

CURSO REGIONAL DE **DIABETES 2021**  
ALAD-DOMINICANA



## Manejo de falla cardíaca en personas con diabetes mellitus

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### Conflictos de interés (últimos 5 años)

- Conferencista: Astra Zeneca, Abbott Nutrición, Novartis Oncology, Novo Nordisk, Merck Sharp & Dohme, Roche, Sanofi Aventis, Bayer, Pfizer, Novartis, Siegfried, Procter & Gamble
- Advisory Board: Sanofi Aventis, Novo Nordisk, Stendhal, Pfizer
- Investigación clínica: Astra Zeneca, Novartis Pharma Logistics Inc., Recordati

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### Agenda

- Asociación entre DM y falla cardíaca
- Impacto de antidiabéticos en falla cardíaca
- Impacto de fármacos de falla cardíaca en DM
- Revisar los iSGLT2 en todo el espectro de falla cardíaca
  - HFpEF
  - Falla cardíaca agua

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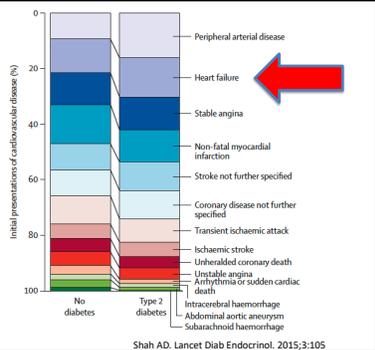
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### Presentación inicial de falla cardíaca




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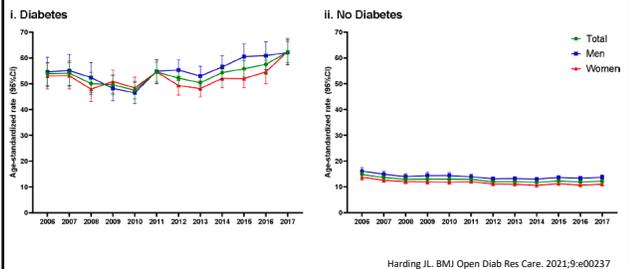
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### Las hospitalizaciones por falla cardíaca en personas con DM en USA van en aumento




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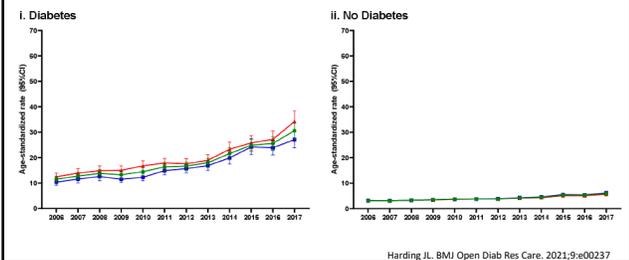
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### Las visitas a urgencias por falla cardíaca en personas con DM en USA van en aumento




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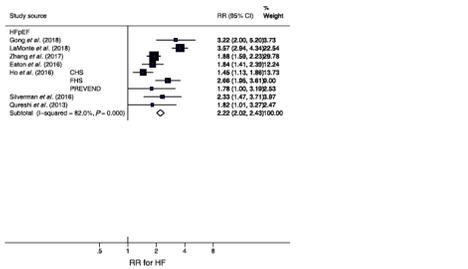
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### DM y riesgo de desarrollar HFpEF



Kodama S. ESC Heart Failure. 2020; online apr 28

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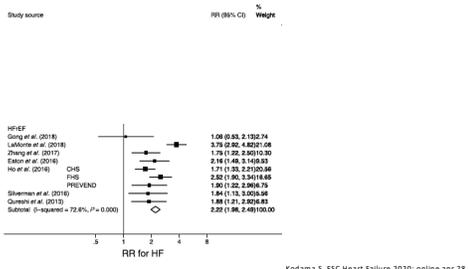
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### DM y riesgo de desarrollar HFrEF



