
5th iHEF CARD
The 5th Indonesian
Symposium on Heart Failure and
Cardiometabolic Disease
Indonesian Working Group
on Heart Failure
and Cardiometabolic Disease
WHFS
World Heart Failure Society
HEART FAILURE SOCIETY
(SINGAPORE)
Metabolic Syndrome
as Heart Failure Stage A
Sally Aman Nasution, MD, PhD
June, 12-14 2025
Sheraton Grand Jakarta Gandaria City, Jakarta, Indonesia
0811-1900-8855 | scientific_ihefcard@inahfcarmet.org | @ina.hf | ihefcard.com

Definition of Heart Failure

Universal Definition and Classification of Heart Failure (HF)

Definition

HF is a *clinical syndrome* with current or prior

- ***Symptoms and or signs caused by a structural and/or functional cardiac***

And corroborated by at least one of the following:

- ***Elevated natriuretic peptide levels***
- ***Objective evidence of cardiogenic pulmonary or systemic congestion***

Stages

AT RISK *(STAGE A)*	Patients at risk for HF, but without current or prior symptoms or signs of HF and without structural cardiac changes or elevated biomarkers of heart disease
PRE-HF *(STAGE B)*	Patients without current or prior symptoms or signs of HF with evidence of one of the following: • *Structural Heart Disease* • *Abnormal cardiac function* • *Elevated natriuretic peptide or cardiac troponin levels*
HF *(STAGE C)*	Patients with current or prior symptoms and/or signs of HF caused by a structural and/or functional cardiac abnormality
ADVANCED HF *(STAGE D)*	Severe symptoms and/or signs of HF at rest, recurrent hospitalizations despite GDMT, refractory or intolerant to GDMT, requiring advanced therapies transplantation, mechanical circulatory support, or palliative care

Classification By EF

HF with reduced EF (HFrEF)
- *HF with **LVEF < 40%***

HF with mildly reduced EF (HFmrEF)
- *HF with **LVEF 41-49%***

HF with preserved EF (HFpEF)
- *HF with **LVEF > 50%***

HF with improved EF (HFimpEF)
- *HF with a baseline LVEF of < 40%, a 10-point increase from baseline LVEF, and a second measurement of LVEF of > 40%*

Language matters! The new universal definition offers opportunities for *more precise communication* and description with terms including ***persistent HF*** instead of "stable HF," and ***HF in remission*** rather than "recovered HF."

Gibson G, Blumer V, Mentz RJ, Lala A. Universal definition and classification of heart failure: a step in the right direction from failure to function [Internet]. Washington: American College of Cardiology; 2021 Jul 13 [cited on 2025 Mar 31].

Clinical significance of HF Stage A

- HF Stages A to D, introduced by ACC/AHA, is based on the development and progression of the structural and functional changes and symptoms.
- Stage 0 is healthy and no risk factor; Stage A is for patients with comorbid diseases but no HF symptoms or structural heart disease.
- Survival steeply decreases from stage A to D; with 9x mortality risk once stage C develops.
- Unlike NYHA, the stages A-D are progressive and cannot return to stage A
- It is critical to address stage A for preventing progression to clinical HF.

