Key Opinion Leader Call – April 15, 2020

Cardiac Complications of Duchenne Muscular Dystrophy

NASDAQ: CAPR

Forward-Looking Statements

Statements in this presentation release regarding the efficacy, safety, and intended utilization of Capricor's product candidates; the initiation, conduct, size, timing and results of discovery efforts and clinical trials; the pace of enrollment of clinical trials; plans regarding regulatory filings, future research and clinical trials; regulatory developments involving products, including the ability to obtain regulatory approvals or otherwise bring products to market; plans regarding current and future collaborative activities and the ownership of commercial rights; scope, duration, validity and enforceability of intellectual property rights; future royalty streams, revenue projections; expectations with respect to the expected use of proceeds from the recently completed offerings and the anticipated effects of the offerings, and any other statements about Capricor's management team's future expectations, beliefs, goals, plans or prospects constitute forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Any statements that are not statements of historical fact (including statements containing the words "believes," "plans," "could," "anticipates," "expects," "estimates," "should," "target," "will," "would" and similar expressions) should also be considered to be forward-looking statements. There are a number of important factors that could cause actual results or events to differ materially from those indicated by such forward-looking statements. More information about these and other risks that may impact Capricor's business is set forth in Capricor's Annual Report on Form 10-K for the year ended December 31, 2019 as filed with the Securities and Exchange Commission on March 27, 2020. All forward-looking statements in this press release are based on information available to Capricor as of the date hereof, and Capricor assumes no obligation to update these forward-looking statements.

CAP-1002 is an Investigational New Drug and is not approved for any indications. None of Capricor's exosome-based candidates have been approved for clinical investigation.

Call Participants

Michael Taylor, M.D., Ph.D. – Director of cardiac MR at Cincinnati Children's Hospital

Linda Marban, Ph.D. – Capricor CEO

Duchenne muscular dystrophy and the heart

Michael D. Taylor, MD, PhD

Director of cardiac MR

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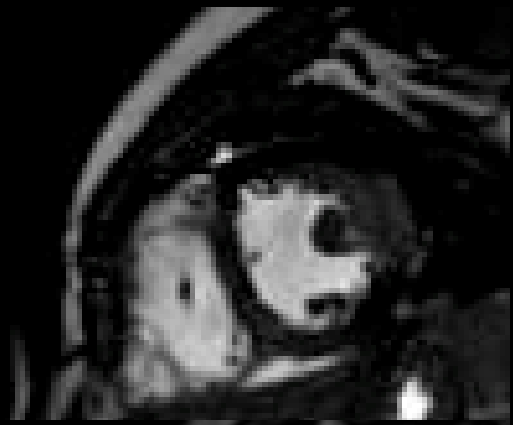
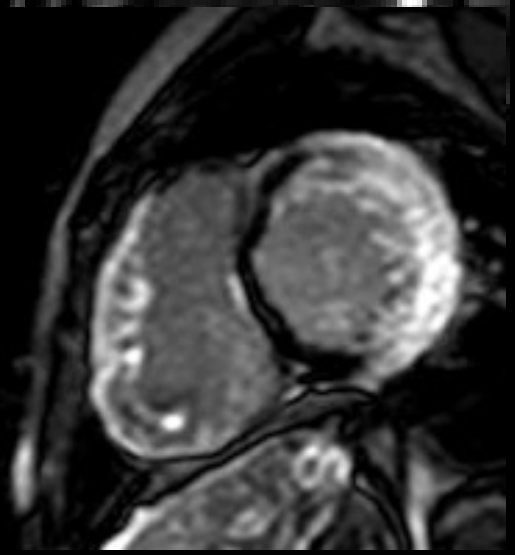
Duchenne muscular dystrophy and the heart

- Duchenne muscular dystrophy: Overview
- Cardiomyopathy of DMD
  - Heart muscle
  - Electrical system
  - Natural history of DMD cardiomyopathy
- Current evaluation and treatment paradigm
- Novel approaches to cardiac therapy





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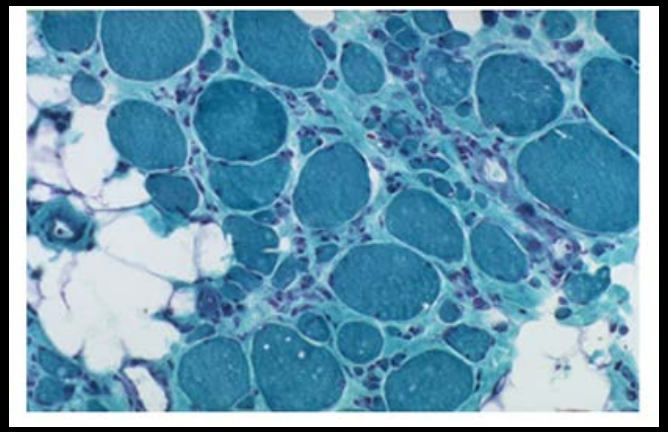
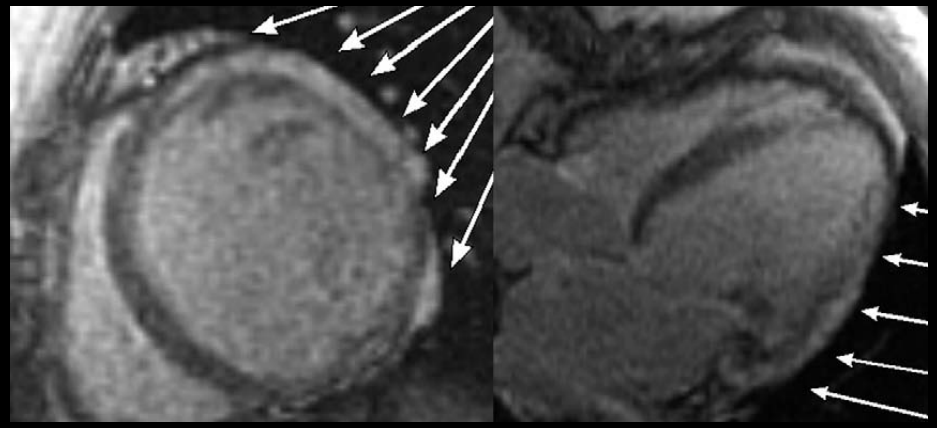
Duchenne Muscular Dystrophy

- *Dystrophin* mutations
- X-linked recessive
- Muscle wasting disease
- Patchy progressive fibrosis

Skeletal myopathy



Cardiomyopathy



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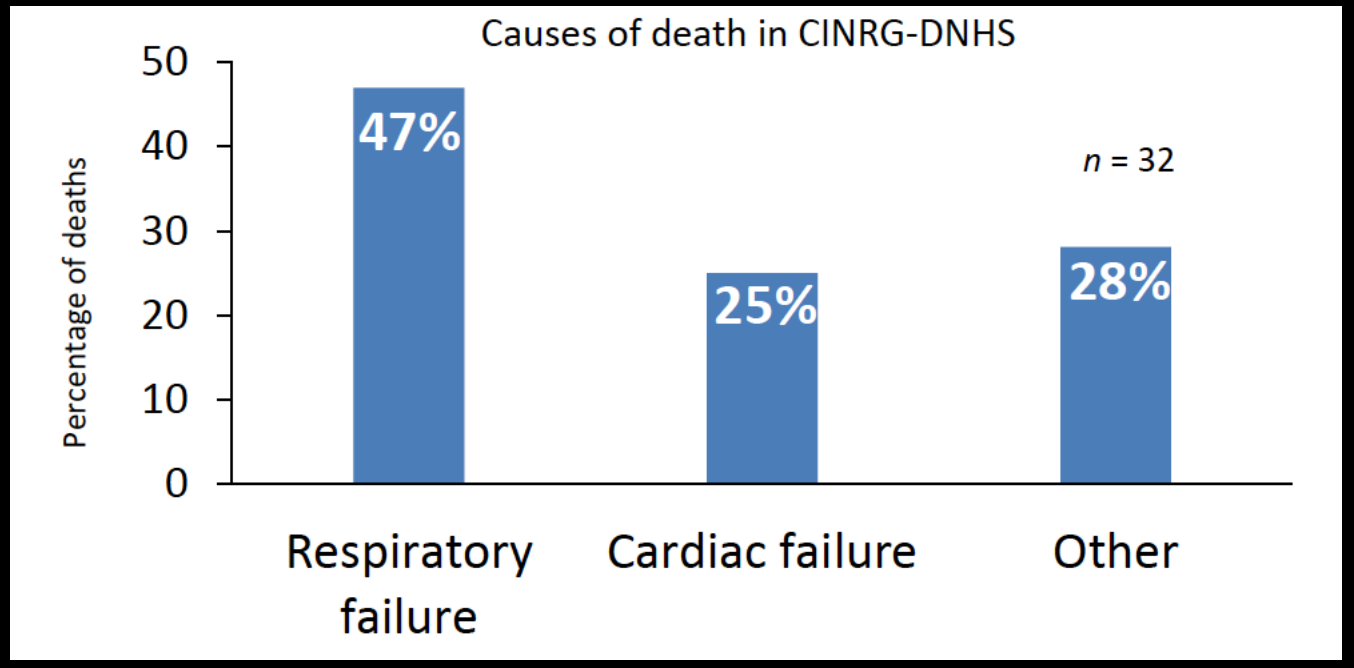

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Neuromuscular diseases with cardiomyopathy

- Duchenne muscular dystrophy
- Becker muscular dystrophy
- Other muscular dystrophies
  - Emery-Dreyfus
  - Myotonic dystrophy I

Neuromuscular diseases

Condition	Gene Locus	Gene Product	Heritance	Cardiac Features		
				Cardiomyopathy	Arrhythmia	Conduction
X-linked recessive muscular dystrophies						
Duchenne	Xp21	Dystrophin	XLR	Common (DCM)	Common (late)	Rare (late)
Becker	Xp21	Dystrophin	XLR	Common	Common	Rare (late)
Emery-Dreifuss	Xq28	Emerin	XLR	Rare	Common	Common (SD)
Limb-girdle muscular dystrophies						
LGMD1B	1q11–q21	Lamin A and C	AD	Common (DCM)	Common (AT, VT)	Common (SD)
LGMD1C	3p25	Caveolin-3	AD	Rare (DCM)	Not reported	Rare (AVB)
LGMD1E	7q36	DNAJB6 (co-chaperone)	AD	Rare	Rare	Rare
LGMD2B	2p13	Dysferlin	AR	Rare (DCM)	Not reported	Not reported
LGMD2C	13q12	γ-Sarcoglycan	AR	Common (DCM)	Rare	Rare
LGMD2D	17q12–q21	α-Sarcoglycan	AR	Common (DCM)	Rare	Rare
LGMD2E	4q12	β-Sarcoglycan	AR	Common (DCM)	Common	Common
LGMD2F	5q33–q34	δ-Sarcoglycan	AR	Rare	Rare	Rare
LGMD2I	19q13.3	Fukutin-related protein	AR	Common (DCM)	Rare	Rare
Associated with mitochondrial dysfunction						
Barth syndrome	Xq28	Tafazzin	XLR	Common (LVNC, DCM, HCM)	Occasional	None
Friedreich ataxia	9q21.11	Frataxin	AR	Common (HCM)	Common (late)	Rare
Myotonic dystrophies						
Myotonic dystrophy (DM) 1	19q13	Myotonin-protein kinase	AD	Occasional (DCM, HCM)	Common (AFL/AF, VT)	Common (SD)
Myotonic dystrophy (DM) 2	3q21	Zinc finger protein 9	AD	Rare in childhood	Rare in childhood	Rare in childhood
Congenital myopathies						
Central core disease	19q13.2	Ryanodine receptor	AD/AR	Rare (DCM)	Not reported	Not reported
Nemaline myopathy	1q21, 2q21–q22, 1q42.13, 19q13.4	α-Tropomyosin, nebulin, skeletal muscle α-actin, troponin T	AR/AD	DCM, HCM	Rare (long QT)	Common (mild)
Multiminicore disease	19q13.2, 1p36.13	Ryanodine receptor, selenoprotein N1	AR	Rare (HCM, RCM)	Unknown	Unknown
Centronuclear myopathy	19p13.2, 2q14, 2q31	Dynamin 2, bridging integrator 1, titin	AD/AR	Rare (DCM)	Rare	Rare
Myotubular myopathy	Xq28	Myotubularin	XLR	Not reported	Not reported	Not reported
Myosin storage myopathy	14q12	β-Myosin heavy chain	AD	Not reported	Not reported	Not reported
Congenital fiber type disproportion	1q21.2, 19q13.2, 1q42.13	α-Tropomyosin, ryanodine receptor, skeletal muscle α-actin	AR/AD	Rare (DCM)	Not reported	Not reported
Myofibrillar myopathies						
	2q35, 5q31, 10q22.3–q23.2, 11q23.1, 7q32–q35, 10q25.2–q26.2, Xq26	Desmin, myotilin, LIM domain binding protein 3, crystallin alpha B, filamin C gamma, BCL2-associated athanogene 3, four-and-a-half LIM domains 1	AD	Common	Rare (late, AF)	Rare (AVB)

Neuromuscular diseases with cardiomyopathy

- Duchenne muscular dystrophy
- Becker muscular dystrophy
- Other muscular dystrophies
  - Emery-Dreyfus
  - Myotonic dystrophy I

	DMD	BMD
Dystrophin protein	Absent	Partially functional
Incidence	1:5,000 male births	1:19,000
Mean age at onset, yrs	3–5	12
Mean age of becoming nonambulatory, yrs	~12	~27
Mean life expectancy, yrs	Mid to late 20s	40s
Onset of cardiomyopathy, yrs	16–18	Variable; cardiomyopathy may precede skeletal symptoms

BMD = Becker muscular dystrophy; DMD = Duchenne muscular dystrophy.

Circulation. 2017;136(13):e200-e231

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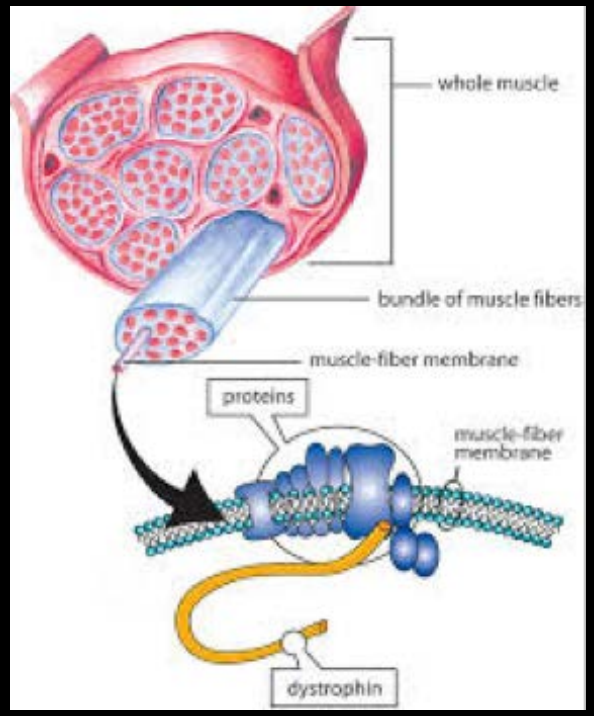
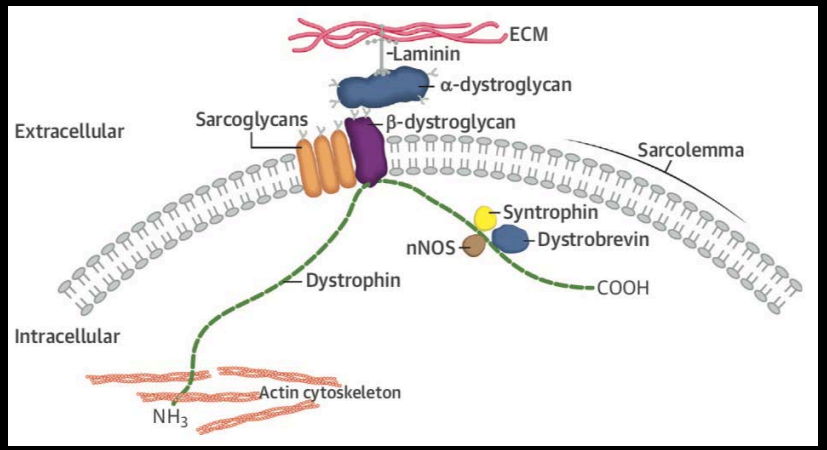
Duchenne cardiomyopathy

- Affects 1 in 3500 males.
- Caused by dystrophin gene mutations
- Results in progressive skeletal muscle weakness.
- Results in progressive heart cell death.
- By 18, 70% have depressed heart function.





