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FRASE DE SALVAMENTO

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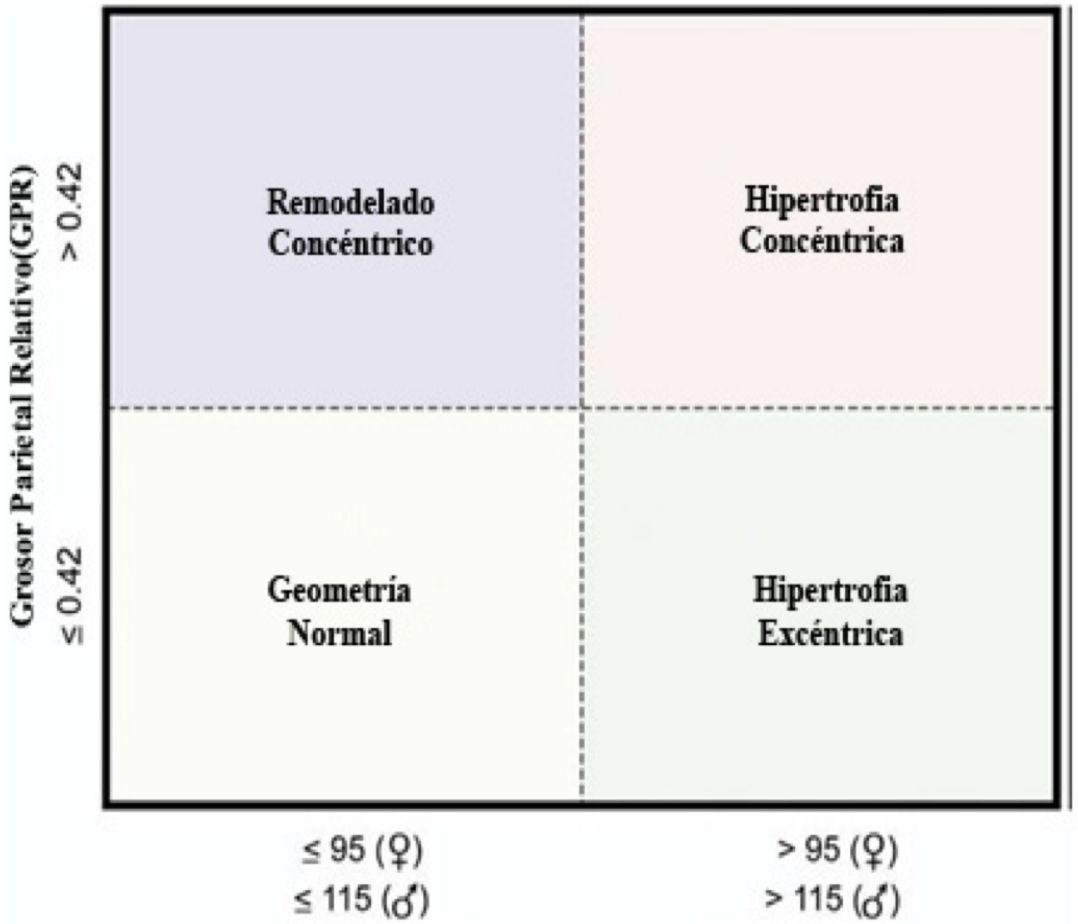
	MUJER	HOMBRE
Método Lineal		
Masa VI (g)	67-162	88-224
Masa VI/ASC (g/m²)	**43-95**	**49-115**
Grosor parietal	0,22-0,42	0,24-0,42
Grosor septal (cm)	**0,6-0,9**	**0,6-1,0**
Grosor pared posterior	**0,6-0,9**	**0,6-1,0**
Método 2D		
Masa VI (g)	66-150	96-200
Masa VI/ASC (g/m²)	**44-88**	**50-102**



J Am Soc Echocardiogr 2010;23:685-713

1868	First pathological description by Vulpian [6] who reported it as idiopathic hypertrophic subaortic stenosis (IHSS).
1957	Brock [9] reported 3 cases of LVOT hypertrophy and attributed it to systemic hypertension.
1958	Teare [1] published series of 8 autopsy cases who had asymmetrical hypertrophy of the heart, 7 of whom died suddenly. Bercu et al. [10] published a case report on 'pseudoaortic stenosis'.
1961	Brockenbrough et al. [11] described the Brockenbrough–Braunwald–Morrow sign.
1963	Nonobstructive form of HCM first described [13].
1964	Morrow et al. [19] performed the first surgical myectomy for HCM.
1965	Bjork [20] postulated that SAM caused LVOTO.
1969	Moreyra et al. [21] pioneered the use of M-Mode echocardiography in HCM diagnosis. Shah et al. [22] described SAM in HCM using echocardiography.
1972	Introduction of cross-section/2D echocardiography [23].
1980	First ICD implanted in a patient with HCM [24].
1990	First pathogenic mutation implicated in HCM [25].
1995	Introduction of alcohol septal ablation (ASA) as an alternative to surgical myectomy by Sigwart [26].
2000	First efficacy study on ICD in the prevention of SCD in the HCM population [27].
2002	ACC/AHA/NASPE guidelines [28] recommended (class IIb) the use of ICD in primary prevention of SCD in HCM.

1639
A

1898
AFD

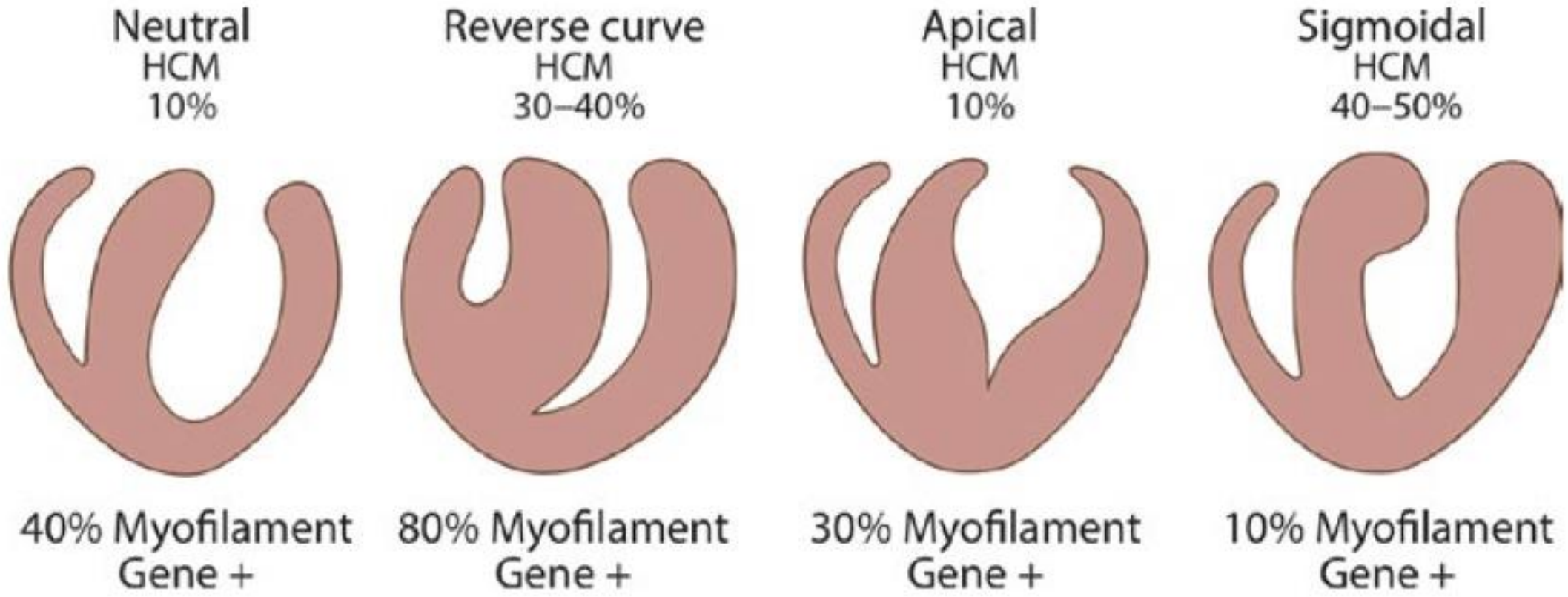
MCH es la que originalmente le dió el nombre a esta división en las **miocardiopatías**.

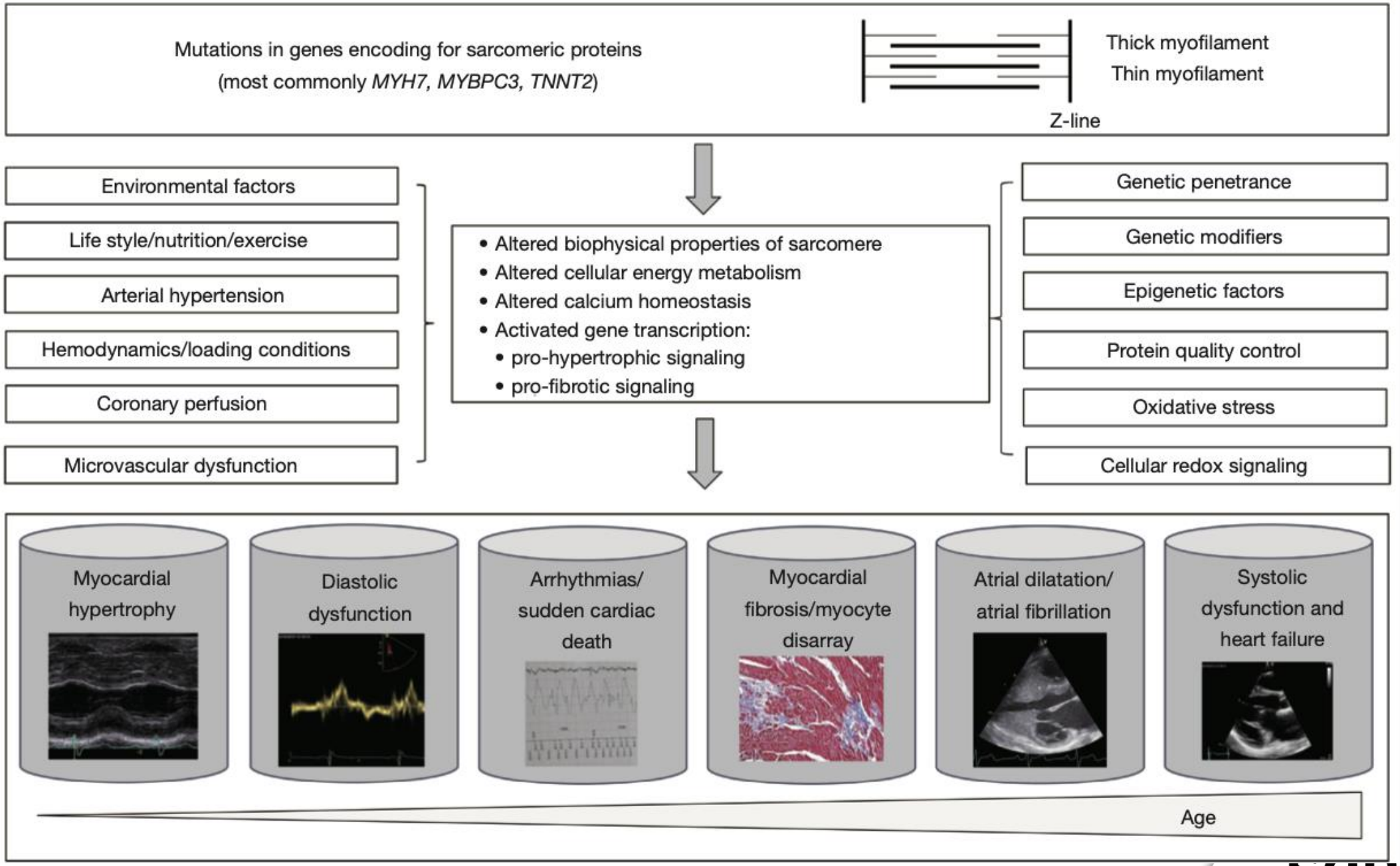
Aspectos Claves que han permitido grandes confusiones en este fenotipo

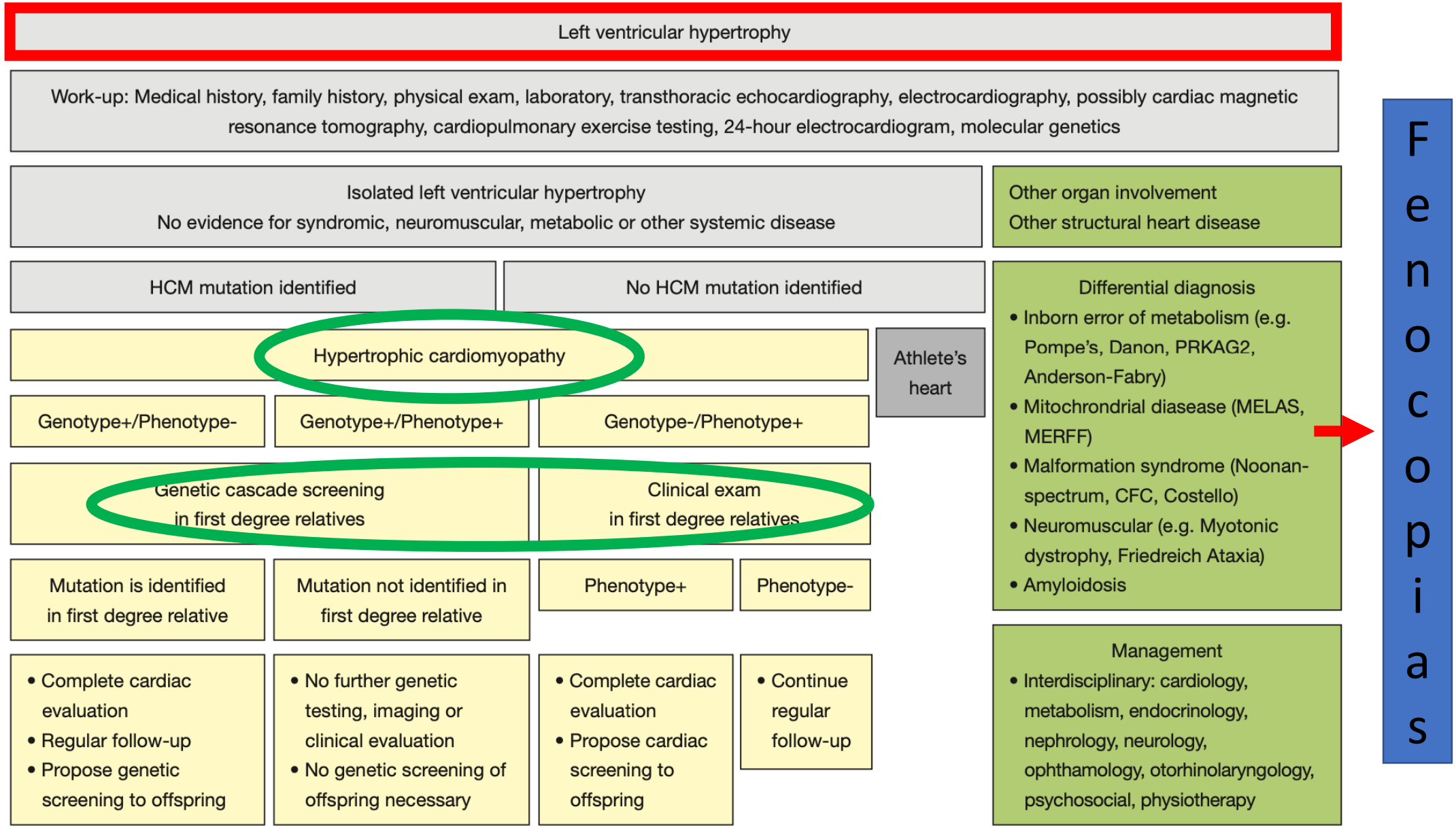
- Condiciones de Carga
- Expresión y penetrancia de su principal representante (MCH)
- Enfoque sólo en la de mayor presencia
- No entendimiento de la genética en Miocardiopatías
- Desconocimiento de enfermedades menos prevalentes/los llamados fenocopias…por su Hipertrofia ventricular izquierda cual sea su distribución.

Glosario Clave

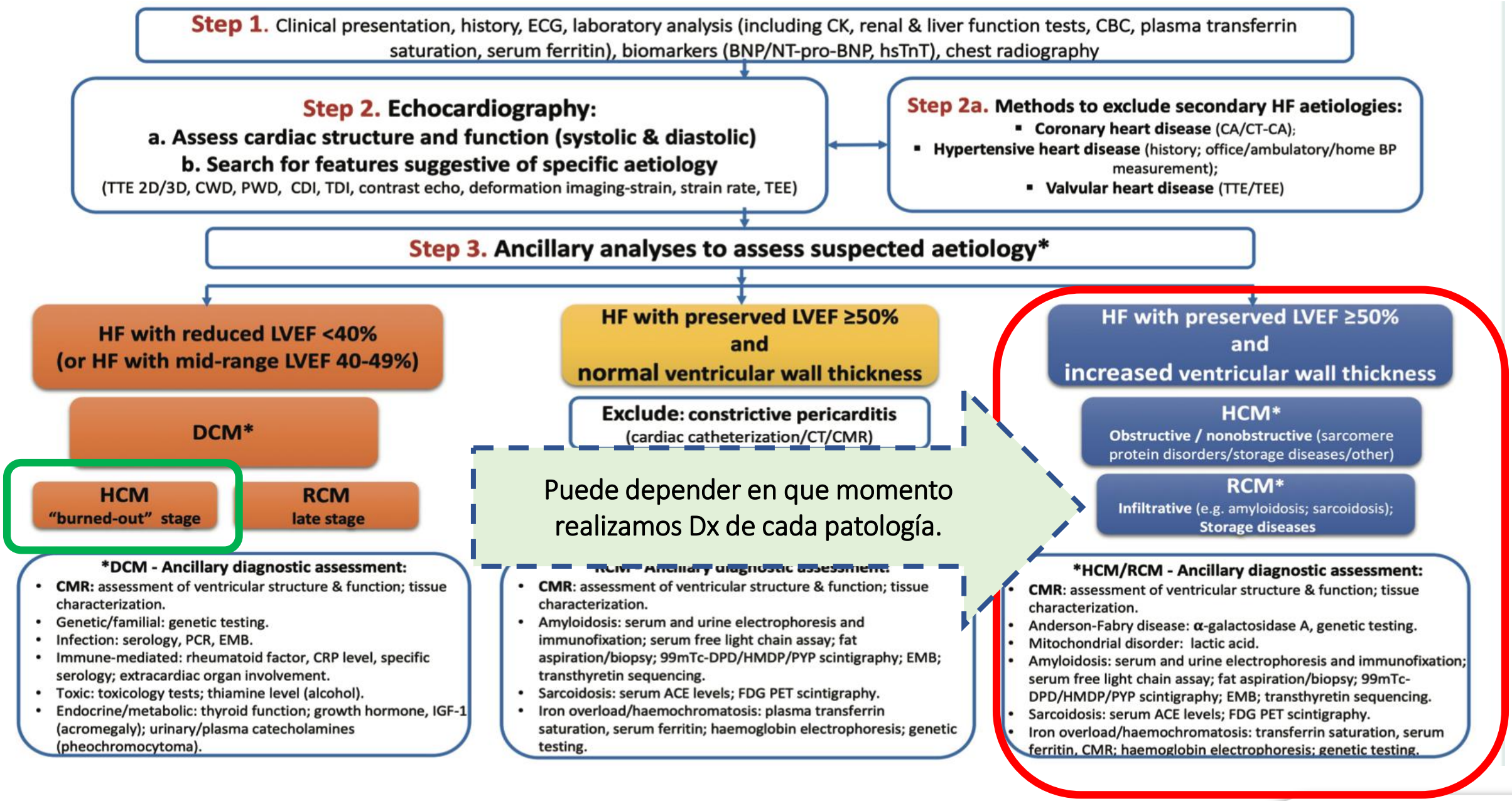
1. **Penetrancia:** % ind con genotipo determinado que muestran o exhiben el fenotipo asociado a ese genotipo.
2. **Expresión:** Grado de Intensidad con que se expresa un genotipo determinado en un individuo.
3. **Tipos de Herencia:** Mendeliana- No mendeliana… Mendeliana (AD, Ar, Lig X D, Lig X r, herencia mitocondrial).
4. **Fenotipo:** lo externo..que vemos
5. **Fenocopia:** lo externo parecido pero que no es.
6. **Genotipo:** Lo interno.. que no vemos.


Neutral
HCM
10%
Reverse curve
HCM
30–40%
Apical
HCM
10%
Sigmoidal
HCM
40–50%
40% Myofilament Gene +
80% Myofilament Gene +
30% Myofilament Gene +
10% Myofilament Gene +


Mutations in genes encoding for sarcomeric proteins
(most commonly *MYH7, MYBPC3, TNNT2*)
Thick myofilament
Thin myofilament
Z-line
Environmental factors
Life style/nutrition/exercise
Arterial hypertension
Hemodynamics/loading conditions
Coronary perfusion
Microvascular dysfunction
• Altered biophysical properties of sarcomere
• Altered cellular energy metabolism
• Altered calcium homeostasis
• Activated gene transcription:
  • pro-hypertrophic signaling
  • pro-fibrotic signaling
Genetic penetrance
Genetic modifiers
Epigenetic factors
Protein quality control
Oxidative stress
Cellular redox signaling
Myocardial hypertrophy
Diastolic dysfunction
Arrhythmias/ sudden cardiac death
Myocardial fibrosis/myocyte disarray
Atrial dilatation/ atrial fibrillation
Systolic dysfunction and heart failure
Age



Cardiovasc Diagn Ther 2019;9(Suppl 2):S388-S415



European Journal of Heart Failure (2019) **21**, 553–576

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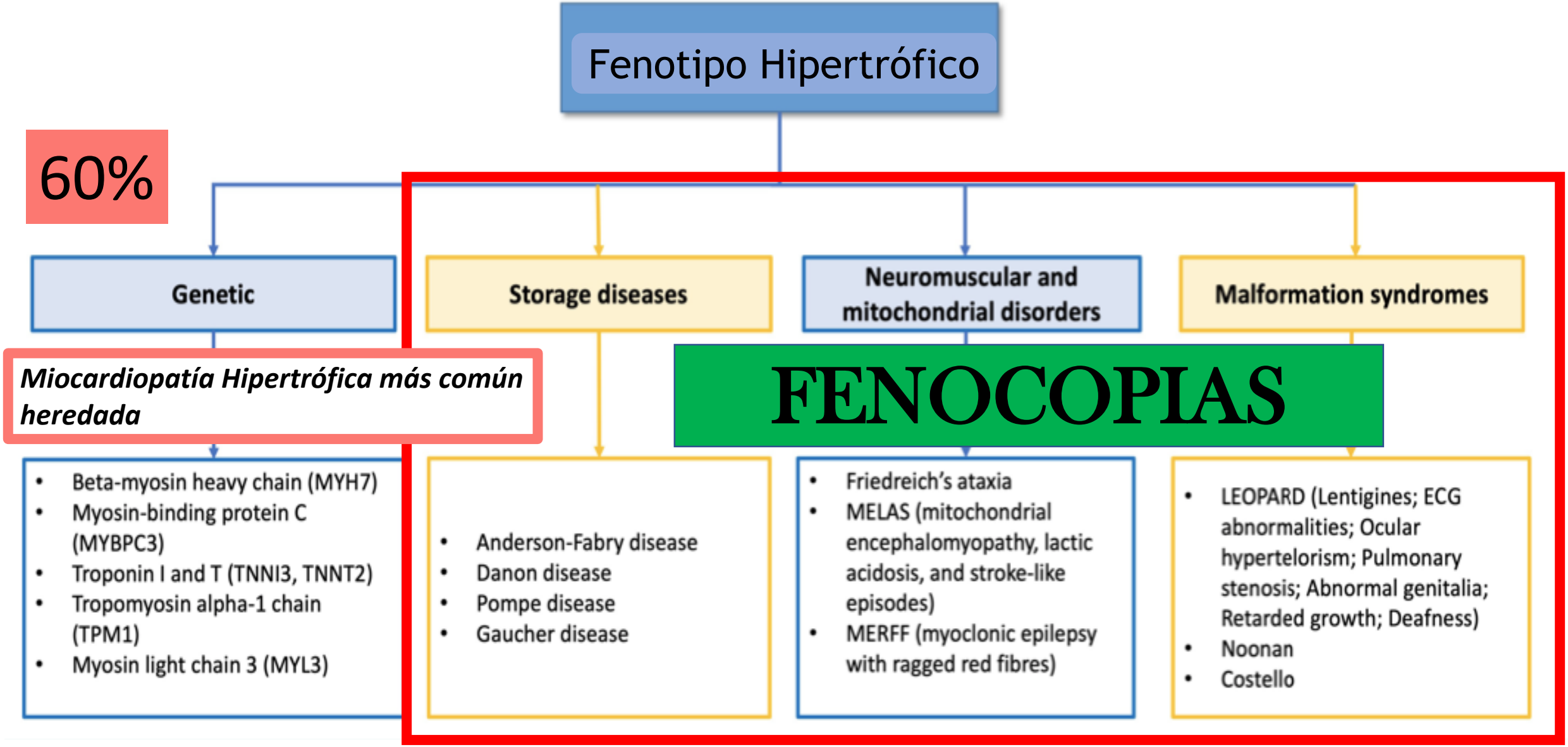


Clin Genet. 2018 Jan;93(1):3-14, European Journal of Heart Failure (2019), 21, 563–576

