Tricuspid Valve Disease: Building Frameworks for Success from Clinical and Real-World Advances

Unmet Needs in the Medical Management of Tricuspid Regurgitation

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Relationships with Industry

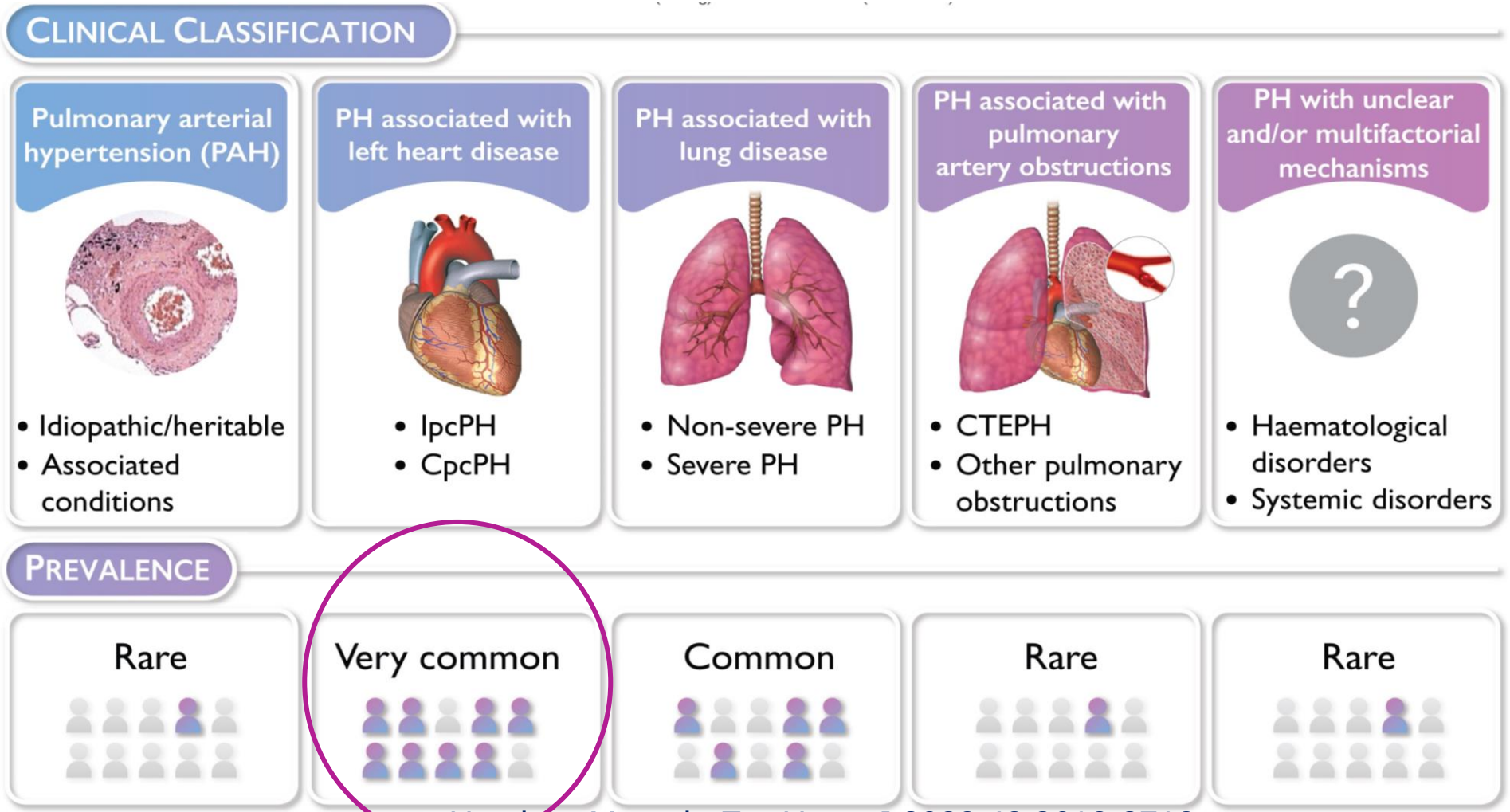
Consulting	**Abbott, ADI, Alleviant, Astra-Zeneca, Boehringer-Ingelheim, Boston Scientific, Cordio, Cytokinetics, CVRx, Edwards Lifesciences, Merck, Medtronic, Vascular Dynamics, Vectorious, Volumetrix, VWave, WhiteSwell**
Grants	**AHA, NIH, AstraZeneca, Cytokinetics, Abbott**

Medical Therapy for Tricuspid Regurgitation

Recommendations for Medical Therapy for TR		
COR	**LOE**	**Recommendations**
2a	**C-EO**	1. In patients with signs and symptoms of right-sided HF attributable to severe TR (Stages C and D), diuretics can be useful.
2a	**C-EO**	2. In patients with signs and symptoms of right-sided HF attributable to severe secondary TR (Stages C and D), therapies to treat the primary cause of HF (eg, pulmonary vasodilators to reduce elevated pulmonary artery pressures, GDMT for HF with reduced LVEF, or rhythm control of AF) can be useful[1,2]

Otto CM et al. Circulation 2021; 143: e72-e227

Classification of Pulmonary Hypertension (Secondary Ventricular TR)



Humbert M et al. Eur Heart J 2022;43:3618-3713

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  - √ Are changes in GDMT worth measuring?
  - √ How good is GDMT?
  - √ GDMT includes CRT/ICD

