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CONSENSUS DOCUMENT
Aging

Frailty in cardiology: definition, assessment and clinical implications for general cardiology. A consensus document of the Council for Cardiology Practice (CCP), Association for Acute Cardio Vascular Care (ACVC), Association of Cardiovascular Nursing and Allied Professions (ACNAP), European Association of Preventive Cardiology (EAPC), European Heart Rhythm Association (EHRA), Council on Valvular Heart Diseases (VHD), Council on Hypertension (CHT), Council of Cardio-Oncology (CCO), Working Group (WG) Aorta and Peripheral Vascular Diseases, WG e-Cardiology, WG Thrombosis, of the European Society of Cardiology, European Primary Care Cardiology Society (EPCCS)

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Abstract

Frailty is a health condition leading to many adverse clinical outcomes. The relationship between frailty and advanced age, multimorbidity and disability has a significant impact on healthcare systems. Frailty increases cardiovascular (CV) morbidity and mortality both in patients with or without known CV disease. Though the recognition of this additional risk factor has become increasingly clinically relevant in CV diseases, uncertainty remains about operative definitions, screening, assessment, and management of frailty. Since the burdens of frailty components and domains may vary in the various CV diseases and clinical settings, the relevance of specific frailty-related aspects may be different. Understanding these issues may allow general cardiologists a clearer focus on frailty in CV diseases and thereby make more tailored clinical decisions and therapeutic choices in outpatients. Guidance on identification and management of frailty are sparse and an international consensus document on frailty in general cardiology is lacking. Moreover, new options linked with eHealth are going to better define and manage frailty. This consensus document on definition, assessment, clinical implications, and management of frailty provides an input to integrate strategies pre- and post-acute CV events with a comprehensive view including out of hospital, office-based diagnostic and therapeutic choices, and based on a multidisciplinary team approach (general cardiologists, nurses, and general practitioners).

Keywords

Frailty • Frailty in cardiovascular diseases • Multimorbidity • Disability • Frailty domains • Frailty components • Frailty evaluation • Frailty screening • Frailty assessment • Frailty trajectory • Frailty prevention • Frailty management • Rehabilitation • Nutrition • Frailty digital health

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Introduction

Ageing leads to pathophysiological changes, the coexistence of several pathological conditions, malnutrition and inactivity, producing a negative impact on health status. These changes, often combined with poor socioeconomical factors, may lead to the development of frailty, which is characterized by a decreased physiologic reserve and ability to maintain homeostasis leading to increased vulnerability to stressors and increased risk of adverse health outcomes.[1,2]

The frailty status is attracting increasing attention due to population ageing, its major implications for clinical practice, the opportunity to contrast an accelerated clinical decline, and the magnitude of impact on healthcare systems.[3] For these reasons in cardiology practice, frailty evaluation deserves to be included as part of the general elderly clinical assessment.[4–7]

A recent position paper from the Acute Cardiovascular Care Association (ACCA) of the European Society of Cardiology (ESC)[8] analysed the impact of frailty on patients mainly in the acute cardiac and critical care setting. Moreover, a document from the Heart Failure Association (HFA) of the ESC focused on frailty as a relevant clinical aspect in complex patients with heart failure (HF).[9]

However, much of cardiac patients' management takes place in an elective care setting and this allows greater scope for pre-assessment and improvement of frail patients' physiological status, prior to any treatment, procedure or intervention.

Therefore, the aim of our paper is to integrate strategies both pre- and post-acute cardiovascular (CV) events, to develop a comprehensive view, encompassing out of hospital, office-based diagnostic and therapeutic choices, and based on a multidisciplinary team approach (general cardiologists, nurses, and general practitioners). This approach should allow the development of a structured management plan, identifying the best treatment for the main CV conditions, but also including home care and social support to family and community levels and the possible use of options/devices linked to e-health technology.

Definitions of frailty, multimorbidity, disability

The multifaceted dynamics between underlying physiological changes, chronic diseases, and simultaneous presence of various pathological conditions can result in health states in older ages that are not captured by traditional disease classifications, and that are commonly known as geriatric syndromes.[10] Disease-based conceptualization may be an inadequate proxy for health in elderly subjects. Rather than the presence or absence of a disease, the most important consideration for older people is likely to be the comprehensive assessment of their functioning.[10]

Various definitions of frailty have been proposed to identify and quantify this complex condition. Frailty has been defined as a loss of functionality leading to an increased vulnerability to adverse stress and health events or as a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance and reduced physiologic function that increases an individual's vulnerability for independency, loss and/or death.[1,11]

McDonagh defined it as a multidimensional syndrome with increased vulnerability to acute stressors, such as hospitalization, falls and infection,[12] whereas in the Frailty Operative Definition-Consensus Conference Project[13] the Experts agreed on a more comprehensive definition of frailty including the assessment of physical performance, gait speed and mobility, nutritional status, mental health, and cognition.