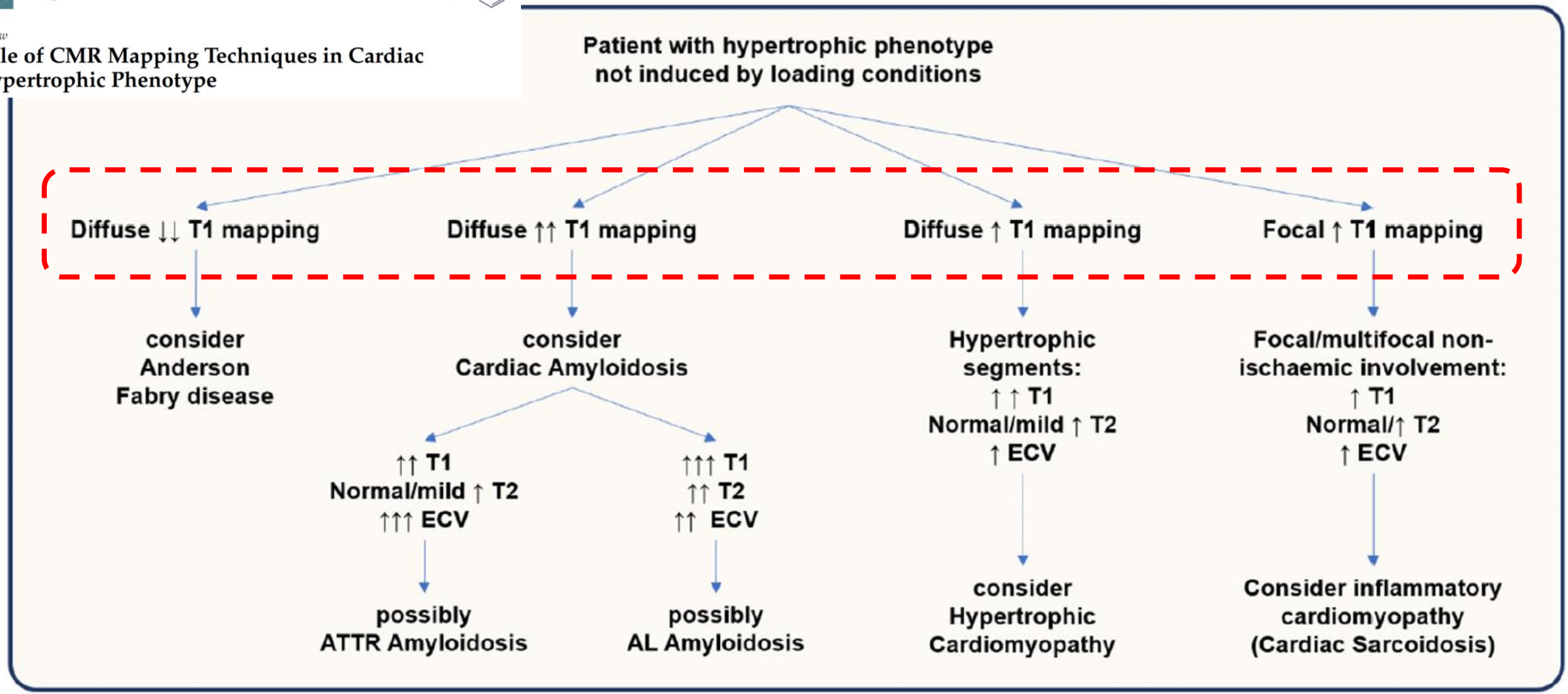
Red Flags de Fenotipo Hipertrófico

diagnostics

MDPI

Review

Role of CMR Mapping Techniques in Cardiac Hypertrophic Phenotype



Diagnostics 2020, 10, 770;

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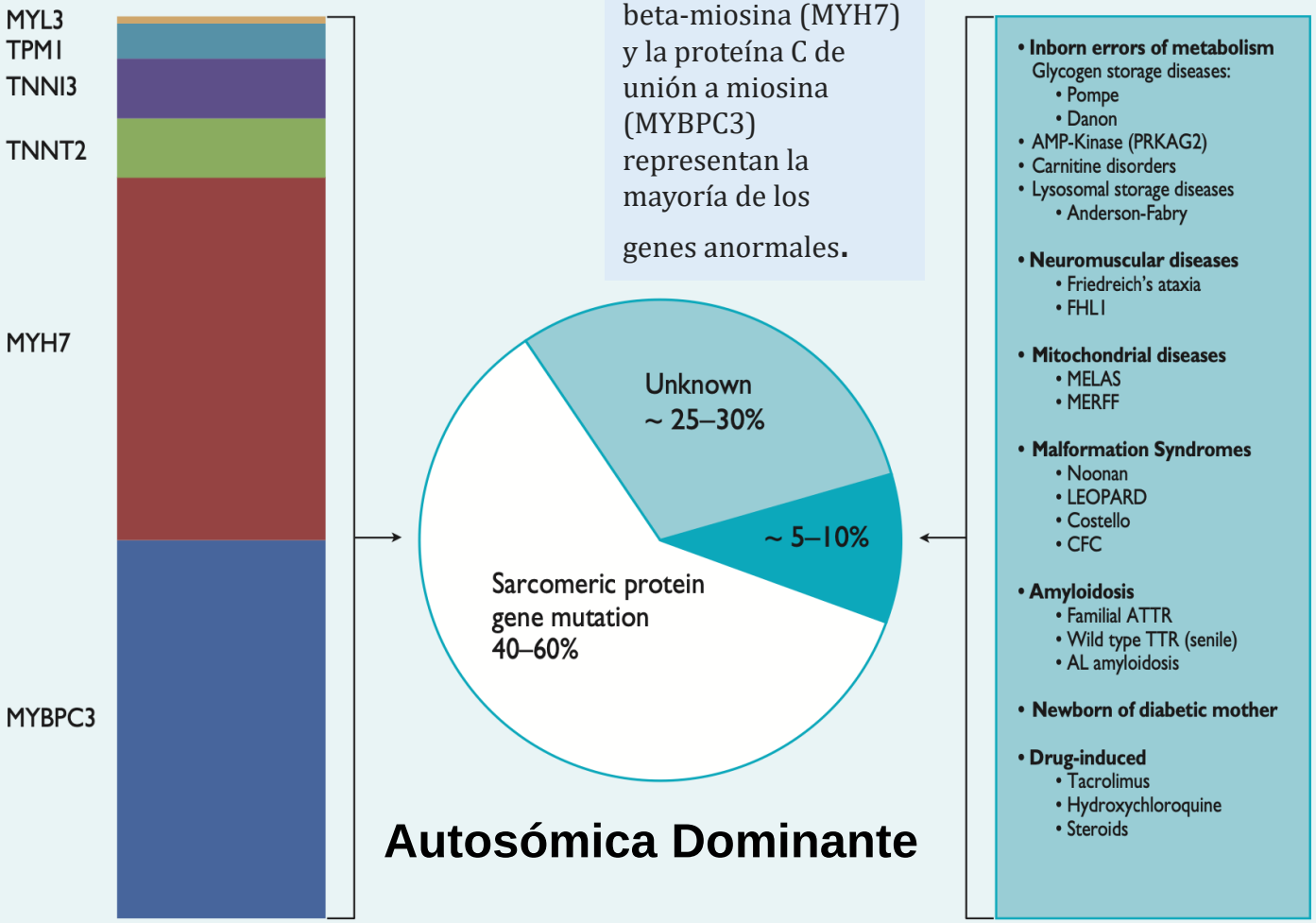
¿Cómo hacer el abordaje inicial y la estratificación de riesgo de falla y muerte súbita?

2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy

Genes que codifican la cadena pesada de beta-miosina (MYH7) y la proteína C de unión a miosina (MYBPC3) representan la mayoría de los genes anormales.



Autosómica Dominante

La miocardiopatía hipertrófica (MCH) se define por la presencia de un aumento en el grosor de la pared del ventrículo izquierdo (VI) que no se explica únicamente por condiciones anormales de carga.

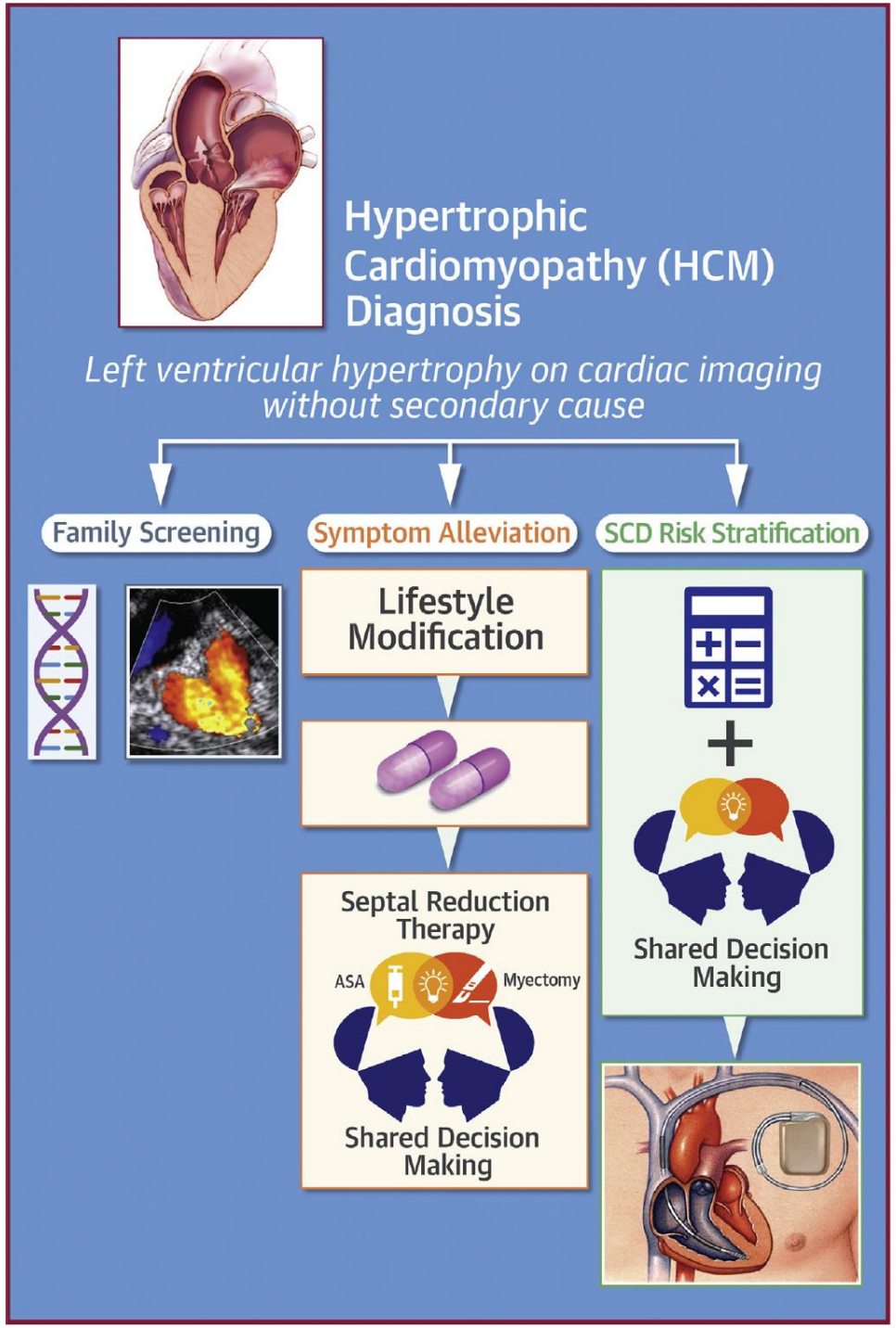
Aunque HCM es una miocardiopatía hereditaria, la causa genética subyacente de la enfermedad solo se encuentra en el 34% de los pacientes.

La evaluación genética es compleja dada la **penetrancia** incompleta, la **expresividad** variable , evaluación de la historia familiar incompleta o imprecisa y la verdadera prevalencia de mutaciones de novo.

European Heart Journal (2014) 35, 2733–2779

CLINICAL PRACTICE GUIDELINE

2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy



- MCH es la miocardiopatía hereditaria más común. Aprox 1 en 500, ó puede ser incluso mayor **1 en 200**). Dx Exclusión.
- Autosómica dominante. Penetrancia incompleta y expresion totalmente variable.
- Pronóstico Bueno y más de manera contemporánea
- Tratamiento multifacético y requiriendo de un heart team para las mejores decisiones.

1 de cada 3 de ustedes han tenido en su consultorio un paciente con fenotipo hipertrófico independientemente del síntoma en la última semana.

TABLE 1 Demographic and Clinical Characteristics of HFpEF Stratified by Presence or Absence of CA

	All Patients (N = 108)	Non-Amyloid HFpEF (n = 93)	HFpEF-CA (n = 15)	p Value
Age (yrs)	66 (57–74)	65 (56–72)	74 (68–79)	0.001
Sex				0.09
Female	66 (61.0)	60 (64.5)	6 (40.0)	
Race				0.23
African American	62 (57.4)	56 (60.2)	6 (40.0)	
Caucasian	43 (39.8)	34 (36.6)	9 (60.0)	
Other	3 (2.8)	3 (3.2)	0 (0.0)	
Hospitalized for HF in the last 12 months	67 (62.0)	61 (65.6)	6 (40.0)	0.08
NYHA functional class				0.14
I	1 (0.9)	1 (1.1)	0 (0.0)	
II	36 (33.6)	28 (30.4)	8 (53.3)	
III	67 (62.6)	61 (66.3)	6 (40.0)	
IV	3 (2.8)	2 (2.2)	1 (6.7)	
Systolic BP (mm Hg)	141 (125–162)	141 (128–163)	125 (111–139)	0.01
Diastolic BP (mm Hg)	70 (65–79)	72 (65–79)	69 (66–77)	0.81
Heart rate (beats/min)	78 (68–88)	77 (66–87)	80 (70–92)	0.16
BMI (kg/m^2)	36.9 (31.5–45.1)	37.6 (33.2–45.6)	29.4 (25.1–34.2)	0.0001
Medical history				
Hypertension	100 (92.6)	91 (97.8)	9 (60.0)	<0.0001
Diabetes mellitus	58 (53.7)	54 (58.1)	4 (26.7)	0.03
Obstructive CAD	15 (13.9)	13 (14.0)	2 (13.3)	1.00
Atrial fibrillation or flutter	34 (31.5)	28 (30.1)	6 (40.0)	0.55
Obstructive sleep apnea	46 (42.6)	44 (47.3)	2 (13.3)	0.02
COPD or asthma	34 (31.5)	33 (35.5)	1 (6.7)	0.03
Medications				
ACE inhibitor	31 (28.7)	30 (32.3)	1 (6.7)	0.06
ARB	33 (30.6)	29 (31.2)	4 (26.7)	1.00
Beta-blocker	65 (60.2)	57 (61.3)	8 (53.3)	0.58
Aldosterone antagonist	31 (28.7)	30 (32.3)	1 (6.7)	0.06
Loop diuretic	105 (97.2)	90 (96.8)	15 (100.0)	1.00
Insulin	33 (30.6)	32 (34.4)	1 (6.7)	0.03
Laboratory studies				
GFR (CKD-EPI), (ml/min/1.73 m^2)	49 (34–70)	49 (34–70)	55 (35–68)	0.79
NT-proBNP (pg/ml)	450 (111–1,433)	353 (100–946)	3,245 (1,012–4,542)	0.0002
Troponin I (ng/ml, n = 83 HFpEF, n = 12 HFpEF-CA)	0.00 (0.00–0.00)	0.00 (0.00–0.00)	0.09 (0.00–0.12)	<0.0001
Troponin I ≥0.04 ng/ml (n = 83 HFpEF, n = 12 HFpEF-CA)	18 (18.95)	10 (12.05)	8 (66.67)	0.0001
Abnormal K/L ratio (<0.26 OR >1.65)	35 (34.3)	28 (32.2)	7 (46.7)	0.38
6-min walk distance (m, n = 55 HFpEF n = 6 HFpEF-CA)	204 (119–348)	203 (118–349)	229 (119–289)	0.91

J Am Coll Cardiol HF 2020;8:712–24

Endomyocardial Biopsy Characterization of Heart Failure With Preserved Ejection Fraction and Prevalence of Cardiac Amyloidosis

Virginia S. Hahn, MD,[a] Lisa R. Yanek, MPH,[b] Joban Vaishnav, MD,[a] Wendy Ying, MD,[a] Dhananjay Vaidya, MBBS, MPH, PHD,[b] Yi Zhen Joan Lee, MD,[a] Sarah J. Riley, MSN, CRNP,[a] Vinita Subramanya, MBBS, MPH,[c] Emily E. Brown, MGC,[a] C. Danielle Hopkins, BS,[a] Sandra Ononogbu, MBBS,[a] Kira Perzel Mandell, BS,[d] Marc K. Halushka, MD, PHD,[d] Charles Steenbergen, JR, MD, PHD,[d] Avi Z. Rosenberg, MD, PHD,[d] Ryan J. Tedford, MD,[e] Daniel P. Judge, MD,[e] Sanjiv J. Shah, MD,[f] Stuart D. Russell, MD,[g] David A. Kass, MD,[a] Kavita Sharma, MD[a]

El campo de la biopsia endomiocárdica en establecer la etiología en cardiomiopatias dilatadas está entre 15 y 37% de pacientes,y con la bx cambiando el diagnóstico en 1|3 de pctes en hfpef

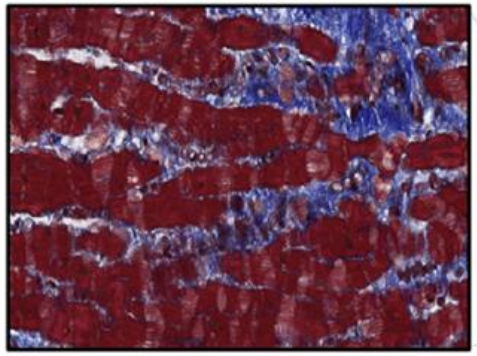
Pero seguimos creyendo que este diagnóstico está lejos ??

Hallazgos Histopatológico y su prevalencia en Falla Cardíaca FSVI preservada y comorbilidades asociadas

HFpEF Myocardial Tissue Findings

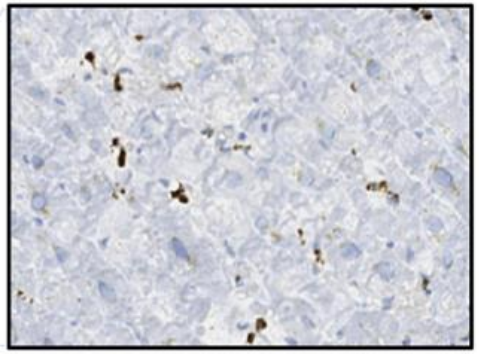
Fibrosis (93%)

- 66% with mild fibrosis
- 27% with moderate or severe fibrosis
- 7% with no fibrosis

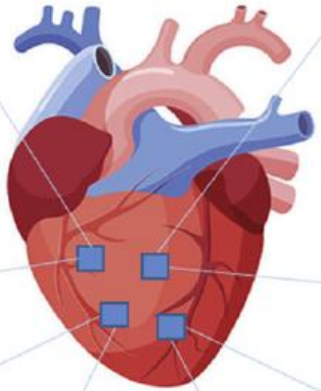


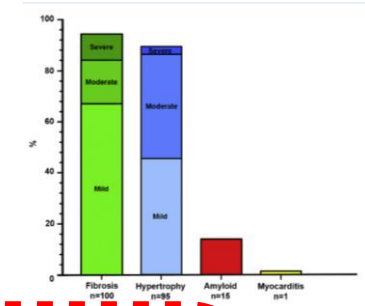
Inflammation

1.9X greater compared to controls*



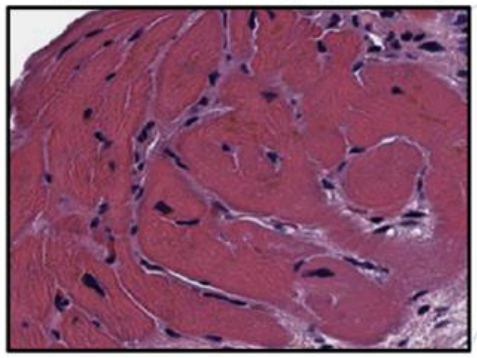
- Older Age
- Renal disease



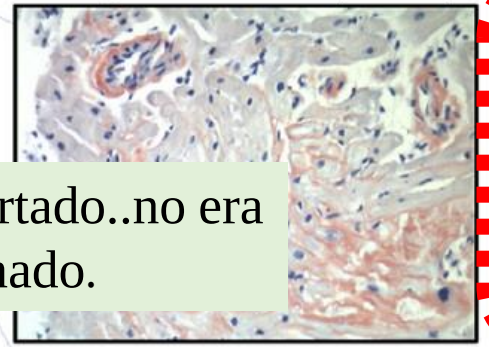


Hypertrophy (88%)

- 45% with mild hypertrophy
- 43% with moderate or severe hypertrophy
- 12% with no hypertrophy



Amyloidosis (14%)



- Older Age
- Lower blood pressure
- Lower BMI
- Fewer comorbidities
- Elevated NT-proBNP
- Elevated Troponin I
- Higher LV mass index

Este 14% reportado..no era sospechado.

J Am Coll Cardiol HF 2020;8:711-724

Relationship between aetiology and left ventricular systolic dysfunction in hypertrophic cardiomyopathy

Stefania Rosmini,[1,2] Elena Biagini,[2] Costantinos O'Mahony,[1,3] Heerajnarain Bulluck,[1,3] Niccolo' Ruozi,[2] Luis R Lopes,[3,4,5] Oliver Guttmann,[1,3] Patricia Reant,[6] Cristina C Quarta,[2,7] Antonis Pantazis,[3] Maria Tome-Esteban,[3] William J Mckenna,[3] Claudio Rapezzi,[2] Perry M Elliott[1,3]

4 + Comunes del fenotipo hipertrófico luego de las sarcoméricas.

Table 1 Summary of diagnostic subgroups at each centre

	Overall n=1697	The Heart Hospital n=987 (58%)	Bologna University Hospital n=710 (42%)
Idiopathic or sarcomeric HCM, n (%)	1288 (76)	826 (49)	462 (27)
Phenocopies, n (%)	409 (24)	161 (9)	248 (15)
AL amyloidosis, n (%)	115 (7)	6 (0.4)	109 (6)
Hereditary TTR amyloidosis, n (%)	86 (5)	6 (0.4)	80 (5)
AFD, n (%)	85 (5)	77 (5)	8 (0.5)
Wild-type or SSA, n (%)	48 (3)	8 (0.5)	40 (2)
Noonan syndrome, n (%)	15 (1)	11 (0.6)	4 (0.2)
Mitochondrial diseases, n (%)	23 (1)	21 (1)	2 (0.1)
Friedreich's ataxia, n (%)	11 (1)	9 (0.5)	2 (0.1)
GSD, n (%)	16 (1)	14 (0.8)	2 (0.1)
LEOPARD syndrome, n (%)	7 (0.4)	6 (0.4)	1 (0.1)
FHL1 mutations, n (%)	2 (0.1)	2 (0.1)	0 (0)
CPT II deficiency, n (%)	1 (0.1)	1 (0.1)	0 (0)

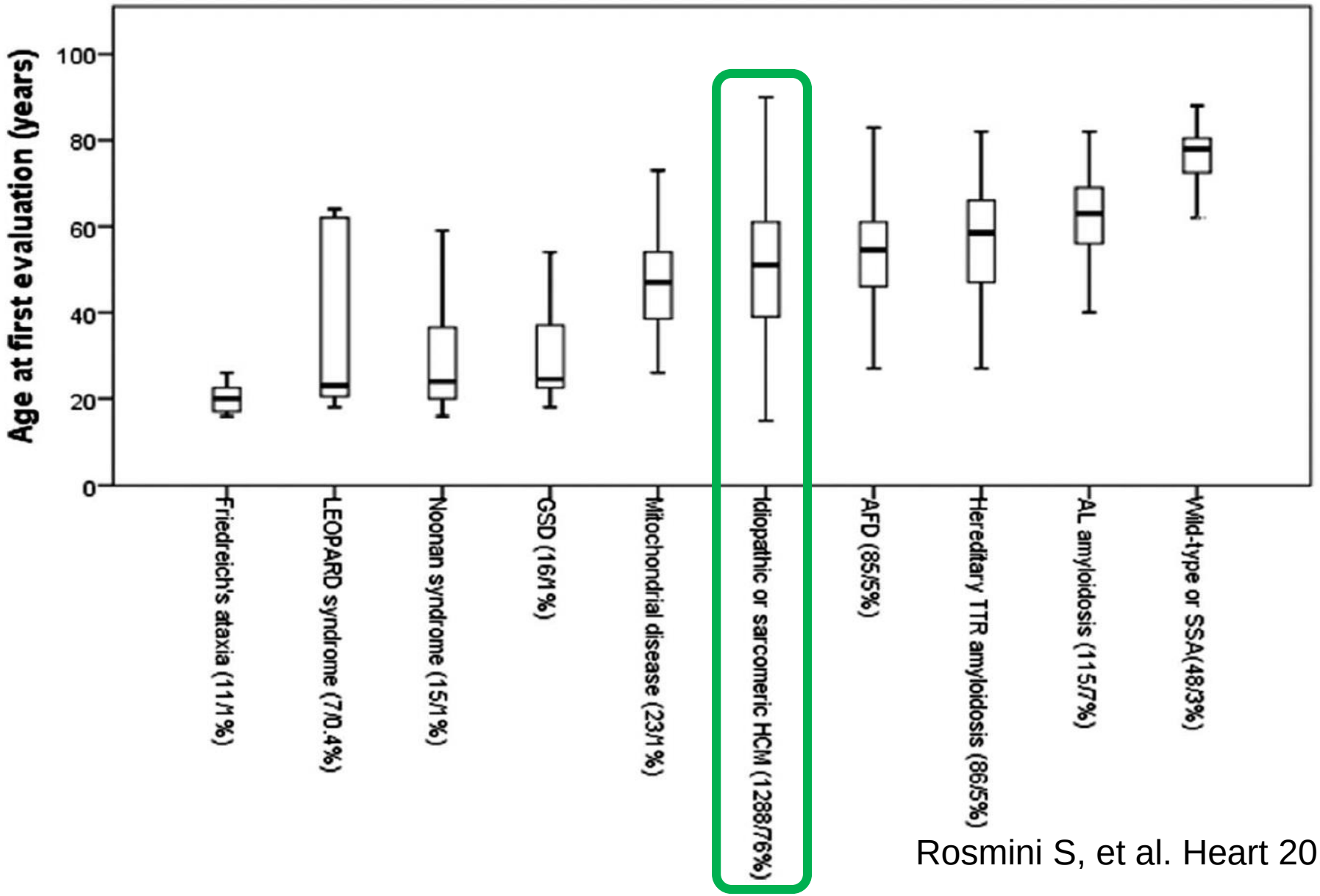
Rosmini S, et al. Heart 2014;100:302-306.