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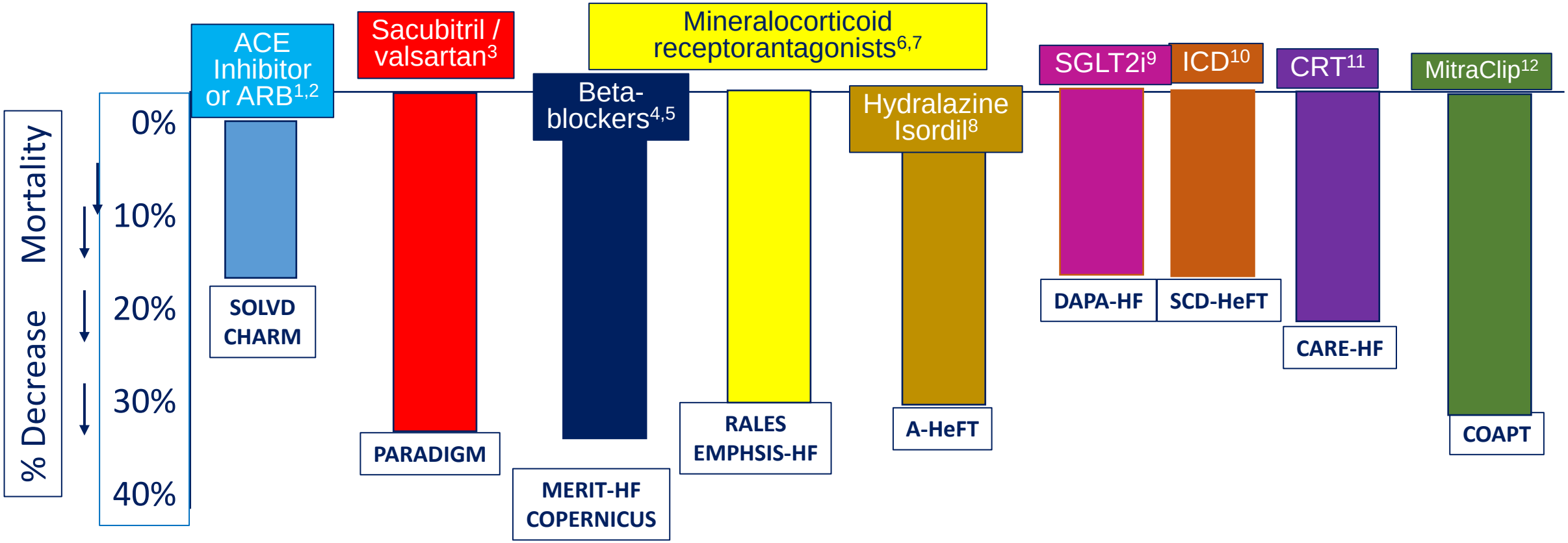
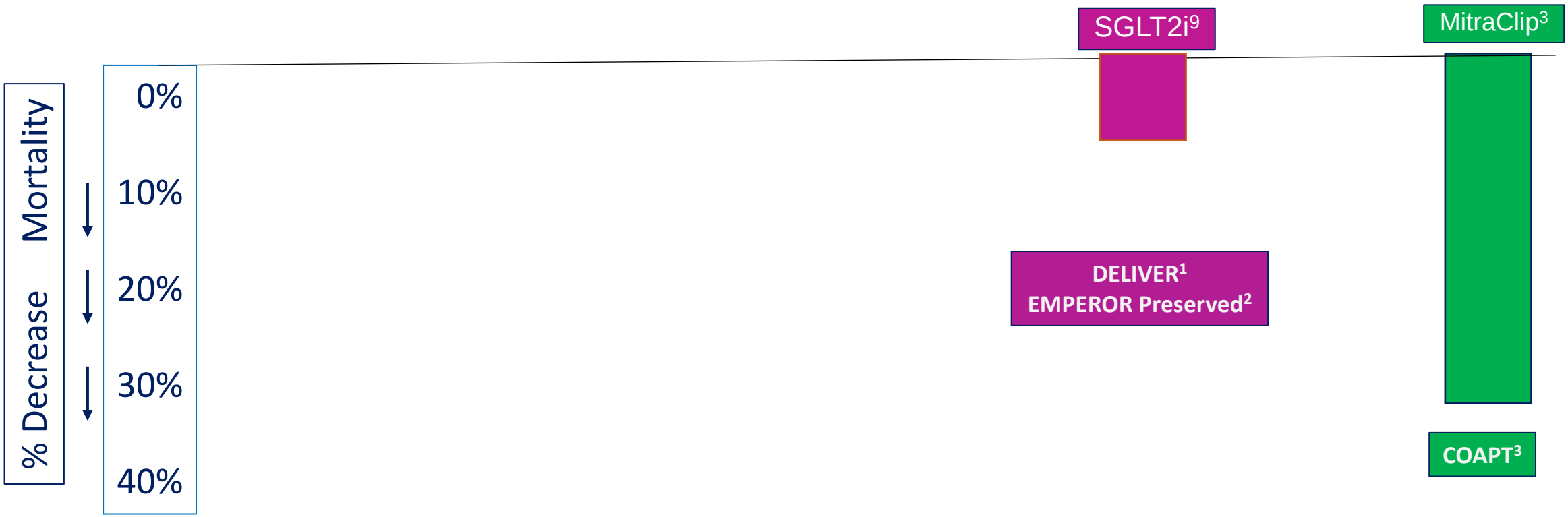
Large Mortality Benefits Observed Across Key Therapies for Treatment of Select HFrEF Patients



