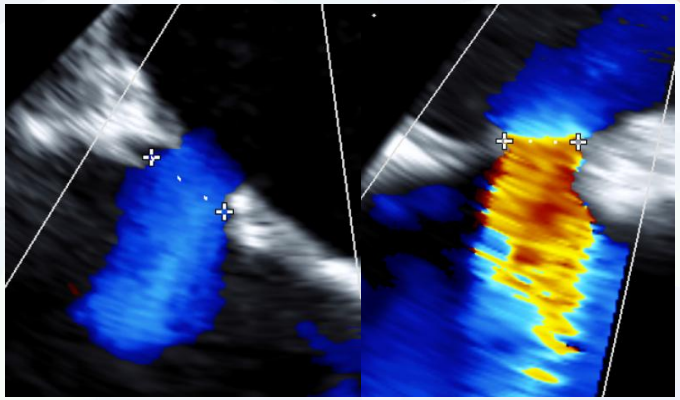
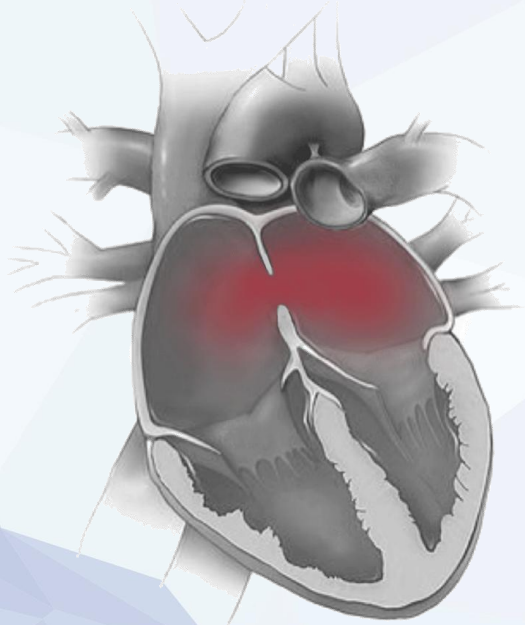


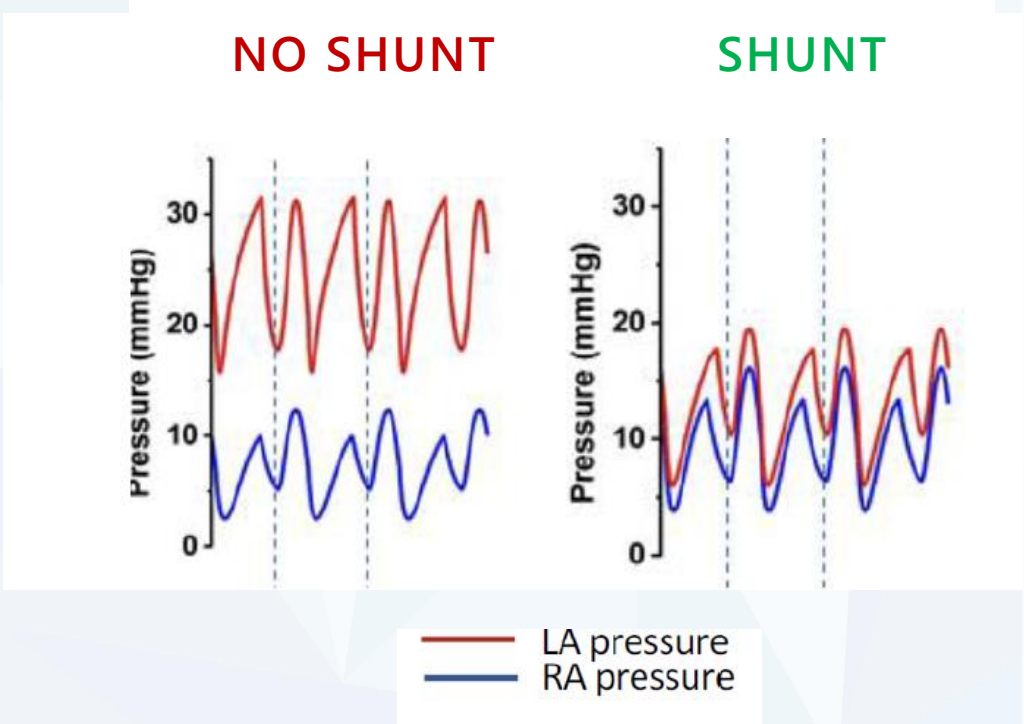
Tratamiento de la IC con shunt inter-atrial ¿Dónde estamos y a dónde vamos?