	Overall (n=1697)	Idiopathic or sarcomeric HCM (n=1288)	Rare phenocopies (n=409)	p Value
Male, n (%)	1160 (68)	860 (67)	300 (73)	0.012
Reason for diagnosis				
Incidental, n (%)	475 (29)	437 (36)	38 (10)	<0.0001
Cardiac symptoms, n (%)	822 (51)	660 (54)	162 (41)	
Family screening, n (%)	180 (11)	128 (10)	52 (13)	
One or more non-cardiac symptoms, n (%)	140 (9)	0 (0)	140 (35)	
Age at diagnosis of HCM, median (IQR)	50 (38–62)	49 (37–60)	58 (44–69)	<0.0001
Age at first evaluation, median (IQR)	52 (40–63)	51 (39–61)	60 (47–69)	<0.0001
NYHA III–IV at first evaluation, n (%)	241 (14)	144 (11)	97 (24)	0.013
Rhythm at first evaluation, n (%)				
Sinus rhythm	1461 (89)	1124 (87)	337 (82)	<0.0001
Atrial fibrillation/atrial flutter	124 (8)	74 (6)	50 (12)	
Paced	53 (3)	33 (3)	20 (5)	
Max LVWT at first evaluation, (mm), median (IQR)	18 (16–21)	18 (16–22)	16 (14–19)	<0.0001
LVED diameter at first evaluation, (mm), median (IQR)	45 (41–49)	45 (41–49)	45 (40–49)	0.145
EF at first evaluation (%), median (IQR)	65 (57–71)	66 (60–72)	60 (48–68)	<0.0001
EF <50% at first evaluation, n (%)	145 (9)	40 (3)	105 (26)	<0.0001
LA diameter at first evaluation (mm), median (IQR)	44 (39–49)	44 (40–49)	44 (38–48)	0.072

EF, ejection fraction; HCM, hypertrophic cardiomyopathy; LA, left atrium; LVED, left ventricular end diastolic; LVWT, left ventricular wall thickness; NYHA, New York Heart Association.

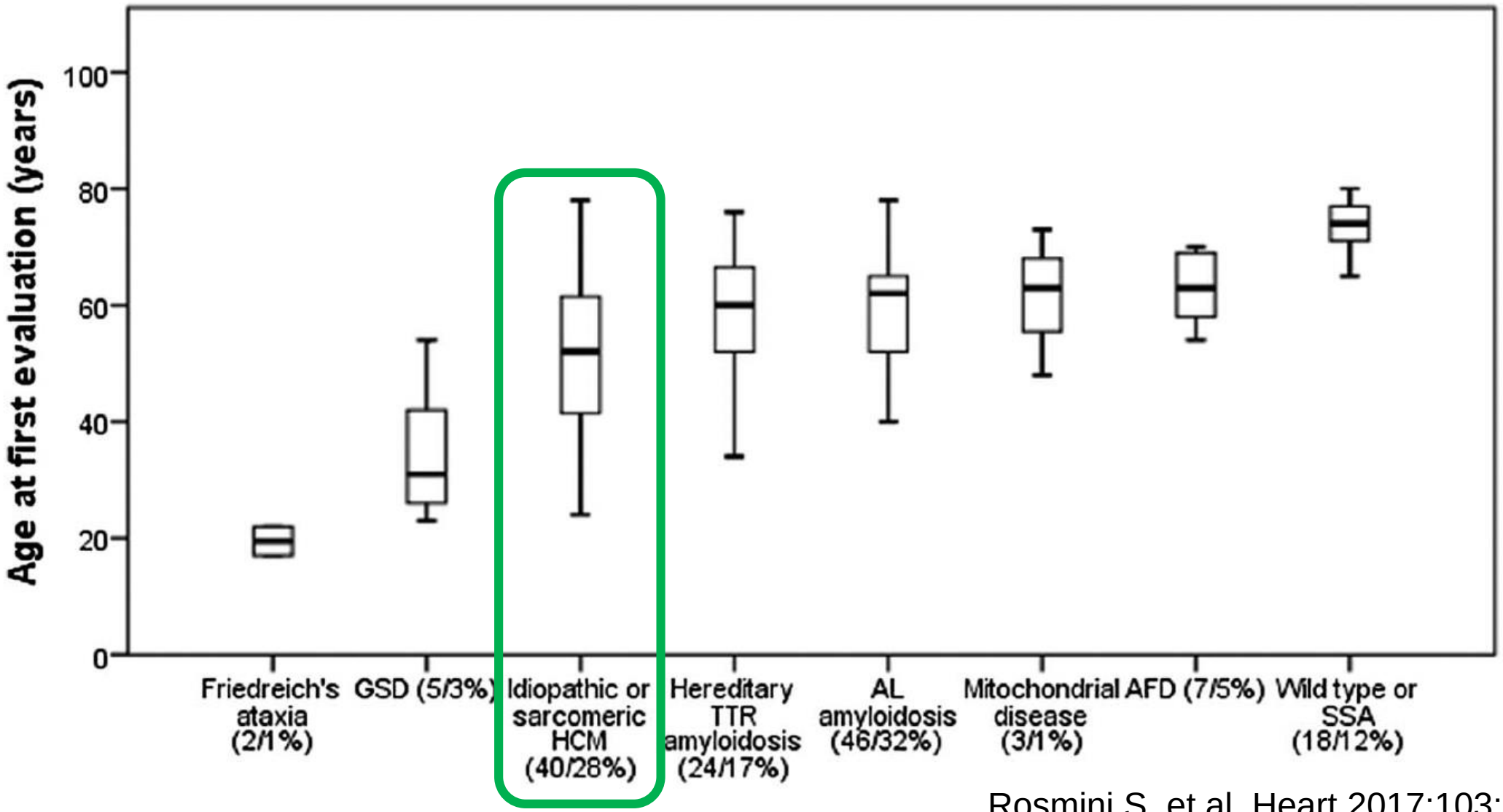
Rosmini S, et al. Heart 2015;101:300–306.

Edad al hacer el Dx en Población General

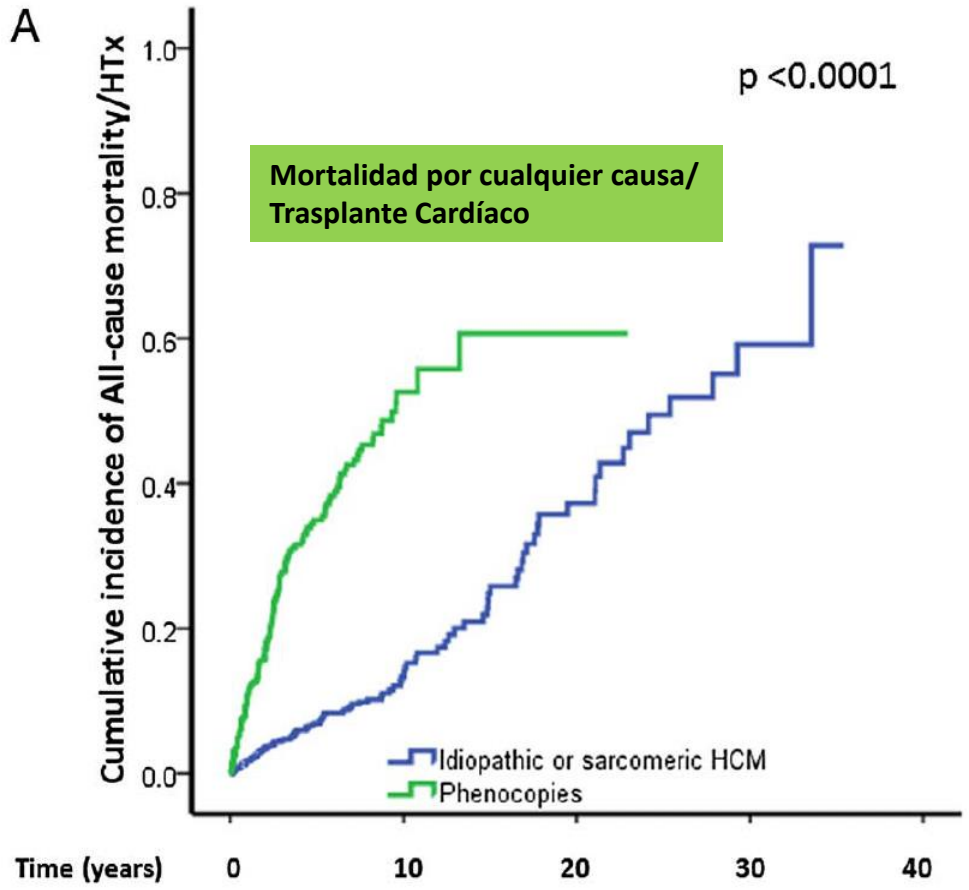


Rosmini S, et al. Heart 2017;103:300–306.

Edad al hacer el Dx en pctes que se presentan con Disfunción ventricular Izquierda



Rosmini S, et al. Heart 2017;103:300-306.



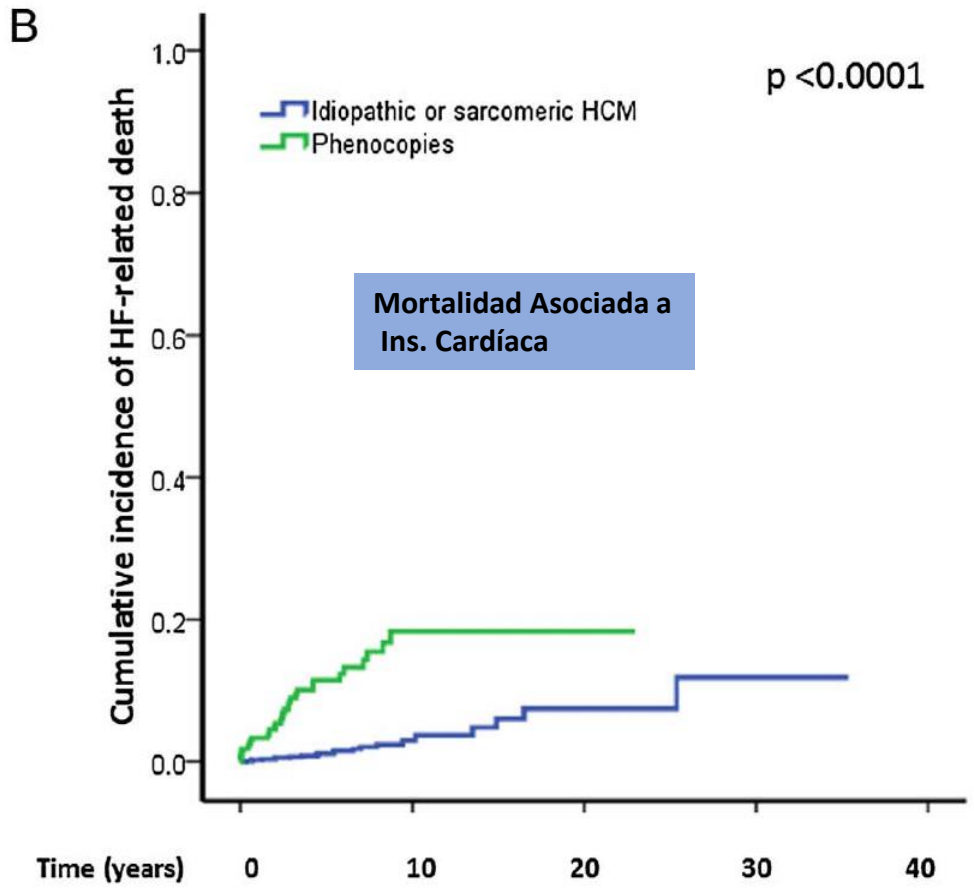


Table 3 Outcomes in the overall population, idiopathic or sarcomeric hypertrophic cardiomyopathy (HCM) and in rare phenocopies

	Overall population (1639 patients)	Idiopathic or sarcomeric HCM (1243 patients)	Rare phenocopies (396 patients)	p Value
All-cause mortality/HTx, n (%)	250 (15)	121 (10)	129 (33)	<0.0001
CV death/HTx, n (%)	160 (10)	89 (7)	71 (18)	<0.0001
HF death, n (%)	55 (3)	21 (2)	34 (9)	<0.0001
HTx, n (%)	33 (2)	18 (1)	15 (4)	0.006
SD, n (%)	60 (4)	41 (3)	19 (5)	<0.0001
Stroke-related death, n (%)	11 (1)	9 (1)	2 (0.5)	
Non-CV death, n (%)	46 (3)	26 (2)	20 (5)	
Unknown, n (%)	50 (3)	6 (0.5)	44 (11)	

CV, cardiovascular; HF, heart failure; HTx, heart transplantation; SD, sudden death.

Desenlaces en pctes con miocardiopatía hipertrófica Sarcomérica Vs Fenocopias

Rosmini S, et al. Heart 2015;101:300-306.

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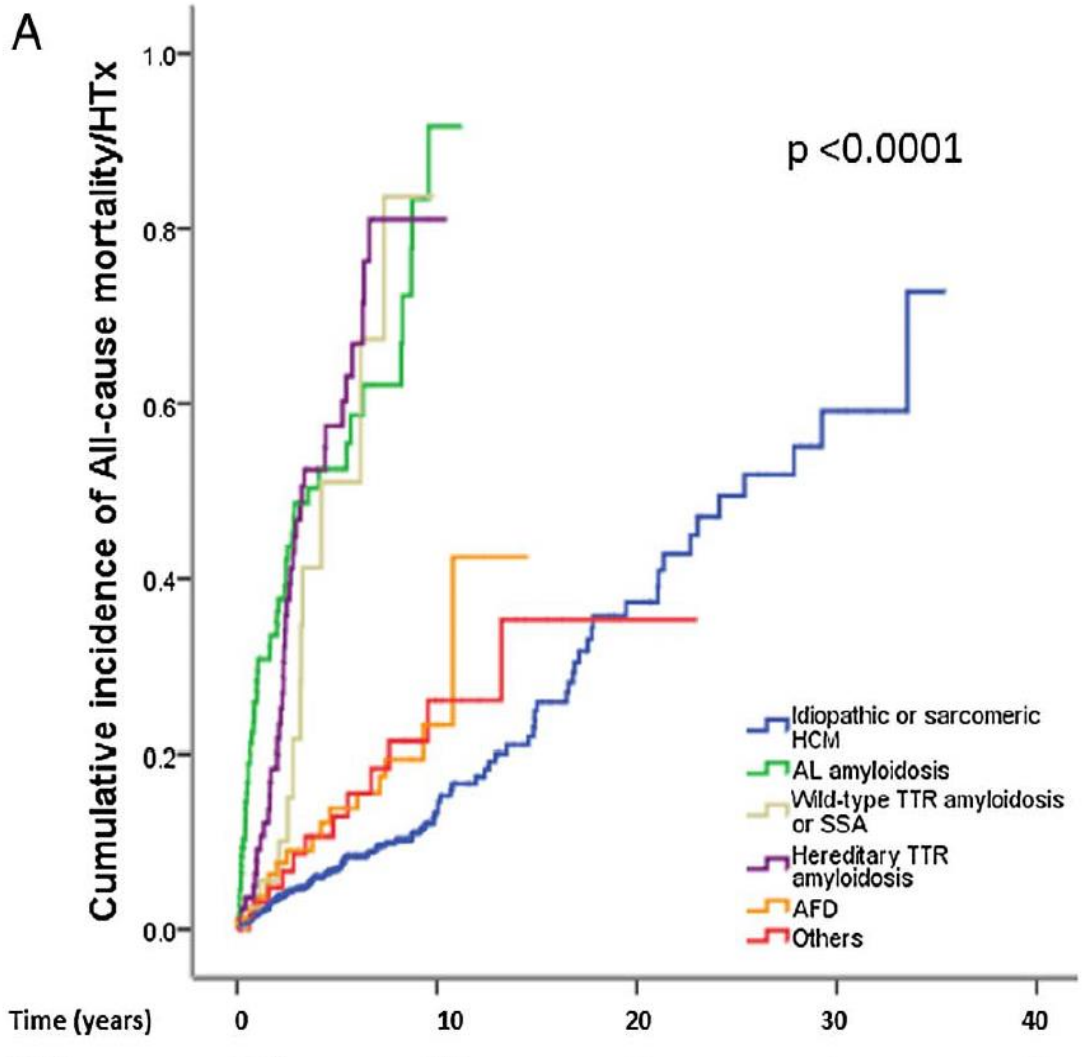
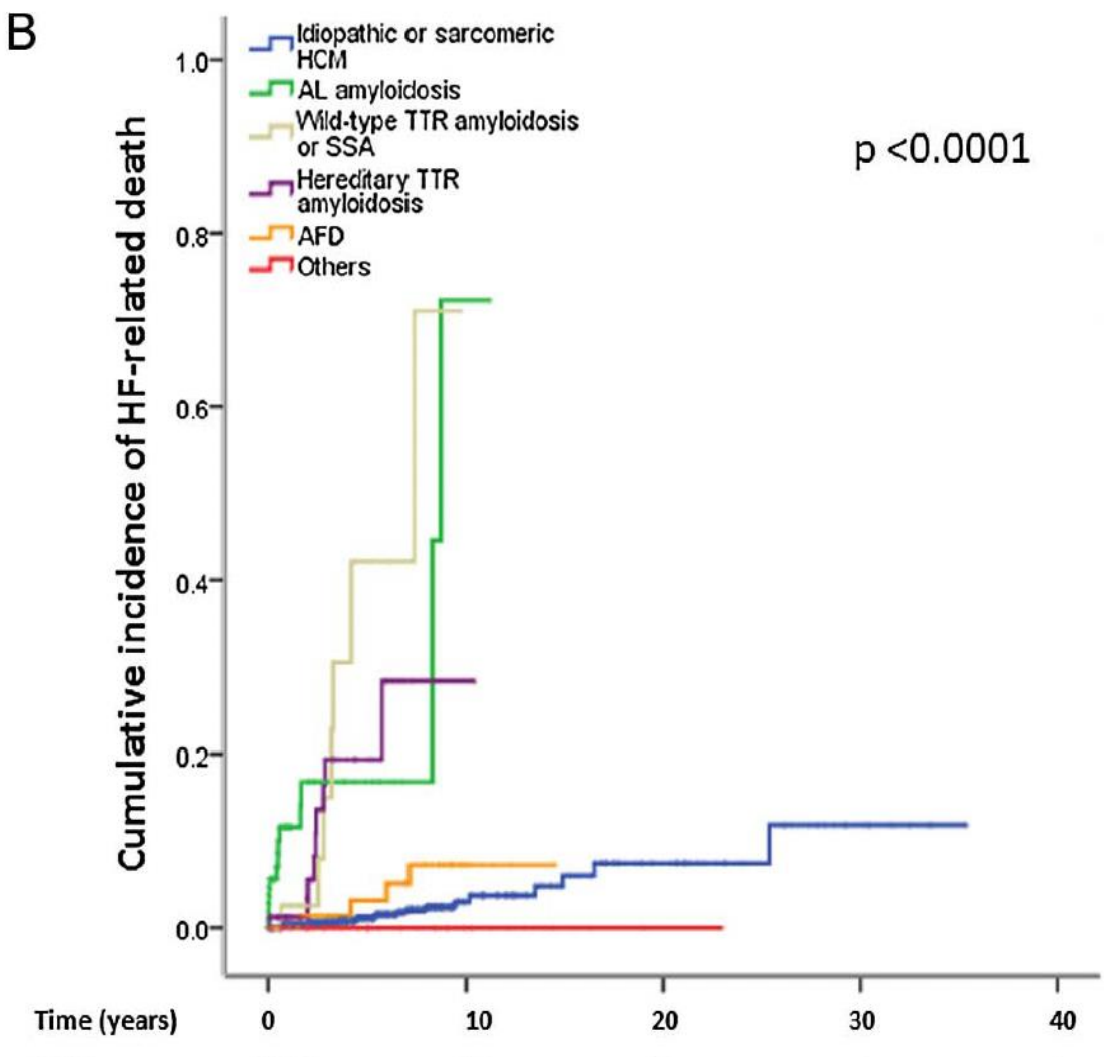
Desenlaces en pctes con miocardiopatía hipertrófica Sarcomérica Vs Fenocopias específicas





Rosmini S, et al. Heart 2015;101:300-306.

Hypertrophic Cardiomyopathy in Adulthood Associated With Low Cardiovascular Mortality With Contemporary Management Strategies

Barry J. Maron, MD,* Ethan J. Rowin, MD,† Susan A. Casey, RN,* Mark S. Link, MD,† John R. Lesser, MD,* Raymond H.M. Chan, MD, MPH,† Ross F. Garberich, MS,* James E. Udelson, MD,† Martin S. Maron, MD†

In a large longitudinally assessed adult HCM cohort, we have demonstrated that contemporary management strategies and treatment interventions, including ICDs for SD prevention, have significantly altered the clinical course, now resulting in a low disease-related mortality rate of 0.5%/year and an opportunity for extended longevity.

J Am Coll Cardiol 2015;65:1915–28

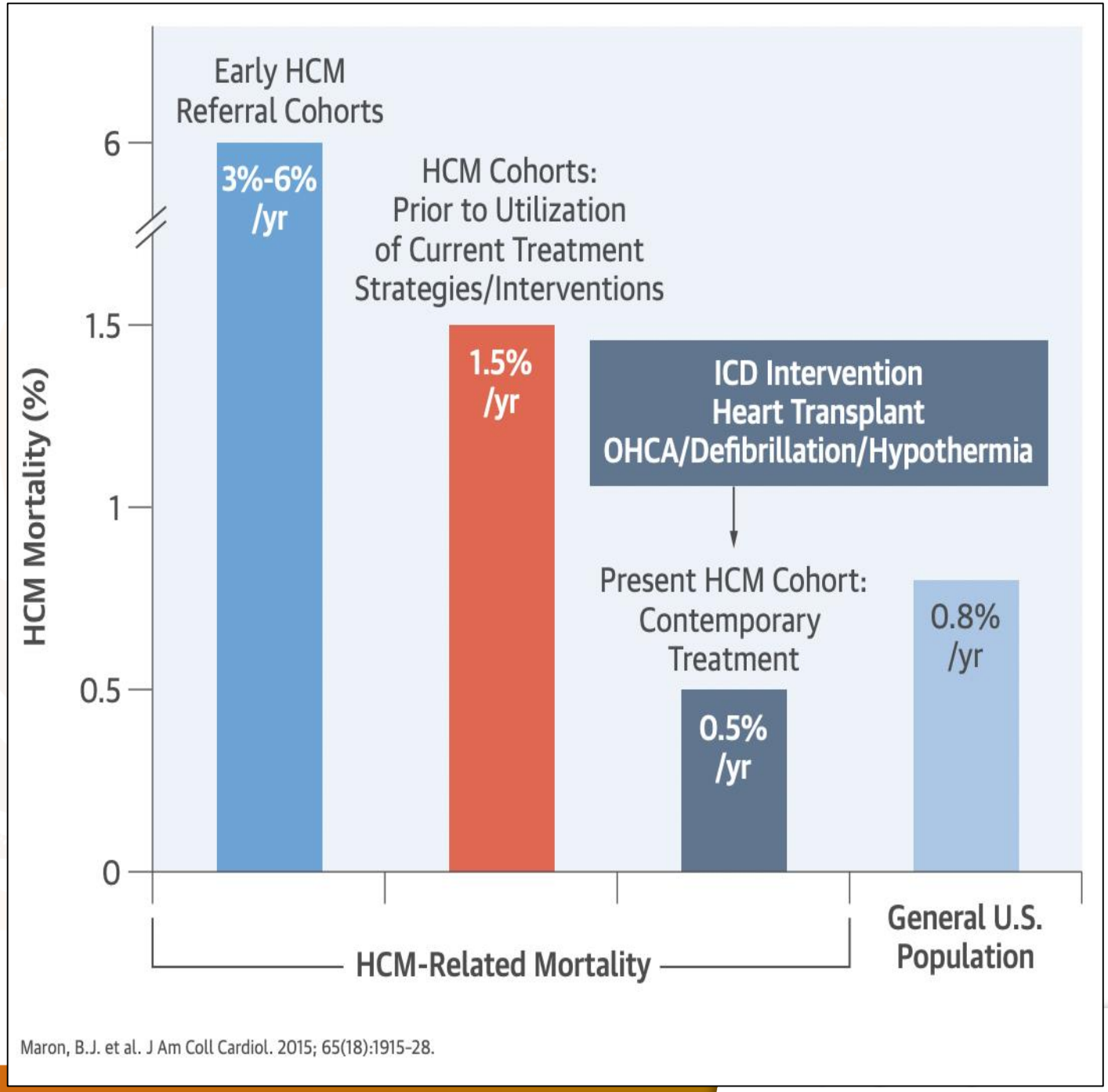


TABLE 3 Univariate and Multivariate Predictors of HCM-Related Mortality or Life-Threatening Event

Parameter	Univariate				Multivariate	
	HCM Death or Event (n = 96)	No HCM Death or Event (n = 904)	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value
Age at diagnosis, yrs	34.8 ± 12.2	41.0 ± 11.0	0.963 (0.947-0.980)	<0.001	0.967 (0.951-0.983)	<0.001
Age of first evaluation, yrs	43.8 ± 8.2	45.9 ± 8.5	0.986 (0.962-1.009)	0.24		
Males	58 (60.4)	645 (71.4)	0.587 (0.389-0.886)	0.011	0.611 (0.400-0.933)	0.023
LVOT gradient ≥30 mm Hg at rest	27 (28.1)	245 (27.1)	1.084 (0.694-1.693)	0.72		
Left atrial dimension, mm	46.0 ± 9.8	41.9 ± 6.7	1.064 (1.040-1.090)	<0.001	1.048 (1.048-1.024)	<0.001
LVED transverse dimension, mm	45.2 ± 6.7	43.7 ± 6.8	1.025 (0.993-1.058)	0.13		
Maximal LV thickness, mm	23.1 ± 6.8	21.6 ± 5.3	1.033 (0.999-1.067)	0.057		
Atrial fibrillation	46 (47.9)	219 (24.2)	1.931 (1.291-2.892)	0.001		
Presence of LGE*	21/25 (84.0)	179/440 (40.7)	5.250 (1.793-15.367)	<0.001		
NYHA functional class at study entry						
I	39 (40.6)	487 (53.9)				
II	27 (28.1)	248 (27.4)	1.544 (0.939-2.539)	<0.001		
III/IV	30 (31.3)	169 (18.7)	2.601 (1.606-4.211)			
NYHA functional class at most recent evaluation						
I	48 (20.0)	576 (65.2)				
II	24 (25.0)	239 (27.1)	1.119 (0.683-1.834)	<0.001	2.488 (1.514, 4.088)†	0.001
III/IV	24 (25.0)	68 (7.7)	3.457 (2.116-5.647)			

Values are mean ± SD or n (%). *n = 465 patients; this variable was excluded from multivariate analysis. †NYHA functional class I was used as a reference at respective time points.
Abbreviations as in Table 1.

