Temporal Trends and Patterns in Heart Failure with Improved Left Ventricular Ejection Fraction: A Retrospective Cohort Study

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Background

Heart failure (HF) with reduced ejection fraction (HFrEF) remains a leading cause of morbidity and mortality. Heart failure with improved ejection fraction (HFimpEF) has better prognosis and outcomes. However, improvement only occurs in a subpopulation of HFrEF.

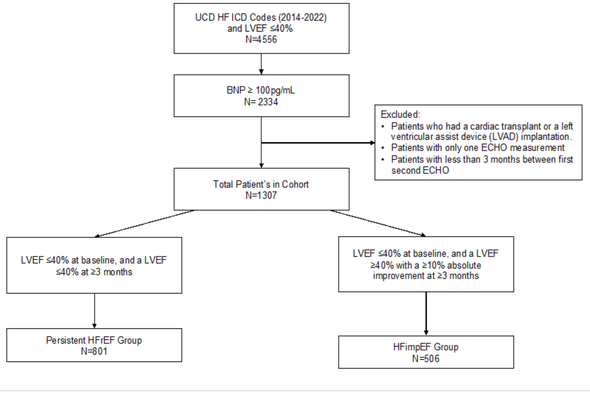
Hypothesis

We hypothesize that by further characterizing the time dependent trajectory of HFrEF and HFrecEF patients, we will be able to discern which parameters are most indicative and predictive of electrical and structural reverse remodeling.

Methods

- This was a single center retrospective cohort study. HFrEF patients were identified from electronic medical records following consensus criterion.
- Patients between January 2014 to January 2022 were identified on electronic medical records.
- Baseline characteristics and longitudinal laboratory, echocardiographic, electrocardiographic, and medication data were obtained.
- We stratified our HF cohort into two groups, HFimpEF group and persistent HFrEF group.
- Longitudinal variables were analyzed using linear mixed models to estimate intercept and slopes.
- Univariate and multivariate Cox regression was used to assess the association between baseline characteristics, slopes, intercepts, and mortality.

