

Frailty syndrome: an emerging clinical problem in the everyday management of clinical arrhythmias. The results of the European Heart Rhythm Association survey

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The age of patients presenting with complex arrhythmias is increasing. Frailty is a multifaceted syndrome characterized by an increased vulnerability to stressors and a decreased ability to maintain homeostasis. The prevalence of frailty is associated with age. The aims of this European Heart Rhythm Association (EHRA) *EP Wire* survey were to evaluate the proportion of patients with frailty and its influence on the clinical management of arrhythmias. A total of 41 centres—members of the EHRA Electrophysiology Research Network—in 14 European countries completed the web-based questionnaire in June 2017. Patients over 70 years represented 53% of the total treated population, with the proportion of frail elderly individuals reaching approximately 10%; 91.7% of the responding centres reported treating frail subjects in the previous year. The respondents usually recognized frailty based on the presence of problems of mobility, nutrition, and cognition and inappropriate loss of body weight and muscle mass. Renal failure, dementia, disability, atrial fibrillation, heart failure, falls, and cancer were reported to characterize the elderly frail individuals. Atrial fibrillation was considered the prevalent arrhythmia associated with frailty by 72% of the responding centres, and for stroke prevention, non-vitamin K antagonist oral anticoagulants were preferred. None of the respondents considered withholding the prevention of thrombo-embolic events in subjects with a history of falls. All participants have agreed that cardiac resynchronization therapy exerts positive effects including improvement in cardiac, physical, and cognitive performance and quality of life. The majority of respondents preferred an Arrhythmia Team to manage this special population of elderly patients, and many would like having a simple tool to quickly assess the presence of frailty to guide their decisions, particularly on the use of complex cardiac implantable electrical devices (CIEDs). In conclusion, the complex clinical condition in frail patients presenting with arrhythmias warrants an integrated multidisciplinary approach both for the management of rhythm disturbances and for the decision on using CIEDs.

Keywords

Anticoagulants • Arrhythmia team • Atrial fibrillation • Cardiac implantable electrical devices
• Elderly • Frailty • EHRA survey • EP wire

Introduction

The aging process of population and improvements in medical therapy have accounted for the progressive increase of elderly patients presenting with a clinically relevant arrhythmia. Aging is frequently

characterized by the coexistence of several comorbid conditions, often reciprocally interacting to produce a greater than additive negative impact on health status. At the same time, sub-clinical malnutrition, inactivity, and low-grade inflammation may exert a hidden effect on several body systems. All these changes are associated with frailty

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development, an age-related phenomenon, characterized by an increased vulnerability to stressors and a decreased ability to maintain homeostasis.¹

The aims of this European Heart Rhythm Association (EHRA) EP Wire survey were to evaluate, among European electrophysiology (EP) centres, the prevalence of frailty in everyday clinical practice and to assess its influence on medical conduct when coping with arrhythmia management.

Methods and results

This survey was based on a questionnaire sent via Internet to the EHRA EP Research Network centres in June 2017. A total of 41 centres from 14 countries in Europe responded to this survey. The majority (78.0%) was university hospitals, 12.2% was non-university hospitals, and 8.8% was private hospitals. After a quality check, we excluded some of the answers of five respondents from the analysis.

Elderly patients in the EHRA electrophysiology research network centres

In the preceding 12 months, patients ≥ 70 years represented the 53% of the entire managed population (70–79 years, 30%; 80–85 years, 15%; and >85 years, 8%). There were wide variations between the responding centres (range 13–100%). Almost all respondents (91.7%) reported treating frail subjects during the previous year.

The definition of frailty among respondents

The majority of participants defined a patient as frail when mobility and cognitive problems were present. Inappropriate reduction of body weight with loss of muscle mass and malnutrition were interpreted as other important markers of the condition. On the contrary, alterations of balance and loss of strength or endurance were not felt as relevant as other signs (Figure 1).

In terms of comorbidities, 75% of the participants considered frailty to be associated with chronic renal failure, a proportion even higher than those observed for dementia and disability (72.2% each). Interestingly, atrial fibrillation (AF) seemed to characterize a frail condition in a high proportion of cases. Chronic heart failure, falls with related injuries, and cancer were also considered to be associated with frailty (Figure 2).