J Am Coll Cardiol 2015;65:1915–28

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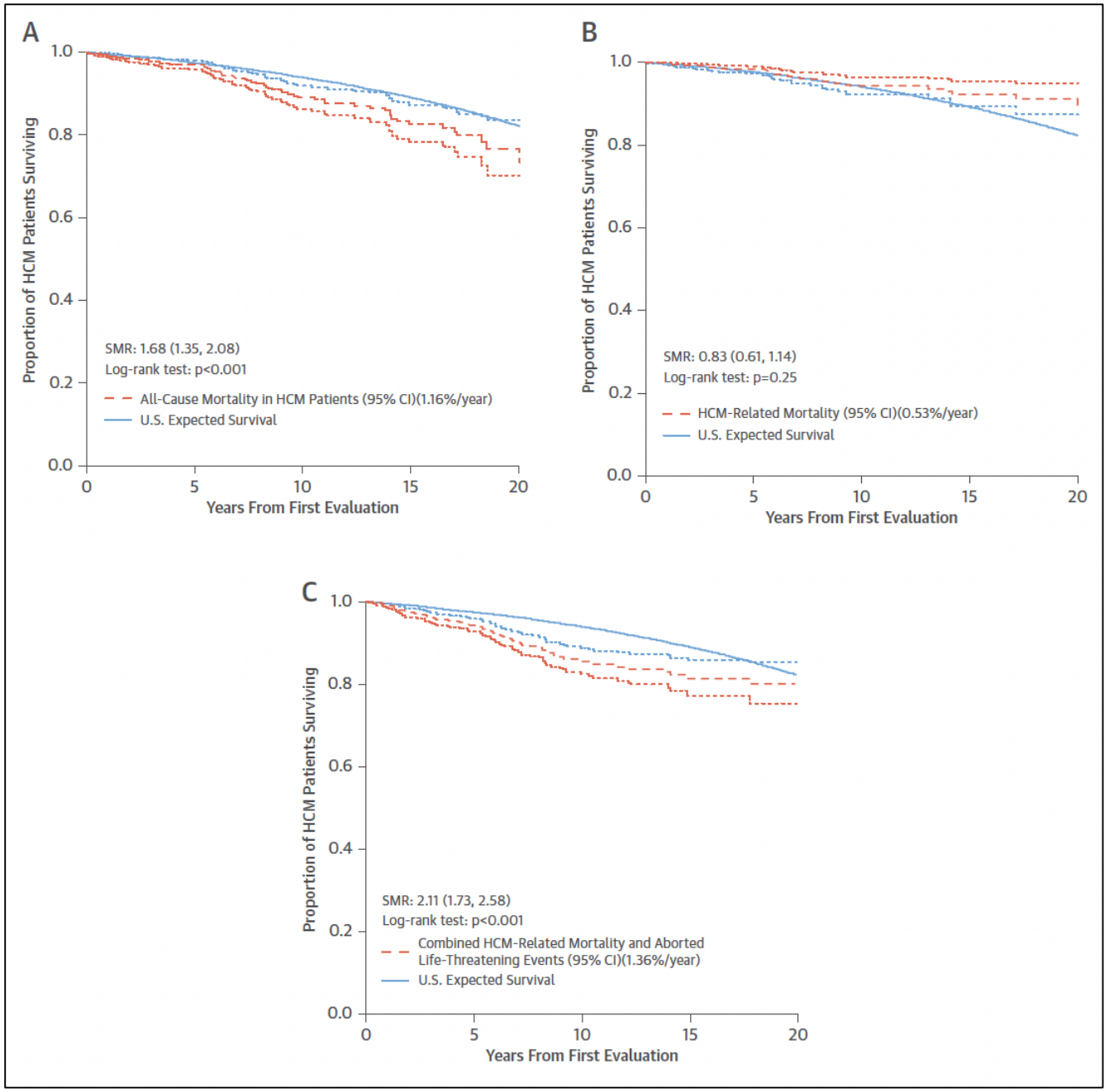
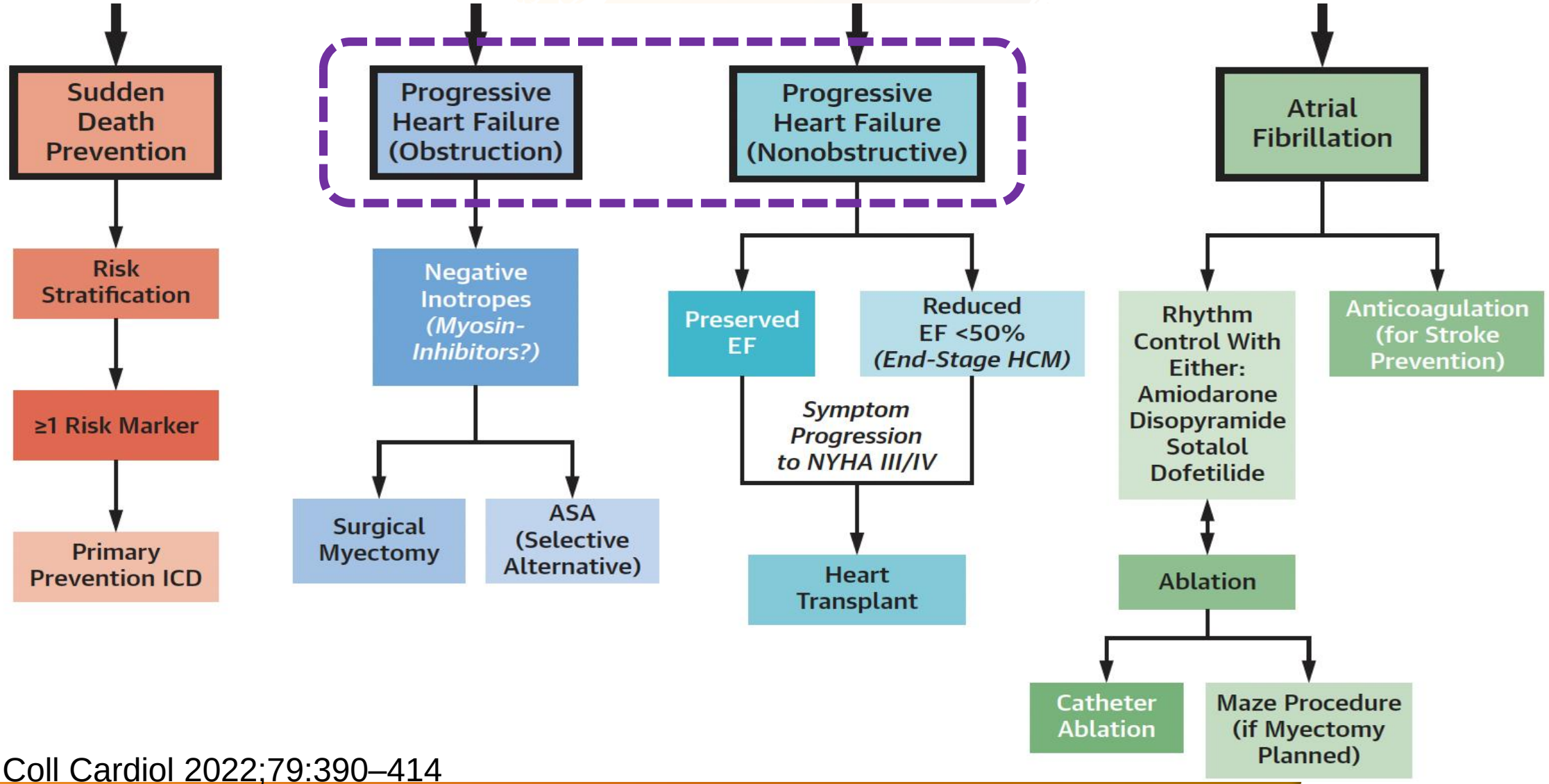


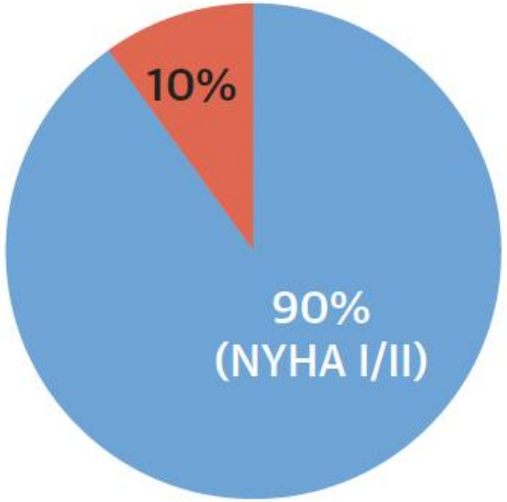
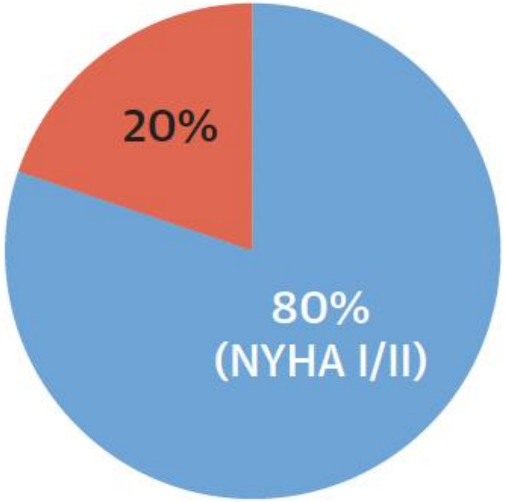
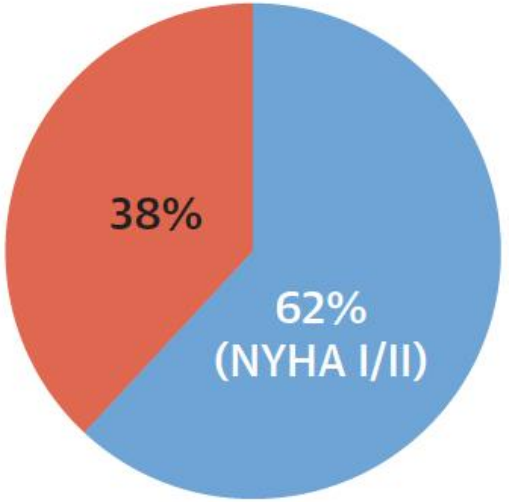
J Am Coll Cardiol 2013;65:1915–28

Perfiles pronósticos en MCH



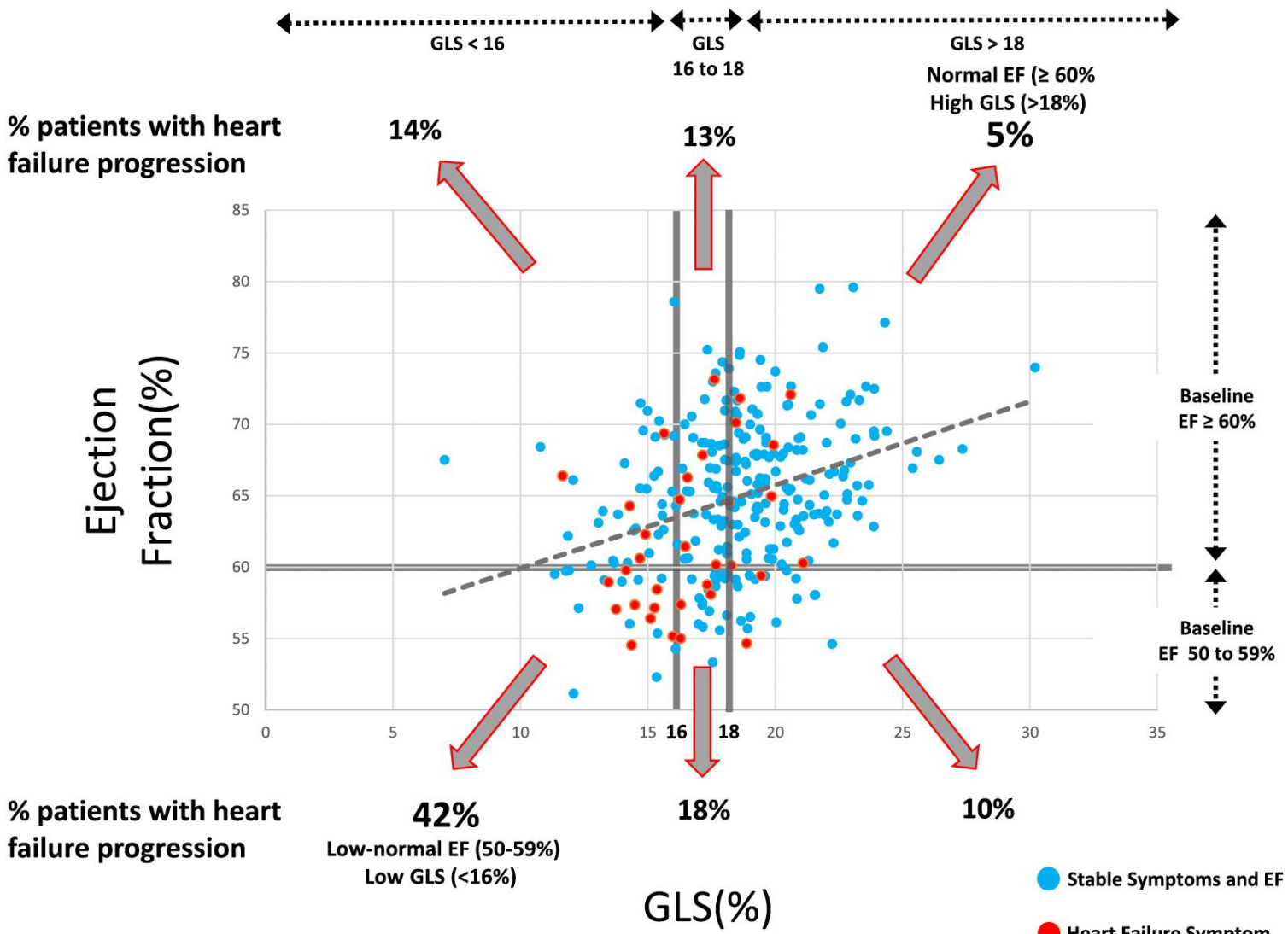
J Am Coll Cardiol 2022;79:390–414

Y qué pasa con la falla cardíaca (NYHA)??

	Nonobstructive	*Provocable Obstruction*	*Rest Obstruction*
Proportion of Patients Who Evolved to NYHA Functional Class III/IV (red)			
Rate of Progression to NYHA Functional Class III/IV (%/y)	1.6%/y	3.2%/y	7.4%/y
Treatment for Progression to NYHA Functional Class III/IV	Transplant (CRT)	Myectomy (ASA)	Myectomy (ASA)

Usefulness of Global Longitudinal Strain to Predict Heart Failure Progression in Patients With Nonobstructive Hypertrophic Cardiomyopathy

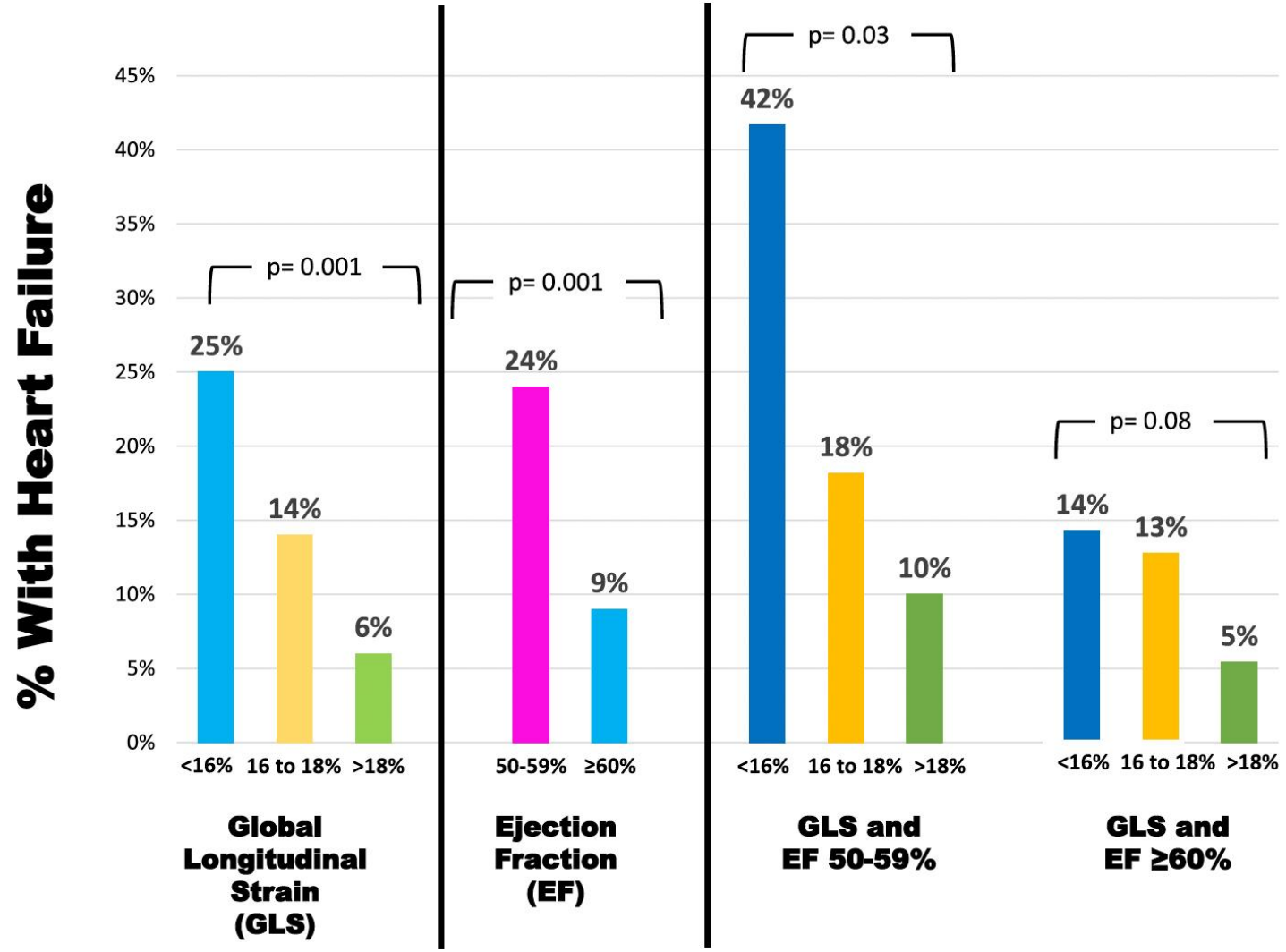
Ethan J. Rowin, MD[a,*], Barry J. Maron, MD[a], Sophie Wells, MD[a], Austin Burrows, BA[a], Christopher Firely, MD[a], Benjamin Koethe, MPH[b], Ayan R. Patel, MD[a], and Martin S. Maron, MD[a]



" In nonobstructive HC with no or mild symptoms and preserved EF, abnormal GLS is a strong independent predictor for subsequent development of progressive heart failure symptoms and/or systolic dysfunction. Furthermore, the greatest power in predicting outcome in nonobstructive HC is achieved by combining GLS with EF to identify HC patients at the highest risk for heart failure progression and systolic dysfunction."

Am J Cardiol 2021;151:86–92)

Porcentaje de pacientes quienes desarrollaron sintomas de falla cardíaca o disfunción sistólica por FE, LGS y la combinación.

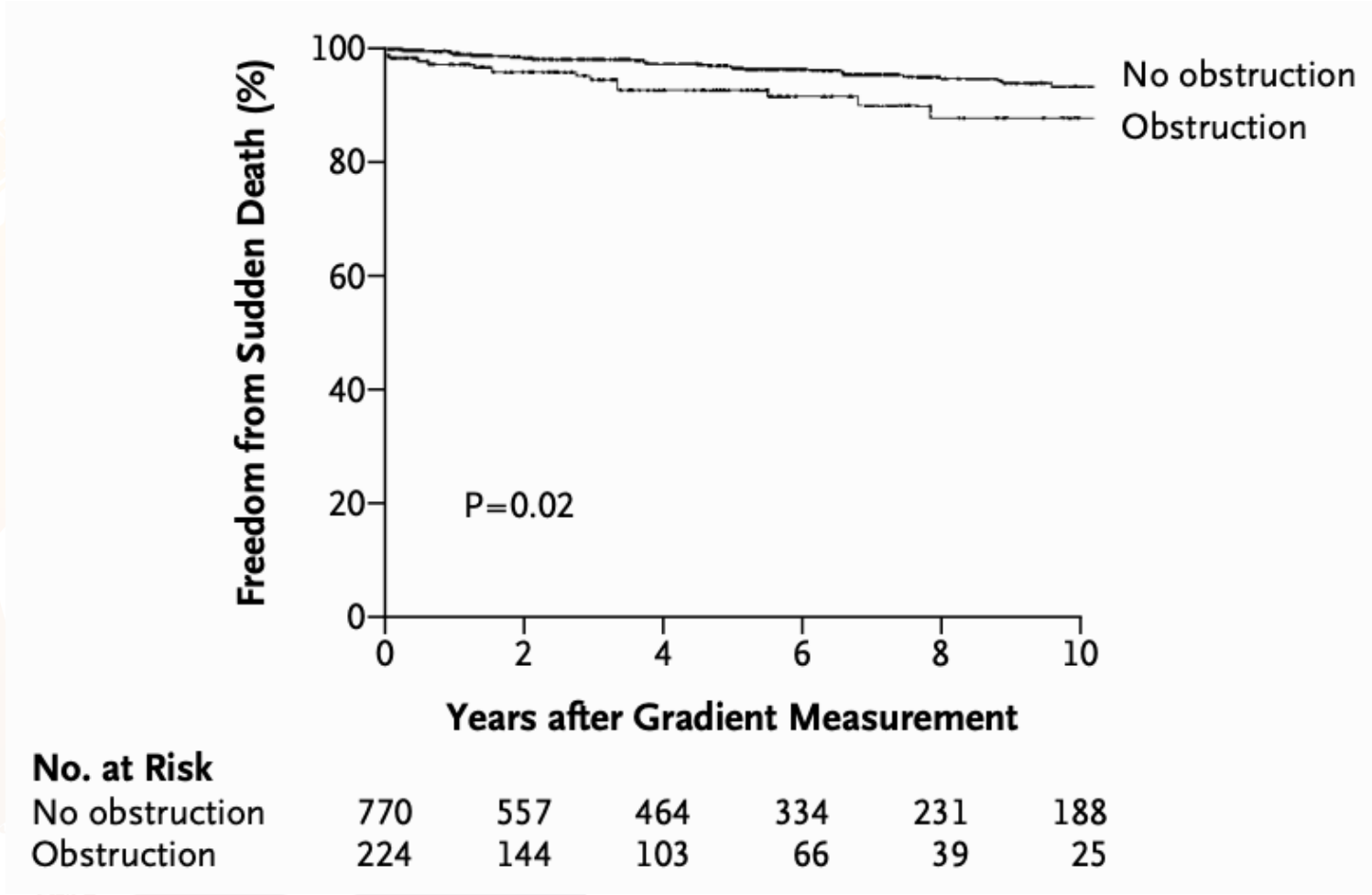


Am J Cardiol 2015;116:91

ORIGINAL ARTICLE

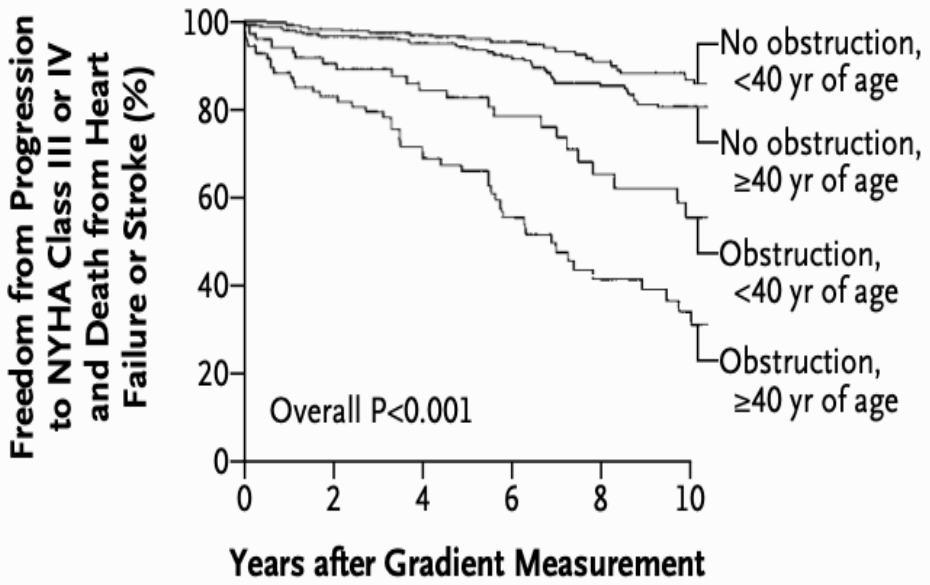
Effect of Left Ventricular Outflow Tract Obstruction on Clinical Outcome in Hypertrophic Cardiomyopathy

Martin S. Maron, M.D., Iacopo Olivotto, M.D., Sandro Betocchi, M.D., Susan A. Casey, R.N., John R. Lesser, M.D., Maria A. Losi, M.D., Franco Cecchi, M.D., and Barry J. Maron, M.D.