Frailty contributors derive from cellular and system physiology alterations, including sarcopenia, reduced nutritional intake, and low physical activity, in addition to associated CV and non-CV chronic diseases.[14]

Recently, neuropsychiatric status, including cognitive impairment and depression, alcohol consumption, and social conditions such as social isolation and loneliness have been shown to contribute to frailty.[15–19]

Comorbidity and disability

Multimorbidity or comorbidity (i.e. the concurrent presence of two or more medically diagnosed diseases in the same individual) are frequently associated with frailty and closely related to ageing[20–24] and disability (i.e. difficulty or dependency in carrying out activities essential to independent living, including self-care tasks, living independently at home, and important desired activities for quality of life—QoL).[25] Therefore, although frailty is a distinct condition overlaps with both comorbidity and disability. Indeed, both frailty and comorbidity predict disability.[25] However, some patients present with frailty alone (e.g. a young homeless person with excess of alcohol assumption and cardiomyopathy) or only multimorbidity (a compensated HF patient with treated diabetes and hypertension) or only disability (a young paraplegic person participating in the Paralympics games) (*Box 1*).

Frailty components and domains

During clinical evaluation, the identification of the main components leading to a clinically relevant frail condition or to the loss of self-care in the individual patient can direct the healthcare team towards the unique needs and the personalized solutions for the subject (*Figure 1*). The burdens of frailty components found at clinical evaluation may be related to the specific settings and purpose of the evaluation. For example, older patients evaluated during hospitalization for acute events or in geriatric communities may more frequently present with social frailty or advanced cognitive impairment than subjects presenting in a cardiology out-patient clinic who are being evaluated for an elective procedure. In the latter patients, the physical frailty burden or multimorbidity may be more relevant for interventional choices.

Various domains of frailty including a medical domain, a physical domain, a cognitive/depressive status domain and a social domain have been identified in the assessment of patients for interventions.[26]

Inclusion of frailty measures in diagnostic algorithms might allow healthcare providers to increase risk prediction capability and

Box 1. Definitions.

FRAILTY:
Multidimensional and multisystem condition characterized by decreased functional reserves and increased vulnerability to stress and acute adverse events.
This condition, a complex system behavior of components, can be described according to:
a) peculiar genesis, including accumulation of damages and dysregulations,
b) peculiar phenotype including physical, nutritional, cognitive/psychological and social aspects, and
c) adverse health-related outcomes

MULTIMORBIDITY:
Concurrent presence of two or more medically diagnosed diseases in the same individual, closely related with ageing

DISABILITY:
Difficulty or dependency in carrying out activities essential for daily living, including tasks needed for self-care and living independently

OVERLAPPING CONDITIONS:
Ageing is associated with frailty, multimorbidity and disability and the three conditions are largely overlapping.

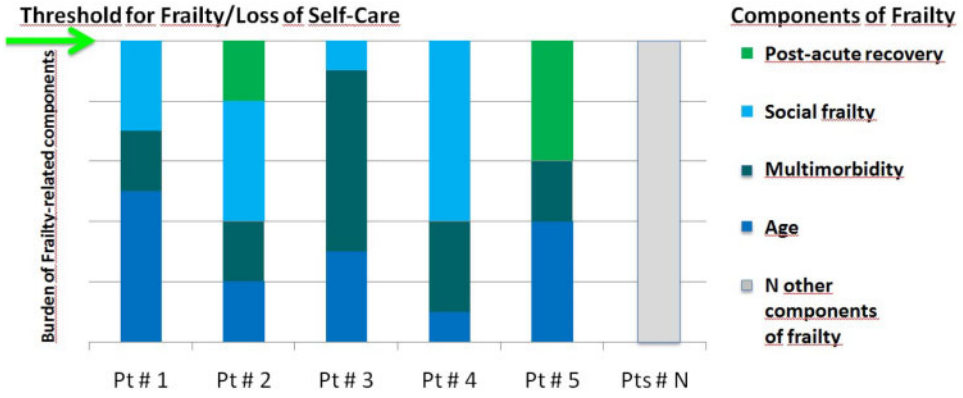

Figure 1 Components of frailty that contribute to reach a frailty status. In subjects who reach the threshold for frailty, the burden of various components is expressed differently. The figure exemplifies how common frailty-related conditions occur differently in frail patients (Pts) to determine the threshold for frailty or loss of self-care and how other numerous (*N*) potential frailty components may be present in other *N* Pts.

thereby make better-founded decisions with more efficient use of healthcare resources, whereas instruments that can disentangle single components of frailty domains would be useful to tailor specific interventions in each patient.

It is important to note that frailty is a dynamic phenomenon, with the possibility of partial restoration of functional independence after temporary disability to a frail or pre-frail individual, depending on the main component leading to loss of self-care. For instance, hospitalization for infection or HF can precipitate a disability status that can be partly reversed after a few weeks of increased family support, whereas installing of long-term social support may be useful in a patient presenting with a high degree of social frailty. Indeed, long-term follow-up data among frailty states have been reported from 16 studies, showing improved health status in 13.7% [95% confidence interval (CI) 11.7–15.8%], worsening in 29.1% (25.9–32.5%) and maintenance of the same frailty status in 56.5% (54.2–58.8%) over about 4 years.[27]

Evaluation of frailty

Various indices and scores, validated as predictive of mortality and/or adverse clinical outcomes in several clinical settings, have been proposed to quantify this multisystem complex condition. Among the operational definitions, there are two basic concepts of frailty: the phenotype model and the cumulative deficit model.[28] Fried *et al.* in 2001 have proposed an operational definition of 'phenotype'-based frailty syndrome (Supplementary material online, *Tables 1aS* and *1bS*), based on the presence of at least three out of five criteria, i.e. unintentional weight loss/sarcopenia, weakness, poor endurance/exhaustion, slowness, and low physical activity level. The identification of one or two items confers an intermediate frailty phenotype or a pre-frail status.[1]