Given the complexity of these patients, 82.3% of the responding centres felt necessary that the decision-making process in the management of a frail individual should involve an Arrhythmia Team. Apart from an electrophysiologist (74.3% of the responses), the cardiac implantable electrical device (CIED) specialist (71.4%), the clinical cardiologist (88.6%), the geriatrician (82.9%), a specialist nurse (68.6%), family members (62.9%), the specialist in internal medicine (37.1%), and an expert in palliative care (37.1%) were nominated to have an active role in the team.

When specifically asked, 77.1% of participants believed that an appropriate intervention (i.e. treatment of AF and CIED implantation) could be beneficial in a robust elderly patient without frailty. However, most respondents similarly agreed that an improvement could also be obtained in subjects with sub-clinical (resilient individuals, with slow or incomplete recovery from stressors; 85.7% of responses), or early frailty (condition is manifest, poor tolerance to stressors, no disability; 85.7% of responses). Awareness of failure of management progressively increased for patients with late (condition is manifest, poor tolerance to stressors, very slow recovery, and disability development) and end-stage frailty (severe condition is manifest, dependency development, and high risk of death in the next 12 months); in these cases, a clinical benefit was expected only by 45.7% and 8.6% of participants, respectively.

Frailty and atrial fibrillation management

A total of 40% of the centres considered that a rate-control strategy was the unique approach for frail patients with AF, whereas 57.1% of the centres believed that both the rate-control and rhythm-control strategy could be chosen according to the clinical context.

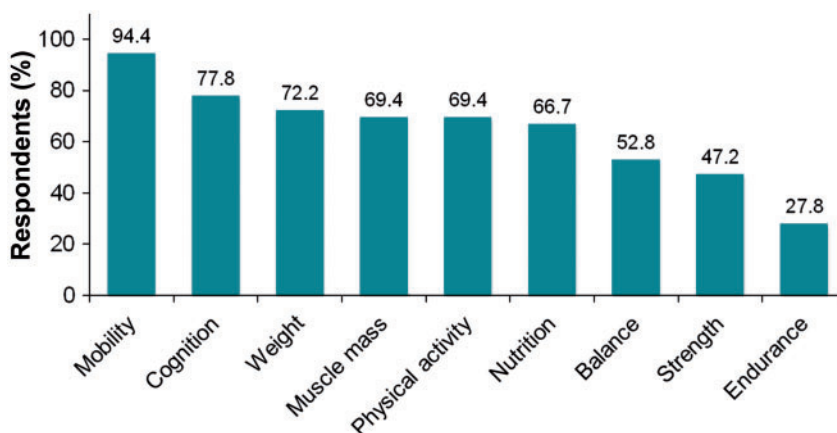


Figure 1 Features that characterize frailty syndrome according to the participants' opinion.

When specifically asked about their preferences on the pharmacological approach to prevention of thrombo-embolic complications in patients with AF, the majority was in favour of non-vitamin K antagonist oral anticoagulants (NOACs; 71.4%) compared with vitamin K antagonists (VKAs; 14.3%). There was a substantial agreement (62.9%) that the decision on anticoagulant treatment should be based on patients' characteristics, such as body weight, renal function, and compliance with therapy or with frequent international normalized ratio (INR) checks. Interestingly, none of the respondents would chose antiplatelet agents or low-molecular-weight heparins, while in 5.7% of cases, it was reported that no antithrombotic agents were appropriate due to a negligible or even negative net clinical effect.

Most common reasons for not prescribing an anticoagulant drug to frail subjects included active bleeding, prior bleed, or high bleeding risk. Dementia, possible lack of compliance, history of falls, and patient's refusal were other frequently reported causes preventing the use of therapy. The presence of comorbidities and the concomitant use of antiplatelet agents were sometimes considered as factors potentially limiting the use of anticoagulants. Age *per se* was associated with the lack of drug prescription only in a minority of the respondents. Indeed, the responses such as 'no existing medical/logistic justification' to prevent the use of anticoagulation and 'the highest possible use of therapy in frail elderly individuals' were selected by 14.3% and 17.1% of the participants, respectively (Figure 3). However, none of