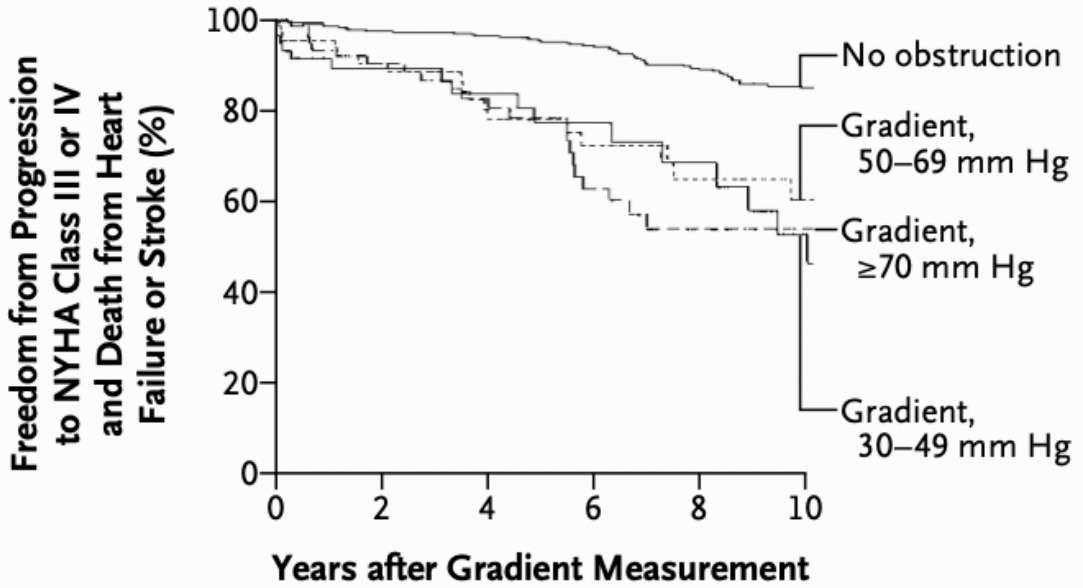
Muerte súbita de acuerdo a LVOT

N Engl J Med 2003;348:295-303.



No. at Risk

No obstruction, <40 yr of age	349	251	206	146	103	80
No obstruction, ≥40 yr of age	421	306	258	188	128	108
Obstruction, <40 yr of age	106	70	52	37	21	15
Obstruction, ≥40 yr of age	118	74	51	29	18	10



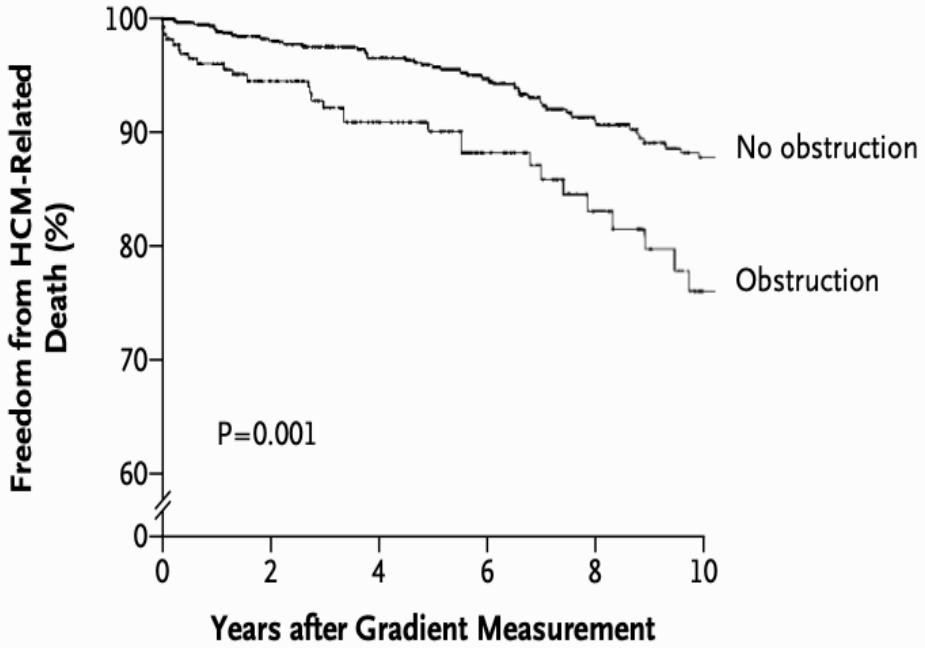
No. at Risk

No obstruction,	770	557	464	334	231	188
Gradient, 30–49 mm Hg	62	38	28	18	12	8
Gradient, 50–69 mm Hg	73	50	37	24	16	10
Gradient, ≥70 mm Hg	89	56	38	24	11	7

Efecto de edad y LVOT de por lo menos 30 mmhg en progresión a falla cardiaca severa o muerte por Ins. Cardíaca ó stroke

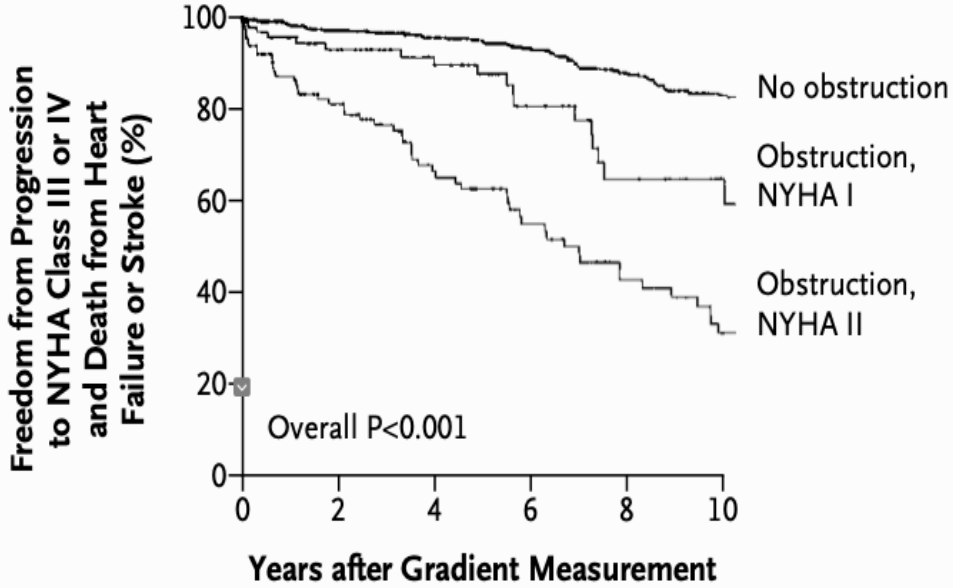
Relación entre la Magnitud del gradiente de LVOT y progresión a falla cardíaca severa (NYHA III-IV) o muerte por falla cardiaca o stroke

N Engl J Med 2003;348:295-303.



No. at Risk

No obstruction	828	594	495	360	247	201
Obstruction	273	178	130	84	54	35



No. at Risk

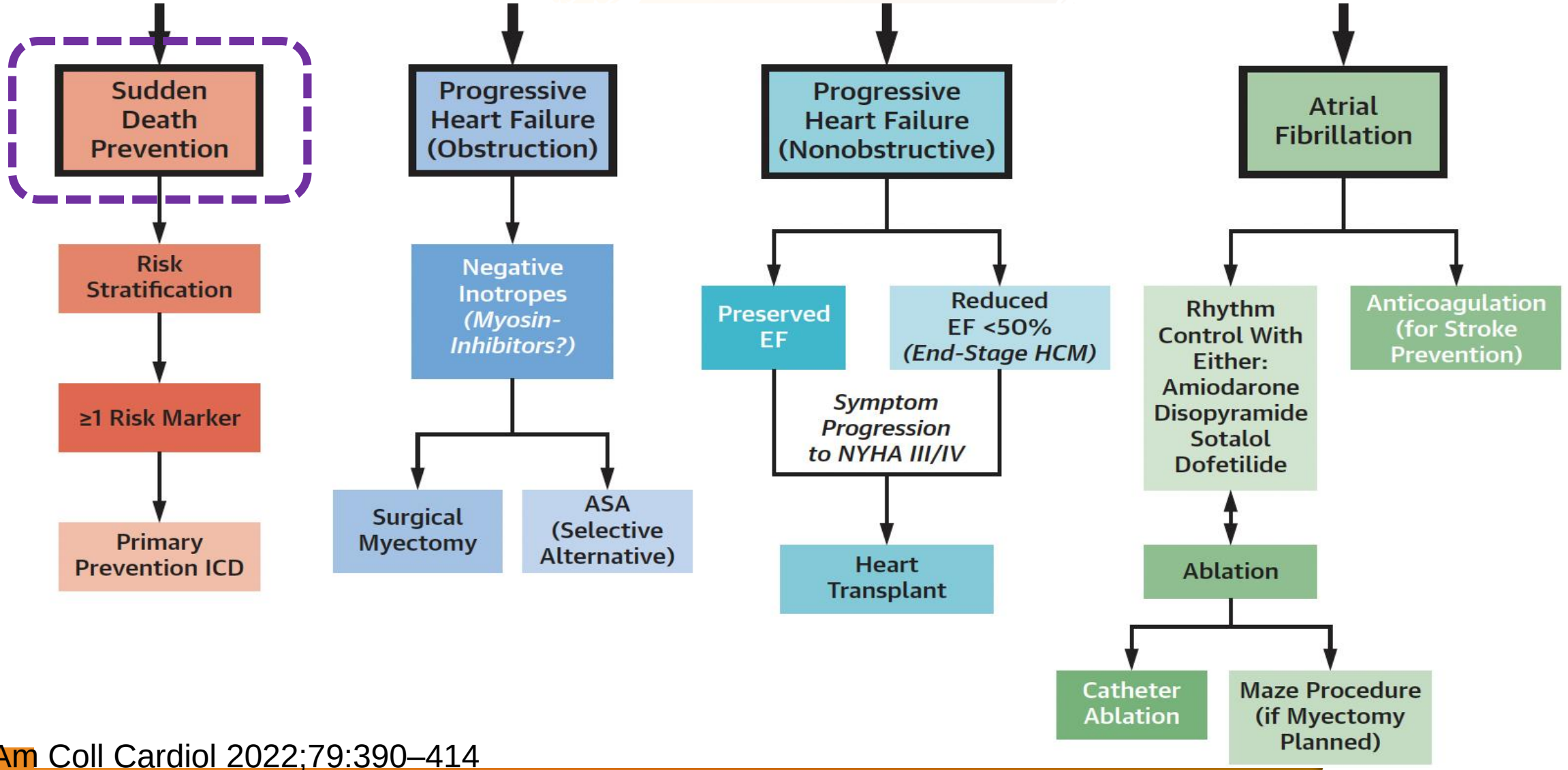
No obstruction	770	557	464	334	231	188
Obstruction, NYHA I	106	69	52	31	18	11
Obstruction, NYHA II	118	75	51	35	21	14

Muerte Cardiovascular relacionada a MCH con gradiente de obstrucción de 30mmhg en condiciones basales

Progresión a Falla Cardíaca severa (NYHA III-IV), o muerte por falla cardíaca o stroke teniendo en cuenta la LVOT

N Engl J Med 2003;348:295-303.

Perfiles pronósticos en MCH



J Am Coll Cardiol 2022;79:390–414

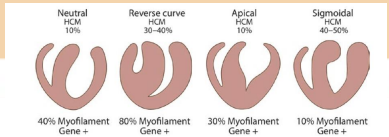
Characterization of a Phenotype-Based Genetic Test Prediction Score for Unrelated Patients with Hypertrophic Cardiomyopathy

J. Martijn Bos, MD, PhD; Melissa L. Will, BS; Bernard J. Gersh, MB, ChB, DPhil; Teresa M. Kruisselbrink, MS, CGC; Steve R. Ommen, MD; and Michael J. Ackerman, MD, PhD

TABLE 3. Multivariate Analysis

Predictor	OR	95% CI	*P* value
Reverse curve HCM	2.97	2.18-4.04	<.001
Age at diagnosis <45 y	2.46	1.78-3.38	<.001
Family history of HCM	2.36	1.74-3.29	<.001
Family history of SCD	1.45	1.01-2.01	.02
MLVWT ≥20 mm	1.72	1.26-2.35	.01
Female sex	1.29	0.95-1.75	.10
Hypertension	0.47	0.33-0.67	<.001

HCM = hypertrophic cardiomyopathy; MLVWT = maximum left ventricular wall thickness; OR = odds ratio; SCD = sudden cardiac death.



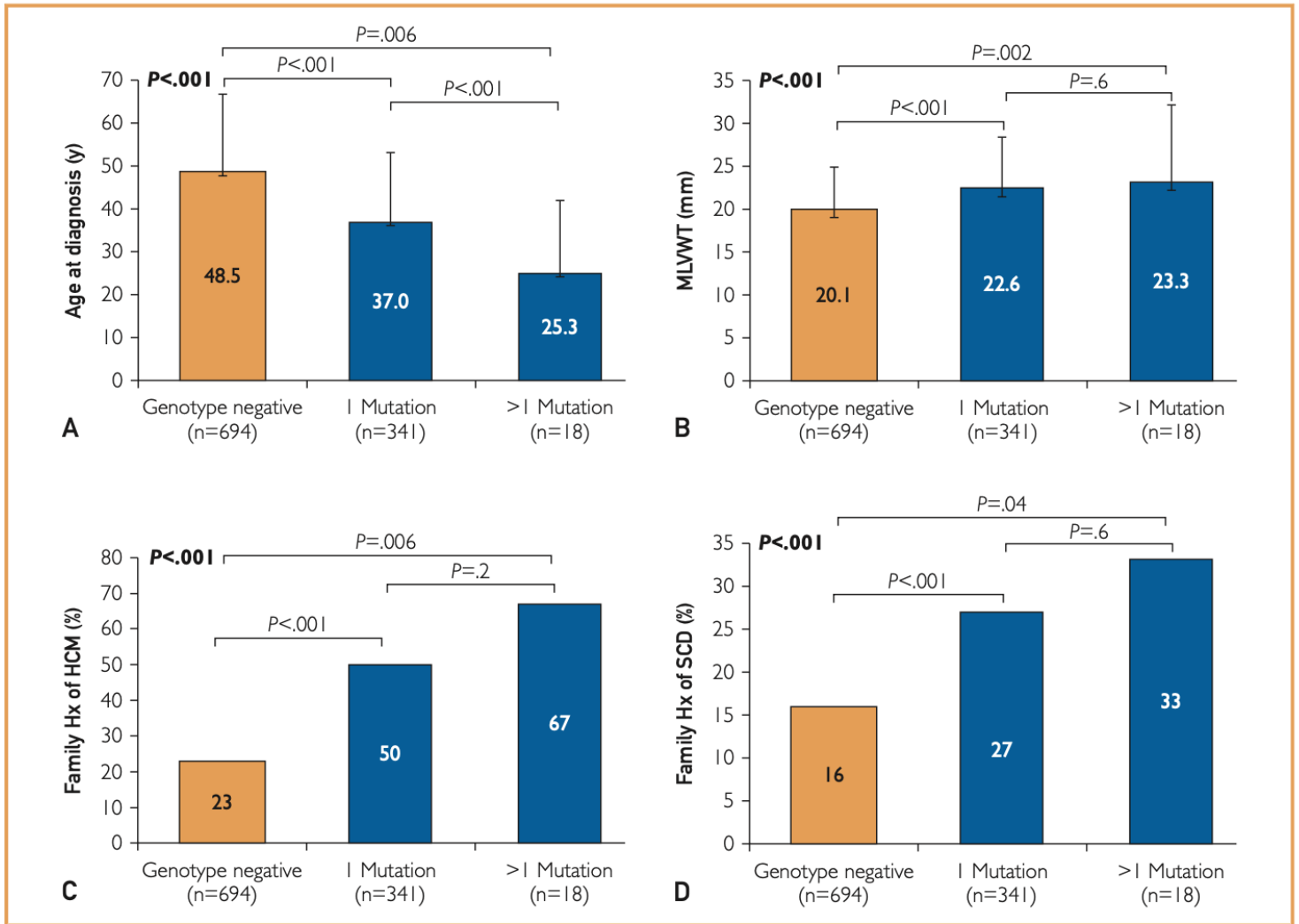


FIGURE 1. Genotype-phenotype analyses for patients with 1 mutation (n=341) or more than 1 mutation (n=18) with respect to age at diagnosis (A), maximum left ventricular wall thickness (MLVWT) (B), family history of hypertrophic cardiomyopathy (HCM) (C), and family history of sudden cardiac death (SCD) (D). Data are given as mean ± SD. Hx = history.

Mayo Clin Proc. 2014 Jun;89(6):727-37

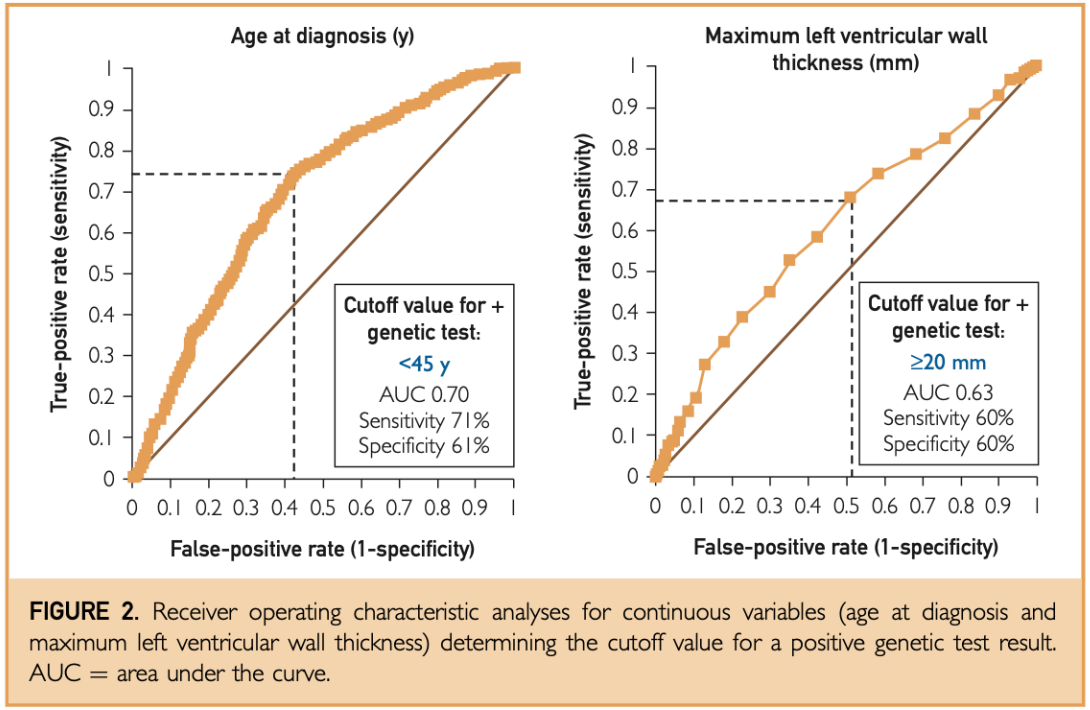


FIGURE 2. Receiver operating characteristic analyses for continuous variables (age at diagnosis and maximum left ventricular wall thickness) determining the cutoff value for a positive genetic test result. AUC = area under the curve.

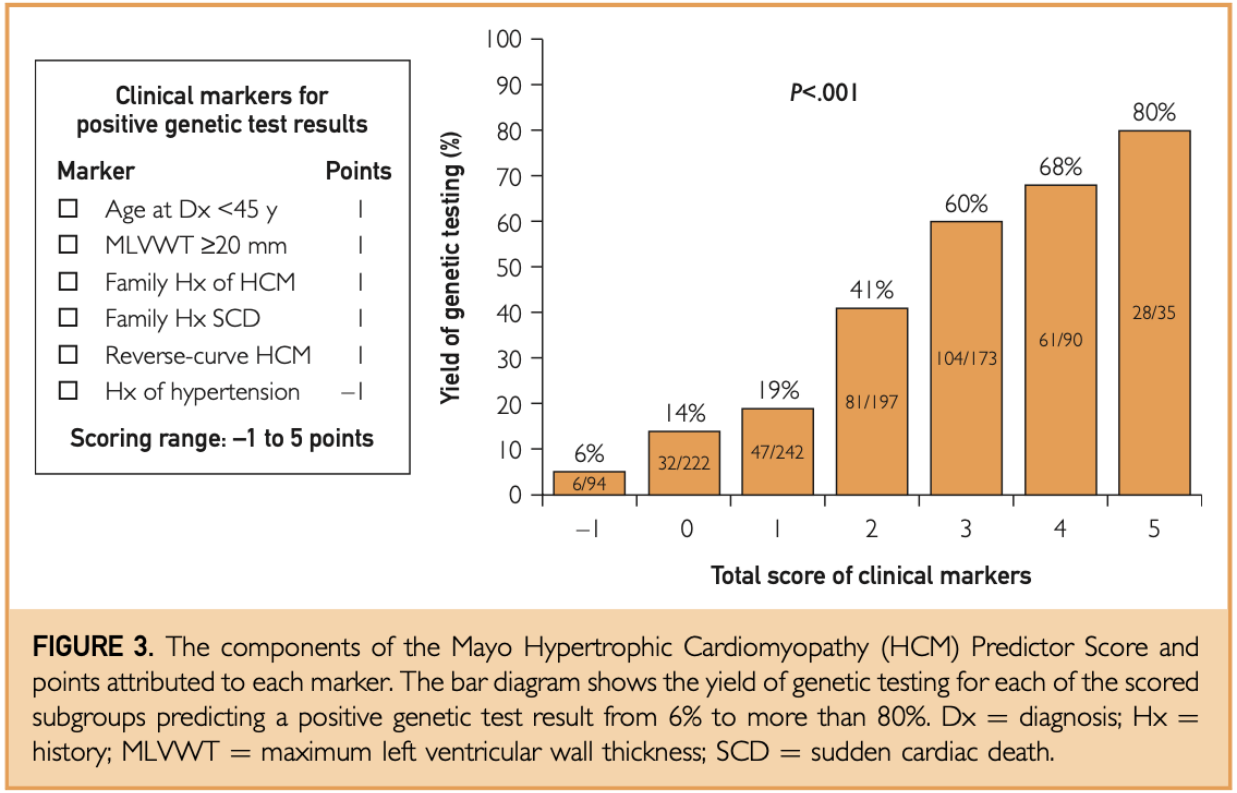
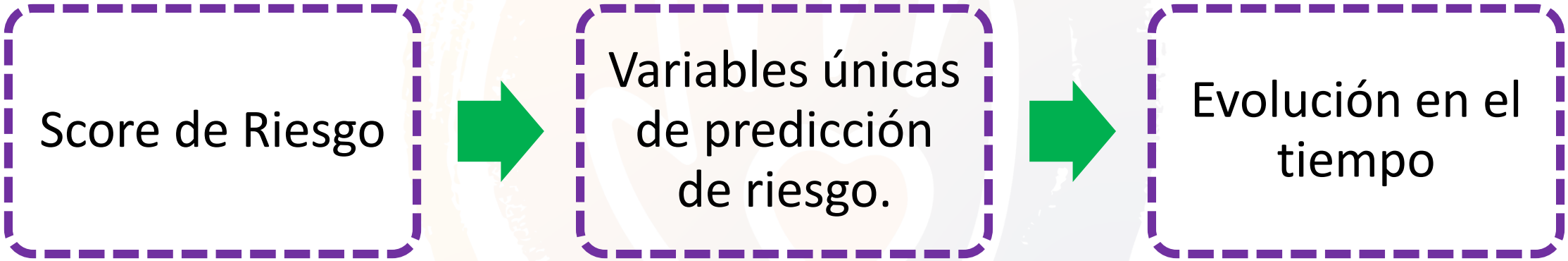
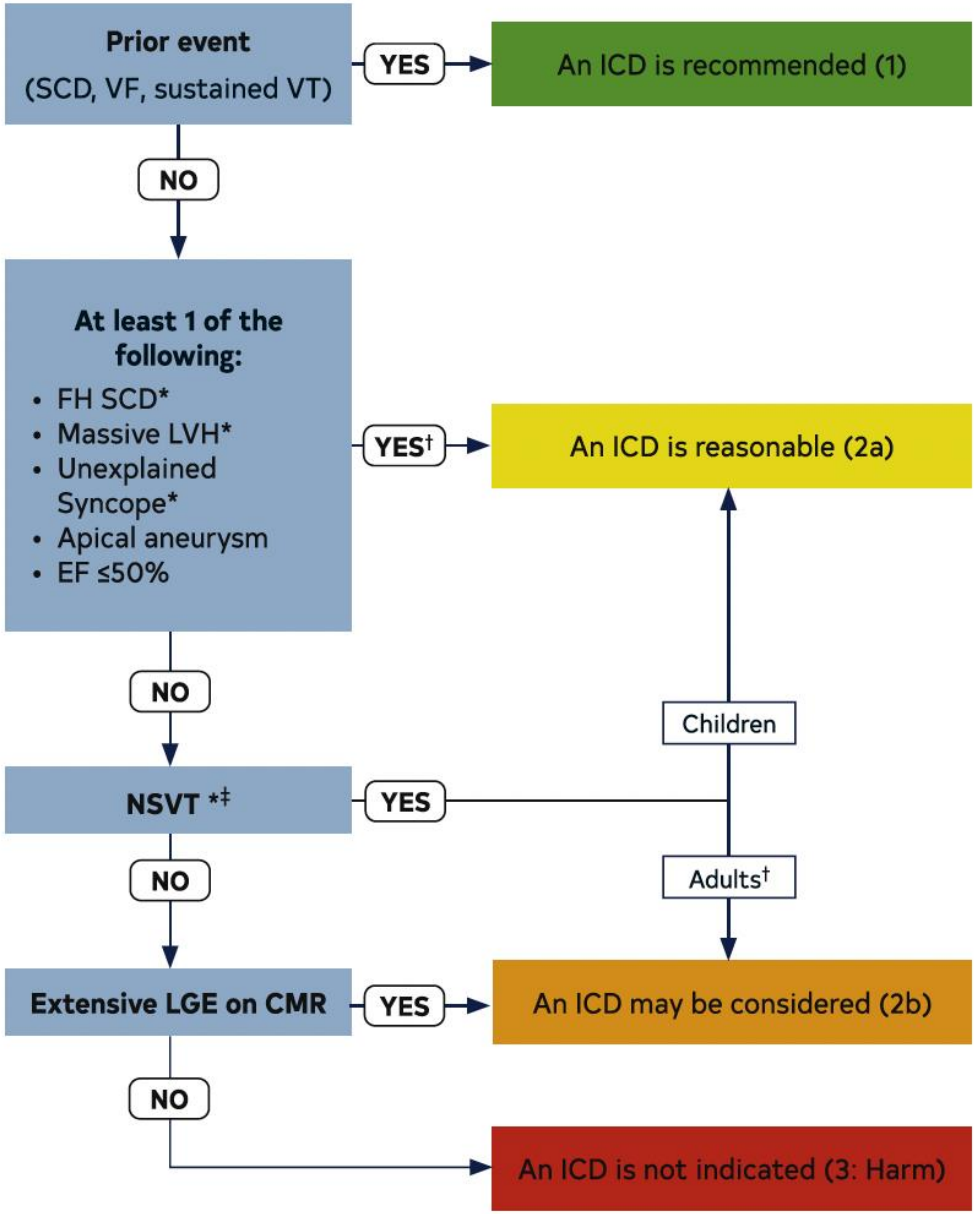


FIGURE 3. The components of the Mayo Hypertrophic Cardiomyopathy (HCM) Predictor Score and points attributed to each marker. The bar diagram shows the yield of genetic testing for each of the scored subgroups predicting a positive genetic test result from 6% to more than 80%. Dx = diagnosis; Hx = history; MLVWT = maximum left ventricular wall thickness; SCD = sudden cardiac death.

