

How to Best Identify Elderly Individuals Who May Develop Heart Failure

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Abstract The prevalence of heart failure grows yearly, and incidence rates are expected to potentiate given the growing aging population. There have been numerous advancements over the past several decades in the management of heart failure, yet the burden of disease in the form of quality of life, frequency of hospitalization, and healthcare cost remains high. Several comorbid conditions, lifestyle factors, pharmacologic agents, and biochemical markers have been associated with increased risk of heart failure resulting in the formulation of risk models for prediction. Although further investigation is still needed in order to more clearly elucidate individuals most at risk for the development of heart failure, this remains a critical objective in order to allow for the implementation of preventive strategies.

Keywords Heart failure · Elderly · Risk factor · Risk score

Introduction

Heart failure (HF) is a growing public health concern, with a prevalence of 5.1 million in the USA and an incidence that increases with age [1]. Over the next 50 years, the aging population is expected to rise with a projected 92 million people aged greater than 65 and 18 million people aged greater than

85 [2]. In spite of the predominance of elderly HF patients, they remain an underrepresented population in clinical trials due to comorbid conditions and concern for polypharmacy [3]. The cost of HF further adds to the burden of this disease in the USA with a projected indirect cost of \$17.4 billion and direct cost of \$77.7 billion in 2030 [4]. The American Heart Association and the American College of Cardiology encourage a proactive approach in the staging of heart failure to include “stage A” for patients with risk factors for heart failure but without structural heart disease [5]. Similarly, patients in “stage B” who have structural heart disease but no overt symptoms are ideal targets for prevention of progression. The anticipated rise in the elderly population and presumed worsening of the heart failure epidemic compounded by its economic strain highlights the paramount need for risk factor identification and implementation of prevention strategies.

Risk Factors for Heart Failure

There are a variety of risk factors that have been described for heart failure, including certain comorbidities, lifestyle factors, biochemical markers, and pharmacologic exposures (Table 1).

Comorbidities

Comorbid conditions such as obesity, hypertension, diabetes, valvular heart disease, and coronary heart disease are independent risk factors for HF [6•]. Among Medicare beneficiaries, more than twice as many patients with HF were greater than 85 compared to 65–69 years of age. The very elderly HF patients were less likely to have underlying coronary artery disease or hypertension and more likely to have worse renal function [7]. Another study of elderly patients found male gender, older age, diabetes, lack of emotional support,

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Table 1 Risk for factors for heart failure

Demographics	Older age, male gender
Socioeconomic status	
Education	
Comorbidities	Hypertension, coronary artery disease, valvular heart disease, diabetes mellitus, obesity, hyperlipidemia, renal insufficiency
Lifestyle factors	Cocaine, tobacco use, excess alcohol consumption, excess caffeine, excess sodium consumption
Pharmacologic exposures	Chemotherapeutic agents, non-steroidal anti-inflammatory drugs, thiazolidinediones, doxazosin
Echocardiographic parameters	Ventricular dysfunction, diastolic filling impairment, ventricular mass, left atrial volume
Biochemical markers	Albuminuria, homocysteine, tumor necrosis factor- α , interleukin-6, C-reactive protein, insulin-like growth factor 1, natriuretic factors
Genetic factors	Adrenergic receptors α_{2C} Del322-325 deletion, B ₁ Arg389 change

hypertension, and increase body mass index to be risk factors for the development of heart failure [8]. Pulse pressure has also been shown to be an independent predictor of HF in the elderly [9]. Hyperlipidemia is a risk for HF; however, it is unclear if this is related to atherosclerosis [10]. Depression in elderly women, but not men, is an independent risk factor for HF [11]. Elderly patients with renal insufficiency have an increased risk of HF, and the risk increases with increasing creatinine level [12]. Sleep-disordered breathing is another important risk factor of HF, independent of other known risk factors [13].

