SESION BIBLIOGRAFICA 29/11/19

Dra Raquel Rodríguez Díez

Circulation

PRIMER

Revisiting the Role of Aspirin for the Primary Prevention of Cardiovascular Disease

Circulation. 2019;140:1115–1124. DOI: 10.1161/CIRCULATIONAHA.119.040205

ORIGINAL RESEARCH ARTICLE

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial

Circulation. 2019;140:1463–1476. DOI: 10.1161/CIRCULATIONAHA.119.042929

ADVANCES IN HEART FAILURE

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis

Circ Heart Fail. 2019;12:e006075. DOI: 10.1161/CIRCHEARTFAILURE.119.006075

TACIT (High Sensitivity Troponin T Rules Out Acute Cardiac Insufficiency Trial)

An Observational Study to Identify Acute Heart Failure Patients at Low Risk for Rehospitalization or Mortality

Junta de Castilla y León
Consejería de Sanidad

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PRIMER

Revisiting the Role of Aspirin for the Primary Prevention of Cardiovascular Disease

- AAS: piedra angular del tto antitrombótico de pacientes con ECV establecida.
- Recomendaciones claras en prevención secundaria.
- Recomendaciones contradictorias en prevención primaria.

Table 1. Summary of Guidelines Recommendations for Aspirin in Primary Prevention of Atherosclerotic Cardiovascular Diseases

Guidelines	Recommendation	Level of Evidence
2019 American College of Cardiology/American Heart Association Guideline on the Primary Prevention of Cardiovascular Disease[6]	Low-dose aspirin (75–100 mg/d orally) might be considered among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk	IIb, A: weak recommendation; high-quality evidence from more than 1 RCT or meta-analyses of high-quality RCTs or 1 or more RCTs corroborated by high-quality registry studies
	Low-dose aspirin (75–100 mg/d orally) should not be administered on a routine basis for the primary prevention of ASCVD among adults >70 years of age	III, B-R: harm; moderate-quality evidence from 1 or more RCTs, or meta-analyses of moderate-quality RCTs
	Low-dose aspirin (75–100 mg/d orally) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding	III, C-LD: harm; randomized or nonrandomized observational or registry studies with limitations of design or execution or meta-analyses of such studies or physiological or mechanistic studies in human subjects
American Diabetes Association Standards of Medical Care in Diabetes 2019[11]	Aspirin 75–162 mg daily for patients with diabetes mellitus at increased cardiovascular risk (who do not have known CVD)	Class C: supportive evidence from poorly controlled or uncontrolled studies
US Preventive Services Task Force 2016 Recommendations for Primary Care Practice[8]	Low-dose aspirin for adults 50–59 years old without CVD but with a ≥10% 10-year CVD risk	B: High certainty that the net benefit is moderate, or moderate certainty that the net benefit is moderate to substantial
	Low-dose aspirin for adults 60–69 years old without CVD but with a ≥10% 10-year CVD risk	C: At least moderate certainty that the net benefit is small
	No recommendation for patients <50 or ≥70 years old without CVD	I: Current evidence is insufficient
European Society of Cardiology 2016 Guidelines on Cardiovascular Disease Prevention in Clinical Practice[9]	Aspirin not recommended in individuals without CVD	III, B: Treatment not recommended, data derived from a single randomized clinical trial or large nonrandomized studies
American Heart Association Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update[12]	Routine use of aspirin in healthy women <65 years of age without CVD is not recommended to prevent myocardial infarction	III, C: Procedure/test not helpful or treatment has no proven benefit, procedure/test excess cost without benefit or harmful or treatment harmful to patients; based on expert opinion, case studies, or standard of care
	Aspirin therapy (75–325 mg/d) is reasonable to use in women with diabetes mellitus without known CVD unless contraindicated	IIa, B: weight of evidence/opinion is in favor of usefulness/efficacy; limited evidence from single randomized trial or other nonrandomized studies
	Aspirin therapy can be useful in women ≥65 y of age without known CVD (81 mg/d or 100 mg every other day) if blood pressure is controlled and benefit for ischemic stroke and myocardial infarction prevention is likely to outweigh risk of gastrointestinal bleeding and hemorrhagic stroke	IIa, B: weight of evidence/opinion is in favor of usefulness/efficacy; limited evidence from single randomized trial or other nonrandomized studies
	Aspirin (81 mg/d or 100 mg every other day) may be reasonable for women <65 y without known CVD for ischemic stroke prevention	IIb, B: usefulness/efficacy is less well established by evidence/opinion; limited evidence from single randomized trial or other nonrandomized studies
Canadian Cardiovascular Society Antiplatelet Guidelines[7,13]	Aspirin not routinely recommended for patients without CVD	III, A: evidence that the treatment is not useful and, in some cases, may be harmful; data derived from multiple randomized clinical trials or meta-analyses
	Aspirin 75–162 mg daily recommended for patients without CVD, if high vascular risk and low bleeding risk[10]	IIb, C: Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the treatment with the usefulness/efficacy less well established; consensus of opinion by experts and/or small studies, retrospective studies, and registries

ASCVD, atherosclerotic cardiovascular disease; CVD, cardiovascular disease; and RCT, randomized controlled trial.

EVIDENCIAS EN PREVENCION PRIMARIA:

Tres Ensayos Controlados Aleatorizados (ARRIVE, ASCEND y ASPREE) que incluyen mas de 47.000 pacientes en 3 poblaciones clave:

- 1. DM
- 2. Persona mayores
- 3. No DM con riesgo intermedio.