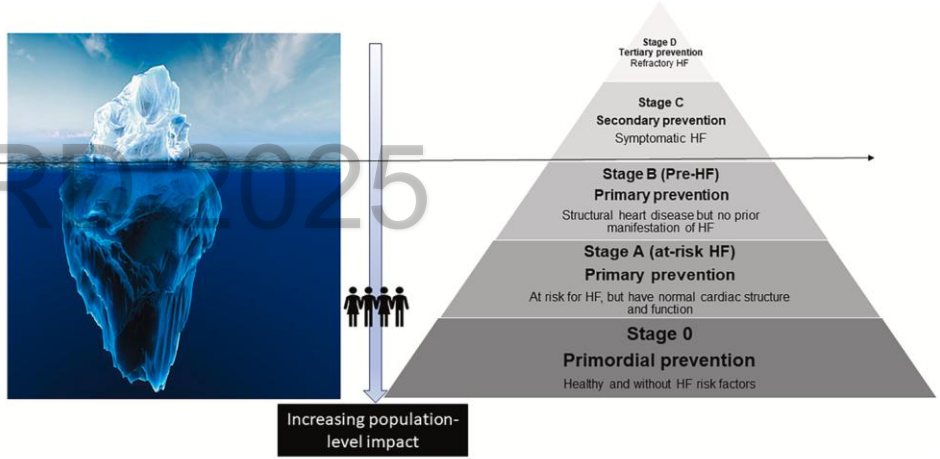
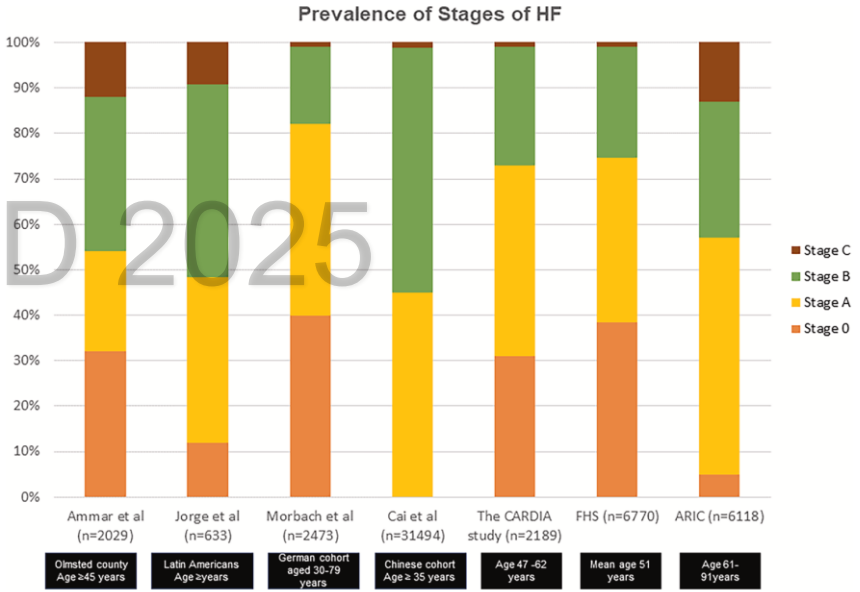


Fig. 1. Clinical significance of Stage A heart failure (HF).

Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.

Clinical significance of HF Stage A

- The effective prevention strategy is to identify the at-risk population before developing the disease.
- From multiple prior cross-sectional studies, the population at risk (stage A and B) is much larger than the symptomatic HF
- Once HF symptoms develop (stage C and D), there is no cure, but only stabilization of the problem
- Primary intervention of HF is imperative before irreversible myocardial damage.



Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.

Metabolic Syndrome (MetS) and Heart Failure

- MetS and HF are steadily increasing conditions, with prevalence of 34% and 1-2% in the general population
- MetS represents a cluster of CV risk factors: hypertension, insulin resistance, lipid abnormalities, and obesity; which are also HF risk factors
- Therefore, MetS will also increase the risk of HF, even in nondiabetic CVD patients (HR 1.32, 95%CI 1.04-1.68)

