# ACC DEFINE LA INSUFICIENCIA CARDÍACA CON FRACCIÓN DE EYECCIÓN RECUPERADA

**La remodelación inversa del ventrículo izquierdo (VI) y la recuperación de su función se asocian con mejores resultados clínicos en pacientes con insuficiencia cardíaca con fracción de eyección reducida (ERHF).**

**Un creciente cuerpo de evidencia científica sugiere que incluso entre los pacientes que experimentan una normalización completa de la FEVI, una proporción significativa desarrollará disfunción del VI recurrente y eventos de IC, aumentando el interés en entender cómo manejar a los pacientes con IC y FE recuperada (ICFErec).**

**Debido a la falta de una definición estándar para ICFErec y la escasez de datos clínicos sobre la historia natural de los pacientes portadores, no existen pautas actuales sobre cómo se debe seguir y tratar a estos pacientes.**

**En este sentido, un panel de expertos de la ACC revisó la biología del remodelado inverso del VI y el curso clínico natural de los pacientes con ICFErec, estableciendo pautas**

**para definir, diagnosticar y tratar a los pacientes con esta nueva entidad clínica.**

**Este documento de consenso definió ICFErec, de acuerdo con la literatura, como (1) FEVI inicial <40%; (2) mejoría absoluta en la FEVI ≥ 10%; y (3) FEVI> 40%, en una segunda medición.**

**Las recomendaciones actuales para el tratamiento y uso de dispositivos para pacientes que cumplen con la definición de ICFErec deben mantenerse indefinidamente hasta que se comprendan mejor la biología y la epidemiología clínica de ICFErec.**

**Los pacientes con ICFErec deben ser controlados a intervalos estrechos debido al alto riesgo de recurrencia de la IC.**

Português

ACC define insuficiência cardíaca com fração de ejeção recuperada

O remodelamento reverso do ventrículo esquerdo (VE) e a recuperação da sua função, estão associados com melhora nos desfechos clínicos em pacientes com insuficiência cardíaca com fração de ejeção reduzida (ICFEr).

Um crescente corpo de evidências científicas sugere que mesmo entre os pacientes que experimentam uma normalização completa da FEVE, uma proporção significativa desenvolverá disfunção recorrente do VE e eventos de IC, aumentando o interesse em se entender como manejar os pacientes com IC e FE recuperada (ICFErec).

Devido à falta de uma definição padrão para a ICFErec e a escassez de dados clínicos em relação à história natural dos pacientes portadores, não existem diretrizes atuais de como esses pacientes devem ser acompanhados e tratados.

Nesse sentido, um painel de especialistas do ACC revisou a biologia do remodelamento reverso do VE e a evolução clínica natural dos pacientes com ICFErec, estabelecendo as diretrizes para definir, diagnosticar e tratar os pacientes com essa nova entidade clínica.

Esse documento de consenso definiu a ICFErec, em concordância com a literatura, como (1) FEVE inicial <40%; (2) melhora absoluta da FEVE ≥10%; e (3) FEVE >40%, em uma segunda medição.

As recomendações atuais de tratamento e o uso de dispositivos para pacientes que se enquadram na definição ICFErec devem ser mantidas indefinidamente, até que a biologia e a epidemiologia clínica da ICFErec sejam melhor compreendidas.

Os pacientes com ICFErec devem ser acompanhados em intervalos próximos devido ao alto risco da recorrência da IC.

English

Jane E Wilcox 1, James C Fang 2, Kenneth B Margulies 3, Douglas L Mann 4. Heart Failure With Recovered Left Ventricular Ejection Fraction: JACC Scientific Expert Panel. J Am Coll Cardiol. 2020 Aug 11;76(6):719-734. doi: 10.1016/j.jacc.2020.05.075.

Affiliations

1. Division of Cardiovascular Medicine, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois. Electronic address: jane-wilcox@northwestern.edu
2. Division of Cardiology, Department of Medicine, University of Utah, Salt Lake City, Utah.
3. Translational Research Center, Department of Medicine, University of Pennsylvania Pearlman School of Medicine, Philadelphia, Pennsylvania.
4. Cardiovascular Division, Department of Medicine, Washington University School of Medicine, St. Louis, Missouri. Electronic address: dmann@wustl.edu.