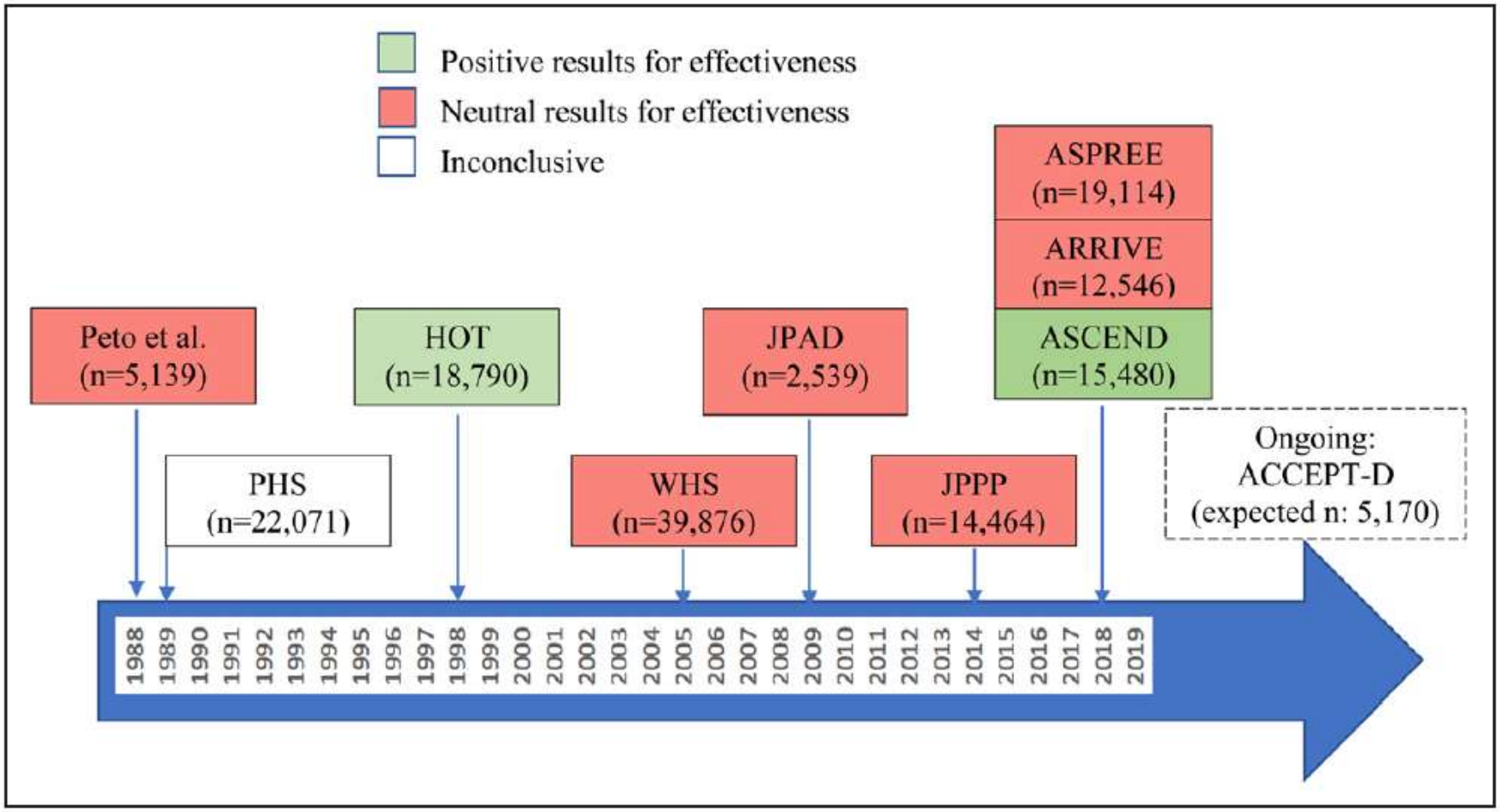

Figure 1. Timeline of major randomized controlled trials of aspirin in primary prevention of atherosclerotic cardiovascular diseases.

Table 2. Summary of the Recent Trials on Aspirin for the Primary Prevention of Atherosclerotic Cardiovascular Disease

Study population	
Age, y	
Sample size	
Median follow-up time, y	
Study interventions	
Primary endpoint	
All-cause mortality	
Bleeding endpoints	

ARRIVE indicates Aspirin to Reduce Risk of Initial Vascular Events; ASCEND, A Study of Cardiovascular Events in Diabetes; and ASPREE, Aspirin in Reducing Events in the Elderly.

Table 3. Key Areas of Residual Uncertainty for the Use of Aspirin for the Primary Prevention of Atherosclerotic Cardiovascular Disease

Areas of Uncertainty	Rationale	Proposed Potential Study

ADD-ASPIRIN indicates A Trial Assessing the Effects of Aspirin on Disease Recurrence and Survival After Primary Therapy in Common Non Metastatic Solid Tumours; ASCEND, A Study of Cardiovascular Events in Diabetes; and ASCVD, atherosclerotic cardiovascular disease.

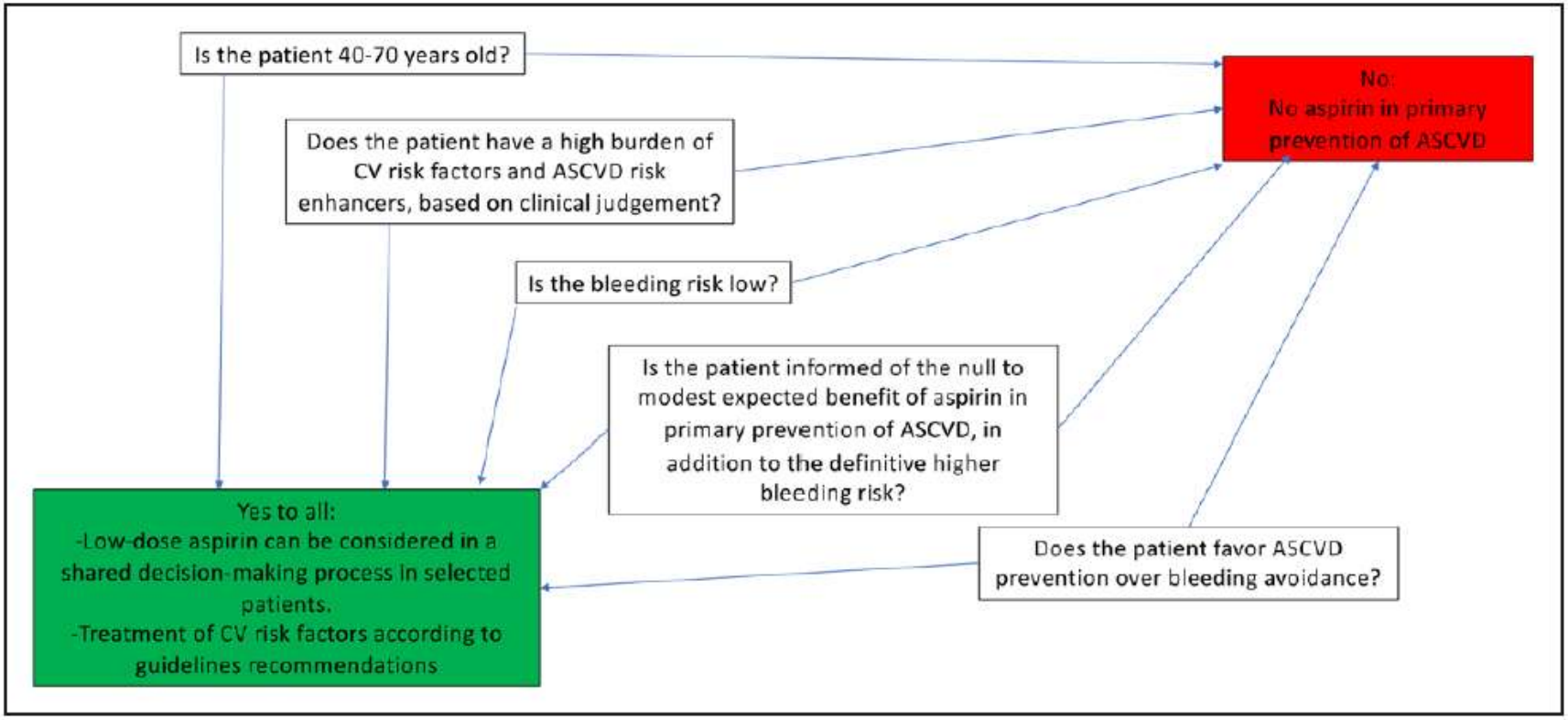

Figure 2. Suggested decisional pathway for the use of aspirin in primary prevention of atherosclerotic cardiovascular disease (ASCVD) for contemporary practice.

CV indicates cardiovascular.

CONCLUSIONES

The positioning of aspirin as a treatment option for the primary prevention of cardiovascular events has been informed by the recent results of 3 large-scale RCTs that collectively question its role for the treatment of patients without established ASCVD. A decisional framework for clinicians to support prescription of aspirin in primary prevention is presented in Figure 2. Key unresolved questions regarding the role of aspirin in primary prevention include the optimal drug formulation, dosing schedule, weight-based dose selection, and interplay between sex and treatment response. Given the desire expressed by regulatory authorities to explore the use of real-world data sources in RCTs, creative approaches are needed in future trials of aspirin in primary prevention. For example, evaluation of the validity and utility of risk calculators derived from real-world data could be conducted to enable their use to inform modeling of eligibility criteria. In the current era, most patients without established ASCVD should not be prescribed aspirin in the absence of established evidence for definitive risk reduction and of decision support tools to tailor patient selection according to the expected net clinical benefits. Rather, aggressive management of comorbidities tailored to the expected cardiovascular risk needs to be emphasized. Informed shared decision making between clinicians and patients regarding the use of aspirin for primary prevention of cardiovascular events is a suitable and laudable approach going forward.[11]

ORIGINAL RESEARCH ARTICLE

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial

- ENSAYO ALETORIZADO DOBLE CIEGO CON 263 PACIENTES CON IC EN FASE ESTABLE (CLASE FUNCIONAL II-III DE NYHA) Y FEVI< 40% A RECIBIR DAPAGLIFOCINA 10 MG FRENTE A PLACEBO.
- **HIPOTESIS:** El tratamiento con Dapaglifocina mejorará los péptidos natriuréticos y el estado de salud (KCCQ) en los pacientes con insuficiencia cardiaca bien fenotipada y óptimamente tratada con y sin DM-2.
- **OBJETIVOS PRIMARIOS:**

  1. Evaluar cambios en NT-proBNP a las 12 semanas

  2. Combinado de cambios categóricos en el cuestionario Kansas City o del NT-proBNP (descenso > 20%)

26 hospitales de USA y patrocinado por ASTRA ZENACA

ORIGINAL RESEARCH ARTICLE

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The DEFINE-HF Trial

- **Criterios de inclusión**: adultos con o sin DM-2 con IC establecida durante al menos 16 semanas, FEVI < 40% y clase funcional II-III de NYHA.

