Risk of Mortality Among Patients with Incident Heart Failure in the Multi-Ethnic Study of Atherosclerosis (MESA)

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Introduction

- Heart failure (HF) is a common condition. Although the recent studies have shown decreasing trends for the incidence of HF, but its prevalence, particularly the HF with preserved ejection fraction (HFpEF) is still substantially high.
- HF is associated with significant morbidity, mortality and resource utilization.
- HF is a heterogeneous disease and despite many studies in the literature, the risk factors associated with mortality in HF patients is not well understood.
- Multi-Ethnic Study of Atherosclerosis (MESA) with extensive longitudinal clinical and imaging data over more than 10 years, provides a unique opprtunity to investigate the mortality of patients with heart failure.

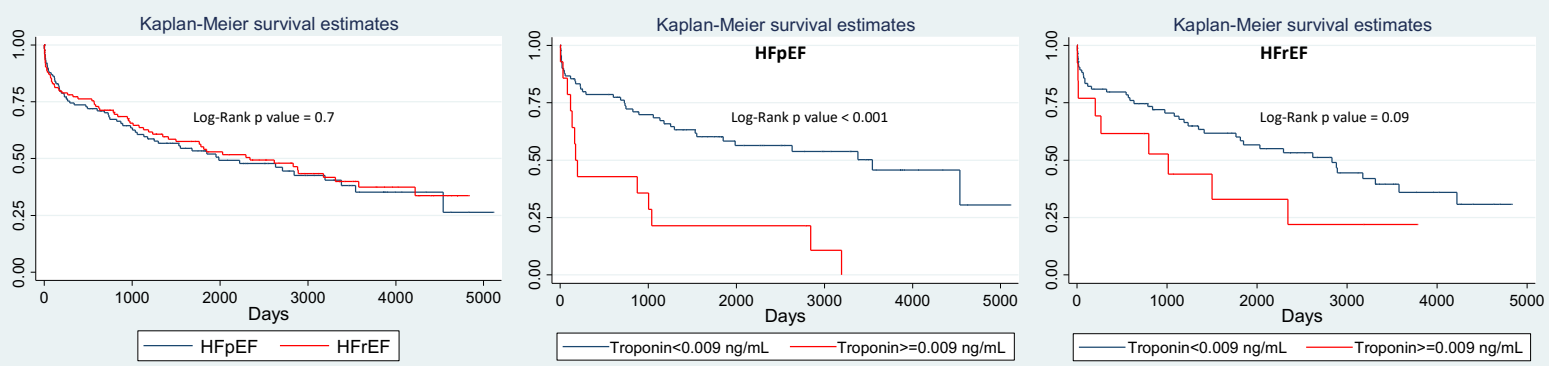
Objective

- To assess the prognostic value of clinical and imaging biomarkers prior to HF diagnosis in relation to the risk of mortality in HF patients in MESA.

Materials and Methods

- The MESA enrolled 6,814 African-American, Caucasian, Hispanic, and Chinese-American men and women without known cardiac disease in 2000 to 2002.
- MESA participants underwent multiple extensive clinical, laboratory and imaging (computed tomography and magnetic resonance imaging) exams from baseline until 10 years later (2010-2012).
- All participants were also followed-up annually for incidence of death and major cardiovascular events (MACE).
- Additional information for adjudication on incident death and MACE were collected through verbal autopsies and hospital medical record.
- MESA participants who developed HF during follow-up were included in the analysis and were followed up for death after HF diagnosis.
- Multivariable Cox regression models assessed the risk of death since HF diagnosis in relation to clinical and imaging biomarkers of cardiovascular diseases (CVD) measured at the closest MESA exam prior to HF diagnosis (median time, 1.5 years).