Lifestyle Factors

Physical inactivity, cigarette smoking, as well as less education are all risk factors for HF [6••]. Moderate alcohol consumption, independent of reduction in myocardial infarction risk, is associated with lower risk of heart failure in the elderly [14]. While there has been discrepancy in the role of caffeine in heart failure, a meta-analysis found an inverse relationship between four cups of coffee per day and incidence of heart failure [15]. In overweight individuals, increased dietary sodium intake is a strong independent risk factor for HF [16].

Pharmacologic Exposures

Among elderly HF patients taking diuretics, the use of non-steroidal anti-inflammatory drugs resulted in a twofold increased risk of first hospitalization for heart failure [17]. Risk of heart failure was also increased in patients taking doxazosin [18]. Among diabetics, use of thiazolidinediones was associated with fluid retention and heart failure [19]. Various chemotherapeutic agents such as anthracyclines, alkylating agents, taxanes, and monoclonal antibodies have all been associated with increased risk of heart failure [20].

Echocardiographic Parameters

In an elderly cohort, ventricular dysfunction and abnormalities in left ventricular diastolic filling was predictive of HF [21]. In addition, left ventricular mass was shown to predict heart failure independent of myocardial infarction [22]. Left atrial volume independently predicted HF in patients with preserved systolic function [23].

Biochemical Markers

Cystatin C, an alternate measure of renal function, was shown to be an independent risk factor for HF in the elderly [24]. Elevations in inflammatory markers such as interleukin-6, tumor necrosis factor- α , and C-reactive protein are also associated with increased risk of HF in elderly patients [25, 26]. In adults without prior myocardial infarction, elevated plasma homocysteine levels independently predicted HF development [27]. Albuminuria, regardless of the presence or absence of diabetes, is a risk factor for cardiovascular events and heart failure hospitalization [28]. Higher rates of insulin-like growth factor-1 are associated with lower incidences of heart failure [29].

Genetic Factors

Polymorphisms of the β_1 -adrenergic receptor (β_1 Arg389) and α_{2C} -adrenergic receptor (α_{2C} Del322-325) are synergistically associated with increased risk of heart failure among black subjects [30].

Risk Factor Models

Although there are numerous known risk factors for HF, individual risk factors are not enough to predict incident HF in the

general population. As such, several risk models have been developed.

Framingham Heart Study

The Framingham Heart Failure Risk Score (FHFRS) assessed the probability of developing heart failure in subjects’ aged 45 through 94 years over the course of a 38-year study period [31••]. A 4-year event score was created based on the variables of age, forced vital capacity, systolic blood pressure, heart rate, left ventricular hypertrophy on electrocardiogram, coronary artery disease, valve disease, diabetes, and cardiomegaly. However, there are several limitations to this model. The population studied was primarily white, and thus, the applicability of this model to individuals in other racial groups is unknown. In addition, subjects were required to have a known history of coronary artery disease, hypertension, or valvular disease. Furthermore, the requirement of chest radiography and pulmonary function testing for certain variables limits the large-scale use of this score in the general population where that data may be unavailable. This model has also not been externally validated in independent cohorts (Table 2).

Health, Aging, and Body Composition Study

The Health, Aging, and Body Composition (Health ABC) study followed patients aged 70–79 years to determine the incidence of HF, the population-attributable risk of independent risk factors for HF, and outcomes of incident HF [27]. Investigators subsequently developed the Health ABC HF Score which included the variables age, heart

rate, fasting glucose, coronary artery disease, smoking, creatinine, left ventricular hypertrophy, albumin, and systolic blood pressure in order to predict 5-year HF risk (Fig. 1) [32••]. In comparison to the FHFRS, the Health ABC HF Score had better discrimination for incident HF. In addition, the score predicted risk equally in both white and male subjects. The variables in the score are readily obtainable in the clinical setting, and eight of the nine variables are modifiable, providing opportunities for prevention. The Health ABC HF model was externally validated in the Cardiovascular Health Study (CHS), a large community-based cohort of individuals aged 65–100 years [33]. Limitations to this model include the lack of data collection on valvular heart disease as well as inclusion of only elderly patients who were relatively healthy, and thus, the applicability of this score to patients of variable ages or with higher burden of comorbid disease remains unknown.