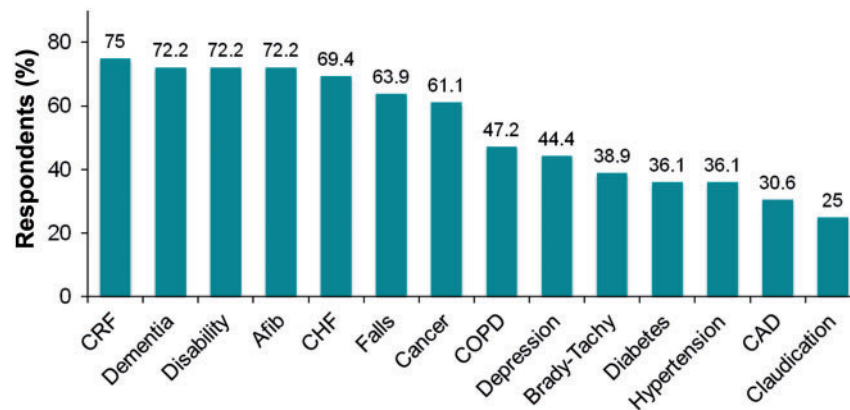


Figure 2 Comorbidities most frequently associated to the frailty syndrome according to the participants' opinion. Afib, atrial fibrillation; Brady-Tachy, bradycardia tachycardia syndrome; CAD, coronary artery disease; CHF, chronic heart failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure.

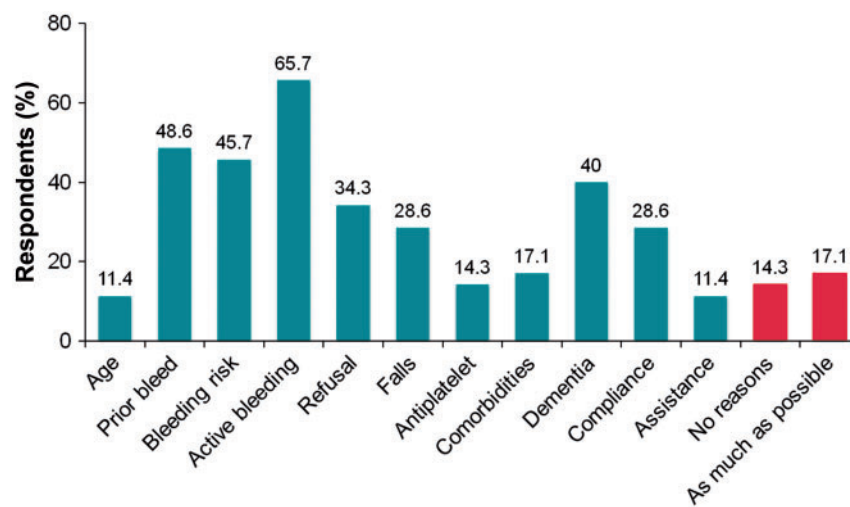


Figure 3 Most important reasons not to prescribe an anticoagulant drug to a frail patient with atrial fibrillation. Red bars indicate responses that are in favour of the use of anticoagulants. Antiplatelet, use of antiplatelet therapy; As much as possible, 'I prescribe anticoagulants as much as possible in these patients'; Assistance, possible lack of assistance; Compliance, possible lack of compliance; No reasons, no existing medical or logistic justifications; Refusal, patient's refusal.