Figure 1. Cohort Curation



Results

Table 1. Baseline Characteristics

Characteristics	Median (IQR) or %					
	All (N=1307)	Persistent HFrEF (N=801)	HFimpEF (N=506)	P-Value[b]	n	Nmiss
Age, years	65 (55-75)	63 (54-74)	66 (58-76)	**0.0006**	1307	0
Sex				**<.0001**	1307	0
Female	420 (32.1)	219 (27.34)	201 (39.72)			
Male	887 (67.9)	582 (72.66)	305 (60.28)			
Race				0.1385	1307	0
White	742 (56.8)	439 (54.81)	303 (59.88)			
Black	229 (17.5)	155 (19.35)	74 (14.62)			
Asian	86 (6.6)	49 (6.12)	37 (7.31)			
Hispanic	7 (0.5)	3 (0.37)	4 (0.79)			
Native American/Hawaiian	41 (3.1)	25 (3.12)	16 (3.16)			
Other	193 (14.8)	126 (15.73)	67 (13.24)			
Unavailable	9 (0.7)	4 (0.5)	5 (0.99)			
Ethnicity				0.9102	1307	0
Hispanic	173 (13.2)	108 (13.48)	65 (12.85)			
Non-Hispanic	1128 (86.3)	689 (86.02)	439 (86.76)			
Unavailable	6 (0.5)	4 (0.5)	2 (0.4)			
Heart rate, b.p.m.	88 (75-102)	86 (73-100)	90 (77-105)	**0.0005**	1306	1
Blood pressure, mm Hg						
Systolic	127 (112-143)	127 (112-142)	127 (112-145)	0.8853	1307	0
Diastolic	77 (67-90)	76 (67-90)	78 (67-90)	0.3453	1307	0
MAP	94.3 (82.7-106.7)	93.7 (82.7-106)	95.3 (83.3-107)	0.3945	1307	0
Weight, Kg	83.5 (71.2-101.1)	83.1 (70.6-98.7)	84.1 (72.4-103.5)	0.1043	1306	1
Body mass index	28.2 (24.5-32.9)	27.9 (24.2-32.2)	28.7 (24.9-33.7)	**0.0238**	1172	135
Medical History					1295	12
Hypertension	967 (74.7)	575 (72.42)	392 (78.24)	**0.0189**		
Diabetes	568 (43.9)	347 (43.7)	221 (44.11)	0.8851		
Hyperlipidemia	574 (44.3)	330 (41.56)	244 (48.7)	**0.0118**		
Coronary artery disease	478 (36.9)	318 (40.05)	160 (31.94)	**0.0032**		
Atrial fibrillation	436 (33.7)	231 (29.09)	205 (40.92)	**<.0001**		
Chronic kidney disease	340 (26.3)	210 (26.45)	130 (25.95)	0.8421		
Laboratory						
BNP, pg/mL	623 (265-1330)	750 (323-1521)	451.5 (209-926)	**<.0001**	1307	0
NT-proBNP, pg/mL	1110 (326-2914)	1242 (431-3339)	874 (218-2852)	0.2144	148	1159
Sodium, mEq/L	138 (135-139)	138 (135-139)	138 (136-140)	0.0671	1306	1
Potassium, mEq/L	4 (3.7-4.4)	4 (3.7-4.4)	4 (3.7-4.4)	0.8134	1306	1
Creatinine, mg/dL	1.2 (0.9-1.5)	1.2 (0.9-1.5)	1.2 (0.9-1.5)	0.9515	1306	1
eGFR, mL/min/1.73 m2	56 (46-60)	57 (47-61)	55 (45-60)	**0.0477**	1232	75
Echocardiogram						
LVEF %	30 (25-40)	30 (20-35)	35 (30-40)	**<.0001**	1307	0
IVSD	1.2 (1-1.3)	1.2 (1-1.3)	1.2 (1.1-1.4)	**<.0001**	1307	0
LVIDd	5.6 (5.1-6.2)	5.8 (5.3-6.4)	5.4 (4.9-5.8)	**<.0001**	1306	1
LVIDs	4.7 (4.1-5.4)	4.9 (4.3-5.6)	4.4 (3.8-4.9)	**<.0001**	1305	2
PASP	41 (30.5-50)	41.5 (31.2-50.4)	40 (29.7-49.7)	0.2926	1240	67
PW	1.2 (1-1.3)	1.1 (1-1.3)	1.2 (1-1.3)	**<.0001**	1307	0
TAPSE	1.8 (1.4-2.1)	1.8 (1.4-2.1)	1.8 (1.4-2.1)	0.8179	1283	24
Electrocardiogram						
QTc, ms	498 (472-528)	499 (474-528)	495.5 (470-527)	0.1605	1287	20