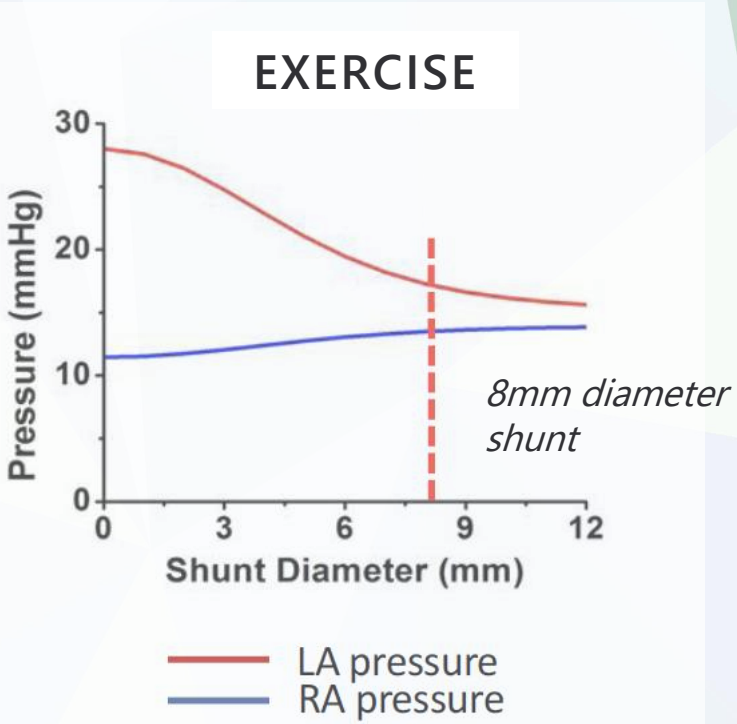
Dr. Julio Núñez

Shunt interatrial: plausibilidad

El shunt interatrial ha mostrado resultados prometedores como tratamiento para pacientes sintomáticos mediante descarga auricular izquierda a derecha.







Kaye et al. J Card Fail. 2014

Reduce LAP-HF II Trial Design[1]

PURPOSE: Evaluate the clinical efficacy and safety of the Corvia Atrial Shunt to improve quality of life and reduce HF related symptoms and events in patients with HFpEF or HFmrEF.

STUDY POPULATION
(N=626 randomized)

- Symptomatic HF
- Ongoing GDMT
- Age ≥40
- LVEF ≥40%
- Preserved RV function
- Elevated exercise PCWP (≥25 mm Hg) with left-to-right gradient (≥5 mm Hg)
- Pulmonary vascular resistance (PVR) <3.5 Wood units at rest or peak exercise

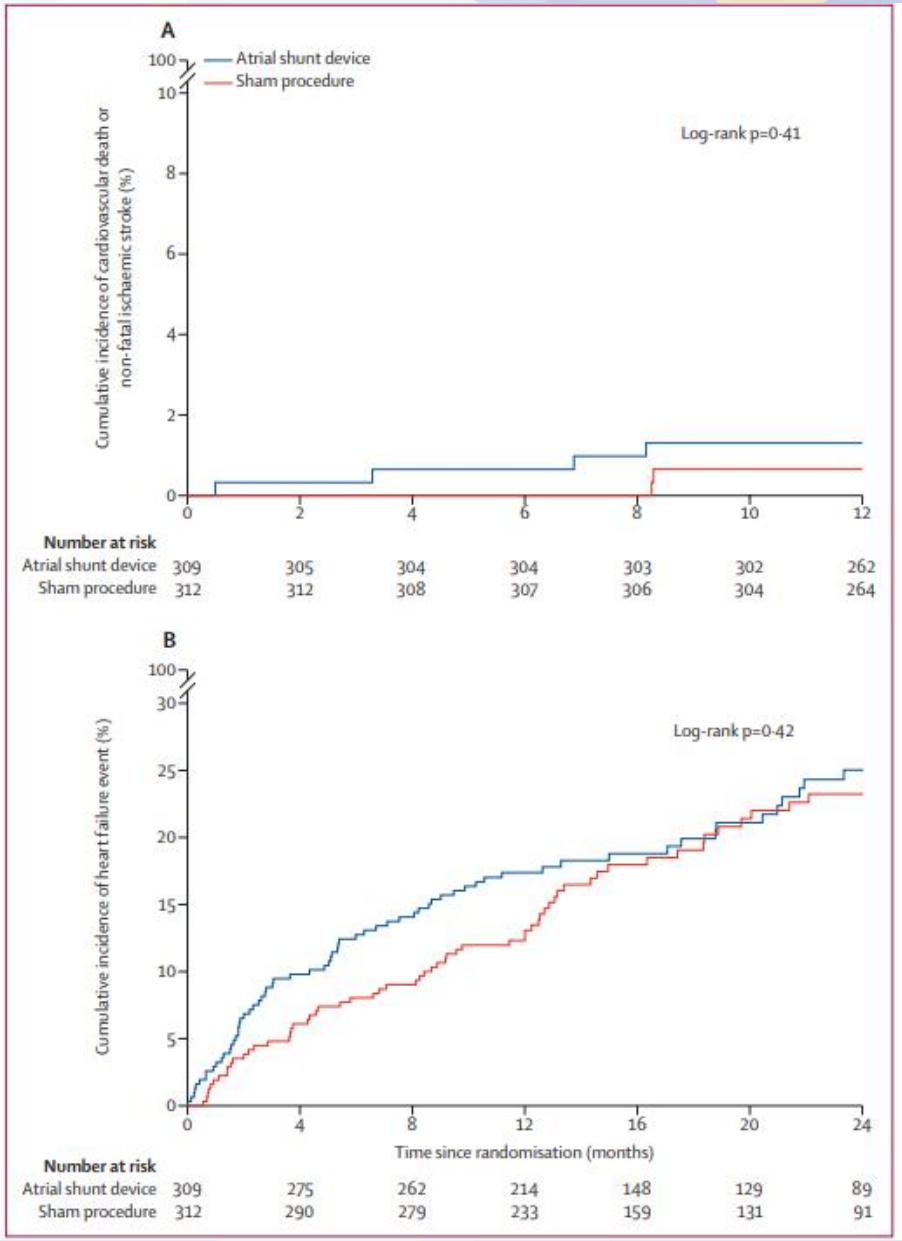
ATRIAL SHUNT TREATMENT
(N=314)

SHAM CONTROL
(N=312)

The primary endpoint was a hierarchical composite of cardiovascular death or non-fatal ischemic stroke at 12 months, rate of total heart failure events up to 24 months, and change in Kansas City Cardiomyopathy Questionnaire overall summary score at 12 months

Shah SJ, et al. Lancet 2022; 399: 1130–40

	Atrial shunt device (n=309)	Sham control (n=312)	p value
Primary endpoint			
Finkelstein-Schoenfeld statistic, T (SE)	-780 (3998)	..	0·85
Probability of favourable distribution (95% CI)	0·50 (0·46 to 0·54)	..	..
Win ratio (95% CI)	1·0 (0·8 to 1·2)	..	..



