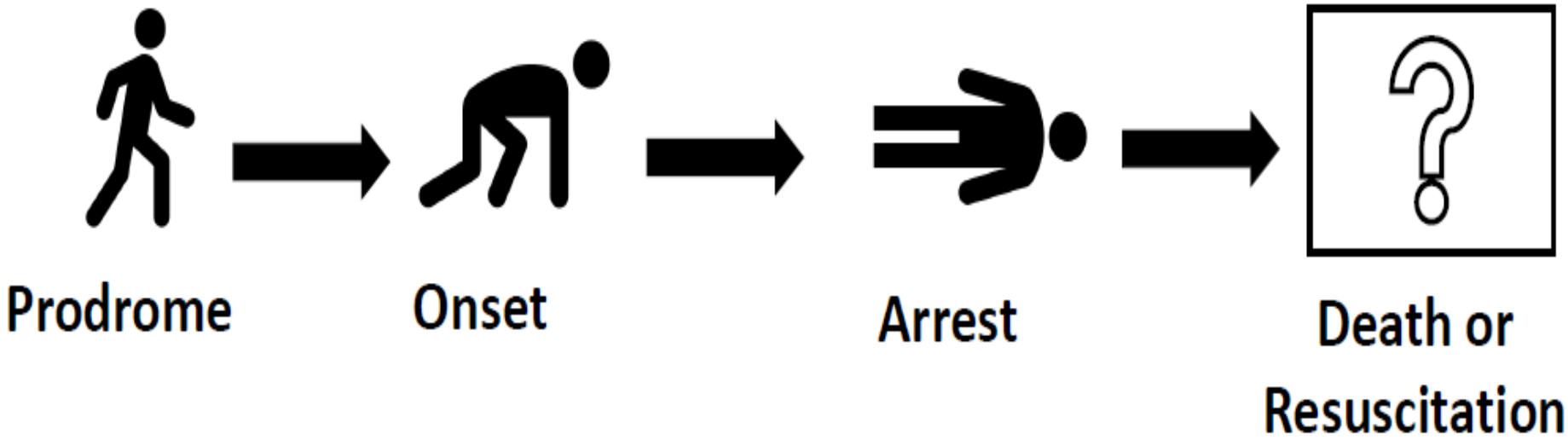
Is there anything beyond EF?

Mehrdad Mirmasoumi MD
Cardiologist
Interventional Electrophysiologist
Tavanir Arrhythmia Clinic

ISMRM ONE COMMUNITY FOR CLINICIANS AND SCIENTISTS

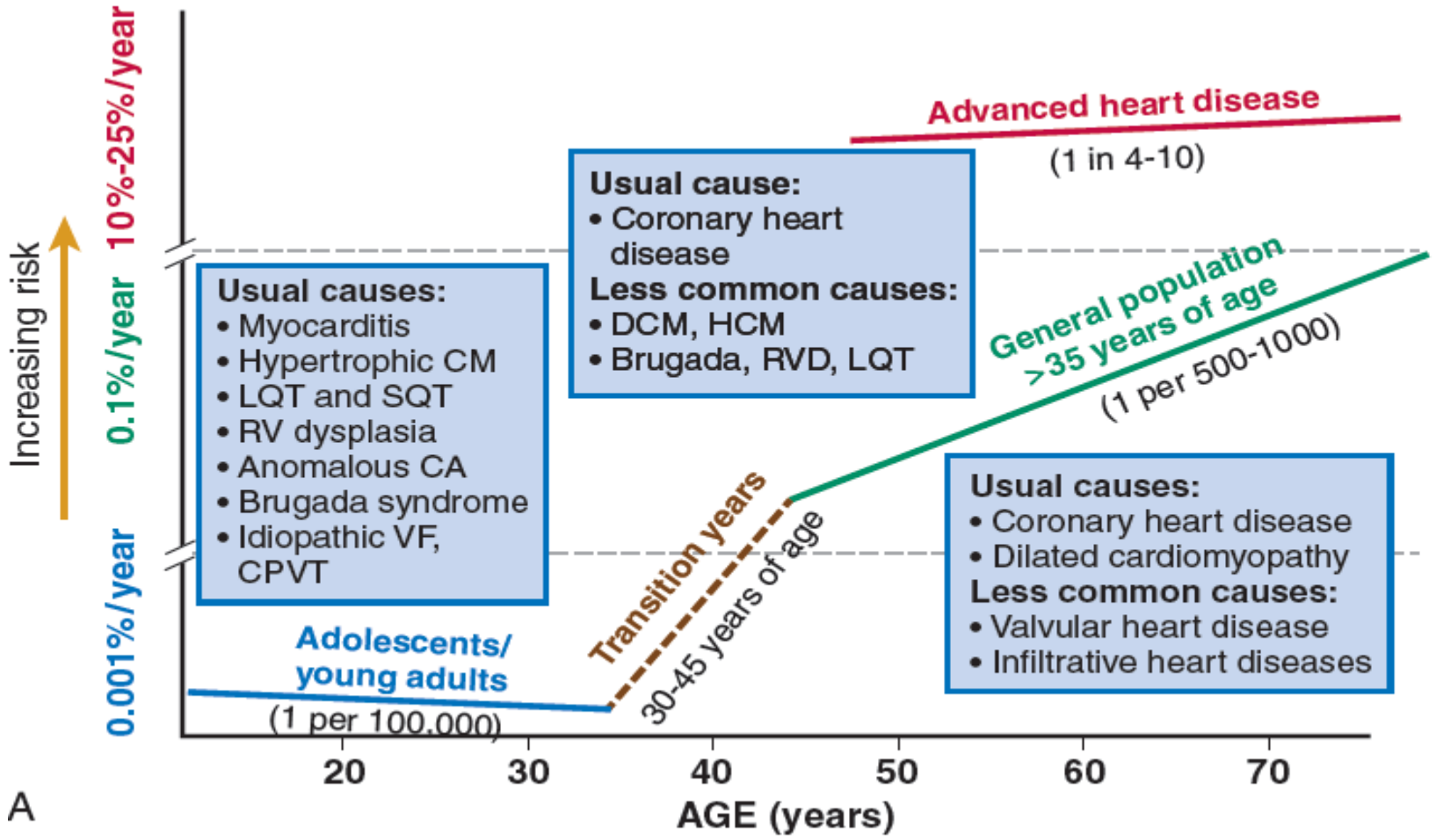
Background

- Abrupt and unexpected cardiac arrest
- Within 1 hour from onset of symptoms
- Devastating for family and community



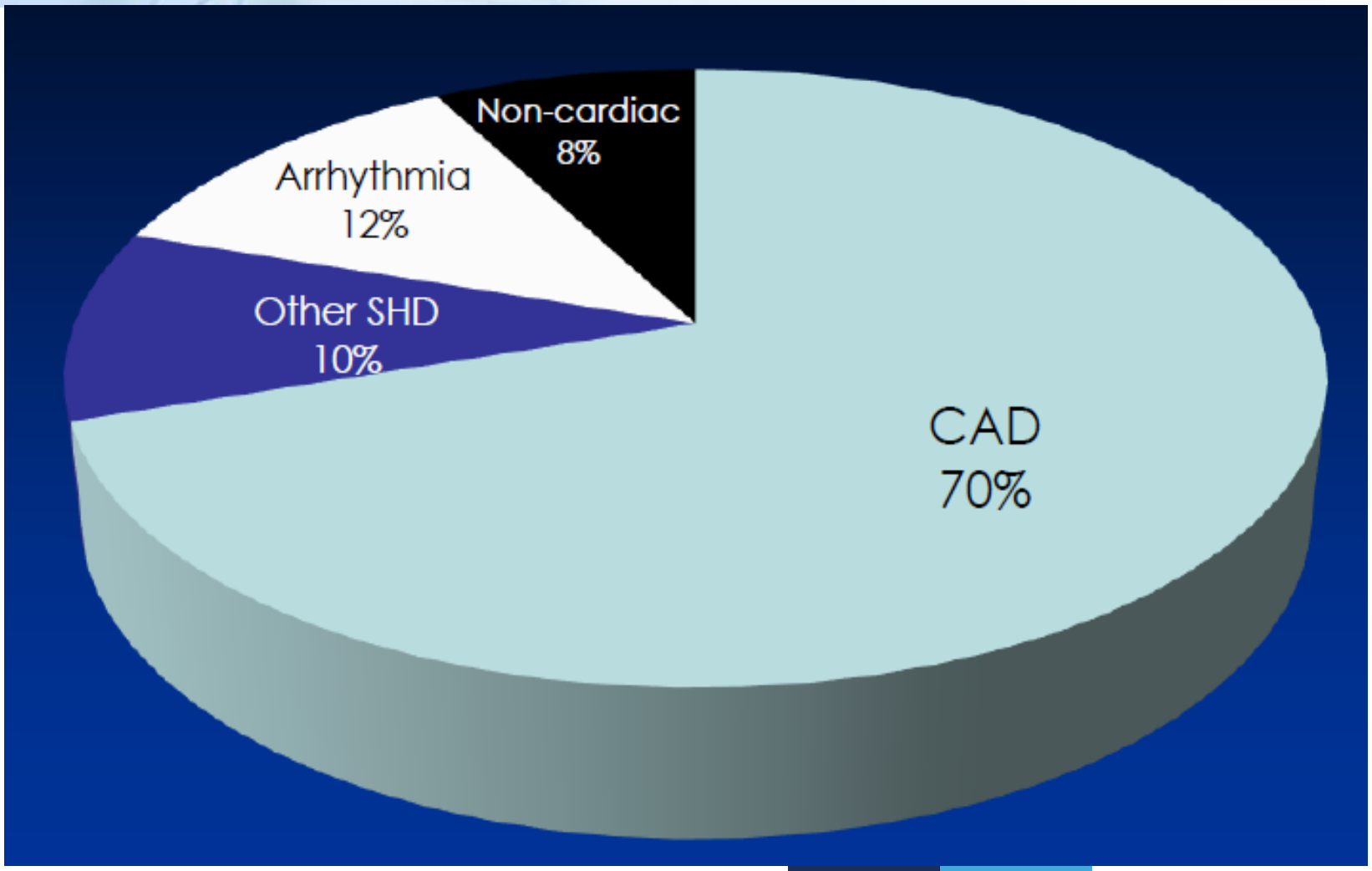
Hugh D. Allen, et al. Moss and Adams' Heart Disease in Infants, Children, and Adolescents.

Age-Related Cause of SCD



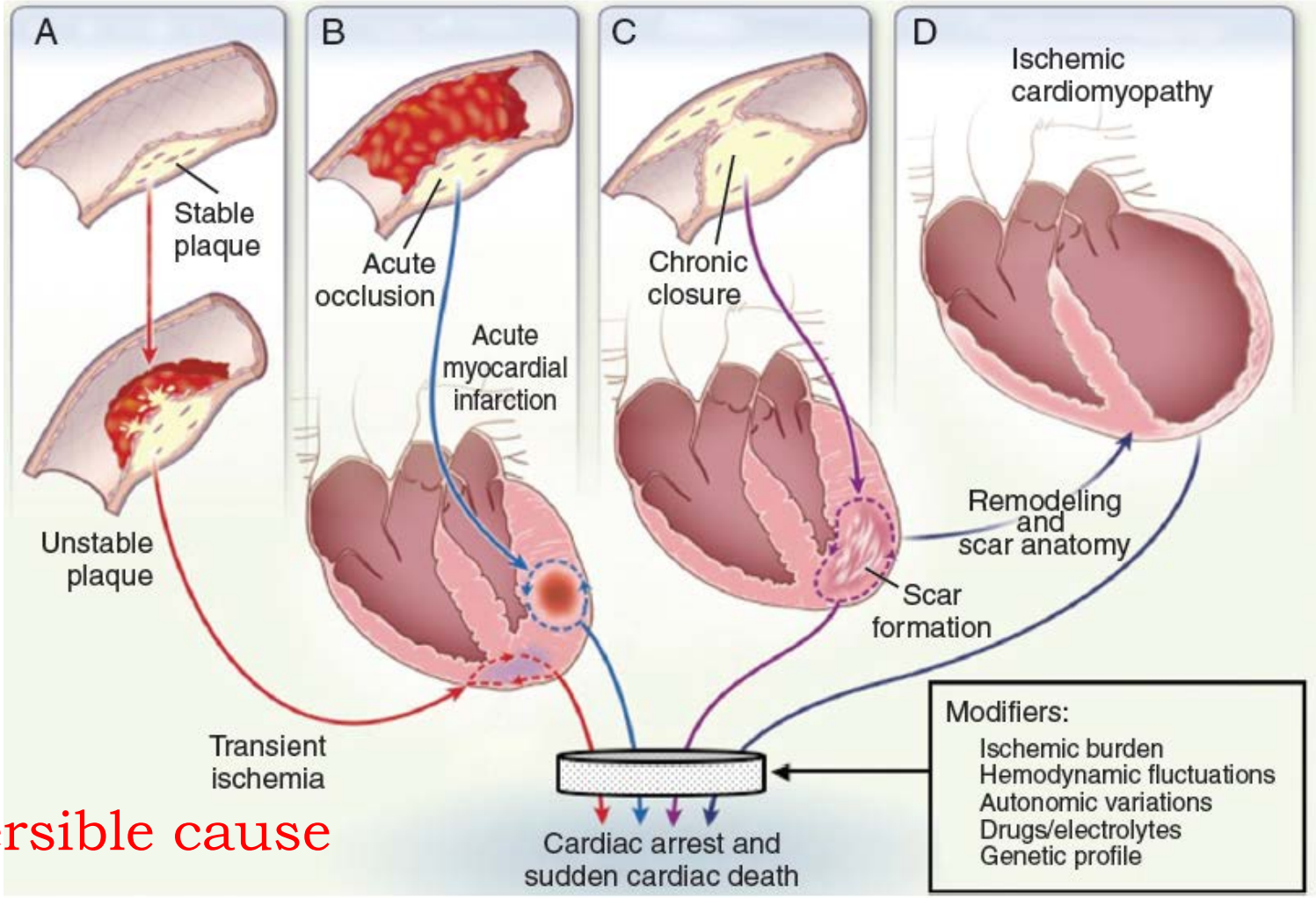
Myerburg RJ. New Engl J Med. 2008;359:2245-2253

Major Causes of SCD



Am J Cardiol 1991;68:1388

Ventricular Tachyarrhythmia The Final Common Pathway In SCD



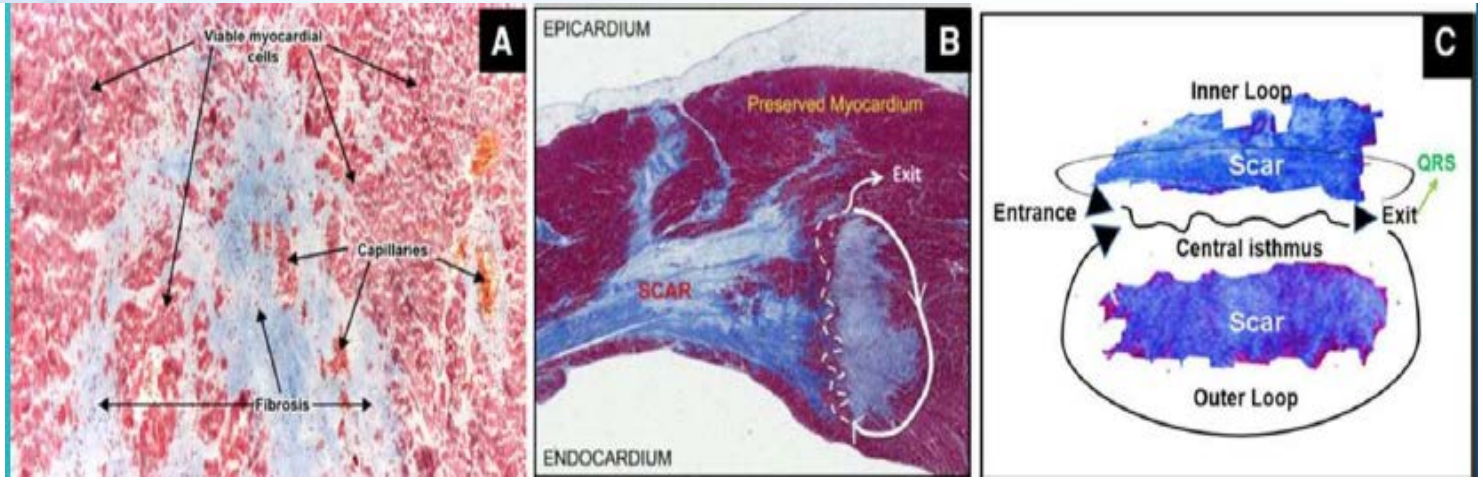
Reversible cause

Irreversible Causes

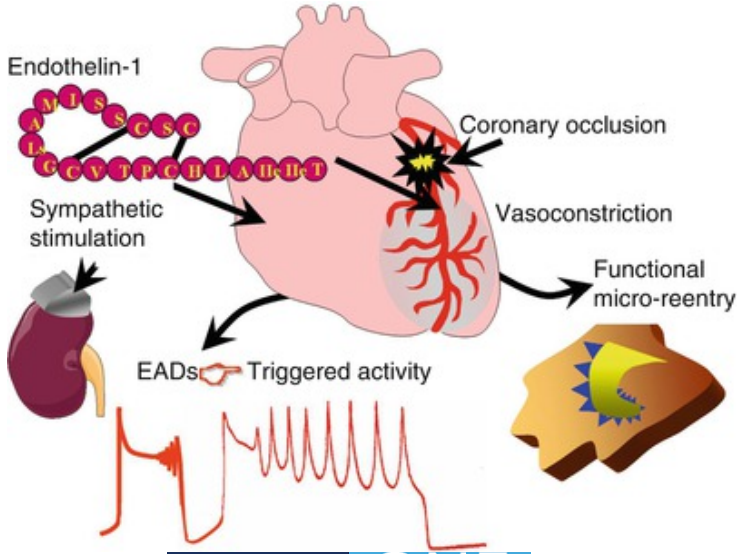
Myerburg RJ. New Engl J Med. 2008;359:2245-2253