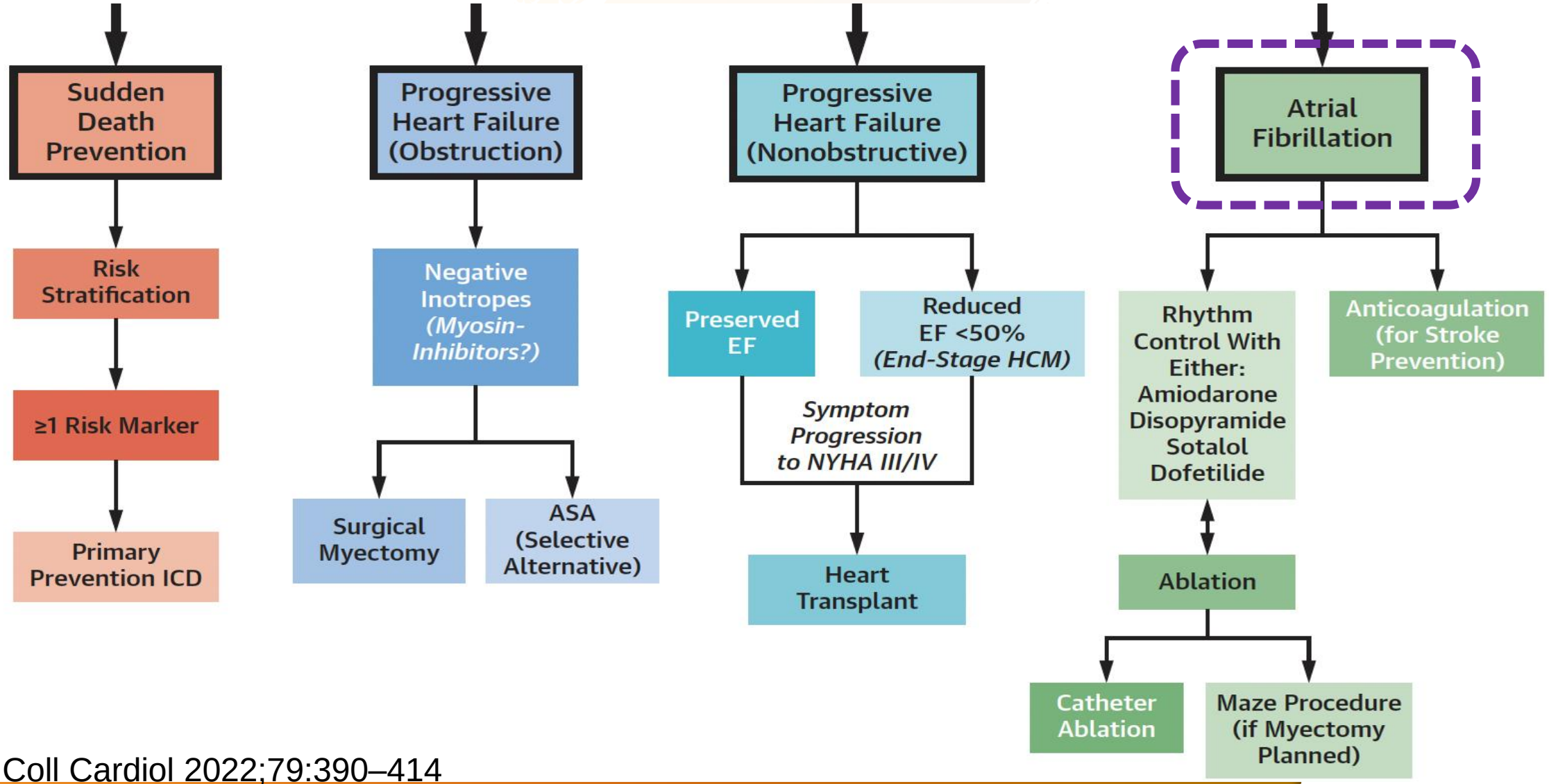
Mayo Clin Proc. 2014 Jun;89(6):727-37


Score de Riesgo
Variables únicas de predicción de riesgo.
Evolución en el tiempo

Historia Familiar de Muerte súbita
Hipertrofia ventricular Izquierda extrema
Síncope reciente no explicado
Taquicardia ventricular no sostenida
Realce Tardío
Miocardiopatía Hipertrófica Estadio Avanzado
Aneurisma apical VI

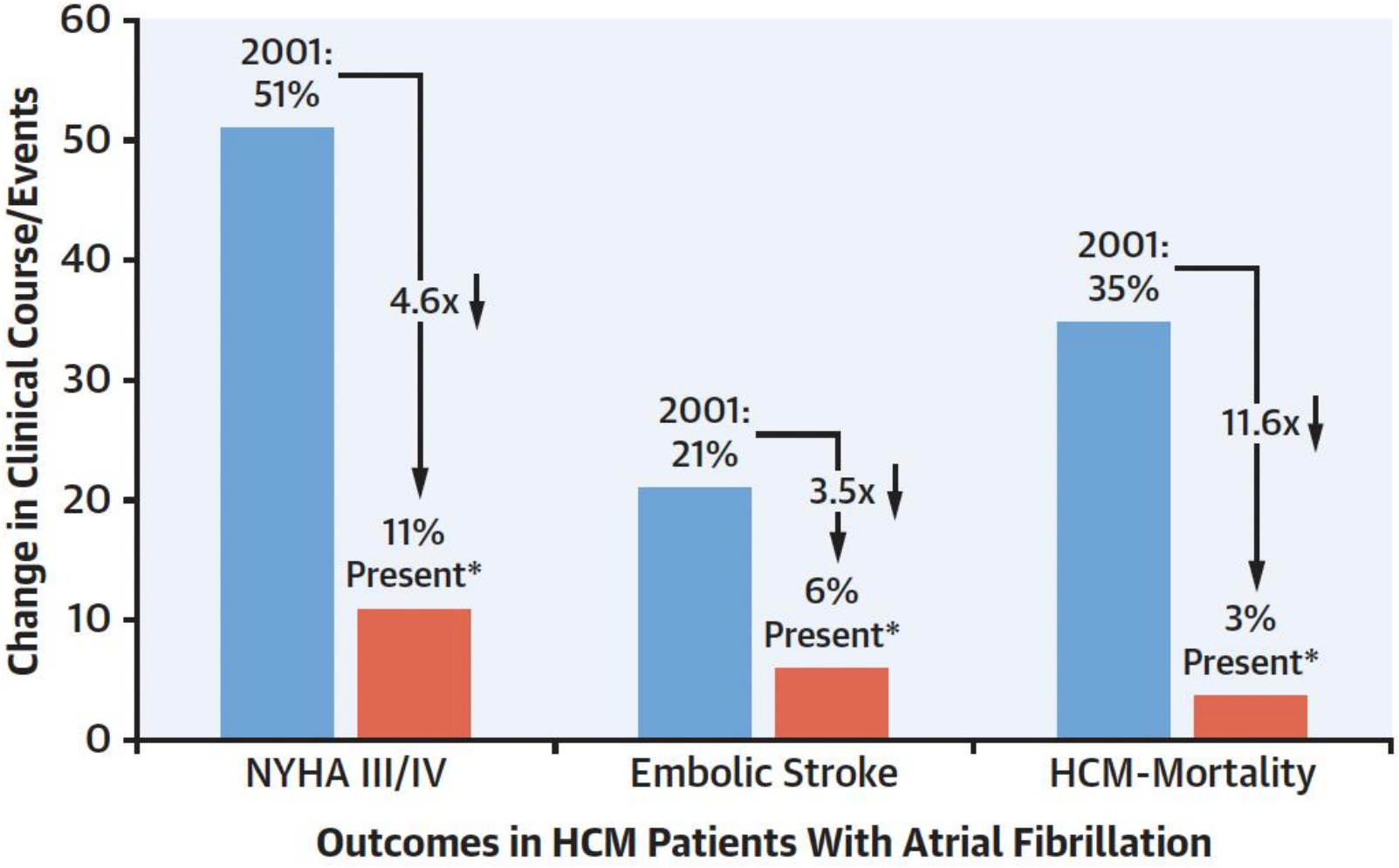

Prior event
(SCD, VF, sustained VT)
YES
An ICD is recommended (1)
NO
At least 1 of the following:
• FH SCD*
• Massive LVH*
• Unexplained Syncope*
• Apical aneurysm
• EF ≤50%
YES†
An ICD is reasonable (2a)
NO
Children
NSVT *‡
YES
NO
Adults†
Extensive LGE on CMR
YES
An ICD may be considered (2b)
NO
An ICD is not indicated (3: Harm)

Perfiles pronósticos en MCH



J Am Coll Cardiol 2022;79:390–414

Y qué pasa con el perfil de la Fibrilación Auricular.

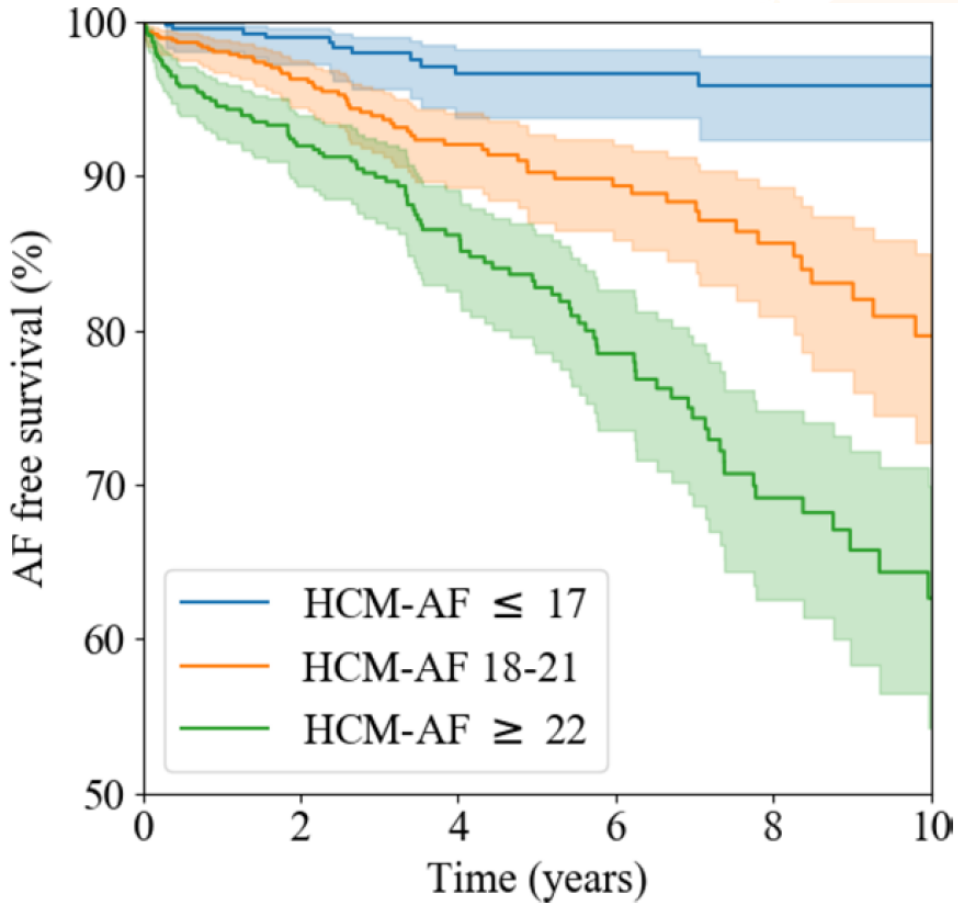


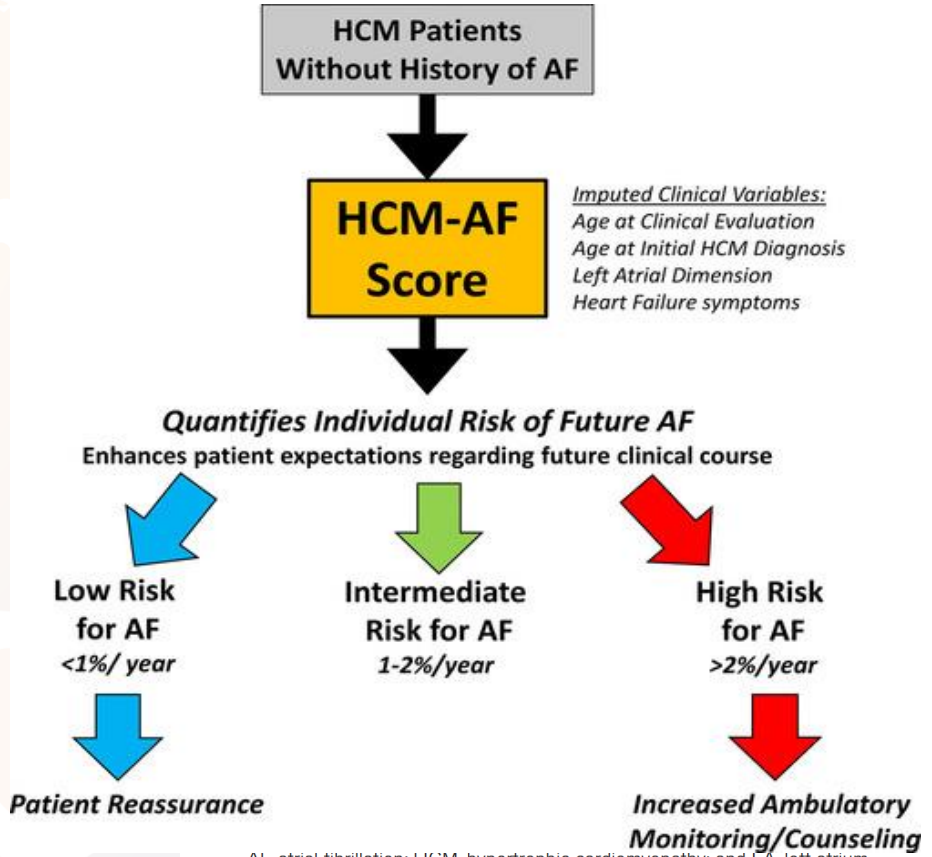
ORIGINAL ARTICLE

Development and Validation of a Clinical Predictive Model for Identifying Hypertrophic Cardiomyopathy Patients at Risk for Atrial Fibrillation

The HCM-AF Score

Richard T. Carrick, MD, PhD; Martin S. Maron, MD; Arnon Adler, MD; Benjamin Wessler, MD; Sara Hoss, MD; Raymond H. Chan, MD, MPH; Aadhavi Sridharan, MD; Dou Huang, MD; Craig Cooper, MD; Jennifer Drummond, MD; Harry Rakowski, MD; Barry J. Maron, MD; Ethan J. Rowin, MD





AF, atrial fibrillation; HCM, hypertrophic cardiomyopathy; and LA, left atrium.

	HCM-AF score ≥18*	HCM-AF score ≥ 22†	LA dimension ≥45 mm
Sensitivity (to detect patients with AF development)	95% [91–99]	58% [50–67]	35% [27–43]‡§
Specificity (likelihood detecting patients not at risk for AF)	25% [23–28]	66% [63–69]	81% [79–83]‡§
Positive predictive value	13% [11–15]	17% [14–24]	18% [13–22]
Negative predictive value	97% [94–99]	93% [91–95]	91% [89–93]‡

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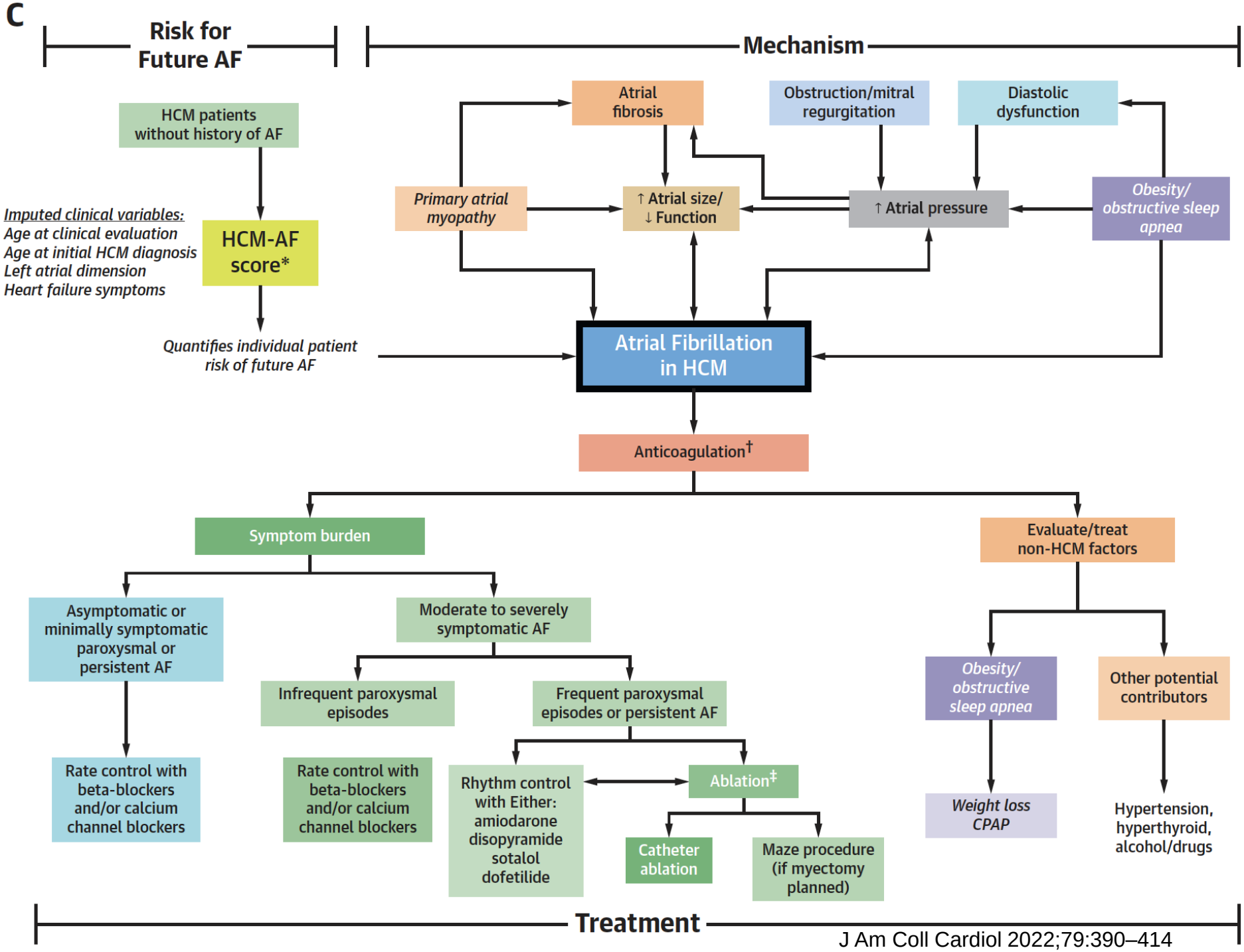

J Am Coll Cardiol 2022;79:390–414

¿Qué nuevas alternativas farmacológicas se pueden utilizar para el manejo?

Obstructivo

No Obstructivo

Mitigar síntomas/No impactan en progresión

Acercamiento Global Inicial sintomático!!

1. BB
2. Calcio antagonistas No dihidropiridínicos.
3. Disopiramida
4. Manejo de comorbilidades adicionales

STATE OF THE ART IN HYPERTROPHIC CARDIOMYOPATHY

JOBS DONE

- ✓ 1957-58 first modern description of HCM
- ✓ 1964 First surgical myectomy
- ✓ 1966 beta-adrenergic blockade in HCM
- ✓ 1980 first ICD implanted in HCM
- ✓ 1982 introduction of disopyramide for oHCM
- ✓ 1990 first genetic mutation identified
- ✓ 1995 alcohol septal ablation
- ✓ 2000 ICD proven effective in SCD prevention
- ✓ 2010's Large HCM international registries
- ✓ *2012 Next generation sequencing*
- ✓ 2014 ESC-SCD risk score calculator
- ✓ 2020 phase III study on mavacamten

OPEN ISSUES

- × Control of symptoms in nonobstructive HCM
- × Control/prevention of atrial fibrillation
- × Pharmacological control of ventricular arrhythmias
- × Prevention of phenotype development
- × Impact on natural history and disease progression
- × Large randomized trial assessing outcome
- × Treatment of pediatric populations
- × Psychological issues and lifestyle
- × Personalized sport prescription
- × Genetic therapy?

Current Heart Failure Reports (2021) 18:169–179

EXPLORER HCM

- 18 años
- Dx MCH
- OTSVI reposo, vaisalba o ejercicio mayor o igual a 50 mmhg.
- Fe 55%
- NYHA II-III
- Capaces de realizar una prueba de ejercicio cardiopulmonar (usual)

Obstructivos

	Mavacamten group (n=123)	Placebo group (n=128)	Difference* (95% CI), p value
Primary endpoint†			
Either ≥1·5 mL/kg per min increase in pVO_2 with ≥1 NYHA class improvement or ≥3·0 mL/kg per min increase in pVO_2 with no worsening of NYHA class	45 (37%)	22 (17%)	19·4 (8·7 to 30·1; p=0·0005)
≥1·5 mL/kg per min increase in pVO_2 with ≥1 NYHA class improvement	41 (33%)	18 (14%)	19·3 (9·0 to 29·6)
≥3·0 mL/kg per min increase in pVO_2 with no worsening of NYHA class	29 (24%)	14 (11%)	12·6 (3·4 to 21·9)
Both ≥3·0 mL/kg per min increase in pVO_2 and ≥1 NYHA class improvement	25 (20%)	10 (8%)	12·5 (4·0 to 21·0)
Secondary endpoints‡			
Post-exercise LVOT gradient change from baseline to week 30, mm Hg	−47 (40), n=117	−10 (30), n=122	−35·6 (−43·2 to −28·1; p<0·0001)
pVO_2 change from baseline to week 30, mL/kg per min	1·4 (3·1), n=120	−0·1 (3·0), n=125	1·4 (0·6 to 2·1; p=0·0006)
≥1 NYHA class improvement from baseline to week 30§	80 (65%)	40 (31%)	34% (22 to 45; p<0·0001)
Change from baseline to week 30 in KCCQ-CSS§	13·6 (14·4), n=92	4·2 (13·7), n=88	9·1 (5·5 to 12·7; p<0·0001)
Change from baseline to week 30 in HCMSQ-SoB§	−2·8 (2·7), n=85	−0·9 (2·4), n=86	−1·8 (−2·4 to −1·2; p<0·0001)

Desenlace primario:

Compuesto entre Rta clínica a semana 30 comparado con el basal (definido cambio como 1.5 ml/Kg/Min ó + en pVO2 ó por lo menos una reducción de clase funcional ó 3 ml/Kg/min ó > de mejoría de pVO2 y no empeoramiento de clase funcional).