Figure 3. Multivariable Cox Regression Analysis

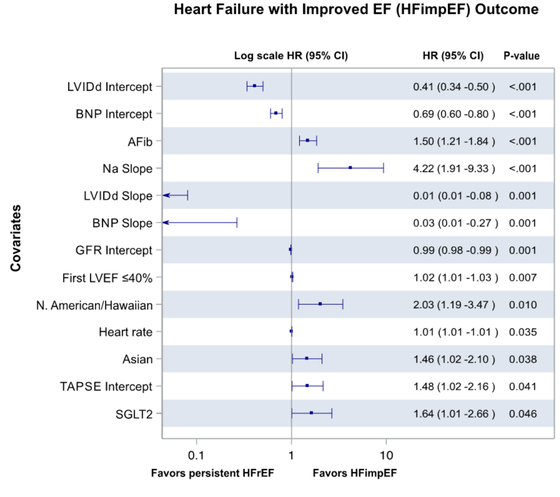


Figure 2. Evolution of EKG, Echocardiographic and Lab Values

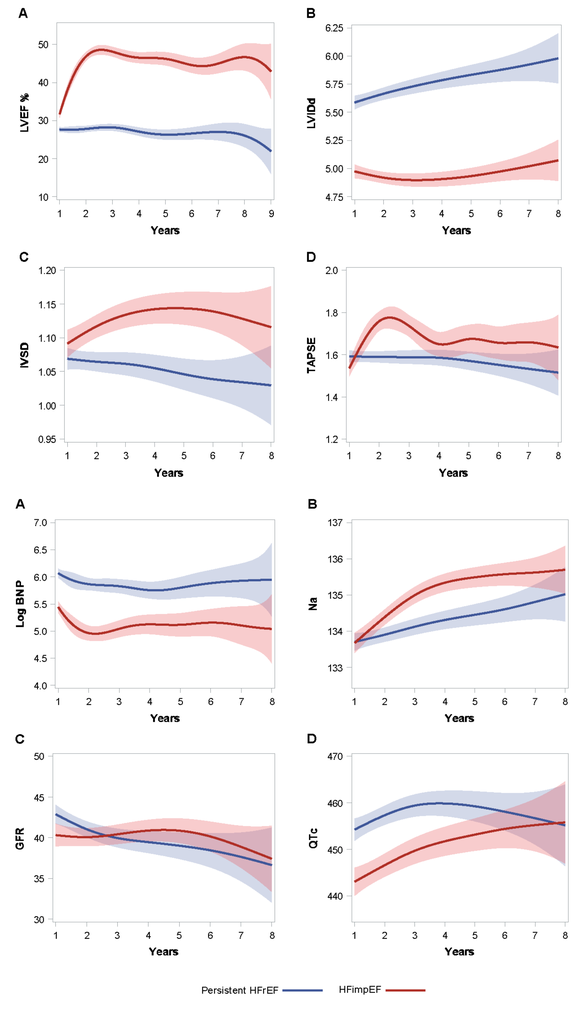


Figure 2. Longitudinal echocardiographic, electrocardiographic and lab parameters. X axis represents time in years. Y axis represents parameter of interest. *Abbreviations: IVSd, Interventricular septum thickness at end-diastole; LVEDD, left ventricle end diastolic diameter; LVEF, left ventricular ejection fraction; LVIDd, left ventricular internal dimension at end -diastole; LVIDs, left ventricular internal dimension at end -systole; PASP, pulmonary artery systolic pressure; TAPSE, tricuspid Annular Plane Systolic Excursion; BNP, B-type natriuretic peptide; eGFR, estimated glomerular filtration rate; QTc, QT corrected for heart rate.*

Figure 3. Forest plot summarizing results from the Multivariable Cox regression analysis for the primary HFimpEF endpoint. *Note: This table only includes the covariates reaching P-value <0.05*

Analysis

- In the HFimpEF group, LVEF changes over time showed that there was a noticeable improvement within the first year and that the LVEF remained above 40% from year 1 to 8. It also showed a persistent decline in LVEF and a level below 40% threshold from years 1 through 8 in the persistent HFrEF group.
- In the HFimpEF group, it was noted that there was an increasing trend in IVSD, PW, LVEF and TAPSE and decreasing trends in LVIDd, LVIDs, and PAS. Furthermore, the HFimpEF group had shorter QTC duration, lower sodium, and serum BNP values over time compared to the persistent HFrEF group.
- Parameters significantly associated with HFimEF (p=<.05) were atrial fibrillation, sodium slope, first LVEF ≤40%, Native American/Hawaiian, heart rate, TAPSE intercept, and SGLT2 use.
- Parameters associated with persistent HFrEF were LVIDd intercept & slope, BNP intercept & slope, and GFR intercept. *Significant covariates parameters remained with a p-values <.05 after a sensitive analysis.*

Conclusion

The longitudinal echocardiographic changes suggest that HFimpEF patients have undergone structural reverse remodeling. HFimpEF patients had significantly improved overall mortality.

Figure 4. Survival Analysis

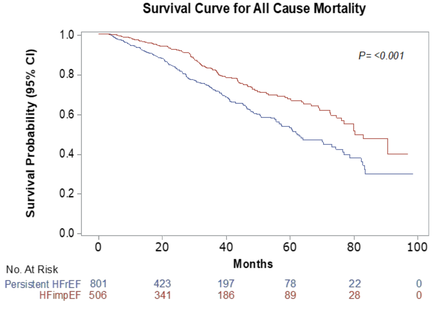


Figure 4. Longitudinal analysis of overall mortality among HFrEF and HFrecEF patient. X axis represents time in years. Y axis represents survival probability.

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References

1. Bozkurt B, Coats et al. Universal Definition and Classification of Heart Failure: A Report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. J Card Fail. 2021 Mar 1:S1071-9164(21)00050-6. doi: 10.1016/j.cardfail.2021.01.022. Epub ahead of print. PMID: 33663906.