Other indices have been proposed: the Short Physical Performance Battery (SPPB), which is measured by three timed physical performance tests—tandem balance, gait speed, and chair raise, the 5-m gait speed, the Study of Osteoporotic Fractures (SOF) index—presence of at least two among unintentional weight loss >5%, inability to raise from a chair five times without using arms and reduced energy level—and the simple Frail Scale.[11,14,29–32]

Alternatively, the Frailty Index (deficit accumulation), defined by Rockwood *et al.*[33] is a 70 item form based on the accumulation of specific deficits (including functional limitations and disabilities, cognitive and sensory impairment, psycho-social variables and a number of diseases). The Authors further developed the 7-point and the 9-point Clinical Frailty Scale (a semi-quantitative global judgement) (Supplementary material online, *Figure 1S*), which was shown to be highly correlated with the Frailty Index.[34]

Therefore, albeit under the same definition, these two different concepts currently recognize completely different subjects and, more importantly, generate different clinical and prognostic implications that may be considered as complementary.[35–37]

The likelihood of multiple overlapping issues may be better explored across several domains and therefore involves several disciplines.[38] Frailty is one of several domains explored within the Comprehensive Geriatric Assessment (CGA) a multidimensional interdisciplinary diagnostic process.[39]

The CGA-derived Multidimensional Prognostic Index[40] includes information on functional basic and instrumental activities of daily living, cognitive and nutritional status, comorbidities and medications.[41] Alternatives include the multidomain-evaluating Edmonton frail scale[42] and a variety of questionnaire-based tools.[43–48] Moreover, some evaluation techniques have been validated to allow the assessment of large electronic data records based on electronic diagnostic codes.[49]

The recently published guidelines by the task force of the International Conference of Frailty and Sarcopenia Research suggest the use of a validated simple evaluation technique, suitable for the specific setting or context, possibly directing the patient towards a more complex CGA after the identification of frailty.[50] Although a standardized CGA may not be routinely performed in clinical practice, there is sufficient evidence to recommend that all persons older

than 70 years should be screened for frailty by healthcare providers.[11]

Finally, several tools have been proposed for the assessment of multimorbidity, including the Acute Physiology and Chronic Health Evaluation (APACHE) score, the Charlson Comorbidity Index and the Cumulative Illness Rating Scale.[51–53] The Basic Activities of Daily Living, the Intermediate Activities of Daily Living and the Advanced Activities of Daily Living scores are the most commonly used tools to assess functional dependence, which represents the core of CGA.[54,55]

Screening for frailty in cardiology

Frailty screening tools should be sensitive, specific, quick to administer, validated for screening, and not requiring specific equipment.[11,14,28,32]

Table 1 lists some of the recommended techniques for initial evaluation of frailty in CV diseases,[4,6,56,57] highlighting the domains and components investigated by the instruments. Of course, some of these methods are only part of an initial identification of frailty (e.g. where laboratory parameters or data from electronic medical records are used together with other information), and ideally the approach to frailty evaluation should be inclusive of all the various domains of frailty.

The ideal technique to screen and assess frailty in any given situation should be chosen according to the characteristics of the subjects, the aim of the assessment and the clinical context. Assessment of frailty for epidemiological purposes or in a clinical context is different. Frailty has particular implications in particular CV diseases and in some of them specific frailty assessment tools have been more studied and validated than in other pathological conditions. For example, the HFA has recently suggested that HF may be better assessed by a multidimensional assessment approach rather than using tools focusing on physical frailty.[9] In some situations, different assessment techniques have different advantages, for example, in older patients who are candidates for complex intervention, indices exploring frailty multidomains (as in the Frailty Index or the Multidimensional Prognostic Index) might be better predictors of death, whereas indices exploring physical frailty (such as the Fried criteria, or the SPPB and gait speed) may be more helpful to identify patients at risk of complications and worsening disability.

It is unlikely that one assessment fits all, and when screening has identified a frail condition, it may be necessary to go through a further in depth assessment of the patient with a comprehensive geriatric evaluation or alternatively further focus on the specific deficit using tailored assessments. For instance, specific cognitive tools or comorbidity and/or disability tools may be administered if a cognitive impairment or multimorbidity has been evidenced. Throughout the assessment process, it should be reminded that the relevance of frailty identification lies in the opportunity it provides to intervene on potentially modifiable components to improve QoL (*Figure 2*).

Digital technology and eHealth for frailty evaluation

eHealth covers newer technologies such as telehealth, mHealth, wearables such as heart rate and activity tracking, utilization of artificial intelligence for analysing non-linear biological information, and sensor technology.