Desenlaces secundario:

Cambio de gradientes LVOT
pVO2
% de pctes con cambio en NYHA
Mejoría de calidad de vida

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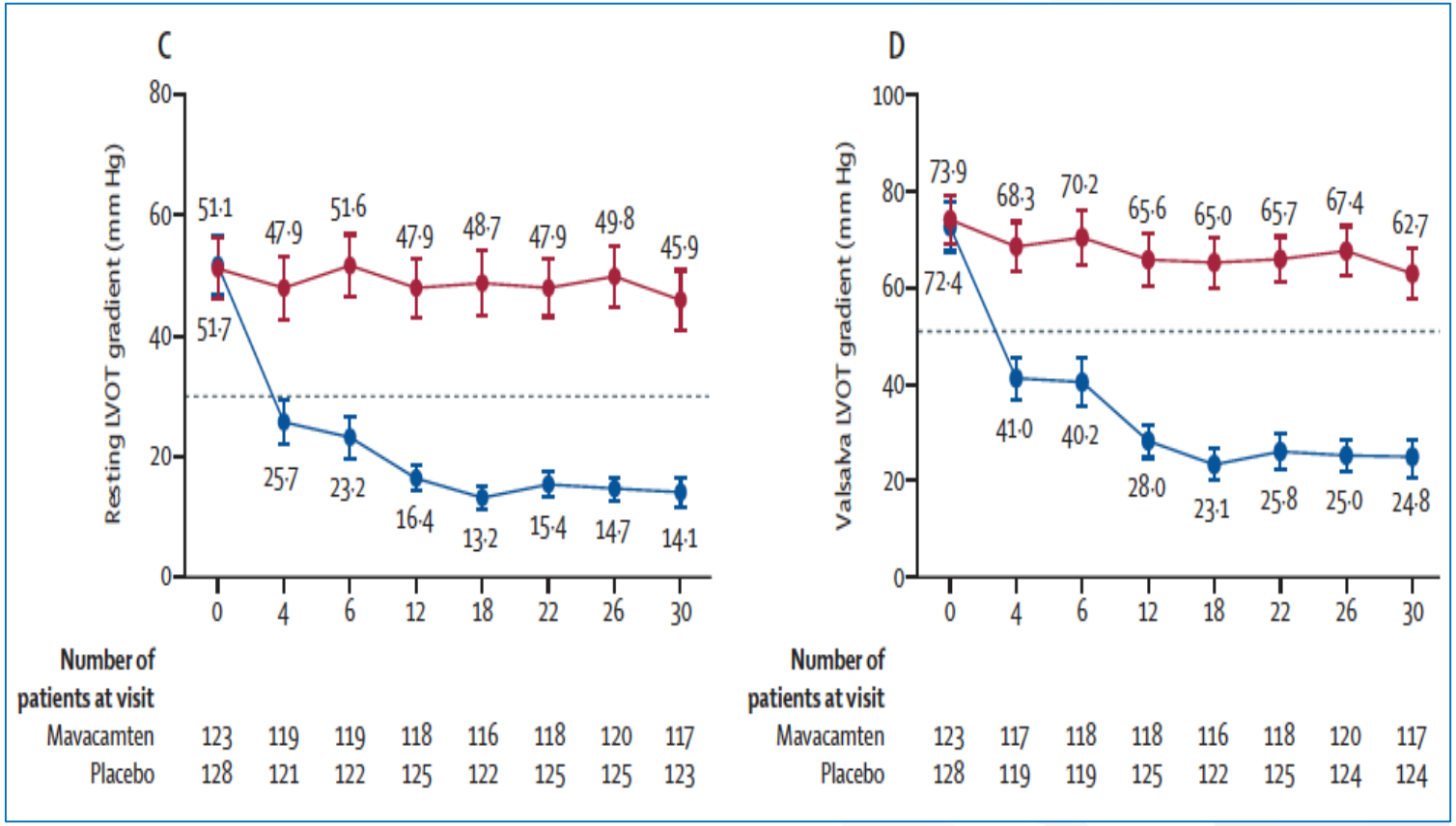


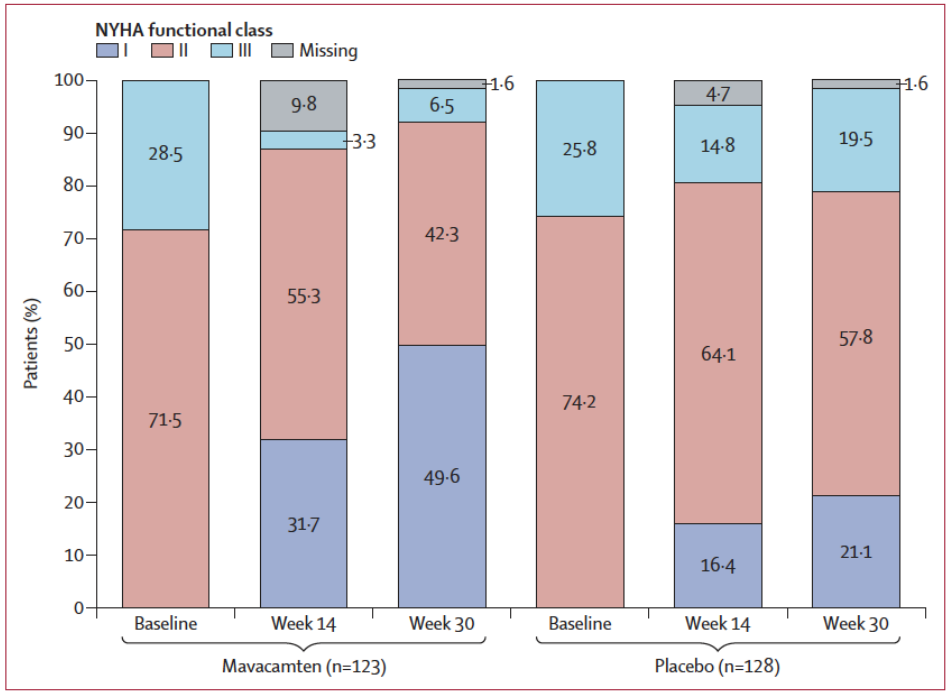


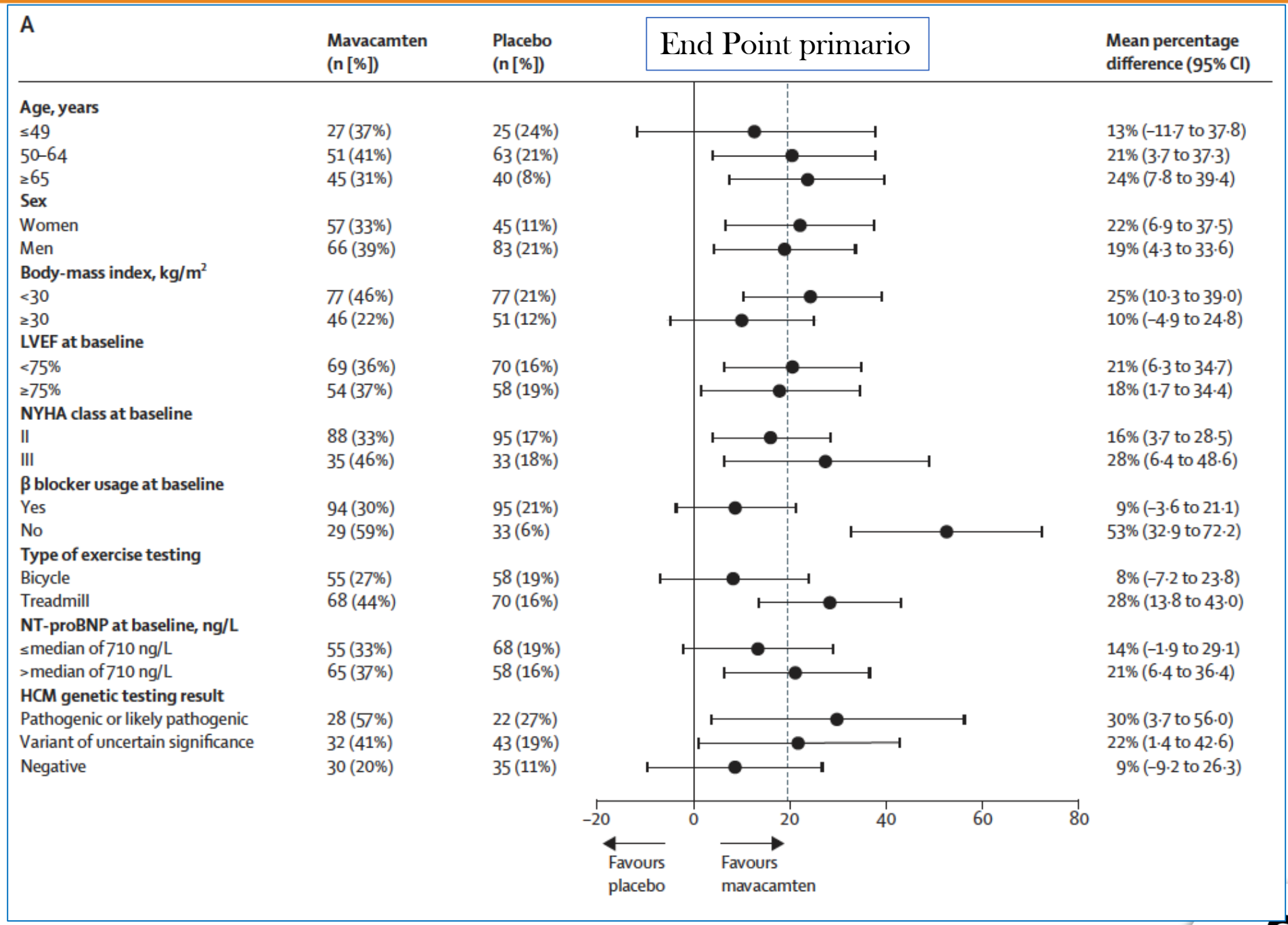
Figure 2: **NYHA functional class**
Percentage of patients who had NYHA class I, II, or III at baseline, after 14 weeks and 30 weeks of treatment, for the mavacamten and placebo groups. NYHA=New York Heart Association.

	Mavacamten group	Placebo group	Difference (95% CI)
Complete response*	32/117 (27%)	1/126 (1%)	26·6 (18·3–34·8)
Post-exercise LVOT peak gradient <50 mm Hg†	75/101 (74%)	22/106 (21%)	53·5 (42·0–65·0)
Post-exercise LVOT peak gradient <30 mm Hg‡	64/113 (57%)	8/114 (7%)	49·6 (39·3–59·9)

Data are n/N (%), unless otherwise indicated. LVOT=left ventricular outflow tract. *Defined as New York Heart Association class I and all LVOT peak gradients less than 30 mm Hg (post exercise, resting, and Valsalva). †Threshold for guideline-based invasive intervention. Only patients with baseline post-exercise LVOT peak gradient of at least 50 mm Hg were assessed. ‡Threshold for guideline-based diagnosis of obstruction. Only patients with baseline post-exercise LVOT peak gradient of at least 30 mm Hg were assessed.

Table 3: **Key exploratory efficacy endpoints**

End Point primario



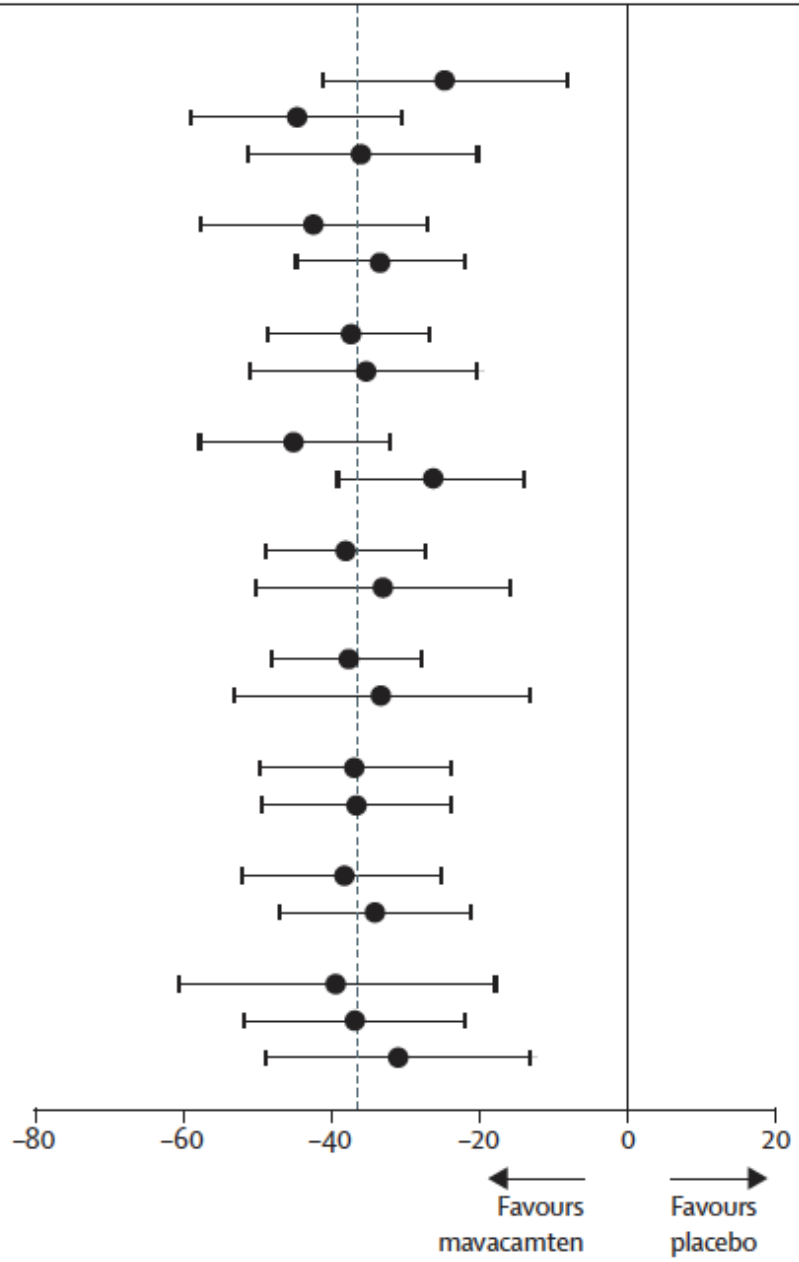
A	Mavacamten (n [%])	Placebo (n [%])	Mean percentage difference (95% CI)
Age, years			
≤49	27 (37%)	25 (24%)	13% (–11·7 to 37·8)
50–64	51 (41%)	63 (21%)	21% (3·7 to 37·3)
≥65	45 (31%)	40 (8%)	24% (7·8 to 39·4)
Sex			
Women	57 (33%)	45 (11%)	22% (6·9 to 37·5)
Men	66 (39%)	83 (21%)	19% (4·3 to 33·6)
Body-mass index, kg/m²			
<30	77 (46%)	77 (21%)	25% (10·3 to 39·0)
≥30	46 (22%)	51 (12%)	10% (–4·9 to 24·8)
LVEF at baseline			
<75%	69 (36%)	70 (16%)	21% (6·3 to 34·7)
≥75%	54 (37%)	58 (19%)	18% (1·7 to 34·4)
NYHA class at baseline			
II	88 (33%)	95 (17%)	16% (3·7 to 28·5)
III	35 (46%)	33 (18%)	28% (6·4 to 48·6)
β blocker usage at baseline			
Yes	94 (30%)	95 (21%)	9% (–3·6 to 21·1)
No	29 (59%)	33 (6%)	53% (32·9 to 72·2)
Type of exercise testing			
Bicycle	55 (27%)	58 (19%)	8% (–7·2 to 23·8)
Treadmill	68 (44%)	70 (16%)	28% (13·8 to 43·0)
NT-proBNP at baseline, ng/L			
≤median of 710 ng/L	55 (33%)	68 (19%)	14% (–1·9 to 29·1)
>median of 710 ng/L	65 (37%)	58 (16%)	21% (6·4 to 36·4)
HCM genetic testing result			
Pathogenic or likely pathogenic	28 (57%)	22 (27%)	30% (3·7 to 56·0)
Variant of uncertain significance	32 (41%)	43 (19%)	22% (1·4 to 42·6)
Negative	30 (20%)	35 (11%)	9% (–9·2 to 26·3)

Lancet. 2020 Sep 12;396(10253):759-769.

B

Gradiente Tracto de salida

	Mavacamten (n [mean])	Placebo (n [mean])	Mean difference, mm Hg (95% CI)
Age, years			
≤49	26 (–37·0)	23 (–12·2)	–24·8 (–41·4 to –8·1)
50-64	48 (–57·1)	61 (–12·2)	–44·9 (–59·2 to –30·6)
≥65	43 (–42·5)	38 (–6·5)	–36·0 (–51·5 to –20·5)
Sex			
Women	54 (–47·9)	43 (–5·5)	–42·4 (–57·7 to –27·1)
Men	63 (–46·7)	79 (–13·1)	–33·6 (–44·8 to –22·4)
Body-mass index, kg/m²			
<30	72 (–47·5)	74 (–9·9)	–37·6 (–48·7 to –26·5)
≥30	45 (–46·9)	48 (–11·3)	–35·6 (–51·1 to –20·1)
LVEF at baseline			
<75%	66 (–52·8)	64 (–7·6)	–45·2 (–58·0 to –32·5)
≥75%	51 (–40·1)	58 (–13·6)	–26·5 (–39·0 to –14·0)
NYHA class at baseline			
II	82 (–48·7)	90 (–10·3)	–38·4 (–49·1 to –27·7)
III	35 (–43·9)	32 (–10·9)	–33·0 (–50·1 to –15·9)
β blocker usage at baseline			
Yes	89 (–47·1)	92 (–9·1)	–37·9 (–48·0 to –27·9)
No	28 (–47·9)	30 (–14·4)	–33·5 (–53·6 to –13·3)
Type of exercise testing			
Bicycle	51 (–48·2)	57 (–11·4)	–36·9 (–49·8 to –23·9)
Treadmill	66 (–46·5)	65 (–9·6)	–36·9 (–49·5 to –24·2)
NT-proBNP at baseline, ng/L			
≤median of 710 ng/L	53 (–48·8)	64 (–10·0)	–38·8 (–51·9 to –25·6)
>median of 710 ng/L	61 (–45·7)	56 (–11·6)	–34·1 (–47·1 to –21·1)
HCM genetic testing result			
Pathogenic or likely pathogenic	25 (–49·8)	21 (–10·5)	–39·4 (–60·6 to –18·1)
Variant of uncertain significance	32 (–49·5)	40 (–12·7)	–36·8 (–51·8 to –21·9)
Negative	28 (–38·9)	34 (–7·9)	–31·0 (–48·8 to –13·2)



Lancet. 2020 Sep 12;396(10253):759-769.

Objetivo Primario

VALOR HCM: Evaluar la seguridad y eficacia de agrega **MAVACAMTEN** a la terapia medica optima con síntomas severos en pacientes con MCH obstructiva, para mejorar los síntomas y ya no cumplan los criterios para terapia de reducción septal o no tener que someterse a la terapia de Reducción septal.

Edad :18 años
Miocardiopatía hipertrófica documentada con un grosor septal :15 mm o 13 mm con historia familiar de miocardiopatía hipertrófica) determinada por eco
Síntomas severos a pesar de terapia medica optima tolerada
Clase fu
Terapia
Gradier
FEVI>60
Debe se
Los pac

End-point primario: compuesto de la decisión del paciente para continuar terapia de reducción septal, o continuar con los criterios de elegibilidad para terapia de reducción septal después de 16 semanas.

End-point secundario: 5 criterios de evaluación de forma jerárquica:

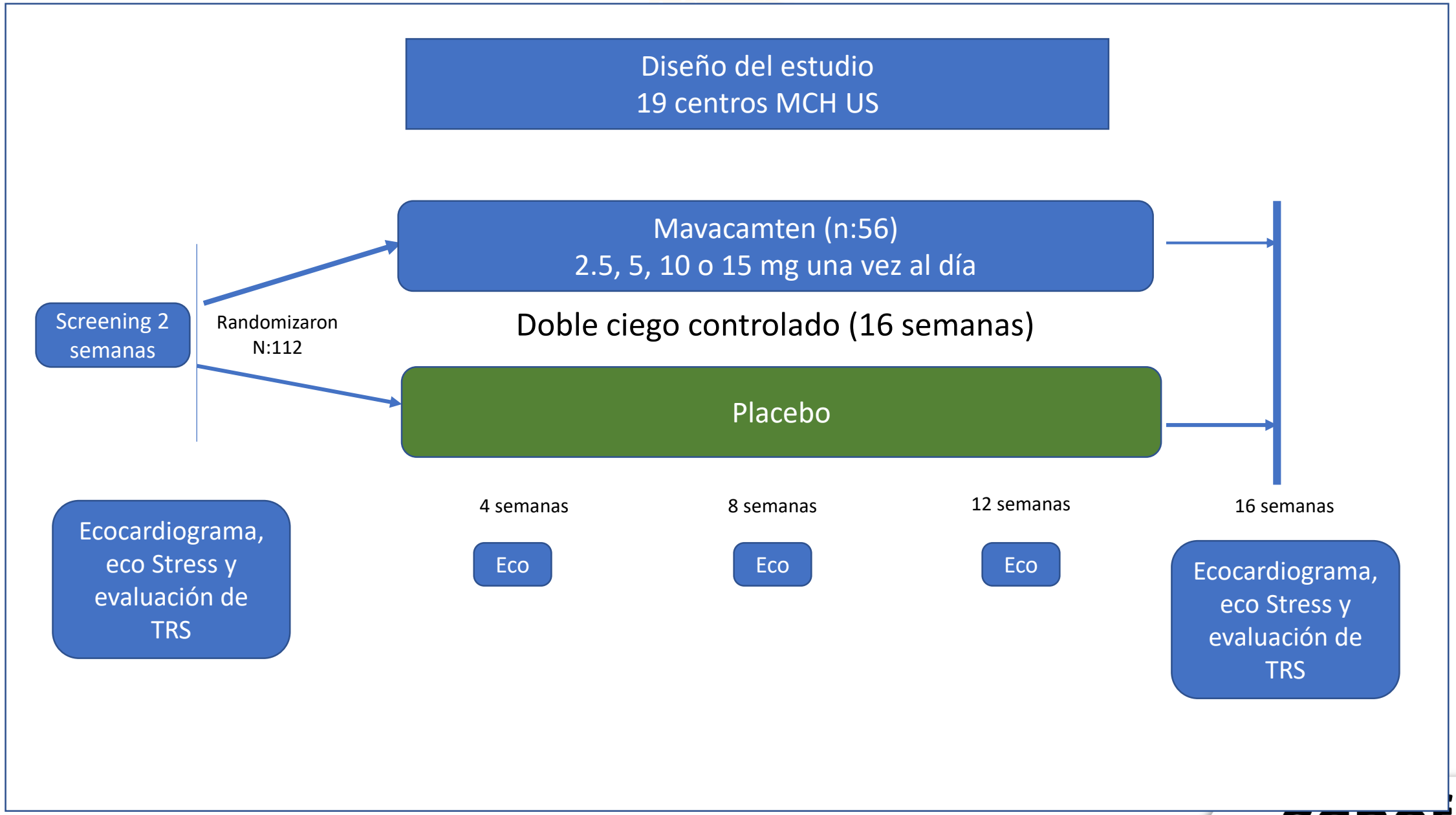
Cambio en el gradiente del tracto de salida VI post ejercicio

Numero de pacientes con mejoría de la clase función a NYHA I

Cambio en el score de calidad de vida

Cambio en el NT-PROBNP

Cambio en la troponina I


Diseño del estudio
19 centros MCH US
Mavacamten (n:56)
2.5, 5, 10 o 15 mg una vez al día
Screening 2 semanas
Randomizaron N:112
Doble ciego controlado (16 semanas)
Placebo
Ecocardiograma, eco Stress y evaluación de TRS
4 semanas
8 semanas
12 semanas
16 semanas
Eco
Eco
Eco
Ecocardiograma, eco Stress y evaluación de TRS

	MAVACAMTEN (56)	Placebo (56)
Edad	59,8	60,9
Sexo femenino	48,2%	50%
Historia familiar de MCH	30,4%	26,8%
NYHA III o mayor	92,9%	92,9%
Tipo de terapia de reducción recomendada -Miectomia -Ablación septal con alcohol	 48 (85,7%) 8 (14,3%)	 49 (87,5%) 7(12,5%)
Terapia medica -Beta bloqueador (Monoterapia) -CA No dihidropiridinico -Terapia combinada	 26 (46.43%) 7 (12,50%) 20 (35,7%)	 25 (44.64%) 10 (17.86%) 16 (12.5%)
Gradiente Tracto de salida en reposo	51,2 mmHg	46.3 mmHg
Gradiente post ejercicio	82.5 mmHg	85,2 mmHg

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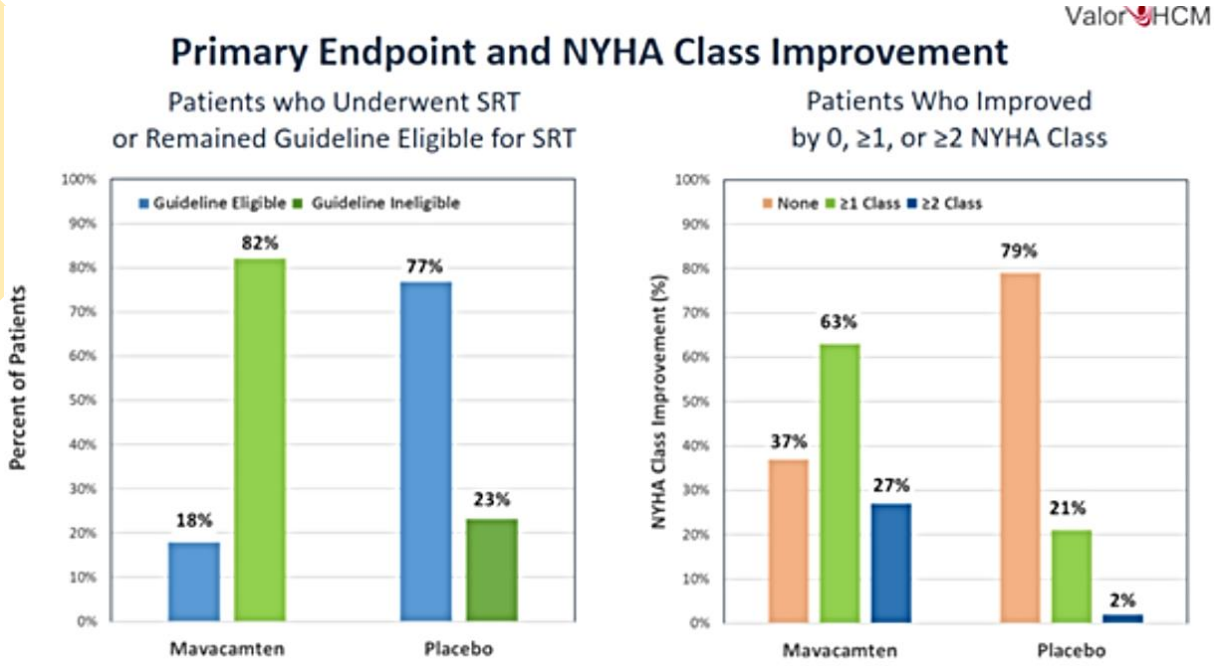
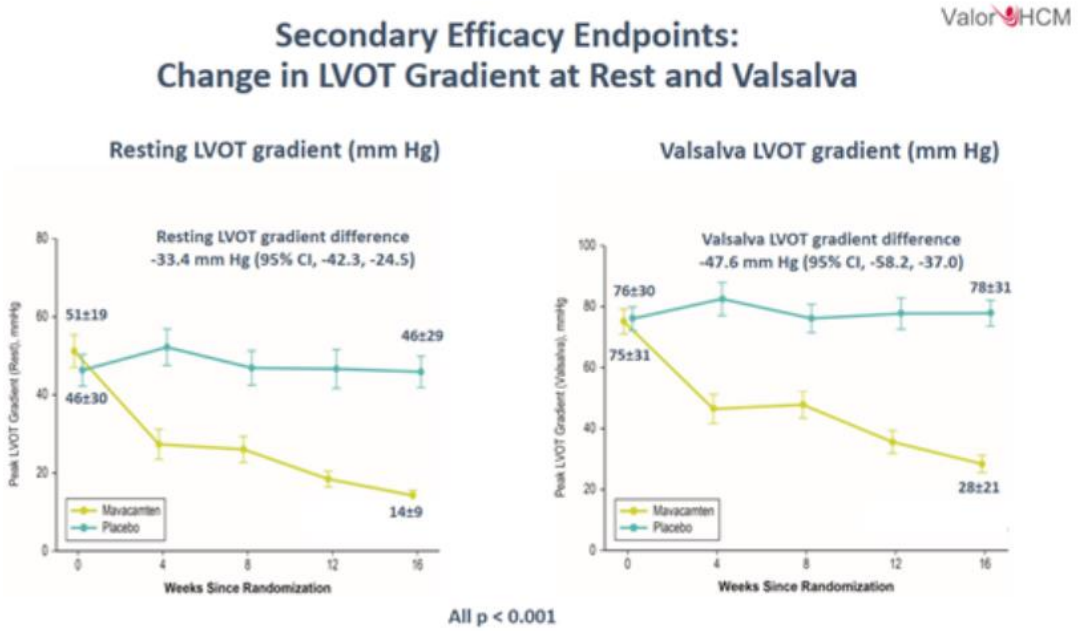
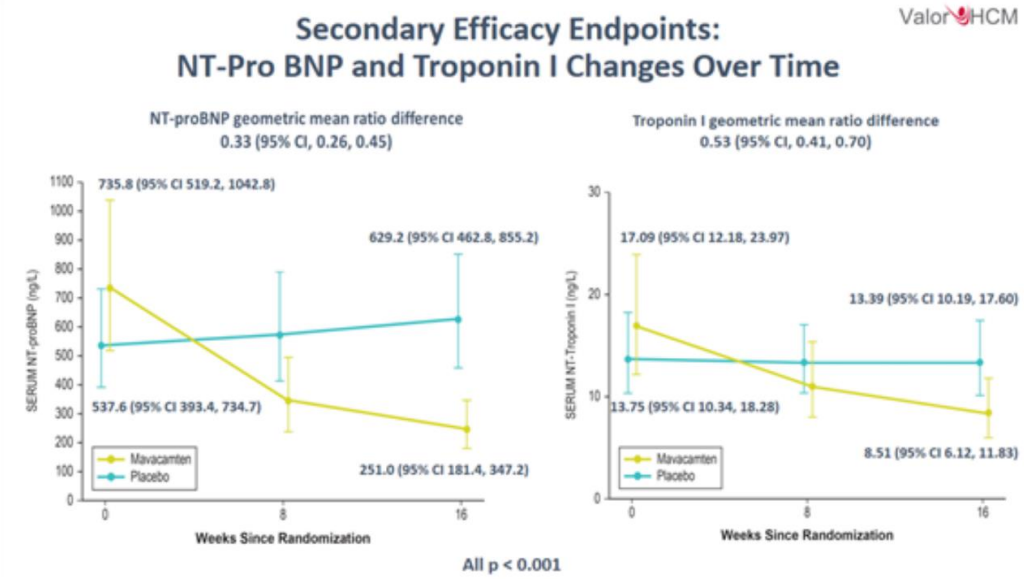
Decisión de continuar con SRT o la guía elegible en la semana 16