Viollet, L. (2012) *Am J Cardiol,* 110(1), 98-102.

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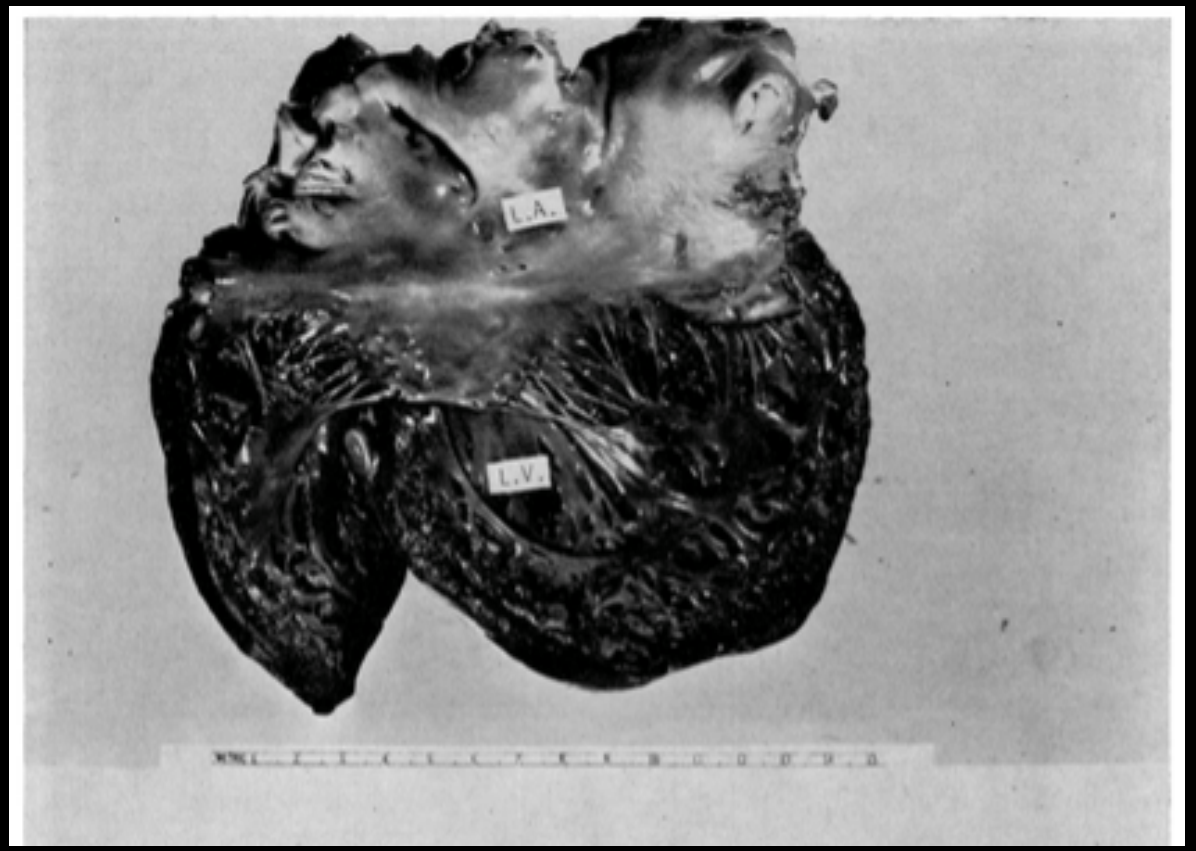
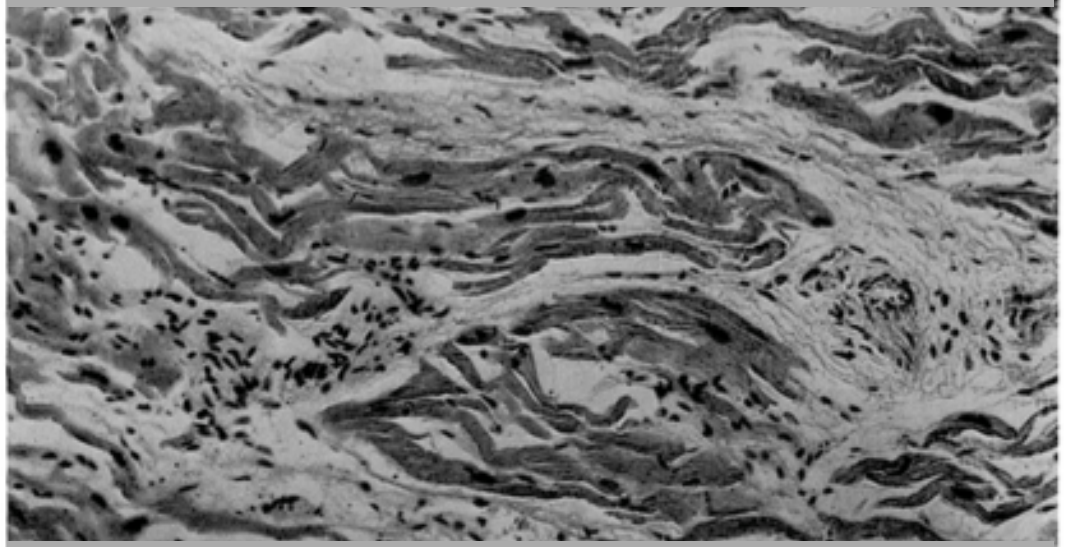
The Cardiomyopathy of Progressive Muscular Dystrophy
JOSEPH K. PERLOFF, ANTONIO C. DE LEON, JR. and DESMOND O'DOHERTY
Circulation 1966;33;625-648



"Multifocal degenerative changes"



"Fibrosed adipose tissue"

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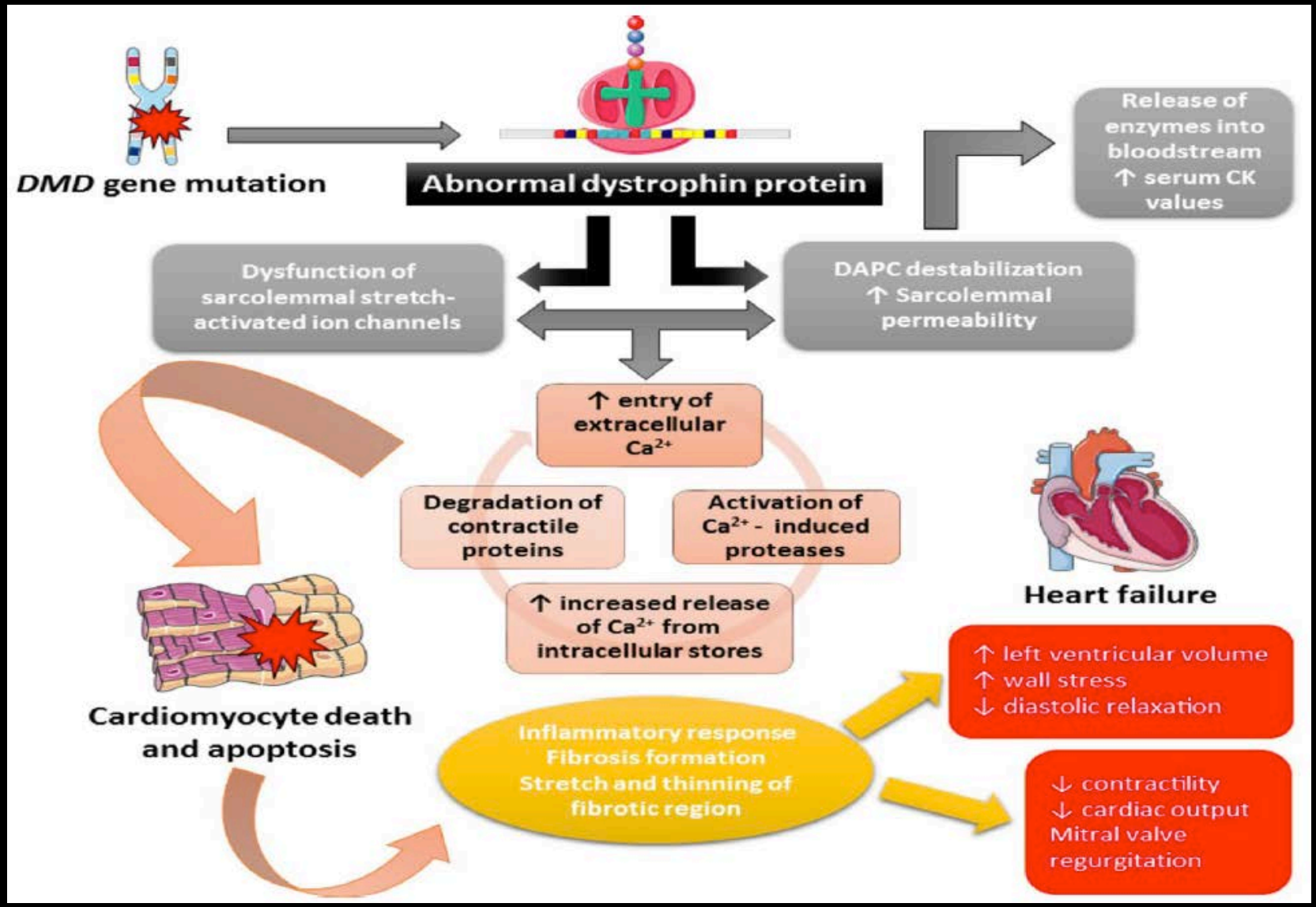
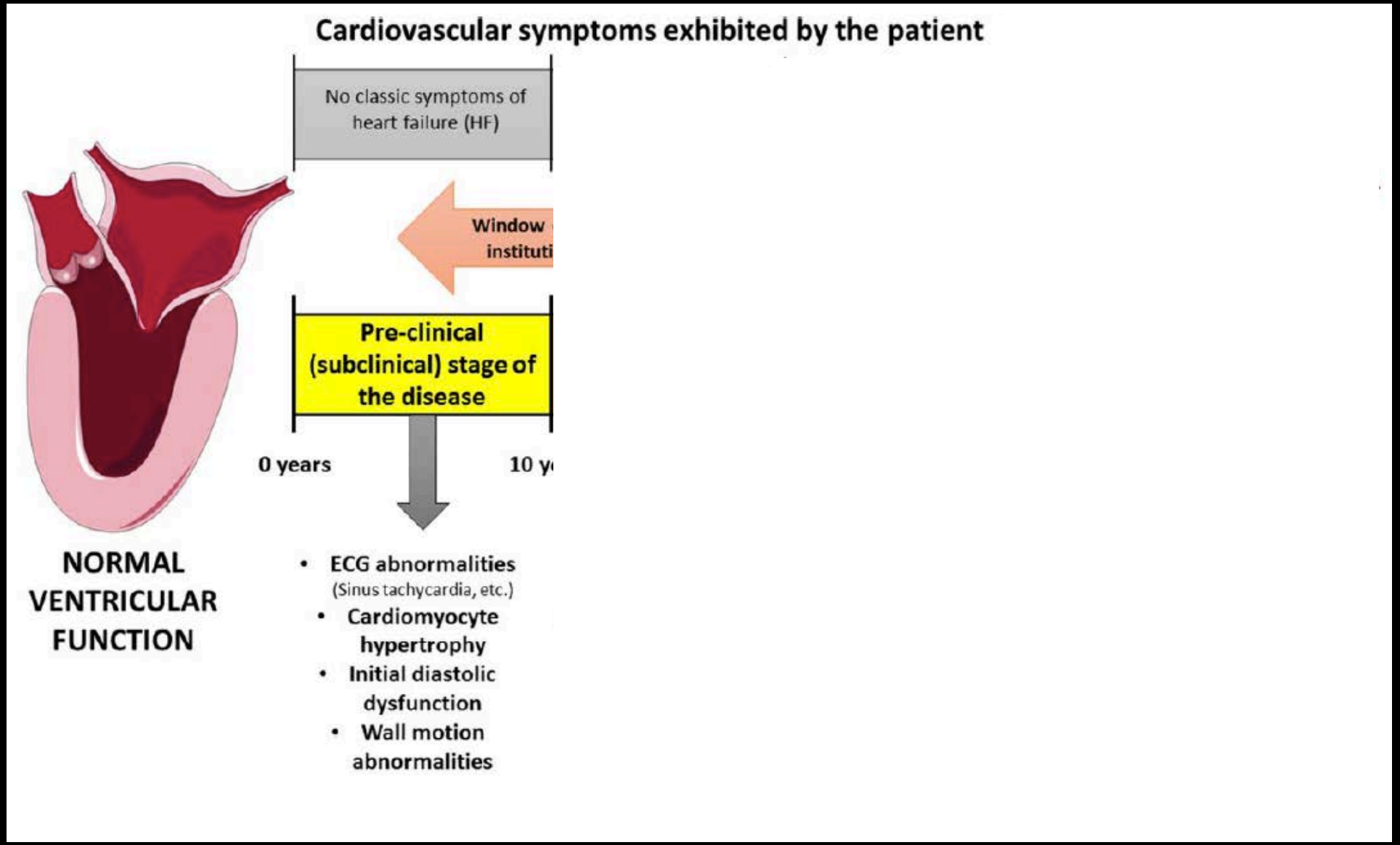


D'Amario D, *Heart*. 2017;103(22):1770-1779.