Kodama S. ESC Heart Failure. 2020; online apr 28

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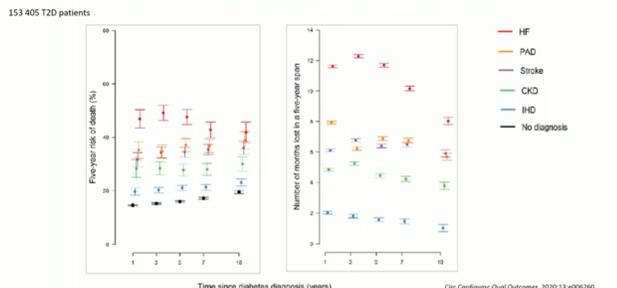
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### The 5-y risk of death and the expected decrease in lifespan in T2D patients in relation to development of 1 cardiovascular or renal diagnosis




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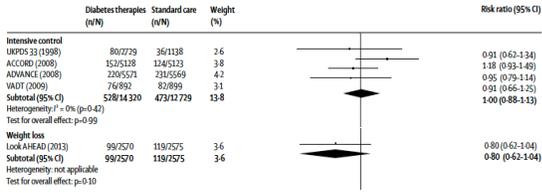
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Metanálisis: intervenciones en DM y falla cardíaca



Ghosh-Swaby OR. Lancet Diab Endocrinol. 2020;8:418.

CUÁL DEBE SER LA META DE HBA1C EN DM + FALLA CARDÍACA?

First author (year)	Description of study population and follow-up	Use of medications for the treatment of diabetes	Relationship of HbA1c with mortality if generally not treated with antidiabetic drugs	Relationship of HbA1c with mortality if generally treated with antidiabetic drugs
Studies that evaluated only patients treated with antidiabetic drugs				
Eskaghan <sup>2</sup> (2006)	123 patients with heart failure and diabetes followed for 2 years	81% treated with antidiabetic drugs, of whom 20% were treated with metformin	Not reported	Inverse relationship, with lower mortality if HbA1c > 7.0%
Aguilar <sup>3</sup> (2009)	5815 patients with heart failure and diabetes followed for 2 years	All treated with antidiabetic drugs, of whom 20%-30% were treated with metformin	Not reported	U-shaped relationship, with lowest mortality if HbA1c 7.1%-7.8%
Romero <sup>4</sup> (2013)	5314 patients with heart failure and diabetes followed for <4 years	Patients with diabetes were treated with metformin (74%), insulin (66%) and sulphonylureas (32%)	Not reported	Direct relationship, with lowest mortality if HbA1c < 6.5%
Grembowski <sup>5</sup> (2014)	1230 patients with heart failure and diabetes followed for 9 years	All treated with antidiabetic drugs, but information about drug classes was not specified	Not reported	Inverse relationship, with lowest mortality if HbA1c < 8.7%
Pastormier <sup>6</sup> (2015)	276 patients with diabetes and heart failure followed for up to 5 years	Use of insulin and oral antidiabetic medications in most patients; use of metformin not described	Not reported	No relationship between HbA1c and mortality if LV ejection fraction <38%
Blecker <sup>7</sup> (2016)	4723 patients with heart failure and diabetes followed for up to 5 years	Majority treated with antidiabetic medications (metformin in 15%-20%)	Not reported	U-shaped relationship, with lowest mortality if HbA1c 8.0%-8.9%

Packer M. Diab Obes Metab. 2018;20:1766





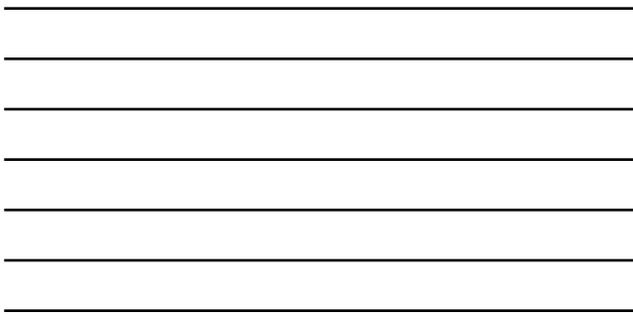
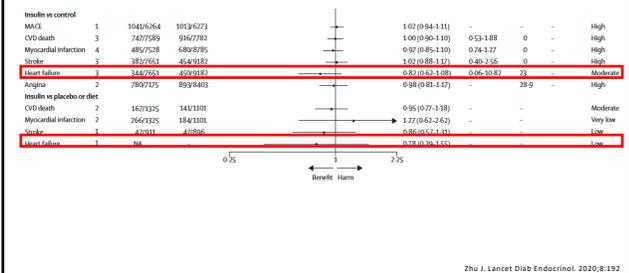
### CAROLINA: linagliptina vs glimepiride