Shah SJ, et al. Lancet 2022; 399:

Resultados heterogéneos

Trial Outcome

50% of the study population benefited significantly from atrial shunt therapy despite an overall neutral trial[2,3]

RESPONDER GROUP (n=313)

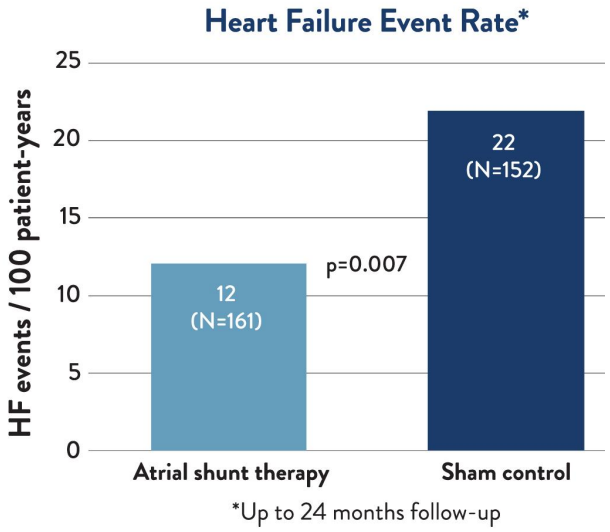
Positive outcome in patients with normal exercise PVR (<1.74 WU)[4] and no cardiac rhythm device (win ratio[5]=1.5, p=0.004)

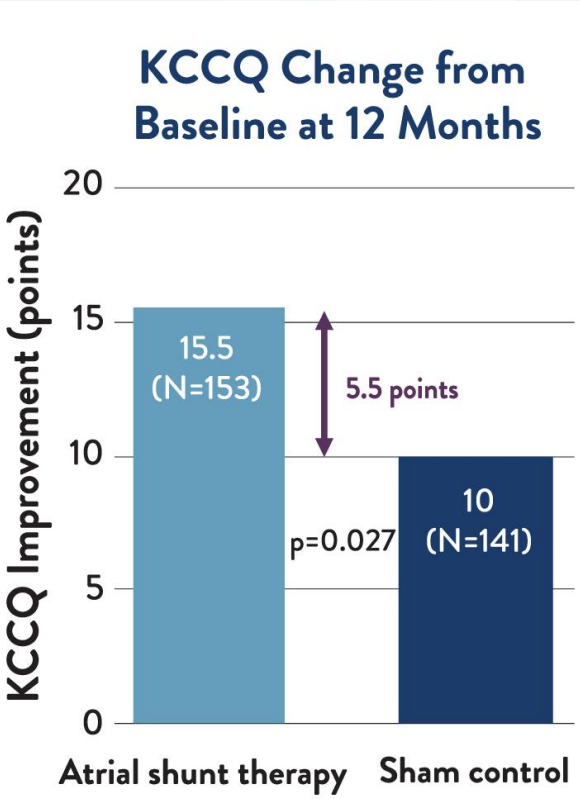
OVERALL POPULATION

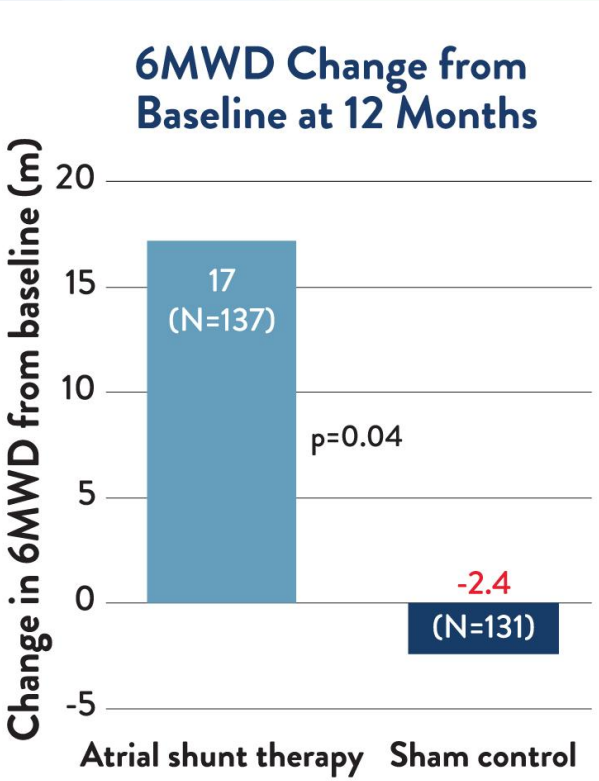
Neutral primary outcome when including all patients (win ratio=1)