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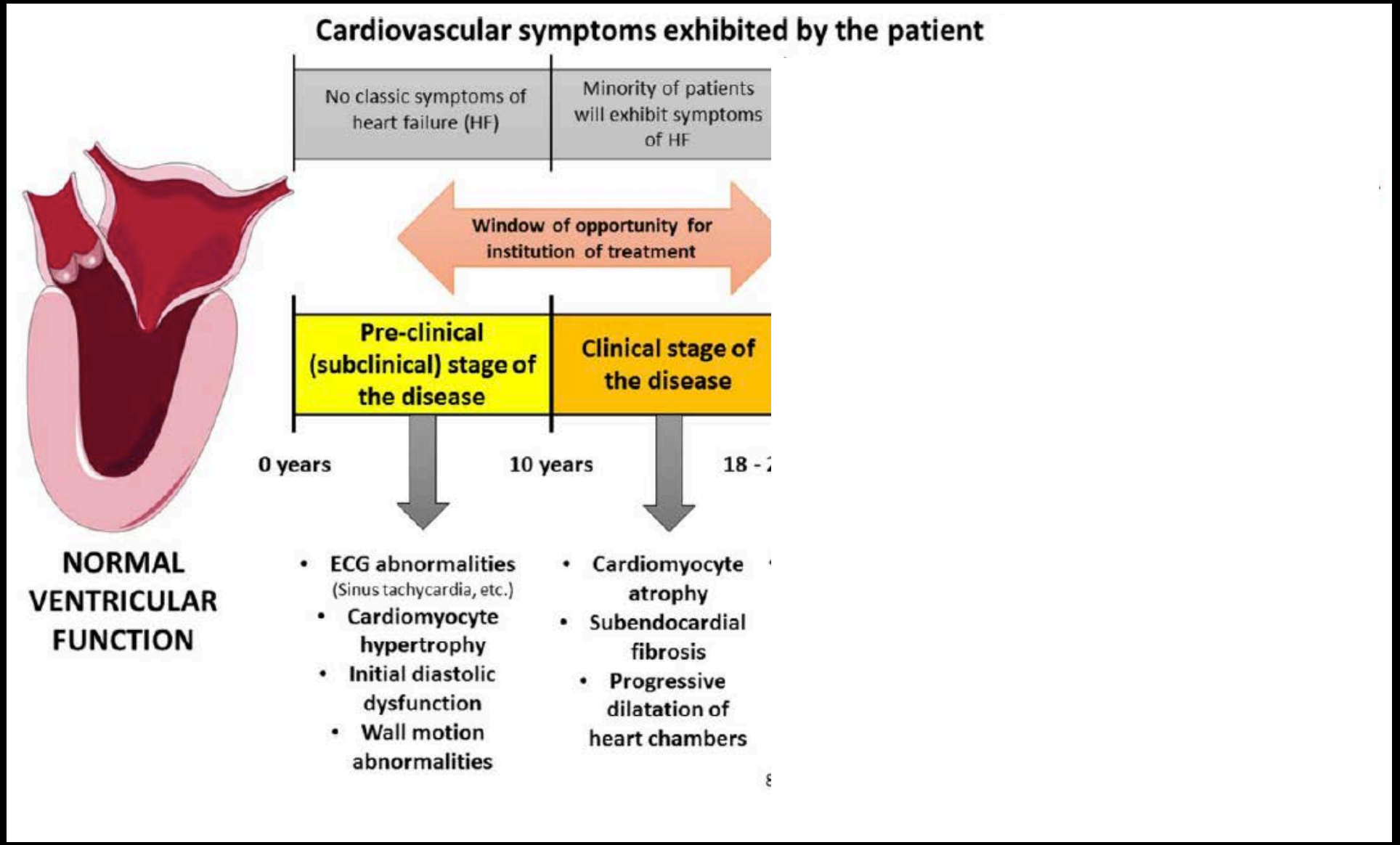

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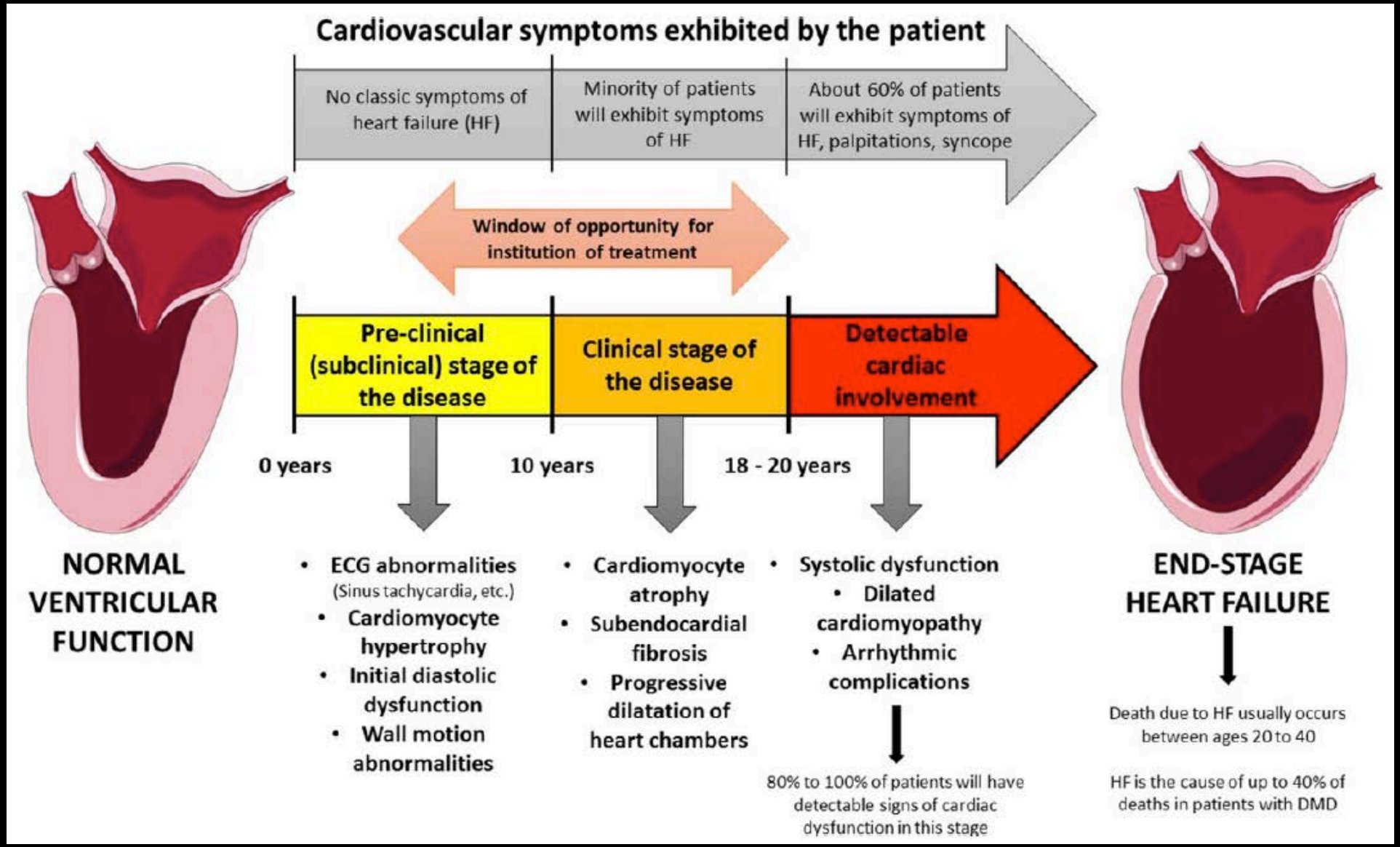

D'Amario D, *Heart*. 2017;103(22):1770-1779.

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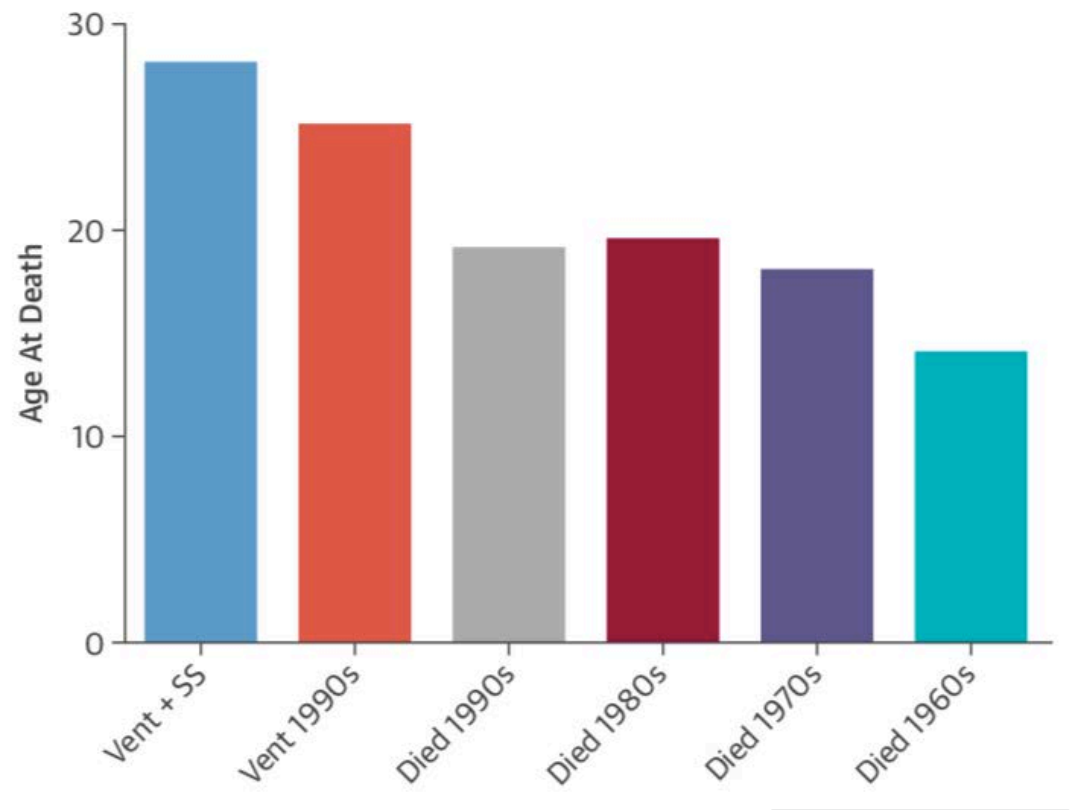
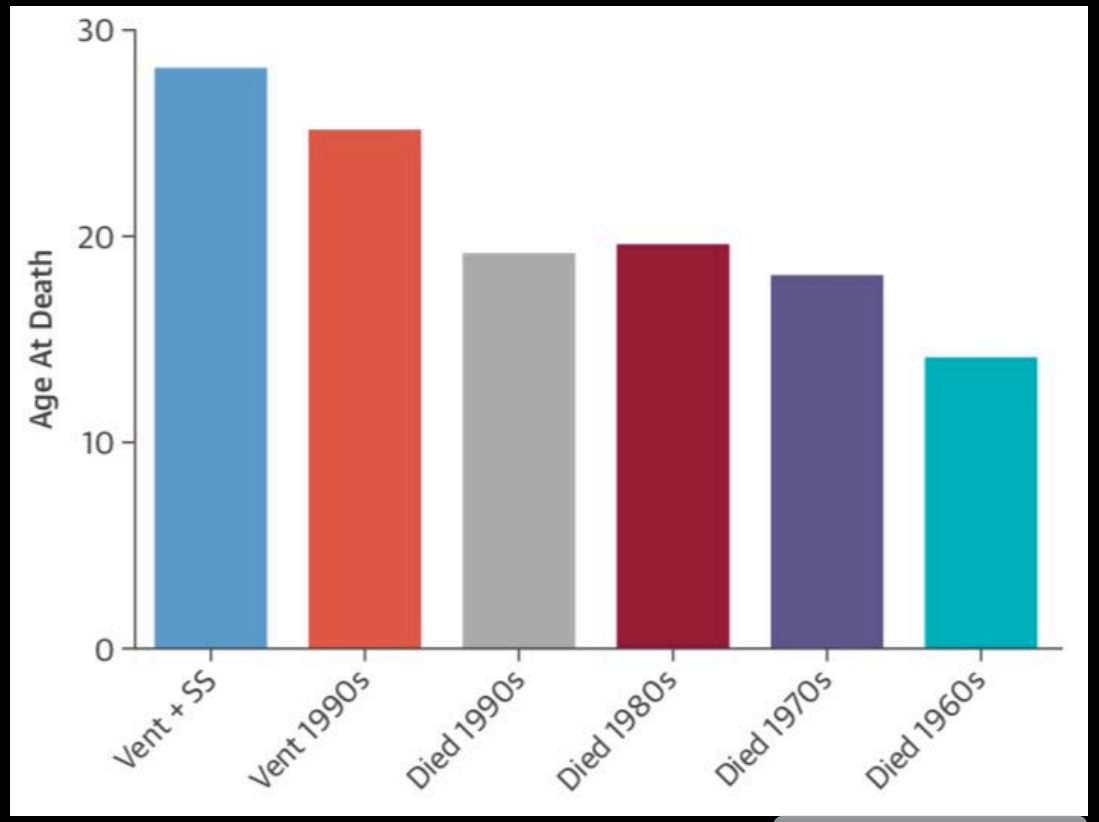
Survival by era



Neuromuscular Disorders. 2002;12(10):926-929.

**SS → spine surgery

Survival by era



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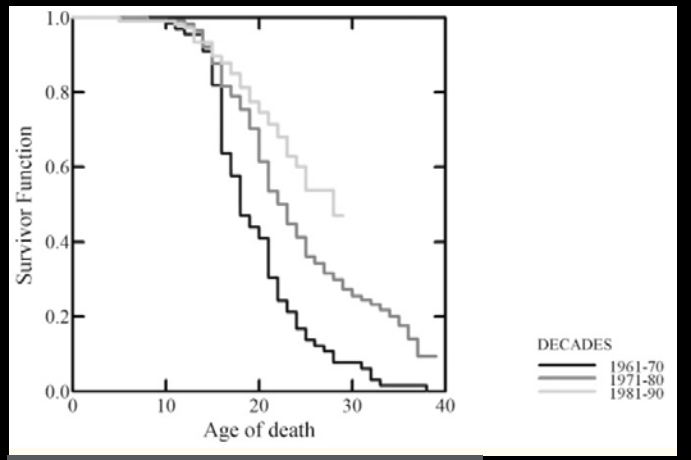
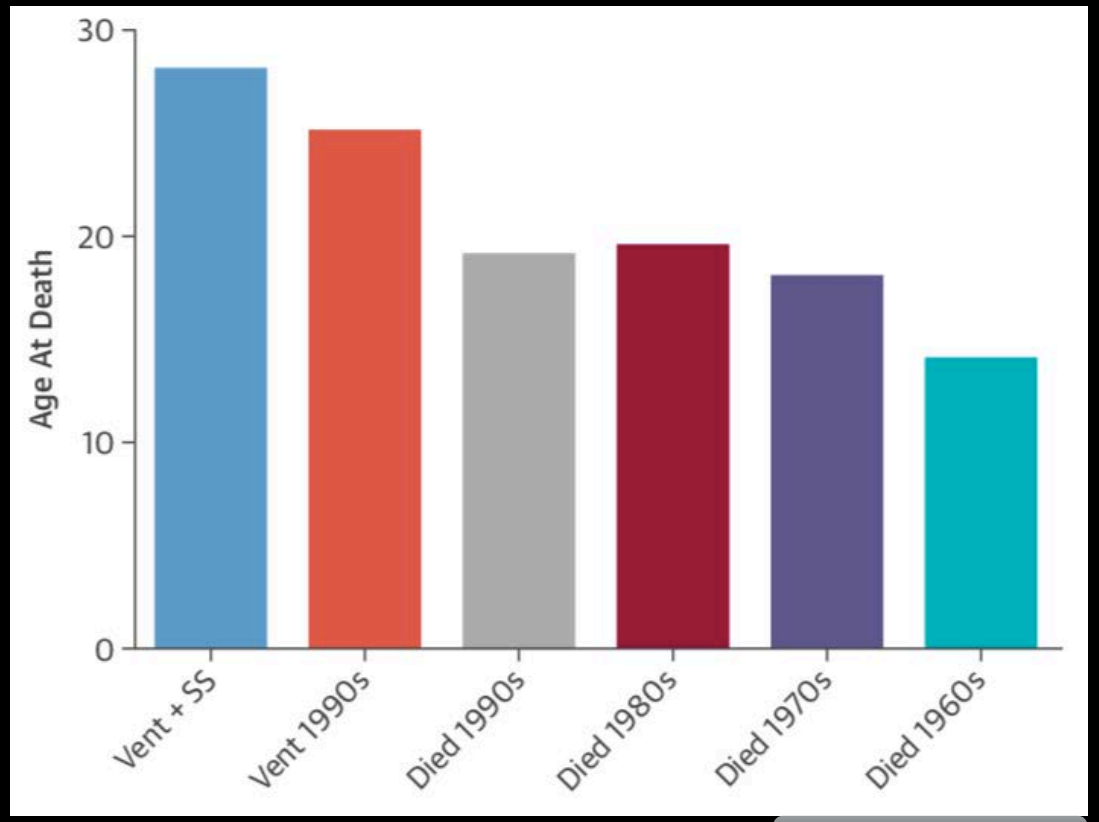


