



Insights into heart failure hospitalizations, management, and services during and beyond COVID-19

Sarah J. Charman^{1,2*} , Lazar Velicki^{3,4}, Nduka C. Okwose^{1,2}, Amy Harwood^{5,6}, Gordon McGregor^{5,6}, Arsen Ristic⁷, Prithwish Banerjee^{5,6}, Petar M. Seferovic⁷, Guy A. MacGowan^{1,2} and Djordje G. Jakovljevic^{1,2,5,6*} 

¹Cardiovascular Research Division, Translational and Biosciences Research Institutes, Newcastle University, Newcastle upon Tyne, UK; ²Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK; ³Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia; ⁴Clinic for Cardiovascular Surgery, Institute of Cardiovascular Diseases Vojvodina, Sremska Kamenica, Serbia; ⁵Faculty of Health and Life Sciences, Coventry University, Coventry, UK; ⁶University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK; ⁷Faculty of Medicine, University of Belgrade, Clinical Centre Serbia, Belgrade, Serbia

Abstract

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus-2. The clinical presentation of this virus mainly manifests in the respiratory system but may also lead to severe complications in the cardiovascular system. The global burden of COVID-19 has led to an unprecedented need to gain further insight into patient outcomes, management, and clinical practice. This review aims to provide an overview of the current literature on heart failure (HF) hospitalizations, management, and care pathways for supporting patients during and beyond this pandemic. A literature review of five areas of interest was conducted and included: (i) HF hospitalization; (ii) recognizing the needs and supporting HF patients during COVID-19; (iii) supporting rehabilitation services; (iv) transitioning to a telehealth framework; and (v) the need for evidence. Patients with new-onset or existing HF are particularly vulnerable, but a significant reduction in HF hospital admissions has been reported. During these periods of uncertainty, the current care pathways for acute and elective cardiac patients have had to change with the relocation of HF services to protect the vulnerable and reduce transmission of COVID-19. Optimizing community HF services has the potential to reduce the pressures on secondary care during the recovery from this pandemic. Telemedicine and virtual health care are emerging technologies and overcome the risk of in-person exposure. Successful remote delivery of cardiac rehabilitation services has been reported during the pandemic. Delivery of a robust telehealth framework for HF patients will improve communication between clinician and patient. The reduction in HF admissions is a concern for the future and may result in unintended mortality. New-onset and current HF patients must understand their diagnosis and future prognosis and seek help and support using the appropriate platform when needed. Realigning HF services and the use of telemedicine and virtual health care has great potential but needs to be carefully understood to ensure engagement and approval in this population to overcome barriers and challenges.

Keywords Heart failure; COVID-19; Hospitalizations; Primary care; Telemedicine

Received: 13 July 2020; Revised: 26 August 2020; Accepted: 25 September 2020

*Correspondence to: Dr Djordje Jakovljevic and Sarah Charman, Cardiovascular Research Division, Translational and Clinical Research Institute, Newcastle University, Newcastle upon Tyne, UK. Tel: +441912088264. Email: sarah.charman@newcastle.ac.uk; djordje.jakovljevic@newcastle.ac.uk

Introduction

The global spread of the novel coronavirus disease 2019 (COVID-19) has been unprecedented since it first emerged in Wuhan, Hubei Province, China, in December 2019.¹ One of the deadliest pandemics in modern history, COVID-19 is

caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).^{2,3} Its clinical presentation mainly affects the respiratory system but also has severe consequences on other organ systems, for example, the cardiovascular and metabolic systems, resulting in multiple organ failure.^{4–6} The global burden of COVID-19 has resulted in 23 918 447 confirmed cases

and 819 945 deaths (as of 26 August 2020).⁷ COVID-19 may only cause mild or even no symptoms,⁸ but typical indicators at hospital admission include fever, shortness of breath, coughing, fatigue, and dyspnoea.^{9,10} The global population is susceptible to this virus, but advancing age, being male, severe obesity, pre-existing co-morbidities, and underlying cardiovascular disease including heart failure (HF) have a poorer prognosis.^{9,11–18}

Patients who are elderly with multiple co-morbidities (both cardiovascular disease and diabetes) are more susceptible to left ventricular hypertrophy, diastolic dysfunction, and HF, which makes them vulnerable to higher pulmonary vascular pressures.¹⁹ New-onset or worsening HF is a common complication in patients with COVID-19,^{20–23} with documented poor survival rates of ~60%.²² Furthermore, nearly 50% of patients who die from COVID-19 with a diagnosis of HF have no previous history of either hypertension or cardiovascular disease.²⁴ A review of the symptom burden of COVID-19 highlighted that dyspnoea is the most prominent symptom, but the primary cause of death is by respiratory failure or HF or both.²⁵ In a large observational study, nearly three-quarters of patients diagnosed with COVID-19 had at least one pre-existing condition, and over half were hypertensive.²⁶ In end-stage HF patients, myocardial injury has resulted from COVID-19,²⁷ but the pathophysiological mechanisms between the virus, cardiac injury, and HF are not yet understood.²⁸ At present, we are unable to determine the long-term effects of COVID-19 on the cardiovascular system and can only rely on the SARS-CoV virus outcomes as an indicator.²⁹ However, deterioration in myocardial function has been reported in the short term with findings suggesting that patients who recently recovered from COVID-19 presented with lower left and right ventricular ejection fraction, higher left ventricular end-diastolic volume, and raised native T1 and T2 values vs. both healthy controls and risk factor-matched controls.³⁰