Mechanism of Ventricular Arrhythmia

- Reentry

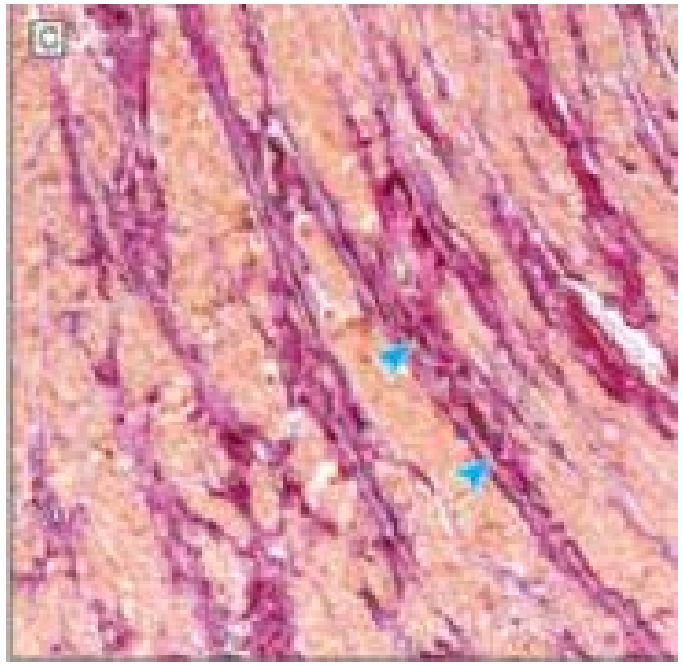


- Automaticity



- Triggered Activity

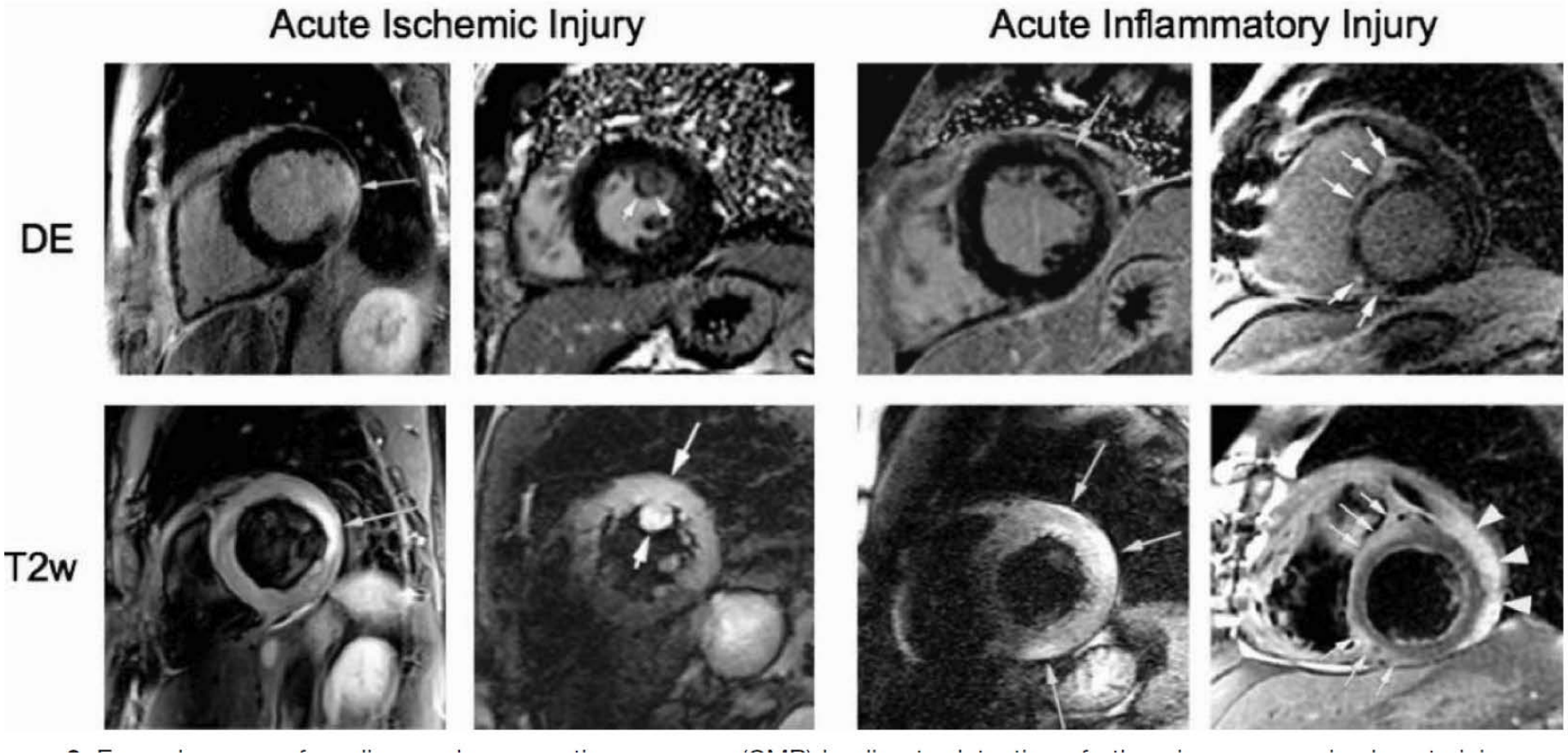
Non-Ischemic Fibrosis & SCD



Sudden death case: Extensive replacement fibrosis

Gulati JAMA 2013; 309:896-908

Reversible Substrate



Increased T2 signal

James A. White, *Circ.Cardiovasc Imaging*. 2012;5:12-20

Cardiac Magnetic Resonance Imaging

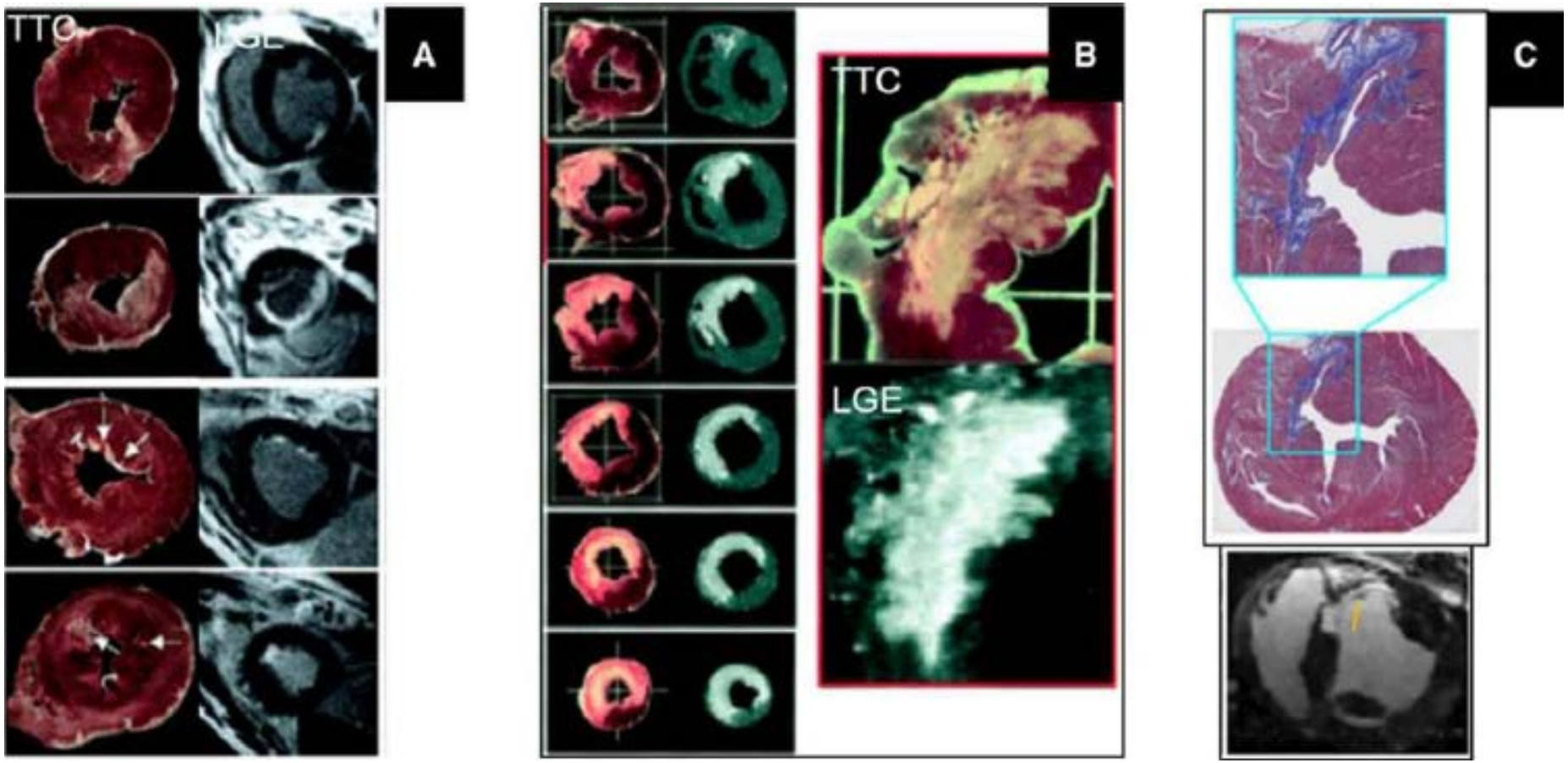
Gold standard for structural, functional assessment

and

tissue characterization, including:

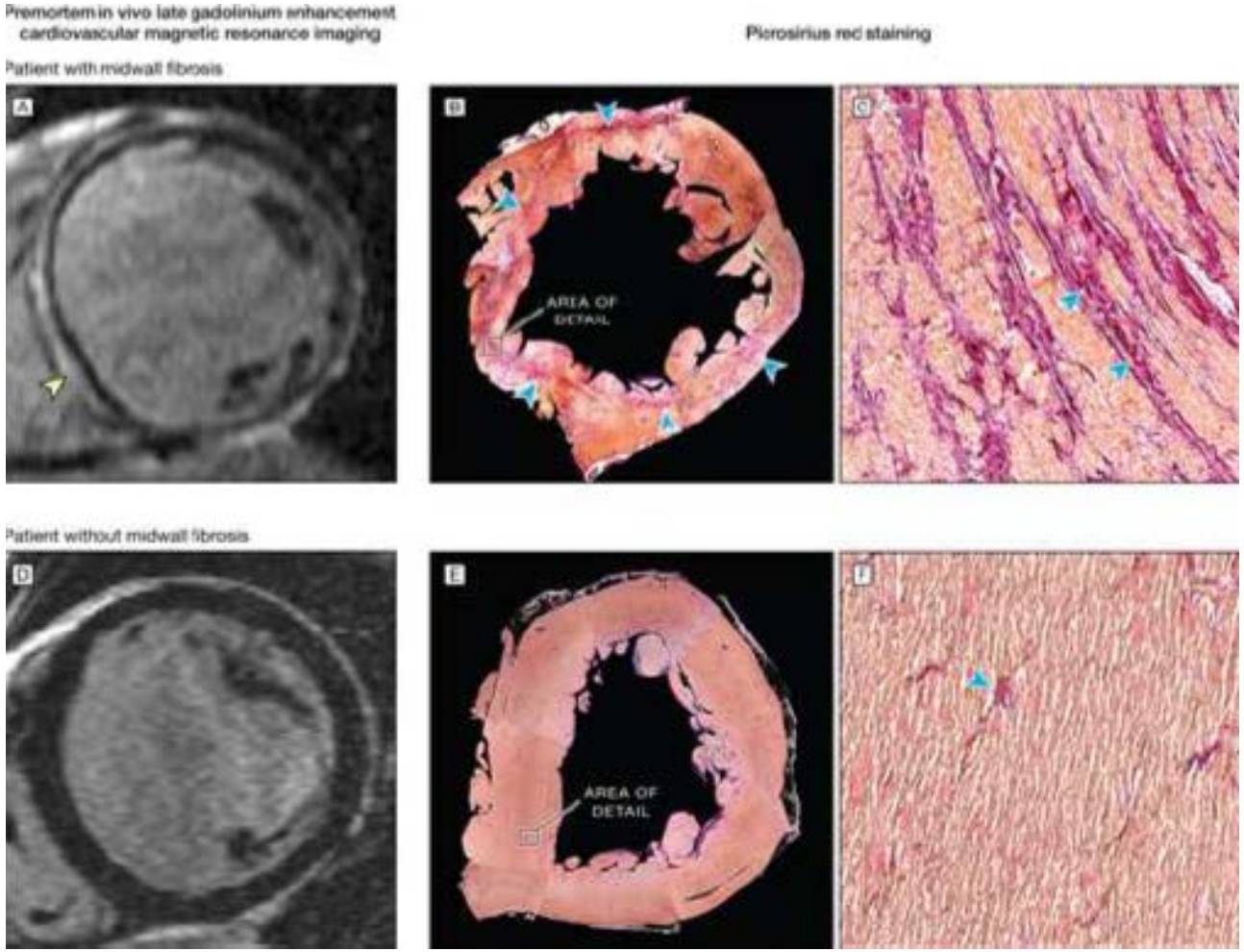
- Late gadolinium enhancement (LGE) for replacement fibrosis
- T1 mapping for interstitial fibrosis
- T2 mapping for myocardial edema/inflammation.

Ischemic Scar: CMR and pathology correlates.



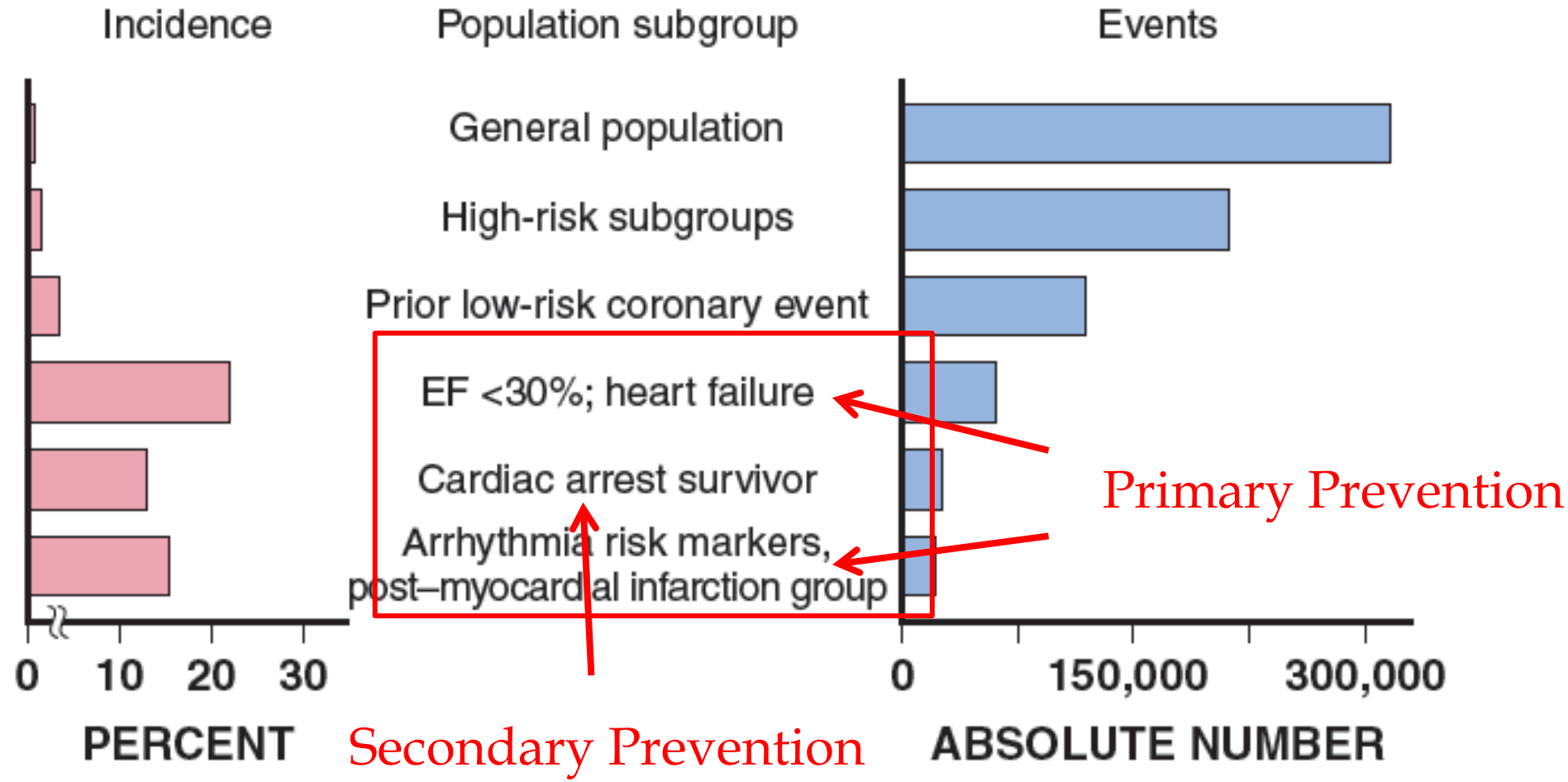
Wu KC, Circ CVIM 2017; e005461

Non-Ischemic Scar: CMR and pathology correlates.



Gulati JAMA 2013; 309:896-908

Incidence Rates and Risk Stratification



Myerburg RJ. J Cardiovasc Electrophysiol 2001;12:369

Primary Prevention

- Cardiovascular diseases the main cause of death
- 25% sudden cardiac death
- Clinical practice guidelines: ICD for the primary prevention of SCD based on LVEF and functional status

Zorzi et al, *J Am Heart Assoc.* 2021

Primary Prevention ICD Trials

TABLE 42.8 Primary Prevention Implantable Cardioverter-Defibrillator Trials

TRIAL (FOLLOW-UP ANALYSIS), YEAR PUBLISHED	STUDY GROUP, DEFINED ENTRY CRITERIA	TIME FROM DIAGNOSIS OF QUALIFYING CONDITION TO RANDOMIZATION	EJECTION FRACTION, ENROLLED PATIENTS	ALL-CAUSE MORTALITY		BENEFIT	
				Control	ICD	Rel RR	Abs RR
MADIT (2-yr analysis), 1996	Prior MI, EF ≤35%, inducible VT, failed IV PA	Entry criterion: ≥3 wk Actual: 75% ≥6 mo Qualifying EF: interval not reported	26% (SD, ±7%)	32%	13%	–59%	19%
CABG Patch (2-yr analysis), 1997	Coronary bypass surgery, EF <36%, SAECG (+)	Diagnosis of CAD: interval not reported Qualifying EF: interval not reported SAECG: day of randomization	27% (SD, ±6%)	18%	18%	N/A	N/A
MUSTT (5-yr analysis), 1999	CAD (prior MI ≈95%), EF ≤40%, N-S VT, inducible VT	Qualifying N-S VT: ≥4 days from MI Time from MI: 17% ≤1 mo 50% ≥3 yr Qualifying EF: interval not reported	30% (21%, 35%) [median (25th, 75th percentile)]	55%	24%	–58%	–31%
				[EP guided arm: AAD vs. ICD at 60 mo]			
MADIT II (2-yr analysis), 2002	Prior MI (>1 mo), EF ≤30%	Entry criteria: ≥1 mo Actual: 88% ≥6 mo Qualifying EF: interval not reported	23% (SD, ±5%)	22%	16%	–28%	–6%
DEFINITE (2½-yr analysis), 2004	Nonischemic CM, Hx HF, EF ≤35%, ≥10 PVCs/hr or N-S VT	Heart failure onset (mean): Controls = 3.27 yr ICD group = 2.39 yr	21% (range, 7%-35%)	14%	8%	–44%	–6%
DINAMIT (2½-yr analysis), 2004	Recent MI (6-40 days), EF ≤35%, abnormal HRV or mean 24-hr heart rate >80/min	Entry criteria: 6-40 days Actual: mean = 18 days	28% (SD, ±5%)	17%	19%	N/A	N/A
SCD-HeFT (5-yr analysis), 2005	Class II-III CHF, EF ≤35%	Entry criteria: interval not reported Qualifying EF: interval not reported	25% (20%, 30%) [median (25th, 75th percentile)]	36%	29%	–23%	–7%

Myerburg RJ. J Am Coll Cardiol 2009;54:747

Primary Prevention

- ICD the most effective strategy
- SCD prevention hampered by over-reliance on LVEF <35%
- About one fifth of patients who experience SCD have LVEF less 35%
- Appropriate ICD therapy in less than a third of ICD recipients with LVEF <35%.