Atherosclerosis Risk in Communities Study

The Atherosclerosis Risk in Communities (ARIC) study analyzed a biracial cohort of middle-aged participants to examine the external validity of the FHFRS and Health ABC scores in addition to the derivation of an ARIC HF risk score [34]. The optimal model for the prediction of 10-year HF risk was determined to include age, race, sex, prevalent coronary heart disease, systolic blood pressure, use of blood pressure lowering medication, diabetes, smoking status, heart rate, and body mass index. Furthermore, the inclusion of N-terminal pro-B-type natriuretic peptide (NT-proBNP) significantly improved HF risk prediction. Overall, the ARIC risk score was found to

Table 2 Risk prediction models for heart failure

Risk score	Risk factors	n	Discrimination	Calibration	Validation
FHFRS	Age, FVC, SBP, HR, LVH, CAD, valve disease, diabetes, cardiomegaly	6354	NR	NR	NR
Health ABC HF	Age, HR, fasting glucose, CAD, smoking status, creatinine, LVH, albumin, SBP	2935	0.73	6.24	Bootstrapping
ARIC	Age, race, sex, prevalent coronary heart disease, SBP, use of BP lowering drug, diabetes, smoking status, HR, BMI	13,555	0.797	NR	Bootstrapping
PEACE	Age, BMI, history of MI, CABG, diabetes, HTN, angina, stroke, smoking status, LVEF, eGFR, use of diuretic, use of digitalis, use of CCB, use of anti-arrhythmic, lack of use of lipid lowering drug	82,890	0.80	NR	NR
MESA	Age, gender, BMI, smoking status, SBP, HR, diabetes, NT-proBNP	6814	0.87	4.84	Bootstrapping
IMRS	Age, sex, hematocrit, hemoglobin, RDW, MVC, RBC, platelet count, MPV, MCH, MCHC, WBC, sodium, potassium, chloride, bicarbonate, BUN, creatinine, glucose, calcium	3927	0.70 (female) 0.67 (male)	NR	NR

BMI body mass index, *BP* blood pressure, *BUN* blood urea nitrogen, *CABG* coronary artery bypass graft, *CAD* coronary artery disease, *CCB* calcium channel blocker, *eGFR* estimated glomerular filtration rate, *FVC* forced vital capacity, *HR* heart rate, *HTN* hypertension, *LVEF* left ventricular ejection fraction, *LVH* left ventricular hypertrophy, *MCH* mean corpuscular hemoglobin, *MCHC* mean corpuscular hemoglobin concentration, *MCV* mean corpuscular volume, *MI* myocardial infarction, *MPV* mean platelet volume, *NT-proBNP* n-terminal pro-B-type natriuretic peptide, *RBC* red blood cell, *RDW* red cell distribution width, *SBP* systolic blood pressure

Fig. 1 The Health ABC Heart Failure Risk Score. From Butler J, Kalogeropoulos A, Georgiopoulou V, et al. Incident heart failure prediction in the elderly: the Health ABC Heart Failure Score, *Circ Heart Fail* 2008;1:125. Reprinted with permission of Wolters Kluwer Health.

Age	
Years	Points
≤71	-1
72-75	0
76-78	1
≥79	2

Heart Rate	
bpm	Points
≤50	-2
55-60	-1
65-70	0
75-80	1
85-90	2
≥95	3

Fasting Glucose	
mg/dl	Points
≤80	-1
85-125	0
130-170	1
175-220	2
225-265	3
≥270	5

Coronary Artery Disease	
Status	Points
No	0
Possible	2
Definite	5

Smoking	
Status	Points
Never	0
Past	1
Current	4

Creatinine	
mg/dl	Points
≤0.7	-2
0.8-0.9	-1
1.0-1.1	0
1.2-1.4	1
1.5-1.8	2
1.9-2.3	3
>2.3	6

LV Hypertrophy	
Status	Points
No	0
Yes	2

Systolic Blood Pressure	
mmHg	Points
≤90	-4
95-100	-3
105-115	-2
120-125	-1
130-140	0
145-150	1
155-165	2
170-175	3
180-190	4
195-200	5
>200	6