Several characteristics associated with frailty are highly suitable for detection and monitoring using technology-based measurements. Information, such as physical activity, gait speed, postural transitions and falls, can be readily detected with current activity and fitness tracking technologies.[58–61] Heart rate and fitness tracking may identify early markers of disease[62,63] or the presence of arrhythmias, and consumer-level products already have widespread use in non-frail individuals.[64] Other clinical information such as cognitive, visual, or sensory impairments potentially might be assessed through telehealth or mHealth technologies and thereby be available for primary or secondary healthcare providers. Sensor technologies are available for other relevant physiological information such as haemoglobin concentration, oxygen saturation, and skin temperature and could therefore contribute to the identification and management of frail individuals.[65,66]

Epidemiology, morbidity, mortality, and consequences of frailty in cardiovascular diseases

Incidence and prevalence

The reported frailty prevalence is highly heterogeneous, closely dependent on the population studied, the clinical setting where the study is conducted (i.e. in hospital database, primary care, outpatient, geriatric clinics, community-based samples, etc.) and on the measure indexes used. A meta-analysis based on 62 papers reporting data from 22 European countries showed an overall estimated frailty prevalence of 18%, ranging from 12% in 53 community-based studies to 45% in 15 non-community-based studies, with a prevalence of 12% in community studies adopting a physical phenotype and 16% for all other definitions.[67]

Besides the clinical phenotype and the presence of multimorbidity, depression is strongly associated with frailty, high levels of loneliness are related to an increased risk of becoming physically frail, and socioeconomic status affects the risk of frailty, multimorbidity and disability.[15,18,19]

In a population-based cohort of 12 844 people aged >65 from six Latin American countries, where nearly 40% had none or some education but did not complete primary school, depression was associated with an increased hazard of incident frailty.[68] Prevalence of frailty and pre-frailty appear higher in community-dwelling older adults in upper middle-income countries, compared with high-income countries. There is limited evidence on frailty prevalence in low middle-income and low-income countries.[69]

Clinical significance of frailty in cardiovascular disease

The prognosis of frail patients is worse than that of robust subjects, is directly influenced by frailty severity, can be evaluated by different indexes and tools, and by its association with disability and comorbidity. This relationship has been described both for adverse CV outcomes and non-CV mortality, across various settings, different diseases and subpopulations.[70–78]

Table 1 Initial evaluation of Frailty in CV disease

Instrument	Frailty domain	Components	Test	Score
5-m gait speed test	Physical function	Slowliness	Patient is positioned behind start line and asked to walk at a comfortable pace past 5-m finish line; cue to trigger stopwatch is first footfall after start line and first footfall after finish line; average of three times	Slow: <0.83 m/s (>6s) Very slow: <0.65 m/s (>7.7 s) Extremely slow: <0.50 m/s (>10 s)
Handgrip strength test	Physical function	Weakness	Patient is asked to squeeze a handgrip dynamometer as hard as possible; repeated three times (once with each hand and then with strongest hand); maximum value is recorded	Men: <30 kg Women: <20 kg
Physical activity questionnaire	Physical function		Many questionnaires have been validated; some provide a measure of activity in kcal/week (e.g. Minnesota Leisure Time Activity, PASE, Paffenbarger Physical Activity Questionnaire)	Men: <383 kcal/week Women: <270 kcal/week
CES-D questionnaire	Physical function	Exhaustion	Two questions administered: How often in the past week did you feel like everything you did was an effort?/like you could not get going? [often (i.e. ≥3 days) or not often (i.e. 0–2 days)]	Positive if often is the answer to either question
Short Physical Performance Battery	Physical function	Three-items: Balance Weakness (chair raise) Gate (5 min gate)	Balance: Patient is asked to stand in semi-tandem position for 10 s; if patient is able, then he/she is asked to stand in full tandem position for 10 s; if patient is not able, then he/she is asked to stand in side-by-side position for 10 s Chair rise: Patient is seated on a straight-backed chair and asked to stand up five times as quickly as possible without using arms; time to complete five sit-to stand repetitions is recorded 5-min gate speed: See above	Balance 0 = side by side 0–9 s or unable 1 = side by side 10 s 2 = full tandem 0–2 s 3 = full tandem 3–9 s 4 = full tandem 10 s Chair rise: 0 = unable 1 = ≥16.7 s 2 = 13.7–16.6 s 3 = 11.2–13.6 s 4 = ≤11.1 s 5-min gate speed: As above Composite score Each item is scored 0–4 Frail if composite score ≤5/12
Weight loss	Medical domain	Nutritional status Shrinking	Self-reported or measured unintentional weight loss	≥10 lbs (≥4.54 kg) in past year
Serum albumin	Medical domain	Nutritional status Shrinking	Laboratory measured serum albumine	<3.5 g/dL
Serum Hb	Medical domain	Nutritional status Multisystem proxy	Laboratory measured serum haemoglobin	<13 g/dL man <12 g/dL women

Continued

Table 1 *Continued*

Instrument	Frailty domain	Components	Test	Score
Electronic medical record	Medical domain and mind and emotion	Comorbidities Polypharmacy Sensory impairment Depression anxiety	Non applicable	Non applicable
Fried frailty index	Medical domain and physical function	Slowness, weakness, low physical activity, exhaustion, and shrinking	See Table 1aS and 1bS Supplemental materials	See Supplemental materials
Clinical frailty scale	Medical domain	Semiquantitative (generic)	See Figure 1S Supplemental material	See Supplemental materials
Essential frailty toolset	Multidomain	Multiple components (four-items): Weakness Cognitive Nutritional status Multisystem proxy	See Figure 2 Ssupplemental material Four-item test: chair stands, cognitive impairment (Mini-Mental State Examination or recall three out of three words after a distractive task), measured lab serum haemoglobin, and serum albumin	The tool is scored 0 (least frail) to 5 (most frail) Chair: ≥15 s or inability to complete five sit-to-stand repetitions without using arms Cognitive: score of <24 on the Mini-Mental State Examination (which is highly unlikely if the patient is able to correctly recall three out of three words after a distractive task and may obviate the need for further cognitive testing) Lab (see above)