Table I Metabolic syndrome definitions

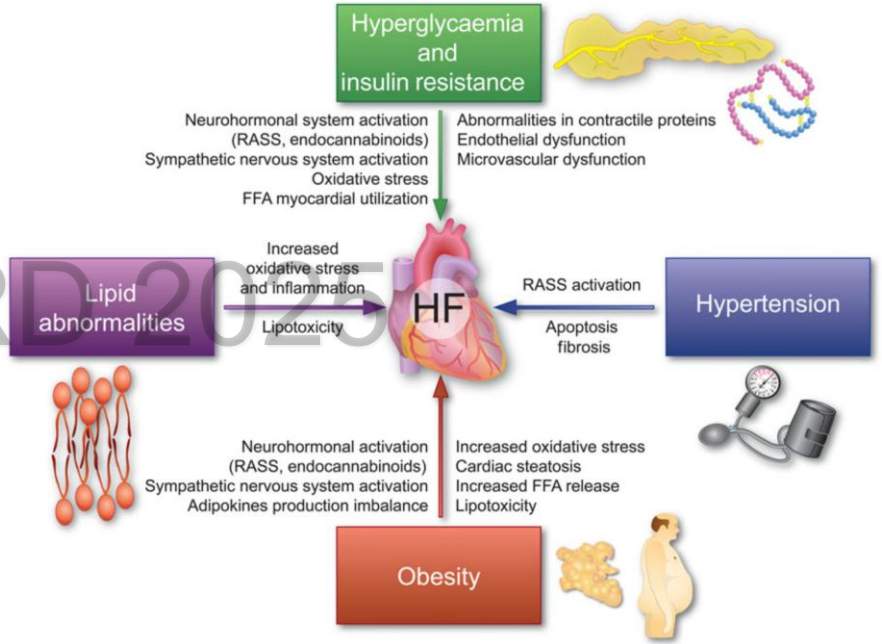
NCEP ATP III[66]	IDF[67]	WHO[68]	EGIR[69]
Three or more of the following five criteria:	Central obesity (defined as waist circumference ≥94 cm for Europid men and ≥80 cm for Europid women, with ethnicity specific values for other groups) plus any two of the following four factors:	Insulin resistance[a] or diabetes plus two of the following five criteria:	Hyperinsulinaemia plus two of the following four criteria:
Fasting blood sugar over 100 mg/dL	Fasting plasma glucose ≥100 mg/dL, or previously diagnosed type 2 diabetes. If above 100 mg/dL, OGTT is strongly recommended but is not necessary to define the presence of the syndrome	–	–
Blood Pressure over 130/85 mmHg	Systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, or treatment of previously diagnosed hypertension	Blood pressure ≥140/90 mmHg	Blood pressure ≥140/90 mmHg or hypertension-specific treatment
Fasting triglyceride level over 150 mg/dL	Triglyceride level ≥150 mg/dL or specific treatment for this lipid abnormality	Fasting triglyceride level over 150 mg/dL or	Fasting triglyceride level ≥177 mg/dL or
Fasting HDL cholesterol level <40 mg/dL (men) or 50 mg/dL (women)	HDL cholesterol <40 mg/dL in males and <50 mg/dL in females, or specific treatment for this lipid abnormality	Fasting HDL cholesterol level <35 mg/dL (men) or 39 mg/dL (women)	Fasting HDL cholesterol level <39 mg/dL
Waist circumference over 40 in. (men) or 35 in. (women)	–	Waist/Hip ratio >0.90 (men) or >0.85 (women); or BMI >30 kg/m^2	Waist circumference ≥94 cm for men and ≥80 cm for women
–	–	Microalbuminuria	–

HDL, high-density lipoprotein.
[a]Insulin resistance defined as: impaired fasting glucose (IFG), defined as a fasting glucose level above a predetermined cut-off, [commonly 100 mg per decilitre (mg/dL)] or impaired glucose tolerance (IGT), defined as a glucose level above a predetermined cut-off, commonly 140 mg/dL, for 120 min after ingestion of 75 g of glucose load during an oral glucose tolerance test or insulin resistance at euglycaemic clamp studies.

Perrone-Filardi P, Paolillo S, Costanzo P, Savarese G, Trimarco B, Bonow RO. The role of metabolic syndrome in heart failure. Eur Hear J. 2015;36:2630–4
Burger PM, Koudstall S, Dorresteijn JAN, Savarese G, van der Meer MG, de Borst GJ, et al. Metabolic syndrome and the riks of incident herat failure in non-diabetic patients with established cardiovascular disease. IJC. 2023;379:66-75.