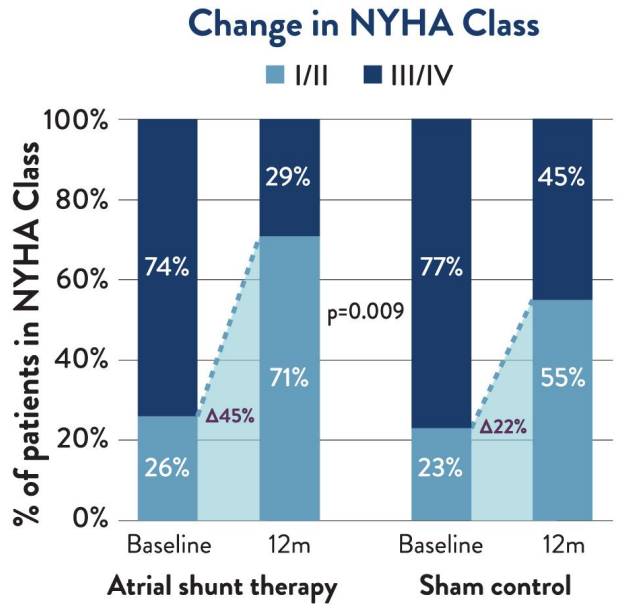
Shah SJ, et al. Lancet 2022; 399: 1130–40

Resultados heterogéneos

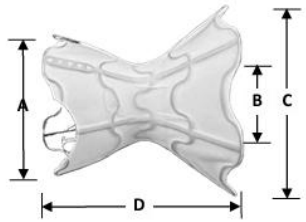






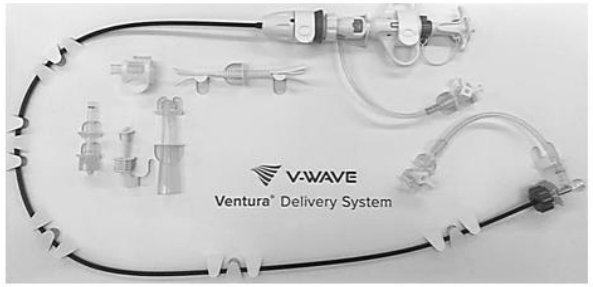


Shah SJ, et al. Lancet 2022; 399: 1130–40



A. Right atrial cone – 11 mm
B. Waist – 5 mm
C. Left atrial cone – 14 mm
D. Length – 12 mm

Ventura Interatrial Shunt



Ventura delivery system

508 patients were randomized at 94 sites to receive
Shunt vs. sham procedure

ORIGINAL RESEARCH ARTICLE

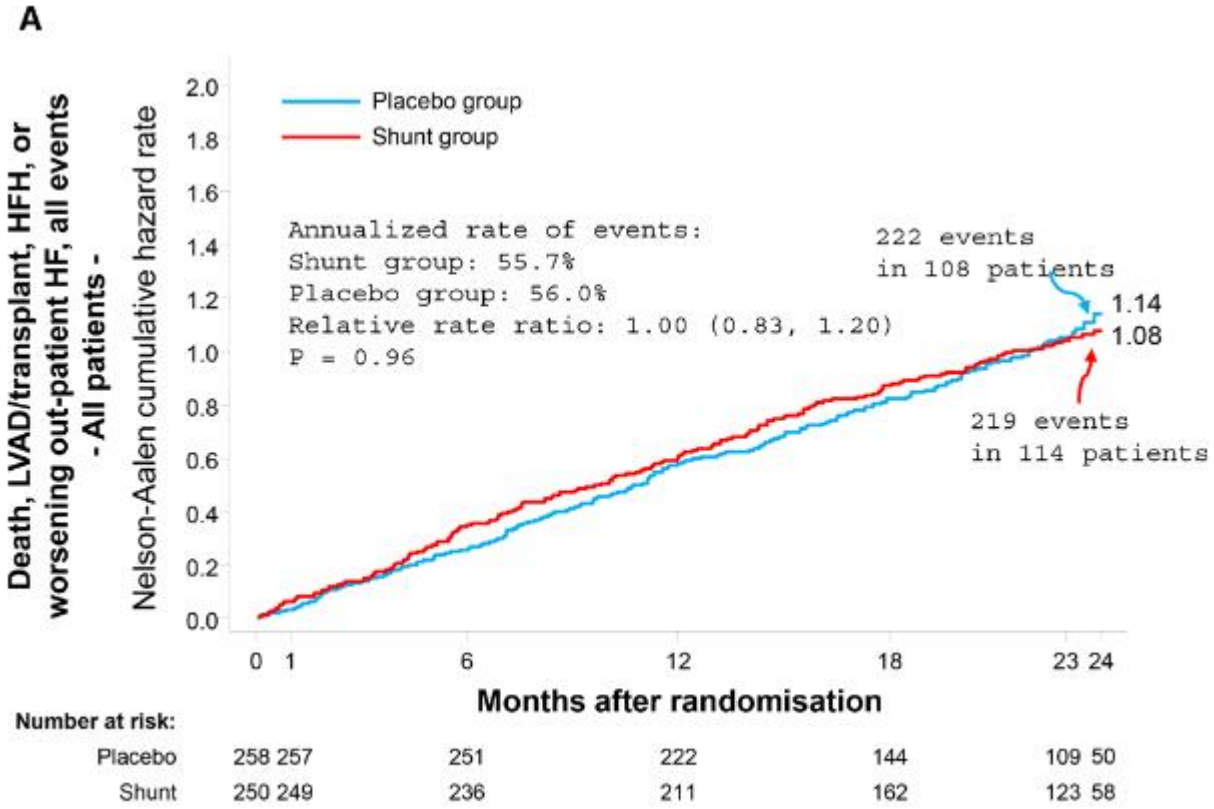
Interatrial Shunt Treatment for Heart Failure: The Randomized RELIEVE-HF Trial