CV mortality seems higher in frail [$N = 540$; hazard ratio (HR) 2.79, 95% CI 2.35–3.30] and pre-frail ($N = 2188$; HR 1.64, 95% CI 1.45–1.85) community-dwelling adults aged 60 or older than in 2244 robust participants in the cross-sectional National Health and Nutrition Survey from 1999 to 2004.[79]

When the relationship between frailty and CV disease was considered in 1432 older adults from the Longitudinal Aging Study Amsterdam, the frailty risk was increased in those with peripheral artery disease and HF.[80]

A meta-analysis including 31 343 subjects showed that frailty as well as pre-frailty were associated with any type of CV disease (pooled risk estimates: total: HR 1.70, 95% CI 1.18–2.45, —from HR 1.26, 95% CI 0.98–1.63 to HR 3.40, 95%CI 1.80-6.41—; total: HR 1.23, 95% CI 1.07–1.36, —from HR 0.13, 95% CI 0.93–1.38 to HR 3.10, 95% CI 1.61–5.95—, respectively).[81] Moreover, frailty was also associated with a ∼3-fold higher risk of CV death in six prospective cohorts including 18 307 participants over a median of 4.4 years (range 1–11.4).[81]

The degree of pre-frailty expressed as the number of Fried criteria has been shown to be related to incident CV events over a 4.4 ± 1.2 years follow-up in a prospective cohort of 1567 community-dwelling individuals aged >65 years without CV disease, frailty or disability at baseline.[7]

Multiple mechanisms (poor physical activity, sub-clinical vascular and cardiac alterations, oxidative stress, deoxyribonucleic acid damage and shorter telomere length, inflammatory markers, endocrine dysregulations, accelerated cellular senescence and epigenetic modifications) may contribute to the association between frailty and symptomatic CV disease.[82–84] The higher risk has been also linked to reduced treatments, considered futile or risky in subjects perceived to be frail. This behaviour may lead to greater occurrence of comorbidity and disability in frail patients instead, further worsening their prognosis. However, the risk of non-CV death should be taken into consideration when assessing the CV death risk and clinical decision making in the frail population. Indeed, when assessing the cause of death in relation to the baseline frailty status among 3135 community-dwelling older men in the MrOS Sleep study in an average follow-up of 9.2 years, the multivariable-adjusted risk of CV death among frail versus robust men was 1.38 (95% CI 0.99–1.92) using the competing risk method versus 1.84 (95% CI 1.35–2.51) using the traditional Cox proportional hazards method.[85]

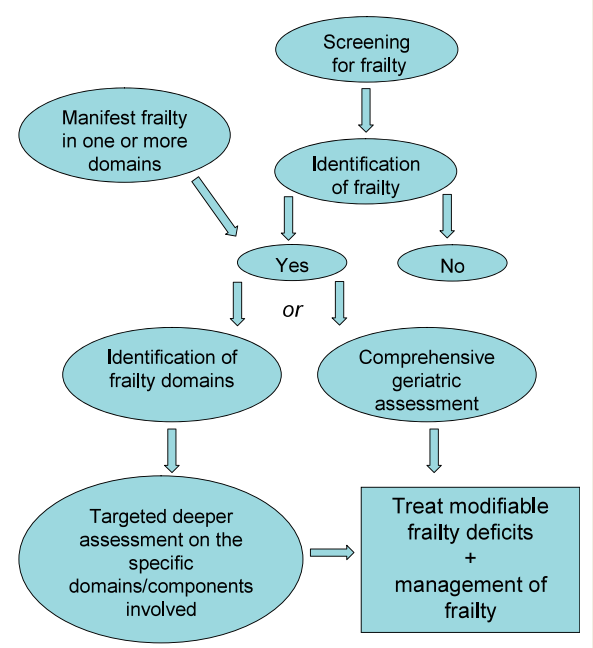

Figure 2 Frailty evaluation. If the presence of frailty is identified after screening, or the patient is presenting a manifest form of frailty, a more detailed assessment of the specific deficit evidenced or a comprehensive geriatric assessment is indicated. It is a crucial step to recognize the frailty domains, their components and their relative weight in order to give a tailored personalized response to the patients' peculiar needs.

Frailty models in specific contexts of cardiovascular diseases

Frailty has been evaluated in many different fields of CV diseases.[86–243] A detailed discussion of frailty models and frailty implications in patients' management is provided in the Supplementary material online, *Annexe 1*. In particular the following chapters are detailed: Frailty and CV prevention (Arterial Hypertension, Dyslipidemia), Cronic coronary syndrome, Arrhythmias (Atrial fibrillation, Cardiac Implantable Electronic Devices), Valvular heart diseases (see a proposed rapid minumum screening in patients considered for transcatheter aortic valve replacement[160], *Figure 3*), Chronic heart failure, Peripheral vascular disease, Coagulation and antithrombotic therapy.