- **Criterios de exclusión**: hospitalización en los últimos 30 dias por IC descompensada, FG < 30 ml/min antecedentes de DM-1.

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial

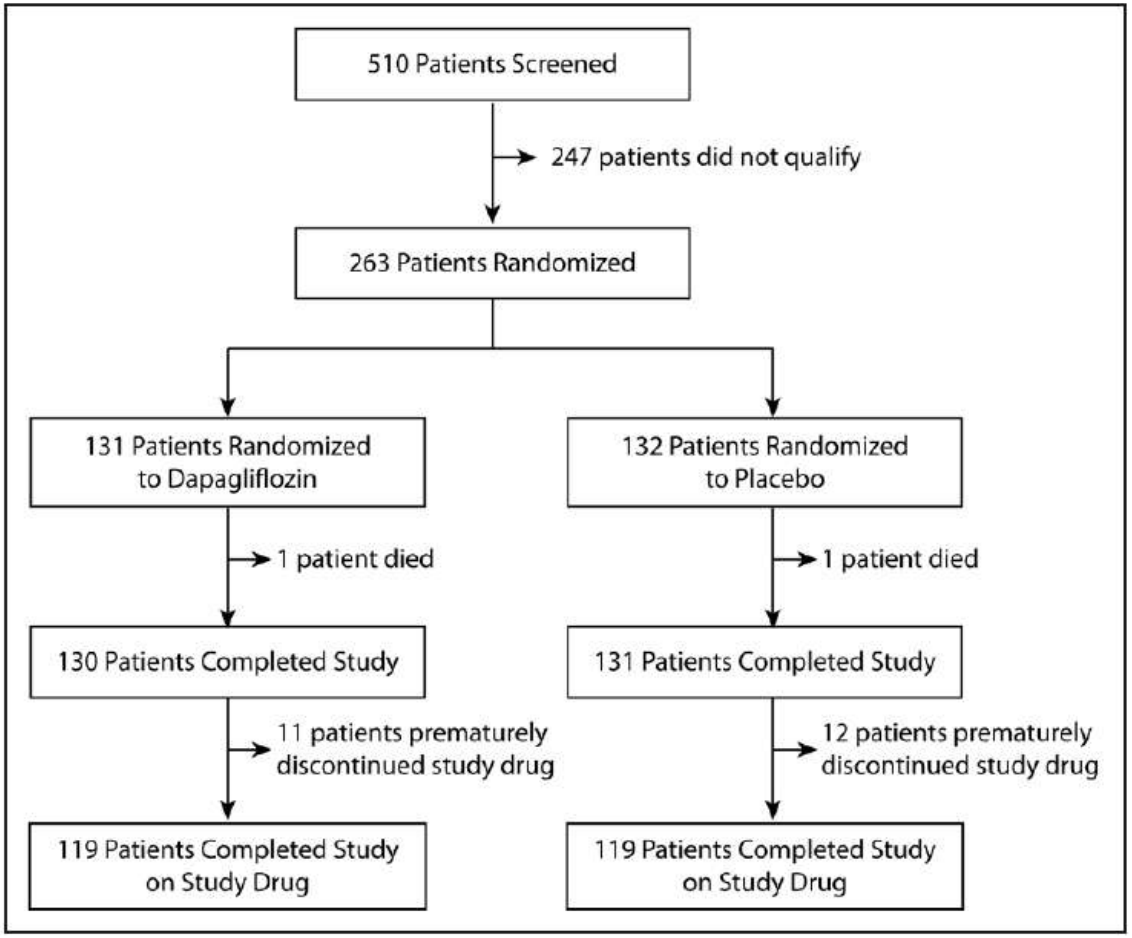


Figure 1. Trial flow chart.

ORIGINAL RESEARCH ARTICLE

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial

- Se aleatorizaron 1:1 a recibir 10 mg de dapaglifocina cada 24 horas durante un periodo de seguimiento de 12 semanas.

- Seguimiento: 4 llamadas telefónicas y dos visitas presenciales a las 6 y 12 semanas. Se realizan los análisis, examen físico, cuestionario KCCQ y test de los 6 minutos antes de la primera dosis de dapaglifocina y a las 12 semanas.

- En la semana 12 se suspende la medicación y se hace una semana adicional de seguimiento para evaluar seguridad y recolectar muestras adicionales.

ORIGINAL RESEARCH ARTICLE

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial

RESULTADOS:

- Edad media 61.3 años

-73% hombres

-40% afroamericanos

-Duración media de la insuficiencia cardiaca 7.1 años

-85% habían sido hospitalizados al menos una vez

-60% DM

-40% FA

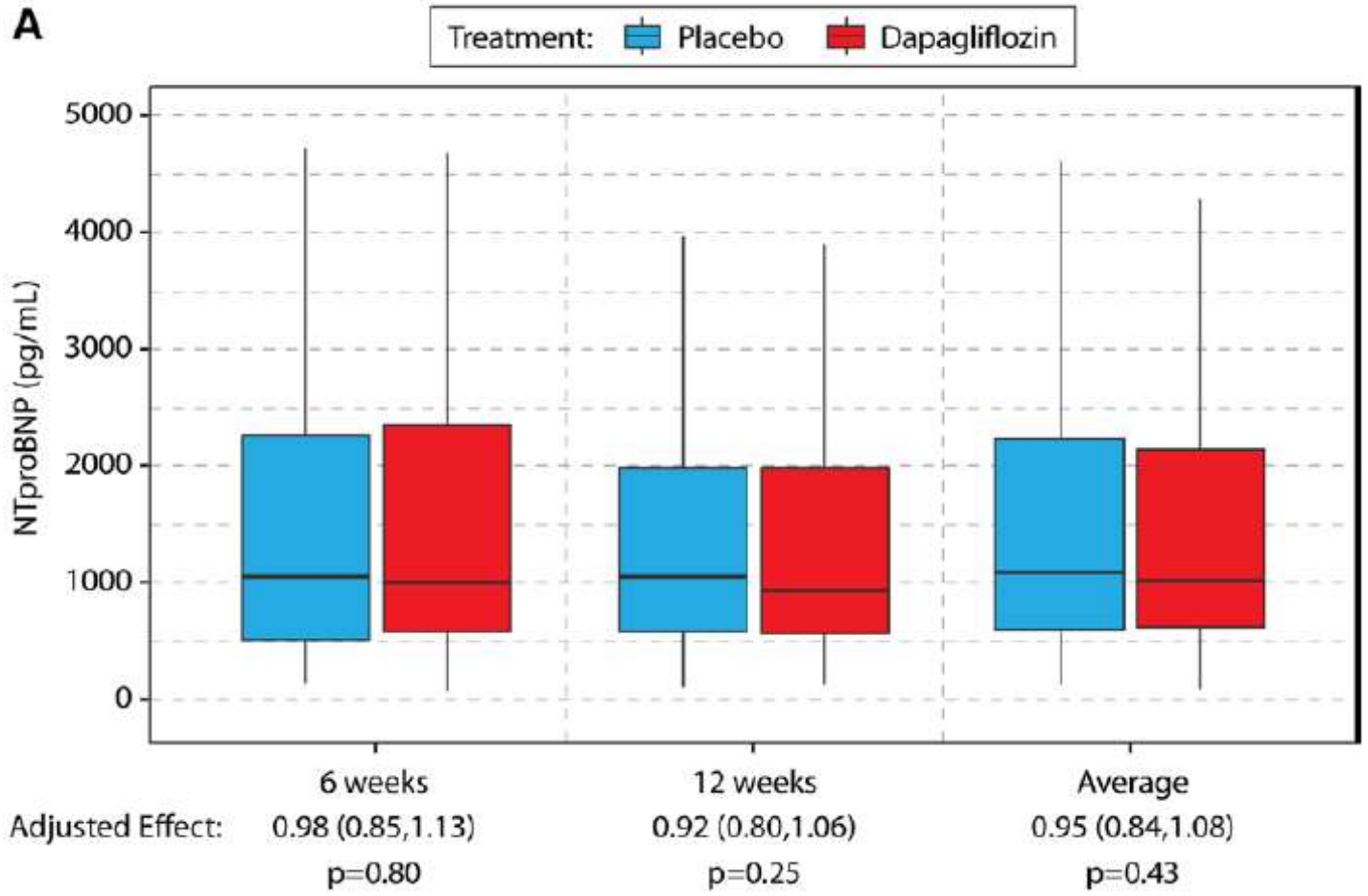
-Clase II 66% y clase III 30.6%

-Tratamiento: 97% BB, 61% AMC, 59% IECA/ARA II, 33% ARNI,62% desfibriladores, 86% diurético de asa

-FEVI media 26%

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial



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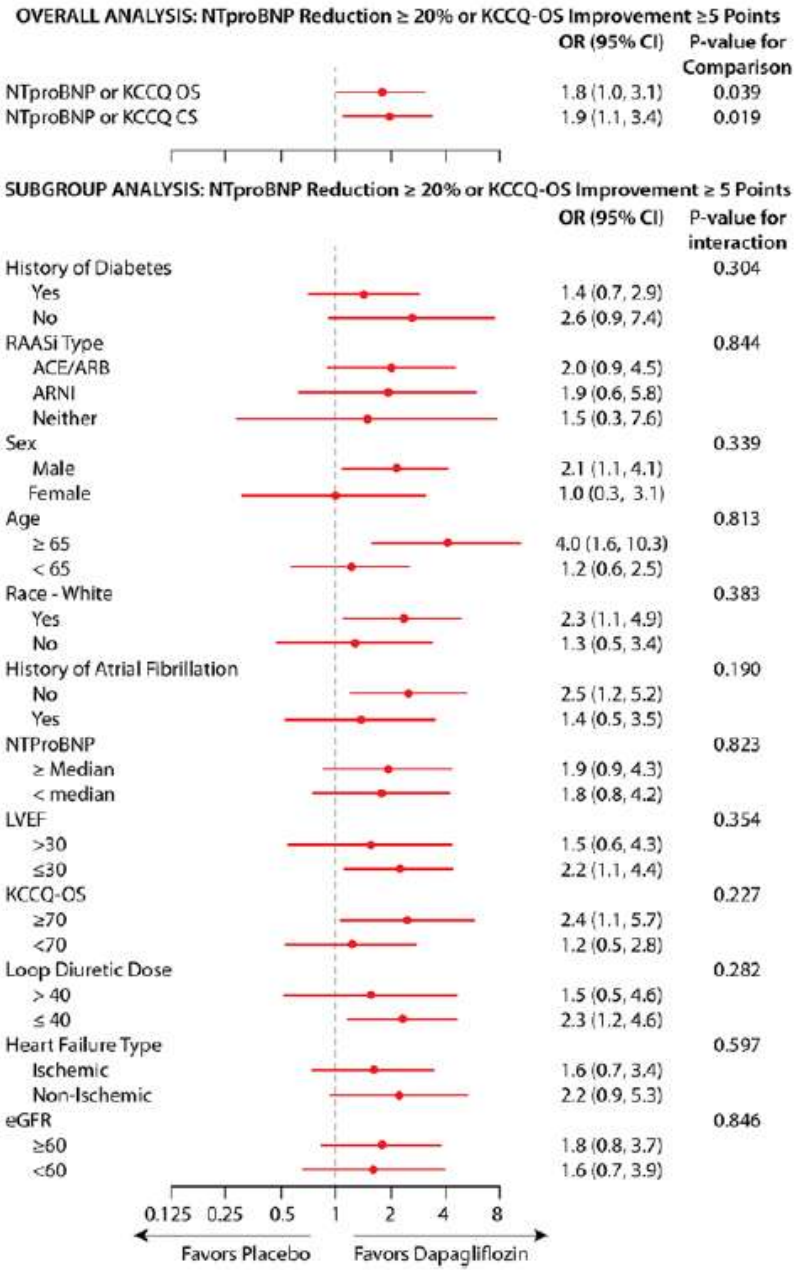

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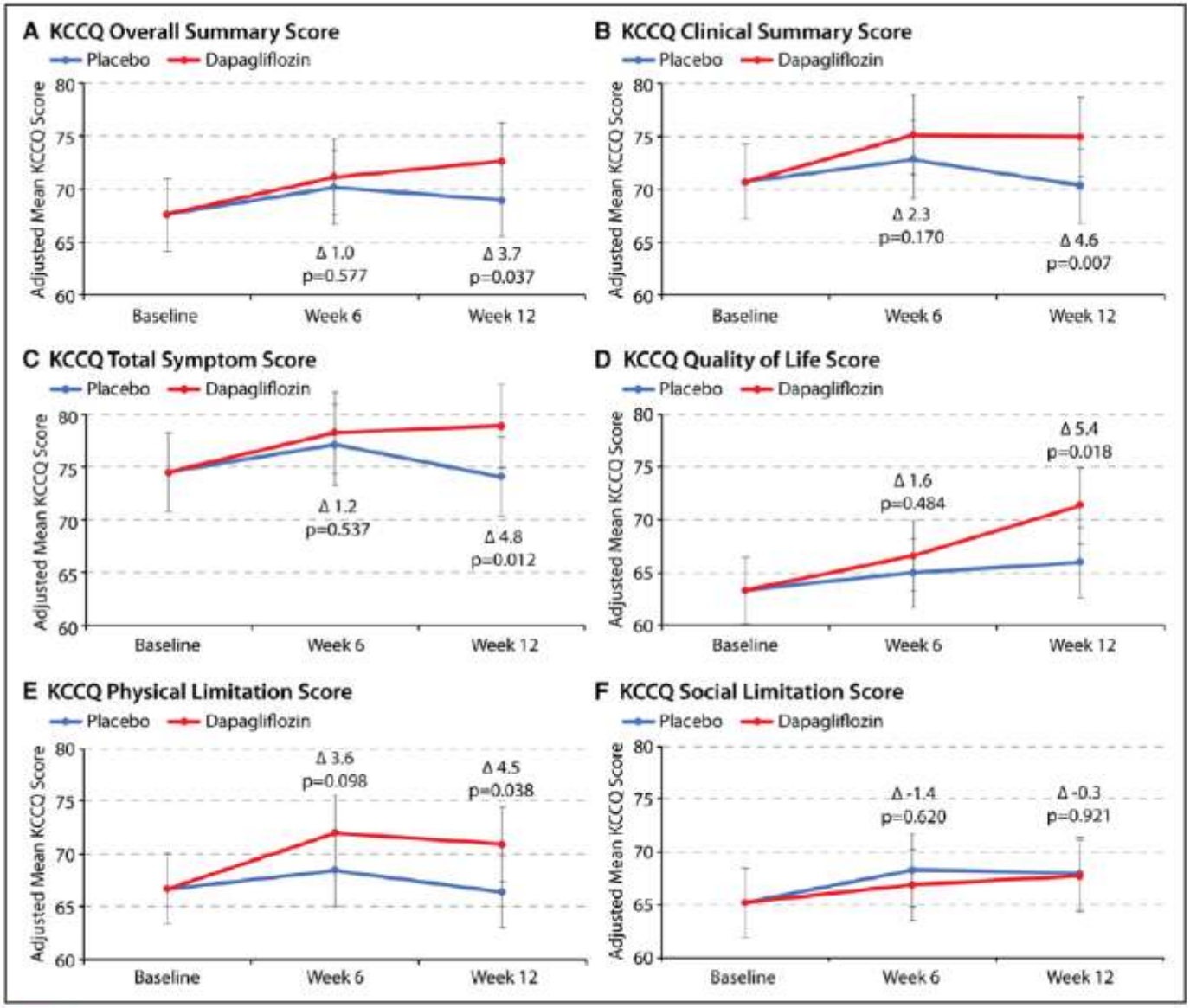

