Heart Failure With Recovered Ejection Fraction

determined whether the accelerated collagen deposition in the hypertensive heart is the result of enhanced cardiomyocyte injury, increased oxidative or nitrosative stress, a direct activation of cardiac fibroblasts that may be predisposed to secrete collagen due to the presence of hypertension, or a combination thereof.

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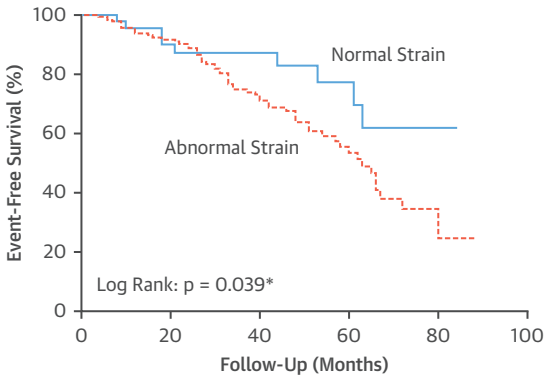
FIGURE 1 Survival Analysis of Death and HF Hospitalization-Free Survival in Patients With Abnormal GLS Versus Normal GLS



Number at risk					
Normal Strain:	44	32	21	12	1
Abnormal Strain:	168	129	74	29	7

This Kaplan-Meier analysis aims to supply information regarding the event-free (hospitalization due to heart failure [HF]) survival of patients who have a normal left ventricular ejection fraction (LVEF) and a normal GLS versus patients with an abnormal GLS. A significant (log-rank = 0.039) beneficial outcome regarding event-free survival is observed in patients with a normal GLS. This finding suggests that in patients with a normal LVEF, additional parameters (such as GLS) can provide additional insight in the cardiac function.

REFERENCES

1. Kotwinski P, Smith G, Cooper J, et al. Body surface area and baseline blood pressure predict subclinical anthracycline cardiotoxicity in women treated for early breast cancer. PloS One 2016;11:e0165262.

2. Mordi IR, Singh S, Rudd A, et al. Comprehensive echocardiographic and cardiac magnetic resonance evaluation differentiates among heart failure with preserved ejection fraction patients, hypertensive patients, and healthy control subjects. J Am Coll Cardiol Img 2018;11:577–85.

3. Meléndez GC, Jordan JH, D'Agostino RB Jr., Vasu S, Hamilton CA, Hundley WG. Progressive 3-month increase in LV myocardial ECV after anthracycline-based chemotherapy. J Am Coll Cardiol Img 2017;10:708–9.

4. Hong YJ, Park HS, Park JK, et al. Early detection and serial monitoring of anthracycline-induced cardiotoxicity using T1-mapping cardiac magnetic resonance imaging: an animal study. Sci Rep 2017;7:2663.

Heart Failure With Recovered Ejection Fraction

Recently, the term heart failure (HF) with recovered ejection fraction (HFrecovEF) was introduced for patients with a normalization of the left ventricular ejection fraction (LVEF) (1). The question remains whether this means true recovery of systolic left ventricular function or simply normalization of LVEF as many patients show remaining abnormalities in biomarker profiles and high hospitalization rate (1). Therefore, this research aims to assess the additional value of global longitudinal strain (GLS) in patients with HFrecovEF as physicians are left with uncertainties regarding the therapeutic approach (e.g., halt or continue HF medication).

Patients were identified via the electronic hospital health record system (EHR) based on the documented, routine LVEF measurement. In total, 212 patients met the inclusion criteria of an initial LVEF <35% with improvement to ≥55%, and had a complete follow-up. Patient characteristics were collected from the EHR. The reason for developing HF was rated according to the current ESC guidelines (2). GLS was measured on routine echocardiographic images at the point of time that LVEF was normalized using automated software (AutoLV module; part of the TomTec-Arena 2.20.10; TomTec Imaging Systems, Unterschleissheim, Germany). GLS was considered normal if ≤−21.5% and abnormal if >−21.5% (3). The primary endpoint was death or hospitalization due to HF during a follow-up of 56 ± 21 months (range 12 to 90 months) analyzed from normalization of LVEF onwards.