Acta Myol. 2012 Oct; 31(2): 121–125

Survival by era



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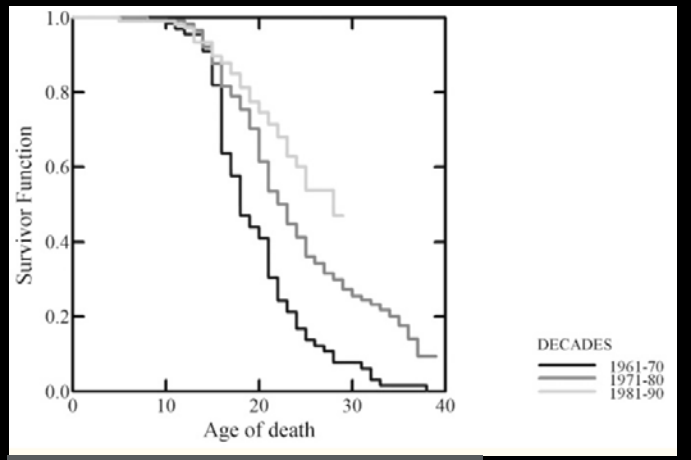

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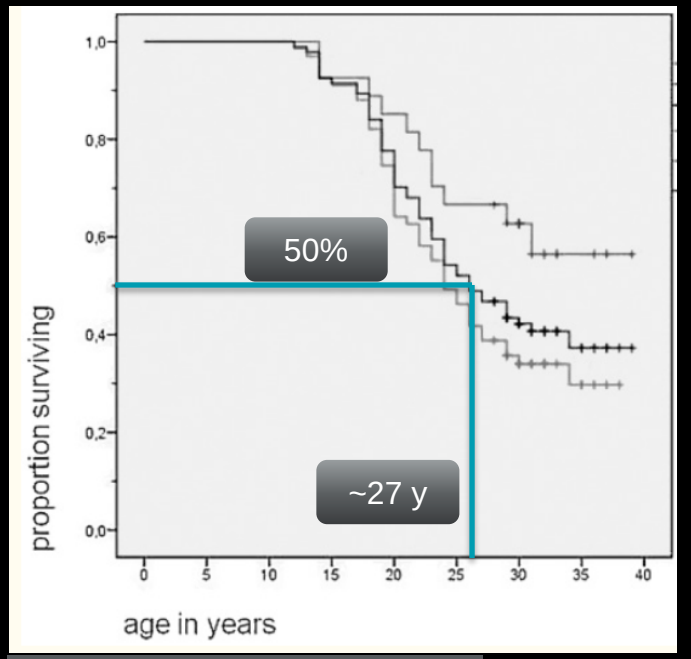

Acta Myol. 2012 Oct; 31(2): 117–120

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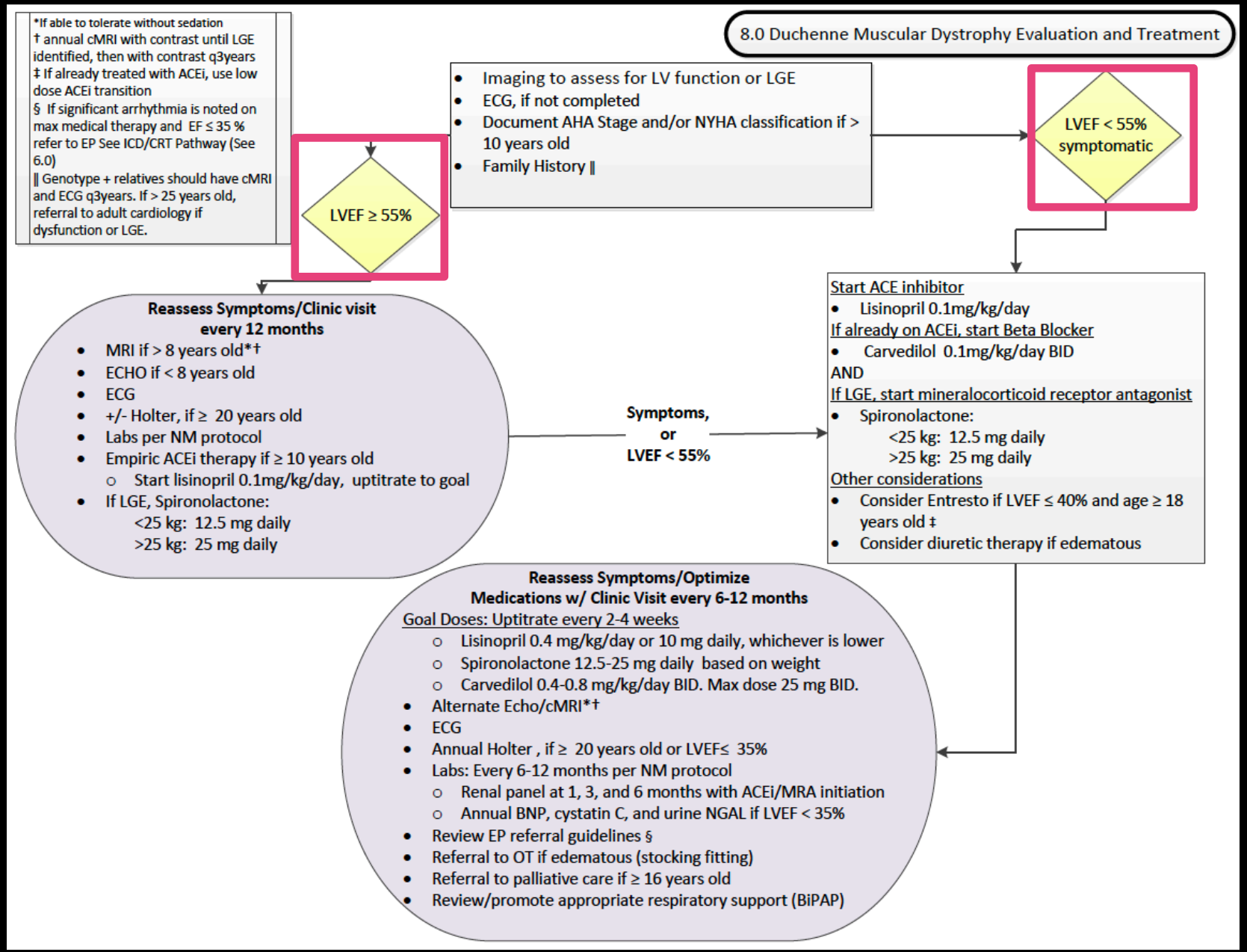

Created by Chet Villa, MD and Tom Ryan, MD
CCHMC Neuromuscular Clinic (2019)

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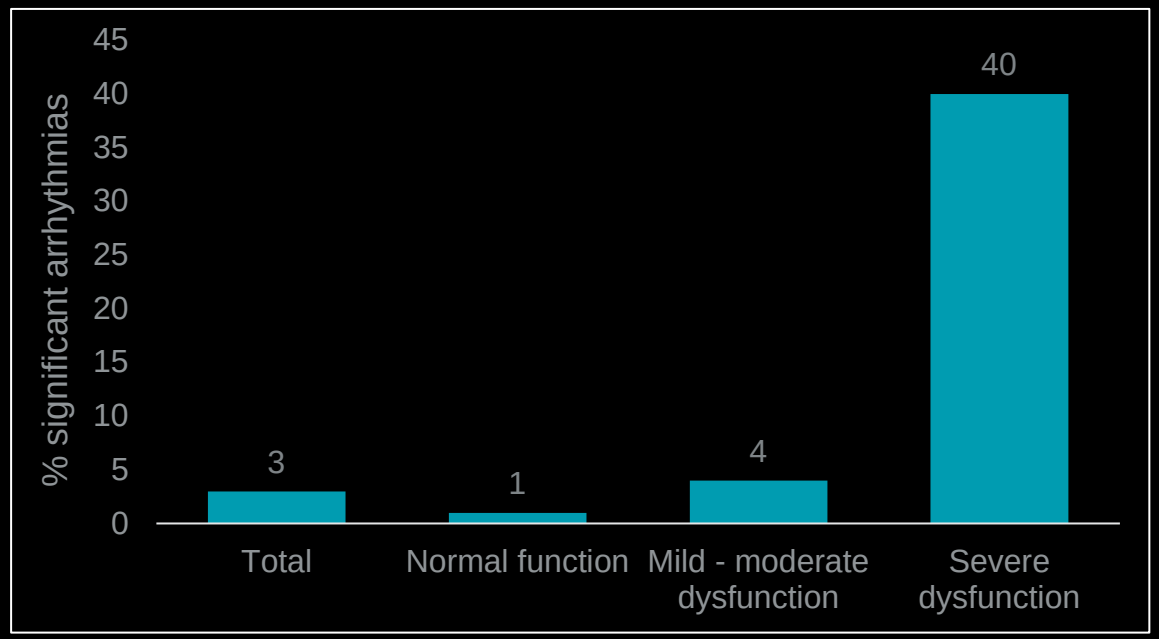
Ambulatory Monitoring and Arrhythmic Outcomes in Pediatric and Adolescent Patients With Duchenne Muscular Dystrophy

Chet R. Villa, MD; Richard J. Czosek, MD; Humera Ahmed, MD; Philip R. Khoury, MS; Jeffrey B. Anderson, MD; Timothy K. Knilans, MD; John L. Jefferies, MD; Brenda Wong, MD; David S. Spar, MD

	Total	EF ≥55%	EF 54% to 35%	EF <35%
Number of patients, n	235	184	46	5
Number of Holters, n	442	337	95	10
Significant Holter finding, n (%)	12 (3)	4 (1)	4 (4)	4 (40)



J Am Heart Assoc. 2015;5(1)

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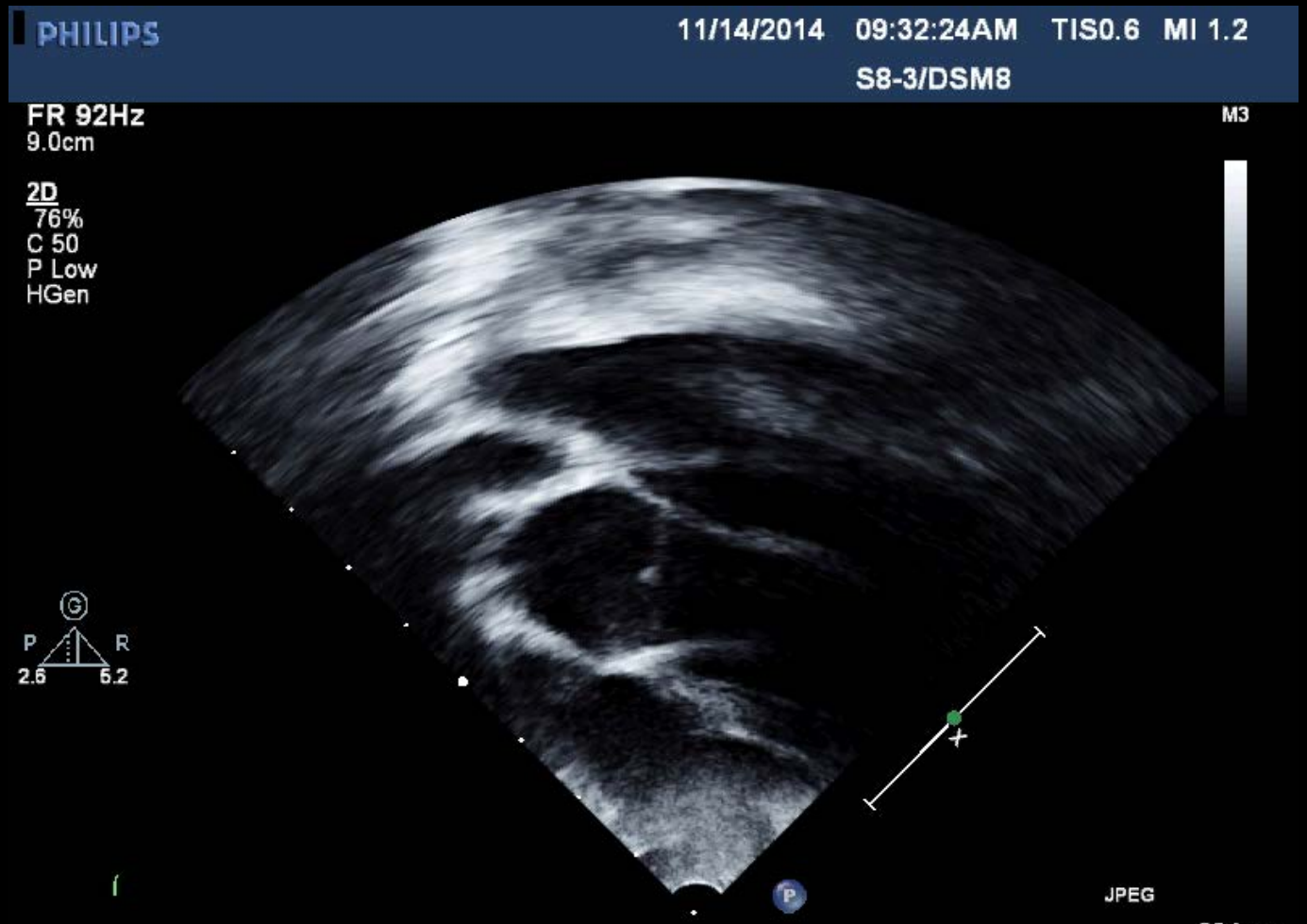
Why cardiac MR ?