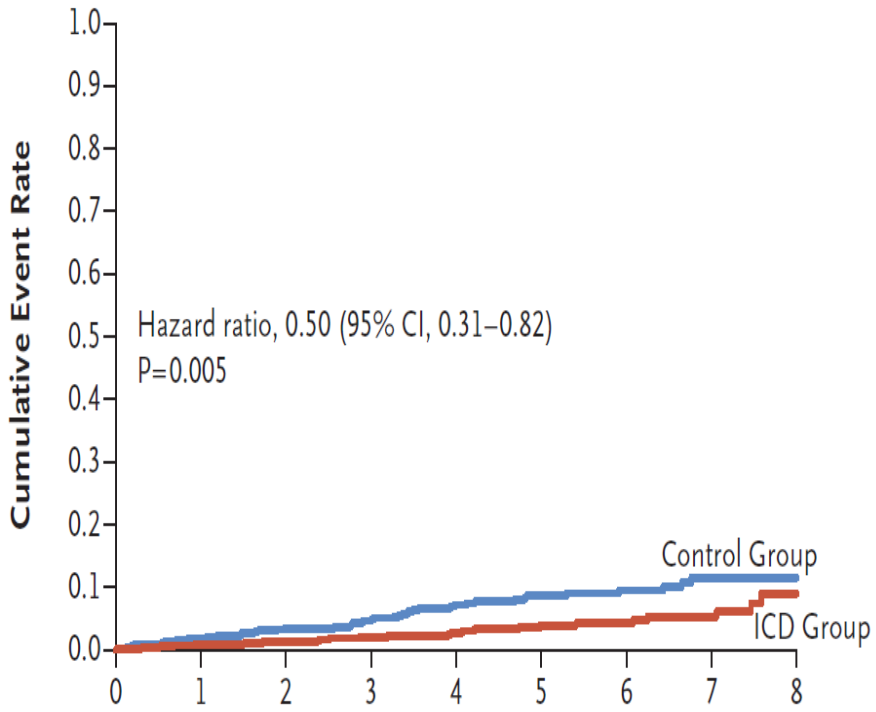
Decision to implant ICD based on the LVEF alone neither sensitive nor specific and far from Ideal

Is there anything beyond EF?

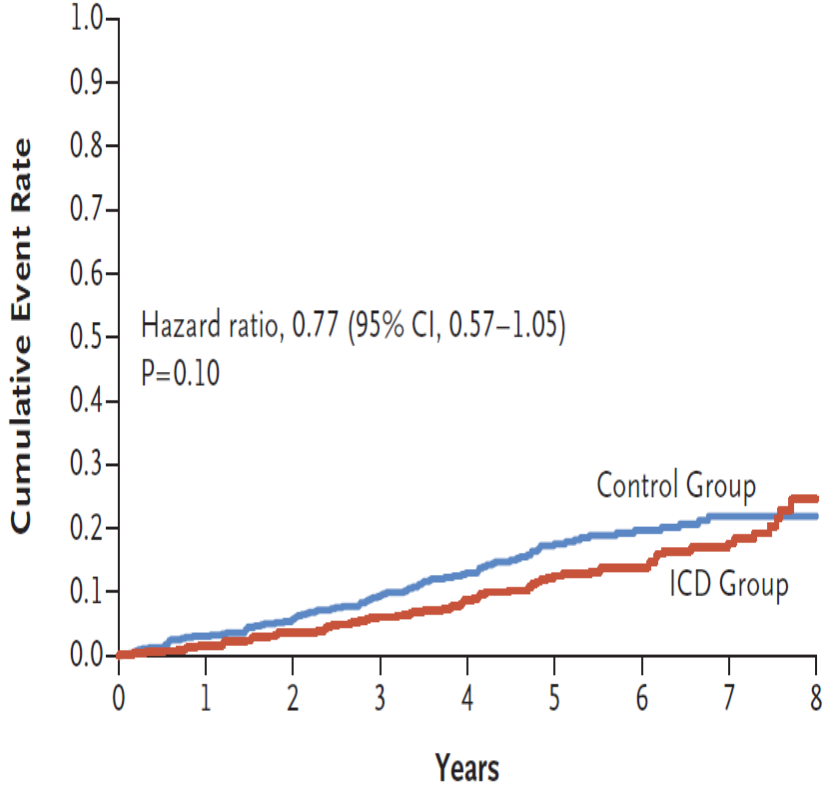
Any thing better than LVEF to predict sudden cardiac death?

DANISH Trial

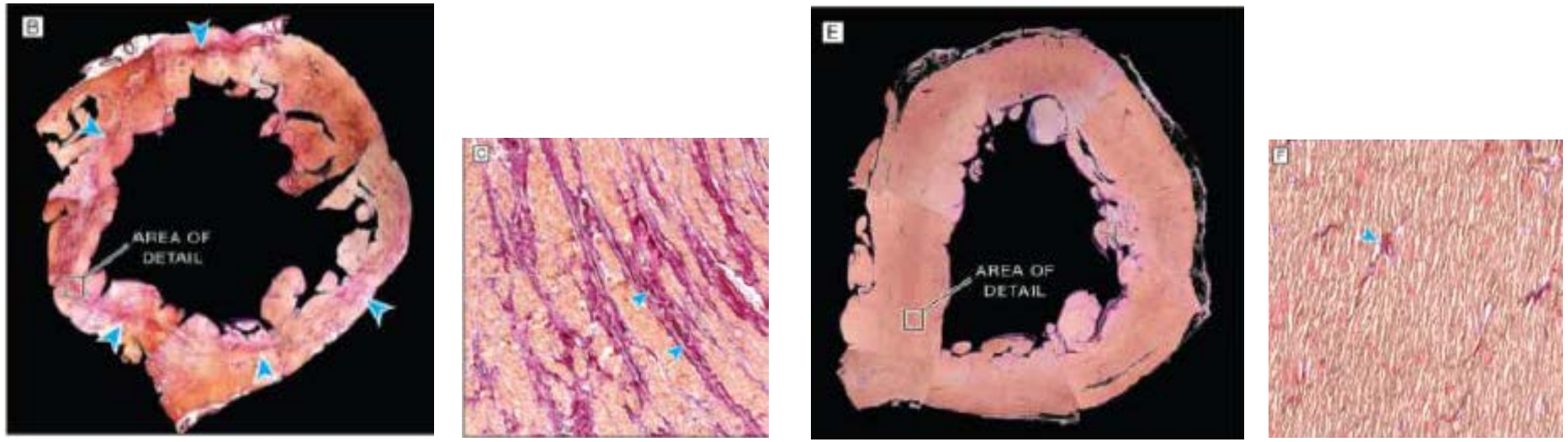
Sudden Cardiac Death



Cardiovascular Death



Myocardial scar promotes ventricular arrhythmia via heterogeneous conduction & electrical reentry



Sudden death case: Extensive replacement fibrosis

At the time of cardiac transplant **NO** replacement fibrosis

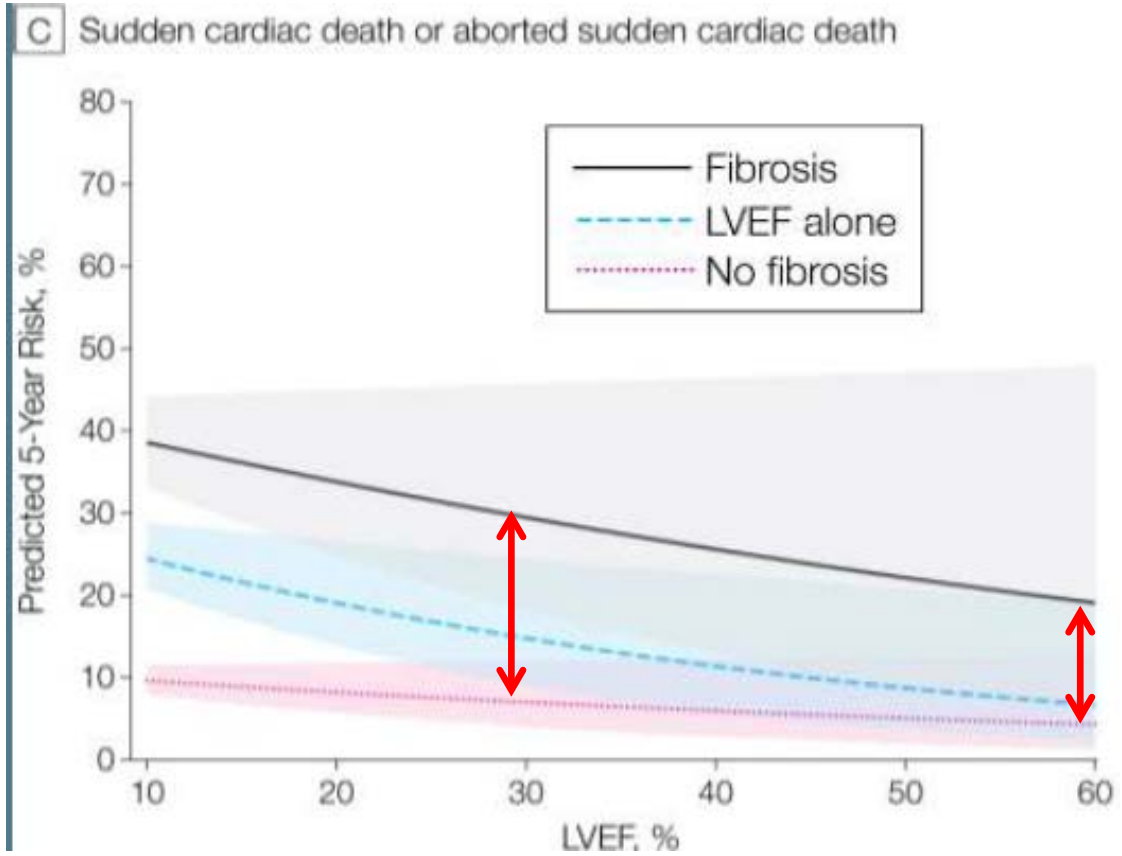
Gulati JAMA 2013; 309:896-908

LGE-CMR and SCD in DCM

- 472 patients with DCM
- Follow-up 5.3 years
- LGE present in 30%
- Aborted SCD

  LGE+ 29.6%

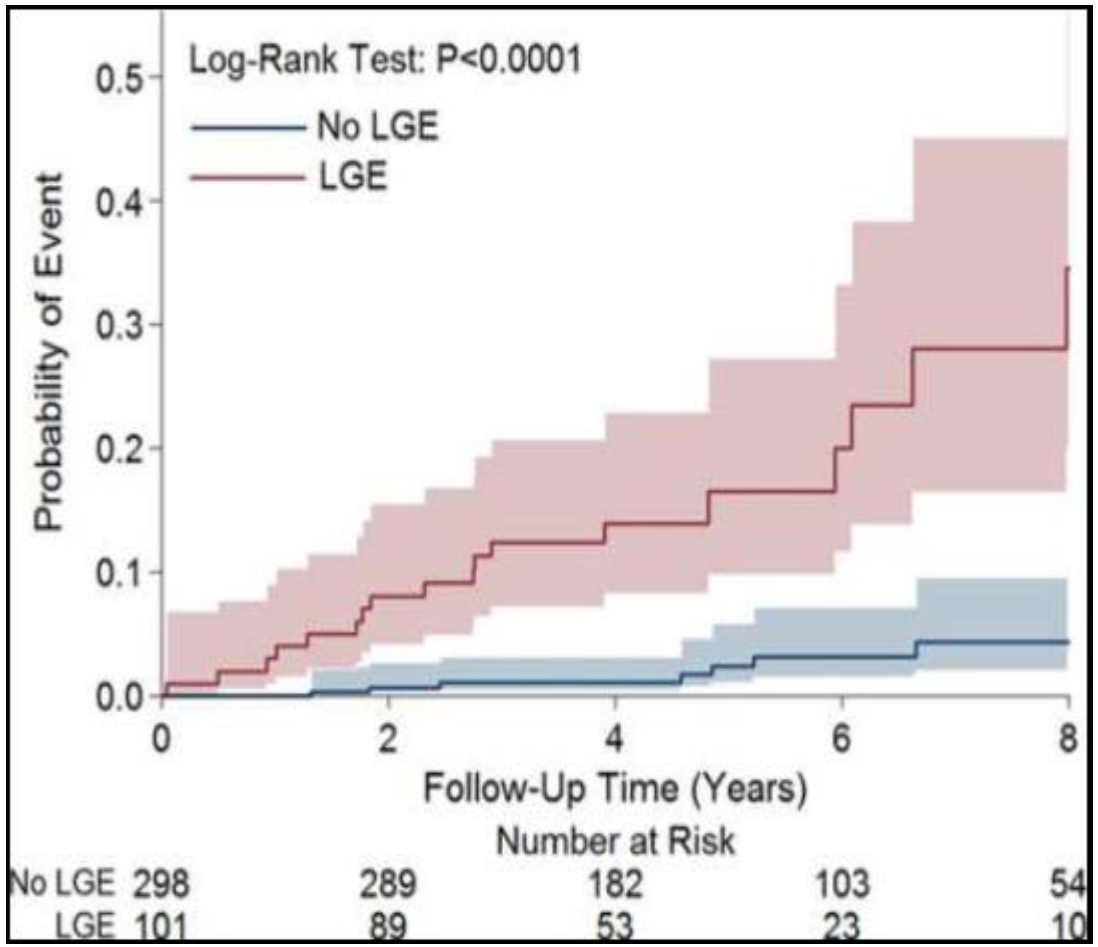
  LGE - 7%
- Adjusted HR for SCD 4.6 (2.8 – 7.7)



Gulati et al. JAMA 2013

LGE and SCD in DCM with relatively preserved systolic function

- 399 patients with DCM and LVEF ≥40% were followed for 4.6y
- LGE present in 25%
- Endpoint SCD / aborted SCD occurred
  - 17.8% LGE+
  - 2.3% LGE-
- Adjusted HR for SCD 9.2 (3.9-21.8)



Halliday et al: Circulation 2017

Meta-Analysis: Subgroup Analysis

TABLE 3 Tachyarrhythmic Event Rate and Odds Ratio in the Different Subgroups of Studies

				LGE-CMR			
	Studies	Patients	% AER	% of LGE+ AER*	% LGE− AER*	OR (95% CI)	p Value
Total	19	2,850	5.3	8.6	1.7	5.62 (4.20-7.51)	<0.00001
ICM	5	358	8.9	13.2	3.3	5.05 (2.73-9.36)	<0.00001
NICM	8	1,443	3.7	7.6	1.3	6.27 (4.15-9.47)	<0.00001
Mixed population	6	1,049	6.8	8.8	1.8	4.92 (2.70-8.98)	<0.00001
Mean EF ≤30%	11	1,178	6.6	10.3	1.2	9.56 (5.63-16.23)	<0.00001
Mean EF >30%	8	1,672	4.6	7.4	2.0	4.48 (3.17-6.33)	<0.00001

Values are n or %. *LGE+/− test results based on the criteria reported in Table 1.

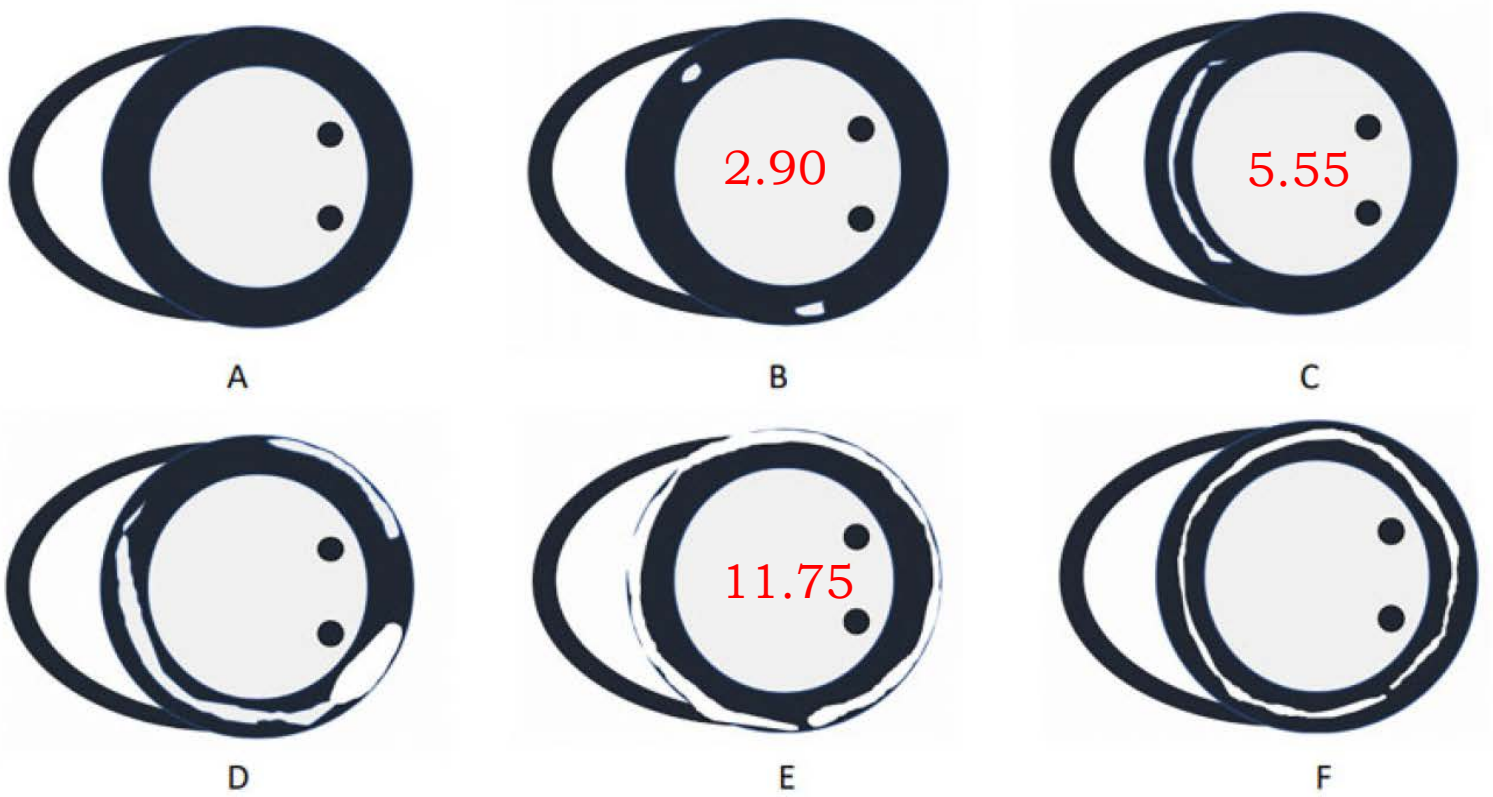
AER = annualized event rate; ICM = ischemic cardiomyopathy; NICM = nonischemic cardiomyopathy; OR = odds ratio; other abbreviations as in Table 1.