Outcome	Linagliptin (n = 3023)		Glimepiride (n = 3010)		Incidence Rate/ 100 Patient-Years	Difference, Linagliptin - Glimepiride (95% CI)	HR <sup>a</sup> /Odds Ratio <sup>b</sup> (95% CI)
	No. (%)	Rate/100 Patient-Years	No. (%)	Rate/100 Patient-Years			
Hospitalization for heart failure	112 (3.7)	0.6	92 (3.1)	0.5	0.1 (-0.1 to 0.3)	1.21 (0.92 to 1.59) <sup>a</sup>	

Rosenstock J. JAMA. 2019; online Sep 19



### Insulina y desenlaces



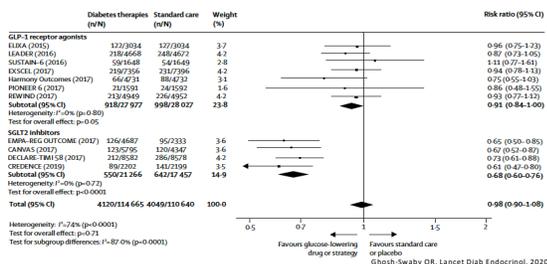
### Summary of CV/Kidney Effects of Epeglenatide

Outcome	N (%)	%/y	N (%)	%/y	HR (95%CI)	Significance
MACE	189 (7.0)	3.9	125 (9.2)	5.3	0.73 (0.58, 0.92)	Primary
MACE/Cor Revasc/UA	257 (9.5)	5.4	158 (11.6)	6.8	0.79 (0.65, 0.96)	Secondary
Renal Composite	353 (13.0)	7.7	250 (18.4)	11.6	0.68 (0.57, 0.79)	Secondary
MACE or Death	216 (7.9)	4.5	143 (10.5)	6.0	0.73 (0.59, 0.91)	Secondary
Renal (no MA) or Death	121 (4.5)	2.5	76 (5.6)	3.1	0.77 (0.57, 1.02)	Secondary
MACE_Death_HF_Renal	243 (8.9)	5.1	164 (12.1)	7.0	0.71 (0.59, 0.87)	Secondary
Fatal or Nonfatal MI	91 (3.3)	1.9	58 (4.3)	2.4	0.75 (0.54, 1.05)	Secondary
Nonfatal MI	85 (3.1)	1.7	53 (3.9)	2.2	0.78 (0.55, 1.10)	Secondary
Fatal or Nonfatal Stroke	47 (1.7)	1.0	31 (2.3)	1.3	0.74 (0.47, 1.17)	Secondary
Nonfatal Stroke	41 (1.5)	0.8	25 (1.8)	1.0	0.80 (0.48, 1.31)	Secondary
CV Mortality	75 (2.8)	1.5	50 (3.7)	2.1	0.72 (0.50, 1.03)	Secondary
Total Mortality	111 (4.1)	2.2	69 (5.1)	2.8	0.78 (0.58, 1.06)	Secondary
Coronary Revascularization	126 (4.6)	2.6	66 (4.9)	2.8	0.93 (0.69, 1.26)	Secondary
New Macroalbuminuria	348 (12.8)	7.6	244 (18.0)	11.3	0.68 (0.58, 0.80)	Secondary
Heart Failure	40 (1.5)	0.8	31 (2.3)	1.3	0.61 (0.38, 0.98)	Secondary