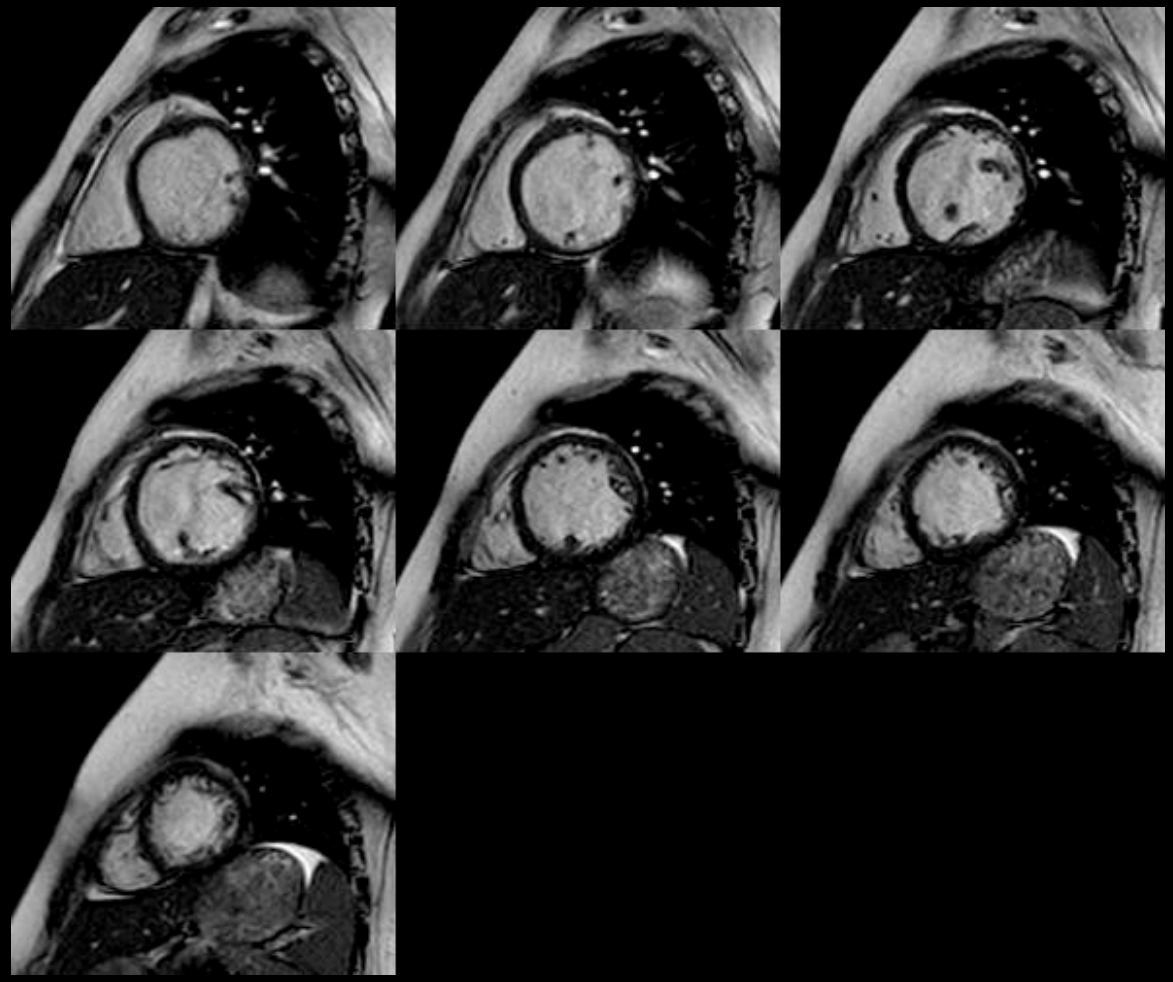


Cardiac MR in Duchenne

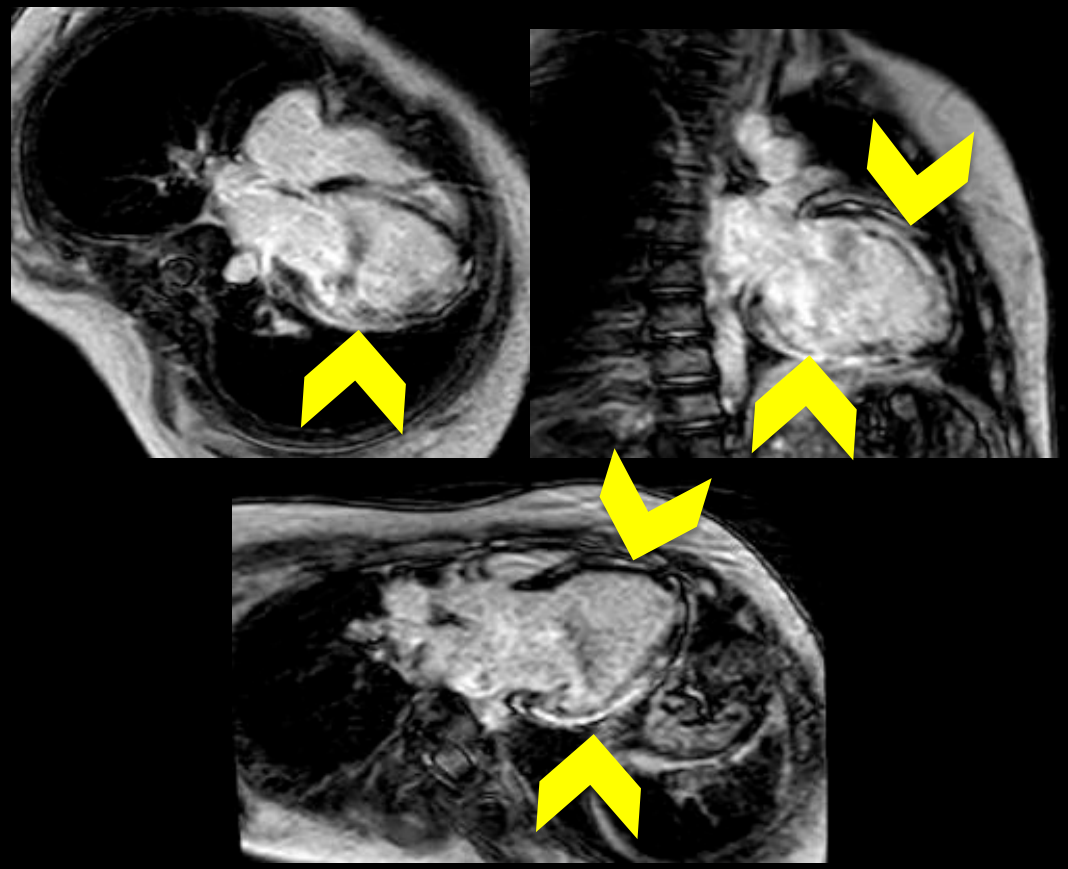
- Replaces echocardiogram after age 6-8
- Patients undergo yearly exams
- No sedation
- Typical exam ~30 minutes
- Abbreviated non-contrast version ~10 minutes
- 2238 exams since 2004

Cardiac MR findings

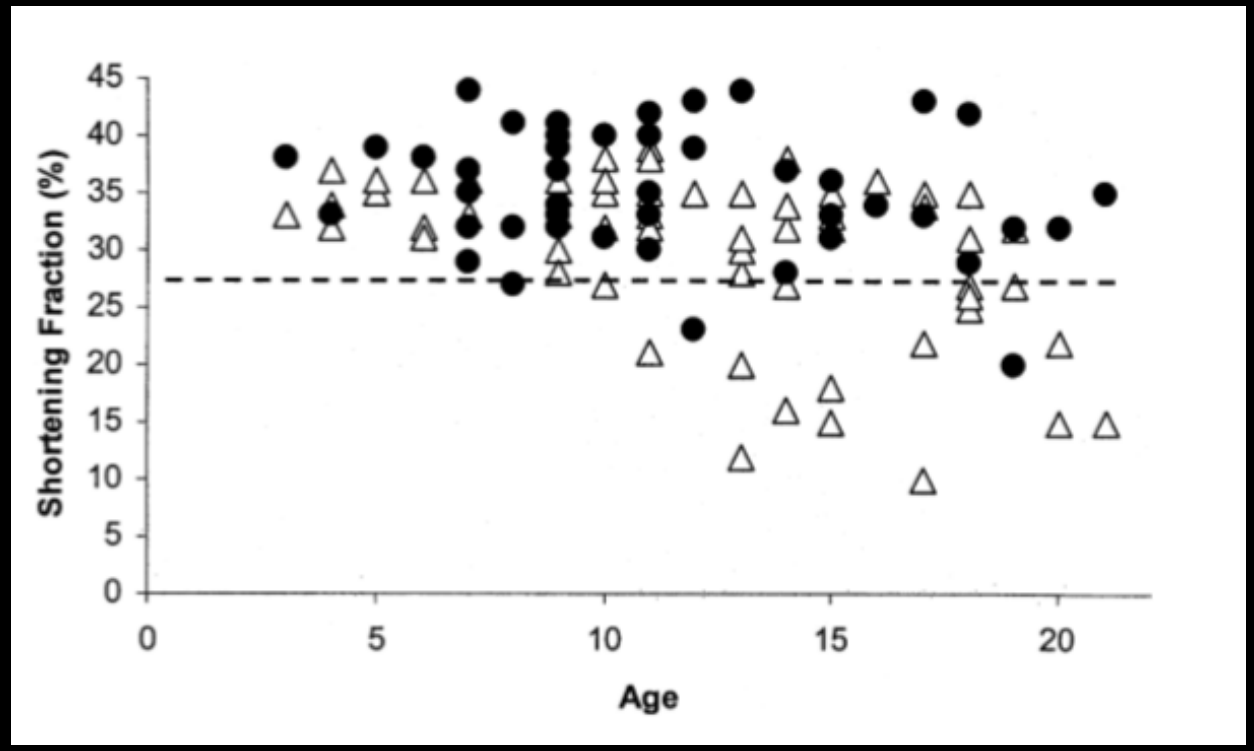
Cardiac function – advanced disease



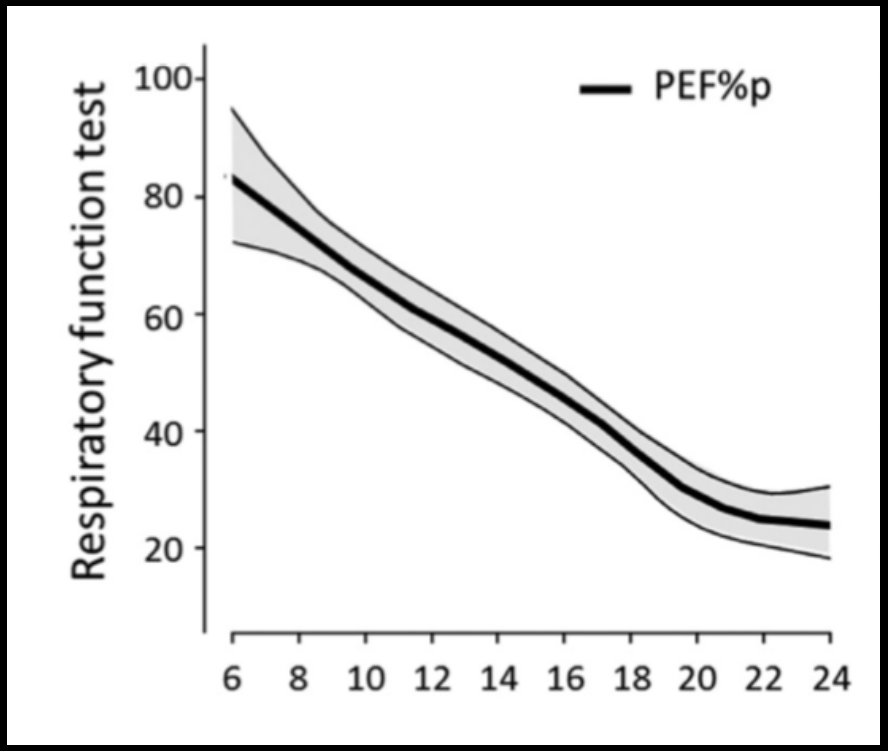
Late gadolinium enhancement (“LGE”)



DMD cardiomyopathy – natural history

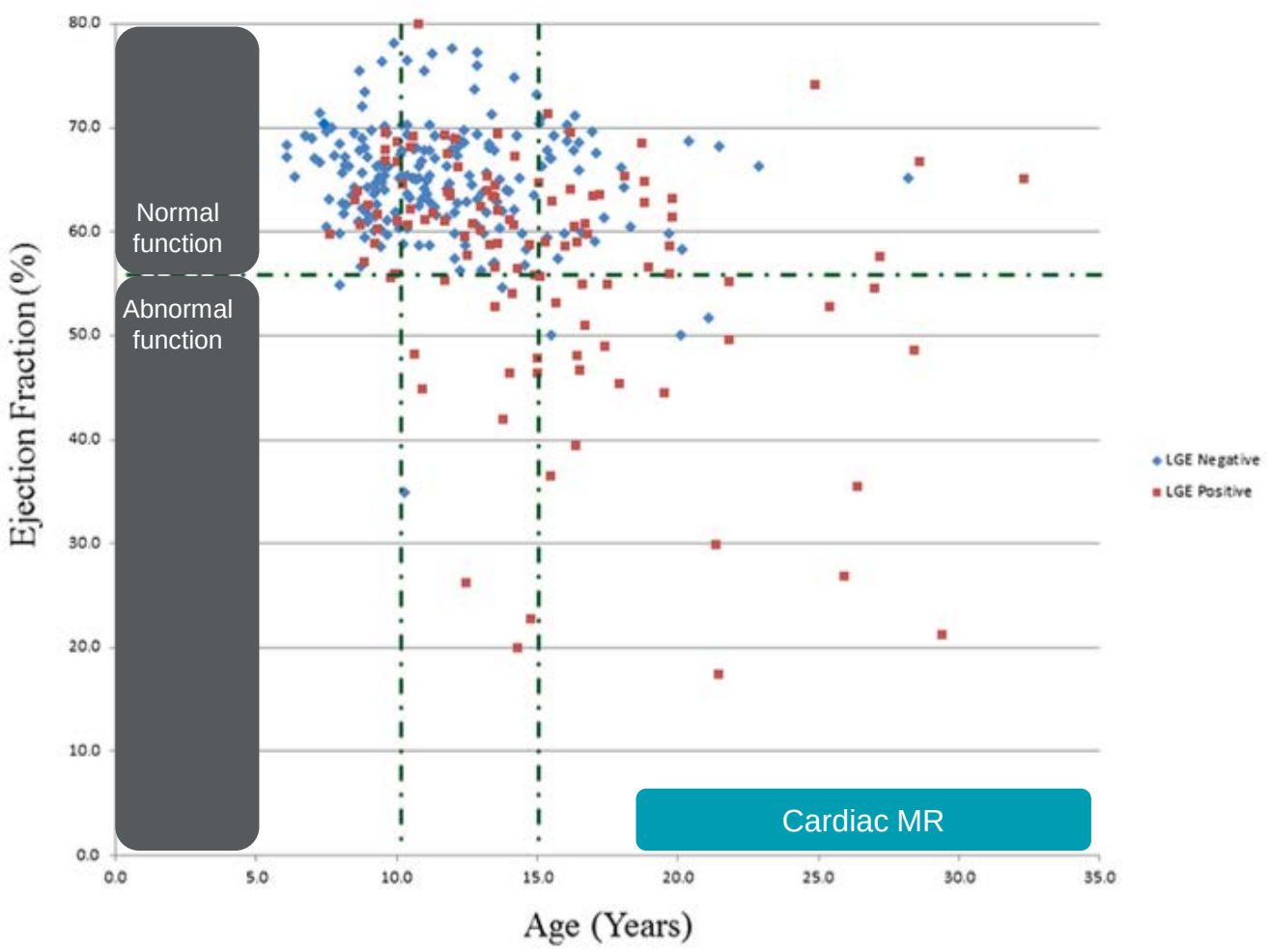


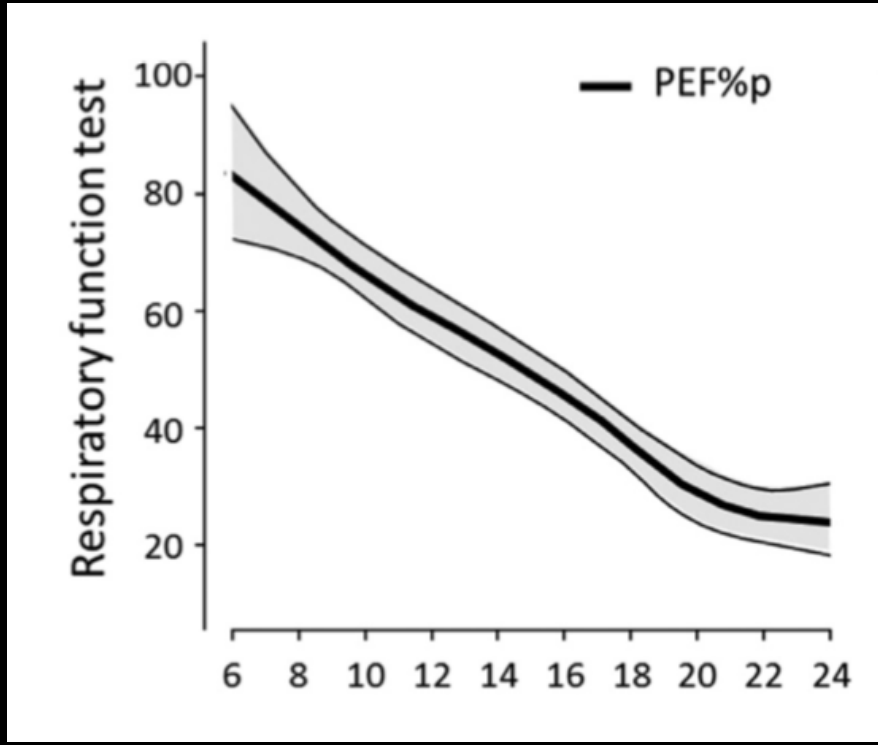
Hor, K. N., et al. (2013). JCMR, *15*(1), 107.