Besides, the prognosis of COVID-19 patients is worse in those with existing conditions such as cardiovascular disease.³⁰ Individuals who are older and have existing cardiac co-morbidities have higher mortality from COVID-19 than non-cardiac patients.³¹ COVID-19-induced myocardial injury, confirmed with higher troponin concentration on admission to hospital, is more likely in those who have a history of coronary artery disease, atrial fibrillation, and HF.² COVID-19-positive patients admitted with both reduced left ventricular ejection fraction or impaired right ventricular function and tricuspid regurgitation > 1 are more likely to have a poorer prognosis than those with normal cardiac function.²⁸ In a case report, acute respiratory distress syndrome in a patient with COVID-19 was found to mimic HF with reduced ejection fraction.³²

A larger proportion of angiotensin-converting enzyme-2 (ACE2)-positive cells in cardiomyocytes, and a greater expression of ACE2 found in HF patients, is associated with greater risk of mortality in comparison with those without underlying

medical conditions.³³ It has been hypothesized that hypertensive patients treated with angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) are at increased risk of developing COVID-19 and potentially worse outcomes.³⁴ The European Society of Cardiology and other cardiology societies encourage treatment with renin-angiotensin system antagonists in patients with cardiovascular disease given the inconclusive data on the association between the up-regulation of systemic or tissue ACE2 and risk of COVID-19.³⁵ A large retrospective cohort study of COVID-19-positive patients found no association with mortality when comparing prior users of ACEIs or ARBs with non-users.³⁶ Tomasoni *et al.* reviewed both the harmful and protective effects of ACEI/ARB treatment but suggested that their use 'may counteract increased angiotensin II AT1 receptors stimulation favoured by the loss of the counter-regulatory effects of the downregulated ACE2'.¹ Although underlying cardiovascular disease increases the risk of a poorer prognosis from COVID-19 and patients with these conditions are more likely to be prescribed with ACEIs or ARBs, the evidence suggests that the use of these medications does not increase the risk of COVID-19.³⁷ Indeed, prior use of ACE inhibitors, ARBs, beta-blockers, calcium channel blockers, or thiazide diuretics showed no association with a higher risk of testing positive for COVID-19.³⁸

Primary care practice has changed dramatically as a result of COVID-19 with the transition to telephone and video consultations, which are reported as more efficient than standard consultations, thereby conserving time.³⁹ Video calls are also being utilized for practice meetings with staff in primary care.³⁹ For HF patients, the usual patterns of care have changed during this pandemic, with the majority of practice converting to telehealth with reduced in-person outpatient visits.⁴⁰ Guidance on the continuation of clinical trials during and after COVID-19 has provided alternative methods for measurement of endpoints and highlighted that practicing physicians and researchers have an obligation even during these difficult times to continue to improve patient outcomes, management, and clinical practice.⁴¹ New communication methods that are being advised between clinical care teams, researchers, and patients such as telehealth, remote assessments, and in-person procedures have been delayed.⁴²

This article provides an overview of the current literature on HF hospitalizations, management, and care pathways for supporting patients during and beyond COVID-19.

Heart failure hospitalization

In London, admission rates for acute HF have been significantly lower during the peak of the pandemic vs. the same period in 2019.⁴³ Likewise, in Italy, a 49% decrease in acute HF admissions was recorded from February to April 2020

compared with the same period in 2019.⁴⁴ A similar trend has been reported in Denmark with significantly lower rates of new-onset HF diagnoses and hospital admissions for worsening HF during the lockdown period of 2020 vs. the same period in 2019.⁴⁵ In Germany, emergency admissions for HF declined by 22% between March and April 2020 vs. the same period in 2019.⁴⁶ Likewise, the USA has reported a similar decline in HF hospitalizations.^{47,48} Despite lower admissions rates, when patients do present, they are at a more critical stage of the disease progression with higher New York Heart Association (NYHA) class III or IV at admission (96% vs. 77%) and more severe peripheral oedema (39% vs. 14%) in 2020 compared with 2019.⁴³ However, no differences in HF severity, admission to intensive care unit, length of stay, or mortality have been reported elsewhere between the pre-COVID-19 and COVID-19 periods.⁴⁸ During the COVID-19 period, HF clinic volume has been reported as one-half less vs. the same period in 2019, and the authors suggest that those with more stable HF will likely have deferred their clinic appointment during this period.⁴⁹

It should not be underestimated that there will be a 'tidal wave' effect shortly owing to HF patients avoiding urgent care during the pandemic.⁵⁰ This will impact on health care services and potentially result in unintended mortality from HF.⁵⁰ A potential 'weathering the storm' mentality may be present in patients owing to fears of contamination in hospitals and a realignment of care pathways for HF treatment and management.⁴⁷ More advanced or severe complications in cardiac conditions are currently presenting⁴³ and may present further post-pandemic, which may lead to a rise in morbidity and mortality.⁵¹ Delayed care or reluctance of patients to seek medical attention earlier may result in valve disease progressing to symptoms of advanced or decompensated HF.⁵²

Barghash and Pinney⁵³ highlighted possible reasons for the dramatic decline in HF hospitalizations, which include reduced dietary indiscretions due to restaurant closures, improvements in medication adherence, virtual follow-up care provided, reduction in daily energy expenditure, and refusal to attend hospital for worsening symptoms owing to fears of exposure to the virus. In contrast, social isolation during the pandemic may result in HF destabilizations and adverse events due to changes in dietary habits such as processed food and lifestyle behaviours (decreased physical activity levels)⁵⁴ as well as quarantine-induced stress resulting in depression, social isolation, and behavioural addiction disorders.⁵⁵