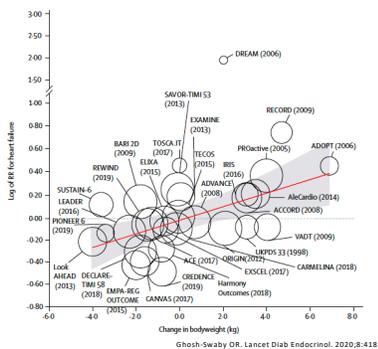
0.25 0.5 HR 1 1.5



### Metanálisis: intervenciones en DM y falla cardíaca



### Metanálisis: cambios en peso y falla cardíaca



### La revolución “inesperada”, inhibidores de SGLT2

HFrEF

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Effects of Dapagliflozin on Worsening HF<sup>a</sup> and Mortality<sup>1</sup>

Outcome, n (%)	Dapagliflozin 10 mg (n=2373)	Placebo (n=2371)	HR (95% CI)	HR (95% CI)	p-value
CV death, HFrEF, or urgent HF visit	386 (16.3)	502 (21.2)		0.74 (0.65, 0.85)	<0.001
HFrEF or urgent HF visit	237 (10.0)	326 (13.7)		0.70 (0.59, 0.83)	0.00003 <sup>b</sup>
Hospitalization for HF	231 (9.7)	318 (13.4)		0.70 (0.59, 0.83)	0.0001 <sup>c</sup>
CV death	227 (9.6)	273 (11.5)		0.82 (0.69, 0.98)	0.029 <sup>d</sup>
CV death or HFrEF	382 (16.1)	495 (20.9)		0.75 (0.65, 0.85)	<0.001
Death from any cause	276 (11.6)	329 (13.9)		0.83 (0.71, 0.97)	0.022 <sup>e</sup>

<sup>a</sup>Worsening HF includes HF with an urgent HF visit. <sup>b</sup>Statistical significance.   
<sup>c</sup>CV = cardiovascular; HF = heart failure; HFrEF = hospitalization for heart failure; HR = hazard ratio.   
<sup>d</sup>M. McMurray JJF et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med*. 2019;381:1995-2008.   
<sup>e</sup>MCMurray JJF et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. Presented at ESC Congress, August 30-September 4, 2019; Paris, France.   
 39   
 1. Pasterkamp GJALM. *ESC 2019 Abstracts*.

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Primary Outcome by Diabetes Status<sup>1</sup>

Dapagliflozin significantly reduced the primary endpoint, regardless of diabetes status and HbA1c in the no T2D group

CV death or hHF or urgent HF visit

Outcome	Dapagliflozin 10 mg, n/N (%)	Placebo, n/N (%)	HR (95% CI)	Interaction p-value <sup>a</sup>
Total population	386/2373 (16.3)	502/2371 (21.2)		0.74 (0.65-0.85)
T2D <sup>b</sup>	215/1075 (20.0)	271/1064 (25.5)		0.75 (0.63-0.90)
No T2D	171/1298 (13.2)	231/1307 (17.7)		0.73 (0.60-0.88)
Normo-glycemic (HbA1c <5.7%)	53/438 (12.1)	71/419 (16.9)		0.67 (0.47-0.96)
Pre-diabetes (HbA1c ≥5.7- <6.5%)	118/860 (13.7)	160/888 (18.0)		0.74 (0.59-0.94)

<sup>a</sup>Includes 1883 patients with a pre-existing diagnosis of diabetes and 154 patients with previously undiagnosed diabetes (HbA1c ≥6.5% at Visits 1 and 2). <sup>b</sup>Non-significant result for an interaction term can be interpreted as consistency of effect across the subgroup.   
<sup>c</sup>CV = cardiovascular; HbA1c = glycated hemoglobin; HF = heart failure; hHF = hospitalization for heart failure; HR = hazard ratio; T2D = type 2 diabetes.   
 39   
 1. Pasterkamp GJALM. *JAMA*. 2019;323:1553-1568.   
 2. Anon M et al. *Dapagliflozin*. *Stat*. 2015;15:1161-1176.