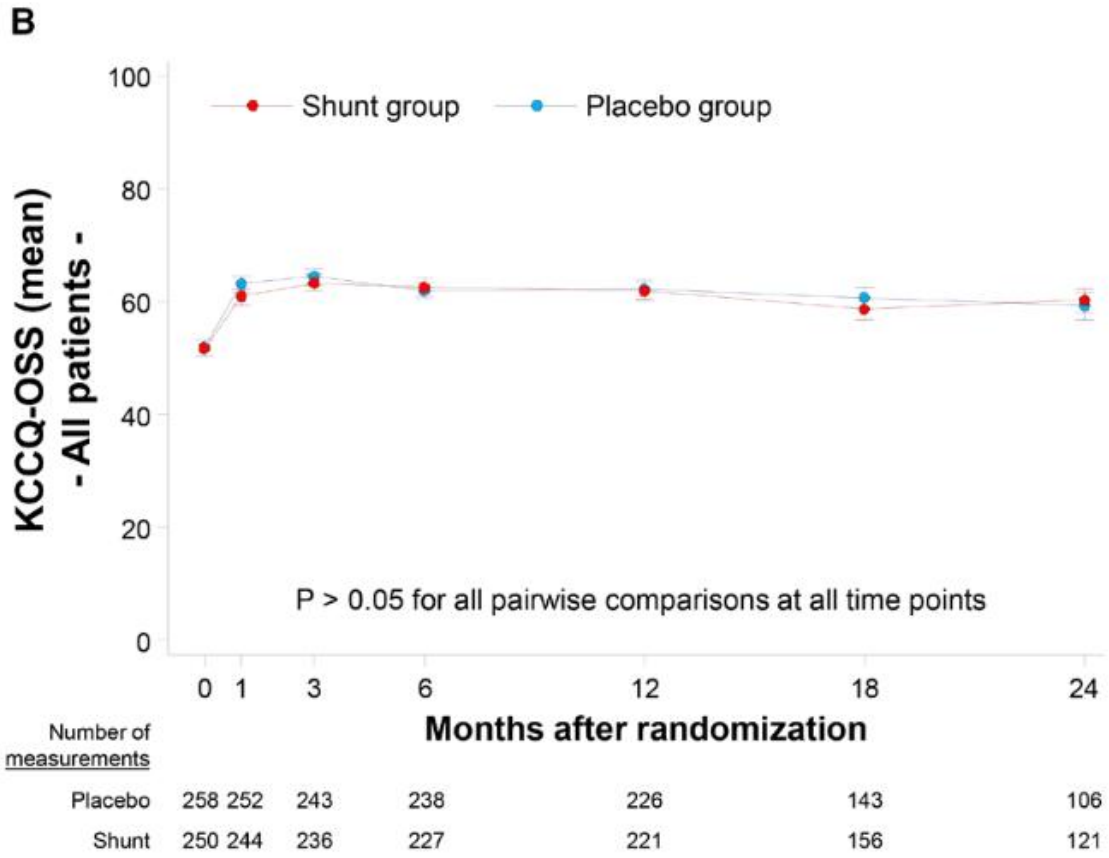
Gregg W. Stone, MD; JoAnn Lindenfeld, MD; Josep Rodés-Cabau, MD, PhD; Stefan D. Anker, MD, PhD; Michael R. Zile, MD; Saibal Kar, MD; Richard Holcomb, PhD; Michael P. Pfeiffer, MD; Antoni Bayes-Genis, MD; Jeroen J. Bax, MD, PhD; Alan J. Bank, MD; Maria Rosa Costanzo, MD; Stefan Verheye, MD; Ariel Roguin, MD, PhD; Gerasimos Filippatos, MD; Julio Núñez; Elizabeth C. Lee, MD; Michal Laufer-Perl, MD; Gil Moravsky, MD; Sheldon E. Litwin, MD; Edgard Prihadi, MD; Hemal Gada, MD; Eugene S. Chung, MD; Matthew J. Price, MD; Vinay Thohan, MD; Dimitry Schewel, MD; Sachin Kumar, MD; Stephan Kische, MD; Kevin S. Shah, MD; Daniel J. Donovan, MD; Yiran Zhang, MS; Neal L. Eigler, MD; William T. Abraham, MD; on behalf of the RELIEVE-HF Investigators*