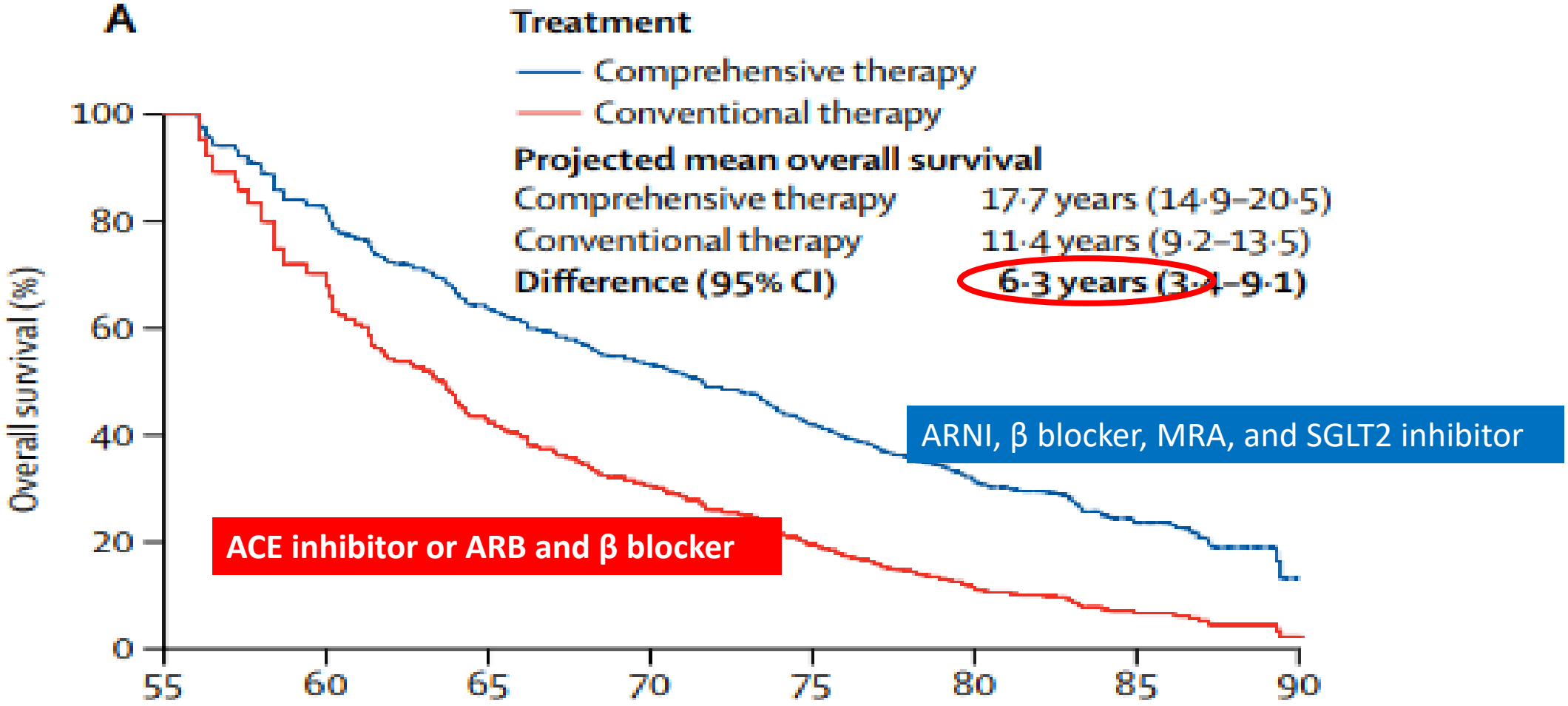
1. SOLVD Invest et al. NEJM 1991:325:293-302
2. Granger CB et al. Lancet 2003;362:722-6
3.. McMurray JJ et al. NEJM 2014;317:993-1004
4. Hjalmarson A et al. JAMA 2000;283:1295-302
5. Packer M et al. NEJM 2001;344:1651-8
6. Pitt B et al. NEJM 1999;344:709-17
7. Zannad F et al. NEJM 2011364:11-21
8. Taylor AL et al. NEJM 2004;351:2049-57
9. McMurray JJV et al NEJM 2019
10. Bardy GH et al. NEJM 2005;352:225-37
10. Cleland JG et al. NEJM 2005;352:1539-
11. Stone GW et al. NEJM 2018;Aug 23

Mortality Benefits Observed Across Key Therapies for Treatment of Select HFpEF Patients



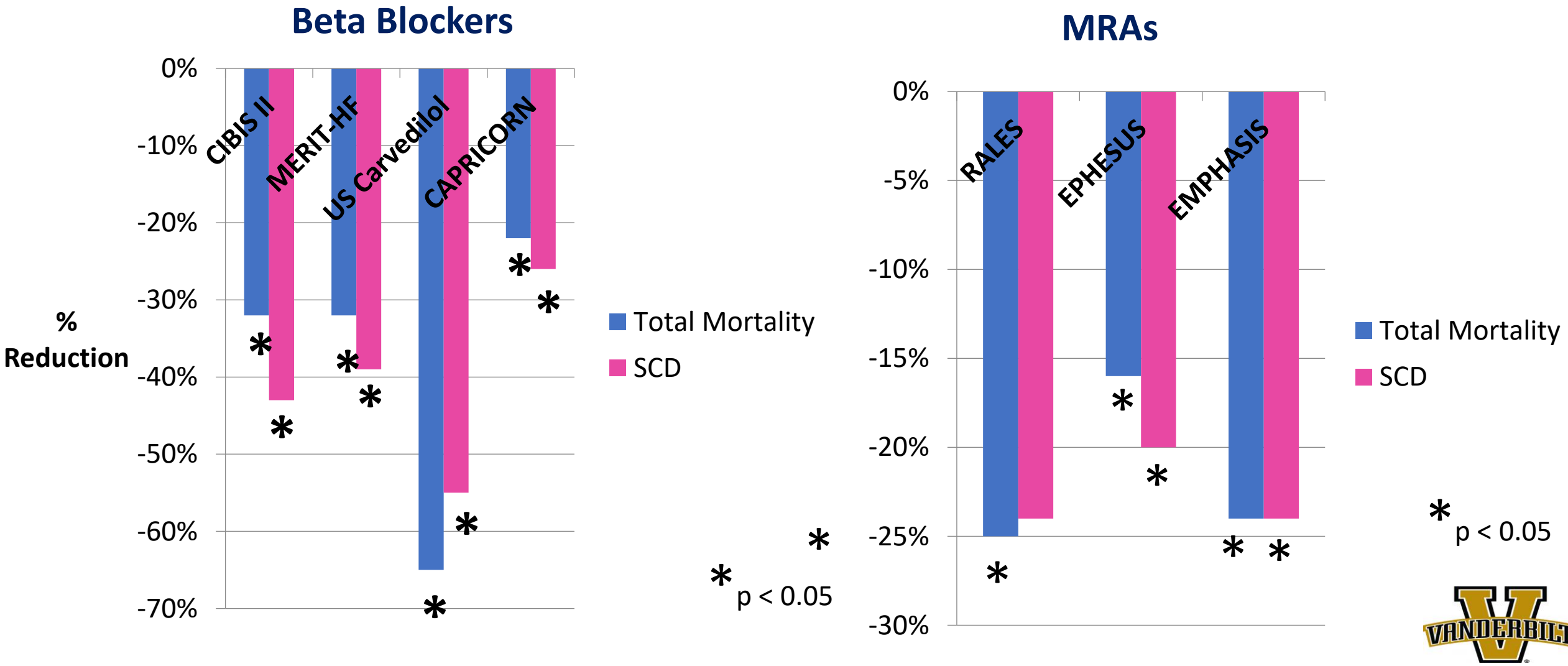
1Anker SD et al NEJM 2021; 2. Solomon SD et al, NEJM 2022 3.Stone GW et al. NEJM 2018