Abstract

Reverse left ventricular (LV) remodeling and recovery of LV function are associated with improved clinical outcomes in patients with heart failure with reduced ejection fraction. A growing body of evidence suggests that even among patients who experience a complete normalization of LV ejection fraction, a significant proportion will develop recurrent LV dysfunction accompanied by recurrent heart failure events. This has led to intense interest in understanding how to manage patients with heart failure with recovered ejection fraction (HFrecEF). Because of the lack of a standard definition for HFrecEF, and the paucity of clinical data with respect to the natural history of HFrecEF patients, there are no current guidelines on how these patients should be followed up and managed. Accordingly, this JACC Scientific Expert Panel reviews the biology of reverse LV remodeling and the clinical course of patients with HFrecEF, as well as provides guidelines for defining, diagnosing, and managing patients with HFrecEF.

Keywords: heart failure with recovered ejection fraction; myocardial recovery.

HIGHLIGHTS

This consensus document was created because there are no guidelines for the management of patients with HFrecEF.

A working definition of HFrecEF that is consistent with the majority of studies in the literature includes the following:

1) documentation of a decreased LVEF 40%.

Guideline-directed medical and device therapy for patients with HFrecEF should be continued indefinitely until the biology and clinical epidemiology of HFrecEF is better understood.

HFrecEF patients should have close clinical follow-up due to the high risk of heart failure relapse.

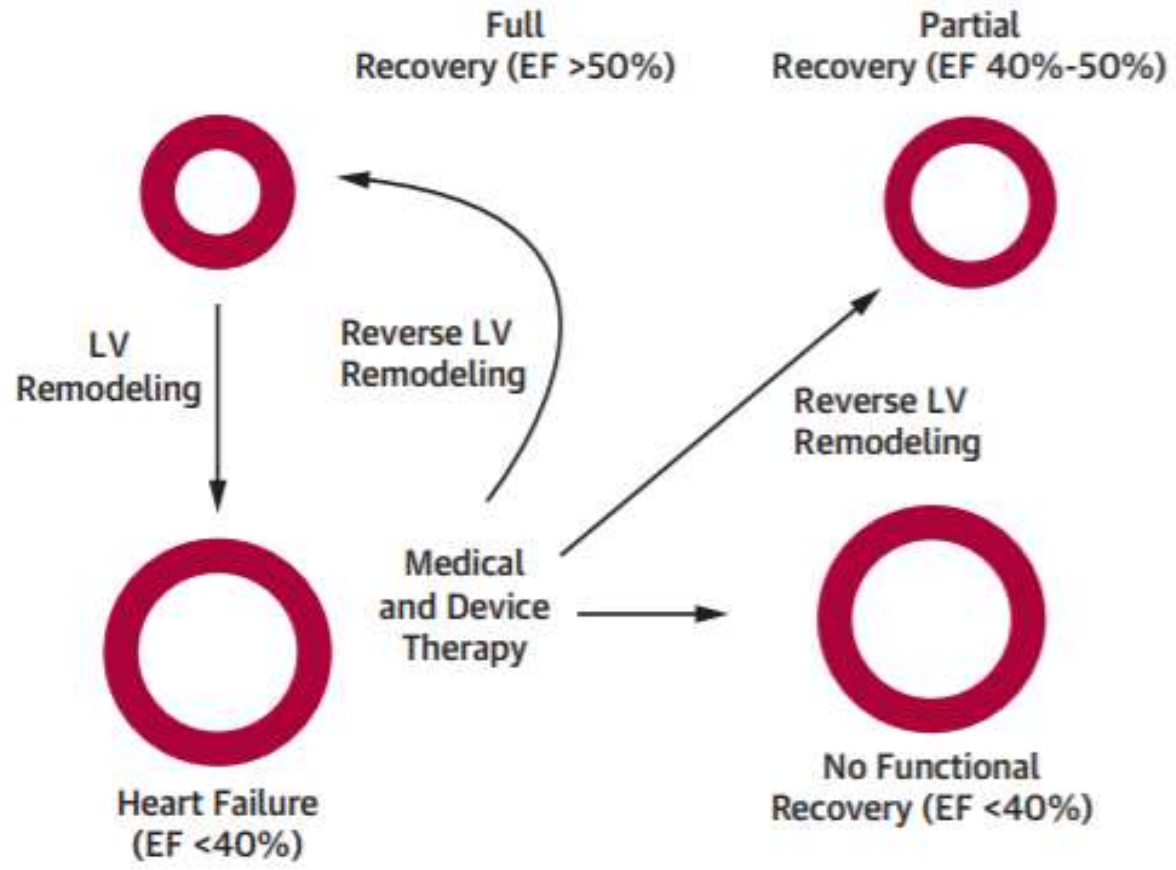
Changes in LVEF With GDMT in Patients With Heart Failure With a Reduced EF

