7th Advances in Heart Failure 2024

10 e 11 de Outubro

FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO

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GET DONE EVENTS

7th Advances in Heart Failure 2024
10 e 11 de Outubro
FACULDADE DE MEDICINA DA UNIVERSIDADE DO PORTO

Age

What is the pathway to a personalized and early approach?

Conceição Queirós
Serviço de Cardiologia – ULS Tâmega e Sousa

10 outubro 2024

Age is among the most potent risk factors independently associated with HF

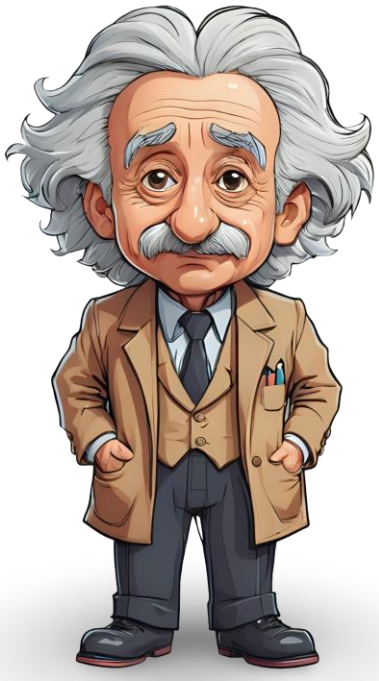
(regardless of ejection fraction, and its outcomes)

References: Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809.

Age is a non-modifiable factor in heart failure…

Age is something we live with, that we know and that we cannot change…

Age is a non-modifiable risk factor… the number of days of life cannot be changed…



But is this the case?

Age belongs to us and is not just a question of being old or young (the **years**), but…
… is associated with an individual, changeable story/history throughout life… associate to an **aging/ageing** process…

Age and Aging

INSTITUTO NACIONAL DE ESTATÍSTICA
STATISTICS PORTUGAL

Sistema de Metainformação

AGE "**Time interval** that elapses between the **date of birth** (day, month and year) and 0 hours on the **reference date.** … is expressed incomplete years, except in the case of children under 1 year old, in which case it must be expressed in complete months, weeks or days.

World Health Organization

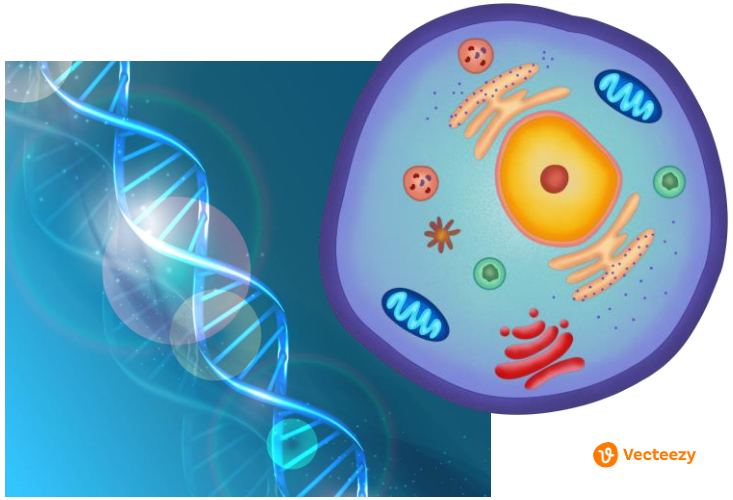
AGEING (=AGING) "At the **biological level**, ageing results from the impact of the accumulation of a wide **variety of molecular and cellular damage over time**. This leads to a gradual **decrease in physical and mental capacity, a growing risk of disease and ultimately death**.

These changes are neither linear nor consistent, and **they are only loosely associated with a person's age in years**. "

Age vs Aging

CHRONOLOGICAL non-modifiable

BIOLOGICAL modifiable /non-modifiable



Chronological age

Chronological - Age

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

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

- **Heart Failure (HF) is a growing health and economic burden** for the United States, **in large part because of the aging population**.

- **Although the absolute number of patients with HF has partly grown as a result of the increasing number of older adults, the incidence of HF has decreased.**

- **Divergent trends in the incidence** of HF have been observed for those with **HFrEF** (**decreasing** incidence) and **HFpEF** (**increasing** incidence).

References: Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032

Chronological - Age

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

- In developed countries, **the age adjusted incidence of HF maybe falling**, presumably reflecting better management of CV disease, but **due to ageing, the overall incidence is increasing.**

- **The prevalence increases with age**: from around 1%f or those aged < 55 years to **> 10% in those aged 70** years or over

- **Due to population growth, ageing, and the increasing prevalence of comorbidities, the absolute number of hospital admissions for HF is expected to increase** considerably in the future

- **HFpEF patients** are older and more often female

References: Theresa A McDonagh, Marco Metra, et al . 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726,

Chronological - Age

EPICA STUDY

- the **prevalence of CHF increases with age** in both sexes and tends to be slightly higher in men up to the age of 70, then it stabilises. **In women**, it continues to increase with age and becomes greater than the prevalence for men in the 70–79 years-old age group

PORTHOS
ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

- HF is a **syndrome associated with aging**, with a **prevalence of 31% in those over 70 years old**; in people between 50 and 59 years old it is 4%.

- **More than 90% of people are unaware of having the disease**, especially women, **those over 70** and patients with the form of **heart failure with preserved ejection fraction**.

References: Ceia, F. et al. Prevalence of chronic heart failure in Southwestern Europe: The EPICA study. *Eur. J. Heart Fail.* 2002, *4*, 531–539.; Baptista R et al. Portuguese Heart Failure Prevalence Observational Study (PORTHOS) rationale and design - A population-based study. Rev Port Cardiol. 2023 Dec;42(12):985-995

HF along Age

Pediatric heart failure:

Table 1 Etiology of pediatric heart failure.

Type of diseases	Pathophisiology	Examples
Congenital heart diseases	Left to right shunt (volume overload)	Ventricular septal defects Complete atrioventricular canal defects Patent ductus arteriosus Aorto–pulmonary windows
	Valvular regurgitation (volume overload)	Mitral regurgitation Aortic regurgitation
	Outflow tract obstruction (pressure overload)	Aortic stenosis Tunnel type subaortic stenosis Supravalvular aortic stenosis Pulmonary stenosis Pulmonary vein stenosis
	Coronary insufficiency (decreased O_2 supply to cardiomyocyte)	Coronary artery anomalies
Cardiomyopathies (inherited or acquired)	Systolic dysfunction (low cardiac output) Diastolic dysfunction (elevated pulmonary capillary pressure)	Dilated cardiomyopathy · Myocarditis · Barth syndrome · Carnitine deficency · Familial dilated cardiomyopathy · Neuromuscular disorder (i.e., Becker dystrophy/ Duchenne dystrophy) Hypertrophic cardiomyopathy · Pompe diseases · Noonan syndrome · Maternal diabetes · Mitochondrial diseases · Familial hypertrophic cardiomyopathy Idiopathic restrictive cardiomyopathy
Arrhythmias	Systolic dysfunction (low cardiac output)	Tachycardia induced cardiomyopathy · Atrio–ventricular node reentry tachycardia · Atrio–ventricular reentry tachycardia · Ectopic atrial tachycardia Congenital third degree atrio–ventricular block
Infection	Systolic dysfunction	Sepsis induced myocardial dysfunction
High output state	Volume overload	Thyrotoxicosis Systemic arteriovenous fistula Severe anemia

Although the **estimated incidence** of heart failure **is relatively low** at 0.9–7.4 per 100,000 children, it is a disease that **carries a high burden of morbidity and mortality**, with an in-hospital mortality rate of 7–26%.