Figure 3. Effects of dapagliflozin versus placebo on KCCQ (overall, and within specific domains).
A, Kansas City Cardiomyopathy Questionnaire (KCCQ) overall summary score (KCCQ-OS) over 12 weeks. **B**, KCCQ clinical summary score (KCCQ-CS) over 12 weeks. **C**, KCCQ total symptom score over 12 weeks. **D**, KCCQ quality of life score over 12 weeks, **E**, KCCQ physical limitation score over 12 weeks, **F**, KCCQ social limitation score over 12 weeks.

Table 4. Safety Analyses

	Dapagliflozin (n=131)	Placebo (n=132)
All-cause death	1 (0.8%)	1 (0.8%)
Cardiovascular death	1 (0.8%)	1 (0.8%)
Nonfatal MI	0 (0.0%)	4 (3.0%)
Stroke	0 (0.0%)	1 (0.8%)
Acute kidney injury	1 (0.8%)	1 (0.8%)
Diabetic ketoacidosis	0 (0.0%)	0 (0.0%)
Volume depletion event	12 (9.2%)	7 (5.3%)
Severe hypoglycemic event	1 (0.8%)	1 (0.8%)
Lower limb amputation	0 (0.0%)	0 (0.0%)
Drug adverse event	3 (2.3%)	3 (2.3%)
AE leading to study drug discontinuation	11 (8.4%)	12 (9.1%)

ORIGINAL RESEARCH ARTICLE

Dapagliflozin Effects on Biomarkers, Symptoms, and Functional Status in Patients With Heart Failure With Reduced Ejection Fraction

The DEFINE-HF Trial

Conclusion

Among patients with HFrEF with and without T2D receiving optimal guideline directed medical therapy, the addition of dapagliflozin for 12 weeks did not affect the mean NT-proBNP but significantly increased the proportion of patients experiencing clinically meaningful improvements in HF disease-specific health status and natriuretic peptides.

ADVANCES IN HEART FAILURE

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis

- Enfermedad causada por fibrillas anormales derivadas de transtirretina, proteína producida fundamentalmente en el hígado, que se deposita en tejidos y órganos.
- Dos variantes: 1. ATTR-m(mutante):Transmisión autosómica dominante con penetrancia variable que aumenta con la edad.

  2.ATTR-wt(salvaje)

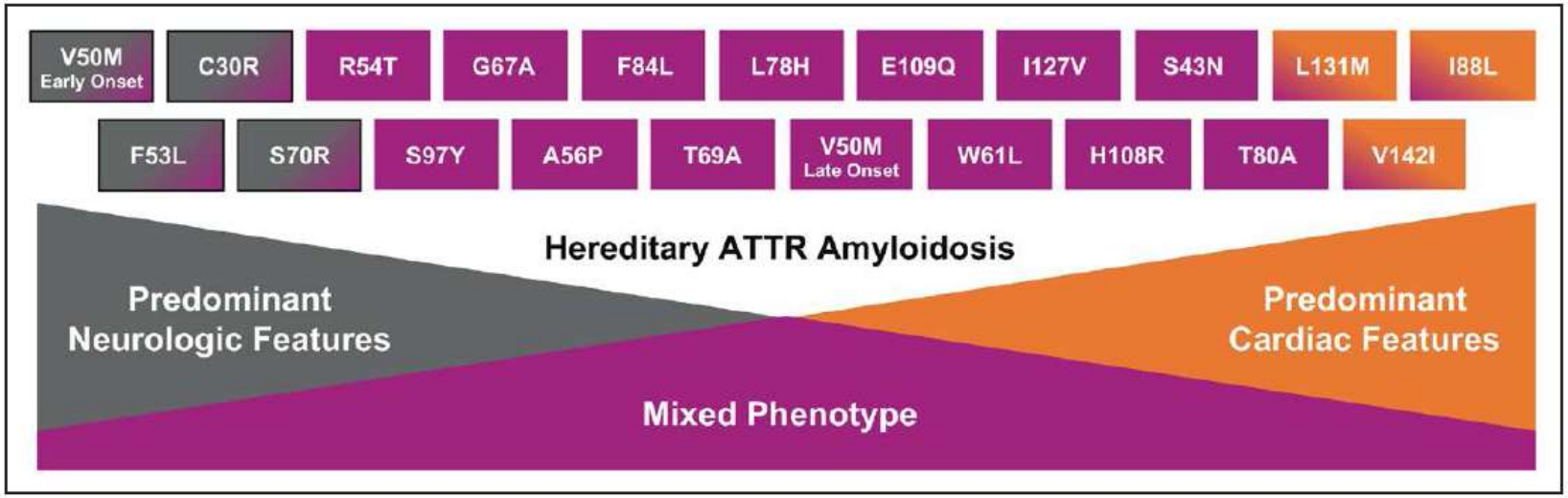

Figure 1. Genotype–phenotype correlations in mutant transthyretin amyloidosis.

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Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis

- Verdadera prevalencia? 25% en 80 años en autopsias, 16% en cirugía de reemplazo valvular, 13% en IC con FEVI preservada, 12.5% en miocardiopatía hipertrófica y 7-8% en sd tunel carpiano.

- Recomendaciones de expertos en USA con la colaboración de empresas que investigan en amiloidosis(GSK, Ionis, Pfizer y Alnylam)

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis

SIGNOS Y SINTOMAS

Table 1. Diagnostic Clues to ATTR-CM

History/examination clues
Evidence of right-sided heart failure (eg, hepatomegaly, ascites, and lower extremity edema)
HFpEF, particularly in men
Intolerance to ACE inhibitors or beta blockers
Bilateral carpal tunnel syndrome
Lumbar spinal stenosis
Biceps tendon rupture
Unexplained peripheral neuropathy (eg, loss of warm/cold discrimination), particularly if associated with autonomic dysfunction (eg, postural hypotension, alternating bowel pattern)
Unexplained atrial arrhythmias or conduction system disease/need for a pacemaker