The 'patient trajectory' before, during, and after critical illness and towards the end of life

Mapping the trajectory of chronic conditions against known disease patterns can help healthcare professionals clarify the type and timing of care required for each individual patient. In the literature there are three distinct trajectories described for people with chronic conditions: the cancer trajectory, the chronic organ/system failure trajectory and the frailty trajectory.[245,246]

The 'cancer trajectory' is characterized by a predictable decline in physical health and function and impaired ability for self-care, usually with a clear terminal phase.[245,247]

The 'chronic organ/system failure trajectory' includes conditions such as HF and is characterized by a progressive functional decline with occasional acute exacerbations. During exacerbations, for example, the unplanned admissions due to an episode of acute HF, the mortality rate is high.[245] In this trajectory, the timing of death is uncertain, making both discussing and initiating the end of life care plan difficult.[248]

Finally, the 'frailty trajectory' includes patients of older age with brain failure or generalized frailty. It is characterized by progressive disability with no clear terminal stage.[245] During this trajectory, an acute event such as pneumonia, may lead to death. Several studies have indicated that frailty is the predominant predictor of poor outcomes such as in-hospital mortality, hospitalization, disability, functional decline, and treatment complications.[249–252] Despite these differences among the chronic conditions, at the end of life, patients may take on one or more of the trajectories described above.

More recently, Freiheit *et al.*, have described a frailty trajectory for people diagnosed and treated for coronary artery disease as having a U-shape, where the Frailty index declines significantly after the initial treatment and then rises after a period of time.[115]

It is estimated that 40% of deaths occur in frail people who have no clear diagnosis, which suggests that the identification of palliative care needs must take into account the different frailty domains and not only disease-centred variables.[253] Frailty seems to be the most prevalent condition at the end of life. Therefore, in clinical practice, frailty must be considered quantitatively to determine the reserve level of the patient.[251,252]

Palliative care in patients with progressive chronic conditions involves optimizing QoL in order to facilitate a peaceful death. An understanding of disease trajectories can be helpful to healthcare professionals in this regard, to predict when progressive deterioration and death may occur. If palliative care is considered only at a late stage, patients and their families may miss opportunities to benefit earlier in the illness.[254] A realistic conversation about the disease trajectory between the patient, family and healthcare professionals can increase supportive care and focus on QoL and symptom control.[253,255]

End-of-life care provision and the patient's acceptance that death is imminent is different among the trajectory types described before.[255] So, when designing their care, engagement with patients and caregivers should commence relatively early and include good communication and education, close attention to the patients' needs, symptoms and preferences, as well as periodic re-evaluation of the care provided and flexible planning.[256] It has recently been proposed that there is a need for so-called "balancing factors" in the management of frailty, i.e. intrinsic and extrinsic resources to meet patients' psychological, social, physical, environmental and/or cognitive frailty challenges and greater focus on how older peoples' wellbeing may be protected and promoted, than how frailty can be resolved or diminished, if sufficient resources are available.[257]

Identification and management of frailty in general cardiology

In a speciality such as cardiology where there are many invasive treatments available, the assessment of frailty is key for determining the appropriatness of these interventions. Therefore, in cardiology practice, screening for frailty should be performed as a minimum in the subjects listed in the *Box 2*. If one or more frailty domains are identified, the patient should then undergo a more comprehensive evaluation (*Figure 2*).

Besides general support to frailty as discussed below, the identification of the specific needs from the individual's frailty components should be addressed to tailor intervention.

There is still debate about the effectiveness of specific actions aimed at modifying the natural course of frailty. However, there is current consensus that physical frailty is potentially, at least in part, reversible and that self-care maintenance can be improved by appropriate intervention.[258,259] In addition, the detection of frailty in the preoperative assessment of older candidates for elective complex cardiology procedures might suggest that there is potential benefit from a short period of more intense exercise training and nutritional support in order to reduce the risk of complications and increase the probability of functional success (*Box 3*).

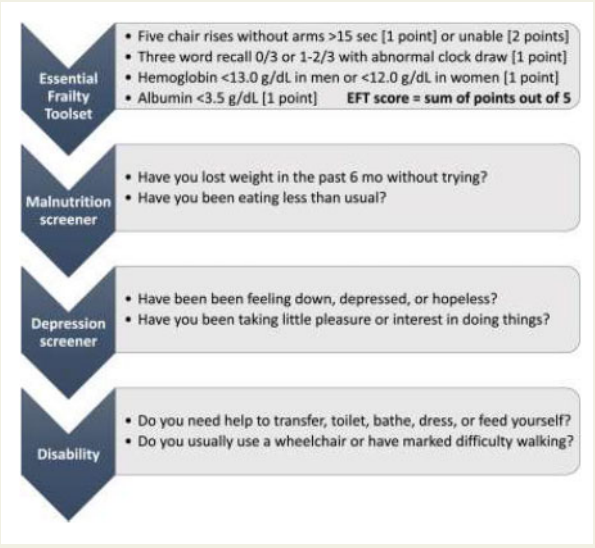

Figure 3 Short multidomain screening (proposed as minimum screening in patients considered for transcatheter aortic valve replacement) including the Essential Frailty Toolset, malnutrition, depression and disability screening (Piankova and Afilalo, *Cardiol Clin*, 2020, see online annexe 1).