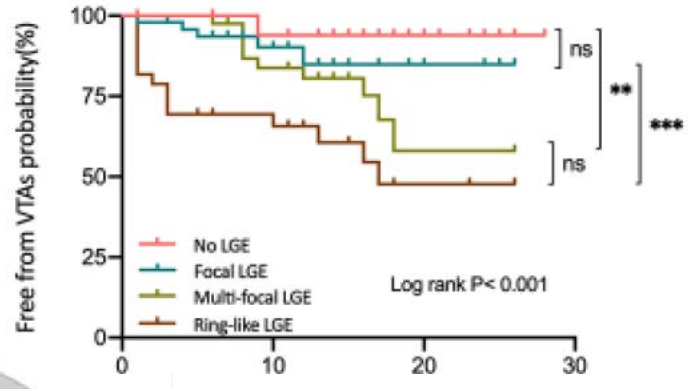
Disertori JACC CVI 2016; 9(9): 1046-55

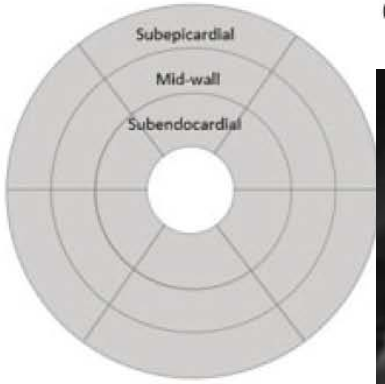
ESC European Society of Cardiology
European Heart Journal - Cardiovascular Imaging (2021) **22**, 1130–1138
doi:10.1093/ehjci/jeab117

Ring-like late gadolinium enhancement for predicting ventricular tachyarrhythmias in non-ischaemic dilated cardiomyopathy

Wensu Chen [1,2†], Wen Qian[3†], Xinwei Zhang[1†], Dongcheng Li[1], Zhiyong Qian[1], Hai Xu[4], Shengen Liao[1], Xing Chen[1], Yao Wang[1], Xiaofeng Hou[1], Amit R. Patel[5], Yi Xu[3]*, and Jiangang Zou [1]*







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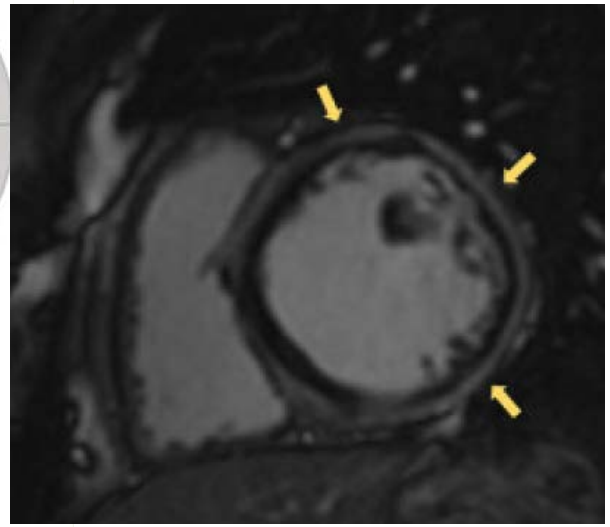

Wensu Chen, European Heart Journal - Cardiovascular Imaging (2021)

Infarct Tissue Heterogeneity by Magnetic Resonance Imaging Identifies Enhanced Cardiac Arrhythmia Susceptibility in Patients With Left Ventricular Dysfunction

André Schmidt, MD*; Clerio F. Azevedo, MD*; Alan Cheng, MD; Sandeep N. Gupta, PhD; David A. Bluemke, MD, PhD; Thomas K. Foo, PhD; Gary Gerstenblith, MD; Robert G. Weiss, MD; Eduardo Marbán, MD, PhD; Gordon F. Tomaselli, MD; João A.C. Lima, MD; Katherine C. Wu, MD

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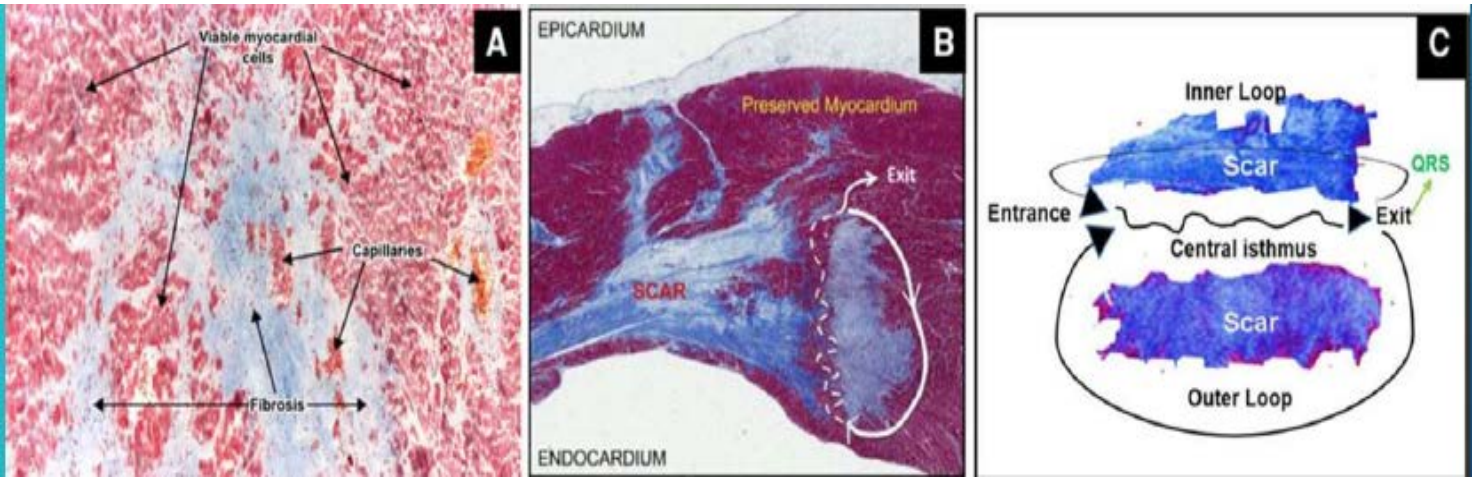
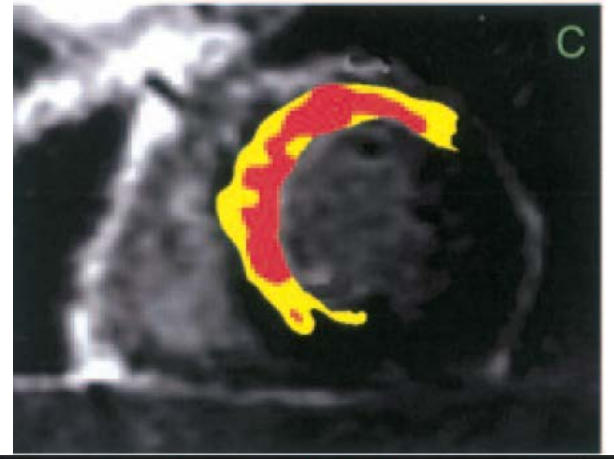
- Association between the extent of the peri-infarct zone by ceMRI and all-cause mortality



André Schmidt, MD, *Circulation*. 2007;115



Gray zone = Area with SI between 9 and 45
Core = Area with SI > 45
Gray + core = Area with SI > 9 (gray+core)

Meta-Analysis: Subgroup Analysis

Table 3 Summary estimates of relative risks and likelihood ratios in 11 studies of late gadolinium enhancement cardiac magnetic resonance imaging to predict ventricular arrhythmic events

Summary estimates	Relative risk (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Patient no.	Events	No. of studies
All	4.33 (2.98–6.29)	1.98 (1.66–2.37)	0.33 (0.24–0.46)	1063	201	11
Subgroups:						
CAD patients only	4.63 (2.48–8.67)	2.01 (1.66–2.44)	0.28 (0.16–0.50)	262	67	4
NICM patients only	3.79 (1.20–11.94)	2.10 (1.60–2.75)	0.46 (0.18–1.20)	227	23	3
Core scar as predictor	3.82 (2.19–6.66)	1.83 (1.57–2.13)	0.40 (0.25–0.64)	488	80	5
Grey zone as predictor	5.94 (2.82–12.52)	2.37 (1.45–3.87)	0.24 (0.13–0.44)	459	86	4
Only appropriate ICD therapy as primary endpoint	6.22 (2.41–16.05)	2.54 (1.73–3.71)	0.27 (0.14–0.52)	294	55	4

Scott PA. Eur J Heart Fail 2013;15:1019-27

Scar channels in cardiac magnetic resonance to predict appropriate therapies in primary prevention

Paula Sánchez-Somonte, MD,*†‡ Levio Quinto, MD,*† Paz Garre, BEng,*†
Fatima Zaraket, MD,*† Francisco Alarcón, BEng,*†‡ Roger Borràs, MSc,*†
Gala Caixal, MD,*† Sara Vázquez, MD,*† Susanna Prat, MD, PhD,*†
Jose T. Ortiz-Perez, MD, PhD,*† Rosario Jesús Perea, MD,†§ Eduard Guasch, MD, PhD *†‡
José Maria Tolosana, MD, PhD,*†‡ Antonio Berruezo, MD, PhD,*†
Elena Arbelo, MD, PhD,*†‡ Marta Sitges, MD, PhD,*†‡ Lluís Mont, MD, PhD,*†‡
Ivo Roca-Luque, MD, PhD*†‡

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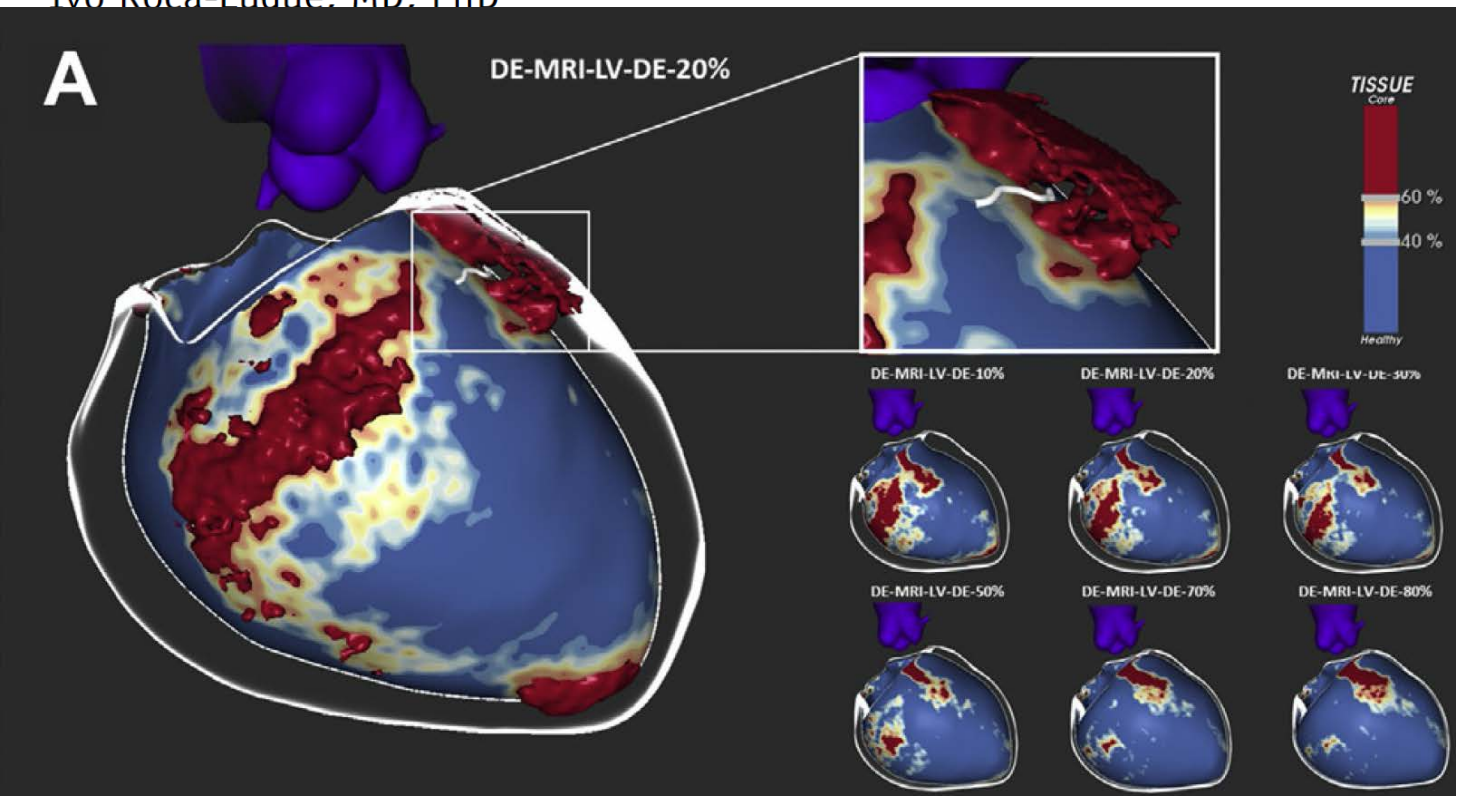
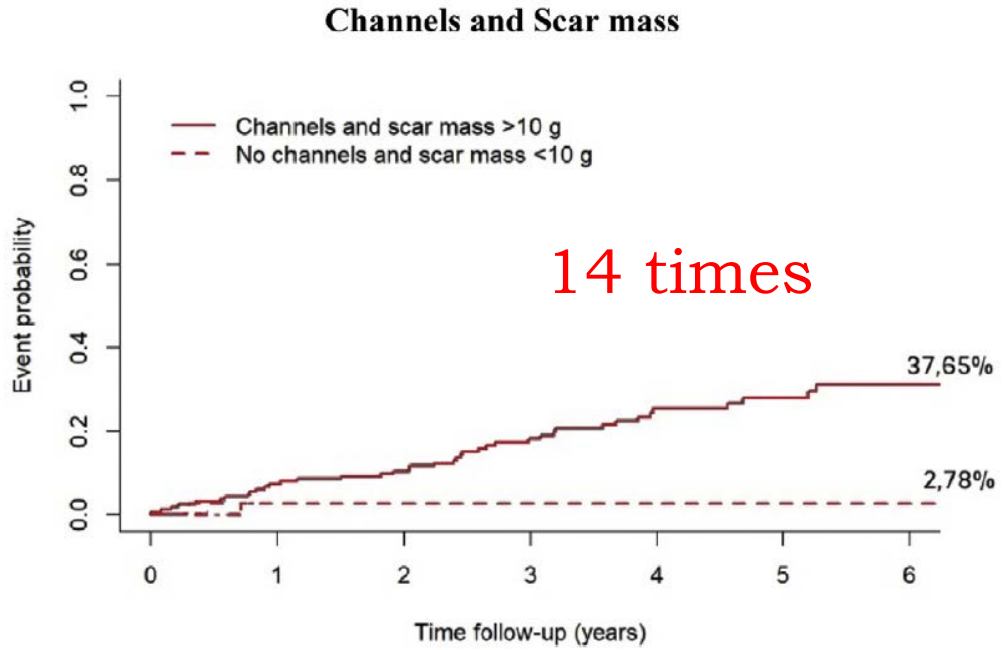




14 times

NPV for patients with no CCs and scar mass < 10 g 97.2%

Paula Sanchez-Somonte, Heart Rhythm 2021;18:1336–1343

Tavanir Arrhythmia Clinic

Scar characteristics

- Scar burden
- Location and pattern of LGE
- Mass and ratio of the peri-infarct border zone
- Quantification of the number of peri-infarct channels
- Interface area between healthy myocardium and hyperenhanced tissue

Predictors of mortality, inducibility of VT at EP study, and ICD therapy

Rubenstein JC, Cardiol J 2013

Let's put an ICD in all cases of aborted SCD!