Albumin	
g/dl	Points
≥4.8	-3
4.5-4.7	-2
4.2-4.4	-1
3.9-4.1	0
3.6-3.8	1
3.3-3.5	2
≤3.2	3

Key:
 Systolic BP to nearest 5mmHg
 Heart Rate to nearest 5bpm
 Albumin to nearest 0.1g/dl
 Glucose to nearest 5mg/dl
 Creatinin to nearest 0.1mg/dl
 HF=Heart Failure

Health ABC HF Risk Score	HF Risk Group	5-yr HF Risk
≤2 points	Low	<5%
3-5 points	Average	5-10%
6-9 points	High	10-20%
≥10 points	Very High	>20%

be superior to the FHFRS and comparable to the Health ABC HF score.

Prevention of Events with Angiotensin-converting Enzyme Inhibition

The Prevention of Events with Angiotensin-converting Enzyme Inhibition (PEACE) study examined 82,890 patients with stable coronary artery disease in order to develop a risk model for the prediction of HF [35]. Characteristics included in the risk score are age, body mass index, history of myocardial infarction, coronary artery bypass graft, diabetes, hypertension, angina, stroke, smoking status, left ventricular ejection fraction, estimated glomerular filtration rate in addition to use of any diuretic, digitalis, calcium channel blocker, antiarrhythmic, and absence of lipid lowering medication.

Multi-Ethnic Study of Atherosclerosis

The Multi-Ethnic Study of Atherosclerosis (MESA) followed 6814 patients without clinical cardiac disease at baseline with the intent to develop a 5-year risk score for incident HF [36]. In this cohort of patients, a model was developed based on age, gender, body mass index, smoking status, systolic blood pressure, heart rate, diabetes, and NT-proBNP. These parameters are all readily available in the clinic setting. Similar to the ARIC study, the addition of NT-proBNP provided the largest contribution to risk assessment.

Intermountain Heart Collaborative Study

The Intermountain Risk Score (IMRS) incorporates information from the complete blood count and basic metabolic panel

in addition to age and sex, initially intended to predict mortality at 30 days, 1 year, and 5 years [37]. The IMRS was shown to also be predictive of HF, left ventricular ejection fraction, readmission for HF, incident HF, myocardial infarction diagnosis, incident myocardial infarction, atrial fibrillation, and chronic obstructive pulmonary disease. The red cell distribution width was shown to be particularly predictive of HF.

Beyond Clinical Risk Factors

Echocardiographic parameters and biomarkers such as natriuretic peptides and troponin have been studied to determine whether they provide an added role in the prediction of HF. In the CHS cohort, ejection fraction, enlarged left atrium, and E/A ratio were independent predictors of HF risk when added to the Health ABC HF Score [38]. In addition, NT-proBNP levels were independently associated with HF risk when added to the ABC HF Risk Score and the combination of NT-proBNP and echocardiography had incremental value over each modality alone. In the same cohort, baseline levels of cardiac troponin T (cTnT) were strongly associated with incident HF and cardiovascular death independent of other risk factors [39]. Furthermore, changes in cTnT over 2–3 years were also associated with increased risk of HF.

The emerging field of genomics adds further potential for risk stratification. Microarrays can allow for the quantification and monitoring of gene expression; however, use is currently limited to the investigational arena [40]. The incorporation of genetic polymorphisms in risk prediction is appealing; however, genetic markers would need to show incremental improvement over validated risk scores and must be uncorrelated with known risk factors to ensure independent risk [41].

Conclusion

Heart failure poses a unique challenge due to the high incidence among the elderly and the burgeoning aging population. The identification of risk factors is critical in order to curb the anticipated rise in disease and healthcare costs. While there are a variety of known risk factors for incident heart failure, individual risk factors are alone not enough to predict who will develop this disease and as a result, several risk models have been proposed. Overall, further investigation is needed prior to the large scale implementation of these screening models in clinical practice.

Compliance with Ethics Standards

Conflict of Interest Drs. Hamo and Butler report no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by the author.

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