Guideline Directed Medical Therapy(GDMT) is Good and Keeps Getting Better in HFrEF

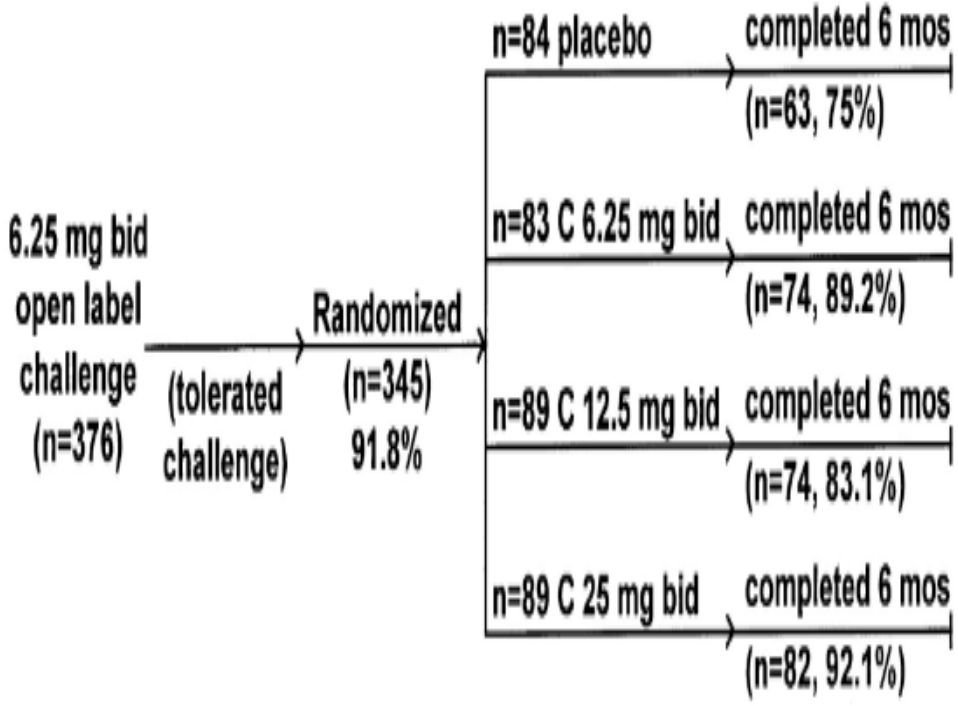


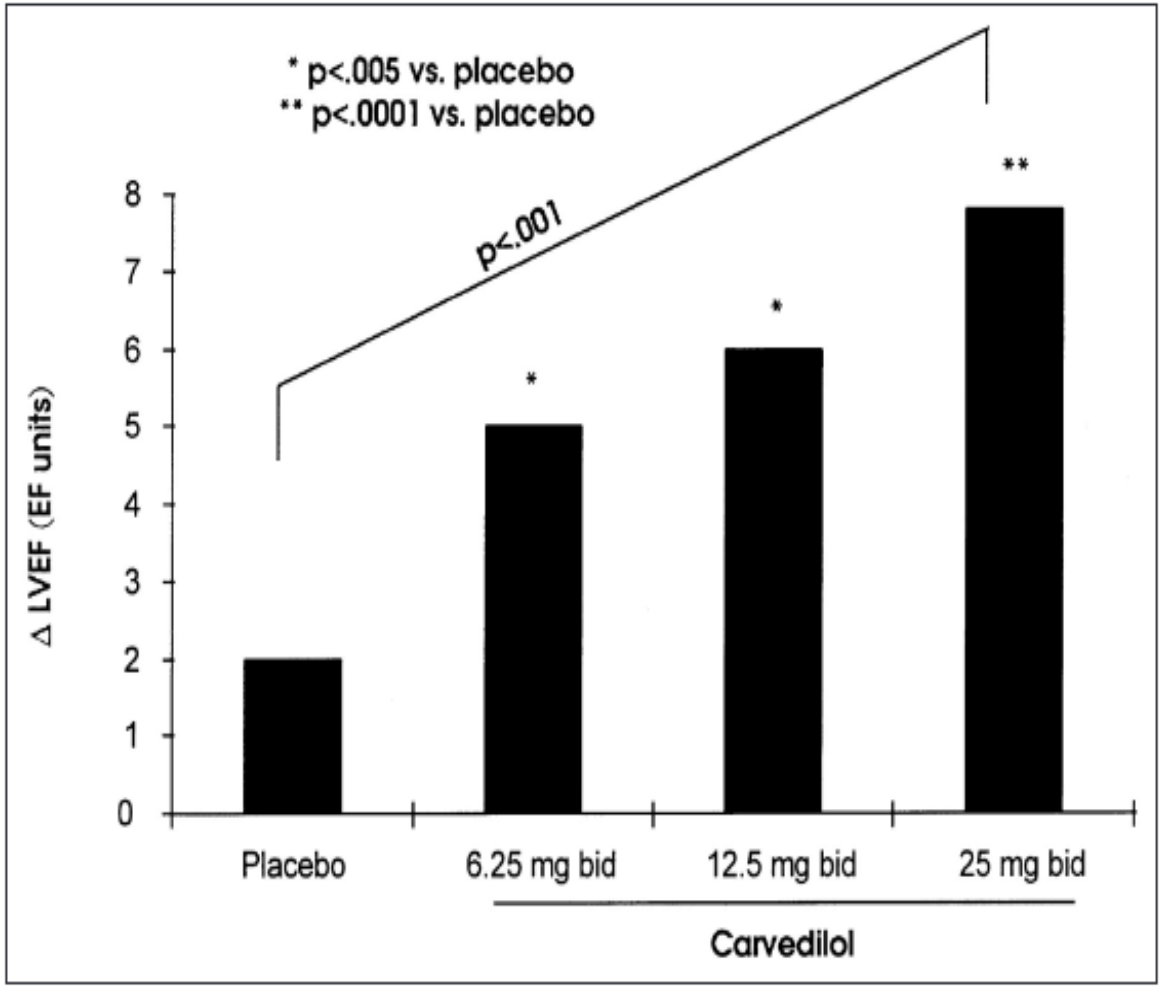
Vaduganathan M, et al. Lancet 2020;396:121-8

Effect of Beta-Blockers and MRAs on Total Mortality and Sudden Cardiac Death in HFrEF



There Appears to Be a Dose-Response Relationship Between Beta Blockers and LVEF





Bristow MR et al. Circulation. 1996;94:2807-16.