- Reversible or treatable causes
- Costly and associated with procedural complications:
  - Infections
  - Inappropriate discharges
  - Device malfunctions
  - Diminished quality of life

- ICD prevents SCD in 2/3 of cases

Fishman GI, Circulation. 2010;122

Diagnostic Tests

- PMH
- Physical examination
- ECG
- Laboratory tests
- Echocardiography
- Coronary Angiography

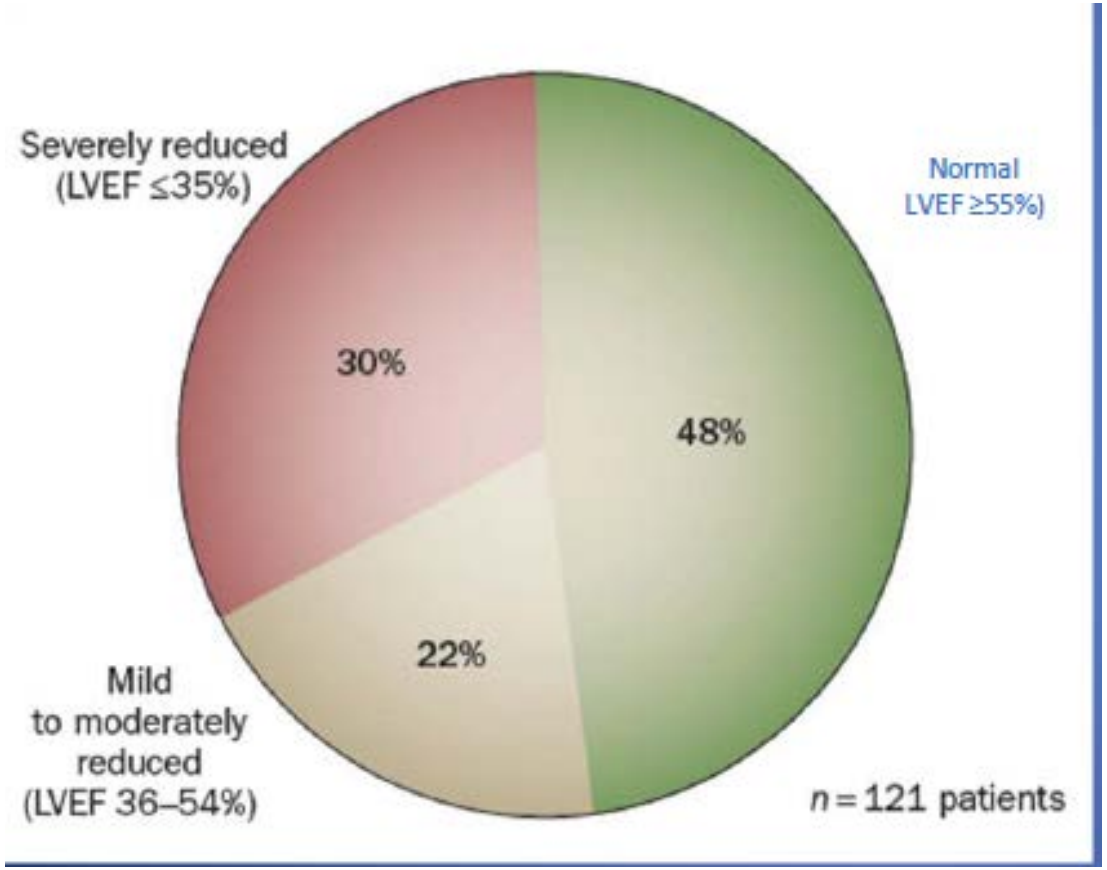
85%

Cardiac MR
Exercise testing
Drug challenge
Holter monitoring
EP study
Genetic Testing

50%

Majority of SCD Patients Have Preserved LVEF

EF <35%: Low Sensitivity



- N=121, retrospective
- Severe LVSD in <30%
- Maastricht Study: Identical findings
- At least 65% - missed by current guidelines

Stecker EC, et al. J Am Coll Cardiol 2006; 47 (6): 1161-6
Gorgels AP, et al. European heart journal. 2003;24:1204-1209

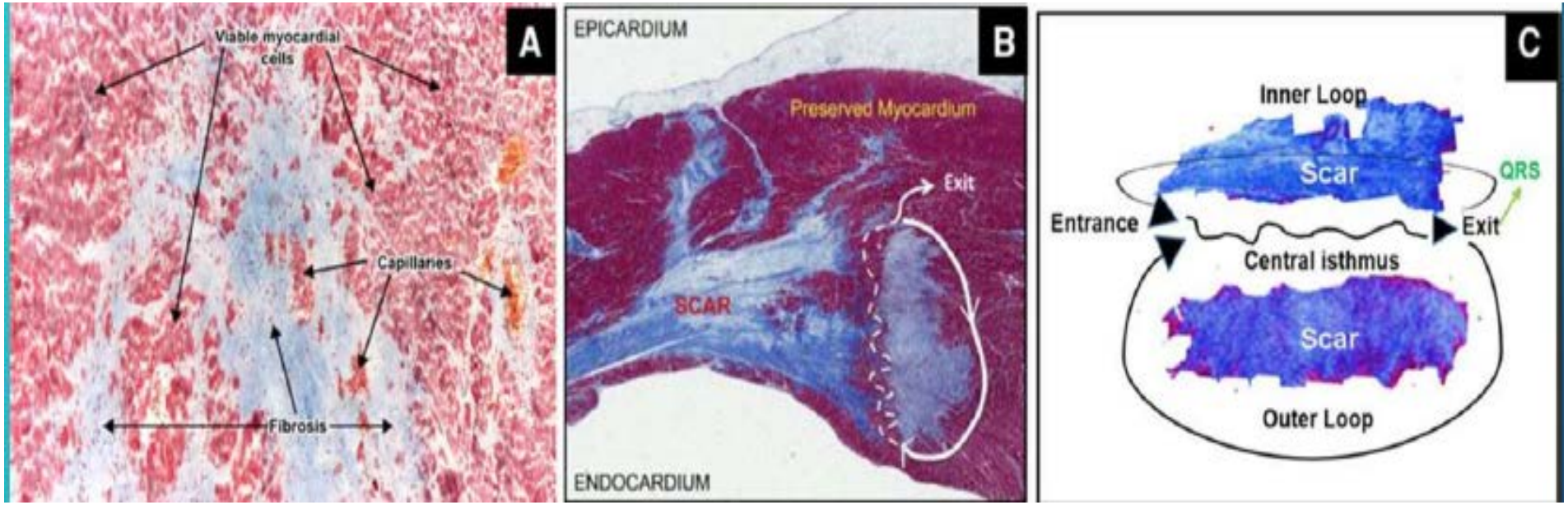
Evaluation of OHCA
"Anything above EF"

- Identification of myocardial tissue changes such as myocardial edema and myocardial fibrosis

- In the evaluation of aborted SCD, the combination of myocardial edema and fibrosis has the potential to distinguish an acute and potentially reversible injury from a chronic and irreversible lesion.

Pathophysiology of VT/VF in coronary heart disease

MYOCARDIAL SCAR forms the established SUBSTRATE for long term risk of VT/VF



Wu KC, Circ CVIM 2017; e005461

JACC: CARDIOVASCULAR IMAGING
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DOI:10.1016/j.jcmg.2008.09.014

Cardiac Magnetic Resonance Monitors Reversible and Irreversible Myocardial Injury in Myocarditis

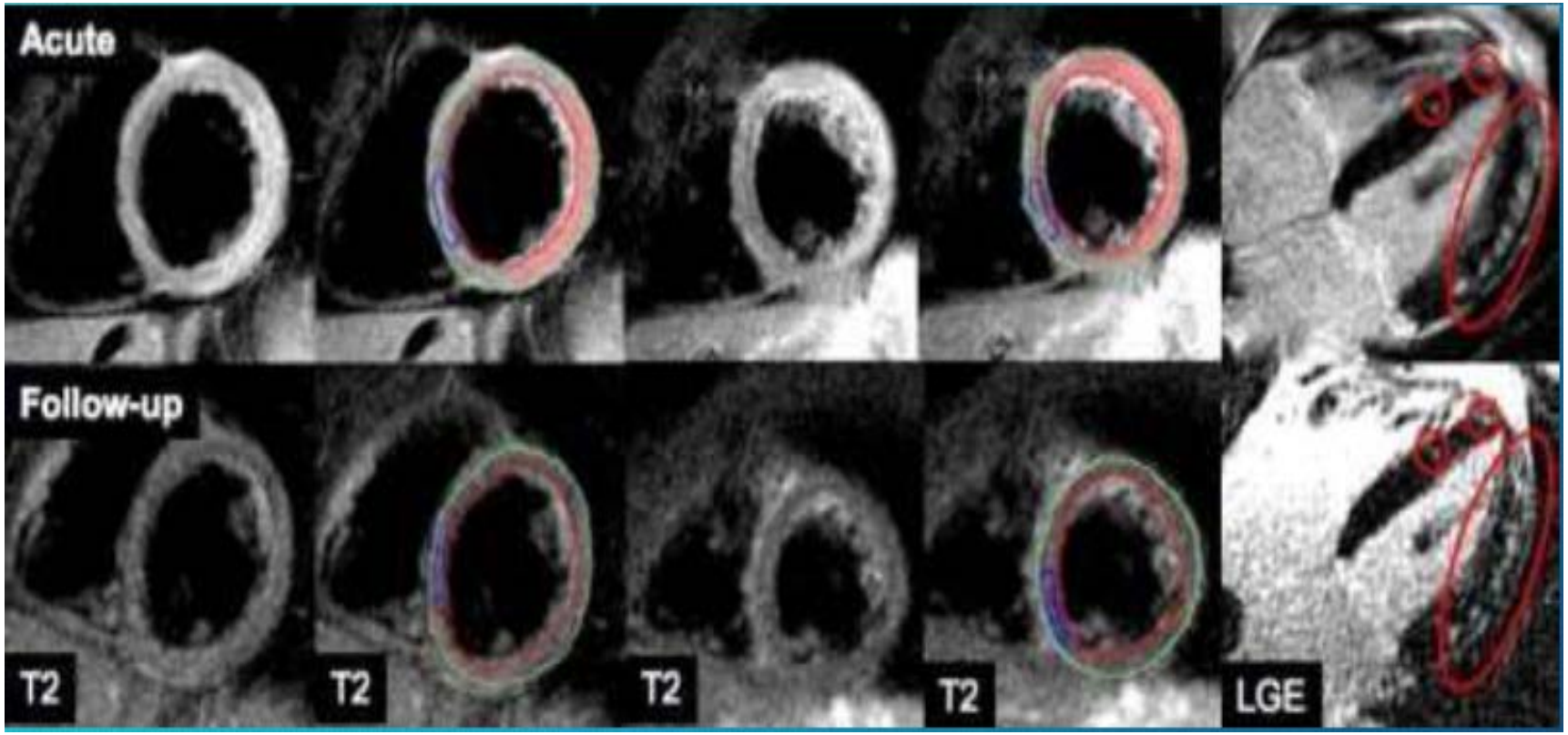
Anja Zagrosek, MD, Hassan Abdel-Aty, MB, BCH, MSc, Philipp Boyé, MD, Ralf Wassmuth, MD, Daniel Messroghli, MD, Wolfgang Utz, MD, Andre Rudolph, MD, Steffen Bohl, MD, Rainer Dietz, MD, Jeanette Schulz-Menger, MD

Berlin, Germany

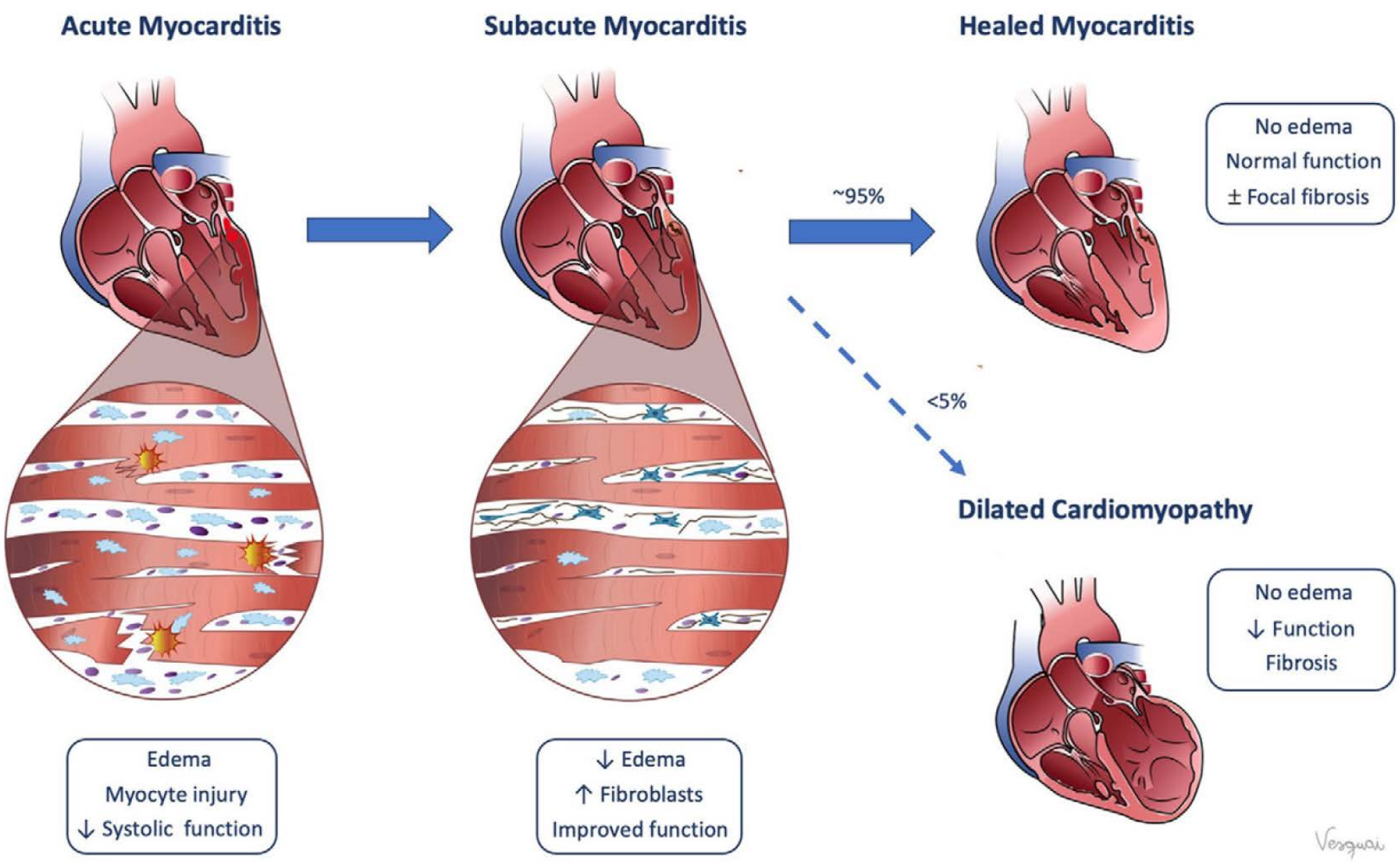
Reversible injuries, namely, myocardial edema (T2-weighted) and increased capillary leakage (gRE), differentiate acute from healed myocarditis whereas necrosis/fibrosis imaging (LGE) alone cannot.

Anja Zagrosek,J Am Coll Cardiol Img 2009;2:131–8) © 2009

- No simultaneous elevation of T2 and gRE during the convalescent phase, resulting in a NPV of 100% to differentiate the 2 phases of the disease.



Anja Zagrosek,J Am Coll Cardiol Img 2009;2:131–8) © 2009

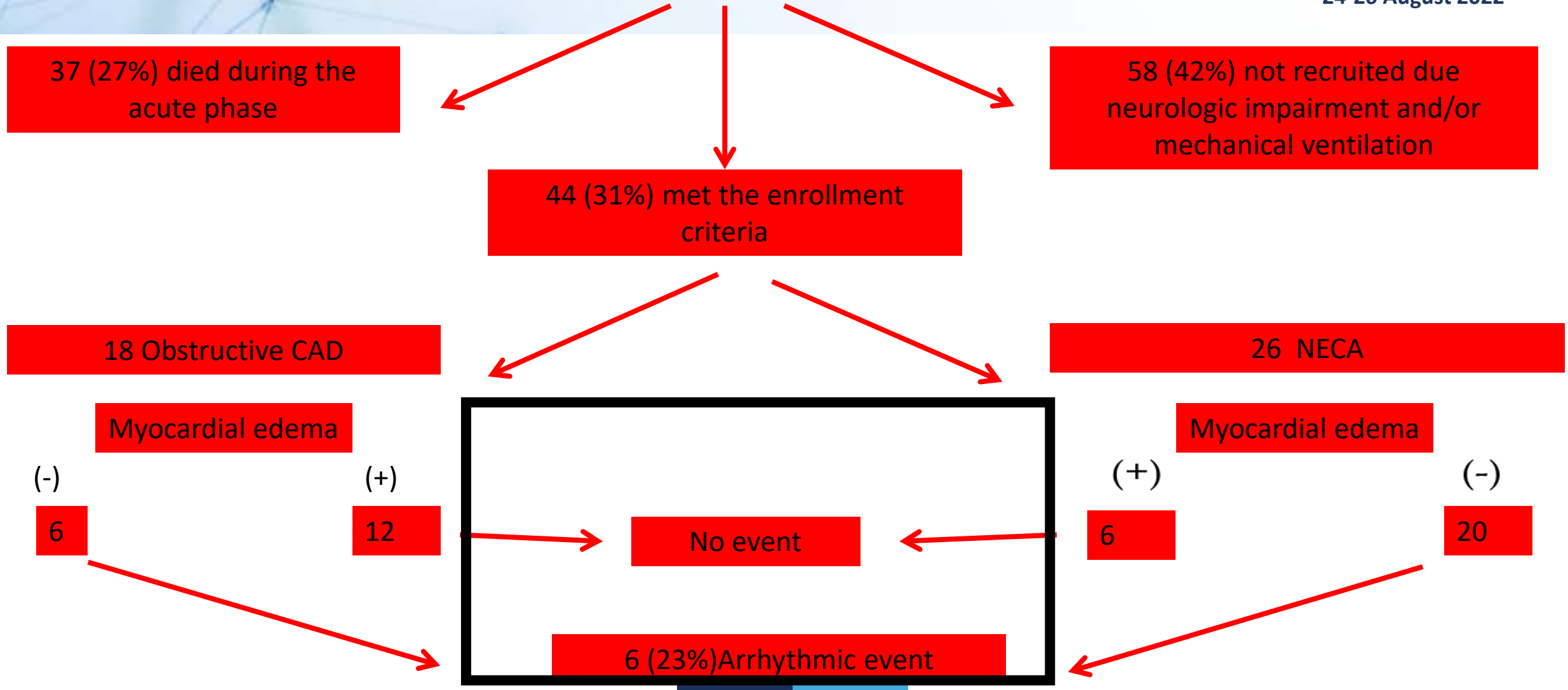

Acute Myocarditis
Subacute Myocarditis
Healed Myocarditis
~95%
No edema
Normal function
± Focal fibrosis
<5%
Dilated Cardiomyopathy
No edema
↓ Function
Fibrosis
Edema
Myocyte injury
↓ Systolic function
↓ Edema
↑ Fibroblasts
Improved function

Diagnostic value and prognostic implications of early cardiac magnetic resonance in survivors of out-of-hospital cardiac arrest