Neuromuscul Disord. 2018;28(11):910-913.

DMD cardiomyopathy – natural history





Neuromuscul Disord. 2018;28(11):910-913.

Hor, K. N., et al. (2013). JCMR, *15*(1), 107.

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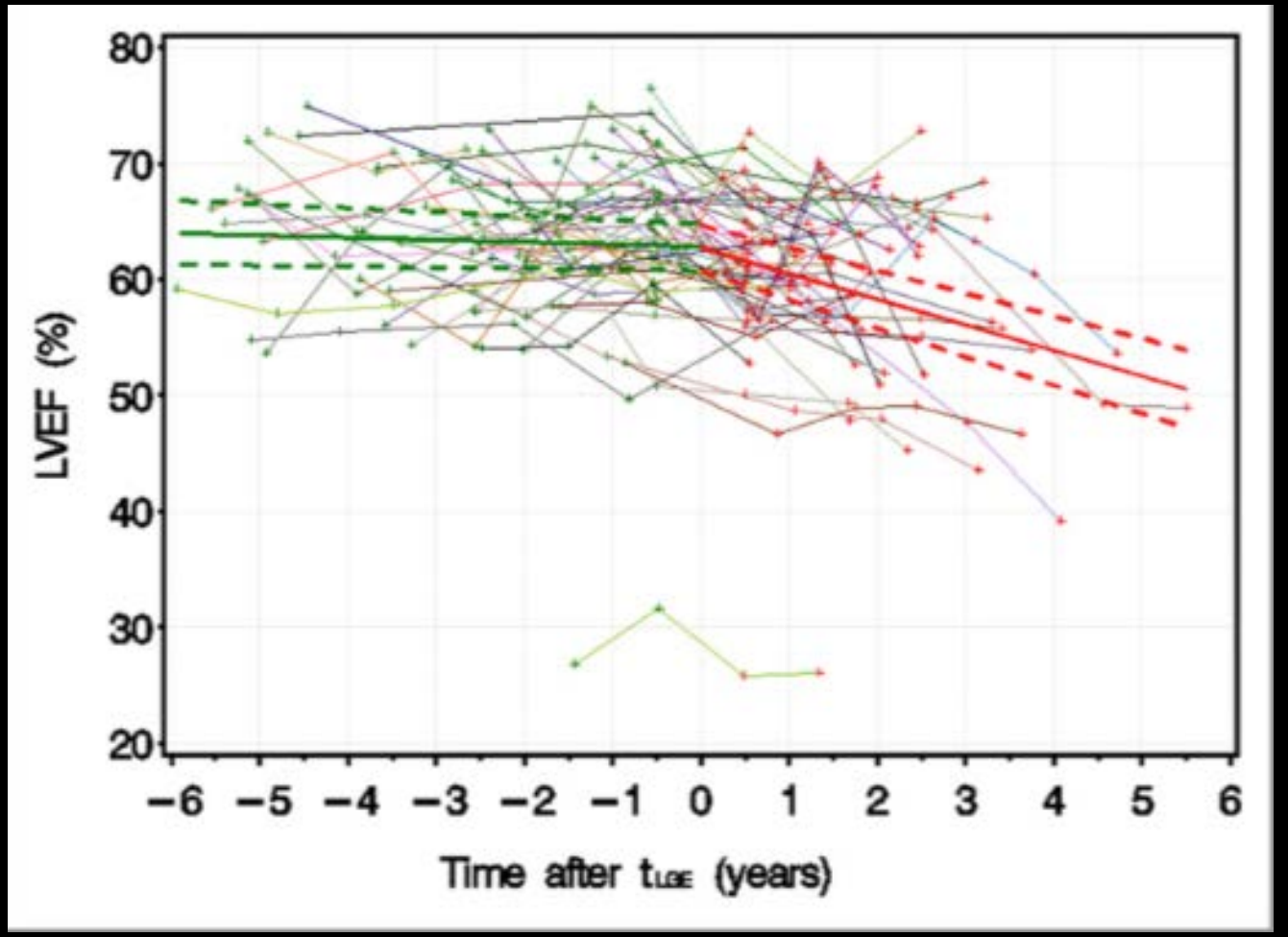
Myocardial Fibrosis Burden Predicts Left Ventricular Ejection Fraction and Is Associated With Age and Steroid Treatment Duration in Duchenne Muscular Dystrophy

Animesh Tandon, MD, MS; Chet R. Villa, MD; Kan N. Hor, MD; John L. Jefferies, MD, MPH; Zhiqian Gao, PhD; Jeffrey A. Towbin, MD, MS; Brenda L. Wong, MD; Wojciech Mazur, MD; Robert J. Fleck, MD; Joshua J. Sticka, MD; D. Woodrow Benson, MD, PhD; Michael D. Taylor, MD, PhD



Tandon, A., et al. (2015). Journal of the American Heart Association, 4(4),

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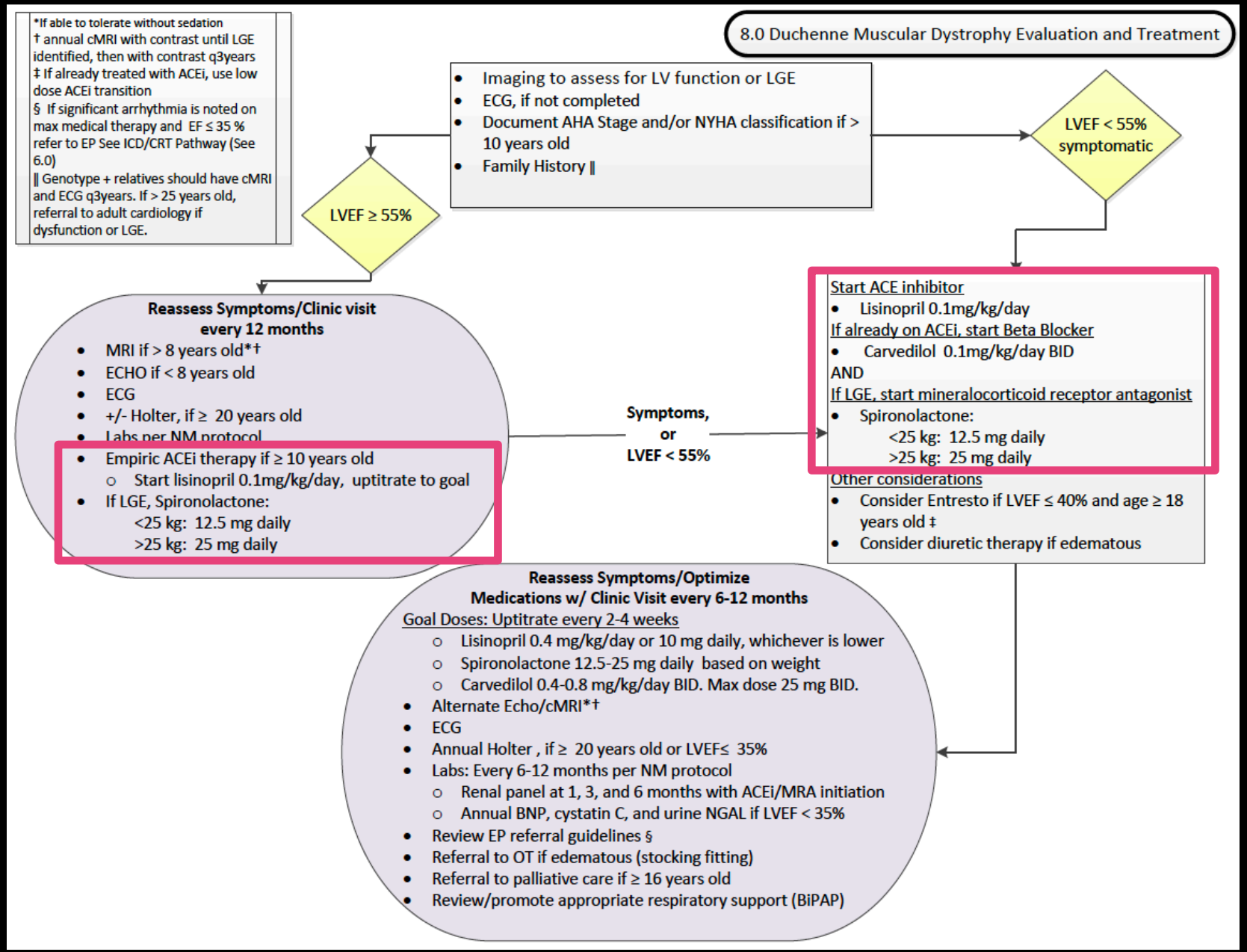

Created by Chet Villa, MD and Tom Ryan, MD
CCHMC Neuromuscular Clinic (2019)

Therapies – current evidence

	Level of Evidence
Corticosteroids	++
ACE inhibitors	+++
Beta-blockers	+
Mineralocorticoid receptor antagonists	+

ACE = angiotensin-converting enzyme; DMD = Duchenne muscular dystrophy.

J Am Coll Cardiol. 2016;67(21):2533-2546.

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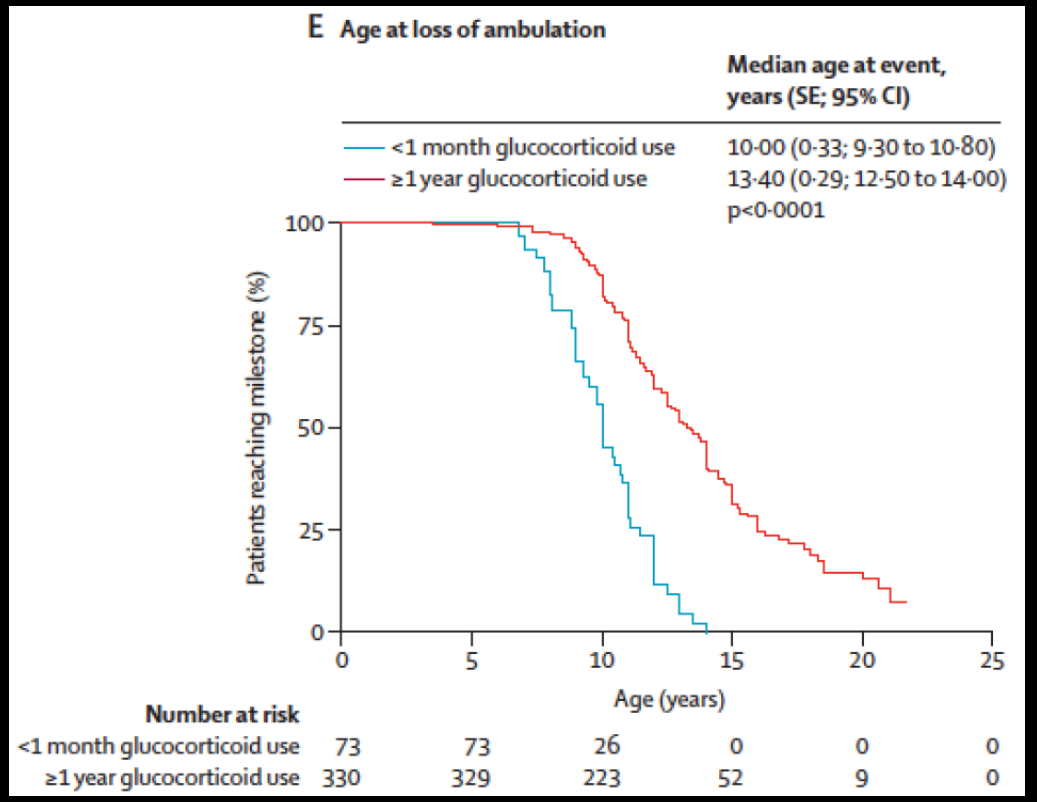
Steroids



Lancet. 2018;391(10119):451-461. doi:10.1016/S0140-6736(17)32160-8.

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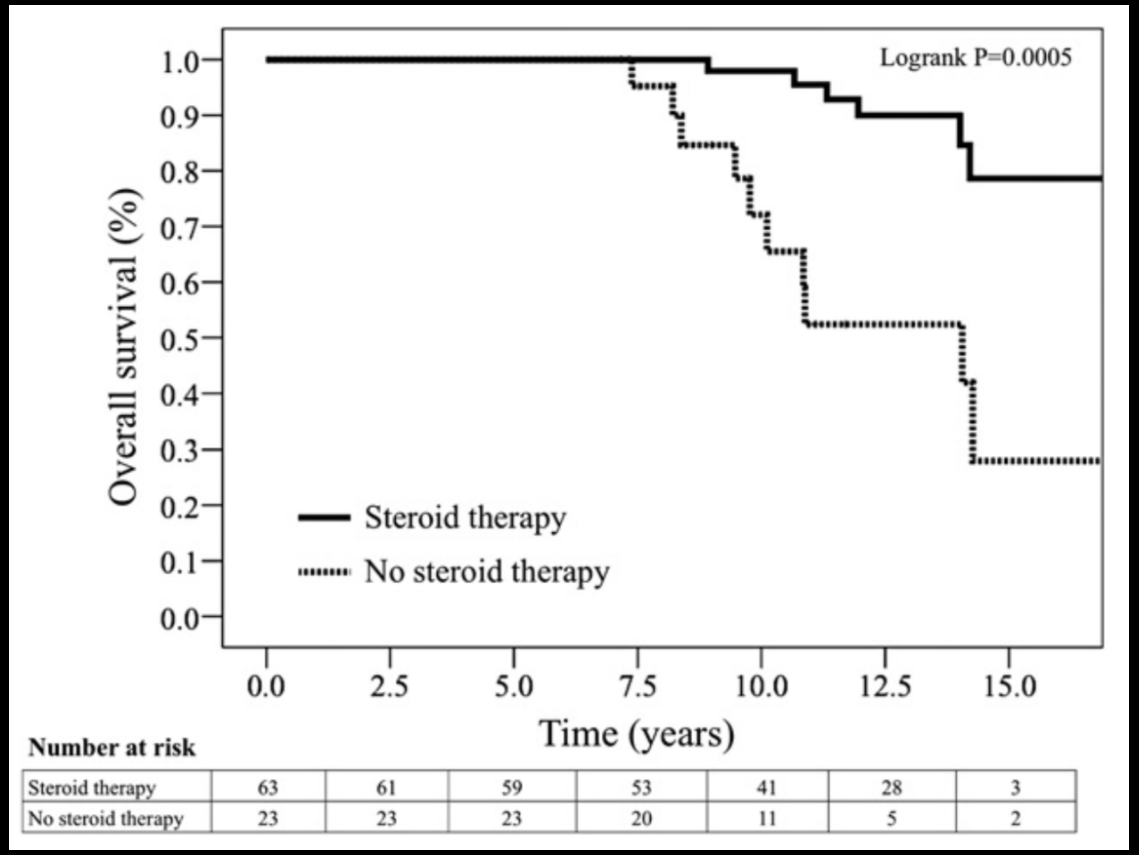

J Am Coll Cardiol. 2013;61(9):948-954.