**TABLE 1 Cellular and Molecular Determinants of Recovery of LV Function**

| | Beta-Blocker | ACE Inhibitor | ARB | Aldosterone Antagonists | LVAD | CRT | CSD |
|---|---|---|---|---|---|---|---|
| Myocyte defects | | | | | | | |
| Hypertrophy | Decreased | Decreased | Decreased | Decreased | Decreased | Decreased | Decreased |
| Fetal gene expression | Decreased | Decreased | Decreased | ND | Decreased | Decreased | Decreased |
| Myocytolysis | Decreased | ND | ND | ND | Decreased | ND | ND |
| Beta-adrenergic desensitization | Decreased | Decreased | Decreased | ND | Decreased | Decreased | Decreased |
| EC coupling | Increased | Increased | Increased | ND | Increased | Increased | Increased |
| Cytoskeletal proteins | ND | ND | ND | Increased | Increased | ND | Increased |
| Myocardial defects | | | | | | | |
| Myocyte apoptosis | Decreased | Decreased | Decreased | ND | Decreased | Decreased | Decreased |
| MMP activation | Decreased | Decreased | Decreased | Decreased | Decreased | Decreased | Decreased |
| Fibrosis | Decreased | Decreased | Decreased | Decreased | Increased* | Decreased | Decreased |
| Angiogenesis | Increased | Increased | Increased | Increased | Decreased | Increased | Increased |
| LV dilation | Decreased | Stabilized | Stabilized | Stabilized | Decreased | Decreased | Decreased |

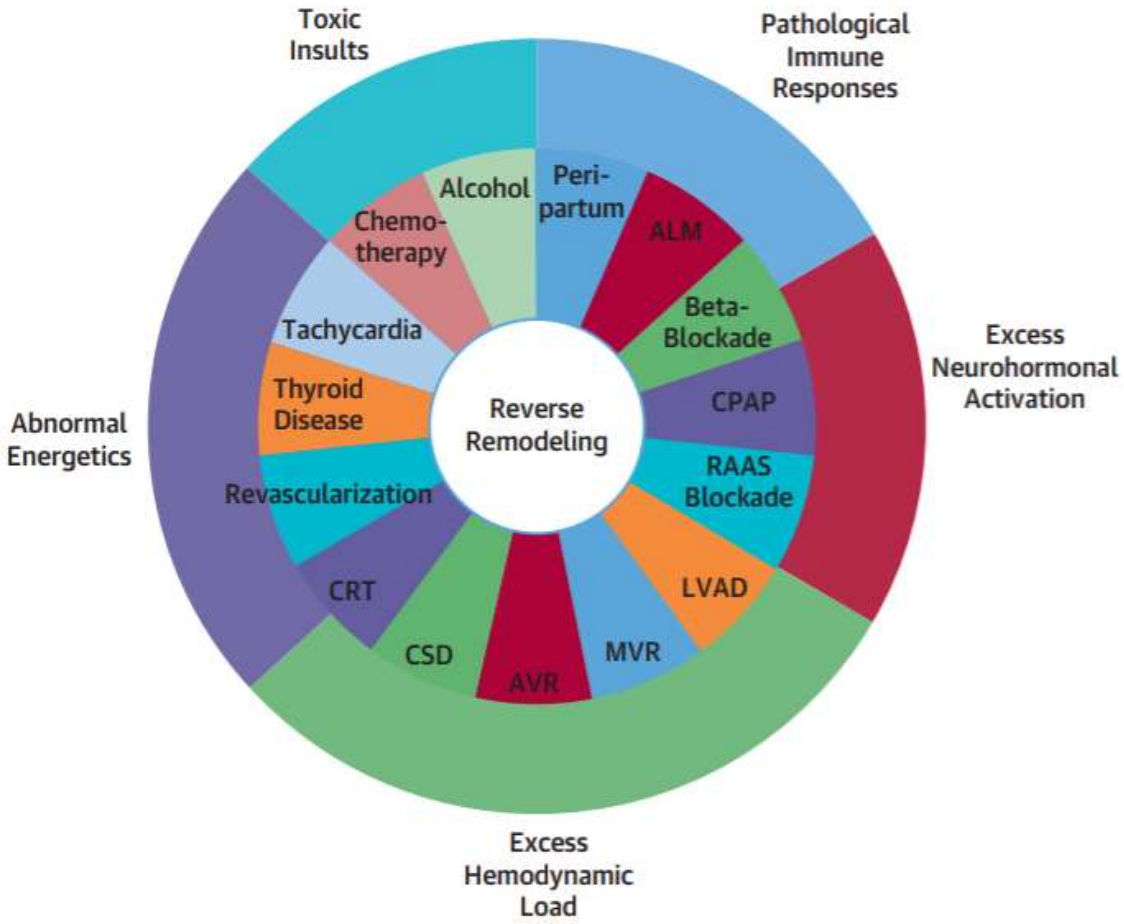
Reproduced with permission from Mann et al. (17)