To improve patient access and confidence in attending care facilities, it has been demonstrated that relocating HF services to isolated areas of admission or peripheral specialty units has prevented transmission of COVID-19 in advanced HF and cardiac transplantation patients and needs to be considered more widely to protect and promote outpatient visits.⁵⁶ For example, colour-coded zones have been implemented in an HF unit in Milan, Italy, to ensure isolation of infected,

suspected, and no-symptom patients.⁵⁷ However, the authors recognize that the zone system was implemented to maximize the lack of personal protective equipment (PPE) and to save time between patients.⁵⁷

Recognizing the needs and supporting heart failure patients during coronavirus disease 2019

The current care pathways for acute and elective cardiac patients have changed dramatically during this pandemic.⁵ There is a need to protect patients from exposure to this virus during these periods of uncertainty.⁵⁸ During the first wave of the pandemic, the highest risk patients were prioritized for review, but now, we are at the recovery phase, and both high-risk and intermediate-risk patient care need initiation to minimize disease progression.⁵⁹ Optimizing community HF services during the recovery from the pandemic has the potential to reduce the pressures on secondary care.⁵⁹ Based on our literature-guided insights, strategies for improved HF management during and after the COVID-19 pandemic is described in *Table 1*. New-onset and current HF patients must understand their diagnosis and future prognosis. Prior to COVID-19, the majority of patients did not understand their diagnosis, and the meaning of the term 'heart failure'⁶⁰ and prognosis discussions have not been a regular feature in the management of HF.⁶¹ Communication between clinician and patient is evolving, and the recommendation is a transition to telehealth, remote monitoring, and virtual health care strategies.⁶² The British Society for Heart Failure recommends facilitating telephone or video consultations as the first method of communication with the patient from those who have suspected HF at the primary care referral stage, recently discharged acute HF, and known HF patients.⁶³ By adopting virtual visits, patients have been given access to a platform to seek medical advice and avoid in-person exposure, which is essential for HF patients.⁶⁴ However, these new methods will have barriers and challenges such as patient access to the internet, the reluctance of the patient to adopt new technology, feeling self-conscious on a video call, and the clinician's inability to perform a full physical examination.⁶⁴

Supporting rehabilitation services

Successful remote delivery of cardiac rehabilitation services has been reported in Belgium during the pandemic with on-line videos, website resources, and emails utilized, which highlights a potential future for cardiac telerehabilitation.⁶⁵ Future-proofing cardiac rehabilitation services to telehealth have been provided by Thomas *et al.* with a transition to

Table 1 Strategies for improved heart failure management during and after the coronavirus disease 2019 pandemic

Patient education at the time of diagnosis	HF education needs to be addressed and the development of an online platform that is user-friendly for all
Prognosis assessment	Information giving regarding prognosis should become a regular feature at the time of diagnosis and future assessments
Risk assessment	High-risk and intermediate-risk patients require optimization of treatment and minimize disease progression
Redesigning cardiac rehabilitation services	Optimizing and transitioning to telehealth. Reduce future hospital admission

Abbreviation: HF, heart failure.

phone management techniques (i.e. for setting goals, advice, and counselling), monitoring and reviewing patients by email, use of mHealth to personalize goals, videoconferencing, and utilizing web resources.⁶⁶ Virtual cardiac rehabilitation guidance has been published in Canada and highlights challenges with using this method such as loss of in-person interactions as well as difficulties with risk stratification.⁶⁷ The evidence suggests that exercise-based cardiac rehabilitation has numerous health benefits by significantly reducing the risk of reinfarction, cardiac, and cardiovascular mortality as well as all-cause mortality.⁶⁸ Redesigned services such as cardiac rehabilitation are needed to ensure that HF patients can receive optimal treatment during and in the recovery from the pandemic,⁵⁵ which may be beneficial in reducing the potential 'tidal wave' in admissions post-pandemic.

Transitioning to a telehealth framework

On reflection, a pre-existing robust telehealth framework for HF patients would have made remote clinical monitoring and early detection of decompensation easier during the pandemic.^{69,70} This is undoubtedly a recommended component of future HF services to improve communication and support between the clinician and patient.^{69,70} We are now reacting to the pandemic rather than preparing, so the implementation and delivery of a telehealth system need to be supported by the clinician to provide an inclusive service to the patient.⁷¹ This is key now more than ever, especially with HF patients, to ensure that home-based delivery is easy and intuitive.⁷¹ Health care professionals should be prepared for future virus outbreaks by becoming efficient and utilizing remote and virtual technology with HF patients.⁵⁹ The current use of PPE makes a person-centred approach between clinician and patient difficult, but reassurance and verbal encouragement from the clinician are vital.⁷² Resources and toolkits for health care professionals to guide palliative and end-of-life care options for HF patients are emerging.^{59,72}

Interestingly, in Italy, Salzano *et al.* described the successful implementation of a telemedicine service (using phone technology) for HF patients, which was provided throughout lockdown with 58% of patients accessing the service.⁷³

Remote cardiac care can detect underlying disease progression and prevent decompensation during this pandemic as demonstrated by colleagues using V-LAP™ System in an NYHA class III patient.⁷⁴ Successful adoption of a telemedicine-based strategy has been integrated into an HF clinic during COVID-19 with a transition to telemedicine services from in-person visits.⁴⁹ However, the authors highlight the invaluable role of in-person services and assessments, which should be recommended to the patient if needed.⁴⁹

