Impact of the COVID-19 pandemic on the management of chronic heart failure

Melanie McGinlay[1], Sam Straw[2], Jacob Jagger[2], Bako Nouri[2], John Gierula[2], Klaus K Witte[2,*]

[1] *Department of Cardiology, Leeds Teaching Hospitals NHS Trust, LS9 7TF Leeds, UK*

[2] *Leeds Institute of Cardiovascular and Metabolic Medicine, University of Leeds, LS2 9JT Leeds, UK*

*Correspondence: k.k.witte@leeds.ac.uk (Klaus K Witte)

The coronavirus disease 2019 (COVID-19) pandemic is an unprecedented challenge. Meeting this has resulted in changes to working practices and the impact on the management of patients with heart failure with reduced ejection fraction (HFrEF) is largely unknown. We performed a retrospective, observational study contrasting patients diagnosed with HFrEF attending specialist heart failure clinics at a UK hospital, whose subsequent period of optimisation of medical therapy was during the COVID-19 pandemic, with patients diagnosed the previous year. The primary outcome was the change in equivalent dosing of ramipril and bisoprolol at 6-months. Secondary outcomes were the number and type of follow-up consultations, hospitalisation for heart failure and all-cause mortality. In total, 60 patients were diagnosed with HFrEF between 1 December 2019 and 30 April 2020, compared to 54 during the same period of the previous year. The absolute number of consultations was higher (390 vs 270; $p = 0.69$), driven by increases in telephone consultations, with a reduction in appointments with hospital nurse specialists. After 6-months, we observed lower equivalent dosing of ramipril (3.1 ± 3.0 mg vs 4.4 ± 0.5 mg; $p = 0.035$) and similar dosing of bisoprolol (4.1 ± 0.5 mg vs 4.9 ± 0.5 mg; $p = 0.27$), which persisted for ramipril (mean difference 1.0 mg, 95% CI 0.018–2.09; $p = 0.046$) and bisoprolol (mean difference 0.52 mg, 95% CI -0.23–1.28; $p = 0.17$) after adjustment for baseline dosing. We observed no differences in the proportion of patients who died (5.0% vs 7.4%; $p = 0.59$) or were hospitalised with heart failure (13.3% vs 9.3%; $p = 0.49$). Our study suggests the transition to telephone appointments and re-deployment of heart failure nurse specialists was associated with less successful optimisation of medical therapy, especially renin-angiotensin inhibitors, compared with usual care.

Keywords

Heart failure; ACE-inhibitors; β-blockers; Specialist nursing

1. Background

The coronavirus disease 2019 (COVID-19) pandemic is an unprecedented challenge to healthcare systems. Meeting this has resulted in dramatic changes to working practices for those caring for patients with chronic diseases. The Leeds Integrated Heart Failure service comprises of physicians, heart failure nurse specialists and dedicated cardiac physiologists, combining hospital and community care. A principle aim of the service is optimising the delivery of guideline-directed medical therapy (GDMT) to improve outcomes for patients with heart failure [1].

The re-deployment of healthcare personnel, transition from face-to-face to telephone consultations and the wider impact of the COVID-19 pandemic on the management of patients with heart failure remains largely unknown. Here we report the changes in frequency and type of follow-up appointments, optimisation of GDMT and outcomes in newly diagnosed patients with heart failure with reduced ejection fraction (HFrEF) during the first wave of the pandemic.

2. Methods

2.1 Study design

We performed a retrospective, observational study in ambulatory patients with newly diagnosed HFrEF attending the Leeds Integrated Heart Failure Service, designed and reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

2.2 Participants

We contrasted patients diagnosed with HFrEF between 1 December 2019 and 30 April 2020 whose diagnosis and subsequent period of dose optimisation of GDMT was during the first wave of the COVID-19 pandemic, with patients diagnosed during the same period the previous year. Inclusion required no previous diagnosis of HFrEF, age $\geq$18 years and left ventricular ejection fraction (LVEF) <50% on transthoracic echocardiogram. Patients who were diagnosed but died within 6-months were excluded from the analysis but are reported in Fig. 1.

