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Introduction to the special issue entitled 'Heart failure management of the elderly patient: focus on frailty, sarcopenia, cachexia, and dementia'

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KEYWORDS

Heart failure; Elderly; Comorbidities; Cachexia; Sarcopaenia; Frailty; Dementia; Cognitive decline This is a special issue focused on heart failure management of the elderly patient with a focus on frailty, sarcopaenia, cachexia, and dementia, all common problems in the contemporary older heart failure (HF) patient. The Heart Failure Association (HFA) of the European Society of Cardiology (ESC) has brought together experts to discuss these topical and clinically difficult areas. There are papers on ageing, demographics, and heart failure, drug treatment of the older patient, the frail heart failure patient and how to recognize frailty and screen for it without the risk segmenting these patients in a form of discrimination of them as less worthy of treatment through 'frailtyism'. This is also discussion of the common problems affecting skeletal muscle, both sarcopaenia and cachexia, as well as dementia and cognitive decline and the crucial issue of planning health care for the older patient with HF most effectively by the use of care plans.

Heart failure (HF) common, currently affecting \sim 26 million patients worldwide. The majority of the HF population is elderly and/or frail patients that commonly have one or more associated comorbidities.² This growing burden of heart failure affecting a particularly at-risk group led the Heart Failure Association (HFA) of the European Society of Cardiology (ESC) to bring together experts to discuss these topical and clinically difficult areas. Now, we are proud to publish individual papers on ageing, demographics, and heart failure, drug treatment of the older patient, the impact of frailty in HF, and how to avoid 'frailtyism'. This is also discussion of the common problems affecting skeletal muscle, both sarcopaenia and cachexia, as well as dementia and cognitive decline and the crucial issue of planning health care for the older patient with HF most effectively by the use of care plans.

In the first paper, Andrew Coats reviews the epidemiology of HF and the impact of the ageing population on

this disorder. He reviews the differing pathophysiological mechanisms of heart failure in older patients and their different background disease burden and possibly different and more prevalent burden of comorbidities.^{3,4} He argues strongly for more studies specifically recruiting older HF patients with more comorbidities, to guide realworld practice, and to assess patient-reported outcomes and quality of life rather more than we have in the past. Both the prevalence of comorbidities and mortality increase with age and of course heart failure with reduced ejection fraction (HFrEF) is more common in younger cohorts (and in most randomized clinical trials) compared to the elderly where the less well trialled heart failure with preserved ejection fraction (HFpEF) predominates. The ageing population has changed HF as often an isolated disorder to one where non-cardiovascular comorbidities are common and can affect the modes and causes of death, in a way which makes clinical trial design and monitoring more difficult. Although subgroup analyses of the major HF RCTs have not suggested differing outcomes with age, still very few studies have specifically recruited older HF patients. There is a

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discussion of the particular effects of comorbidities in this regard.

Ewa A. Jankowska et al. review drug therapy in elderly heart failure patients. They review the evidence-base of pharmacotherapy in elderly patients with heart failure, including the most recent major trials PARADIGM-HF trial, of sacubitril-valsartan combination compared to enalapril in HFrEF and the DAPA-HF trial of dapagliflozin. They summarize that the pharmacotherapy of HFrEF in elderly patients is recommended to be the same as for patients in all other age groups being based on angiotensin converting enzyme (ACE) inhibitors [or angiotensin receptor blocker (ARB) or angiotensin receptor neprilysin inhibitor (ARNI)], betablockers, mineralocorticoid receptors, ivabradine to improve clinical outcomes, along with loop diuretics and sometimes digoxin to further alleviate HF symptoms. 5 They stress the risk of inappropriate prescribing and the risk of side effects because of frailty and the impact of multiple comorbidities. Cristina and Loreena Hill review the issues of frailty in HF and whilst stressing the importance of screening for and detecting frailty within any cohort of HF patients they also caution against 'frailtyism'. Frailtyism they liken to ageism as prejudice or discrimination based on the presence of frailty. They quite rightly point out that because of its major prognostic and therapeutic implications, the identification of frailty is of major importance, and that it is of significance in HF⁸ as in any other area of medicine, perhaps even more so than most. They talk about the efforts of the HFA to devise and then validate an objective and easy to use measurement that can help detect and document frailty within a HF population in our effort to prevent or manage poor outcomes in this at-risk group, ultimately enabling more effective and tailored plans of care to suit the needs of the patient. The very limited number of interventional trials to date needs to increased. Later in the issue, Loreena Hill also gives practical advice concerning the need and mechanisms of creating a care plan for the elderly HF patient. 10