The European Society of Cardiology⁷⁵ HF guidelines promote the use of telephone and remote monitoring in the management and follow-up of HF patients. Home monitoring of HF patients with non-invasive and/or implantable devices is being adopted and has the capacity to transmit haemodynamic data to the clinician, which allows for assessment and guides HF management, thereby reducing in-person visits.⁷⁶ Remote titration strategies using telemonitoring have been effective in HF patients and resulted in reduced clinic visits, decreased time to dose optimization, and a greater number of patients achieving target doses (vs. standard titration).⁷⁷ Standardizing HF telemedicine is essential, and there is potential to improve patient care and reduce costs to health care services.⁷⁸

The need for evidence

Editors clearly have an obligation to support and disseminate the latest findings from COVID-19, but the need for randomized controlled clinical trials, larger cohort studies (>100 patients), case reports, and design papers have been highlighted in the HF population.⁷⁹ The publication of protocols such as the BRACE CORONA Trial will be of interest.⁸⁰ Clinical trials for HF are currently restricted during this pandemic, and telehealth methods have been introduced for follow-up to reduce the risk of missing data.⁸¹ Systematic literature reviews provide readers and cardiologists with the latest communication on COVID-19 and cardiovascular complications.^{82,83} Researchers have to adapt to different ways of working with reduced opportunities in cardiovascular research for data collection, networking, presenting, and funding with strategic opportunities for online options needed.⁸⁴

Conclusions

The need to gain information about the effect of COVID-19 on HF presentation and management is ever more present. The reduction in hospitalizations for HF is a concern, and the potential 'tidal wave' in admissions may result in more severe or advanced cases of HF in the near future. There is still a need to shield the most vulnerable, and future outbreaks may occur. Lessons should have been learnt from the current pandemic to provide better support for HF patients and optimize clinical services. More research is needed to ensure telehealth is acceptable and sustainable in this population now and during the recovery from the pandemic.

Conflict of interest

Sarah J. Charman, Lazar Velicki, Nduka C. Okwose, Amy Harwood, Gordon McGregor, Arsen Ristic, Prithwish Banerjee, Petar M. Seferovic, Guy A. MacGowan, and Djordje G. Jakovljevic declare that they have no conflict of interest.

Funding

This work was supported by the European Union's Horizon 2020 Research and Innovation Programme under Grant Agreement no. 777204, and Research Councils UK Centre for Ageing and Vitality (L016354).

References

- Tomasoni D, Italia L, Adamo M, Inciardi RM, Lombardi CM, Solomon SD, Metra M. COVID 19 and heart failure: from infection to inflammation and angiotensin II stimulation. Searching for evidence from a new disease. *Eur J Heart Fail* 2020; **22**: 957–966.
- Lala A, Johnson KW, Januzzi JL, Russak AJ, Paranjpe I, Richter F, Zhao S, Somani S, Van Vleck T, Vaid A, Chaudhry F, De Freitas JK, Fayad ZA, Pinney SP, Levin M, Charney A, Bagiella E, Narula J, Glicksberg BS, Nadkarni G, Mancini DM, Fuster V. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. *J Am Coll Cardiol* 2020; **76**: 533–546.
- Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, Haagmans BL, Lauber C, Leontovich AM, Neuman BW, Penzar D, Perlman S, Poon LLM, Samborskiy DV, Sidorov IA, Sola I, Ziebuhr J. Coronaviridae Study Group of the International Committee on Taxonomy of V. The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol* 2020; **5**: 536–544.
- Bavishi C, Bonow RO, Trivedi V, Abbott JD, Messerli FH, Bhatt DL. Acute myocardial injury in patients hospitalized with COVID-19 infection: a review. *Prog Cardiovasc Dis* 2020. <https://doi.org/10.1016/j.pcad.2020.05.013>
- Boukhris M, Hillani A, Moroni F, Annabi MS, Addad F, Ribeiro MH, Mansour S, Zhao X, Ybarra LF, Abbate A, Vilca LM, Azzalini L. Cardiovascular implications of the COVID-19 pandemic: a global perspective. *Can J Cardiol* 2020; **36**: 1068–1080.
- Du RH, Liu LM, Yin W, Wang W, Guan LL, Yuan ML, Li YL, Hu Y, Li XY, Sun B, Peng P, Shi HZ. Hospitalization and critical care of 109 decedents with COVID-19 pneumonia in Wuhan, China. *Ann Am Thorac Soc* 2020; **17**: 839–846.
- Coronavirus Resource Centre. Johns Hopkins University & Medicine [cited 26 August 2020]. <https://coronavirus.jhu.edu/map.html> (26 July 2020).
- Wang Y, Wang Y, Chen Y, Qin Q. Unique epidemiological and clinical features of the emerging 2019 novel coronavirus pneumonia (COVID-19) implicate special control measures. *J Med Virol* 2020; **92**: 568–576.
- Du Y, Tu L, Zhu P, Mu M, Wang R, Yang P, Wang X, Hu C, Ping R, Hu P, Li T, Cao F, Chang C, Hu Q, Jin Y, Xu G. Clinical features of 85 fatal cases of COVID-19 from Wuhan. A retrospective observational study. *Am J Respir Crit Care Med* 2020; **201**: 1372–1379.
- Liu K, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, Xiao W, Wang YN, Zhong MH, Li CH, Li GC, Liu HG. Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl)* 2020; **133**: 1025–1031.
- Gao Q, Hu Y, Dai Z, Xiao F, Wang J, Wu J. The epidemiological characteristics of 2019 novel coronavirus diseases (COVID-19) in Jingmen, Hubei, China. *Medicine (Baltimore)* 2020; **99**: e20605.
- Palmieri L, Vanacore N, Donfrancesco C, Lo Noce C, Canevelli M, Punzo O, Raparelli V, Pezzotti P, Riccardo F, Bella A, Fabiani M, D'Ancona FP, Vaianella L, Tiple D, Colaizzo E, Palmer K, Rezza G, Piccioli A, Brusaferrero S, Onder G. Clinical characteristics of hospitalized individuals dying with COVID-19 by age group in Italy. *J Gerontol A Biol Sci Med Sci* 2020; **75**: 1796–1800.
- Escalera-Antezana JP, Lizon-Ferrufino NF, Maldonado-Alanoca A, Alarcon-Dela-Vega G, Alvarado-Arnez LE, Balderrama-Saavedra MA, Bonilla-Aldana DK, Rodriguez-Morales AJ. Risk factors for mortality in patients with coronavirus disease 2019 (COVID-19) in Bolivia: an analysis of the first 107 confirmed cases. *Infez Med* 2020; **28**: 238–242.
- Böhm M, Frey N, Giannitsis E, Sliwa K, Zeiher AM. Coronavirus disease 2019 (COVID-19) and its implications for cardiovascular care: expert document from the German Cardiac Society and the World Heart Federation. *Clin Res Cardiol* 2020; **27**: 1–14. <https://doi.org/10.1007/s00392-020-01656-3>
- Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell L, Chernyak Y, Tobin KA, Cerfolio RJ, Francois F, Horwitz LI. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. *BMJ* 2020; **369**: m1966.
- Palaiodimos L, Kokkinidis DG, Li W, Karamanis D, Ognibene J, Arora S, Southern WN, Mantzoros CS. Severe obesity, increasing age and male sex are independently associated with worse in-hospital outcomes, and higher in-hospital mortality, in a cohort of patients with COVID-19 in the Bronx. *New York Metabolism* 2020; **108**: 154262.
- Zhao XY, Xu XX, Yin HS, Hu QM, Xiong T, Tang YY, Yang AY, Yu BP, Huang ZP. Clinical characteristics of patients with 2019 coronavirus disease in a non-Wuhan area of Hubei Province, China: a retrospective study. *BMC Infect Dis* 2020; **20**: 311.
- Ciceri F, Castagna A, Rovere-Querini P, De Cobelli F, Ruggeri A, Galli L, Conte C, De Lorenzo R, Poli A, Ambrosio A, Signorelli C, Bossi E, Fazio M, Tresoldi C, Colombo S, Monti G, Fominskiy E, Franchini S, Spessot M, Martinenghi C, Carlucci M, Beretta L, Scandroglio AM, Clementi M, Locatelli M, Tresoldi M,