Characteristics	Shunt group (n=250)	Placebo group (n=258)
Age, y	74.0 (67.0, 79.0)	72.0 (65.0, 78.0)
Sex,* male	162 (64.8)	157 (60.9)
Race, White	227 (90.8)	232 (89.9)
Ethnicity, Hispanic	20 (8.0)	26 (10.1)
Body mass index, kg/m²	30.0 (25.6, 34.9)	30.3 (26.2, 36.0)
Diabetes	124 (49.6)	125 (48.4)
Insulin-treated	49 (19.6)	48 (18.6)
Hypertension	209 (83.6)	216 (83.7)
Hyperlipidemia	201 (80.4)	195 (75.6)
Current or previous smoker	133 (53.2)	137 (53.1)
Previous stroke or transient ischemic attack	43 (17.2)	48 (18.6)
Chronic obstructive lung disease	43 (17.2)	52 (20.2)
Ischemic cardiomyopathy	114 (45.6)	120 (46.5)
Nonischemic cardiomyopathy	136 (54.4)	138 (53.5)
At least one HFH in the previous year	128 (51.2)	127 (49.2)
Known coronary artery disease	169 (67.6)	160 (62.0)
Previous myocardial infarction	104 (41.6)	103 (39.9)
Previous PCI	103 (41.2)	96 (37.2)
Previous CABG	65 (26.0)	58 (22.5)
History of atrial fibrillation or flutter	170 (60.8)	159 (61.2)
Baseline rhythm is atrial fibrillation or flutter	76 (30.4)	64 (24.8)
ICD or CRT-D	115 (46.0)	123 (47.7)
CRT-D or CRT-P	70 (28.0)	59 (22.9)
NYHA class		
I	0 (0.0)	0 (0.0)
II	9 (3.6)	7 (2.7)
III	239 (95.6)	251 (97.3)
IV	2 (0.8)	0 (0.0)
KCCQ-OSS	52.1 (35.4, 66.9)	50.8 (34.6, 66.4)
Six-minute walk distance	264.8 (195.5, 325.0)	270.9 (198.0, 330.0)
LVEF (biplane, core laboratory assessment), %	45.4 (33.4, 58.9)	45.3 (33.3, 57.4)
≤40% (reduced LVEF)	101/250 (40.4)	105/258 (40.7)
>40% (preserved LVEF)	149/250 (59.6)	153/258 (59.3)
Troponin I or T >ULN	79/227 (34.8)	109/240 (45.4)
B-type natriuretic peptide	237.9 (117.2, 412.5)	221.0 (101.0, 518.3)