Medical Treatment of Tricuspid Regurgitation(TR) in Seconary Ventricular TR

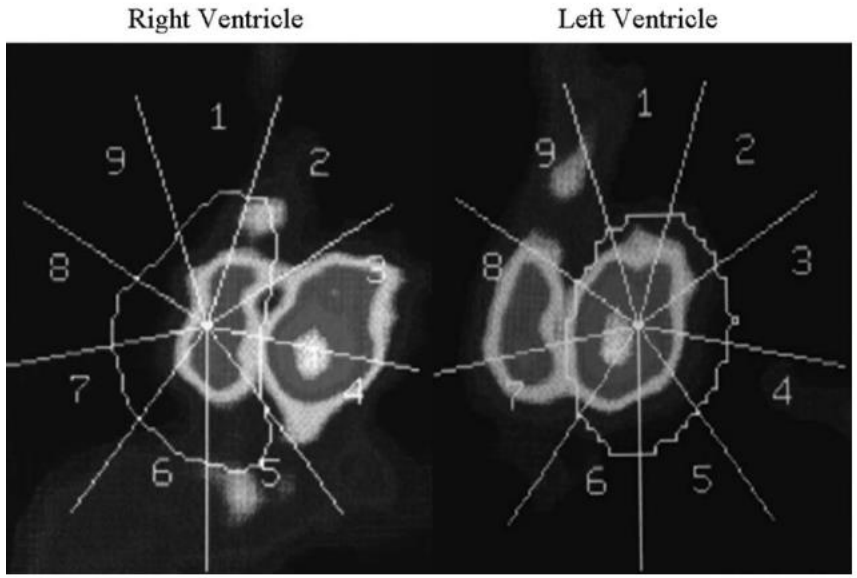
- Right Ventricular Afterload

- Right ventricular function
  - √ Right ventricular free wall
  - √ Septum (LV function)

Right Ventricular Systolic Function in Organic Mitral Regurgitation

Impact of Biventricular Impairment

Thierry Le Tourneau, MD, PhD; Guillaume Deswarte, MD; Nicolas Lamblin, MD, PhD; Claude Foucher-Hossein, MD; Georges Fayad, MD; Marjorie Richardson, MD; Anne-Sophie Polge, MD; Claire Vannesson, MD; Yan Topilsky, MD; Francis Juthier, MD, PhD; Jean-Noel Trochu, MD, PhD; Maurice Enriquez-Sarano, MD; Christophe Bauters, MD, PhD



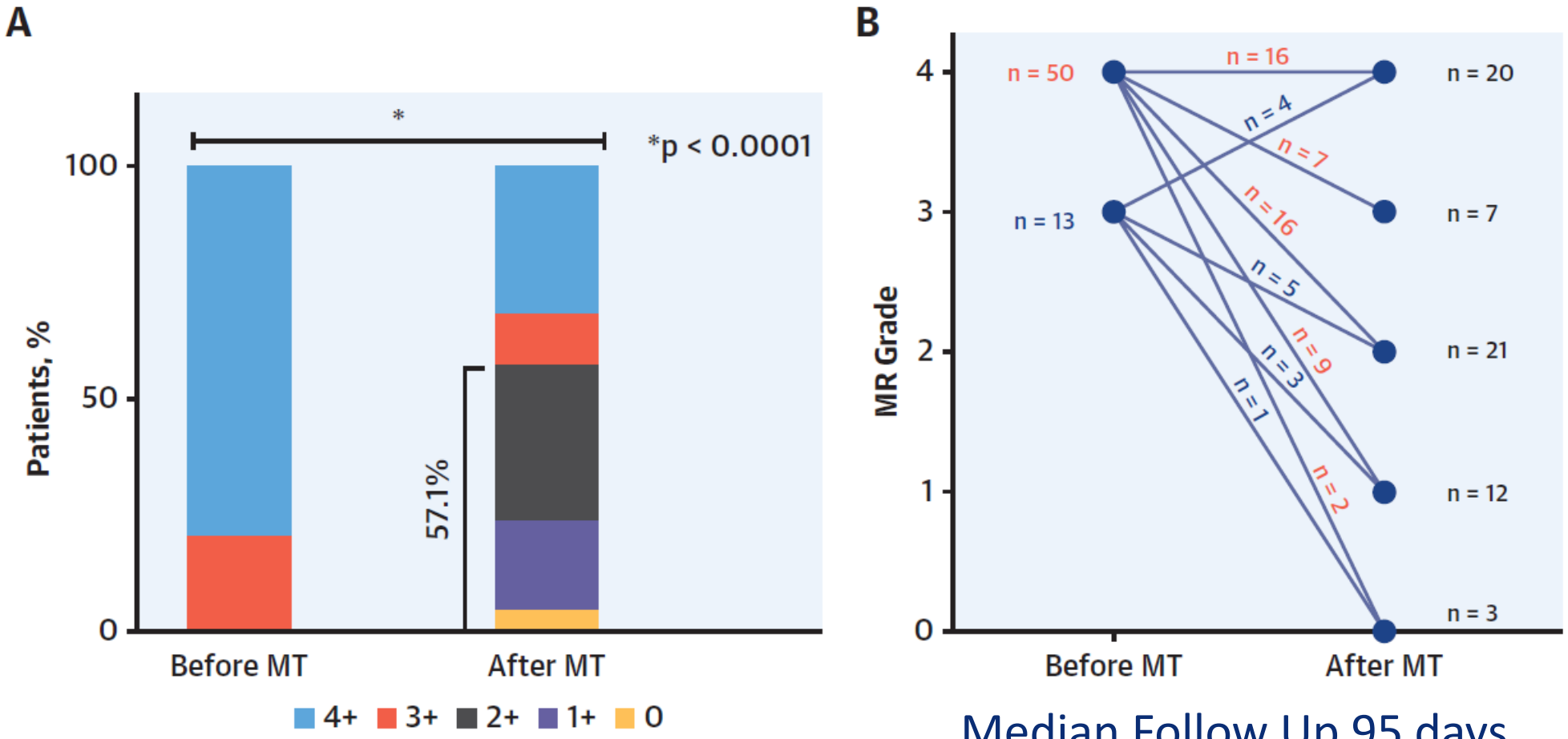
N =218

Table 3. Echocardiographic and Isotopic Predictors of RV EF in Multivariate Analysis

	R	β	P
Overall group (n=208)	0.55		
LV septal function		0.42	<0.0001
LV EDD index		−0.22	0.002
PASP		−0.14	0.047
With MR quantitation (n=84)	0.35		
Mitral ERO		−0.28	0.012

Le Tourneau T et al. Circulation. 2013;127:1597-1608.)