In the modern era, **infants account for the majority (64%) of heart failure admissions in patients ≤18 years of age**.

The primary cardiac diagnosis at the time of admission is **congenital heart disease - CHDs** (69% - valvular, coronary, left to right shunts, outflow tract obstruction), followed by **arrhythmias** (12–15% - tachy or congenital 3rd degree atrio-ventricular block), **cardiomyopathy** (13–14%- inherited or acquired), and **myocarditis** (~2%).

Other causes are: hight output states (like hyrotoxicosis, systemic AV fistula, severe anemia), infectious and inflammatory diseases, oncologic processes, metabolic syndromes, renal failure, and malnutrition

References: Daniele et al. Pediatric Heart Failure: A Practical Guide to Diagnosis and Management Masarone, Pediatrics & Neonatology, Volume 58, Issue 4, 303 – 312; Masarone D, et al Pediatric Heart Failure: A Practical Guide to Diagnosis and Management. Pediatr Neonatol. 2017 Aug;58(4):303-312.; Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.

HF along Age

At birth – fetal **cardiomyopathies** or **extracardiac conditions** (such as sepsis, hypoglycaemia, and hypocalcaemia)

In the **1st week** - **CHDs with ductus-dependent systemic circulation** (such as severe aortic stenosis/aortic coarctation and hypoplastic left heart syndrome), in which the closure of the ductus arteriosus causes severe reduction of end-organ perfusion, are the main cause.

In the **1st month** of life - **CHDs with left to right shunt** (such as ventricular septal defects, patent ductus arteriosus, and aorto-pulmonary windows), in which pulmonary blood flow progressively increases with the fall of pulmonary resistance.

In **adolescence and young adults** HF is rarely secondary to CHDs, but is more often related to **cardiomyopathies** or **myocarditis**

References: Daniele et al. Pediatric Heart Failure: A Practical Guide to Diagnosis and Management Masarone, Pediatrics & Neonatology, Volume 58, Issue 4, 303 – 312; Masarone D, et al Pediatric Heart Failure: A Practical Guide to Diagnosis and Management. Pediatr Neonatol. 2017 Aug;58(4):303-312.; Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.

HF along Age

Given the relative rarity of heart failure in pediatrics, and the heterogeneity of this population, there has been a **paucity of clinical trials** that have been performed primarily in pediatric patients. As a result, **clinical guidelines for the treatment of pediatric heart failure have historically been reliant on expert consensus, and the extrapolation of data from trials performed in adults.**

References: Daniele et al. Pediatric Heart Failure: A Practical Guide to Diagnosis and Management Masarone, Pediatrics & Neonatology, Volume 58, Issue 4, 303 – 312; Masarone D, et al Pediatric Heart Failure: A Practical Guide to Diagnosis and Management. Pediatr Neonatol. 2017 Aug;58(4):303-312.; Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.

HF along Age

Vecteezy

Young Adults:

- **increase of HF incidence in young adults (< 50 years old)** … differs from the general trend noted in older patients.

- **men seemed to be more vulnerable to premature HF than women** (new heart failure presenting during pregnancy - **PPCM**)

References: Lecoeur E, et al. Epidemiology of heart failure in young adults: a French nationwide cohort study. Eur Heart J. 2023 Feb 1;44(5):383-392. doi: 10.1093/eurheartj/ehac651. Erratum in: Eur Heart J. 2024 Jul 9;45(26):2335. doi: 10.1093/eurheartj/ehae187. PMID: 36452998; PMCID: PMC9890267

HF along Age

- **myocarditis–cardiomyopathy and IHD** were major **causes of HF admission**, with inverse probability trends according to age group (in the young population, and especially in young men, **ischaemic HF** was the predominant form of HF, and … data suggest that it is **progressively increasing:**

… it may reflect true epidemiological changes linked to **increased prevalence of cardio-metabolic risk factors** in young people

- the **young adults hospitalized for premature HF** also presented with **high rates** of major **modifiable risk factors for ischaemic HF,** including **obesity, dyslipidaemia, smoking, hypertension**, and **diabetes.**

The observed **proportion of re-hospitalization for HF or from any cause within 2 years** after the first HF event **is alarming**.

References: Lecoeur E, et al. Epidemiology of heart failure in young adults: a French nationwide cohort study. Eur Heart J. 2023 Feb 1;44(5):383-392. doi: 10.1093/eurheartj/ehac651. Erratum in: Eur Heart J. 2024 Jul 9;45(26):2335. doi: 10.1093/eurheartj/ehae187. PMID: 36452998; PMCID: PMC9890267

HF along Age

Elderly :

- **more than 10% in those aged 70** years or over have HF

- **HFpEF** patients are **older**

- **some of the comorbidities of HF are more common in the elderly:** arrhythmias and conduction disturbances (AF, pauses and atrioventricular block), stroke, frailty, sarcopenia, iron deficiency and anaemia, kidney dysfunction, arthritis, depression, … **They can:**

  … **limit the use of certain medications or compliance with non-pharmacological measures**

  … **promote the adoption of incorrect actions** (eg. self-administeredNSAIDs)

References: Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metra, et al . 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726,

HF along Age

- elderly tends to **have a greater burden of illness and longer survival time with the syndrome and/or diseases "causing HF"** (coronary disease, genetic or acquired cardiomyopathies such as **Amyloidosis**, DMC after cancer therapy, valvular disease (**aortic stenosis**, …), ...

- **have more frequently limitations in accessing pharmacological and non-pharmacological therapy:**

  … lower purchasing power, and more polypharmacy,

  … eg. exercise less frequently given the greater likelihood of physical limitations

References: Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metra, et al . 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726,

HF along Age

Elderly :

... due to his condition, less access to advanced HF therapies...