NT-proBNP ≈2000 p

Circulation.
2024;150:00-00

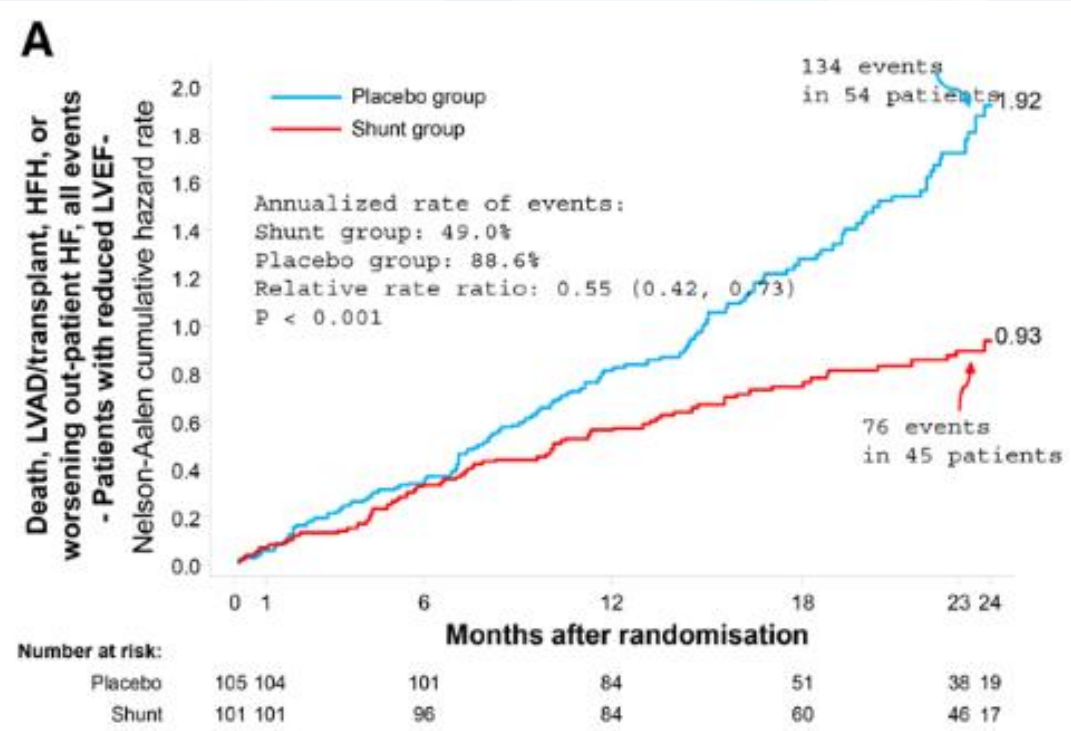




Circulation.
2024;150:00-00

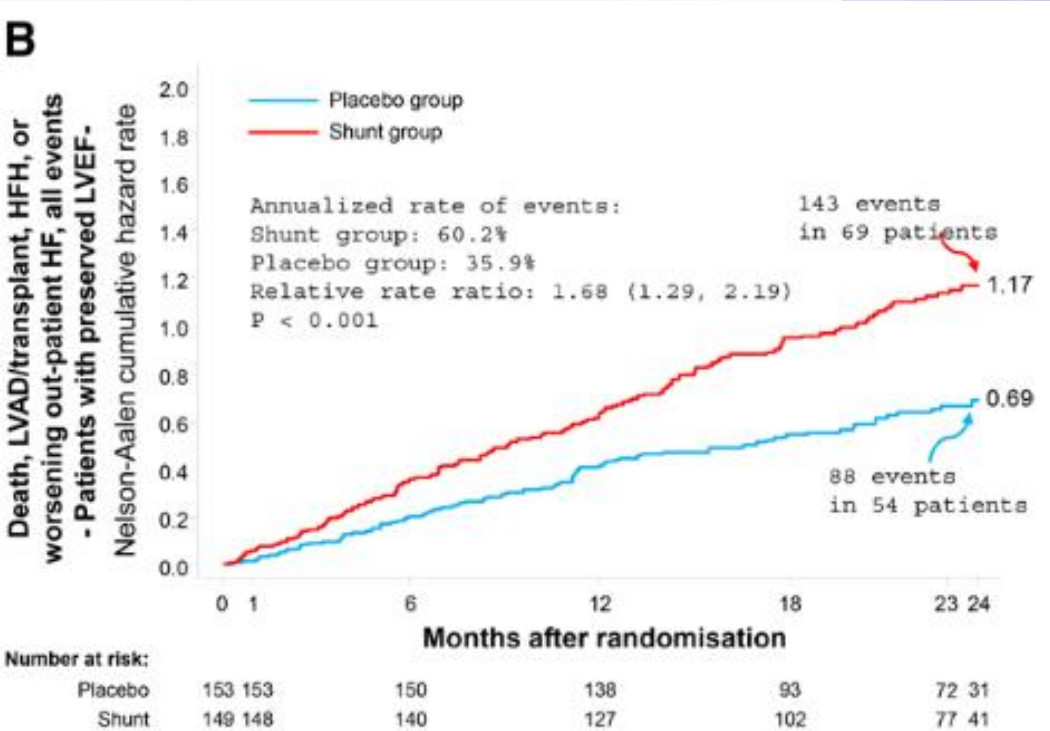
Resultados heterogéneos

HFrEF



Reducción del riesgo del 45%

HFpEF



Incremento del riesgo del 68%

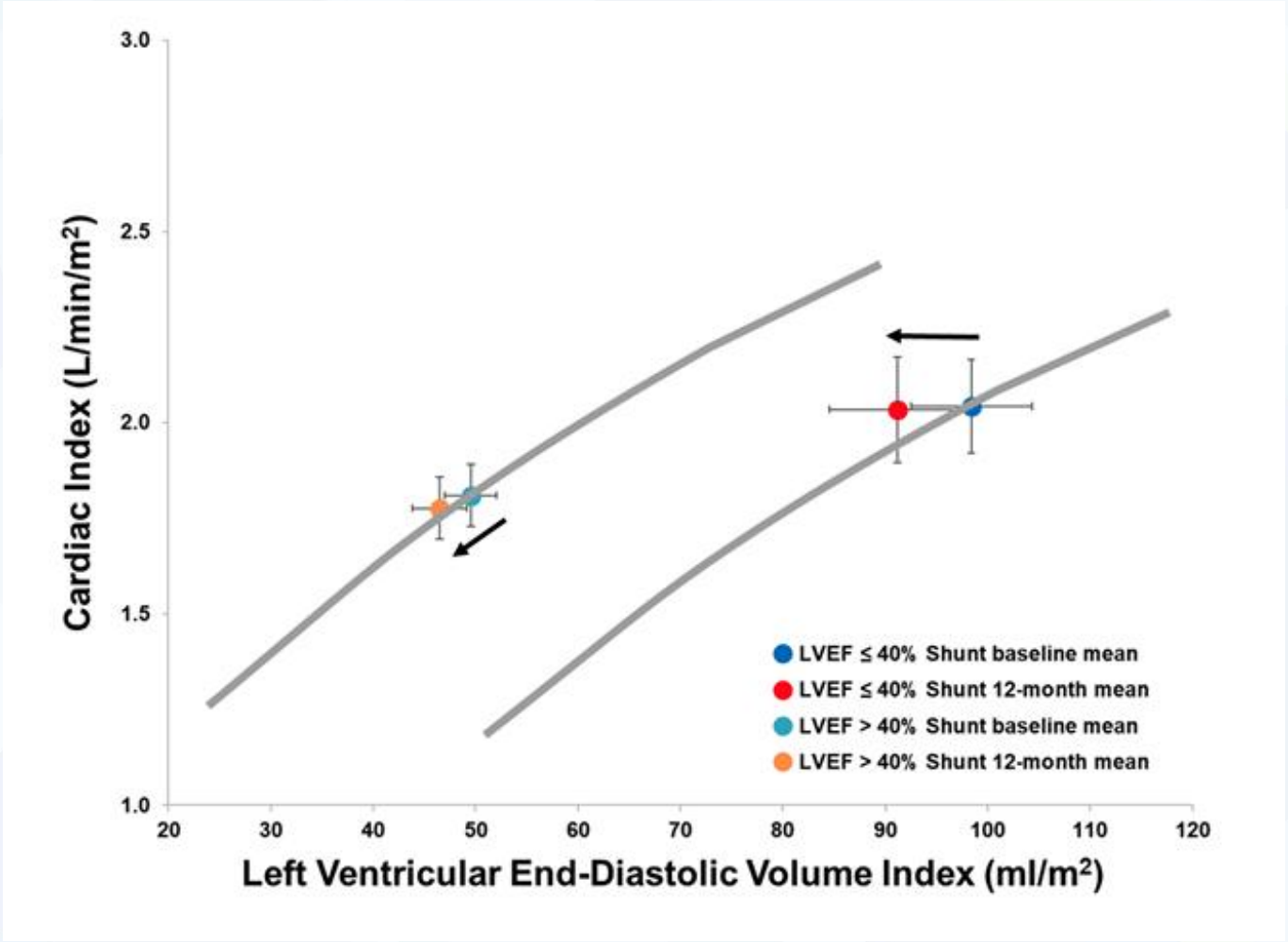
Circulation.

¿Por qué deletéreo en ICFEP?