We then have review articles written by experts in the field on two complex and partially inter-related complications of HF, that being cachexia and sarcopaenia. 11 Cachexia is a state of energy deprivation or wasting where body weight loss leads to loss of skeletal muscle as well as other tissue compartments. 12 Sarcopaenia, in contrast, is a purer form of skeletal muscle loss and associated functional weakness. Both are common in the elderly, ^{13,14} and both are common in HF. 15 Sarcopaenia formally defined as reduced skeletal muscle mass associated with either a decline in muscle strength or low physical performance is common¹⁶ as the populations of developing nations are ageing. 17,18 It has a particularly high prevalence (>20%) in HF, where it further impairs patients already with markedly reduced exercise capacity due to their HF and leads to an increased hospitalization burden. 19 Sarcopaenia also increases mortality, and impairs quality of life, frequently making the difference between the ability to self-care or not. The pathophysiological mechanisms underlying sarcopaenia are discussed, as is the treatments we have to date to prevent this disabling condition, mainly involving resistance training combined with nutritional protein supplements. Cardiac cachexia (the cachexia complicating HF)

has a long history with a first plausible description being found in the writings of Hippocrates. As Dr Lena and colleagues from the leading cachexia centre (Charité, Berlin) review, cachexia is a complex multifaceted disorder characterized by a pathological shift in the balance between anabolism (growth) and catabolism (wasting). It is a common complication of many chronic disease processes, and these include HF. In patients at risk, cachexia is seen crosssectionally in about 10% of HF patients, but longitudinally it is far more incident than that because once acquired it is associated with an extremely high mortality rate, so that sufferers frequently die within months of reaching the cachectic state. There is an urgent need to find new effective therapies²⁰ and despite extensive effort, the only effective therapy to date remains cardiac transplantation in patients so affected, although beta-blockers have shown some efficacy.²¹ The other important organ that suffers 'wasting' as a consequence or in association with HF is the brain, and the resulting dementia and cognitive impairment is a major public health problem as well as a potentially catastrophic complication. Professor Doehner, who may well be unique as a professor in both HF and stroke medicine, reviews the interaction between heart and brain disorders²² and how in HF patients, especially the older patients strokes, dementia, and depression are all prevalent and the cause of major clinical and management difficulties. Loss of ability to selfcare is a contributor to very poor quality of life and often leads to a dramatic increase in health care expenditure. I recommend this series of up to date review articles to our readership, in our efforts as the HFA to improve the care and quality of life of all HF sufferers.

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References

- Ambrosy AP, Fonarow GC, Butler J, Chioncel O, Greene SJ, Vaduganathan M, Nodari S, Lam CSP, Sato N, Shah AN, Gheorghiade M. The global health and economic burden of hospitalizations for heart failure: lessons learned from hospitalized heart failure registries. J Am Coll Cardiol 2014;63:1123-1133.
- van Deursen VM, Urso R, Laroche C, Damman K, Dahlström U, Tavazzi L, Maggioni AP, Voors AA. Co-morbidities in patients with heart failure: an analysis of the European Heart Failure Pilot Survey. Eur J Heart Fail 2014;16:103-111.
- 3. Iorio A, Senni M, Barbati G, Greene SJ, Poli S, Zambon E, Di Nora C, Cioffi G, Tarantini L, Gavazzi A, Sinagra G, Di Lenarda A. Prevalence and prognostic impact of non-cardiac co-morbidities in heart failure outpatients with preserved and reduced ejection fraction: a community-based study. Eur J Heart Fail 2018; 20:1257-1266.
- Wolsk E, Claggett B, Køber L, Pocock S, Yusuf S, Swedberg K, McMurray JJV, Granger CB, Pfeffer MA, Solomon SD. Contribution of cardiac and extra-cardiac disease burden to risk of cardiovascular outcomes varies by ejection fraction in heart failure. Eur J Heart Fail 2018;20:504-510.
- Komajda M, Cowie MR, Tavazzi L, Ponikowski P, Anker SD, Filippatos GS; QUALIFY Investigators. Physicians' guideline adherence is associated with better prognosis in outpatients with heart failure with reduced ejection fraction: the QUALIFY international registry. Eur J Heart Fail 2017;19:1414-1423.