Pathophysiology

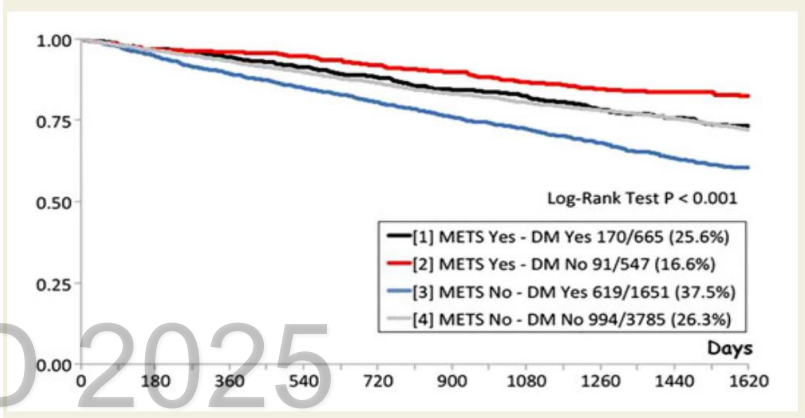
1. Insulin resistance and hyperglycemia → increase in AGEs and ROS → cellular damage to contractile proteins and myocardial cells → impaired diastolic performance
2. Obesity is associated with reduced level of myocardial protective adiponectin and enlarged end-diastolic volume (eccentric hypertrophy)
3. Hypertension causes concentric LV hypertrophy by mechanical stress due to increase pressure load together with RAAS activation
4. Lipid accumulation causes lipotoxicity that impairs cardiac function and promotes HF. Reduced HDL in metS means reduced protective role of HDL (anti-inflammatory and anti-oxidant)



Perrone-Filardi P, Paolillo S, Costanzo P, Savarese G, Trimarco B, Bonow RO. The role of metabolic syndrome in heart failure. Eur Hear J. 2015;36:2630–4

Obesity paradox in HF

- Paradox: prognostic impact of obesity in HF patients
- Oreopoulos et al (meta-analysis in 28,209 HF patients) found lower rate of all-cause mortality and CV mortality in overweight and obese patients compared to normoweight
- This counterintuitive association has been consistent, regardless of age, gender, systolic or diastolic HF, central or peripheral obesity, and chronic or acutely decompensated HF.



Graph shows survival analysis for HF patients with/without MetS and DM

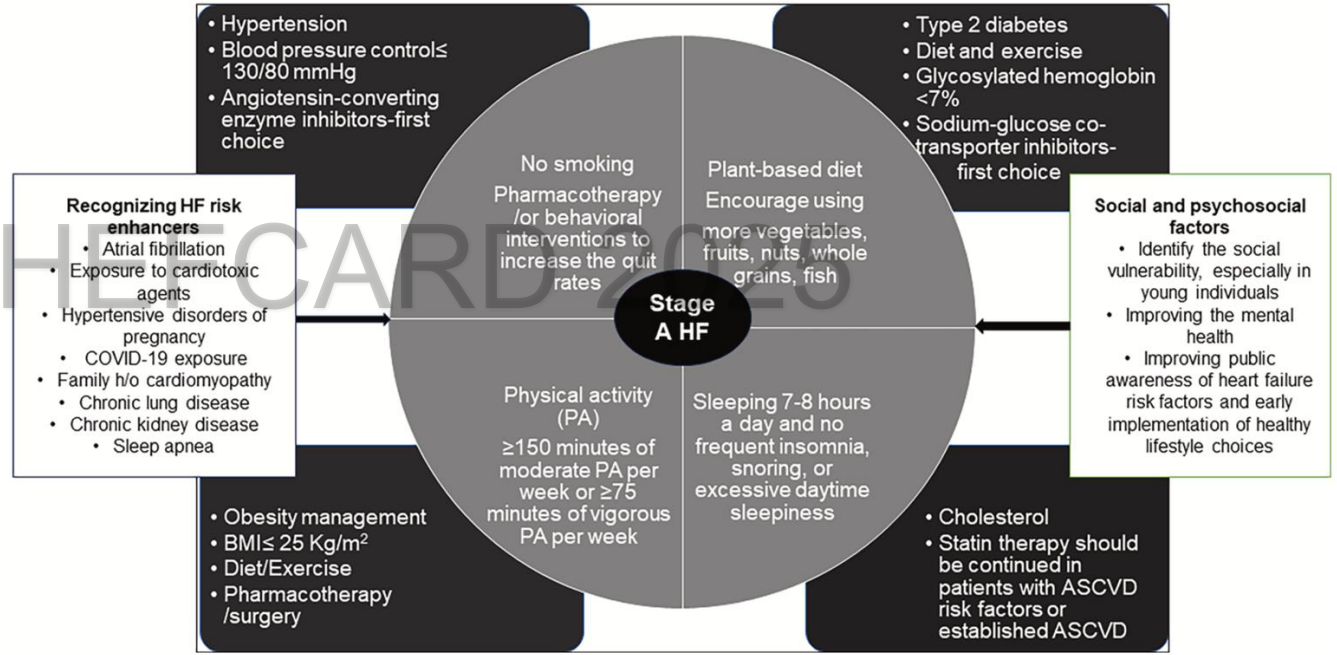
- HF patients with DM but no MetS showed the poorest survival
- DM but not overweight affects poor prognosis in HF patients