Secondary prevention
An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients who have recovered from a ventricular arrhythmia causing haemodynamic instability, and who are expected to survive for >1 year with good functional status, in the absence of reversible causes or unless the ventricular arrhythmia has occurred <48 h after a MI.[162–164]

Primary prevention
An ICD is recommended to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of an ischaemic aetiology (unless they have had a MI in the prior 40 days—see below), and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.[161,165]
An ICD should be considered to reduce the risk of sudden death and all-cause mortality in patients with symptomatic HF (NYHA class II–III) of a non-ischaemic aetiology, and an LVEF ≤35% despite ≥3 months of OMT, provided they are expected to survive substantially longer than 1 year with good functional status.[161,166,167]

Table 19. Indications and Contraindications to Durable Mechanical Support[37]

Contraindications:
Absolute
Irreversible hepatic disease
Irreversible renal disease
Irreversible neurological disease
Medical nonadherence
Severe psychosocial limitations
Relative
Age >80 y for destination therapy
Obesity or malnutrition
Musculoskeletal disease that impairs rehabilitation
Active systemic infection or prolonged intubation
Untreated malignancy
Severe PVD
Active substance abuse
Impaired cognitive function
Unmanaged psychiatric disorder
Lack of social support

References: Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metraet al. ESC Scientific Document Group , 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726

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HF along Age

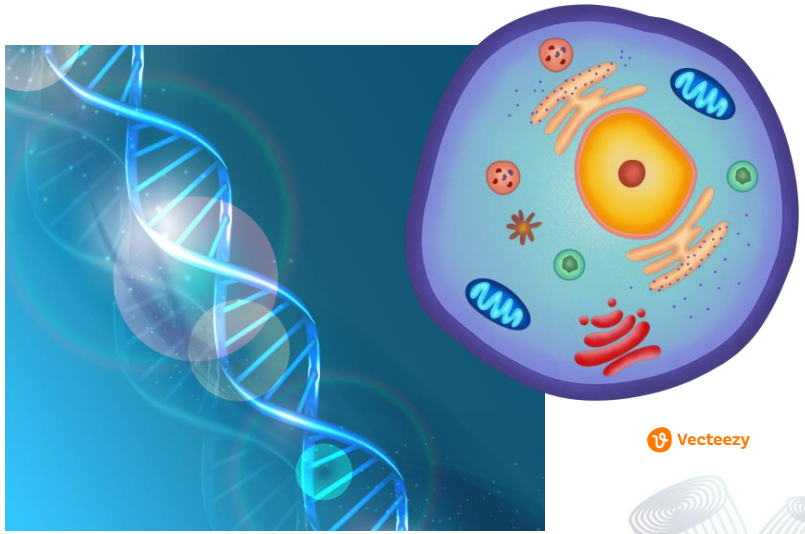
Elderly :

Older adults, especially **those aged 75 years and with multiple disabilities, are underrepresented** in most cardiovascular **clinical trials**, resulting in **knowledge gaps** related to cardiovascular care for this population

There is **great heterogeneity and biological diversity** in this population, which are independent of age

References: Lazzeroni D, Villatore A, Souryal G, Pili G, Peretto G. The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24):16033

Biological age



Biological - Aging

Although the **passage of time allows for greater exposure to known causes of HF** (eg, coronary artery disease**), it appears with age** **even in the absence of overt myocardial injury**,…

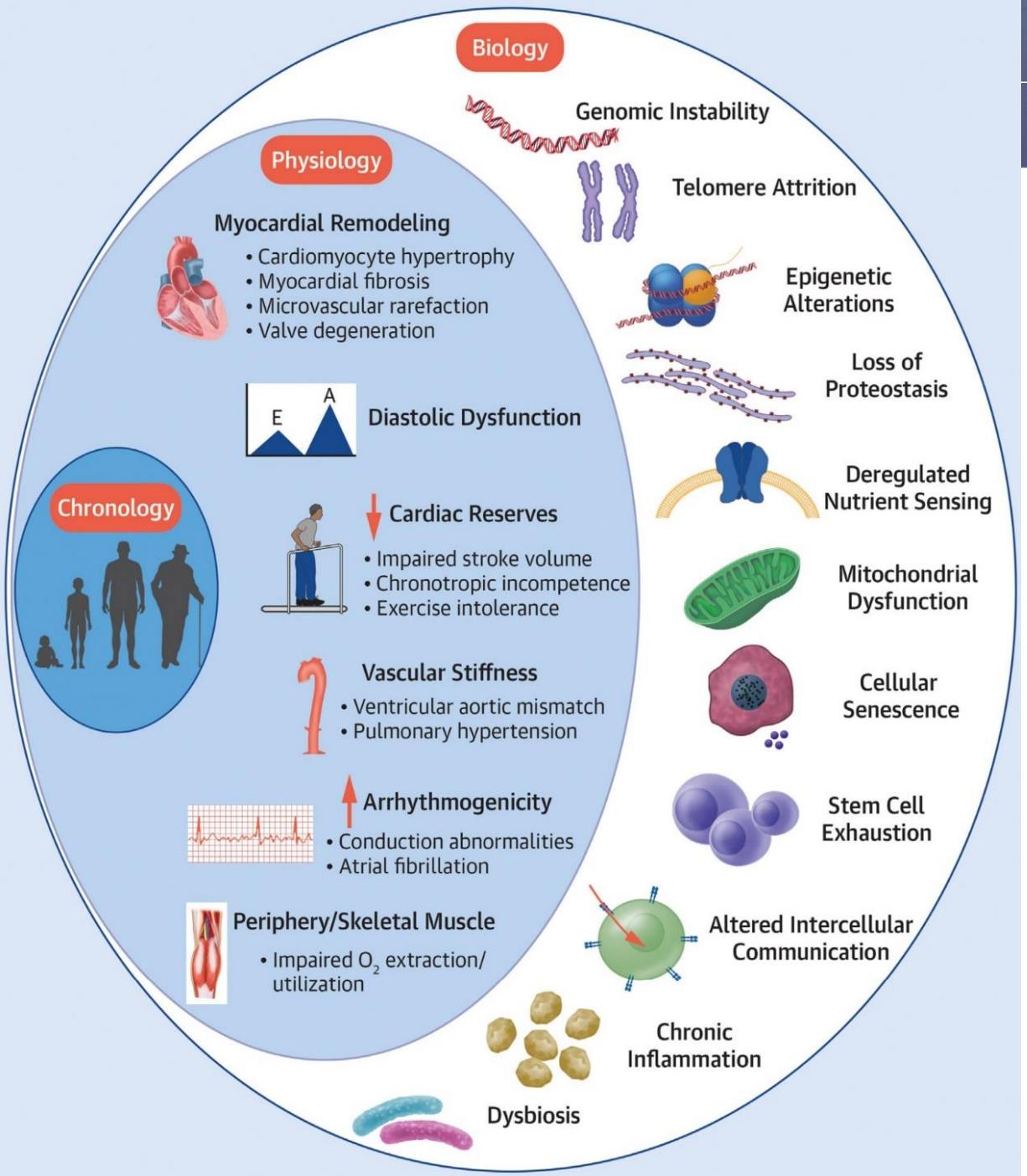
… **Biological Aging** **is the gradual deterioration of functional characteristics in living organism**

(this the **decline in intracellular quality control systems,** across all organ systems **does not "age" at the same rate**)

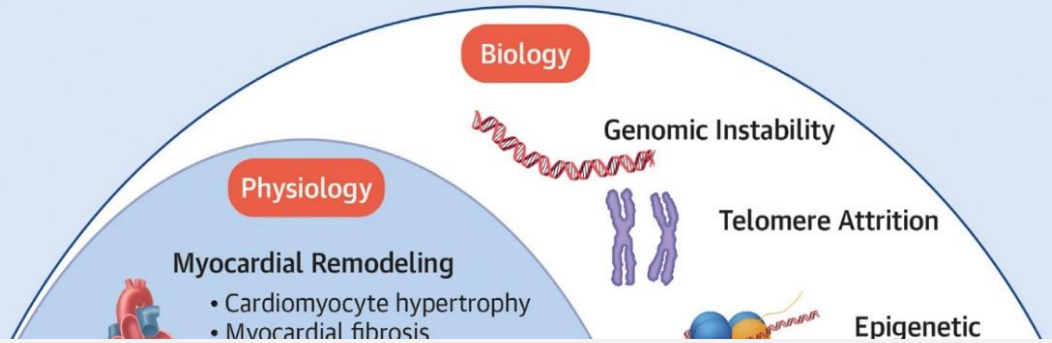
… **the aging cardiovascular system mirrors many of the phenotypes in HF**

References: Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809; Lazzeroni D, Villatore A, Souryal G, Pili G, Peretto G. The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24):16033.