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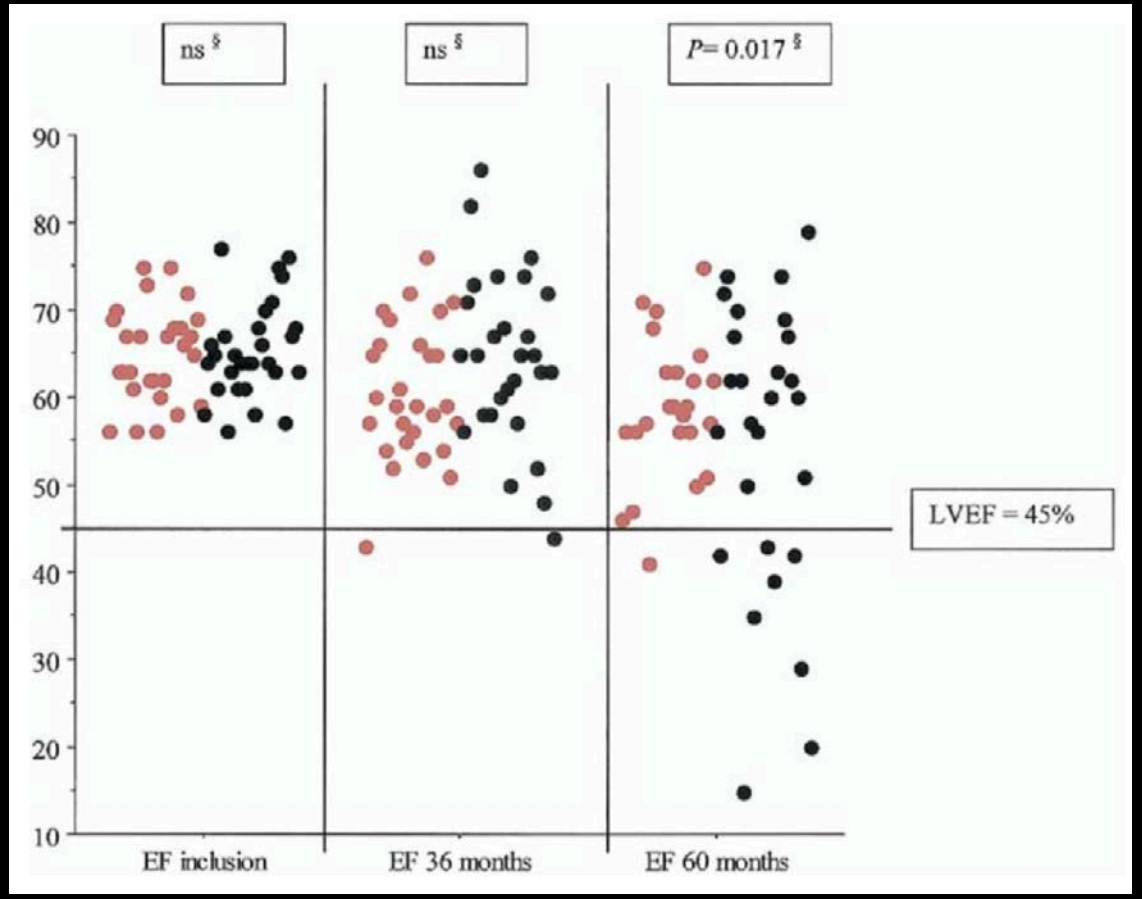
ACE inhibitors



Am J Cardiol. 2006;98(6):825-827

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ACE inhibitors	+++
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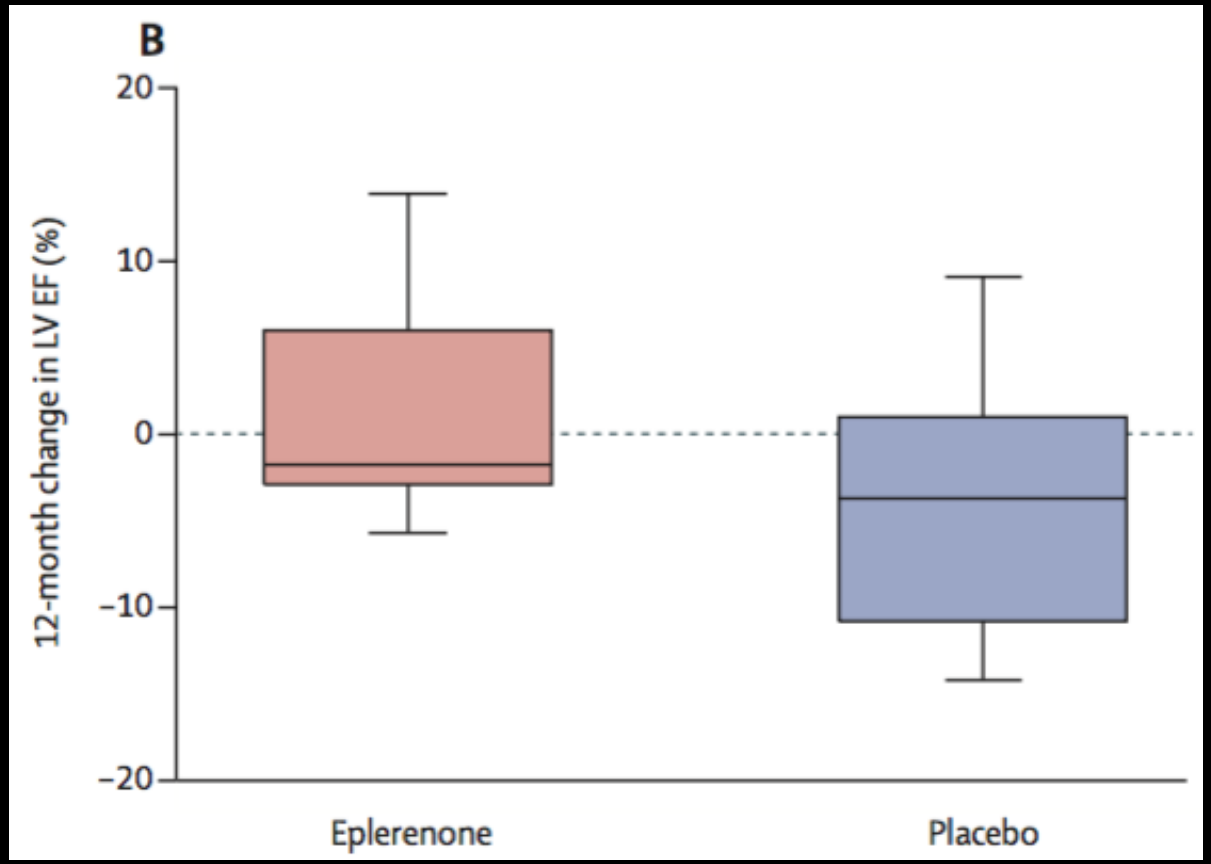
J Am Coll Cardiol. 2016;67(21):2533-2546.

Mineralcorticoid receptor antagonists



Lancet Neurology (2014) 14(2), 1–9.

Eplerenone for early cardiomyopathy in Duchenne muscular dystrophy: a randomised, double-blind, placebo-controlled trial

Subha V Raman, Kan N Hor, Wojciech Mazur, Nancy J Halnon, John T Kissel, Xin He, Tam Tran, Suzanne Smart, Beth McCarthy, Michael D Taylor, John L Jefferies, Jill A Rafael-Fortney, Jeovanna Lowe, Sharon L Roble, Linda H Cripe

	Eplerenone	Placebo	p value
Imaging			
Left ventricular strain, %	0·84% (2·68)	0·38% (2·56)	0·602
Left ventricular ejection fraction, %	0 (−3·8 to 4·0)	1·0% (−5·0 to 2·1)	0·474
EDV, mL	1·50 (14·35)	0·87 (13·70)	0·893
ESV, mL	1·4 (−4·5 to 6·6)	1·7 (−2·9 to 3·6)	0·915
LGE, % of left ventricular mass	−2% (6)	4% (6)	0·034
Blood			
Troponin-I, ng/mL	0 (−0·01 to 0·01)	0 (−0·02 to 0·01)	0·840
Total creatine kinase, U/L	−590 (−1868 to 4)	−520 (−3156 to 1205)	0·589
Creatine kinase MB, %	0·19% (1·52)	0·13% (1·68)	0·616
Osteopontin, ng/mL	−13·25 (42·12)	−11·06 (33·56)	0·859

Data are mean (SD) or median (IQR). LGE=late gadolinium enhancement. EDV=end-diastolic volume. ESV=end-systolic volume.

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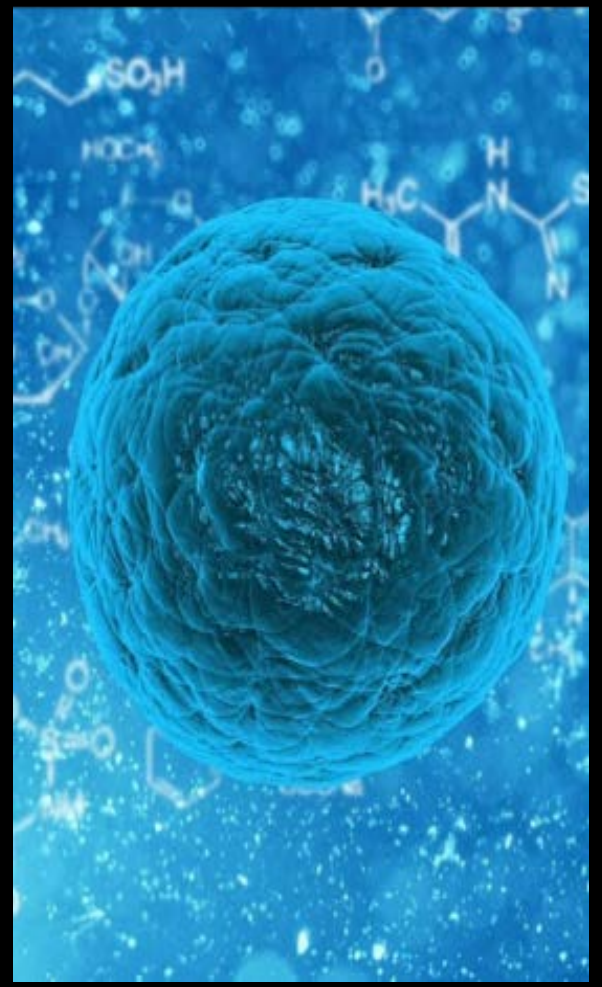
Lancet Neurology (2014) 14(2), 1–9.

Capricor's CAP-1002 Technology

CAP-1002 is a biologic consisting of allogeneic cardiosphere-derived cells (CDCs)

- Manufactured from donated heart muscle
- Does not act by "stemness" - the cells do not engraft into host tissue
- Mechanism: cells secrete exosomes:
  - Contain miRNA, non-coding RNAs and proteins
  - Internalized by target cells
  - Stimulate diverse and lasting changes in cellular behavior
  - 3 known miRNAs drive CAP-1002 potency
- **CAP-1002 has been investigated in multiple independent clinical trials and more than 150 human subjects to date**



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HOPE-Duchenne Focused on Older DMD Patients

- Phase I/II study: 25 patients, randomized and open-label
- One-time, multi-vessel, intracoronary delivery of cells
- HOPE population were all on stable corticosteroids
- Very limited options for this patient population

https://n.neurology.org/content/92/8/e866

RESULTS

- Reduction in cardiac scar at 6 and 12 months measured by MRI
- Improvement in cardiac function (systolic wall thickening) at 6 and 12 months
- Improvements shown in PUL (mid + distal)
  - Best improvement shown within the first 3 months
- Study published in February 2019 in Journal of Neurology

35

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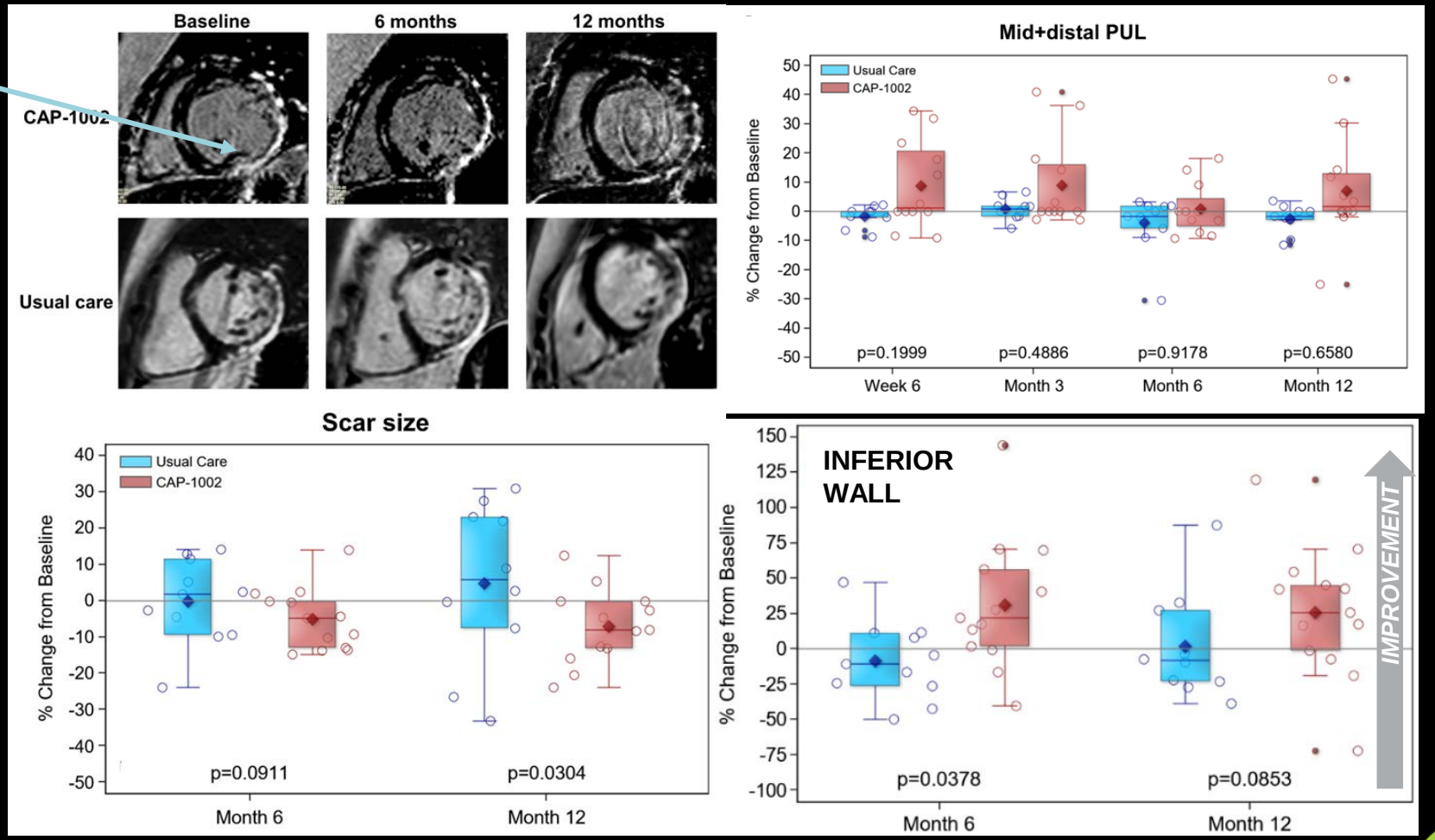
HOPE-Duchenne:

Reduced Cardiac Scar and Improved PUL



Taylor M, Jefferies J, Byrne B, et al. Cardiac and skeletal muscle effects in the randomized HOPE-Duchenne trial. *Neurology*. 2019;92(8):e866-e878.