Cardiac rehabilitation

Cardiac rehabilitation programs usually include patient evaluation both before and after the program and have a specific focus on nutrition and exercise. Multicomponent programs are important for frail patients, as the EAPC position paper on frailty emphasises[260] and are designed to improve the prognosis of old frail individuals and/or give benefits in terms of QoL. However, they need to be carefully designed and individually tailored, depending on the severity of frailty and the existence of CV disease and comorbidities, to achieve the best results safely.

During rehabilitation after an acute CV event, in a large number of frail patients, finishing the program was related to an improvement in frailty levels, although greater frailty was associated with higher dropout.[261]

Nutrition, exercise and combined interventions

Nutrition is a very important part of the multidimensional intervention in the very elderly and frail or sarcopenic/cachectic patients,[262] poor nutritional status being one of the main pathophysiological mechanisms for frailty. A systematic review on nutrition in old frail individuals reported an association between low intake of specific micronutrients and the frailty syndrome, and an association of higher protein and higher dietary antioxidant intake and lower risk of frailty.[263] Although not unequivocally demonstrated, it was suggested that improving nutritional status may reduce the risk of frailty and that nutrition may improve the functional outcome of elderly and frail patients.[259,264–272]

We highlight the importance of dental care, quantitative (energy intake) and qualitative (nutrient quality) factors of nutrition in the optimization of the frailty syndrome management.

Exercise in older people was shown to confer beneficial effects on body composition, muscle function, and functional ability.[273,274] However, the effects of exercise intervention on physical functioning of old frail people have been evaluated in very few trials. In frail elderly, moderate intensity aerobic and resistance training exercise programs increased the risk of falls and are not advised whereas it is thought that weighted low-intensity strength training could be indicated in most frail people.[275–277] Specific sessions on balance training using adapted tai-chi exercises have been shown to be beneficial in the prevention of falls, but hip protectors should be used and environmental modification may be required to avoid problems.[275–277]

Interventional trials designed to evaluate the benefits of cognitive training often combined with other interventions in reversing frailty and its physical manifestations, showed the possibility of reversing the degree of frailty.[267,278–283]

Other interventions and role of eHealth in frailty management

Other key areas for consideration include avoiding inappropriate prescribing and polypharmacy, careful selection of medical and surgical interventional procedures, planning for a shorter stay in hospitals where possible and long-term support after any discharge. Inappropriate prescribing has been consistently demonstrated to be associated with increased risk of hospitalization, geriatric syndromes and mortality in older adults in several settings.[284–286] The Beers criteria in North America, and the STOPP-START criteria in Europe, are the screening tools most widely used in geriatric medicine to avoid potentially inappropriate prescriptions, to alert doctors to the most appropriate treatment, to adjust doses of drugs according to renal function, and to identify drug–drug interactions known to be associated with harm in older adults.[287–289]

Box 2. Identification of frailty.

IDENTIFICATION OF FRAILTY:

patients ≥ 70 years with an acute or chronic CV disease

patients ≥ 70 years with a chronic CV disease with worsening of chronic health conditions

patients with a CV disease known to be closely related to frailty such as HF and AF

or presenting multi-morbidity

patients ≥ 70 years with CV disease hospitalized for:

CV acute events

or non CV acute events

or undergoing major surgery

patients ≥ 70 years candidate to cardiac interventional procedures (PM, ICD-CRT, TAVR, PCI, etc.)

Box 3. Management of frailty.

MANAGEMENT OF FRAILTY:

Focus on:

Nutrition (from dental care to dietary counselling and prepared meals)

Exercise (tailored exercise)

Cognitive domain / emotional support (cognitive and emotional interventional approaches)

Cardiac rehabilitation multi-component program

(after an acute event, possibly before programmed interventions/procedures)

Focus on enviromental aspects to reduce falls

(such as avoiding architectonic barriers at home, carpets, etc)

Target inappropriate polypharmacy

Reduce the hospitalization periods when needed

Support self-care behaviour

(- intensify the support to the patients when needed, for instance after an acute event

- support sensory impairment

- act at a community level if the individual or family level of support are inadequate)

Consider potential new interventions from eHealth technology

There is at present insufficient evidence to recommend specific e-Health-related interventions for frail individuals.[290] Although no controlled data are available on clinical outcomes, the use of e-Health has already become part of daily monitoring of some frail patients who live independently (for instance videocameras which are monitored by family members using phone apps so they can intervene rapidly if health threatening circumstances occur—falls, syncope, etc.—, alerting devices to remember the timing of drug assumption, thus increasing adherence, . . .).

Although several issues must be addressed before these technologies can be generally recommended, technology-based risk stratification may, however, be used for personalized management of individuals at risk and may, in the near future, not only identify high-risk individuals but also aid in the choice of intervention suited for the frail individual.[61,291] New studies are needed to determine which the best protocols for frailty management are.

Special role for the cardiovascular team

Development of a structured integrated management plan for frailty in cardiology should be the responsibility of a multidisciplinary team which includes nurses, general practitioners, and cardiologists, with a role for geriatricians when in-deep assessments are needed (*Box 4*, Supplementary material online, *Annexe 2*). Professionals acting as part of the frailty team are involved in specific clinical aspects to optimize the frail patient peculiarities and management (*Figure 4*).

Box 4. The frailty health team.