Age – what



References: Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809.



Lopez-Otin et al published the first reports on the **"hallmarks of aging,"** where they described the **fundamental biological processes** that dictate organismal **aging**

…**all** of them are connected with complex interactions and interdependence and **all contribute to HF pathophysiology**:

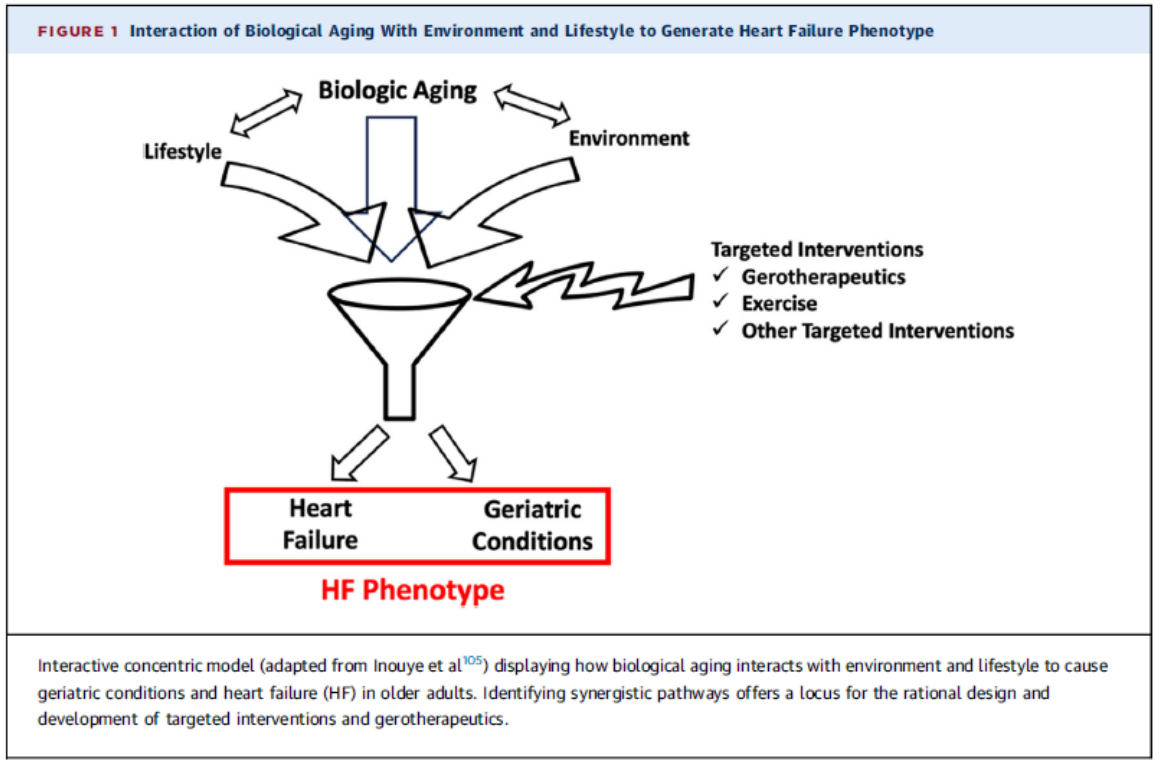
1. impaired proteostasis and autophgy (Amyloidosis, Sarcopenia)
2. mitochondria dysfunction: oxidative stress, metabolic reprogramming (Dementia, Frailty, Sarcopenia)
3. deregulated nutrient sensing (Cognitive impairment)
4. inflammation (Cachexia)
5. altered intercellular communication
6. telomere shortening
7. epigenetic alterations
8. cellular senescence
9. dysbiosis
10. stem cell exhaustion
11. Genomic instability
12. …

and also dependent of **lifestyle and environment factors**

References: Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809.

Biological - Aging

Several **geriatric conditions**, including malnutrition and cachexia, sarcopenia, frailty, and cognitive impairment, **coexist with HF** in part because of **shared mechanisms of dysregulated biological aging**

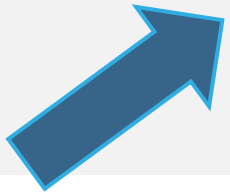


References: Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809. doi: 10.1016/j.jchf.2024.02.021.

Biological - Aging

Geriatric conditions complicate management in HF given their well-known associations with **adverse outcomes**, including **impaired quality of life**, **hospitalization**, and **reduced life expectancy** **even after adjustment for chronologic age.**

Frailty and **sarcopenia** are particularly important



References: Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809. doi: 10.1016/j.jchf.2024.02.021.

Biological age in HF

HF can accelerate Cardiac aging:

Heart failure promotes accelerated cardiac aging through several interconnected mechanisms:

1. **Increased Oxidative Stress**: HF leads to an overproduction of reactive oxygen species
2. **Inflammation**: chronic inflammation is a hallmark of heart failure leading to fibrosis and reduced heart function
3. **Mitochondrial Dysfunction**: energy deficits and increased oxidative stress
4. **Telomere Shortening**: a marker of cellular aging and can lead to cell death or dysfunction.
5. **Cellular Senescence**: cells stop dividing and release inflammatory factors
6. **Impaired Autophagy**: accumulation of damaged proteins and organelles, which accelerates aging

References: Shono, A., Matsumoto, K., Yamada, N. *et al.* "Accelerated aging" of the heart as heart failure with preserved ejection fraction—analysis using leg-positive pressure stress echocardiography. *Int J Cardiovasc Imaging* **37**, 2473–2482 (2021).; Li H, Hastings MH, Rhee J, et al, A. Targeting Age-Related Pathways in Heart Failure. Circ Res. 2020 Feb 14;126(4):533-551.; Lazzeroni D, Villatore A, et al The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24)

These mechanisms lead to:

1. **Structural Changes**: thickening, stiffening of the heart walls, which are also common in the natural aging process
2. **Impaired Function**: includes reduced cardiac reserve and impaired diastolic function.
3. **Increased risk of arrhythmias:** which can further damage the heart.