ADVANCES IN HEART FAILURE

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis

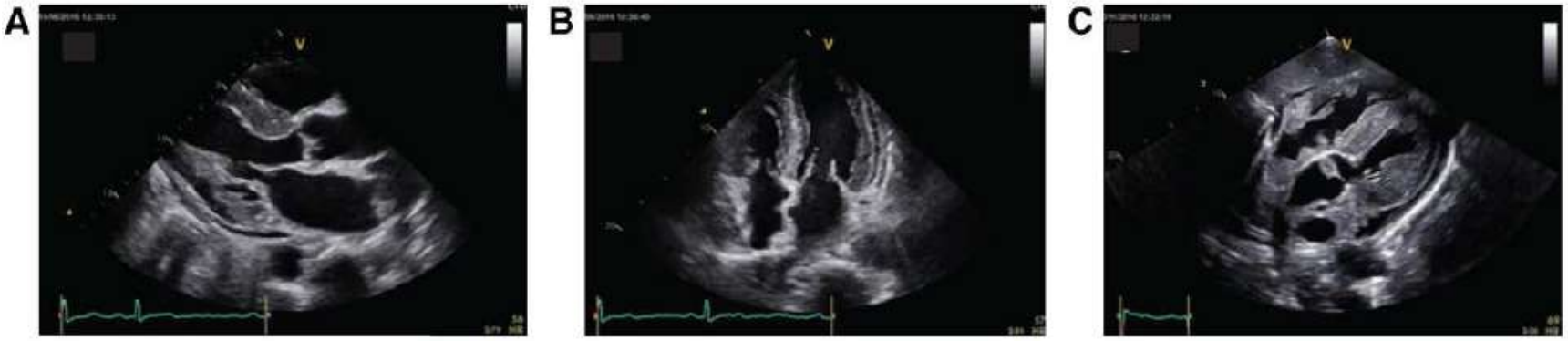
BIOMARCADORES

- Niveles elevadamente desproporcionados deBNP.
- Elevación de troponina en hipertrofia ventricular.
- Proteína de unión a retinol circulante 4

ECG E IMÁGENES CARDIACAS

- ECG: Bajo voltaje, a pesar de hipertrofia. Patrón de onda Q de pseudoinfarto.
- ETT: disfunción diastólica, engrosamiento de pared de VI, tamaño pequeño de cavidad de VI, agrandamiento biauricular, válvulas engrosadas, presión sistólica de VD elevada, refringencia del miocardio, patrón restritivo.
- RM: realce tardío difuso con gadolinio subepicárdico o transmural.
- Gammagrafía miocárdica. Alteración temprana.

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis



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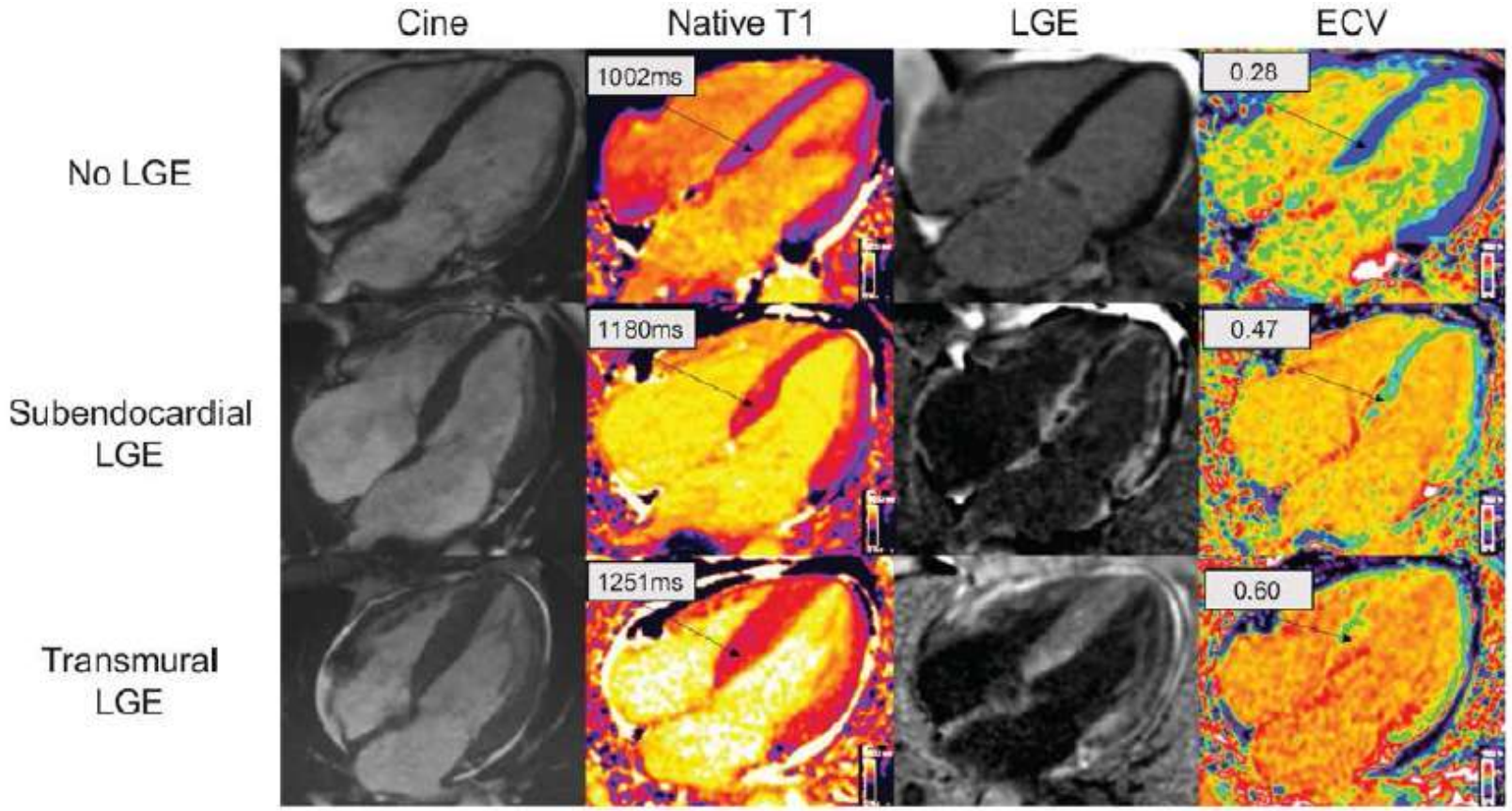