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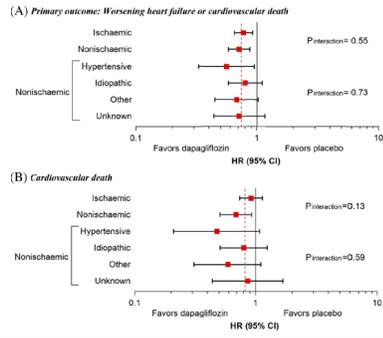
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Beneficio de dapagliflozina independiente de la etiología de FC



Butt JW. Eur J Heart Fail. 2021.

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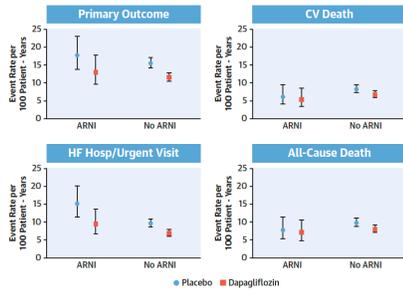
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Beneficio de dapagliflozina independiente del uso basal de ARNI



Solomon SD. J Am Coll Cardiol HF. 2020.

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### EMPEROR-Reduced: Effect on Individual Components of the Primary Endpoint

	Empagliflozin (n=1863)		Placebo (n=1867)		Hazard ratio (95% CI)	P value
	Number of events (%)	Events/100 patient-yr	Number of events (%)	Events/100 patient-yr		
Primary composite outcome	361 (19.4%)	15.8	462 (24.7%)	21.0	0.75 (0.65 – 0.86)	<0.0001
First hospitalization for heart failure	246 (13.2%)	10.7	342 (18.3%)	15.5	0.69 (0.59 – 0.81)	
Cardiovascular death	187 (10.0%)	7.6	202 (10.8%)	8.1	0.92 (0.75 – 1.12)	

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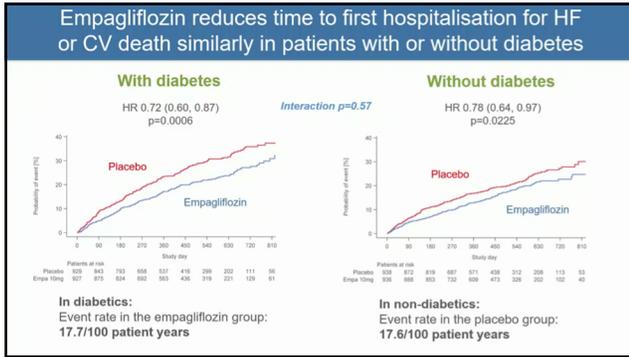
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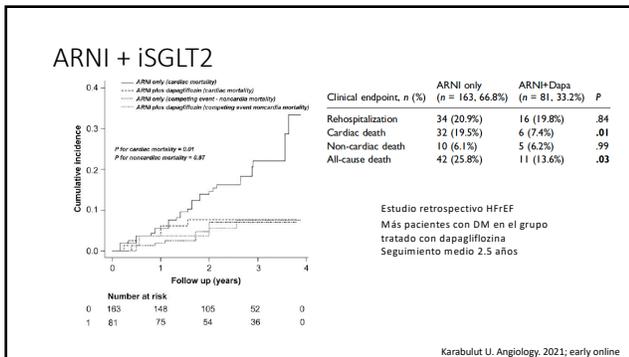
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**Efecto de tratamiento de falla cardíaca en glucosa**

- IECA/ARA: no aumentan glucosa, algunos estudios con reversión a normoglicemia en pacientes con prediabetes
- Beta bloqueadores:
  - Carvedilol mejora resistencia a la insulina
  - Metoprolol aumento discreto Hba1c
- MRA:
  - Espironolactona: aumenta hasta 0.2% Hba1c
  - Eplerenona: neutro
- ARNI:
  - Reducción de hasta 0.26% de Hba1c