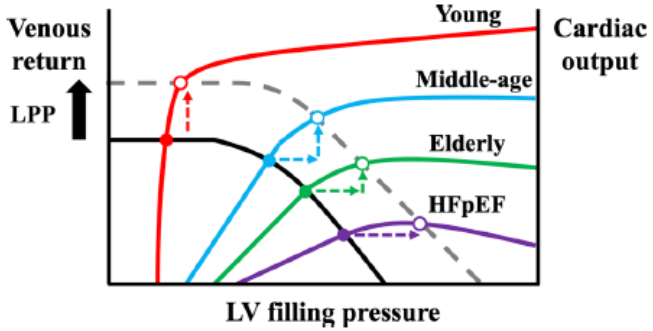


Fig. 3 Schematic presentation of the hemodynamic responses on the Guyton diagram for each subgroup during acute preload-increasing maneuver. The difference in hemodynamic responses to the increased preload according to age groupss and HFpEF are schematically presented in the Guyton diagram. *LPP* leg-positive pressure, *LV* left ventricular, *HFpEF* heart failure with preserved ejection fraction

These changes can lead to a decline in overall heart health and function…

These are the structural and hemodynamic are the **hallmarks of HFpEF**:

… concentric hypertrophy,

… diastolic abnormalities,

…delayed relaxation,

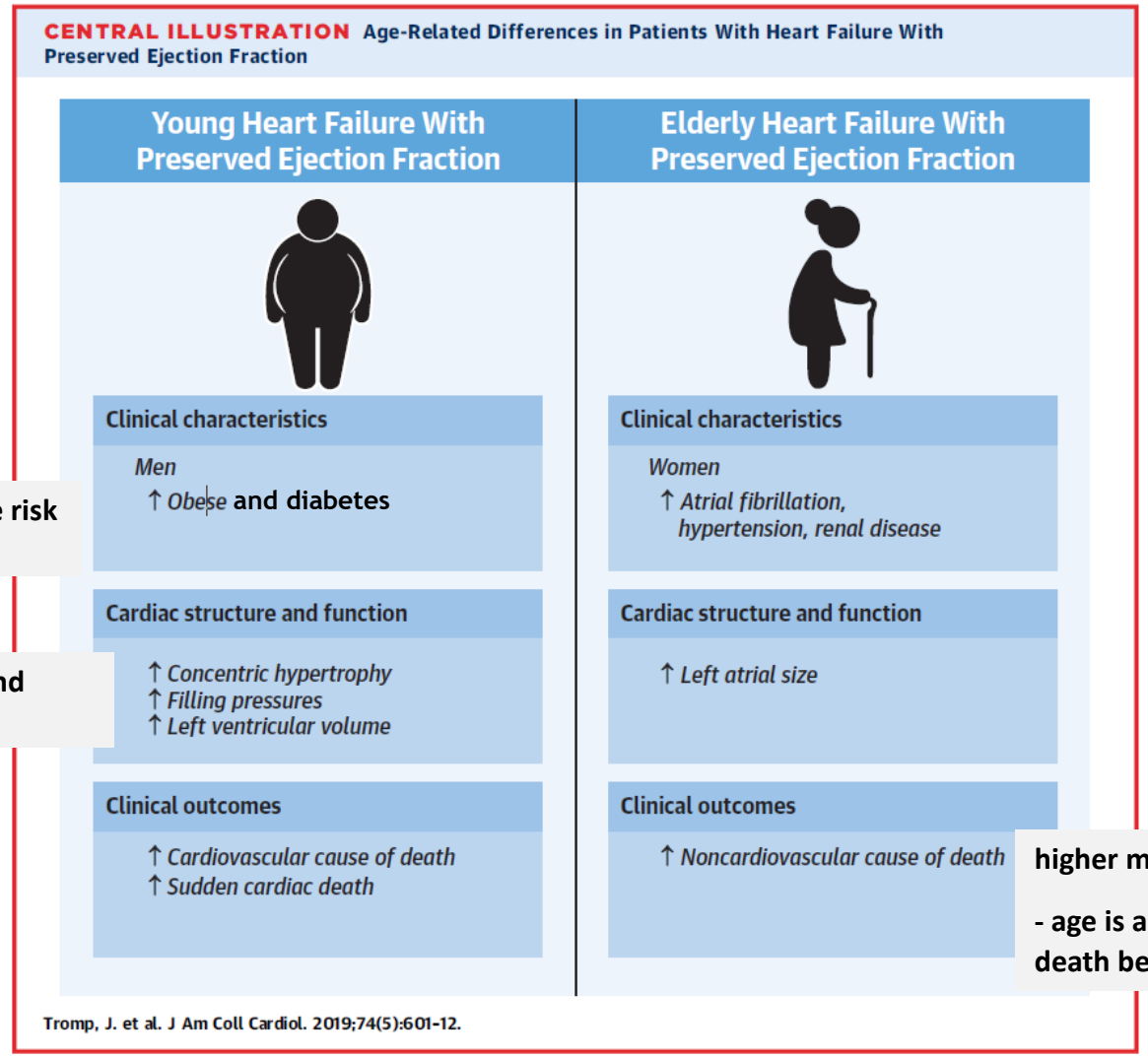
… myocardial stiffening

,… impairment of filling dynamics.

References: Shono, A., Matsumoto, K., Yamada, N. *et al.* "Accelerated aging" of the heart as heart failure with preserved ejection fraction—analysis using leg-positive pressure stress echocardiography. *Int J Cardiovasc Imaging* **37**, 2473–2482 (2021).; Li H, Hastings MH, Rhee J et al, Targeting Age-Related Pathways in Heart Failure. Circ Res. 2020 Feb 14;126(4):533-551.; Lazzeroni D, Villatore A, Souryal G, et al, The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24)

HFpEF

CENTRAL ILLUSTRATION Age-Related Differences in Patients With Heart Failure With Preserved Ejection Fraction



Tromp, J. et al. J Am Coll Cardiol. 2019;74(5):601-12.

Derangements following diabetes might be a possible risk factor for developing HFpEF at a younger age

less objective evidence of fluid overload and were less often treated with diuretic

higher mortality rates:

- age is an important predictor of non-CV death because of higher comorbidity burden ?

References: Tromp J, Shen L, Jhund PS, et al, Age-Related Characteristics and Outcomes of Patients With Heart Failure With Preserved Ejection Fraction. J Am Coll Cardiol. 2019 Aug 6;74(5):601-612)

How can we be more personalized in care and have an early approach to HF in terms of age?

REMEMBE
R

AGE and AGING

How can we be more personalized in care and have an early approach to HF in terms of age?