- Scarpellini P, Martino G, Bosi E, Dagna L, Lazzarin A, Landoni G, Zangrillo A. Early predictors of clinical outcomes of COVID-19 outbreak in Milan. *Italy Clin Immunol* 2020; **217**: 108509.
19. Mehra MR, Ruschitzka F. COVID-19 illness and heart failure: a missing link? *JACC Heart Fail*. 2020; **8**: 512–514.
 20. Aggarwal S, Garcia-Telles N, Aggarwal G, Lavie C, Lippi G, Henry BM. Clinical features, laboratory characteristics, and outcomes of patients hospitalized with coronavirus disease 2019 (COVID-19): early report from the United States. *Diagnosis (Berl)* 2020; **7**: 91–96.
 21. Liu PP, Blet A, Smyth D, Li H. The Science Underlying COVID-19: implications for the Cardiovascular System. *Circulation* 2020; **142**: 68–78.
 22. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, Guan L, Wei Y, Li H, Wu X, Xu J, Tu S, Zhang Y, Chen H, Cao B. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet* 2020; **395**: 1054–1062.
 23. Chen Q, Xu L, Dai Y, Ling Y, Mao J, Qian J, Zhu W, Di W, Ge J. Cardiovascular manifestations in severe and critical patients with COVID-19. *Clin Cardiol* 2020; [epub ahead of print 20 June 2020]; **43**: 796–802.
 24. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, Ma K, Xu D, Yu H, Wang H, Wang T, Guo W, Chen J, Ding C, Zhang X, Huang J, Han M, Li S, Luo X, Zhao J, Ning Q. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. *BMJ* 2020; **368**: m1091.
 25. Keeley P, Buchanan D, Carolan C, Pivodic L, Tavabie S, Noble S. Symptom burden and clinical profile of COVID-19 deaths: a rapid systematic review and evidence summary. *BMJ Support Palliat Care* 2020. <https://doi.org/10.1136/bmjspcare-2020-002368>
 26. Iaccarino G, Grassi G, Borghi C, Ferri C, Salvetti M, Volpe M. Age and multimorbidity predict death among COVID-19 patients: results of the SARS-RAS study of the Italian Society of Hypertension. *Hypertension* 2020; **76**: 366–372.
 27. Dong N, Cai J, Zhou Y, Liu J, Li F. End-stage heart failure with COVID-19: strong evidence of myocardial injury by 2019-nCoV. *JACC Heart Fail* 2020; **8**: 515–517.
 28. Rath D, Petersen-Urbe Á, Avdiu A, Witzel K, Jaeger P, Zdanyte M, Heinzmann D, Tavlaki E, Müller K, Gawaz MP. Impaired cardiac function is associated with mortality in patients with acute COVID-19 infection. *Clin Res Cardiol* 2020; **14**: 1–9. <https://doi.org/10.1007/s00392-020-01683-0>
 29. Goha A, Mezue K, Edwards P, Nunura F, Baugh D, Madu E. COVID-19 and the heart: an update for clinicians. *Clin Cardiol* 2020. <https://doi.org/10.1002/clc.23406>
 30. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, Ji R, Wang H, Wang Y, Zhou Y. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. *Int J Infect Dis* 2020; **94**: 91–95.
 31. Inciardi RM, Adamo M, Lupi L, Cani DS, Di Pasquale M, Tomasoni D, Italia L, Zaccone G, Tedino C, Fabbriatore D, Curnis A, Faggiano P, Gorga E, Lombardi CM, Milesi G, Vizzardi E, Volpini M, Nodari S, Specchia C, Maroldi R, Bezzi M, Metra M. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur Heart J* 2020; **41**: 1821–1829.
 32. Sattar Y, Connerney M, Ullah W, Rauf H, Mamtani S, Luddington S, Alraies MC. Coronavirus disease 2019 with acute respiratory distress syndrome mimicking heart failure exacerbation: time to rethink. *Cardiol Res* 2020; **11**: 196–199.
 33. Guo J, Wei X, Li Q, Li L, Yang Z, Shi Y, Qin Y, Zhang X, Wang X, Zhi X, Meng D. Single-cell RNA analysis on ACE2 expression provides insights into SARS-CoV-2 potential entry into the bloodstream and heart injury. *J Cell Physiol* 2020; **235**: 9884–9894.
 34. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? *Lancet Respir Med* 2020; **8**: e21.