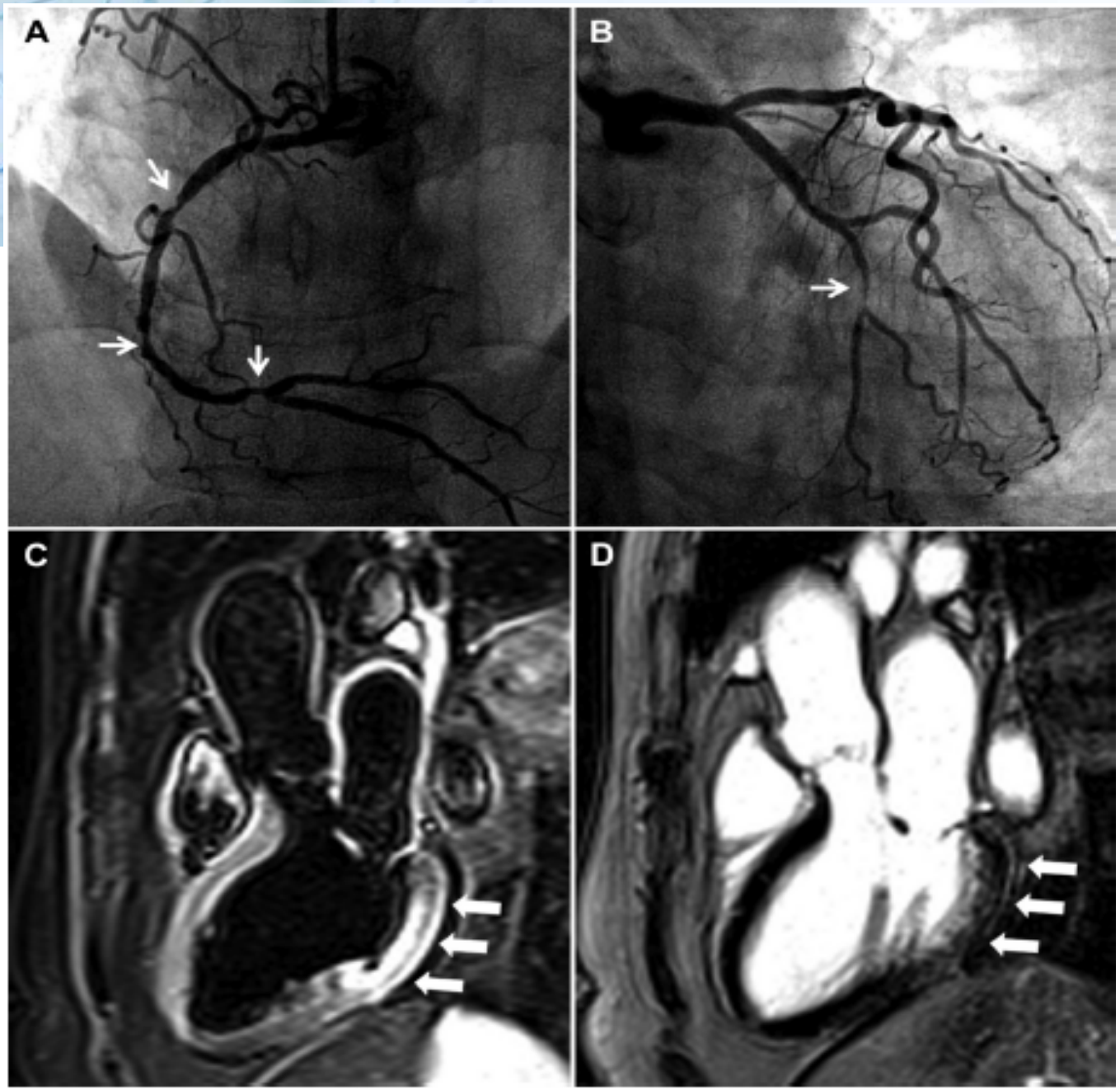
Alessandro Zorzi, MD, PhD,* Angela Susana, MD,* Manuel De Lazzari, MD, PhD,* Federico Migliore, MD, PhD,* Giovanni Vescovo, MD,* Daniele Scarpa, MD,* Anna Baritussio, MD,*‡ Giuseppe Tarantini, MD, PhD,* Luisa Cacciavillani, MD, PhD,* Benedetta Giorgi, MD,† Cristina Basso, MD, PhD,* Sabino Iliceto, MD,* Chiara Bucciarelli Ducci, MD, PhD,‡ Domenico Corrado, MD, PhD,* Martina Perazzolo Marra, MD, PhD*

*From the *Division of Cardiology, Department of Cardiac, Thoracic and Vascular Sciences, University of Padova, Padova, Italy, †Division of Radiology, Department of Medicine, Az. Ospedaliera di Padova, Padova, Italy, and ‡Bristol NIHR Cardiovascular Biomedical Research Unit, Bristol Heart Institute, University of Bristol, Bristol, United Kingdom.*

Alessandro Zorzi, Heart Rhythm 2018;15:1031–1041

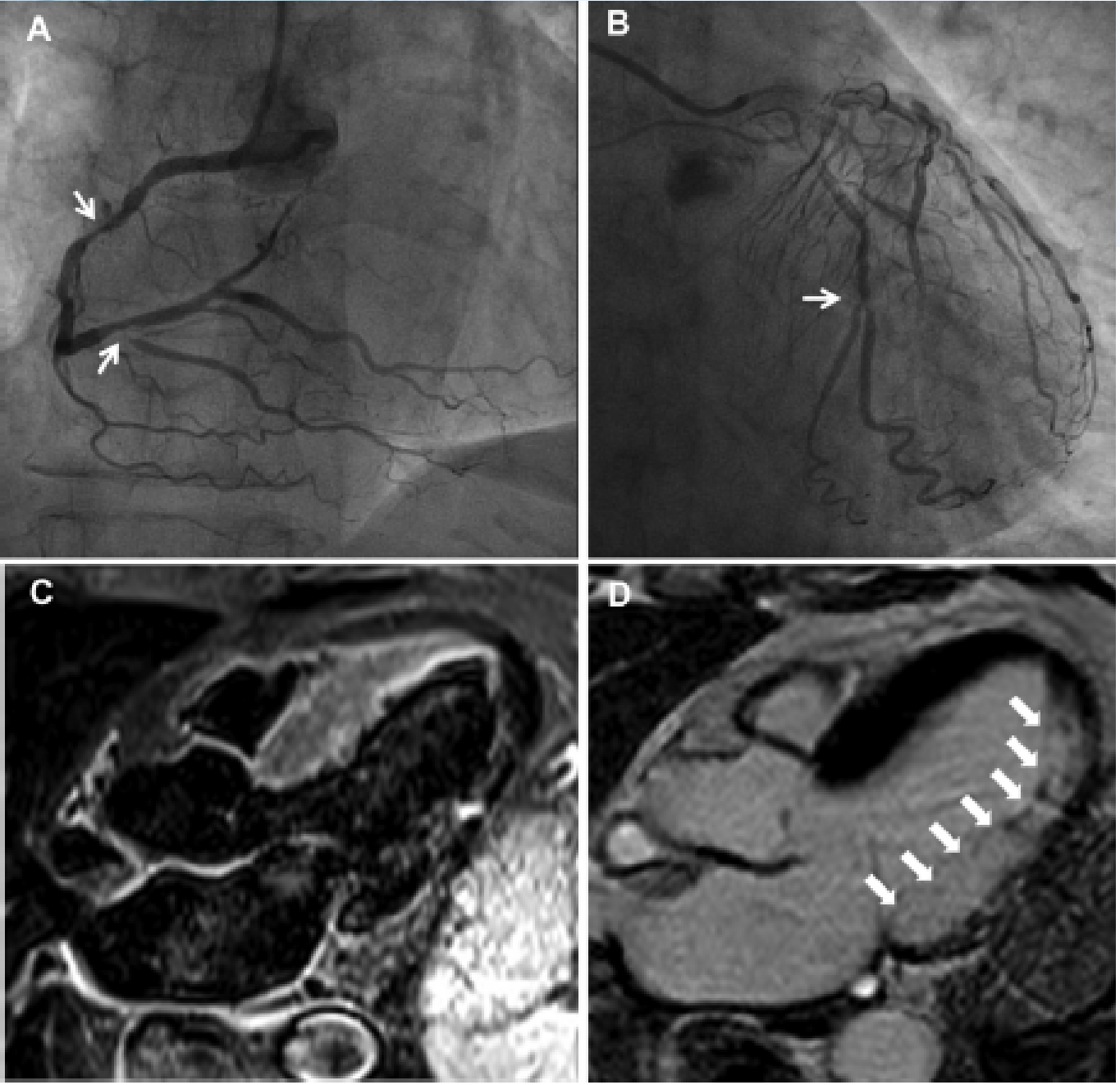


Alessandro Zorzi,Heart Rhythm 2018;15:1031–1041



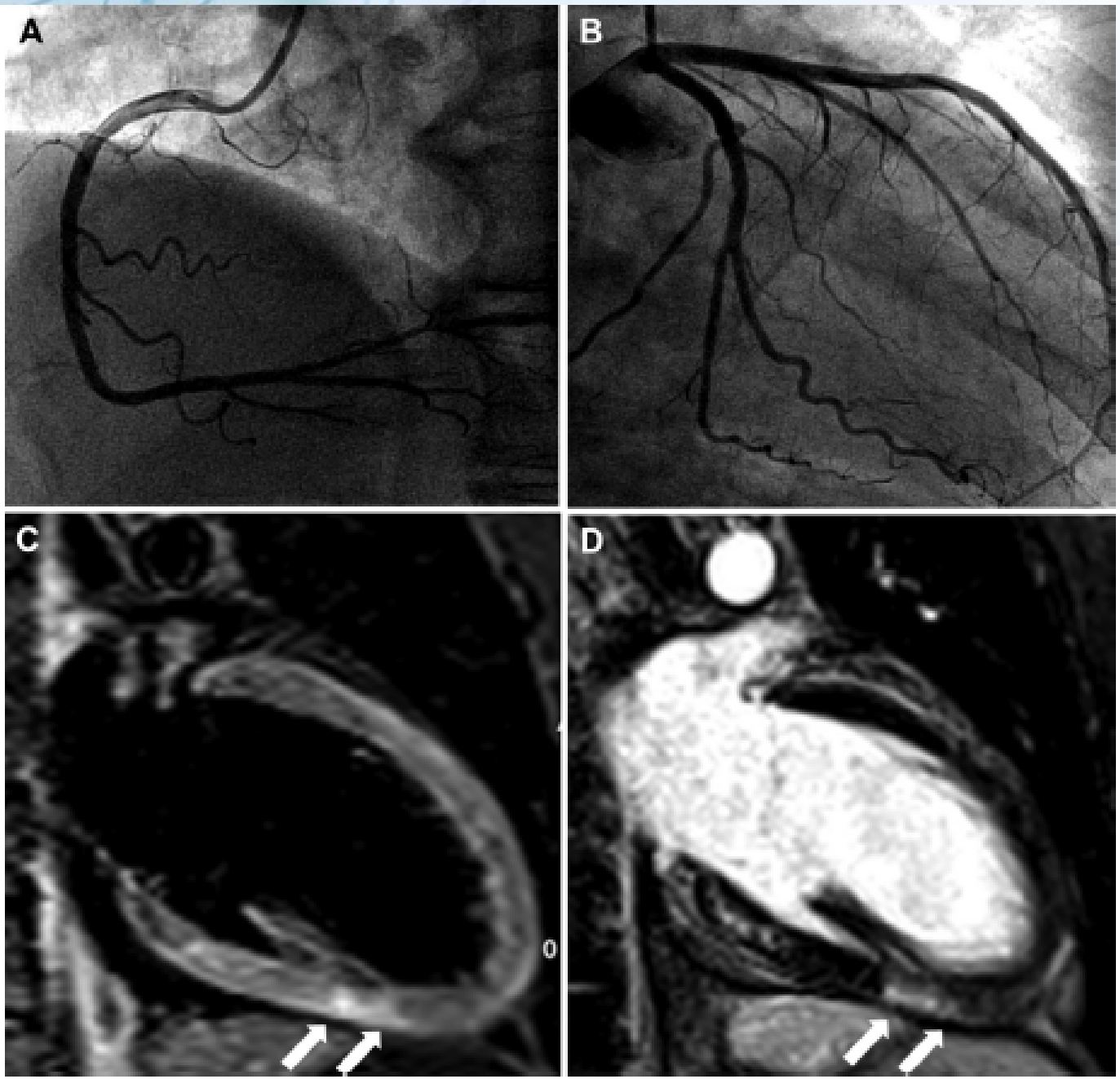
- Aborted SCD in a case of ACS

Alessandro Zorzi, Heart Rhythm 2018;15:1031–1041



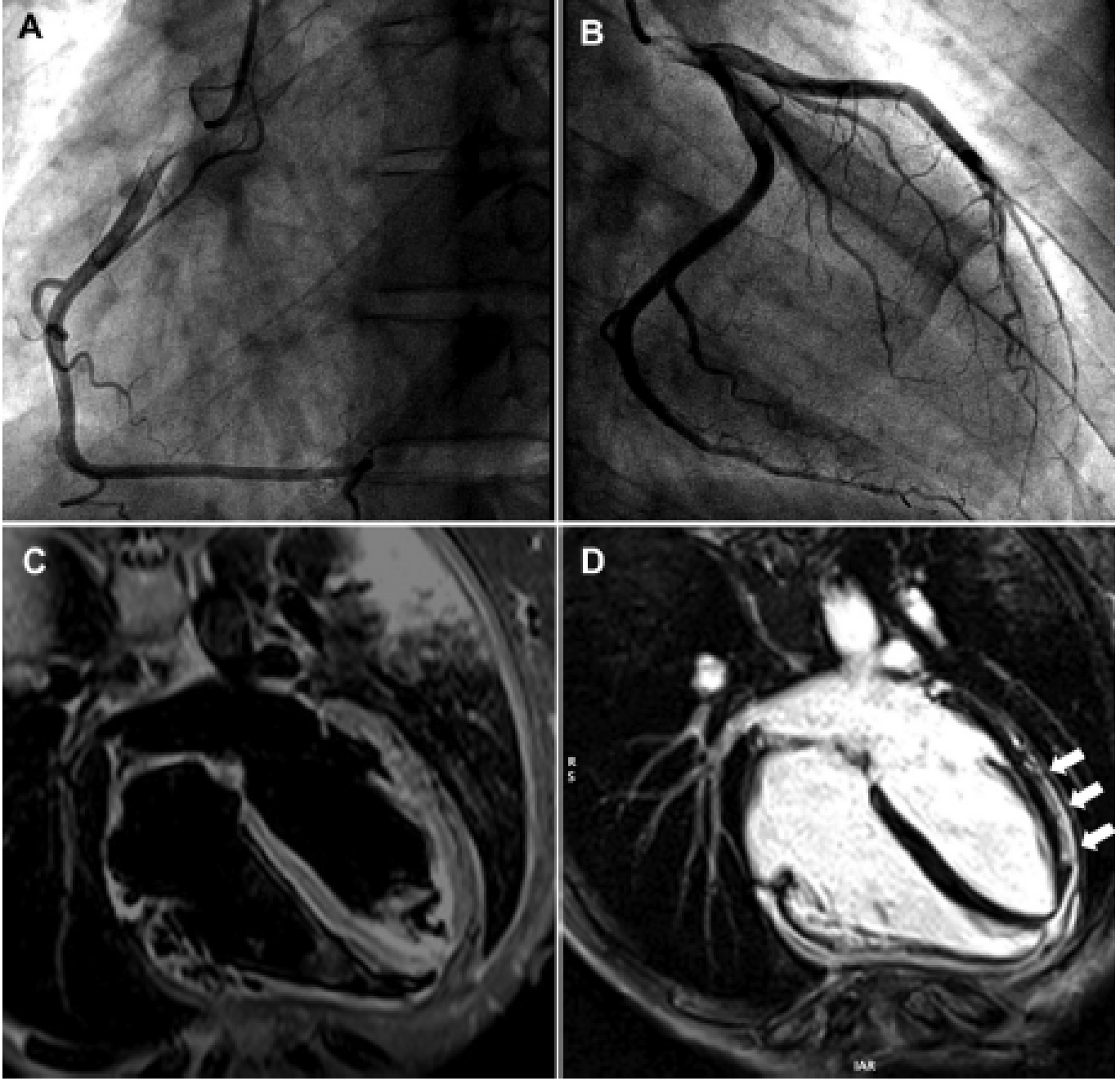
- Aborted SCD in a case of old MI

Alessandro Zorzi, Heart Rhythm 2018;15:1031–1041



- Aborted SCD in a case of myocarditis

Alessandro Zorzi, Heart Rhythm 2018;15:1031–1041



Aborted SCD in a case with an isolated non-ischemic left ventricular scar

Alessandro Zorzi, Heart Rhythm 2018;15:1031–1041

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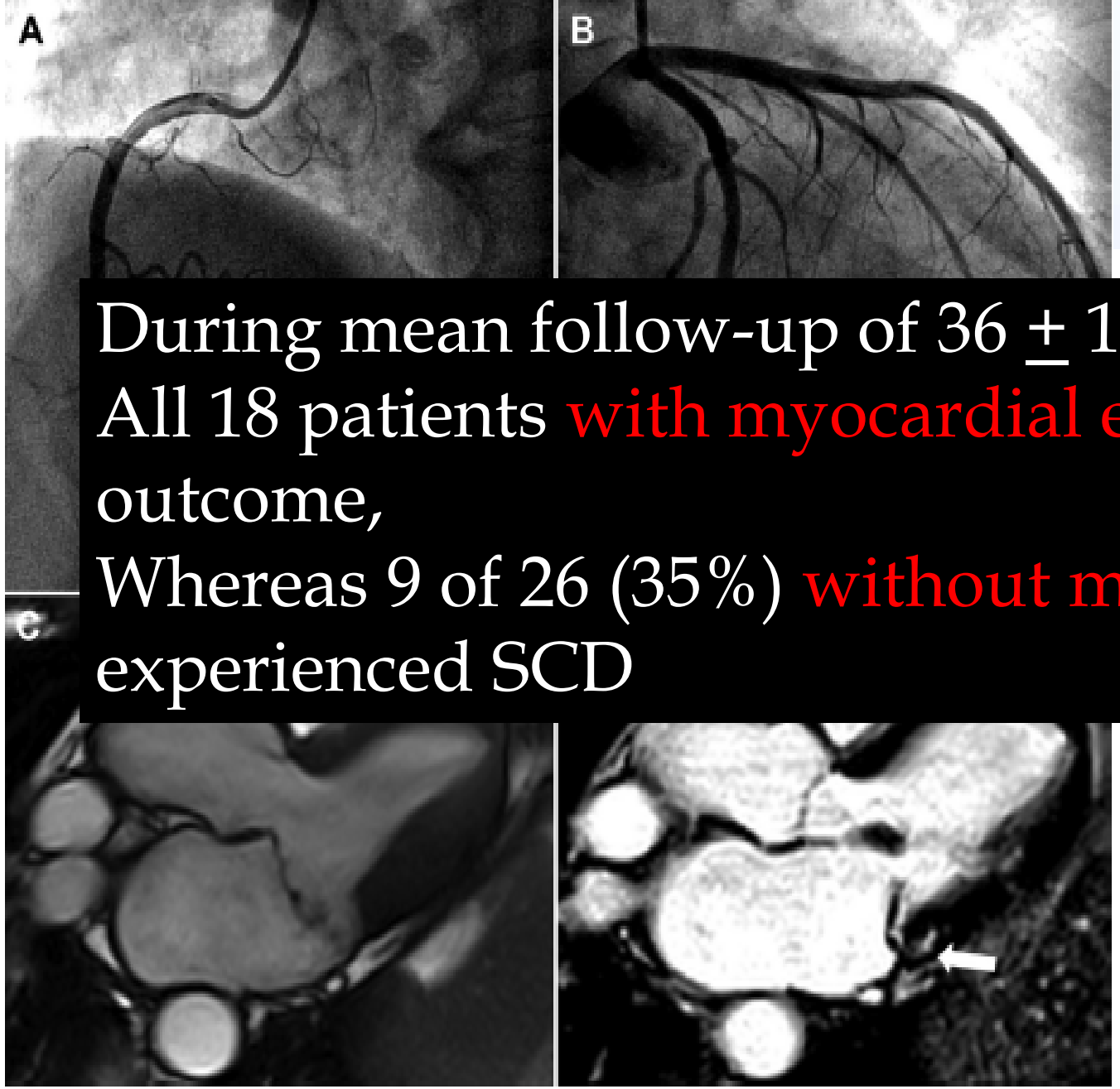