Table 10 Risk factors for the development of heart failure and potential corrective actions

Risk factors for heart failure	Preventive strategies
Sedentary habit	Regular physical activity
Cigarette smoking	Cigarette smoking cessation
Obesity	Physical activity and healthy diet
Excessive alcohol intake[286]	General population: no/light alcohol intake is beneficial Patients with alcohol-induced CMP should abstain from alcohol
Influenza	Influenza vaccination
Microbes (e.g. *Trypanosoma cruzi*, Streptococci)	Early diagnosis, specific antimicrobial therapy for either prevention and/or treatment
Cardiotoxic drugs (e.g., anthracyclines)	Cardiac function and side effect monitoring, dose adaptation, change of chemotherapy
Chest radiation	Cardiac function and side effect monitoring, dose adaptation
Hypertension	Lifestyle changes, antihypertensive therapy
Dyslipidaemia	Healthy diet, statins
Diabetes mellitus	Physical activity and healthy diet, SGLT2 inhibitors
CAD	Lifestyle changes, statin therapy

CAD = coronary artery disease; CMP = cardiomyopathy; SGLT2 = sodium-glu-

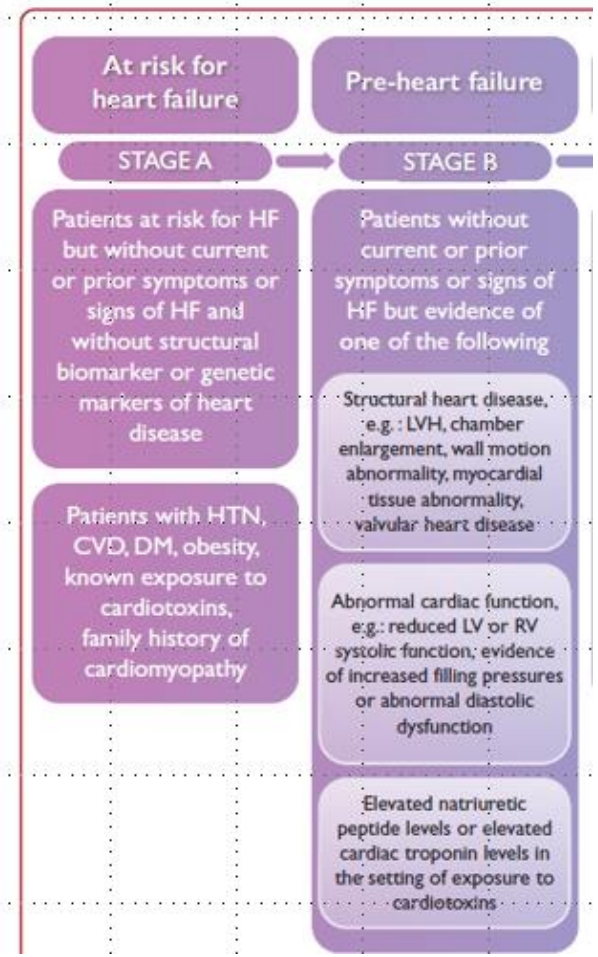
Firstly – prevention:

… promote healthy life style habits: diet, regular exercise, healthy weight management, limit Alcohol and quit Smoking:

… **treat** adequately the most important **risk factors for the onset of HF**, such as diabetes, hypertension and obesity, excessive alcohol intake, coronary heart disease, …

References: Theresa A McDonagh, Marco Metraet al. ESC Scientific Document Group , 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726

How can we be more personalized in care and have an early approach to HF in terms of age?



Second – high suspicion and early diagnosis:

… think about at-risk populations, particularly individuals **over 50**, but also **children** where diagnosis can sometimes be challenging (“the primary presenting complaints are often respiratory and/or gastrointestinal symptoms that can mimic more common pediatric illnesses, leading to incorrect and/or late diagnoses…”) ...

… identify early individuals with subclinical or symptomatic cardiac pathology that could develop into heart failure;

Primary Care plays a fundamental role in the **early referral** of patients with strong diagnostic suspicion to **specialized HF Units/Consultations** so that the most improved etiological study can be carried out quickly:
... **in Portugal**, access to NTproBNP and echocardiography determine the initial approach

References: Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.; Theresa A McDonagh, Marco Metraet et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726

How can we be more personalized in care and have an early approach to HF in terms of age?

After diagnosis treat well to slow progression and anticipate exacerbations:

… **early institution and optimization of guideline-recommended therapy** (this is **a challenge for children**, given the rarity of heart failure in pediatrics and the heterogeneity of this population, leading to a lack of clinical trials in this population and also in the **Elderly**)

AHA/ACC/HFSA CLINICAL PRACTICE GUIDELINE

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

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure

References: Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.; Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metraet et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726.

How can we be more personalized in care and have an early approach to HF in terms of age?

After diagnosis treat well to slow progression and anticipate exacerbations:

… **Team Work** - **Primary Health Care vs Hospital HF Units**, with patients moving between the two types of care according to their need and complexity is the ideal scenario:

- **in the stabilization phase of the Syndrome, the role of Primary Health Care is vital to reinforce non-pharmacological measures**, namely vaccination, weight loss, strengthening the importance of exercise, supervine compliance with therapy and optimization according to the guidelines; treating co-morbidities, give psychosocial support, …

- **facilitate the access to care** in **decompensation**

- **pay attention to self-care …**

References: Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.; Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metraet et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726.

How can we be more personalized in care and have an early approach to HF in terms of age?

Self-care:

- Many health and social factors are associated with poor HF self-care:

… Depression

… Frailty

… Social isolation.

… poor Social support

… inadequate/marginal Health literacy

… Cognitive impairment

… Homelessness or housing insecurity

… These are more common in the elderly

References: Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metraet et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726.

How can we be more personalized in care and have an early approach to HF in terms of age?

Some age groups have particularities:

… **Children -** there is a lack of randomized clinical trials and international guidelines and optimal therapeutic

… **Young adults -** pregnancy, job, hobbies (travel, sports,...) family/small children

… **Elderly**

…

References: Ahmed H, VanderPluym C. Medical management of pediatric heart failure. Cardiovasc Diagn Ther. 2021 Feb;11(1):323-335.; Heidenreich PA, Bozkurt B, Aguilar D, 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:e895-e1032; Theresa A McDonagh, Marco Metraet et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: Developed by the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) With the special contribution of the Heart Failure Association (HFA) of the ESC, *European Heart Journal*, Volume 42, Issue 36, 21 September 2021, Pages 3599-3726. ; https://www.heartfailurematters.org/

Age – what is the pathway to a personalized and early apporach?

Elderly

TABLE 4 Strategies and Potential Interventions for Managing Geriatric Conditions

Geriatric Condition	Strategies for Enhanced Care Provision	Interventions Requiring Additional Study
Malnutrition	• Referral to dietitian/nutritionist • Consideration of nutritional supplements • Dietary recommendations (eg, increasing caloric intake and/or liberalizing dietary restrictions) • Assessment of external factors that may be contributing to malnutrition (eg, financial means, taste, dental issues, social support)	• Dietary modifications • Nutritional/caloric supplementation • Combining nutritional interventions with exercise • Home-delivered meals • Micronutrient supplementation
Cachexia	• Consideration of nutritional supplements • Dietary recommendations (eg, increasing caloric intake and/or liberalizing dietary restrictions) • Consideration for palliative care	• Treatment of underlying causes such as heart failure and other comorbid conditions • Appetite stimulants • Dietary modifications • Nutritional/caloric supplementation
Sarcopenia	• Referral to physical and/or occupational therapy; provision of exercise prescription • Exercise and resistance training • Reassessment of prognosis and risk-benefit ratio of management options	• Treatment of underlying causes such as heart failure (eg, effect of GDMT) and other comorbid conditions • Nutritional/caloric supplementation • Resistance exercise training • Testosterone replacement
Frailty	• Reassessment of prognosis and risk-benefit ratio of management options • Emphasis on lifestyle recommendations such as exercise (home programs, cardiac rehabilitation programs, and strength-training) and nutrition	• Exercise
Cognitive impairment	• Engagement of social support (caregivers, family), services • Referral for formal assessment and/or discussion with other clinicians (geriatrics and/or memory center) • Reassessment of health goals/priorities • Reassessment of prognosis and risk-benefit ratio of management options (especially related to medications) • Consideration of novel agents to treat early Alzheimer dementia if present • Consideration for palliative care	• Treatment of underlying causes such as heart failure and other comorbid conditions • Exercise

GDMT = guideline-directed medical therapy.

References Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809av

Age – what is the pathway to a personalized and early apporach?

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GDMT = guideline-directed medical therapy.

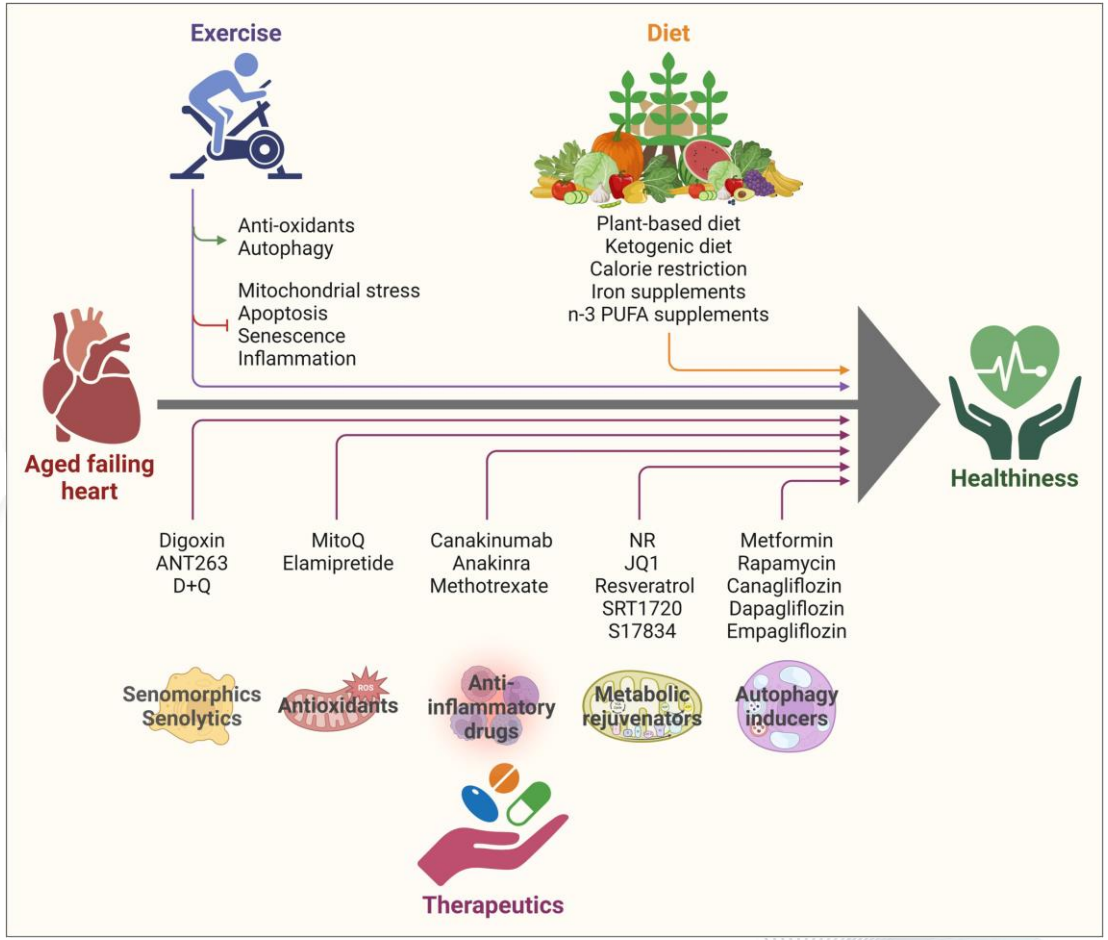
Adopting a patient-centered-approach, which considers individual comorbidities, life expectancy, cognitive function, frailty, and patient preferences, is critical for establishing the optimal management strategy

References Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809av; Lazzeroni D, Villatore A, Souryal G, Pili G, Peretto G. The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24):16033

How can we be more personalized in care and have an early approach to HF in terms of age?

In the Biological age:

Pre-clinical and clinical research
demonstrates that dietary restriction with adequate intake of specific nutrients, as well as
regular exercise, stress management, and smoking cessation, are effective ways to prevent
or delay the accumulation of molecular damage that results in tissue degeneration and
cardiometabolic dysfunction



References Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809av; Fang Z, Raza U, et al. Systemic aging fuels heart failure: Molecular mechanisms and therapeutic avenues. ESC Heart Fail. 2024 Jul 22; Lazzeroni D, Villatore A, Souryal G, Pili G, Peretto G. The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24):16033

How can we be more personalized in care and have an early approach to HF in terms of age?

- Exercise:

… Physical activity regular and moderate promotes beneficial adaptations, **affecting all hallmarks of aging and enhancing resiliency in essentially every organ system** not only **attenuates or reverses many of the cardiac phenotypes associated with aging**, but it also **improves the cellular mechanism associated to cellular decline** like inflammation, mitochondrial function, proteostasis, metabolism, epigenetic alterations, telomerase activity, and even had **regenerative potential of the heart**

- Amiloidosis Therapeutics
- omega-3 and omega-6 polyunsaturated FAs (PUFAs), Coenzyme Q10,
- metformin
- canakinumab,
- anakinra, colchicine, methotrexate, infliximab
- pirfinidona
- empaglifozin
- …

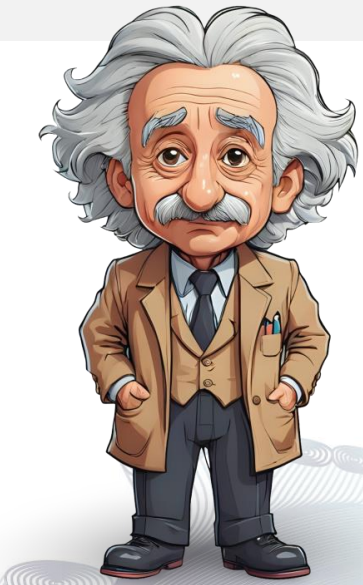
References Goyal P, Maurer MS, Roh J. Aging in Heart Failure: Embracing Biology Over Chronology: JACC Family Series. JACC Heart Fail. 2024 May;12(5):795-809av

Take-Home Messages

Chronological age is immutable but is accompanied by problems, sometimes characteristic of each stage of life, which can be intervened on …

Biological age is susceptible to interventions designed to slow the process of cellular and tissue degradation... but there is still a long way to go...

molecular damage that results in tissue d
With the growing impact of aging, it is essential to reassess CV research, including the increased use of real-world studies to measure long-term effects. Clinical decision-making should integrate molecular and genetic indicators, pointing to personalized therapy. Remarkably, the identification of new molecular targets, as well as improved clinical characterization of older patients, may enhance knowledge and therapy f the aging heart.