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; CRT = cardiac resynchronization therapy; CSD = cardiac support device; EC = excitation-contraction; LV = left ventricular; LVAD = left ventricular assist device; MMP = matrix metalloproteinase; ND = not done.




**Changes in LVEF With GDMT in Patients With Heart Failure With a Reduced EF**
**Patients with heart failure with recovered ejection fraction (HFrecEF) treated with guideline-directed medical and device therapies (GDMT) may have a complete recovery of left ventricular ejection fraction (LVEF) >50%, partial recovery of LVEF (EF 40% to 50%), or no functional recovery of LVEF (EF <40%).**

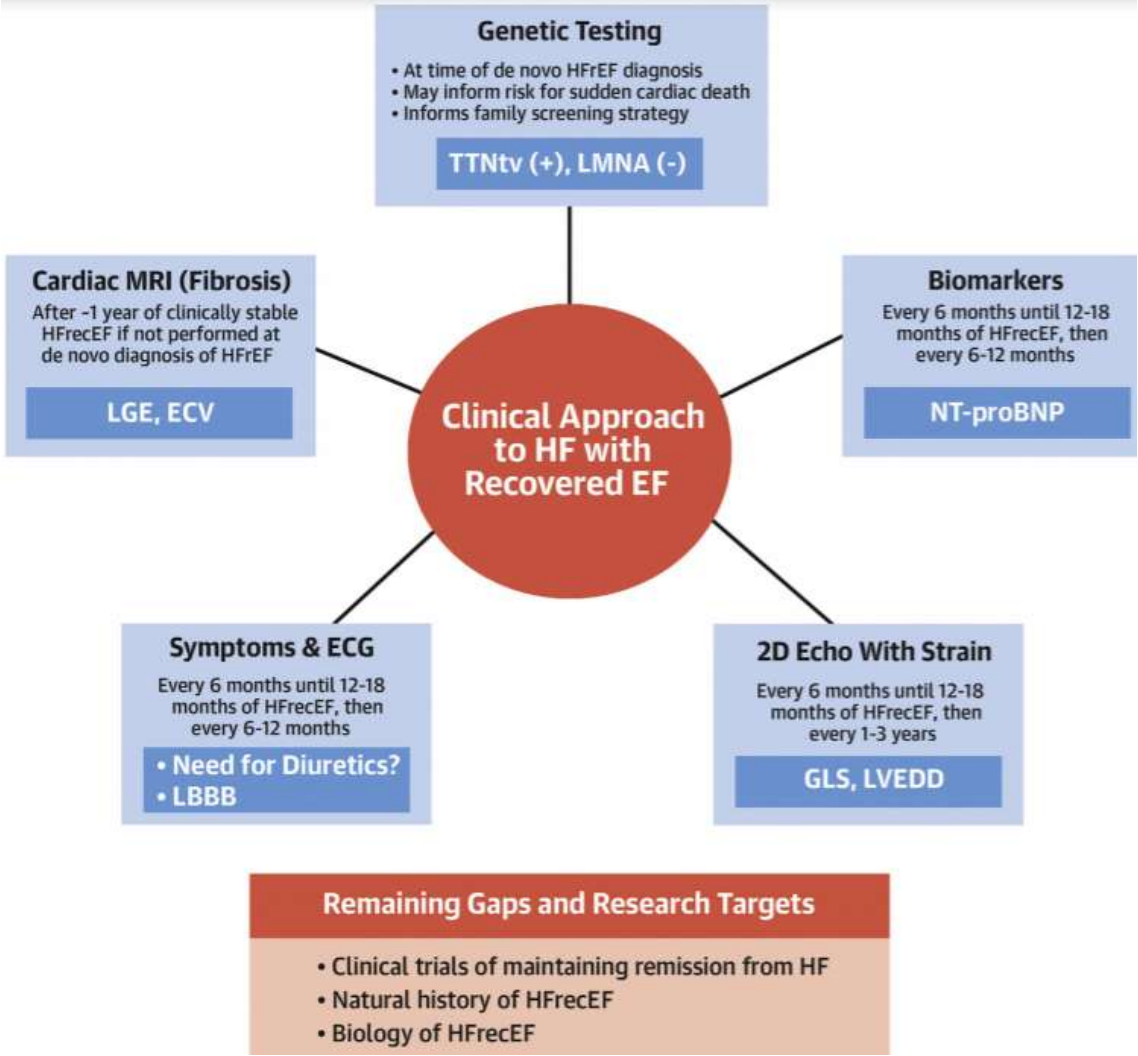
**Recovery of LVEF in Clinical Settings**