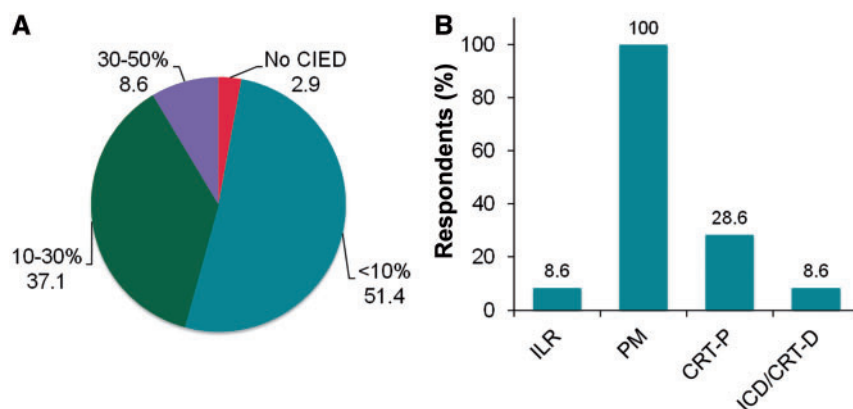


Figure 4 (A) Proportions of pre-frail or frail patients (FP) who received a CIED in the previous 12 months in the participating centres. No CIED, CIEDs are not implanted in such patients; <10%, FP are implanted in < 10% of all procedures; 10–30%, FP are implanted in 10–30% of all procedures; 30–50%, FP are implanted in 30–50% of all procedures. (B) Most frequently used devices in frail or pre-frail patients in the responding centres. CRT-D, cardiac resynchronization therapy-defibrillator; CRT-P, cardiac resynchronization therapy-pacemaker; ICD, implantable cardioverter-defibrillator; ILR, implantable loop recorder; PM, pacemaker.

the respondents thought that a history of falls represented a valid reason to avoid anticoagulant therapy. Most of the participants indicated NOACs as their preferred choice for this kind of patients (51.4%). In 37.1% of cases, the response was that either NOACs or VKAs could be prescribed, according to the individual clinical conditions, whereas only 5.7% of the participants indicated VKAs as their preferred option. In a small number of cases (5.7%), left atrial appendage closure appeared as the most useful solution for the frail elderly at risk of falls.

Frailty and cardiac implantable electrical devices

When analysing the activities of the previous 12 months, pre-frail or frail patients who received CIED usually represented <10% of all implanted population. Only a negligible proportion of participants reported not to work with pre-frail or frail individuals (Figure 4A). Pacemakers were the devices most frequently used; about one-third of the respondents affirmed that also cardiac resynchronization therapy-pacemaker (CRT-P) therapy was a common choice in such a population; however, <10% indicated an implantable cardioverter-defibrillator (ICD), or CRT-defibrillator (CRT-D) or a loop recorder implantation as a common procedure if frailty was present (Figure 4B). Overall, 57.1% of the centres believed that the new capabilities of CIEDs to monitor patients' activities during the daily life could be of some help to identify the development of a frail condition and to rapidly start an effective treatment.

Cardiac resynchronization therapy-pacemaker was generally acknowledged as an important therapy in the frail elderly. In particular, 40% of the participants reported that it could be as useful as in younger robust patients. In other 40% of cases, when compared with CRT-D, it was considered even more favourable, because of the lower risk of inappropriate shocks, the different characteristics and complications of severe heart failure in the elderly, and because of costs. Indeed, CRT-P-mediated improvements were reported in

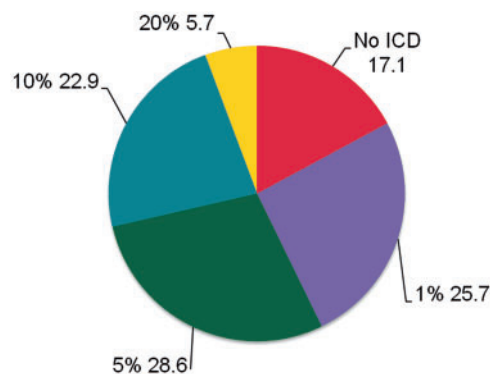


Figure 5 Proportions of frail patients (FP) receiving an ICD on the total ICD implanted population in the participating centres. No ICD, ICD are not implanted in FP; 1%, FP are implanted in 1% of all procedures; 5%, FP are implanted in 5% of all procedures; 10%, FP are implanted in 10% of all procedures; 20%, FP are implanted in 20% of all procedures. ICD, implantable cardioverter-defibrillator.

cardiac (51.4%) and physical performance (37.1%), in health-related quality of life (54.3%), and in neurocognitive profile (14.3%), with a consequent reduction of disability. Only 20% of the respondents thought that CRT-P was not so useful in frail individuals and did not use this therapy in their patients.

Frail subjects were excluded from ICD therapy in 17.1% of the participating centres. In most cases, it was answered that the prevalence of frail individuals receiving an ICD was between 1 and 10% of the total population (Figure 5).