Results



Multivariable Cox proportional hazard ratio to predict mortality of participants with HF in MESA, Hazard ratio (p value)

	HFpEF (n=126, 66 died)	HFrEF (n=125, 65 died)
Age, years	**1.6(0.005)**	**2.1(<0.001)**
Male gender	1.3(0.34)	1.4(0.44)
Race		
Caucasians (n=123, 64 died)	ref	ref
Chinese (n=23, 10 died)	0.48(0.18)	**9.8(0.04)**
African-American (n=96, 54 died)	1.6(0.22)	1.3(0.4)
Hispanics (n=66, 37 died)	0.89(0.75)	1.4(0.41)
Framingham risk score	0.98(0.89)	1.1(0.69)
Diabetes Mellitus		
Normal (n=154, 71 died)	ref	ref
Impaired fasting glucose (n=54, 34 died)	1.99(0.06)	1.5(0.28)
Diabetes Mellitus (n=100, 60 died)	1.33(0.46)	1.8(0.08)
Coronary artery calcium score	1.1(0.63)	0.97(0.84)
Interleukin-6, pg/ml	0.9(0.52)	1.3(0.09)
Glomerular filtration rate<60 ml/min/1.73 m2 (n=97, 65 died)	1.5(0.17)	1.7(0.08)
NTproBNP, pg/ml	1.2(0.36)	**1.4(0.03)**
Troponin>0.009 ng/mL (n=34, 29 died)	**4.9(<0.001)**	2.3(0.06)
Interleukin-10, pg/ml	**1.8(0.002)**	1.3(0.39)
End diastolic volume, ml	1.4(0.21)	0.9(0.68)
End systolic volume, ml	1.3(0.29)	1.2(0.36)
End diastolic mass, gr	1.4(0.15)	**1.7(0.02)**
Ejection fraction, %	0.83(0.40)	0.7(0.06)
Stroke volume, ml	1.25(0.37)	**0.6(0.02)**
Left atrial total ejection fraction, %	**0.63(0.02)**	0.8(0.27)
Left atrial active ejection fraction, %	**0.66(0.04)**	0.84(0.48)
Left atrial passive ejection fraction, %	1.1(0.75)	0.7(0.11)

Cox models for each clinical or imaging marker (each row) were adjusted for age, gender, race, Framingham risk score, interim myocardial infarction, HF medications, and income
Log transformed values were used for Coronary artery calcium score, interleukin-6, NTproBNP, and interleukin-10
Hazard ratios for continuous variables are per one standard deviation increase for each covariate

- In total, 308 MESA participants developed HF (defined as first hospitalization for HF) with the mean age of 75(9) years at the time of HF diagnosis. Of those, 59% were male, 40% were Caucasians, 7.5% were Chinese, 31.2% were African-American, and 21.4% were Hispanics.
- 165 (53.6%) HF patients died during 6.3 (4.8-7.9) median years of follow-up after HF diagnosis (20% coronary heart disease, 4.2% stroke, 24.2% other CVD, 51.5% non-CVD death).
- Ejection fraction (EF) at the time of HF diagnosis was available for 251 subjects to categorize preserved (HFpEF, ≥45%) or reduced (HFrEF, <45%) EF.
- 126 patients were classified as HFpEF, while 125 had HFrEF at the time of HF diagnosis.
- There was no difference in mortality of HFpEF (52.4% died) and HFrEF (52% died) patients (log-rank p=0.7).
- In HFpEF, higher age, troponin level, interleukin (IL)-10 (a pro-fibrotic cytokine) and lower left atrial (LA) total and active EF were associated with higher mortality.
- In HFrEF, higher age, brain natriuretic peptide and end-diastolic mass, and lower stroke volume were associated with higher mortality.

Conclusion

- The mortality rate of HFpEF patients is not lower than those with HFrEF.
- Aging, myocyte damage, pro-fibrotic state, and diastolic dysfunction indexed as lower left atrial ejection fraction are associated with mortality in HFpEF.
- Aging, myocardial stress, ventricular hypertrophy and lower stroke volume are associated with mortality in HFrEF.

The authors thank the other investigators, the staff, and the participants of the MESA study for their valuable contributions. A full list of participating MESA investigators and institutions can be found at http://www.mesa-nhlbi.org/ (UID: NCT00005487).This research was supported by contracts N01-HC-95159 through N01-HC-95168 from the National Heart, Lung, and Blood Institute.