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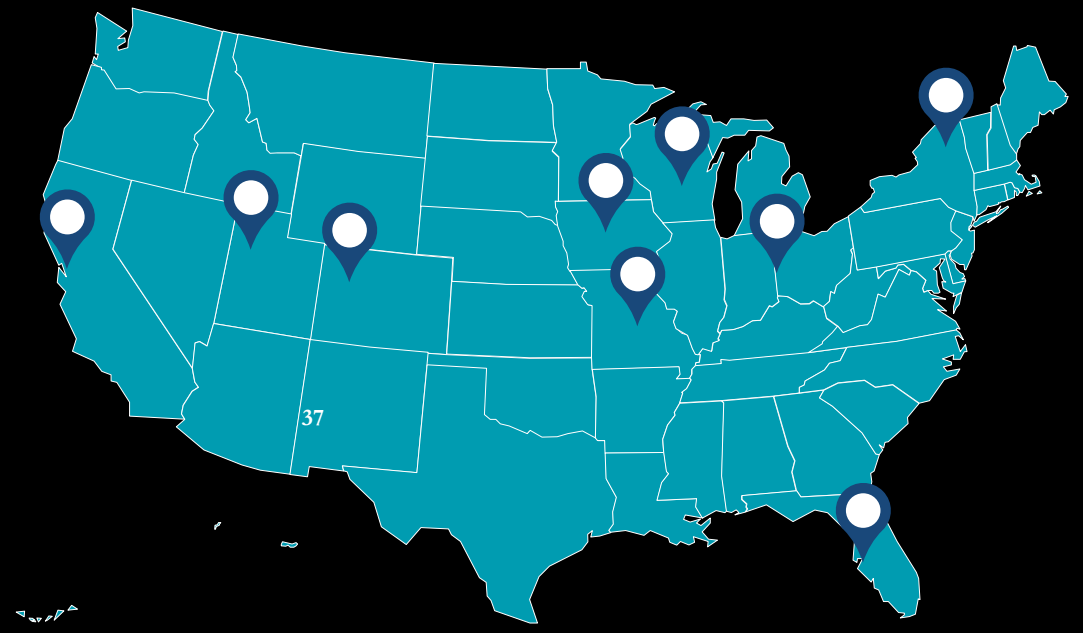
HOPE-2 Clinical Trial

- **Design:** Phase II, randomized, double-blind, placebo-controlled trial in participants with DMD and reduced skeletal muscle function
- **Objective:** Evaluate safety and efficacy of CAP-1002
- **Dosing Regimen:** 150M cells delivered intravenously every 3 months
- **Sites:** 9 sites (USA)
- **Interim Analysis:** ITT population **-** 20 subjects
- **Demographics**
  - Mean age: 14.3 years
  - All patients were on corticosteroids
  - ~ 80% of patients were non-ambulant



https://www.clinicaltrials.gov/ct2/show/study/NCT03406780.

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Advanced heart failure therapies

- 2019 study of 43 DMD patients with severe dysfunction
- Ventricular assist device – 4
- Heart transplant – 1

Age at implant (years)
17
17
29
15

Device implanted	Goal of LVAD[a]	Home on device	LVAD[a] complication (months from implant)	Alive as of 1/1/2018 (mo from implant)
HeartWare	Destination therapy	Yes	Yes, pump thrombosis (16)	Yes, with device (18)
HeartMate II	Bridge to transplant	Yes	No	Yes, heart transplant (10)
HeartMate II	Destination therapy	Yes	Yes, gastrointestinal bleed (10)	No, deceased (15)
HeartWare	Bridge to decision	Yes	Yes, stroke (5)	No, deceased (5)

Selected characteristics of Duchenne muscular dystrophy cases with severe Left Ventricular Systolic Dysfunctio (*N* = 43).

	Died during study period (*N* = 12)[a]	Alive at study end (*N* = 29)[a]	*p* value
Median age at death/study end	20.8 (IQR 15-9-24.6) years	19.6 (IQR 17.0–22.1) years	0.61
Median age ambulation ceased[b]	9 (IQR 9–12) years	11 (IQR 10–13) years	0.15
Current/past steroid use	6 (50%)	22 (75.9%)	0.11
Heart failure admission	5 (41.7%)	7 (24.1%)	0.26
VAD implanted	1 (8.3%)	2 (6.9%)	0.87
ICD implanted	0 (0%)	9 (31%)	0.03
Medication use at last cardiac evaluation[c]			
Ace-inhibitor/angiotensin Receptor Blocker	10/11 (90.9%)	28/31 (90.3%)	0.96
Beta-Blocker	7/11(63.6%)	20/31 (64.5%)	0.96
Ace-inhibitor/Angiotensin Receptor Blocker + Beta-Blocker	6/11 (54.5%)	18/31 (58.1%)	0.84

Prog Pediatr Cardiol. 2019;53:11-14.

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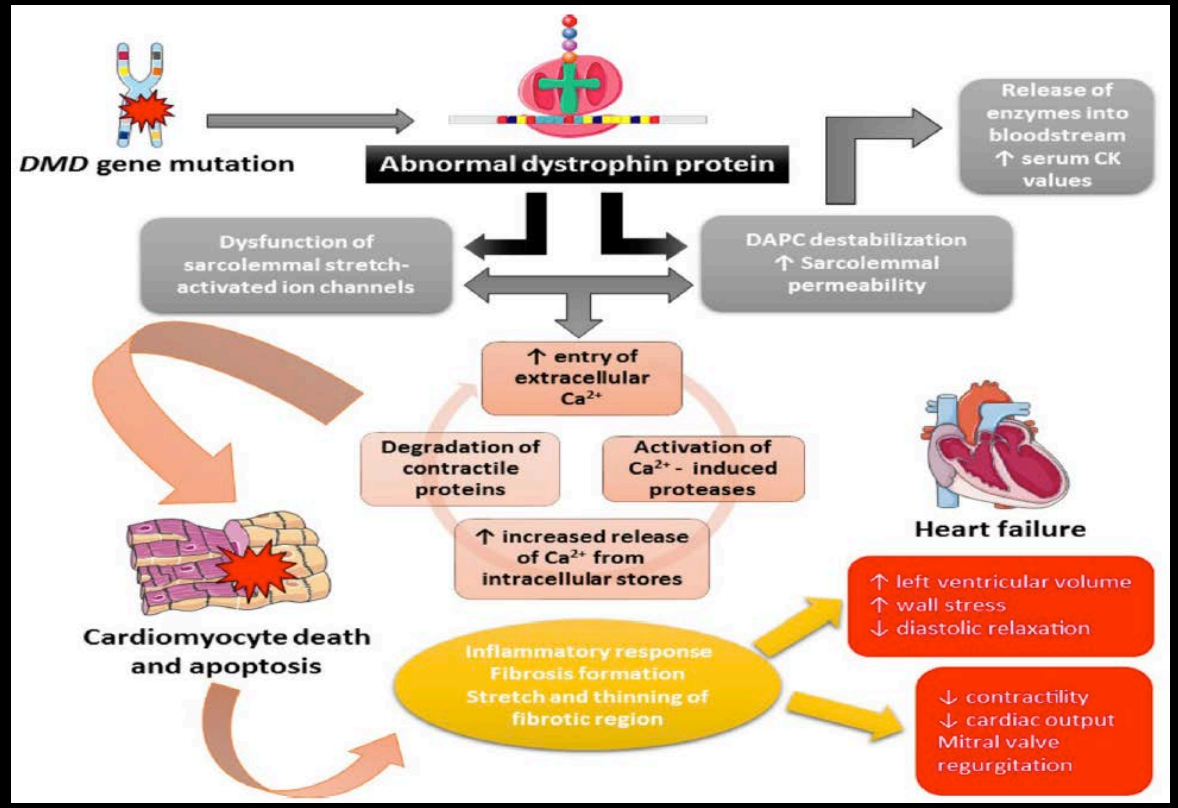
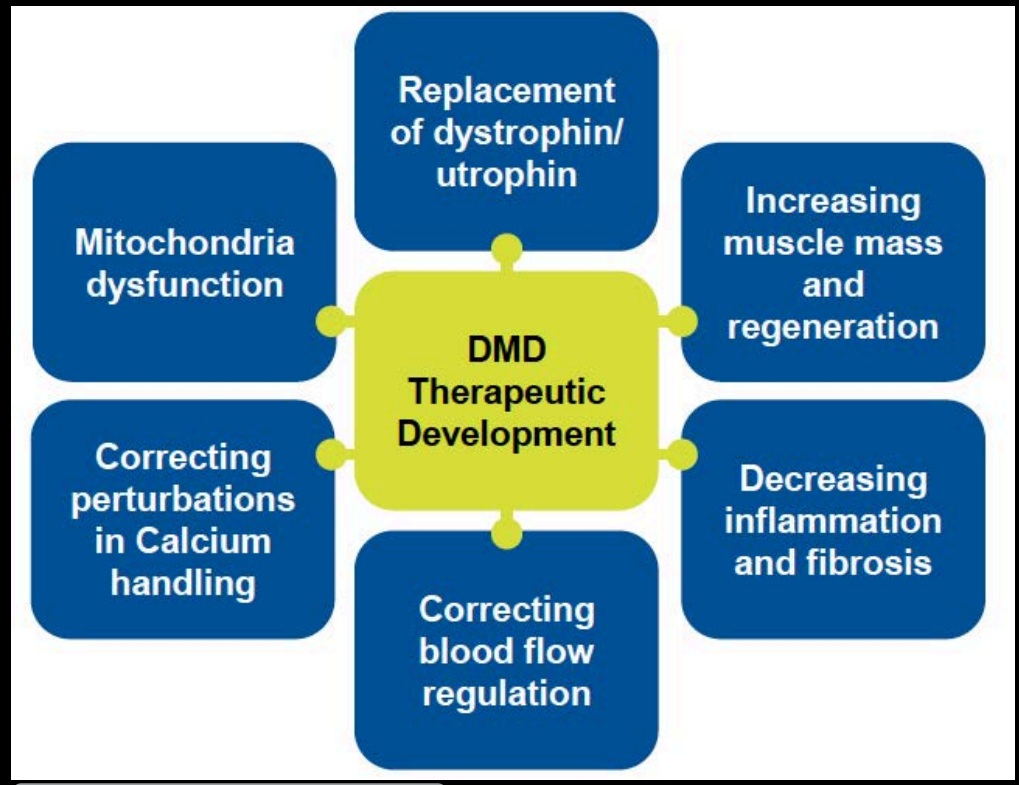
Therapeutic strategies





Courtesy of Craig McDonald, MD

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Summary

- Duchenne associated cardiomyopathy is an inexorably progressive disease with variable onset.
- Current therapies provide marginal therapeutic benefit.
- These patients need a transformative therapy that prevents the replacement of cardiac muscle cells or provides new muscle cells.

Thank you

Question and Answers

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Cardiac magnetic resonance group

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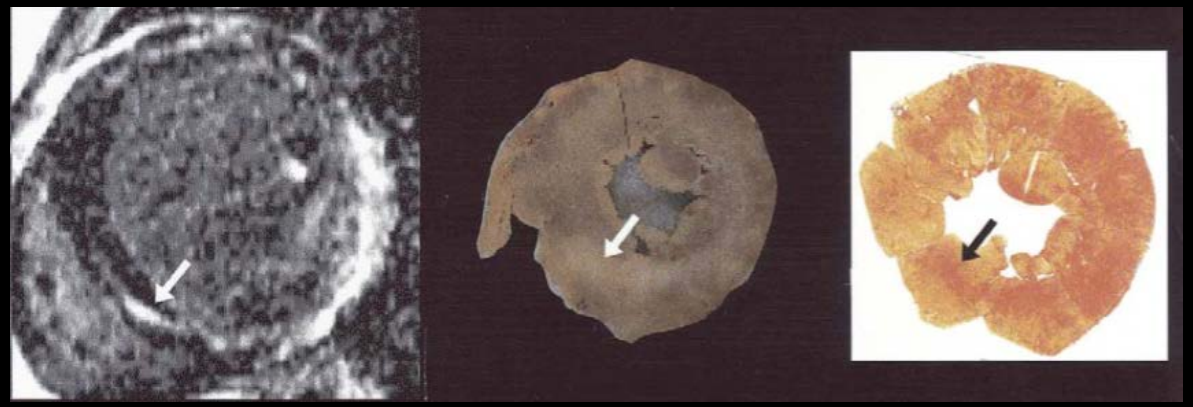
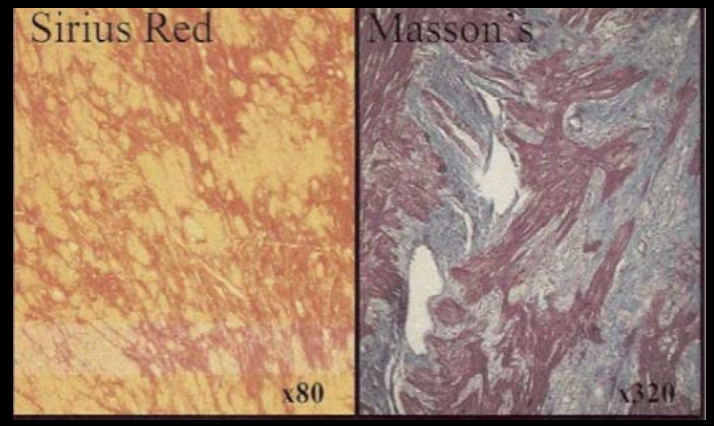
LGE → What is it really showing?

- Collagen replacement
- Gross fibrosis
- Protein infiltration
- Myocardial disarray
- Fine interstitial fibrosis without disarray





Moon, J. C. C., et al. (2004).. *JACC*, *43*(12), 2260–2264.

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Circumferential Strain Analysis Identifies Strata of Cardiomyopathy in Duchenne Muscular Dystrophy

A Cardiac Magnetic Resonance Tagging Study

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