Effect of GDMT in 63 patients with HFrEF and SMR grade 3-4+ referred for mTEER



Median Follow Up 95 days

Sannino A et al JACC 2020; 76: 883-884

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Signs and Symptoms of Tricuspid Regurgitation and Right Ventricular Failure

- Hypotension
- Fatigue
- Peripheral Edema
- Abdominal Distension
- Early satiety and anorexia
- Ascites
- Elevated LFTs
- Cardiorenal syndrome

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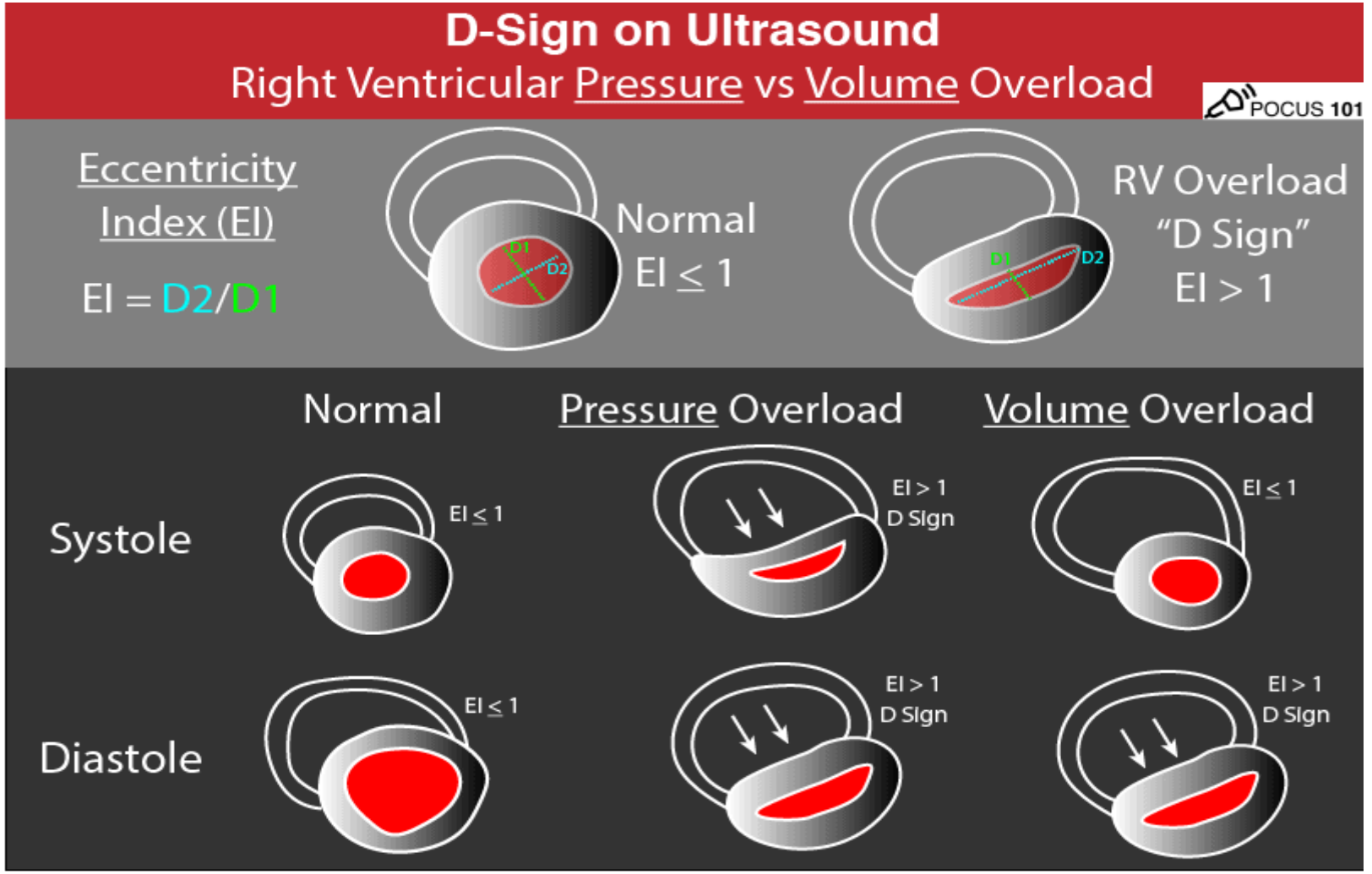
- Cardiorenal syndrome
- Rales
- Orthopnea and PND

Is Septal Position Important to Septal Function?



https://www.pocus101.com/the-d-sign-right-heart-strain-from-pressure-vs-volume-overload/