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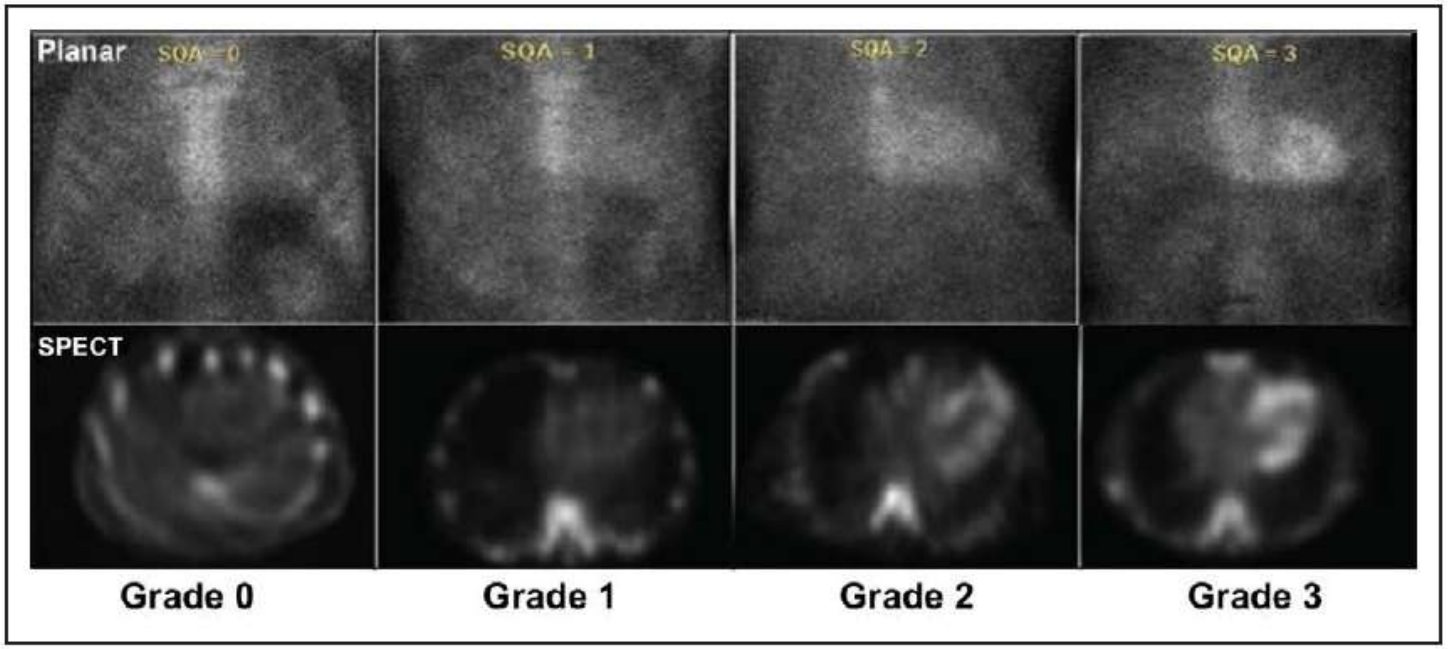
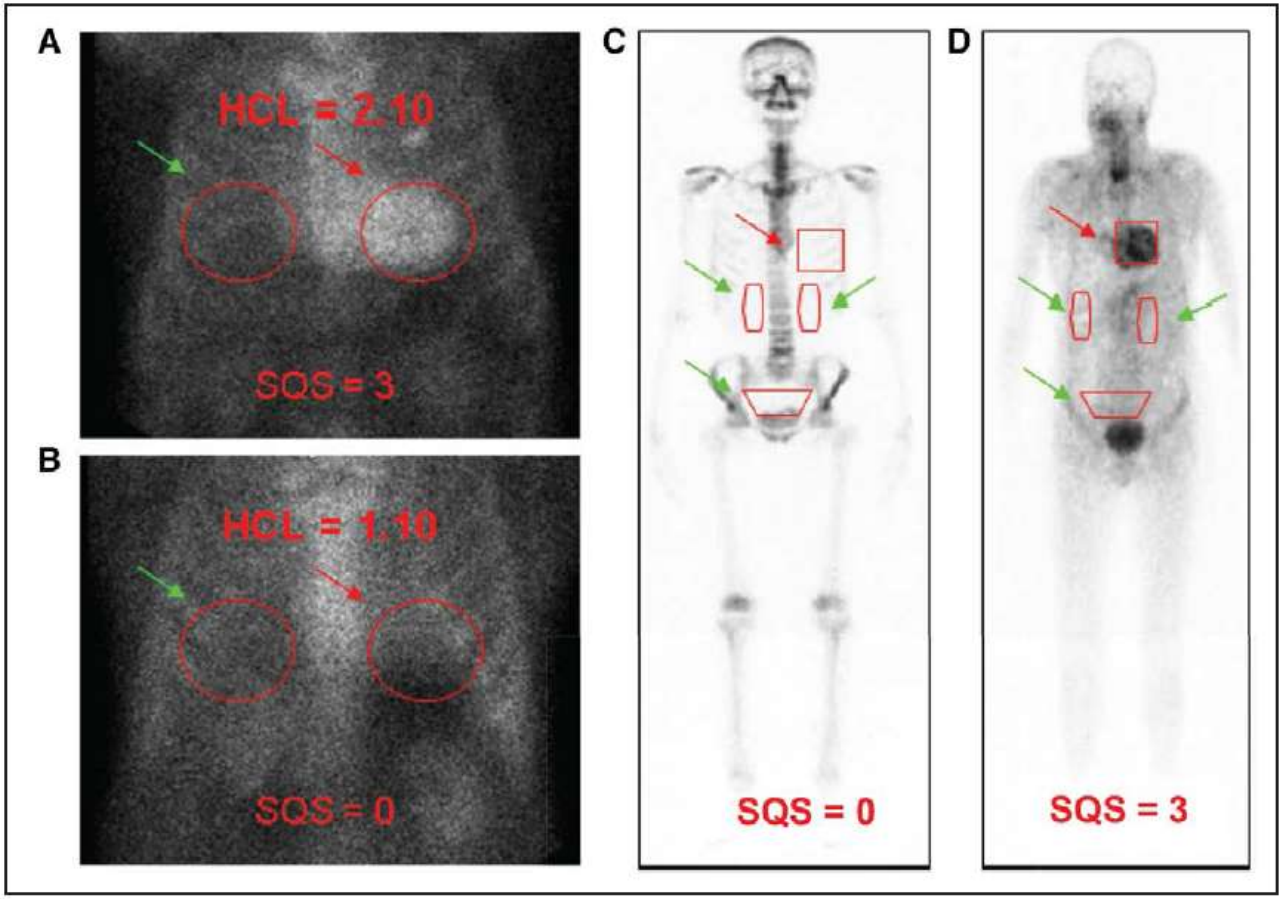


Figure 4. ^{99m}Technetium imaging procedures for cardiac amyloidosis.

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis



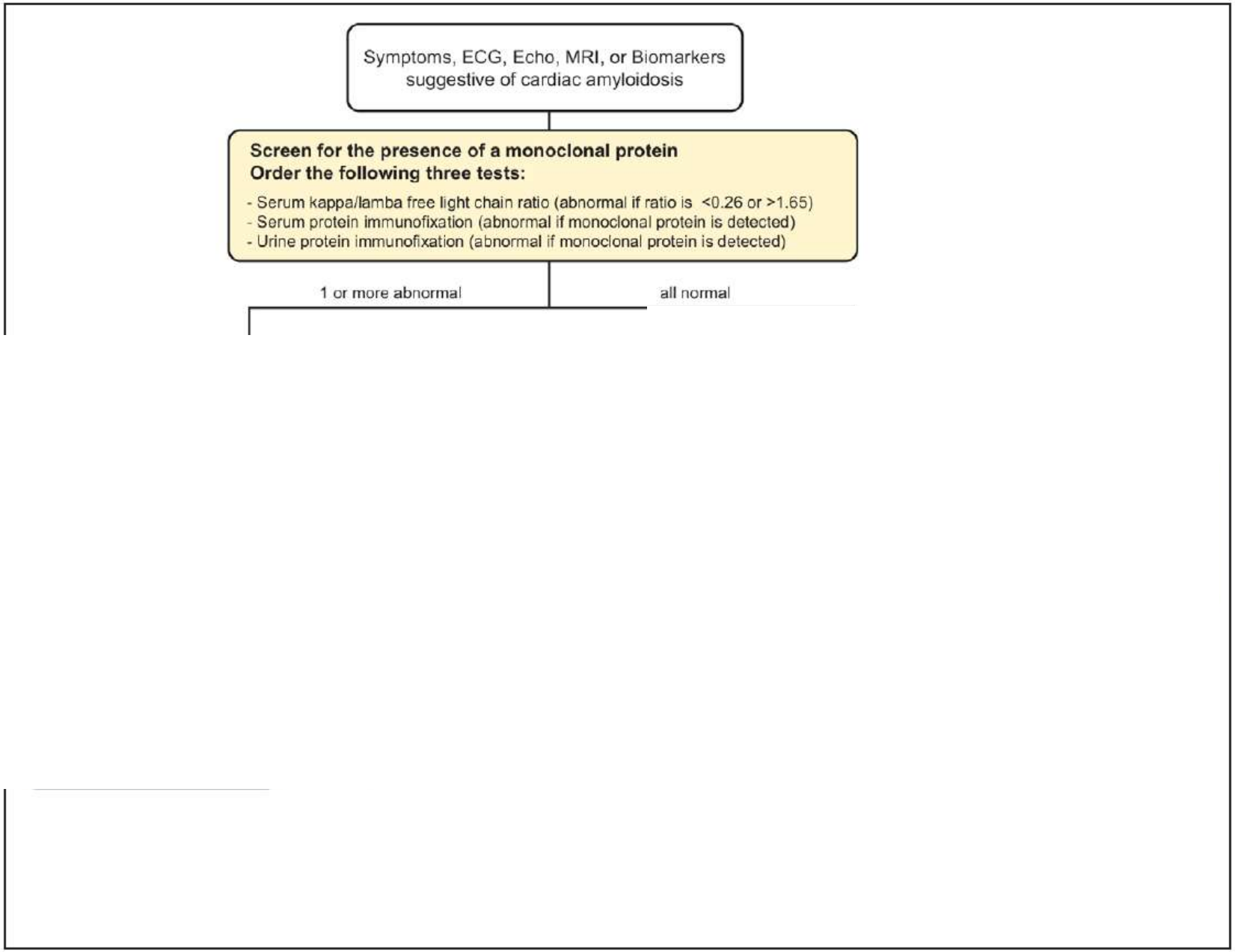
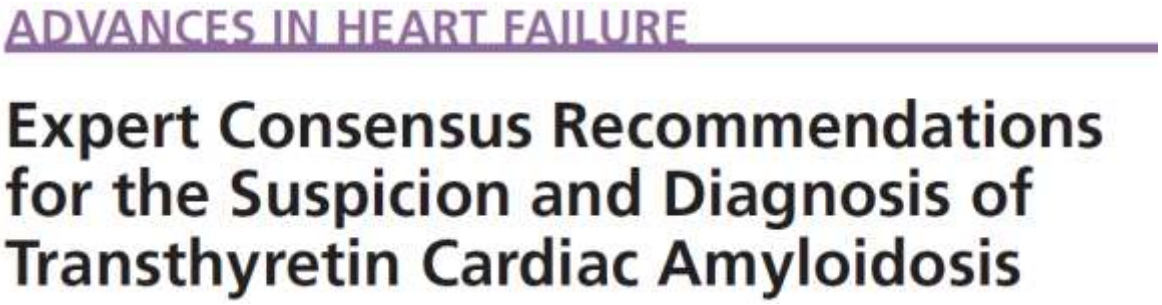