	MAVACAMTEN	PLACEBO	Diferencia en el Tto
Decisión de continuar con SRT o la guía elegible en la semana 16	10/56)17,9%	43/56)76,8%	58,93 P<0.0001
Se procedió con TRS en la semana 16	2 (3,6)	2 (3,6)	
Criterios de TRS en la semana 16 y no se procedió	8 (14,3)	39 (69,6)	
No se evaluó TRS) incumplimiento de criterio	0	2 (3,6)	







En Pacientes con Miocardiopatía hipertrófica obstructiva con síntomas intratables, referidos para TRS, la administración de MAVACAMTEN:

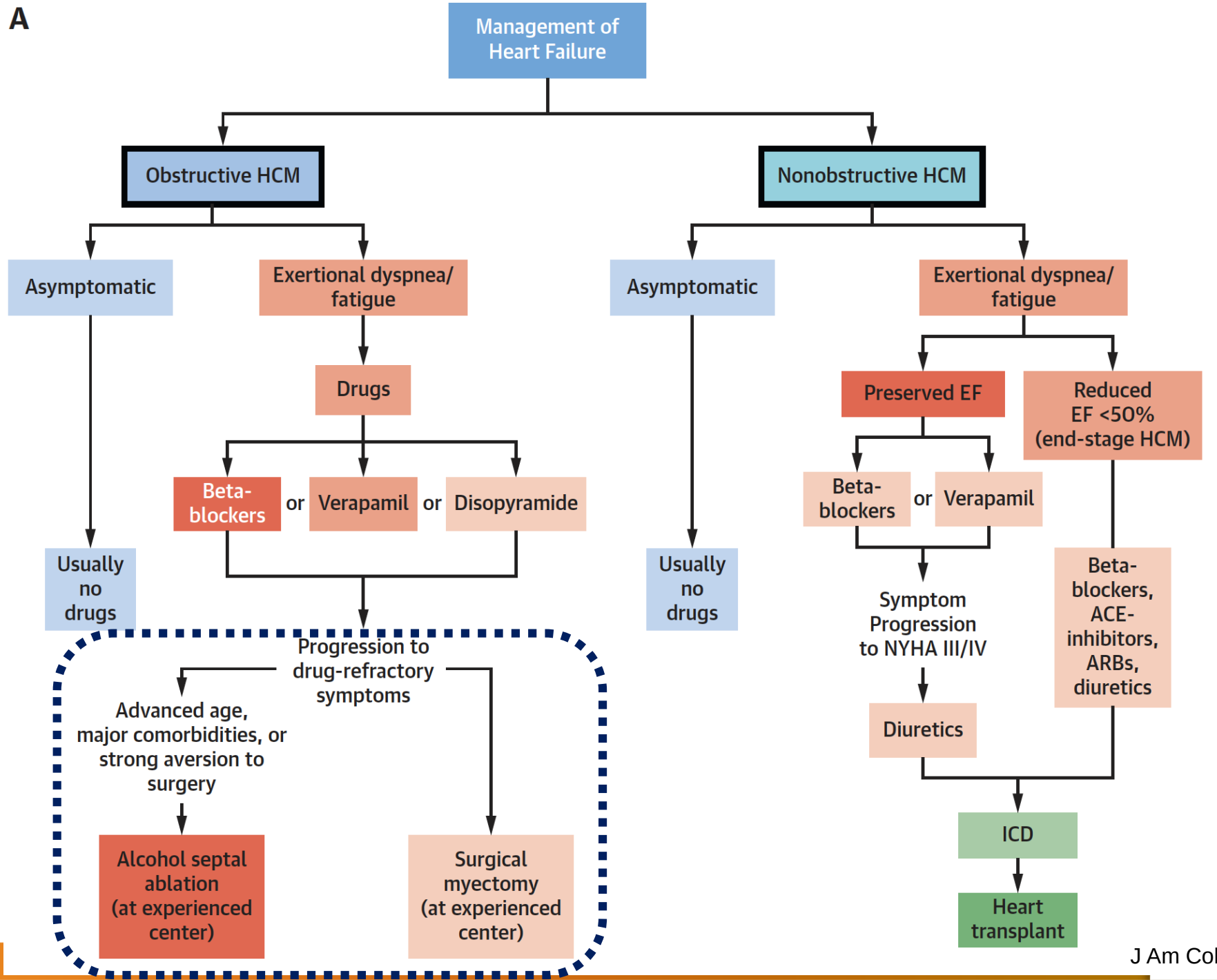
Disminución significativa de la terapia invasiva de reducción septal a las 16 semanas de Tto (P<0.0001)

Se vio beneficios en los endpoints secundarios (p:<0.0001)

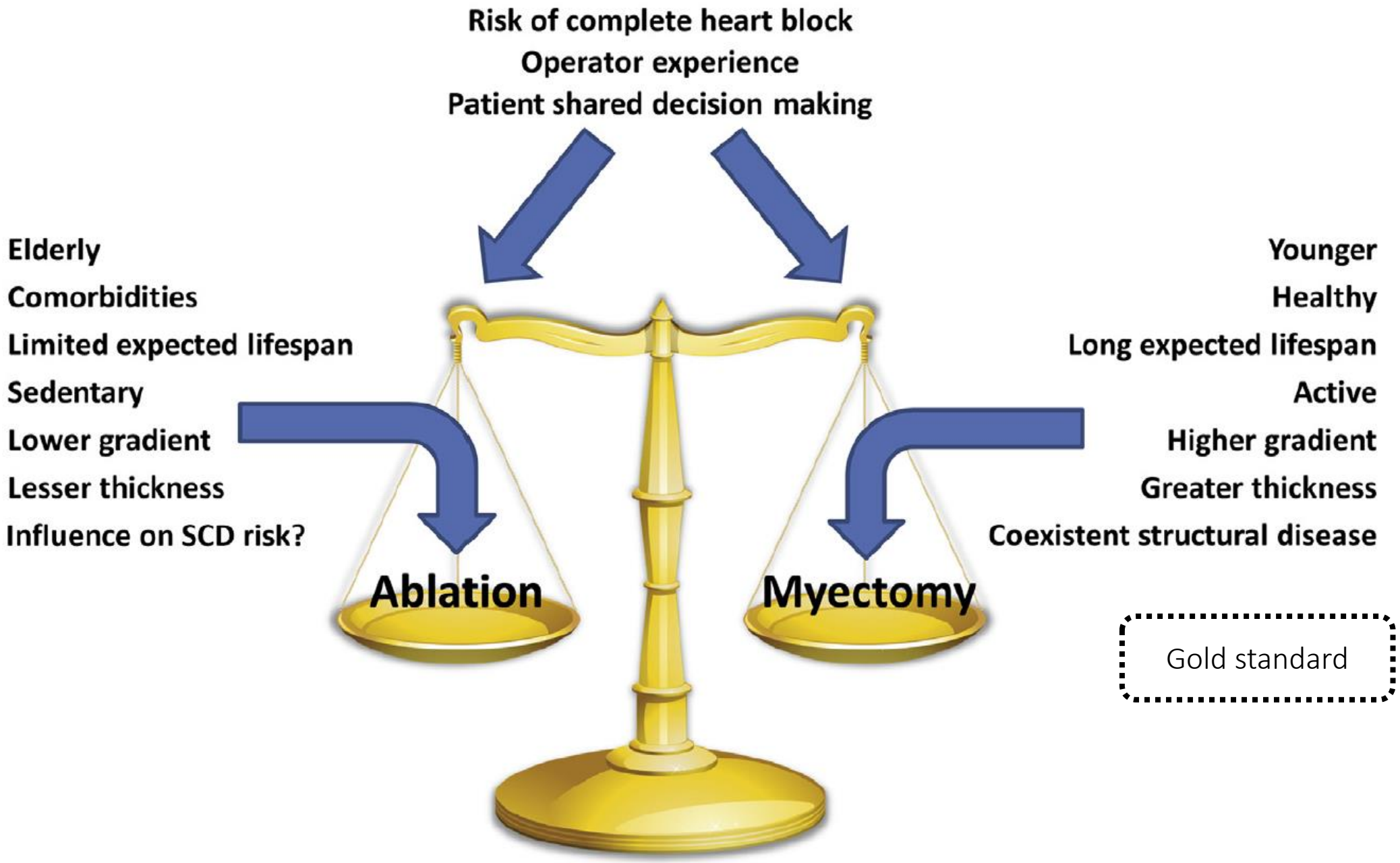
Reducción gradiente TSVI post ejercicio
Mejoría de la clase funcional
Mejoría del score de calidad de vida
Reducción del NT – PROBNP – Troponina I

Qué elementos necesitamos para determinar si el paciente con CMPH requiere intervención invasiva (miectomía/ASA)

Obstrucción del tracto de Salida del Ventrículo Izquierdo
Reposo
Ejercicio
Síntomas refractarios al manejo médico



J Am Coll Cardiol 2022;79:390-414

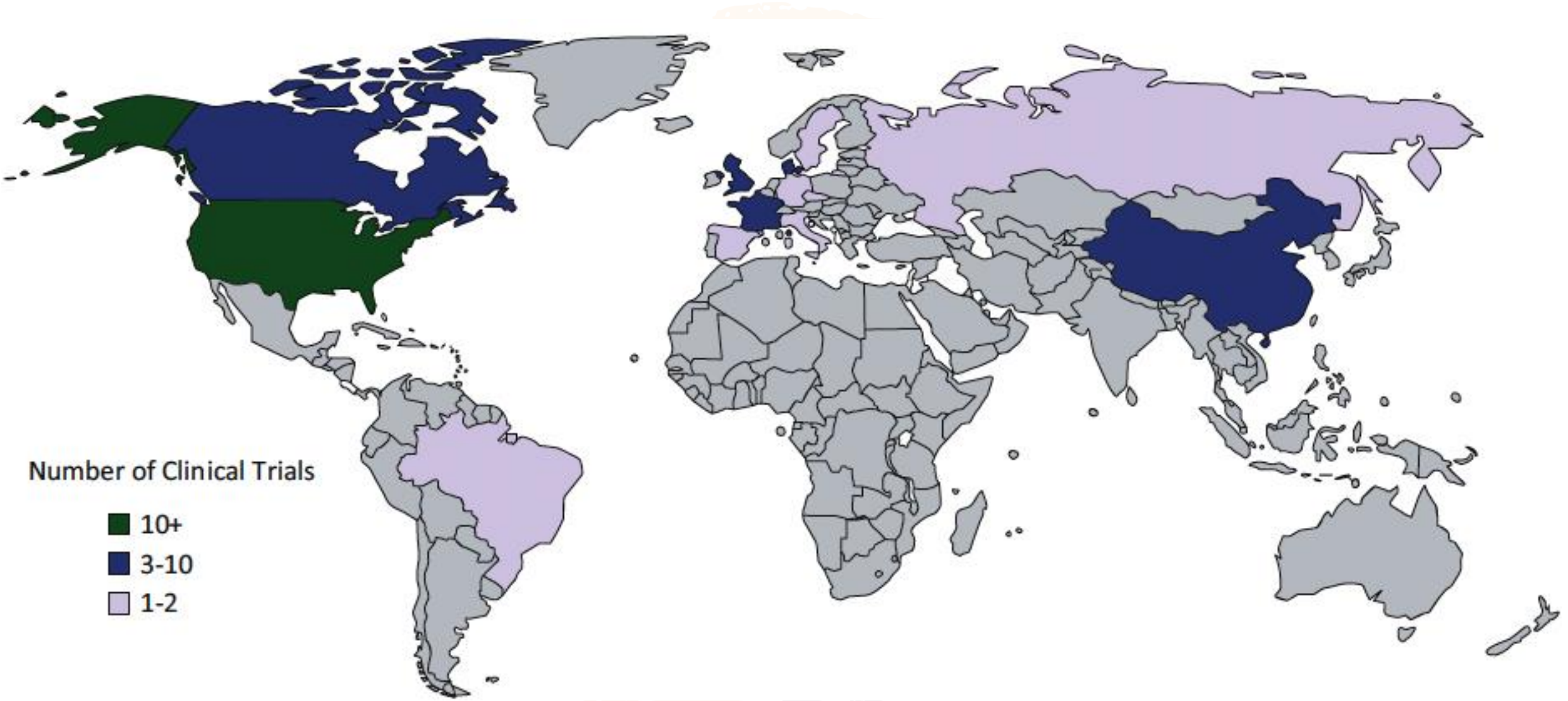


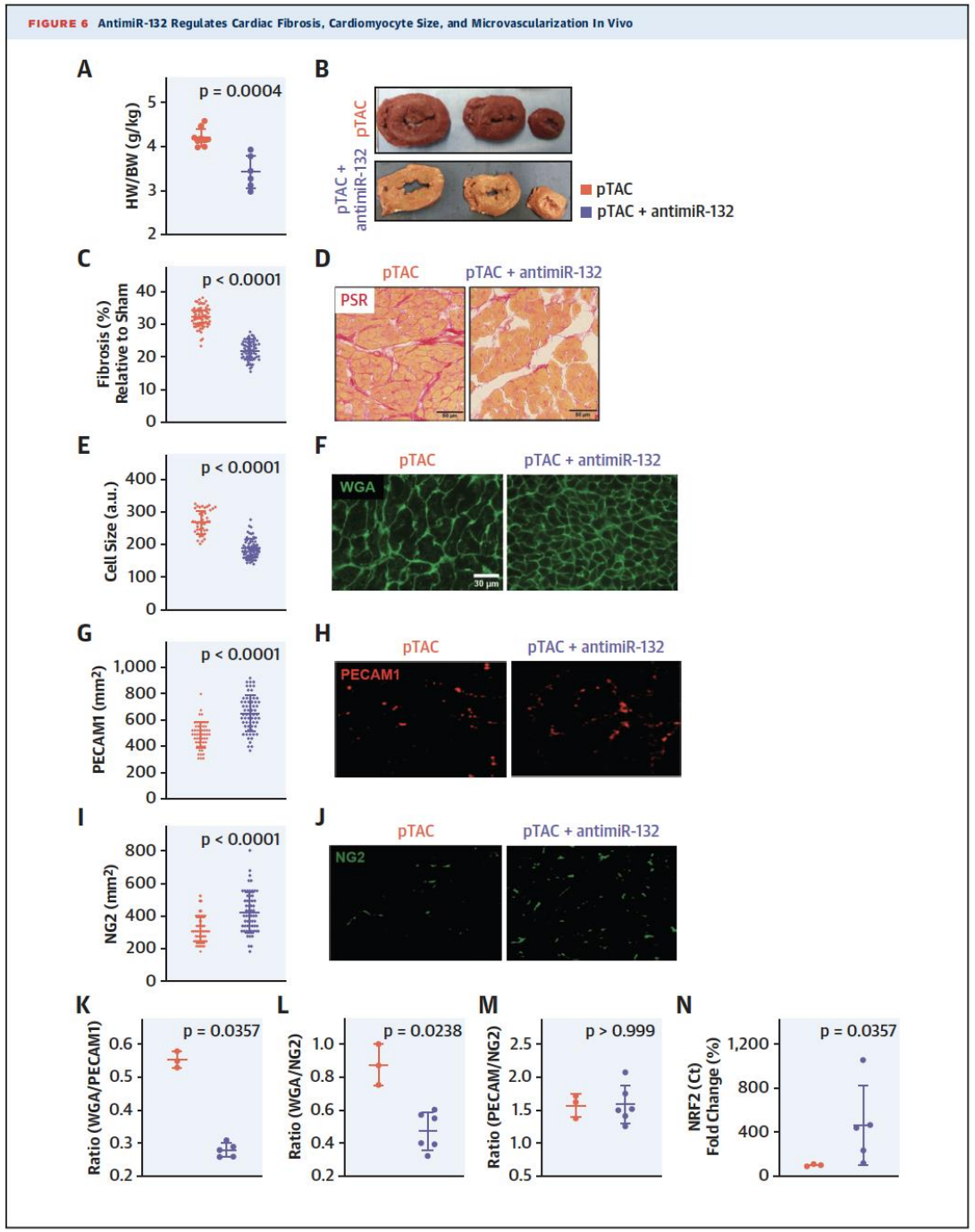
J Am Coll Cardiol HF 2018;6:364–75

First Author	Year	Title	NCTID	Enrolled	Phase	Intervention	Inclusion Criteria	Primary Outcome Measure	Result
Ho	2015	Diltiazem treatment for preclinical hypertrophic cardiomyopathy sarcomere mutation carriers: a pilot randomized trial to modify disease expression	NCT00319982	38	II/III	• Drug: diltiazem • Drug: placebo	Preclinical HCM (identified sarcomere mutation with no clinical evidence of LVH) and able to provide informed consent (or parental consent)	Increase, stability of, or decrease in the decline of diastolic function as reflected by the global early myocardial relaxation (E′) velocity	Preclinical administration of diltiazem is safe and may improve early LV remodeling in HCM
Axelsson	2016	Functional effects of losartan in hypertrophic cardiomyopathy-a randomised clinical trial	NCT01447654	130	II	• Drug: losartan • Drug: placebo	Diagnosed HCM, >18 yrs of age and has normal sinus rhythm	LVH	Treatment with losartan had no effect on cardiac function or exercise capacity compared with placebo; losartan fail to improve myocardial performance and failed to alter the progression of the disease
Axelsson	2015	Efficacy and safety of the angiotensin II receptor blocker losartan for hypertrophic cardiomyopathy: the INHERIT randomised, double-blind, placebo-controlled trial	NCT01447654	130	II	• Drug: Losartan • Drug: Placebo	Diagnosed HCM, >18 yrs of age and has normal sinus rhythm	LVH	Findings challenge the view that ARBs reduce cardiac hypertrophy; treatment with losartan was safe, suggesting that it can be used for other indications in patients with HCM, irrespective of obstructive physiology
Coats	2019	Effect of trimetazidine dihydrochloride therapy on exercise capacity in patients with nonobstructive hypertrophic cardiomyopathy: a randomized clinical trial	NCT01696370	90	II	• Drug: Trimetazidine • Other: Placebo capsule	Nonobstructive HCM (gradient <30 mm Hg at rest), NYHA functional class ≥II, peak VO_2 ≤80% predicted for age and gender and heart rate <90 beats/min at rest	Peak oxygen consumption	In symptomatic patients with nonobstructive HCM, trimetazidine therapy does not improve exercise capacity
Shimada	2013	Effects of losartan on left ventricular hypertrophy and fibrosis in patients with nonobstructive hypertrophic cardiomyopathy	NCT01150461	20	II	• Drug: losartan • Drug: placebo	Patients with HCM, left ventricular outflow tract gradient <30 mm Hg at rest and 18 yrs of age or older	Percentage change from baseline in extent of LV fibrosis at 1 yr as assessed by cardiac magnetic resonance	This study suggests attenuation of progression of myocardial hypertrophy and fibrosis with losartan in patients with nonobstructive HCM
Nerbass	2016	Acute effects of nasal CPAP in patients with hypertrophic cardiomyopathy	NCT01631006	26	—	• Device: CPAP	Both genders, over 18 yrs of age, hemodynamically stable, no other cardiac disease and consent form signed	Cardiac performance by echocardiography	The acute application of CPAP is apparently safe in patients with HCM, because CPAP does not lead to hemodynamic compromise

Penicka	2009	The effects of candesartan on left ventricular hypertrophy and function in nonobstructive hypertrophic cardiomyopathy: a pilot, randomized study	NCT00430833	-	II	• Drug: candesartan	HCM diagnosed on the basis of echocardiography showing a nondilated, hypertrophied LV (any wall thickness >15 mm) in the absence of known causes of LVH, hypertension, or valvular disease		Candesartan induced regression of LVH, and improved LV function and exercise tolerance with no side effects in patients with nonobstructive HCM
Hersi	2016	Statin induced regression of cardiomyopathy trial: a randomized, placebo-controlled double-blind trial	NCT00317967	22	III	• Drug: atorvastatin • Drug: placebo	18 yrs of age and over with HCM in the absence of another cardiac or systemic disease capable of producing a prespecified wall thickening	Change in left ventricular mass at 12 months from baseline	Atorvastatin did not cause LV mass regression or improvements in LV diastolic function
Marian	2018	Hypertrophy Regression With N-Acetylcysteine in Hypertrophic Cardiomyopathy (HALT-HCM): a randomized, placebo-controlled, double-blind pilot study	NCT01537926	42	I	• Drug: N-acetylcysteine • Drug: placebo	Diagnosis of HCM, have at least an LV end-diastolic wall thickness of at least 15 mm on a 2-dimensional echocardiogram and known to have mutations in genes encoding sarcomeric proteins	Recruitment rate	Treatment with NAC for 12 months had small effect sizes on indices of cardiac hypertrophy or fibrosis
Lee	2017	Pediatric cardiomyopathies	NCT01912534	211	II	• Drug: valsartan • Drug: placebo	All subjects must have a pathogenic or likely pathogenic HCM sarcomere mutation	A combined single composite *Z*-score will serve as primary surrogate endpoint to monitor response to valsartan treatment	Within 2 yrs of presentation, normalization of function occurs in 20% of children with dilated cardiomyopathy, and 40% die or undergo transplantation; infants with HCM have a 2-yr mortality of 30%, whereas death is rare in older children
Bogachev-Prokophiev	2017	Mitral valve repair or replacement in hypertrophic obstructive cardiomyopathy: a prospective randomized study	NCT02054221	82	—	• Procedure: myomectomy • Procedure: mitral valve surgery	• ≥18 yrs of age, obstructive HCM, surgically significant mitral insufficiency, NYHA functional class II—IV, average systolic pressure gradient >50 mm Hg. Art. at rest; and basal or medium ventricular obstruction	The function of the mitral valve	Both mitral valve repair and valve replacement in addition to extended myectomy are effective methods of surgical treatment in patients with hypertrophic obstructive cardiomyopathy who have severe mitral regurgitation

First Author	Year	Title	NCTID	Enrolled	Phase	Intervention	Inclusion Criteria	Primary Outcome Measure	Result
Abozguia	2010	Metabolic modulator perhexiline corrects energy deficiency and improves exercise capacity in symptomatic hypertrophic cardiomyopathy	NCT00500552	44	II	• Drug: perhexiline • Drug: placebo	Symptomatic patients with HCM with abnormal peak VO_2, no significant LVOT obstruction at rest (gradient <30 mm Hg) and normal sinus rhythm	Peak oxygen consumption	In symptomatic HCM, perhexiline ameliorates cardiac energetic impairment, corrects diastolic dysfunction, and increases exercise capacity
Olivotto	2016	Novel approach targeting the complex pathophysiology of hypertrophic cardiomyopathy: the impact of Late Sodium Current Inhibition on Exercise Capacity in Subjects with Symptomatic Hypertrophic Cardiomyopathy (LIBERTY-HCM) trial	NCT02291237	172	II/III	• Drug: eleclazine • Drug: placebo	Established diagnosis of HCM defined by standard criteria as a maximal left ventricular wall thickness ≥15 mm at initial diagnosis Exertional symptoms including at least 1 of the following: NYHA functional class ≥II dyspnea, Canadian Cardiovascular Society Class ≥II angina, screening peak VO_2 <80% of predicted for age, sex, and weight and ability to perform an upright treadmill cardiopulmonary exercise test	Change in peak oxygen uptake achieved during cardiopulmonary exercise testing from baseline to week 24	
Ho	2016	Evolution of hypertrophic cardiomyopathy in sarcomere mutation carriers	NCT00319982	38	II/III	• Drug: diltiazem • Drug: placebo	Preclinical HCM and able to provide informed consent (or parental consent)	Increase, stability of, or decrease in the decline of diastolic function as reflected by the global early myocardial relaxation (E′) velocity	LV relaxation, ECG changes, mitral leaflet length, and serum NT-proBNP concentrations appeared more prominently abnormal at baseline in preclinical sarcomere mutation carriers who imminently progressed to HCM; LVH appears to stabilize within 2 yrs of onset


Number of Clinical Trials
10+
3-10
1-2



AntimiR-132 Attenuates Myocardial Hypertrophy in an Animal Model of Percutaneous Aortic Constriction

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J Am Coll Cardiol 2015;65:2728–35

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