2.3 Variables and data sources

We recorded patient demographics, aetiology of heart failure, past medical history, functional capacity according to New York Heart Associated (NYHA) classification. Transthoracic echocardiogram was performed at the point of first attendance at the integrated heart failure service and we measured LVEF according to Simpson's biplane method, left ventricular (LV) end-diastolic diameter, right ventricular impairment and presence of regional wall motion abnormal-
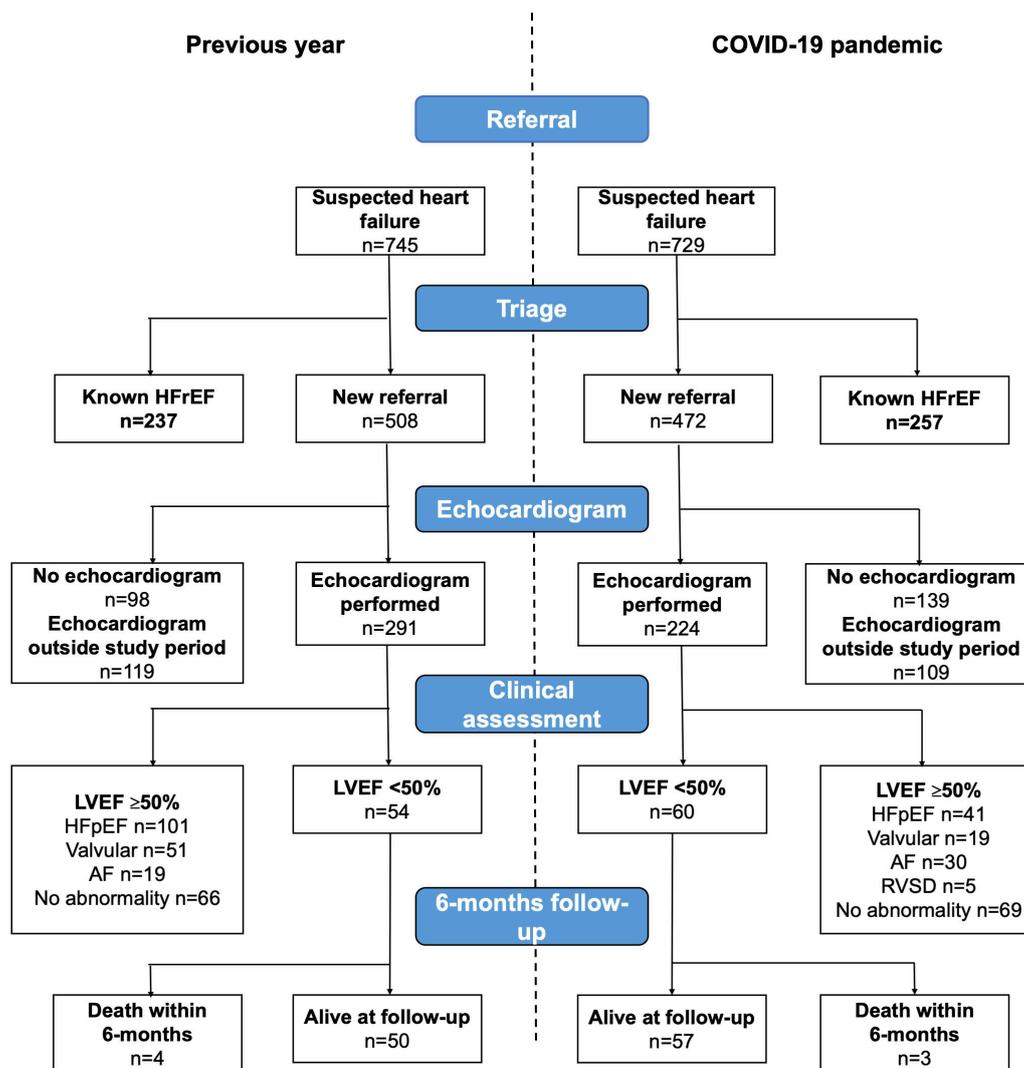
Fig. 1. Study flow chart. Description: Inclusion and exclusion criteria of patients referred to the Leeds integrated heart failure service.

ity according to national recommendations [2]. We recorded dosing of guideline-directed medical therapy at enrolment and at 6-months. We assessed the frequency and type of follow-up consultations, outpatient blood tests, change in dosing of angiotensin converting enzyme inhibitors (ACEi) or angiotensin II receptor blockers (ARB), β-blockers and loop diuretics.

2.4 Definitions

The date of the first echocardiogram showing LVEF <50% was regarded as the time of diagnosis. For the purposes of analysis, the doses of renin-angiotensin system inhibitors, β-blockers and loop diuretics are expressed as equivalent doses relative to the maximum licensed doses of ramipril, bisoprolol and furosemide, respectively.