- Tsutsumimoto K, Doi T, Makizako H, Hotta R, Nakakubo S, Makino K, Suzuki T, Shimada H. Aging-related anorexia and its association with disability and frailty. J Cachexia Sarcopenia Muscle 2018;9:834-843.
- Sanders NA, Supiano MA, Lewis EF, Liu J, Claggett B, Pfeffer MA, Desai AS, Sweitzer NK, Solomon SD, Fang JC. The frailty syndrome and outcomes in the TOPCAT trial. Eur J Heart Fail 2018;20:1570-1577.
- Vidán MT, Blaya-Novakova V, Sánchez E, Ortiz J, Serra-Rexach JA, Bueno H. Prevalence and prognostic impact of frailty and its components in non-dependent elderly patients with heart failure. Eur J Heart Fail 2016:18:869-875.
- Chan DD, Tsou HH, Chang CB, Yang RS, Tsauo JY, Chen CY, Hsiao CF, Hsu YT, Chen CH, Chang SF, Hsiung CA, Kuo KN. Integrated care for geriatric frailty and sarcopenia: a randomized control trial. J Cachexia Sarcopenia Muscle 2017;8:78-88.
- 10. Hill E, Taylor J. Chronic heart failure care planning: considerations in older patients. *Card Fail Rev* 2017;3:46-51.
- Morley JE. Anorexia of ageing: a key component in the pathogenesis of both sarcopenia and cachexia. J Cachexia Sarcopenia Muscle 2017:8:523-526.
- 12. Scherbakov N, Doehner W. Cachexia as a common characteristic in multiple chronic disease. *J Cachexia Sarcopenia Muscle* 2018;9:1189-1191.
- Dodds RM, Granic A, Davies K, Kirkwood TB, Jagger C, Sayer AA. Prevalence and incidence of sarcopenia in the very old: findings from the Newcastle 85+ study. J Cachexia Sarcopenia Muscle 2017; 8:229-237.
- Boengler K, Kosiol M, Mayr M, Schulz R, Rohrbach S. Mitochondria and ageing: role in heart, skeletal muscle and adipose tissue. J Cachexia Sarcopenia Muscle 2017;8:349-369.
- 15. Emami A, Saitoh M, Valentova M, Sandek A, Evertz R, Ebner N, Loncar G, Springer J, Doehner W, Lainscak M, Hasenfuß G, Anker SD, von Haehling S. Comparison of sarcopenia and cachexia in men with chronic heart failure: results from the Studies Investigating Comorbidities Aggravating Heart Failure (SICA-HF). Eur J Heart Fail 2018;20:1580-1587.

- Martone AM, Bianchi L, Abete P, Bellelli G, Bo M, Cherubini A, Corica F, Di Bari M, Maggio M, Manca GM, Marzetti E, Rizzo MR, Rossi A, Volpato S, Landi F. The incidence of sarcopenia among hospitalized older patients: results from the Glisten study. J Cachexia Sarcopenia Muscle 2017:8:907-914.
- Tieland M, Trouwborst I, Clark BC. Skeletal muscle performance and ageing. J Cachexia Sarcopenia Muscle 2018;9:3-19.
- Makizako H, Shimada H, Doi T, Tsutsumimoto K, Lee S, Lee SC, Harada K, Hotta R, Nakakubo S, Bae S, Harada K, Yoshida D, Uemura K, Anan Y, Park H, Suzuki T. Age-dependent changes in physical performance and body composition in community-dwelling Japanese older adults. J Cachexia Sarcopenia Muscle 2017;8:607-614.
- Yang M, Hu X, Wang H, Zhang L, Hao Q, Dong B. Sarcopenia predicts readmission and mortality in elderly patients in acute care wards: a prospective study. J Cachexia Sarcopenia Muscle 2017;8: 251-258.
- Haehling S. Casting the net broader to confirm our imaginations: the long road to treating wasting disorders. J Cachexia Sarcopenia Muscle 2017;8:870-880.
- Clark AL, Coats AJ, Krum H, Katus HA, Mohacsi P, Salekin D, Schultz MK, Packer M, Anker SD. Effect of beta-adrenergic blockade with carvedilol on cachexia in severe chronic heart failure: results from the COPERNICUS trial. *J Cachexia Sarcopenia Muscle* 2017;8: 549-556.
- 22. van Bilsen M, Patel HC, Bauersachs J, Böhm M, Borggrefe M, Brutsaert D, Coats AJS, de Boer RA, de Keulenaer GW, Filippatos GS, Floras J, Grassi G, Jankowska EA, Kornet L, Lunde IG, Maack C, Mahfoud F, Pollesello P, Ponikowski P, Ruschitzka F, Sabbah HN, Schultz HD, Seferovic P, Slart R, Taggart P, Tocchetti CG, Van Laake LW, Zannad F, Heymans S, Lyon AR. The autonomic nervous system as a therapeutic target in heart failure: a scientific position statement from the Translational Research Committee of the Heart Failure Association of the European Society of Cardiology. Eur J Heart Fail 2017;19:1361-1378.