 35. Brojakowska A, Narula J, Shimony R, Bander J. Clinical implications of SARS-CoV-2 interaction with renin-angiotensin system: JACC review topic of the week. *J Am Coll Cardiol* 2020; **75**: 3085–3095.
 36. Fosbøl EL, Butt JH, Østergaard L, Andersson C, Selmer C, Kragholm K, Schou M, Phelps M, Gislason GH, Gerds TA, Torp-Pedersen C, Køber L. Association of angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use with COVID-19 diagnosis and mortality. *JAMA* 2020; **324**: 168–177.
 37. Mancia G, Rea F, Ludergnani M, Apolone G, Corrao G. Renin-angiotensin-aldosterone system blockers and the risk of Covid-19. *New England Journal of Medicine*. 2020; **382**: 2431–2440.
 38. Reynolds HR, Adhikari S, Pulgarin C, Troxel AB, Iturrate E, Johnson SB, Hausvater A, Newman JD, Berger JS, Bangalore S, Katz SD, Fishman GI, Kunichoff D, Chen Y, Ogedegbe G, Hochman JS. Renin-angiotensin-aldosterone system inhibitors and risk of Covid-19. *New England Journal of Medicine* 2020; **382**: 2441–2448.
 39. Thornton J. Covid-19: how coronavirus will change the face of general practice forever. *BMJ* 2020; **368**: m1279.
 40. McIlvennan CK, Allen LA, DeVore AD, Kaltenbach LA, Granger CB, Granger BB. Changes in care delivery for patients with heart failure during the COVID-19 pandemic: results of a multicenter survey. *J Card Fail* 2020; **26**: 635–636.
 41. Anker SD, Butler J, Khan MS, Abraham WT, Bauersachs J, Bocchi E, Bozkurt B, Braunwald E, Chopra VK, Cleland JG, Ezekowitz J, Filippatos G, Friede T, Hernandez AF, Lam CSP, Lindenfeld J, McMurray JJV, Mehra M, Metra M, Packer M, Pieske B, Pocock SJ, Ponikowski P, Rosano GMC, Teerlink JR, Tsutsui H, Van Veldhuisen DJ, Verma S, Voors AA, Wittes J, Zannad F, Zhang J, Seferovic P, Coats AJS. Conducting clinical trials in heart failure during (and after) the COVID-19 pandemic: an Expert Consensus Position Paper from the Heart Failure Association (HFA) of the European Society of Cardiology (ESC). *Eur Heart J* 2020; **41**: 2109–2117.
 42. Abraham WT, Fiuzat M, Psotka MA, O'Connor CM. Heart failure collaborative statement on clinical trials in the landscape of COVID-19. *JACC Heart Fail*. 2020; **8**: 423–425.
 43. Bromage DI, Cannata A, Rind IA, Gregorio C, Piper S, Shah AM, McDonagh TA. The impact of COVID-19 on heart failure hospitalization and management: report from a Heart Failure Unit in London during the peak of the pandemic. *Eur J Heart Fail* 2020; **22**: 978–984.
 44. Colivicchi F, Di Fusco SA, Magnanti M, Cipriani M, Imperoli G. The impact of the coronavirus disease-2019 pandemic and Italian lockdown measures on clinical presentation and management of acute heart failure. *J Card Fail* 2020; **26**: 464–465.
 45. Andersson C, Gerds T, Fosbøl E, Phelps M, Andersen J, Lamberts M, Holt A, Butt JH, Madelaire C, Gislason G, Torp-Pedersen C, Køber L, Schou M. Incidence of new-onset and worsening heart failure before and after the COVID-19 epidemic lockdown in Denmark: a nationwide cohort study. *Circ Heart Fail* 2020; **13**: e007274.
 46. Bollmann A, Hohenstein S, Meier-Hellmann A, Kühlen R, Hindricks G. Emergency hospital admissions and interventional treatments for heart failure and cardiac arrhythmias in Germany during the Covid-19 outbreak Insights from the German-wide Helios hospital network. *Eur Heart J Qual Care Clin Outcomes* 2020; **6**: 221–222.
 47. Hall ME, Vaduganathan M, Khan MS, Papadimitriou L, Long RC, Hernandez GA, Moore CK, Lennep BW, McMullan MR, Butler J. Reductions in heart failure hospitalizations during the COVID-19 pandemic. *J Card Fail* 2020; **26**: 462–463.
 48. Cox ZL, Lai P, Lindenfeld J. Deceases in acute heart failure hospitalizations during COVID-19. *Eur J Heart Fail* 2020; **22**: 1045–1046.
 49. Umapathi P, Cuomo K, Riley S, Hubbard A, Menzel K, Sauer E, Gilotra NA. Transforming ambulatory heart failure