References Lazzeroni D, Villatore A, Souryal G, Pili G, Peretto G. The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24):16033

7th Advances in Heart Failure 2024
10 e 11 de Outubro

Age - what is the pathway to a personalized and early apporach?

ELSEVIER
Ageing Research Reviews
Volume 9, Supplement, November 2010, Pages S59-S66

Review

microRNA and aging: A novel modulator in regulating the aging network

Li-Hsin Chen [a c 1], Guang-Yuh Chiou [a d 1], Yi-Wei Chen [a d 1], Hsin-Yang Li [b d], Shih-Hwa Chiou [a c d]

Review | Open access | Published: 24 April 2023

A state-of-the-art review on the MicroRNAs roles in hematopoietic stem cell aging and longevity

Geovanny Genaro Reivan Ortiz, Yasaman Mohammadi, Ahmad Nazari, Mehrnaz Ataeinaeini, Parisa Kazemi Saman Yasamineh, Bashar Zuhair Talib Al-Naqeeb, Haider Kamil Zaidan & Omid Gholizadeh

Cell Communication and Signaling **21**, Article number: 85 (2023) | Cite this article

Hum Genet. 2020 March ; 139(3): 291–308. doi:10.1007/s00439-019-02046-0.

MicroRNAs as modulators of longevity and the aging process

Holly E Kinser[1], **Zachary Pincus**[2]

[1]Department of Biomedical Engineering, Washington University in St. Louis

[2]Department of Developmental Biology and Department of Genetics, Washington University in St. Louis

Abstract

MicroRNAs (miRNAs) are short, non-coding RNAs that post-transcriptionally repress translation or induce mRNA degradation of target transcripts through sequence-specific binding. miRNAs target hundreds of transcripts to regulate diverse biological pathways and processes, including aging. Many microRNAs are differentially expressed during aging, generating interest in their use as aging biomarkers and roles as regulators of the aging process. In the invertebrates *C. elegans* and *Drosophila*, a number of miRNAs have been found to both positive and negatively modulate longevity through canonical aging pathways. Recent studies have also shown that miRNAs regulate age-associated processes and pathologies in a diverse array of mammalian tissues, including brain, heart, bone, and muscle. The review will present an overview of these studies, highlighting the role of individual miRNAs as biomarkers of aging and regulators of longevity and tissue-specific aging processes.

Review | J Int Med Res. 2024 Oct;52(10):3000605241279190. doi: 10.1177/03000605241279190.

Impact of microRNAs on cardiovascular diseases and aging

Md Sayed Ali Sheikh [1], Umme Salma [2]

Affiliations + expand

PMID: 39370977 DOI: 10.1177/03000605241279190

Free article

Abstract

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality for both men and women among all ethnicities worldwide. Although significant improvements in the management of CVD occurred in the 20th century, non-invasive, universal, early diagnostic biomarkers and newer therapeutic drugs are needed for clinical treatment by physicians. MicroRNAs (miRNAs) are a class of endogenous, non-coding, single-stranded, small RNA molecules that are critically controlled by all human biological processes. Moreover, dysregulated miRNA expression is directly involved in various CVDs, including stable coronary artery disease and acute coronary syndrome. Several miRNAs that are enriched in the plasma of CVD patients have potential as clinical biomarkers, and overexpression or inhibition of specific miRNAs has novel therapeutic significance in the management of CVD. Aging is a multifactorial physiological process that gradually deteriorates tissue and organ function and is considered a non-modifiable major risk factor for CVDs. Recently, several studies established that various miRNAs essentially regulate aging and aging-related disease processes. This narrative review briefly discusses the recently updated molecular involvement of miRNAs in CVDs, their possible diagnostic, prognostic, and therapeutic value, and their relationship to the aging process.

Keywords: Cardiovascular disease; aging; diagnosis; microRNA; prognosis; therapeutic.

Victor Ambros e Gary Ruvkun – foto REUTERS – Ken McGagh

International Journal of Molecular Sciences

Review

The Aging Heart: A Molecular and Clinical Challenge

Davide Lazzeroni [1], Andrea Villatore [2,3], Gaia Souryal [2], Gianluca Pili [2] and Giovanni Peretto [2,3,*]

- **MicroRNAs**

microRNAs (miRNAs) are involved in the aging process and help to regulate many mechanisms underlying cardiac changes in the elderly [17]. Aging is specifically associated with an increased expression of miR-34a, which is caused by an upregulation of p53 signaling. Indeed, the miR-34 family induces apoptosis, which emphasizes the central role of miR-34a in the mechanisms underlying aging [18]. Moreover, in aged cells, a reduced amount of miR-146a is found. MiR-146a reduces oxidative stress by downregulating the expression of NOX4, which is the major catalytic subunit of NADPH oxidase [19]. Some miRNAs, including the senescence-associated miR-17-92 cluster, have been shown to inhibit apoptosis [20]. Finally, the expression of miR-17, which is reduced by hypoxia, causes a downregulation of Casp9 and apoptotic protease-activating factor 1 (Apaf-1) [21].

- **MicroRNAs inhibition**

MiR-217 is a biomarker of vascular aging and cardiovascular risk, as it regulates an endothelial signaling hub and downregulates a network of eNOS, including VEGF, which results in diminished eNOS expression [184]. A recent study by De Yebénes et al. [184] found out that the inhibition of endogenous vascular miR-217 in apoE$^{-/-}$ mice improved vascular contractility and diminished atherosclerosis, highlighting the therapeutic potential of miR-217 inhibitors.

Circulation Research

REVIEW

Targeting Age-Related Pathways in Heart Failure

Haobo Li, Margaret H. Hastings, James Rhee, Lena E. Trager, Jason D. Roh, Anthony Rosenzweig

MicroRNAs (miRNAs) are endogenous small ncRNAs, approximately 22 nucleotides long that work as post-transcriptional regulators by binding to complementary sequences of messenger RNAs (mRNAs) to inhibit mRNA translation or to promote mRNA degradation.[154] A number of miRNAs have been found to have pathophysiological roles in HF. In a screen for 380 miRNAs in cardiomyocytes, miRNA (miR)-22 was identified as an abundant and strong inhibitor of cardiac autophagy, whose expression level increased during aging in mice in vivo and in cardiomyocytes in vitro by a p53-dependent mechanism.[155] Pharmacological

References Lazzeroni D, Villatore A, Souryal G, Pili G, Peretto G. The Aging Heart: A Molecular and Clinical Challenge. Int J Mol Sci. 2022 Dec 16;23(24):16033; Li H, Hastings MH, Rhee J, Trager LE, Roh JD, Rosenzweig A. Targeting Age-Related Pathways in Heart Failure. Circ Res. 2020 Feb 14;126(4):533-551

Muito obrigada pela vossa atenção!