**The segments of the outmost ring highlight pathophysiological processes implicated by reverse left ventricular remodeling, in particular clinical settings that comprise the middle ring. Reproduced with permission from Hellowell et al. (1). ALM ¼ acute lymphocytic myocarditis; AVR ¼ aortic valve replacement; CPAP ¼ continuous positive airway pressure; CRT ¼ cardiac resynchronization therapy; CSD ¼ cardiac support device; LVAD ¼ left ventricular assist device; LVEF ¼ left ventricular ejection fraction; MVR ¼ mitral valve repair/replacement; RAAS ¼ reninangiotensin-aldosterone system.**

1. **Hellawell JL, Margulies KB. Myocardial reverse remodeling. Cardiovasc Ther 2012; 20:172–81**.

**Clinical Assessment of Patients With Recovered Left Ventricular Ejection Fraction**




**Clinical Assessment of Patients With Recovered LVEF**

**Clinical assessment of symptoms and ECG can identify patients with HF with recovered EF (HFrecEF) at higher risk of relapse. The need for persistent diuretics and LBBB represents higher risk subgroups. Absence of late gadolinium enhancement (LGE) on cardiac magnetic resonance imaging is a strong predictor of recovery or remodeling and is associated with improved prognosis. Elevated extracellular volume (ECV) values (suggested of edema or fibrosis) can also improve diagnostic understanding of specific cardiomyopathies. Higher absolute global longitudinal strain (GLS) (e.g., >16%) is associated with stability of LVEF over short-term follow-up and higher GLS even among dilated hearts is associated with HFrecEF status. Prognosis in genetic dilated cardiomyopathy varies, with truncating variants of the titin gene (TTNtv) more likely to respond favorably to guideline directed medical therapy and achieve HFrecEF status, and LMNA mutations less likely to respond and confer high risk for SCD despite HFrecEF status. Greater reductions in N-terminal pro–B-type natriuretic peptide (NT-proBNP) with neurohormonal heart failure (HF) therapy is associated with greater improvements in LV structure and function, as well as improved clinical outcomes. A rise in NT-proBNP in HFrecEF patients may precede HF relapse. Gaps remain with regard to development of inception cohorts to better understand the natural**