Mehta A. Clin Geriatr Med. 2020;36:447

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Falla cardíaca aguda

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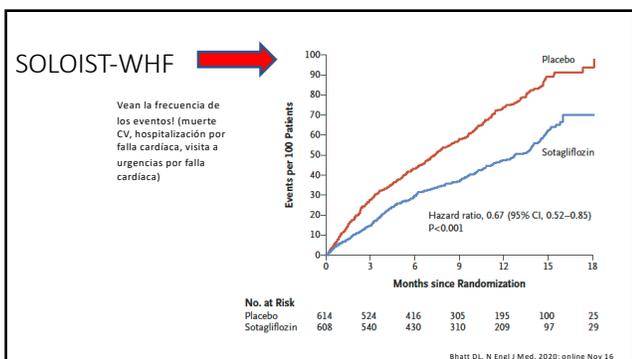
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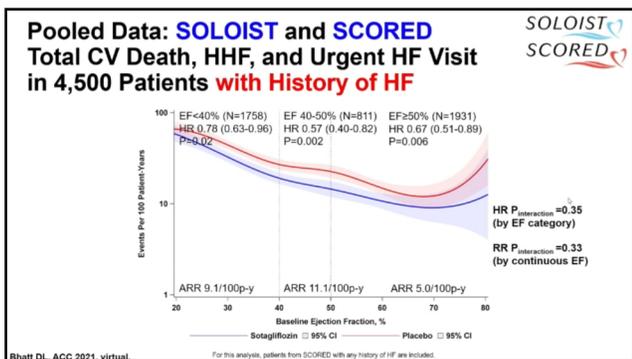
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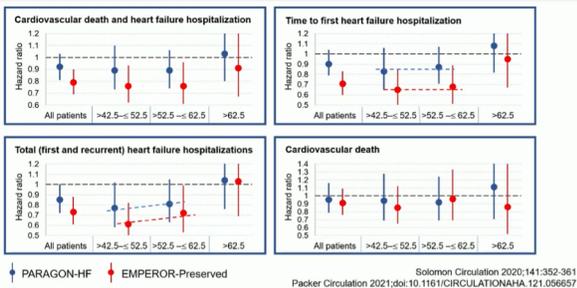
### EMPEROR-Preserved: Results

Subgroup	Empagliflozin No. of patients with events/total no.	Placebo No. of patients with events/total no.	HR (95% CI)
Overall	415/2997	511/2991	0.79 (0.69-0.90)
Diabetes at baseline			
Yes	239/1466	291/1472	0.79 (0.67-0.94)
No	176/1531	220/1519	0.78 (0.64-0.95)
LVEF at baseline			
<50%	145/995	193/988	0.71 (0.57-0.88)
≥50% to <60%	138/1028	173/1030	0.80 (0.64-0.99)
≥60%	132/974	145/973	0.87 (0.69-1.10)

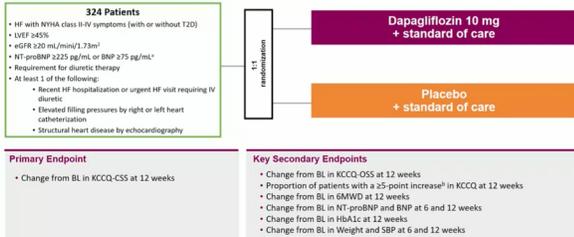
Consistent results across diabetes status and LVEF at baseline (interaction P>0.10)

CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction  
Anker S, et al. N Engl J Med 2021; doi:10.1056/NEJMoa2010158 (pub ahead of print)

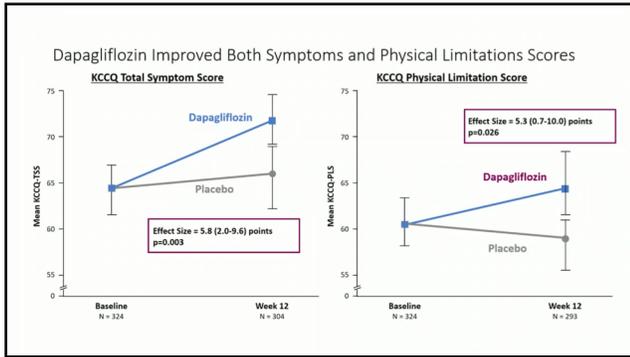
### Side-by-Side Display of EMPEROR-Preserved and PARAGON-HF in Ejection Fraction Subgroups (Post Hoc)



### PRESERVED-HF: Effects of Dapagliflozin on Biomarkers, Symptoms and Functional Status in Patients with Preserved Ejection Fraction Heart Failure<sup>1,2</sup>



<sup>1</sup> N Engl J Med. 2021;384(12):1117-1127. doi:10.1056/NEJMoa2010158. <sup>2</sup> JAMA. 2021;325(12):1117-1127. doi:10.1001/jama.2020.2010158




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Qué papel tienen los iSGLT2 en las guías de FC del 2021?