Study Description

145 subjects, mean left ventricular ejection fraction 20± 8%

↓

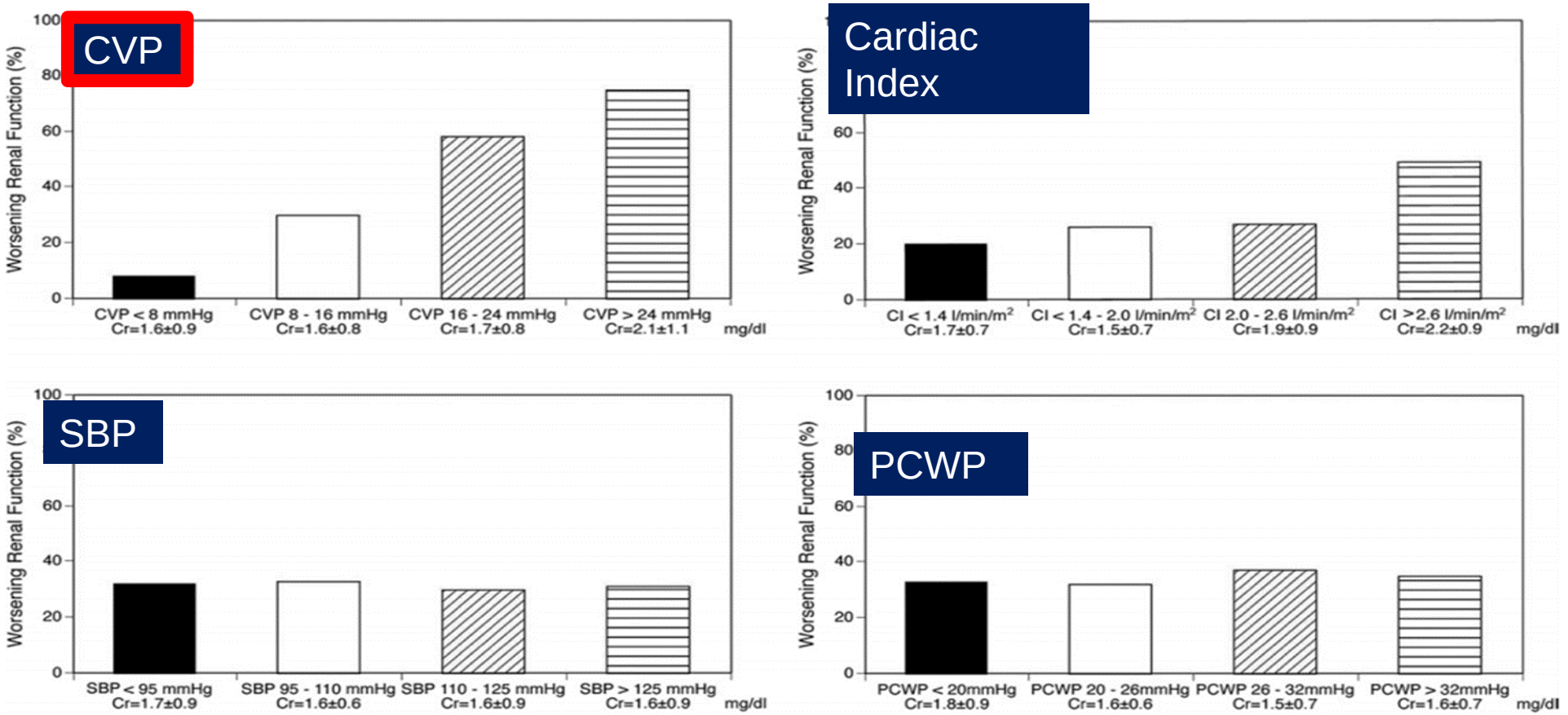
Acute Decompensated HF
Intensive medical therapy guided by pulmonary artery catheter (PAC)
NYHA class III to IV symptoms

↓

Worsening Renal Function(WRF) defined as an increase of serum creatinine 0.3 mg/dl during hospitalization.

Mullens W et al. JACC 2009;53:589-96

Incidence of Worsening Renal Function(WRF) by is most closely correlated with CVP, not PCWP, SBP, or CI



Mullens W et al. JACC 2009;53:589-96

Diuretics

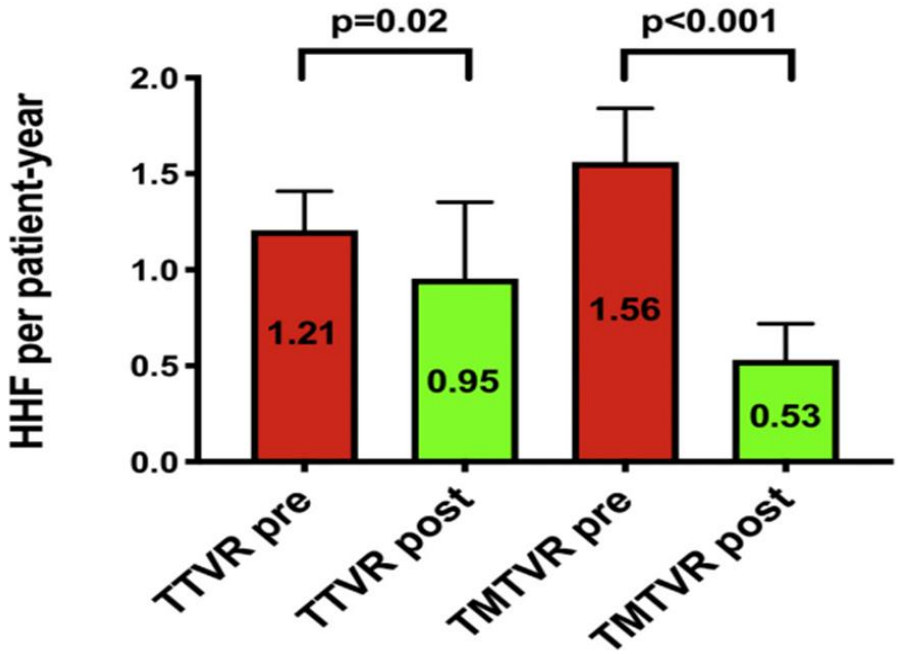
Primary Diuretic Therapy: Loop Diuretics			
Bumetanide	PO/IV	0.5 – 4mg PO 1-2x Daily 1 – 10mg IV 2-3x Daily	Document dose, number of doses/day, and changes over time in clinical trials
Furosemide	PO/IV	20 – 160mg PO 1-2x Daily 40 – 500mg IV 2-3x Daily	
Torsemide	PO	10 – 100mg PO 1-2x Daily	
Diuretics to add with Loop Diuretics as Combination Diuretic Therapy			
Acetazolamide	PO/IV	500mg IV Daily	Rarely used chronically
Thiazides/Thiazide-like			
Metolazone	PO	2.5 - 10mg 1-2x Daily	Document dose per day and changes over time in clinical trials
Hydrochlorothiazide	PO	25 – 100mg 1x Daily	
Chlorothiazide	PO/IV	500mg – 1g IV 1-2x Daily	
Chlorthalidone	PO	25 – 100mg 1x Daily	
Guideline-Directed Medical Therapies with Diuretic Actions			
Sodium glucose co-transporter 2 inhibitors*			
Dapagliflozin	PO	10 – 25 mg PO 1x Daily	Document dose per day and changes in clinical trials
Empagliflozin	PO	10 – 25 mg PO 1x Daily	
Mineralocorticoid Receptor Antagonist**			
Eplerenone	PO	12.5 – 50mg 1x Daily	Document dose per day and changes in clinical trials
Spironolactone	PO	12.5 – 50mg 1x Daily	