The reason for HF in the HFrecovEF patients was classified as: nonischemic (n = 41), due to arrhythmias (n = 70), abnormal loading conditions (n = 34), and "other" (e.g., Takotsubo) (n = 38). Patients with

an ischemic cause (n = 29) showed similar survival and combined primary endpoint results as compared with patients with a nonischemic etiology (n = 183) (p = 0.91 and p = 0.92, respectively). The duration between onset of symptoms and initial echocardiogram was overall 10 ± 7 (1 to 18) weeks, between initial echocardiogram and follow-up echo was 16 ± 8 (5 to 23) months. Overall, image quality was rated as good (91%), moderate in 8%, and poor in 1% (p = 0.26 between GLS groups).

Seventy-nine percent (n = 168) of patients still had an abnormal GLS despite normalization of LVEF. No significant differences regarding symptoms, medication, physical findings, further echocardiographic measurements (e.g., mitral annular plane systolic excursion, diastolic function) or underlying etiologies of HF were detected comparing patients with normal and abnormal GLS during follow-up. Also, no significant differences regarding interventions, operations, or new diagnoses were observed between GLS groups. The vast majority of patients (96%) showed a normal diastolic function at the time of normalization of LVEF with no significant difference between patients with normal/abnormal GLS (p = 0.11). Importantly, an abnormal GLS was associated with a significantly worse outcome of all-cause death and hospitalization due to HF (**Figure 1**) compared with patients having a normal GLS. There were 22 deaths in the group with abnormal GLS and only 1 in the other group (p = 0.05).

Thus, HFrecovEF is purely defined on improvement/normalization of LVEF. Still, normalization of geometry and/or LVEF does not necessarily mean full myocardial recovery (4). This difference is clinically important as decisions are taken based on dimensions and function rather than on tissue characteristics. Therefore, the mere depiction of LVEF, that is, volumetric changes, does not seem to be a sufficiently comprehensive marker of systolic function. GLS seems to provide additional characterization of systolic function as a significantly better death and HF hospitalization-free survival was seen in patients with normal GLS. These findings may have 2 direct implications for physicians caring for patients with HFrecovEF: 1) because systolic function remains altered in most patients, medication should not be ceased in patients with HFrecovEF; and 2) because many physicians rely on the measurement of LVEF, it calls for implementation of modern imaging tools (e.g., GLS or stress echocardiography).

In conclusion, the majority of patients with HFrecovEF still have an abnormal systolic function, as measured by GLS. Patients with an abnormal GLS, despite normalization of LVEF, showed a significantly worse outcome. Further studies should evaluate therapeutic consequences.

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REFERENCES

1. Basuray A, French B, Ky B, et al. Heart failure with recovered ejection fraction: clinical description, biomarkers, and outcomes. Circulation 2014;129:2380–7.

2. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure of the European Society of Cardiology (ESC). Eur Heart J 2016;37:2129–200.

3. Farsalinos KE, Daraban AM, Unlu S. Head-to-head comparison of global longitudinal strain measurements among nine different vendors: the EACVI/ASE inter-vendor comparison study. J Am Soc Echocardiogr 2015;28:1171–81.

4. Cohn JN, Ferrari R, Sharpe N, on Behalf of an International Forum on Cardiac Remodeling. Cardiac remodeling–concepts and clinical implications: a consensus paper from an international forum on cardiac remodeling. J Am Coll Cardiol 2000;35:569–82.

Infective Endocarditis and Valve-Pathogen Predilection

We read with great interest the excellent work of Zegri-Reiriz et al. (1), who have provided critical insight into the syndrome of infective endocarditis