During mean follow-up of 36 ± 17 months
All 18 patients with myocardial edema had an uneventful outcome,
Whereas 9 of 26 (35%) without myocardial edema experienced SCD

Alessandro Zorzi, Heart Rhythm 2018;15:1031–1041

Journal of the American Heart Association

ORIGINAL RESEARCH

Prognostic Role of Myocardial Edema as Evidenced by Early Cardiac Magnetic Resonance in Survivors of Out-of-Hospital Cardiac Arrest: A Multicenter Study

Alessandro Zorzi, MD, PhD; Giulia Mattesi, MD; Enrico Baldi, MD; Mauro Toniolo, MD; Federico Guerra, MD; Filippo Maria Cauti, MD; Alberto Cipriani, MD; Manuel De Lazzari, MD, PhD; Daniele Muser, MD; Giulia Stronati, MD; Lina Marcantoni, MD; Massimiliano Manfrin, MD; Leonardo Calò, MD; Chiara Lanzillo, MD; Martina Perazzolo Marra, MD, PhD; Simone Savastano, MD; Domenico Corrado, MD, PhD

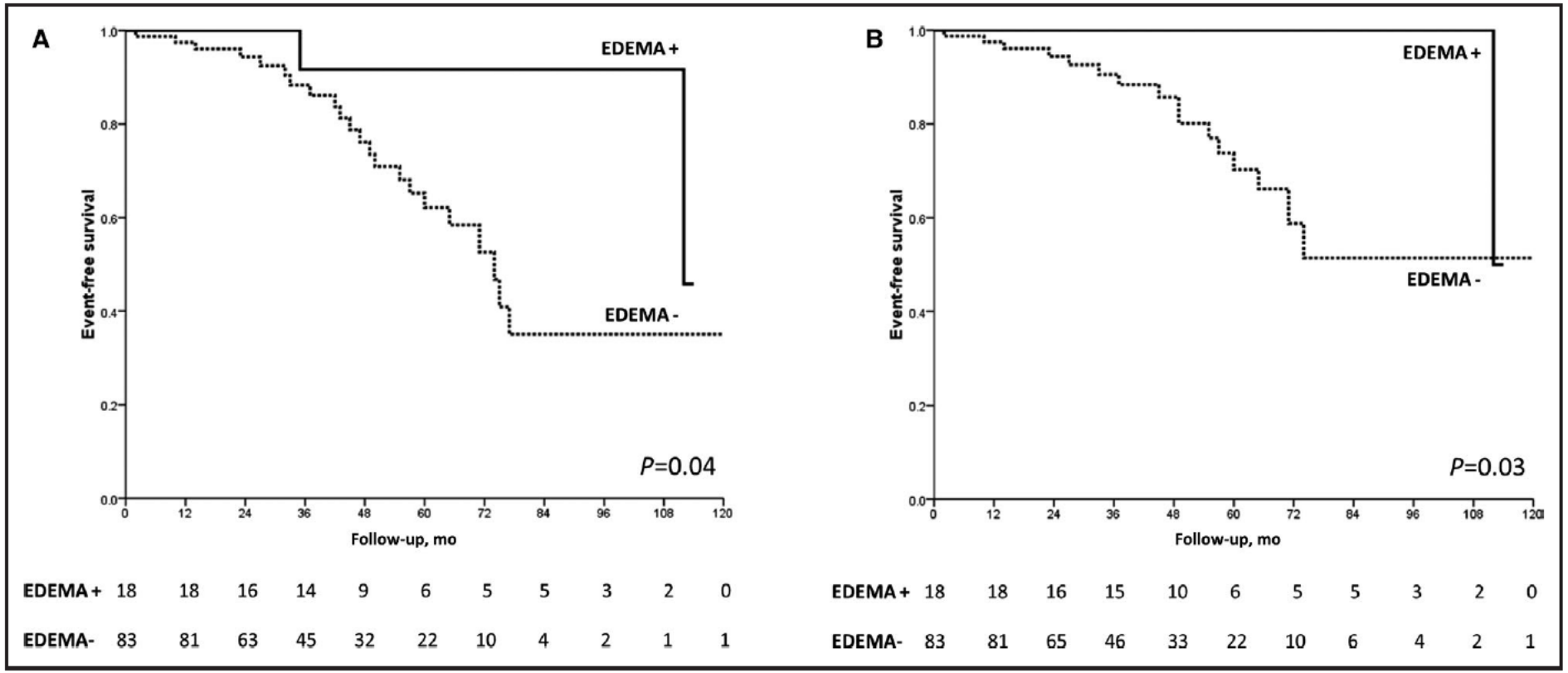

Figure 3. Survival free from appropriate implantable cardioverter-defibrillator (ICD) intervention according to the presence of myocardial edema (ME).

Kaplan-Meier analysis of survival free from appropriate ICD interventions (antitachycardia pacing or shock [**A**] or shock only [**B**] according to the presence of ME on cardiac magnetic resonance).

Zorzi et al, *J Am Heart Assoc.* 2021

Case Presentation

- 48 year old man admitted with aborted SCD
- ECG at admission polymorphic VT
- History of ACS 6 months earlier
- LVEF 50%
- No Enzyme changes

ECG

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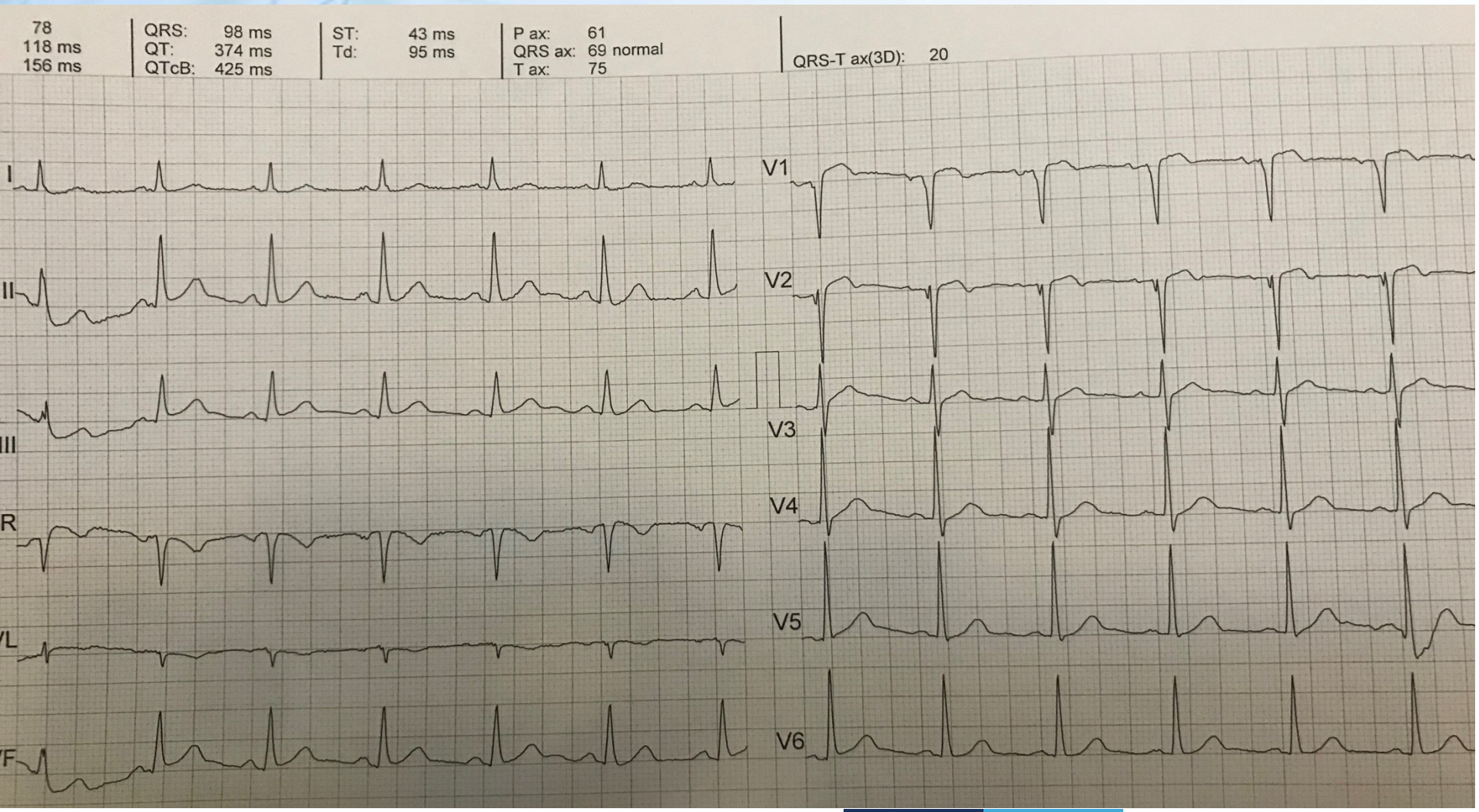

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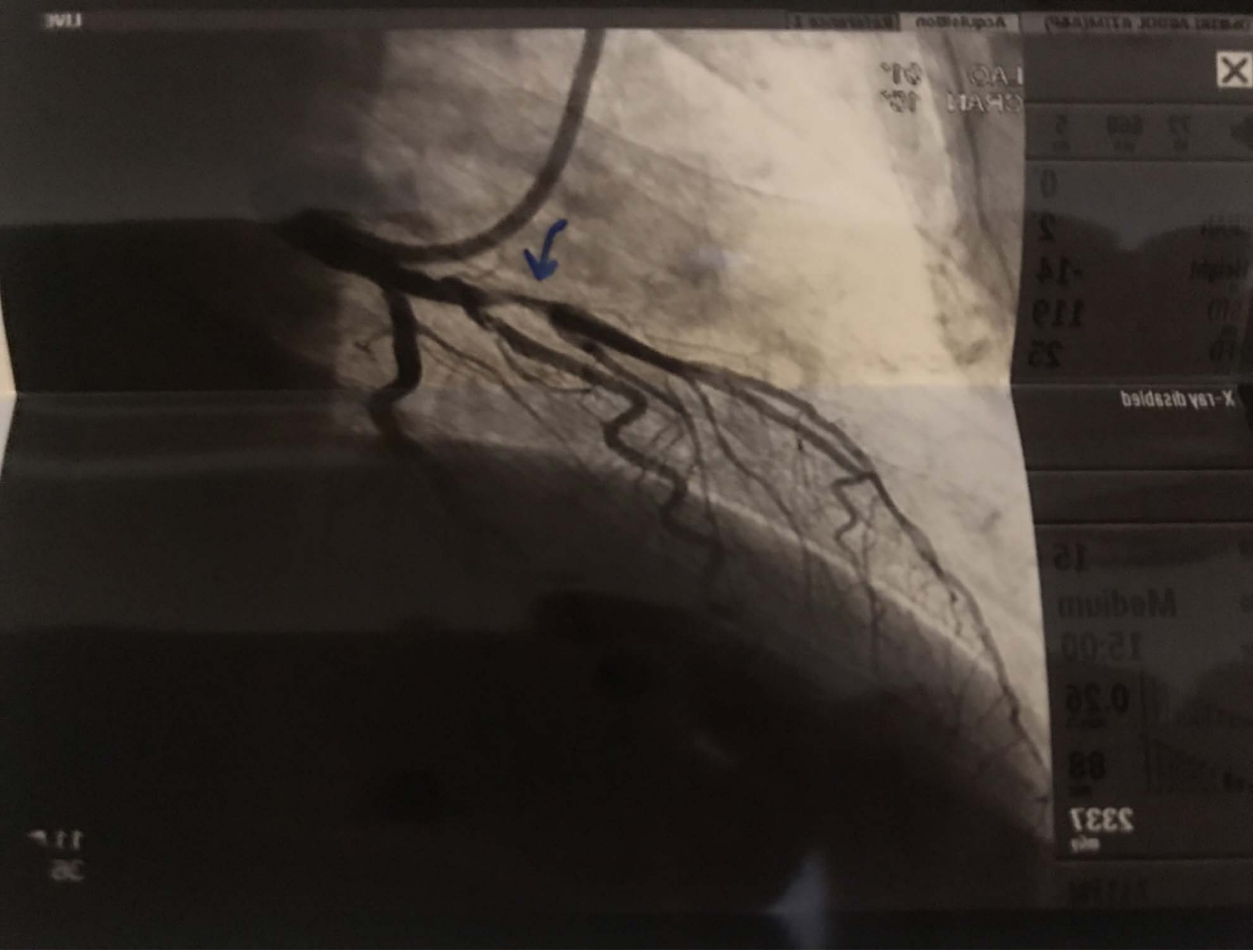

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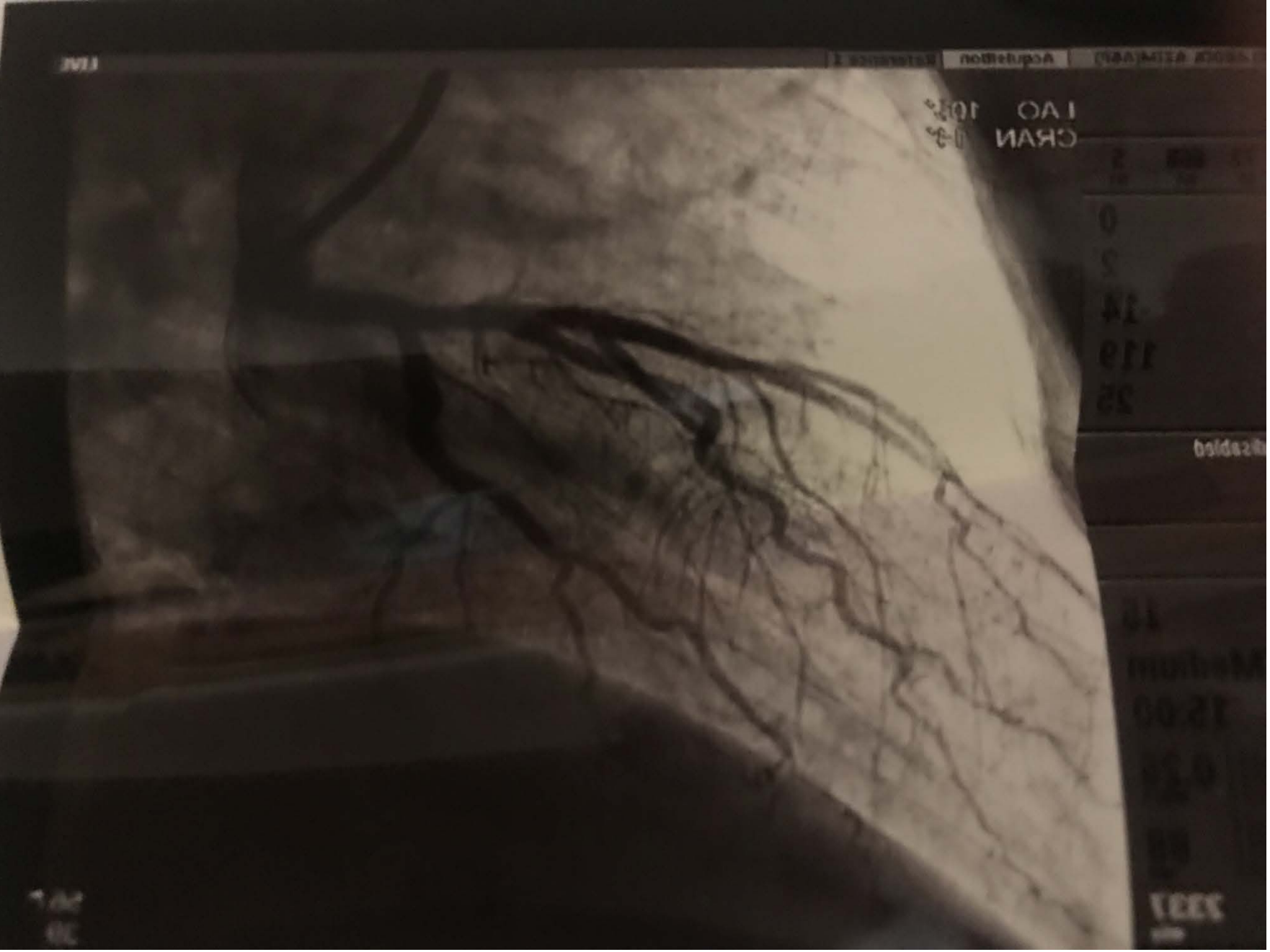