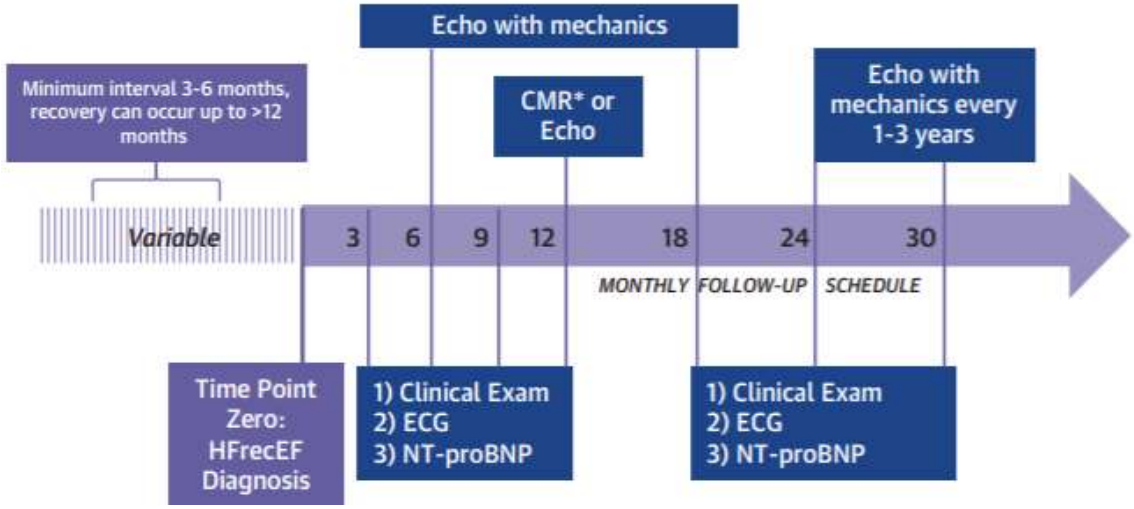
**history of HFrecEF, and additional clinical trials are needed to define which elements of clinical care are important for maintaining clinical remission, as well as basic studies to better define the biology of HFrecEF in order to develop new therapeutic targets. Echo ¼ echocardiography; HFrEF ¼ HF with reduced ejection fraction; LVEDD ¼ LV end diastolic dimension; MRI ¼ magnetic resonance imaging**

Recommended Interval Follow-Up for HFrecEF

| Interval Follow-Up Time Period (After Meeting the HFrecEF Definition) | Clinical Examination and ECG | Holter Monitoring (24 h) | NT-pro BNP | Echocardiography With Mechanics (Strain) | CMR |
|---|---|---|---|---|---|
| Every 6 months (until 12–18 months of HFrecEF). | X | | X | X | |
| After ~1 yr of "clinically stable" HFrecEF | | | | | X* |
| Every 6–12 months (at minimum). | X | | X | | |
| Optimal interval of echocardiography/imaging is unknown. It is reasonable clinical practice to assess durability every 1–3 yrs after stable recovery depending on etiology. | | | | X | |
| Every 1–2 yrs for certain genetic cardiomyopathies at risk of atrial dysrhythmias (e.g., *TTN*). | | X | | | |

*Consider CMR if one was not performed at de novo diagnosis of HFrEF.
CMR = cardiac magnetic resonance; ECG = electrocardiogram; HFrecEF = heart failure with recovered ejection fraction; other abbreviations as in Table 2.

Sample Follow-Up and Clinical Testing Schedule for an HFrecEF Patient Deemed High-Risk for Recurrence of HF




**Patients with heart failure with recovered ejection fraction (HFrecEF) at high risk of relapse (persistent left bundle branch block, genetic dilated cardiomyopathy, higher biomarker profiles, or more comorbidities) require close clinical follow-up, with biomarker and imaging, with shorter intervals immediately following HFrecEF diagnosis out to 12 months, and longer intervals thereafter. Abnormal or worsening global longitudinal strain (GLS) may identify patients at higher risk of HF relapse. *Consider CMR if was not performed at de novo time of HFrEF diagnosis. CMR ¼ cardiac magnetic resonance; ECG ¼ electrocardiogram; Echo ¼ echocardiography; HF ¼ heart failure; HFrEF ¼ heart failure with a reduced ejection fraction; NT-proBNP ¼ N-terminal pro–B-type natriuretic peptide.**