SPECIAL ROLE FOR GENERAL CARDIOLOGISTS
Pursuing prevention of cardiovascular diseases
Consider specific treatment aspects of cardiovascular diseases
Improve cardiovascular protocols impacting on frailty
Clinical evaluation of frailty in single patient
Use of tools addressing specific issues

SPECIAL ROLE FOR GENERAL PRACTITIONERS
Initial screening for frailty and contact with specialists
Informing the patient and meeting the patient's family
Planning for the patient support: the interface with the primary care
Monitoring the patient with frailty
Clinical management of frailty

SPECIAL ROLE FOR NURSES
Follow a holistic, individualized, person-centered approach
Intervention impacting on frailty aimed at maintenance of homeostasis
Case/care management

Future perspectives

The progressive increase of the elderly population is stressing world health systems. The frailty epidemic is growing and the improvement in acute and chronic disease management will increase the number of older patients and therefore more prone to become frail.

Frail patients are often excluded from large CV trials and the cardiology societies should design studies to target frail patients. Although most guidelines are suggesting careful attention to age, co-morbidities and frail-associated components (body size, mobilization, kidney function, cognitive status, nutritional assessment, and life expectancy), frail patients' management at the moment generally follows the recommendations as non-frail subjects.

The use of standardized methods for frailty evaluation could allow clinicians to use common criteria to interpret the results from different studies. However, the current heterogeneity of the available screening and assessment tools should not limit the routine assessment of frailty in daily practice, avoiding the use of the clinical subjective judgments (eyeball test or foot-of-the-bed assessment).

The identification of frailty according to simple, validated, universally accepted methods will allow us to define the additional risk frailty brings and possibly aid the frailty health team to

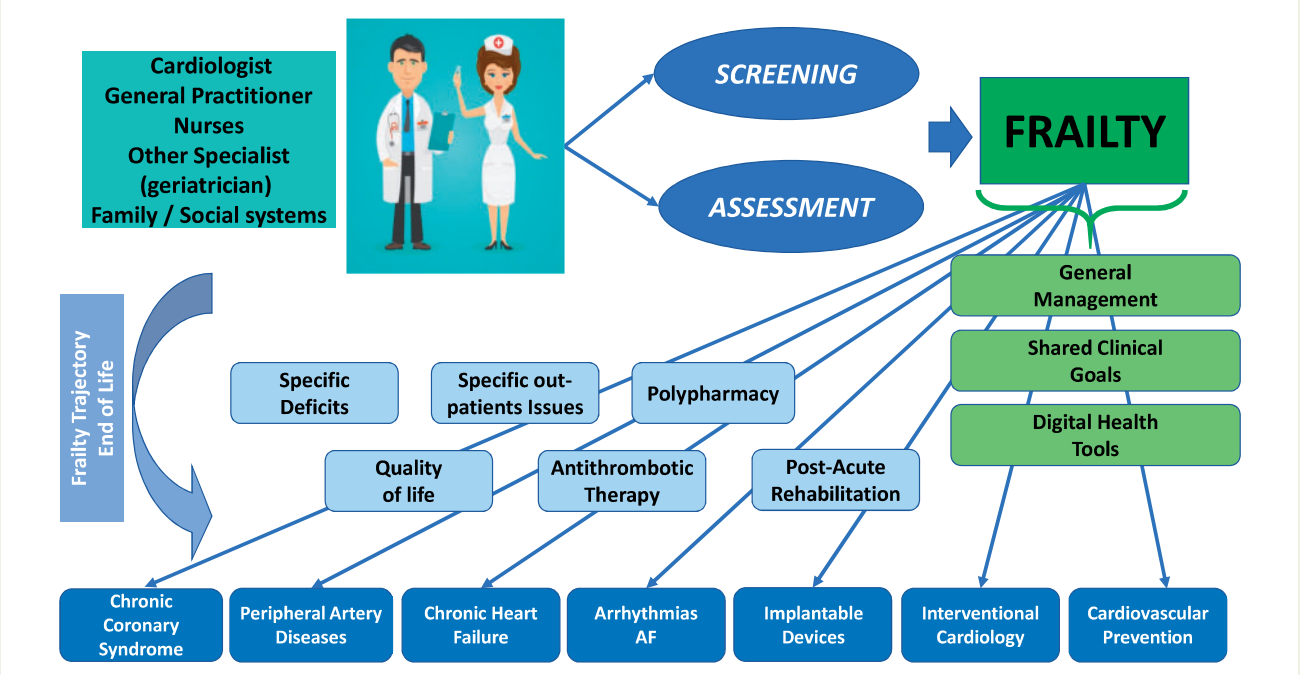

Figure 4 The frailty galaxy: specific peculiarities in general cardiology.

tailor CV and non-CV interventions to optimize the clinical outcomes.

New epidemiological and clinical challenge such as world pandemics are going to reconsider the whole health system clinical pathways. In this view a comprehensive evaluation of multimorbidities and frail profiling is going to be required to stratify the global risk of elderly patients.

In older frail patients the goals of treatment have to be shared with the patients, taking into account the patients' needs and attainable objectives, and frailty-directed specific interventions.

Digital health will probably have a prominent role in CV medicine in frail individuals for identification, monitoring, and personalizing treatment.

Conflict of interest: none declared.

References

References are provided in the Supplementary material online, *Annexe 3*.