- care in the COVID-19 era: initial experience from a heart failure disease management clinic. *J Card Fail* 2020; **26**: 637–638.
50. Moayed Y, Alba AC, Lee DS, Wijeyesundara HC, Ross HJ. The next wave of health care strain related to COVID-19: heart failure patients coming back in force: we must not fail them. *Can J Cardiol* 2020; **36**: 993–994.
 51. Lazaridis C, Vlachogiannis NI, Bakogiannis C, Spyridopoulos I, Stamatelopoulos K, Kanakakis I, Vassilikos V, Stellos K. Involvement of cardiovascular system as the critical point in coronavirus disease 2019 (COVID-19) prognosis and recovery. *Hellenic J Cardiol* 2020. <https://doi.org/10.1016/j.hjc.2020.05.004>
 52. George I, Salna M, Kobsa S, Deroo S, Kriegel J, Blitzer D, Shea NJ, D'Angelo A, Raza T, Burlansky P, Takeda K, Takayama H, Bapat V, Naka Y, Smith CR, Bacha E, Argenziano M. The rapid transformation of cardiac surgery practice in the coronavirus disease 2019 (COVID-19) pandemic: insights and clinical strategies from a centre at the epicentre. *Eur J Cardiothorac Surg* 2020; **667**–675.
 53. Barghash MH, Pinney SP. Heart failure in the COVID-19 pandemic: where has all New York's congestion gone? *J Card Fail* 2020; **26**: 477–478.
 54. Reza N, DeFilippis EM, Jessup M. Secondary impact of the COVID-19 pandemic on patients with heart failure. *Circ Heart Fail* 2020; **13**: e007219.
 55. Neth Heart Mureddu GF, Ambrosetti M, Venturini E, La Rovere MT, Mazza A, Pedretti R, Sarullo F, Fattiroli F, Faggiano P, Giallauria F, Vigorito C, Angelino E, Brazzo S, Ruzzolini M. Cardiac rehabilitation activities during the COVID-19 pandemic in Italy. Position Paper of the AICPR (Italian Association of Clinical Cardiology, Prevention and Rehabilitation). *Monaldi Arch Chest Dis* 2020; **90**.
 56. Walsh MN, Ravichandran AK, Seator E, Salerno CT. Clinical distancing of hospitalized patients with advanced heart failure and cardiac transplantation during COVID-19. *J Heart Lung Transplant* 2020; **39**: 730.
 57. Agostoni P, Mapelli M, Conte E, Baggiano A, Assanelli E, Apostolo A, Alimento M, Berna G, Guglielmo M, Muratori M, Susini F, Palermo P, Pezzuto B, Salvioni E, Sudati A, Vignati C, Merlino L. Cardiac patient care during a pandemic: how to reorganise a heart failure unit at the time of COVID-19. *Eur J Prev Cardiol* 2020; **27**: 1127–1132.
 58. Harjai KJ, Agarwal S, Bauch T, Bernardi M, Casale AS, Green S, Harostock M, Ierovante N, Mascarenhas V, Matsumura M, Nawaz Y, Scott T, Singh D, Stella JJ, Vijayaraman P, Yost G, Blankenship JC. Coronary and structural heart disease interventions during COVID-19 pandemic: a road map for clinicians and health care delivery systems. *Cardiovasc Revasc Med*. Washington DC; 2020. <https://doi.org/10.1016/j.carrev.2020.06.013>
 59. British Society for Heart Failure. *Planned Recovery Phase of Essential Heart Failure Services during Covid-19 Pandemic: A Position Statement from the British Society for Heart Failure*. 2020.
 60. Banerjee P, Gill L, Muir V, Nadar S, Raja Y, Goyal D, Koganti S. Do heart failure patients understand their diagnosis or want to know their prognosis? Heart failure from a patient's perspective. *Clin Med (Lond)* 2010; **10**: 339–343.
 61. Banerjee P, Watson C, Ali D. Discussing prognosis in heart failure: a questionnaire-based study of the patient's view. *JACC Heart Fail*. 2018; **6**: 803–804.
 62. Virani SA, Clarke B, Ducharme A, Ezekowitz JA, Heckman GA, McDonald M, Mielniczuk LM, Swigum E, Van Spall HGC, Zieroth S. Optimizing access to heart failure care in Canada during the COVID-19 pandemic. *Can J Cardiol* 2020; **36**: 1148–1151.
 63. British Society for Heart Failure. *Retention of Essential Heart Failure Services during COVID-19 Pandemic: A Position Statement from the British Society for Heart Failure*. London, UK; 2020.
 64. Gorodeski EZ, Goyal P, Cox ZL, Thibodeau JT, Reay RE, Rasmusson K, Rogers JG, Starling RC. Virtual visits for care of patients with heart failure in the era of COVID-19: a statement from the Heart Failure Society of America. *J Card Fail* 2020; **26**: 448–456.
 65. Scherrenberg M, Frederix I, De Sutter J, Dendale P. Use of cardiac telerehabilitation during COVID-19 pandemic in Belgium. *Acta Cardiol* 2020. <https://doi.org/10.1080/00015385.2020.1786625>
 66. Thomas E, Gallagher R, Grace SL. Future-proofing cardiac rehabilitation: transitioning services to telehealth during COVID-19. *Eur J Prev Cardiol* 2020; **204748732092292**.