Figure 6. Diagnostic algorithm for patients with suspected cardiac amyloidosis.



ESTRATIFICACION PRONOSTICA

BNP y TROPONINAS evalúan el riesgo y la respuesta al tratamiento.

Diferencias entre amiloidosis ATTR y AL

ETAPAS: 1. NP-proBNP< 3000 pg/ml y tpT < 0.05ng/ml

2. NP-proBNP> 3000 pg/ml o tpT > 0.05ng/ml

3. NP-proBNP>3000 pg/ml y tpT > 0.05ng/ml

Expert Consensus Recommendations for the Suspicion and Diagnosis of Transthyretin Cardiac Amyloidosis

CONCLUSIONS

ATTR amyloidosis is a progressive disease associated with increased morbidity and mortality and occurs in inherited (ATTRm or hereditary ATTR) or acquired (ATTRwt) forms. Disease-related cardiac dysfunction in patients with ATTR amyloidosis is associated with particularly poor outcomes and is a manifestation of many of the genetic variants and the wild-type form of ATTR amyloidosis.

Diagnosis of ATTR-CM is often missed or mistaken as hypertrophic cardiomyopathy or heart failure with preserved ejection fraction of unknown cause. Although considered a rare disease, the true prevalence of ATTR-CM is unclear and is likely higher than appreciated. Physicians should consider systemic signs and symptoms along with evidence from biomarkers and imaging to build suspicion for ATTR-CM. To facilitate early diagnosis of ATTR-CM, evaluation of myocardial uptake on bone scintigraphy should be considered in patients with HF, unexplained neuropathy, family history of amyloidosis, or unexplained increased LV wall thickness. Appropriate evidence on echocardiography or cardiac MRI—combined with no light chain clone, grade ≥2 myocardial uptake of ^{99m}Tc-pyrophosphate, diphosphono-1,2-propanodicarboxylic acid, and hydroxymethylene diphosphonate—is diagnostic of ATTR-CM, in which case endomyocardial biopsy is unnecessary. Genetic testing should be performed to differentiate ATTRm from ATTRwt causes of ATTR-CM.

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EL PAÍS ECONOMÍA

CincoDías

Compañías

MEDICAMENTOS •

Críticas a las pastillas para el corazón de Pfizer que cuestan 200.000 euros al año

- Los propios médicos que ayudaron a su desarrollo cuestionan el alto precio fijado

EMMA COURT (BLOOMBERG)

Una caja de pastillas de Vyndaqel, nombre comercial del tafamidis.

Ir a comentarios

20 NOV 2019 - 11:31 CET

Una caja de pastillas de Vyndaqel, nombre comercial del tafamidis.

Ir a comentarios

20 NOV 2019 - 11:31 CET

Con un sombrero tricornio de la era revolucionaria, el médico Mathew Maurer se puso en pie frente a una audiencia de colegas cardiólogos en Filadelfia para **denunciar el precio de un nuevo medicamento** con capacidad para ayudar a muchos de sus pacientes con insuficiencia cardíaca.

El medicamento, tafamidis, de Pfizer, cuesta **651 dólares al día,** dijo Maurer, lo mismo que el presupuesto para alimentación de un paciente durante un mes. Los medicamentos no funcionan si la gente no puede tomarlos, dijo, y el precio de 225.000 dólares (algo más de 200.000 euros) al año de la compañía farmacéutica está muy fuera de los límites.

Maurer no es un crítico cualquiera. Como profesor del Centro Médico Irving de la Universidad de Columbia, **trabajó en estrecha colaboración con Pfizer para desarrollar el innovador medicamento.** Fue el autor principal de un estudio científico fundamental financiado por la compañía con el que se logró la aprobación de tafamidis a principios de este año.

Bloomberg habló con **Maurer y otros tres médicos involucrados en los ensayos**

TACIT (High Sensitivity Troponin T Rule Out Acute Cardiac Insufficiency Trial)

An Observational Study to Identify Acute Heart Failure Patients at Low Risk for Rehospitalization or Mortality

- **ESTUDIO PROSPECTIVO OBSERVACIONAL, MULTICENTRICO EN PACIENTES CON INSUFICIENCIA CARDIACA AGUDA DE BAJO RIEGO ATENDIDOS EN URGENCIAS PARA DETERMINAR SI LA TROPONINA T DE ALTA SENSIBILIDAD IDENTIFICA PACIENTES DE BAJO RIESGO DE REHOSPITALIZACION Y MORTALIDAD.**

TACIT (High Sensitivity Troponin T Rule Out Acute Cardiac Insufficiency Trial)

An Observational Study to Identify Acute Heart Failure Patients at Low Risk for Rehospitalization or Mortality

- Se determinó la Troponina T basalmente y a las 3 horas.
- Seguimiento telefónico a los 30 y 90 días.
- Objetivo primario: compuesto de mortalidad por todas las causas, rehospitalización y visitas al servicio deUrgencias a los 90 días.
- Objetivo secundario: mortalidad por todas las causas a los 30 días y a los 90 días.
- 570 pacientes
- Edad media 62 años, 60% hombres, 57% raza negra
- Media de TpT 26.4 ng/l.

TACIT (High Sensitivity Troponin T Rule Out Acute Cardiac Insufficiency Trial)

An Observational Study to Identify Acute Heart Failure Patients at Low Risk for Rehospitalization or Mortality

RESULTADOS:

99(21%) eventos del objetivo compuesto a los 30 días

13 (2.7%) muerte a los 30 días

25 (8.2%) muerte a los 90 días

La seriación deTpT con valores por debajo del percentil 99 no se asoció con menor riesgo en el objetivo compuesto a 90 días .

No hubo ninguna muerte a los 30 días y solo 1 a los 90 días en los que tenían la TpT por debajo del percentil 99.

CONCLUSION: los niveles de TpT seriados no identificaron a los pacientes con bajo riesgo para el resultado primario compuesto de rehospitalización, visitas a Urgencias y mortalidad a los 90 días.