The great majority of the respondents was in favour of a clinical tool allowing the quick assessment of the presence and degree of frailty in patients undergoing ICD implantation. This instrument was needed to better guide treatment (e.g. use of CRT and optimization

of medical therapy; 65.7% of answers) and to exclude subjects in whom the intervention would likely be futile (e.g. upgrade or replacement of a device; 34.3% of answers). Only 8.6% of respondents claimed that they could use such a tool to exclude all frail individuals from ICD implantation.

Discussion

In recent years, frailty has become the 'core' of geriatric medicine because its prevalence greatly increases with age, exposing the 'oldest old' to a higher risk of medical instability, disability, acute illnesses, and iatrogenesis. All these factors determine greater health-care resources utilization, with higher rates of hospitalization and institutionalization, and an augmented risk of mortality and incomplete recovery from disease. On this basis, one of the most important aims of geriatric medicine is the early identification, evaluation, and treatment of frail elderly individuals to prevent the cascade of events leading from functional decline to disability development and death.¹

The results of this *EP Wire* have demonstrated that the proportion of elderly individuals with arrhythmia-related problems is high because of the aging process of the population and the improvement of care. Despite a wide inter-centre variability, patients ≥ 80 years constitute almost a quarter of the whole group of subjects managed by the participating centres.

Interestingly, in the survey, the most often identified components of the frailty syndrome were those associated to mobility, cognition, and loss of muscle mass. Indeed, important characteristics, such as those related to the reduction of balance, strength, and endurance,² gained less attention. Frailty can be explained by two different series of processes. In the first one, an accumulation of potentially unrelated diseases across different parts or systems of the body leads to sub-clinical dysfunctions and disabilities; in this case, frailty represents the resultant of all defects, which are also associated with mortality following a dose–response relationship.³ The alternate mechanism proposes that frailty is a unique process able to compromise physiologic functions and homeostatic pathways through changes in production, distribution, and utilization of energy. These alterations could involve at the same time endocrine, immune, inflammatory, musculoskeletal, and nervous systems and could lead to a defective regulation of several functions with a progressive loss of homeostasis and, ultimately, death.⁴ Atrial fibrillation was related to frailty by 72.2% of the respondents. Indeed, the arrhythmia, when associated with other diagnosis, identified older and more frequently disabled in-hospital patients, who also showed higher prevalence of comorbidities and longer hospitalizations. On this basis, AF could be interpreted as an emerging marker of frailty.⁵ To strengthen this concept, more recently, the Health, Aging, and Body Composition Study showed that, in older subjects living in community, the development of the arrhythmia was associated to a higher risk of decline in physical performance.⁶

Regarding AF therapy, only a low proportion of participants thought that anticoagulation might not be safe in frail elderly individuals. Following current guidelines recommendations,⁷ the results of this *EP Wire* survey clearly show that NOACs are used more often than VKAs for the prevention of thrombo-embolism, whereas antiplatelet agents and low-molecular-weight heparins are no more

prescribed. Dementia, possibly because of fear of lack of compliance, could justify the reluctance to use an anticoagulant. However, evidence seems to suggest that the interruption of warfarin in demented patients could be associated with a significant increase in mortality during follow-up.⁸ A high risk or a history of falls is a relevant reason to avoid anticoagulation in a frail patient reported by 28.6% of the respondents to the survey. However, when specifically asked, this at-risk population was left without therapy in no cases. Only 5.7% of participants considered using a left atrial appendage closure device. According to the results of a recent sub-study of the Effective Anticoagulation with Factor Xa Next Generation in Atrial Fibrillation-Thrombolysis In Myocardial Infarction 48, NOACs were preferred over VKAs because of a significant reduction in severe bleeding and mortality.⁹

Depending on the clinical characteristics and situation, both the rate-control and rhythm-control strategy can be considered for the treatment of a frail AF patient by 57.1% of the respondents. This uncertainty is also expressed in a recent scientific statement from the American College of Cardiology, the American Heart Association, and the American Geriatrics Society in which it is reported that studies are needed to test the differences between rate- and rhythm-control strategies on clinical outcomes relevant to older populations.¹⁰

About 70% of participants considered congestive heart failure to be a condition related to frailty.