	Heart failure with reduced ejection fraction (≤40%)			Heart failure with preserved ejection fraction (>40%)		
	Shunt group (N=86)	Placebo group (N=84)	Difference [95% CI]	Shunt group (N=124)	Placebo group (N=138)	Difference [95% CI]
Left ventricular end-diastolic volume (biplane), mL	177.0 (144.0, 225.0)	176.0 (139.0, 230.5)	-0.8 [-21.0, 19.5][1]	89.0 (68.0, 113.5)	98.0 (74.5, 136.3)	-10.3 [-19.5, -1.0][1]
Left ventricular end-systolic volume (biplane), mL	118.5 (91.0, 163.0)	120.5 (88.5, 165.5)	-1.8 [-18.5, 15.0][1]	37.5 (26.5, 52.3)	43.5 (28.0, 62.8)	-4.8 [-10.0, 0.5][1]
Left ventricular ejection fraction (biplane), %	32.4 (25.5, 39.1) 32.9 ± 8.9	29.5 (25.3, 39.1) 32.0 ± 9.0	0.9 [-2.0, 3.7][2]	57.6 (50.1, 63.0) 56.2 ± 9.1	56.6 (48.8, 61.9) 55.2 ± 9.3	0.8 [-1.4, 3.1][2]
Left atrial volume (biplane), mL	84.5 (61.5, 108.5)	80.5 (57.5, 102.5)	3.5 [-6.5, 13.5][1]	77.8 (63.0, 91.5)	71.0 (57.5, 91.5)	3.8 [-2.5, 10.0][1]
Stroke volume, mL	54.0 (43.0, 70.0)	56.0 (41.0, 65.0)	1.0 [-5.0, 7.0][1]	49.0 (37.0, 60.0)	52.0 (42.0, 67.0)	-5.0 [-9.0, -1.0][1]
Stroke volume index, mL/m^2	28.4 (20.7, 34.0)	25.8 (19.7, 32.3)	1.2 [-1.5, 3.9][1]	24.3 (19.9, 29.0)	27.0 (21.7, 32.7)	-2.3 [-4.3, -0.4][1]
Cardiac output, L/min	3.74 (2.94, 4.74)	3.91 (2.85, 4.78)	0.11 [-0.54, 0.33][1]	3.34 (2.60, 3.92)	3.61 (2.88, 4.52)	-0.37 [-0.67, -0.07][1]
Cardiac index, L/min/m^2	1.89 (1.38, 2.28)	1.94 (1.39, 2.26)	0.01 [-0.21, 0.18,][1]	1.65 (1.34, 1.93)	1.84 (1.50, 2.18)	-0.18 [-0.30. -0.06][1]
Right ventricular fractional area change, %	37.5 (34.5, 42.9)	35.9 (30.4, 40.0)	2.2 [0.0, 4.4][1]	40.0 (35.3, 43.8)	39.5 (35.3, 43.8)	0.4 [-1.2, 1.9][1]
Tricuspid annular plane systolic excursion, mm	17.0 (14.0, 19.0)	15.0 (13.0, 19.0)	1.0 [0.0, 2.0][1]	18.0 (14.0, 21.0)	17.0 (15.0, 20.0)	0.0 [-1.0, 1.0][1]
Pulmonary artery systolic pressure. mmHg	30.0 (23.0, 41.5)	32.0 (23.0, 40.0)	-0.5 [-5.0, 4.0][1]	37.0 (31.0, 44.0)	31.0 (24.0, 37.0)	6.0 [3.0, 9.0][1]
Right ventricular end-diastolic area index, cm^2/m^2	10.2 (8.8, 13.4)	10.2 (7.9, 12.2)	0.6 [-0.4, 1.6][1]	10.2 (9.0, 12.6)	9.5 (7.8, 11.7)	0.9 [0.2, 1.5][1]
Inferior vena cava diameter max, cm	1.7 (1.2, 2.0)	1.6 (1.2, 2.0)	0.0 [-0.2, 0.2][1]	1.8 (1.4, 2.2)	1.5 (1.2, 1.9)	0.3 [0.1, 0.4][1]
Mitral regurgitation moderate or greater	12/86 (14.0%)	8/84 (9.5%)	4.4 [-5.2, 14.1][2]	11/123 (8.9%)	15/138 (10.9%)	-1.9 [-9.2, 5.3][2]
Tricuspid regurgitation moderate or greater	7/86 (8.1%)	8/81 (9.9%)	-1.7 [-10.4, 7.0][2]	26/123 (21.1%)	16/137 (11.7%)	9.5 [0.5, 18.5][2]

Circulation.

¿Por qué deletéreo en ICFEP?



Circulation.

PIVOTAL Trials – "Finding the Strike zone"

Precision medicine: inclusion if exercise right heart catheterization*

1. Elevated left atrial pressure during exercise right heart catheterization (greater than or equal to 25 mmHg)
2. Exercise PVR < 1.8 WU

What Insights have we gained?

corvia

REDUCE LAP-HF II[1]
(HFpEF RCT PIVOTAL)

HFpEF responder group identified
RESPONDER-HF

HFpEF Non - Responders

V-WAVE

RELIEVE-HF[2]
(RCT PIVOTAL)

HFrEF responder group identified
(FDA Submission pending)

ALLAY-HF

ALLAY-HF
(HFpEF RCT PIVOTAL)

ALLAY-HF
(HFrEF RCT PIVOTAL
in development)

ALLAY-HF capitalizing on key learnings from Corvia & V-Wave

1. REDUCE LAP-HF II: NCT03088033
2. RELIEVE-HF: NCT03499236

El shunt inter-atrial emerge como estrategia de tratamiento promisoria en:

Pacientes con ICFEr tratamiento médico optimo que persisten muy sintomátic

En ICFEp, futuros estudios en paciente con predominio de IC izquierda
y ausencia de remodelado vascular pulmonar significativo desvelarán su utilida