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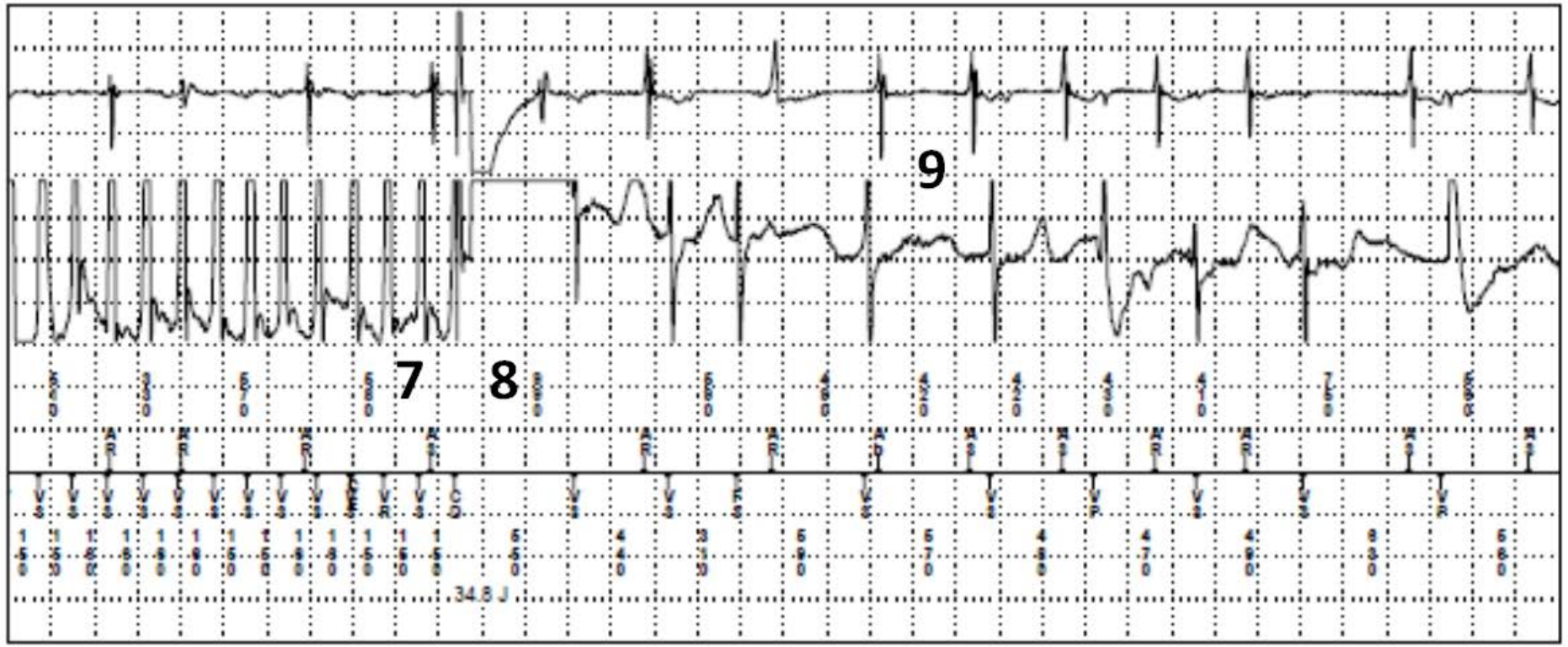
More Investigation?

- Near normal LVEF
- Proximal LAD lesion
- ACS?
- Any substrate

Two years later



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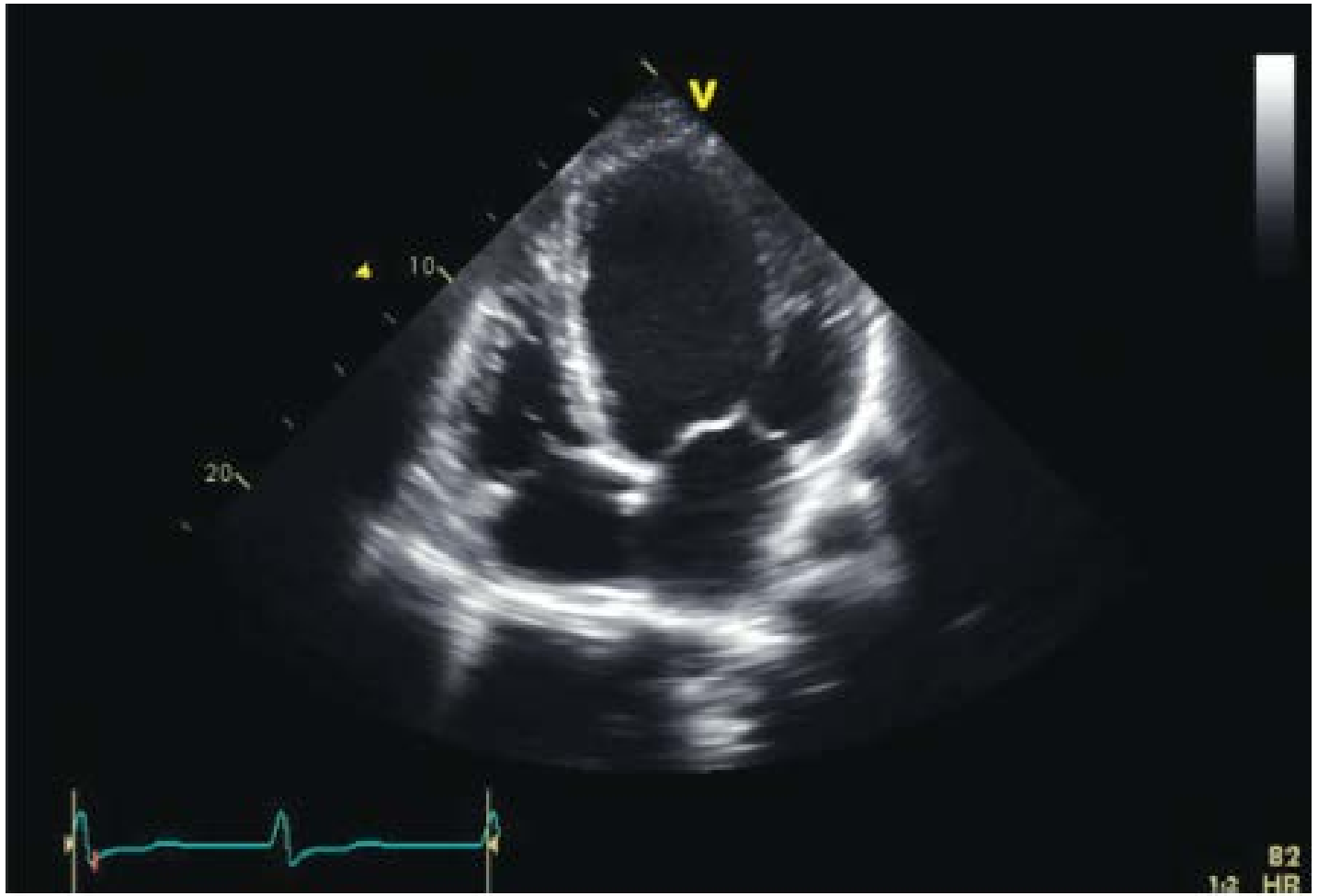
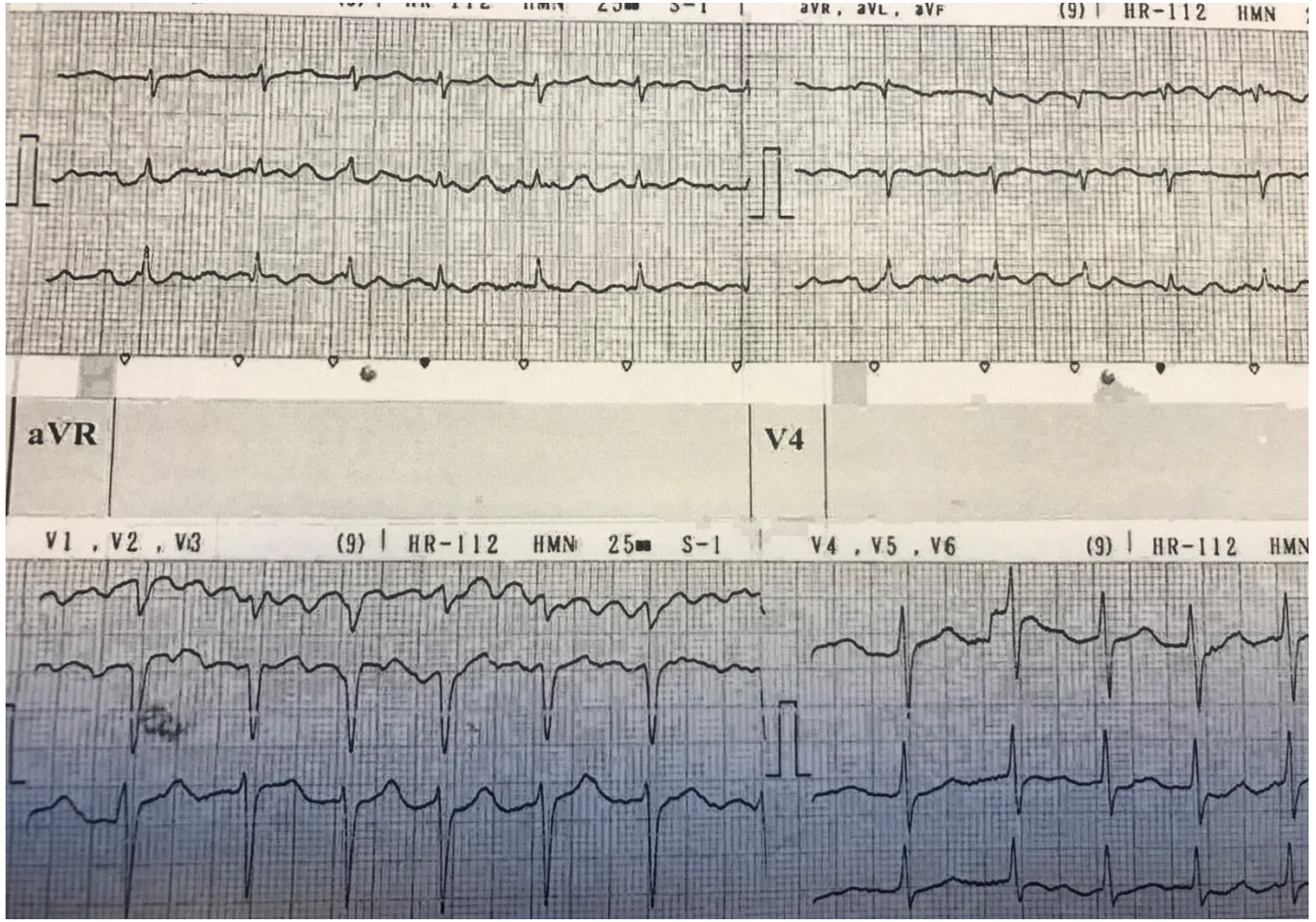
Case Presentation

- 58 year old man admitted because of collapse (5 minutes CPR , no DC shock)
- No previous symptom
- No family history of SCD
- Off drug
- Echo LVEF 25%
- NECA
- Normal neurologic evaluation

Echo findings: EF 25%, LVED 5.8, LVES 4.8, LA 4.2, No valvular abnormality



ECG at Admission

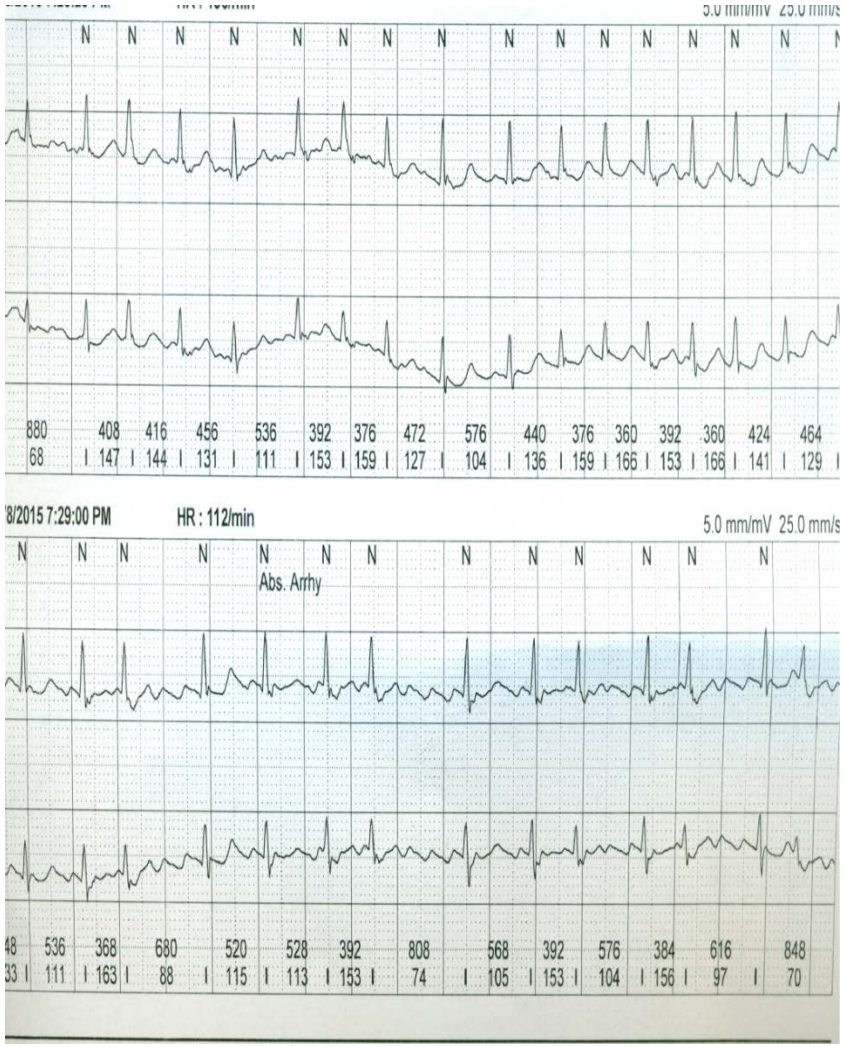


ECG at CCU

What is the next step?

- ICD implantation
- Medical follow up
- DC cardioversion
- RF ablation
- Or
- CMR

Holter Monitoring
Min 75, Mean 124, Max 191
PVCs 7400



MRI findings:
LVEF 30% with
no fibrosis

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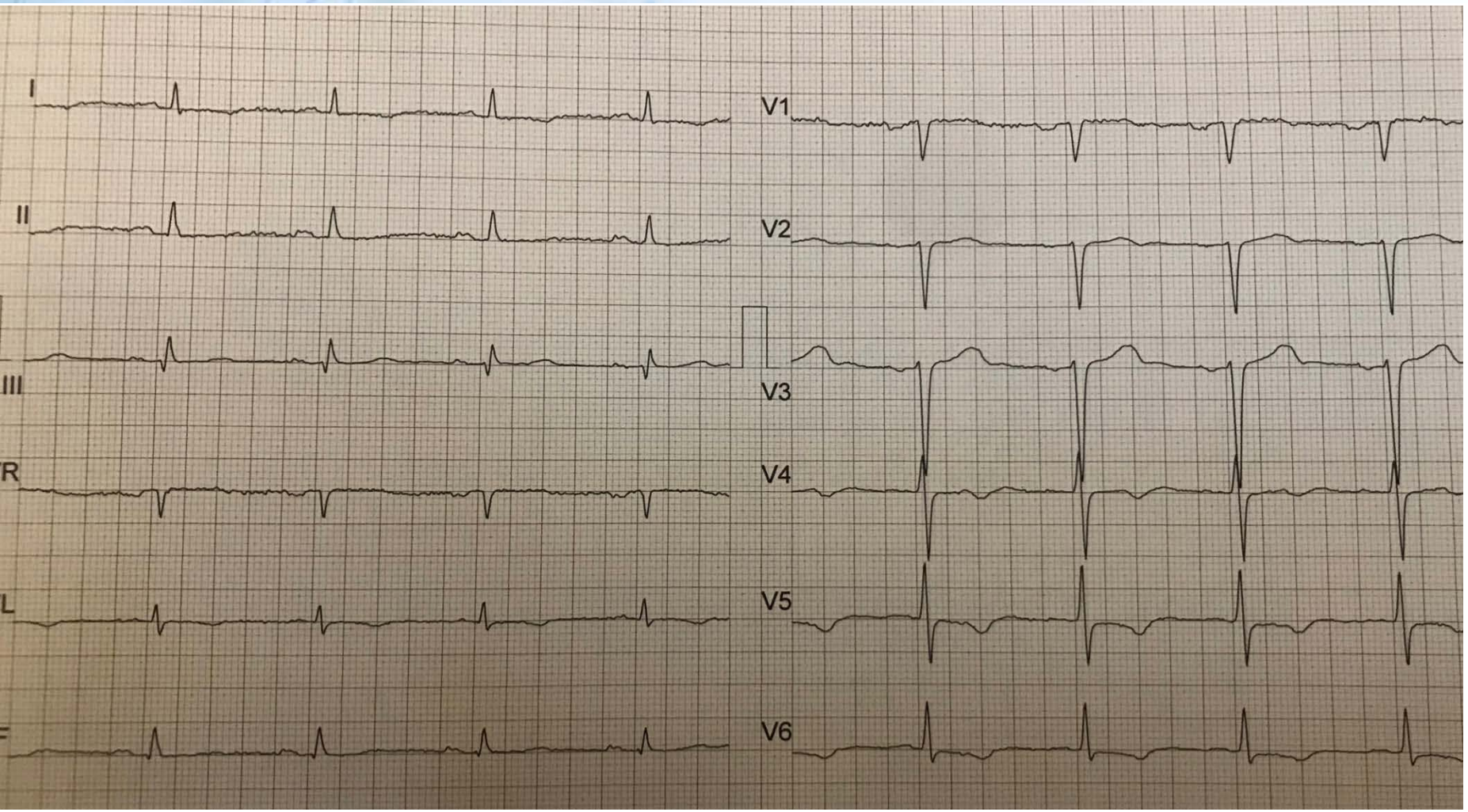
- EP study: no inducible VT at baseline or on Isuprel
- DC cardioversion performed.
- On Amiodarone and NOAC for 6 weeks
- In 6 weeks ECG : NSR
- Echocardiography: LVEF 55% LVED 5.4
- Normal Holter recordings
- PVI performed.

Last Visit



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Taking Home Message

- CMR imaging an important tool in the risk stratification of high risk patients and the standard-of-care test in SCA survivors
- But not a "Fortune Teller Machine"
- In primary prevention consider LGE on CMR
- Genetic mutations (Laminin, Filamin C and RMB20), different types of CMP

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THANK YOU
For attending the 1st annual meeting of ISMRM Iranian Chapter

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See you next year!

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