Everyone agreed that pacemakers for bradyarrhythmias control should always been implanted in a frail or a pre-frail patient. It was shown that a pacemaker could reduce the risk of falls,¹¹ improve or maintain quality of life, and prevent worsening heart failure by maintaining heart rhythm and the subsequent functional decline of major organs. The device can also be considered an instrument allowing to reach the endpoints of palliative care.¹²

Under this perspective, CRT-P devices can show similar properties.¹² Accordingly, about 30% of respondents frequently used them in frail or pre-frail individuals. Clinical evidence supports this practice. Real-world data demonstrate that CRT can improve left ventricular performance and functional capacity independently of age and that the proportion of the responders to therapy, as evaluated with traditional instrumental variables, was not different in elderly subjects.¹³ Data from the European CRT Survey show that, after 1 year, health-related quality of life was improved in 81% of the patients treated with CRT.¹⁴ More recently, it was observed that after 6 months, CRT determined an improvement not only of left ventricular ejection fraction and New York Heart Association class but also of physical and cognitive profile. Interestingly, the older population showed the greater changes of functional performance.¹⁵ All these data indicate that CRT should be considered in elderly patients with heart failure.¹⁶

In clinical practice, about one in four patients receiving an ICD is aged ≥ 75 years.^{17,18} However, the use of a defibrillator in frail subjects is more controversial.¹⁹ About 20% of the respondents affirm not to implant at all such patients; only 8.6% of participants reported that an ICD/CRT-D was frequently used. In the majority of participating centres, elderly frail individuals represent a proportion ranging between 1% and 10% of the entire implanted population. An analysis of Medicare database from the National Cardiovascular Data Registry ICD Registry showed that in heart failure patients receiving a primary prevention ICD, the prevalence of frailty and dementia was 10% and

1%, respectively. One-year mortality after the procedure was significantly greater in patients showing one of the two conditions (frailty, 22%; dementia, 27%) when compared with that observed in the whole population (12%).²⁰ Some evidence suggests that the benefit of the device could be lower at advanced age because of a more complex clinical condition.^{18,21} Indeed, traditional clinical predictors of survival seem to lose their importance in elderly subjects that received an ICD.¹⁷

In addition, the majority of the participants to the survey agree with the perspective of a tool that quickly allows detecting frailty. This could improve the quality of treatment and help exclude patients at risk of a futile procedure. The Short Physical Performance Battery could reveal a useful option; it consists of a battery of tests used to assess lower extremity function, measuring balance, gait speed, and strength and endurance; it can predict disability at 4 years even in those who are not disabled at baseline.²²

In general, the complexity of elderly frail patients can explain why 82.3% of the respondents preferred the cooperation of several professionals to improve the management of such a particular population. Electrophysiologists, clinical cardiologists, geriatricians, internists, specialists in palliative care, nurses, and family members could all take part in the decision-making process in these patients through the activity of an Arrhythmia Team. In a previous *EP Wire*, the majority of respondents thought that an Arrhythmia Team should be implemented in every centre, to cope with difficult situations represented by refractory forms of arrhythmias, or with complex clinical conditions, represented by inherited arrhythmic disorders, comorbidities, difficult therapeutic schemes, and, obviously, frailty.²³ An integrated approach has already revealed its benefit in terms of survival and reduction of disability and costs.²⁴

Limitations

The main limitation of this survey is that the conclusions that can be drawn are valid only for the physicians who participated. However, centres from 14 different European countries with different types of activity (university, non-university, and private hospitals) participated, and results can, at least in part, represent how specialized facilities behave when facing such a complex problem.

Conclusions

Frailty is a multifaceted syndrome characterized by loss of homeostasis. It is associated to several components and comorbidities. The number of frail elderly individuals presenting with relevant arrhythmias is progressively increasing and constitutes about 10% of patients in the responding centres. This clinical and epidemiological trend could create important problems of management. Most centres used oral anticoagulants for AF in frail patients. Decisions to implant CIEDs varied among centres with most of them using pacemakers and CRT-P in frail subjects, while decisions regarding ICD implantations were more difficult. The presence of a multidisciplinary Arrhythmia Team was wanted by most centres to help to solve many clinical questions and ideally to reverse frailty by a timely intervention.

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