Perrone-Filardi P, Paolillo S, Costanzo P, Savarese G, Trimarco B, Bonow RO. The role of metabolic syndrome in heart failure. Eur Hear J. 2015;36:2630–4

MetS Management to intervene HF Stage A

At Risk for HF (Stage A)	
Patients with hypertension	Optimal control of BP (1)
Patients with type 2 diabetes and CVD or high risk for CVD	SGLT2i (1)
Patients with CVD	Optimal management of CVD (1)
Patients with exposure to cardiotoxic agents	Multidisciplinary evaluation for management (1)
First-degree relatives of patients with genetic or inherited cardiomyopathies	Genetic screening and counseling (1)
Patients at risk for HF	Natriuretic peptide biomarker screening (2a)
Patients at risk for HF	Validated multivariable risk scores (2a)

Preventing New-Onset Heart Failure: Intervening at Stage A



Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.
Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145.e859-e1032

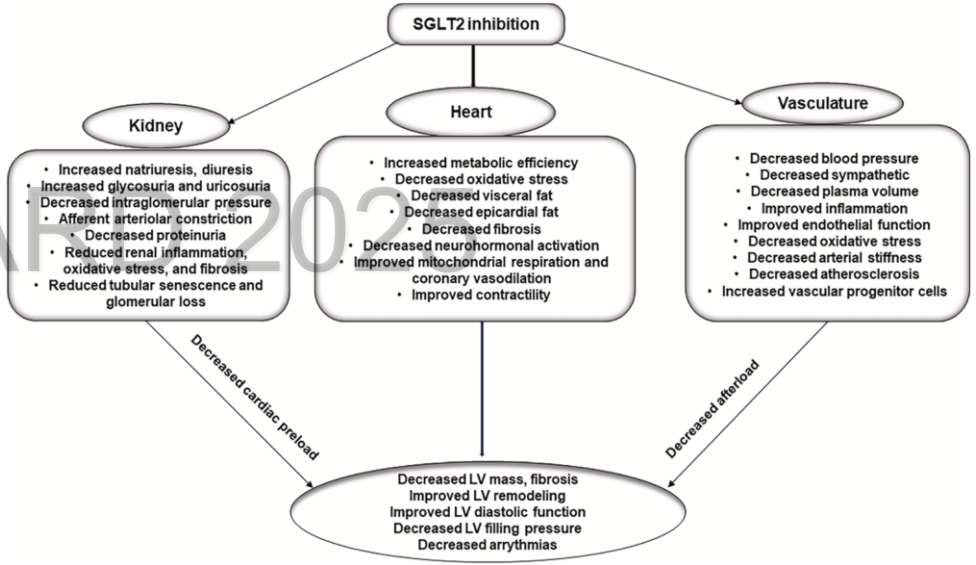
Blood Pressure Management

- Many trials have shown that hypertension control reduces the risk of HF
- SPRINT trial: control to SBP goal <120 mmHg decreases HF incident than SBP goal <140 mmHg by 38% and lower mortality by 23%
- ACC/AHA recommendation: optimal BP should be <130/80 mmHg
- ESC recommendation: for all patient should be <140/90 mmHg, and if tolerated SBP 120-129 mmHg for patients aged under 65.
- ACEi and ARB should remain the drug of choice for high-risk ASCVD patients
- Recent meta-analysis showed the most significant impact on HF prevention results from the magnitude of BP lowering, independent of the antihypertensive class

Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.
Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145.e859-e1032

Diabetes Management

- Most guidelines recommend target HbA1c <7.0% for most adult diabetic patients with no significant comorbidities (HF Stage A)
- Multiple RCTs and meta-analysis show SGLT2i prevent HF hospitalization and reduces the risk for HF in patients with or without MI and CAD.
- All HF stage A patients with eGFR ≥20 mL/min/1.73m2 should be on SGLT2i to prevent incident HF
- Proposed mechanism of HF prevention: reductions in plasma volume, cardiac preload and afterload, alterations in cardiac metabolism, and reduced arterial stiffness.



Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.
Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145.e859-e1032

Obesity Prevention and Management

- For every 1 kg/m2 increase in BMI, the risk of HF increased by 5% in men and 7% in women.
- Diet and regular exercise as the cornerstone of weight management
- Adjunctive pharmacotherapy for adults with BMI >30 or >27 with comorbidities, such as GLP1RAs.
- Gastric bypass surgery may also be needed in selected patients

Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.
Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145.e859-e1032

Lipid Management

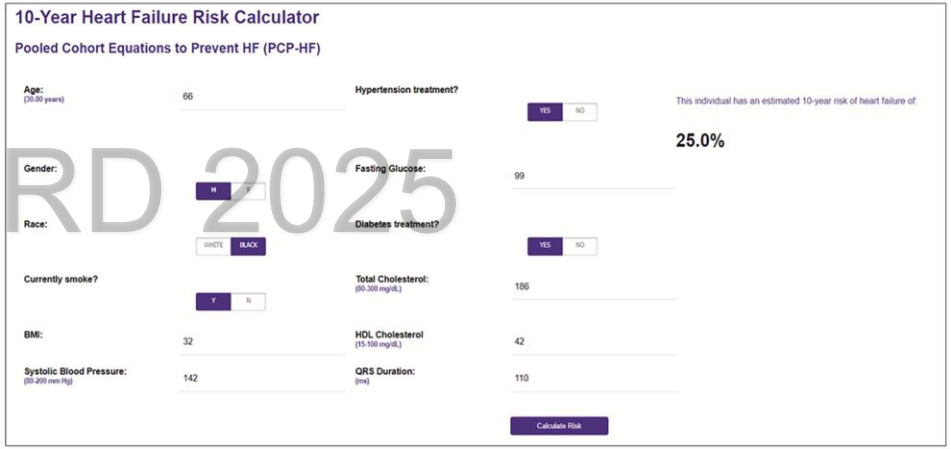
- Statin therapy seems beneficial in reducing the incidence of HF in patients with stable CAD or previous ACS by mechanisms partly independent from MI prevention
- Statin therapy should be continued in patients with ASCVD risk factors or established ASCVD to prevent HF

Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.
Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145.e859-e1032

HF Prediction Tools

- HF risk prediction tools combine risk factor levels to facilitate preventive interventions based on absolute risk level
- The most recent prediction tools is the Pooled Cohort equations to Prevent HF (PCP-HF) that can provide race- and sex-specific 10 year-risk equations
- Predictors of HF include age, MetS (obesity, hypertension, DM, dyslipidemia), smoking, and QRS duration.

An example of calculating the Heart Failure (HF) risk score for a 66-year-old individual is shown below.



10-Year HF Risk Calculator: Pooled Cohort Equations to Prevent HF (PCP-HF). Available at: http://hf-risk-calculator.surge.sh/

Khan SS, J Am Coll Cardiol. 2019 May 21;73:2388-2397

Upadhya B, Hegde S, Tannu M, Stacey RB, Kalogeroupolos A, Schocken DD. Preventing new-onset heart failure: intervening at stage A. AJPC. 2023;16:100609.
Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145.e859-e1032

Conclusion

- Metabolic syndrome represents a cluster of risk factors, which are also risk factors of heart failure
- HF stage A are patients with these risk factors, but have not developed myocardial damage seen in HF
- Long term comorbidities of MetS will cause permanent myocardial damage through increase AGEs and ROS, lipotoxicity, arterial stiffening, and RAAS activation
- Preventing MetS will also prevent HF Stage A to progress into symptomatic HF