*Common doses may need to be exceeded in patients with severe tricuspid regurgitation

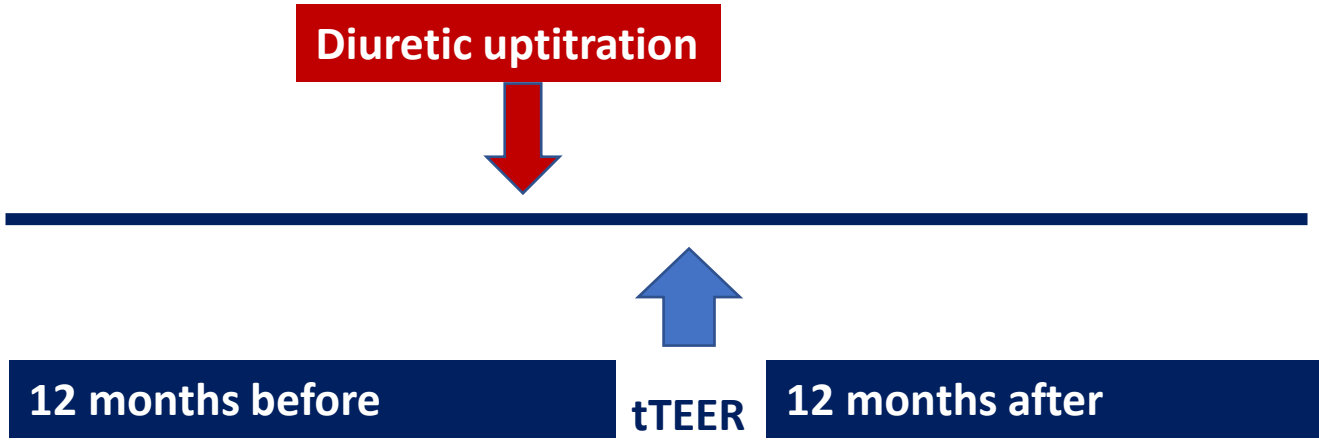
Hahn R et al. *JACC HF submitted*

Transcatheter Edge-to-Edge Tricuspid Repair for Severe Tricuspid Regurgitation Reduces Hospitalizations for Heart Failure

Mathias Orban, MD,[a,b,*] Karl-Philipp Rommel, MD,[c,*] Edwin C. Ho, MD,[d,e,*] Matthias Unterhuber, MD,[c] Alberto Pozzoli, MD,[e] Kim A. Connelly, MD, PhD,[d] Simon Deseive, MD,[a,b] Christian Besler, MD,[c] Geraldine Ong, MD, MSc,[d] Daniel Braun, MD,[a] Jeremy Edwards, MD,[d] Mizuki Miura, MD, PhD,[e] Gökhan Gülmez, MD,[e] Lukas Stolz, cand.med,[a] Mara Gavazzoni, MD,[e] Michel Zuber, MD,[e,f] Martin Orban, MD,[a,b] Michael Nabauer, MD,[a] Francesco Maisano, MD,[e] Holger Thiele, MD,[c] Steffen Massberg, MD,[a,b] Maurizio Taramasso, MD, PhD,[e] Neil P. Fam, MD, MSc,[d,†] Philipp Lurz, MD, PhD,[c,†] Jörg Hausleiter, MD[a,b,†]



The furosemide-equivalent dose was significantly increased from the year before TTVR to baseline but remained stable from the intervention to follow-up: 70 mg (95% CI: 54 to 87 mg) to 85 mg (95% CI: 67 to 104 mg) to 83 mg (95% CI: 58 to 109 mg; p = 0.03)



TTVR = transcatheter tricuspid valve repair
TTMVR = transcatheter tricuspid and mitral valve repair

Orban M et al. JACC HF 2020;8:265-76

Impact of Outpatient Diuretic Optimization(ODI) in the TOPCAT Trial

ODI = any increase
In loop diuretics or
New prescription

Table 2 Impact of outpatient loop diuretic dose intensification or new initiation of loop diuretics (among patients not on loop diuretics at baseline) on subsequent (time-updated) outcomes

Outcome	Overall population		Placebo arm		Spironolactone arm		Interaction p-value
	Event rate (per 100 py)	HR (95%CI) p-value*	Event rate (per 100 py)	HR (95% CI) p-value*	Event rate (per 100 py)	HR (95% CI) p-value*	
HFH/CVD	No ODI 10.4 (9.3–11.5) ODI 14.6 (12.5–17.0)	1.67 (1.36–2.04) $p < 0.001$	No ODI 11.3 (9.8–13.0) ODI 15.4 (12.5–18.8)	1.73 (1.31–2.27) $p < 0.001$	No ODI 9.6 (8.3–11.1) ODI 13.5 (10.6–17.3)	1.60 (1.18–2.16) $p = 0.002$	0.97
CVD	No ODI 3.1 (2.6–3.7) ODI 7.3 (6.0–8.8)	2.17 (1.64–2.87) $p < 0.001$	No ODI 3.2 (2.5–4.2) ODI 8.5 (6.7–10.8)	2.65 (1.81–3.89) $p < 0.001$	No ODI 3.0 (2.4–3.9) ODI 5.7 (4.1–7.9)	1.61 (1.04–2.49) $p = 0.034$	0.21
ACM	No ODI 5.6 (4.9–6.4) ODI 11.2 (9.6–13.0)	1.75 (1.41–2.16) $p < 0.001$	No ODI 5.8 (4.8–7.0) ODI 12.0 (9.9–14.6)	1.81 (1.34–2.43) $p < 0.001$	No ODI 5.4 (4.5–6.5) ODI 10.0 (7.9–12.8)	1.60 (1.16–2.20) $p = 0.005$	0.61

Ferreira JP et al European J Heart Failure 2022;24:378-384.;

Are we asking the right questions?

Tim McGraw and Faith Hill

Tug McGraw

Tug was asked when pitching in Houston if he prefered grass or Astroturf

"I dunno. I never smoked any Astroturf"