 67. Moulson N, Bewick D, Selway T, Harris J, Suskin N, Oh P, Coutinho T, Singh G, Chow CM, Clarke B, Cowan S, Fordyce CB, Fournier A, Gin K, Gupta A, Hardiman S, Jackson S, Lamarche Y, Lau B, Légaré JF, Leong-Poi H, Mansour S, Marelli A, Quraishi AUR, Roifman I, Ruel M, Sapp J, Small G, Turgeon R, Wood DA, Zieroth S, Virani S, Krahn AD. Cardiac rehabilitation during the COVID-19 era: guidance on implementing virtual care. *Can J Cardiol* 2020; **36**: 1317–1321.
 68. Lawler PR, Filion KB, Eisenberg MJ. Efficacy of exercise-based cardiac rehabilitation post-myocardial infarction: a systematic review and meta-analysis of randomized controlled trials. *American Heart Journal* 2011; **162**: 571–84.e2.
 69. De Filippo O, D'Ascenzo F, De Ferrari GM. Heart failure related hospitalisation and management during COVID-19 pandemic: are we ready to reflect?—reply. *Eur J Heart Fail* 2020. <https://doi.org/10.1002/ejhf.1939>
 70. Shah N, Ahmed I, Nazir T. Heart failure related hospitalisation and management during COVID-19 pandemic: are we ready to reflect? *Eur J Heart Fail* 2020. <https://doi.org/10.1002/ejhf.1931>
 71. Cleland JGF, Clark RA, Pellicori P, Inglis SC. Caring for people with heart failure and many other medical problems through and beyond the COVID-19 pandemic: the advantages of universal access to home telemonitoring. *Eur J Heart Fail* 2020; **22**: 995–998.
 72. Hill L, Beattie JM, Geller TP, Baruah R, Boyne J, Stolfo GD, Jaarsma T. Palliative care: essential support for patients with heart failure in the COVID-19 pandemic. *Eur J Cardiovasc Nurs* 2020; **19**: 469–472.
 73. Salzano A, D'Assante R, Stagnaro FM, Valente V, Crisci G, Giardino F, Arcopinto M, Bossone E, Marra AM, Cittadini A. Heart failure management during COVID-19 outbreak in Italy. Telemedicine experience from a heart failure university tertiary referral centre. *Eur J Heart Fail* 2020; **22**: 1048–1050.
 74. D'Amario D, Restivo A, Canonico F, Rodolico D, Galli M, Burzotta F, Vergallo R, Trani C, Aspromonte N, Crea F. Experience of remote cardiac care during Covid-19 pandemic: the V-LAP™ device in advanced heart failure. *Eur J Heart Fail* 2020; **22**: 1050–1052.
 75. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, Gonzalez-Juanatey JR, Harjola VP, Jankowska EA, Jessup M, Linde C, Nihoyannopoulos P, Parissis JT, Pieske B, Riley JP, Rosano GM, Ruilope LM, Ruschitzka F, Rutten FH, van der Meer P. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: the Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur Heart J* 2016; **37**: 2129–2200.
 76. Iellamo F, Sposato B, Volterrani M. Telemonitoring for the management of patients with heart failure. *Card Fail Rev* 2020; **6**: e07.
 77. Kirk V. Evaluation of the impact of remote titration combined with telemonitoring on the optimization of guideline directed medical therapy for patients with heart failure. MSc Thesis. Health Policy, Management and Evaluation 2020.
 78. Eurlings CGMJ, Boyne JJ, de Boer RA, Brunner-La Rocca HP. Telemedicine in heart failure—more than nice to have? *Neth Heart J* 2019; **27**: 5–15.
 79. O'Connor CM. Heart failure editorial emergencies in the COVID-19 era. *JACC: Heart Failure* 2020; **8**: 518.
 80. Lopes RD, Macedo AVS, Silva PGM d BE, Moll-Bernardes RJ, Feldman A,

- D'Andréa Saba Arruda G, de Souza AS, de Albuquerque DC, Mazza L, Santos MF, Salvador NZ, Gibson CM, Granger CB, Alexander JH, de Souza OF. Continuing versus suspending angiotensin-converting enzyme inhibitors and angiotensin receptor blockers: impact on adverse outcomes in hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)—the BRACE CORONA Trial. *Am Heart J* 2020; **226**: 49–59.
81. Ozkan J. Trying times for heart failure trials during the COVID-19 pandemic. *Eur Heart J* 2020; **41**: 1715.
82. Sugimoto T, Mizuno A, Kishi T, Ito N, Matsumoto C, Fukuda M, Kagiya N, Shibata T, Ohmori T, Oishi S, Fuse J, Kida K, Kawai F, Ishida M, Sanada S, Komuro I, Node K. Coronavirus disease 2019 (COVID-19) information for cardiologists—systematic literature review and additional analysis. *Circ J* 2020; **84**: 1039–1043.
83. Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. *Am J Emerg Med* 2020; **38**: 1504–1507.
84. Climie RE, Marques FZ. Impact, strategies, and opportunities for early and midcareer cardiovascular researchers during the COVID-19 pandemic. *Circulation* 2020; **141**: 1838–1840.