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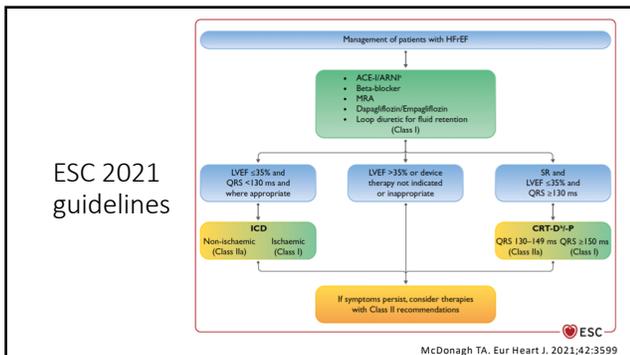
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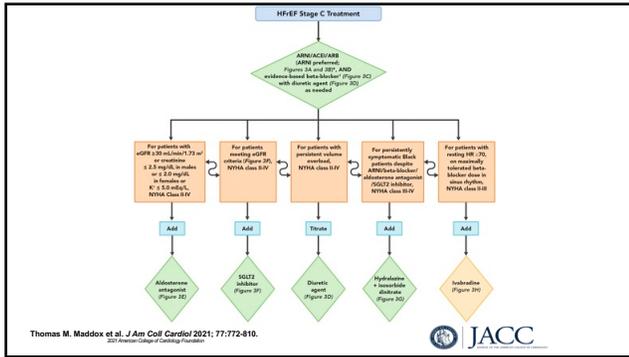
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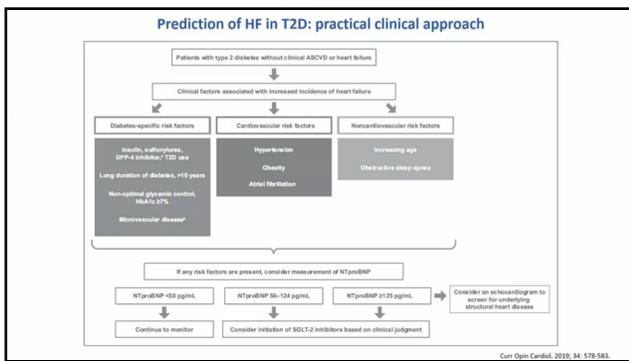
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Conclusiones

- Falla cardíaca puede ser la primera manifestación de enfermedad cardiovascular en pacientes con DM
- Es igual o más prevalente que IAM, ictus y muerte cardiovascular
- El tratamiento estándar de HFrEF no produce deterioro del control glicémico
- Hay una correlación entre impacto en peso con anti diabéticos y empeoramiento de falla cardíaca
- Los iSGLT2 tienen beneficio en todo el espectro de falla cardíaca

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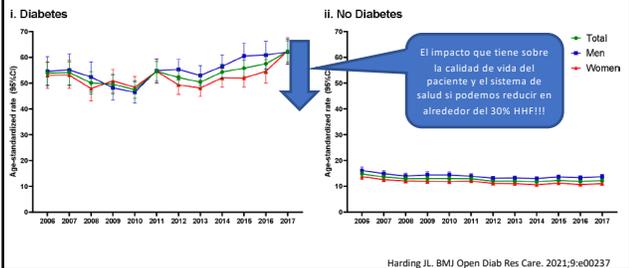
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Las hospitalizaciones por falla cardíaca en personas con DM en USA van en aumento




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Preguntas...

[chenku2409@gmail.com](mailto:chenku2409@gmail.com)

Puede descargar la presentación en:



[www.EndoDrChen.com](http://www.EndoDrChen.com)

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