2.5 Assessment of outcomes

Patients were followed up until death or 6-months following diagnosis. Outcomes data were obtained from the electronic Patient Pathway Manager Plus care record, which

updates mortality events daily directly from the UK Office of National Statistics. The primary outcome was the change in equivalent dosing of ramipril and bisoprolol between the time of diagnosis and 6-months. Secondary outcomes were the number and type of follow-up consultations, hospitalisation for heart failure and all-cause mortality during the 6-month period following diagnosis.

2.6 Statistics

All statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Corporation, Armonk, NY, USA). Unless otherwise stated, continuous variables are expressed as mean $\pm$ SEM and discrete variables as number (percentages). Groups were compared using Student's t-test, Mann-Whitney U test or χ^2 as appropriate. Changes in dosing of GDMT between study cohorts was compared by one-way analysis of covariance adjusted for baseline dosing. In all analyses statistical significance was defined as $p < 0.05$.

3. Results

3.1 Patients

A total 60 patients were newly diagnosed with HFrEF following referral to the integrated heart failure service between 01 Dec 2019 and 30 April 2020, compared to 54 during the same period in the previous year (Fig. 1). Patients had a mean age of 74.7 ± 1.2 years and 70 (61.4%) were male. At baseline, the majority of patients were receiving a beta-blocker (70.2%) and an ACEi/ARB (64.0%). The majority of patients were New York Heart Association Class II (57.9%) or III (35.1%) and the mean LVEF was 33.1 ± 1.1%. Patients were well matched between study periods with no differences in co-morbidities, measured parameters or dosing of medications (Table 1).

3.2 Consultations

In the first 6-months following diagnosis the absolute number of consultations was higher during the COVID-19 pandemic (390 vs 270; $p = 0.69$) compared to the previous year (Table 2). This was primarily driven by increases in the number telephone consultations with community heart failure nurses (185 vs 53; $p = 0.008$). However, the number of consultations with hospital heart failure specialist nurses was less, no patients were seen face-to-face (28 vs 0; $p = 0.001$) and only one had telephone follow-up (3 vs 1; $p = 0.26$) during the study period. Although the number of consultations with physicians was similar, we observed a transition from face-to-face (76 vs 61; $p = 0.033$), to telephone appointments (0 vs 21; $p < 0.001$). Additionally, the median number of outpatient blood tests was less during the COVID-19 pandemic, compared to the previous year (4 (2–6) vs 3 (1–4); $p = 0.03$).

3.3 Dosing of medical therapy

Equivalent doses of ramipril (3.1 ± 0.44 mg vs 2.7 ± 0.44 mg; $p = 0.56$) and bisoprolol (3.8 ± 0.49 mg vs 3.2 ± 0.42 mg; $p = 0.35$) were similar between study periods at baseline. After 6-months we observed lower equivalent dosing of ramipril during the pandemic compared with the previous year (3.1 ± 3.0 mg vs 4.4 ± 0.5 mg; $p = 0.035$), although equivalent dosing of bisoprolol was similar (4.1 ± 0.5 mg vs 4.9 ± 0.5 mg; $p = 0.27$) (Fig. 2). These observations persisted after adjustment for dosing at baseline, with mean difference of equivalent dosing of ramipril of 1.0 mg (95% CI 0.018–2.09; $p = 0.046$) and for bisoprolol 0.52 mg (95% CI –0.23–1.28; $p = 0.17$) between study periods. The dosing of loop diuretic was similar at baseline and at follow-up (mean change 18.9 ± 6.5 vs 11.1 ± 5.6 mg; $p = 0.36$).

3.4 Heart failure hospitalisation and survival

We observed no differences in the proportion of patients who died (5.0% vs 7.4%; $p = 0.59$) or were hospitalised with heart failure (13.3% vs 9.3%; $p = 0.49$) between study periods.

4. Discussion

In this retrospective analysis of newly diagnosed patients with HFrEF referred to the Leeds Integrated Heart Failure Service, we observed that during the COVID-19 pandemic patients were more often managed by telephone consultations and the optimisation of GDMT, especially ACEi/ARB was less successful compared to the previous year.

Recent reports have highlighted that patients with HFrEF are at high-risk of severe disease from COVID-19 [3, 4], and that the pandemic has also resulted in significant disruption to heart failure service including the cancellation or postponement of appointments and investigations [5]. Additionally, reports have highlighted a reluctance to seek medical attention, with reduced attendances with worsening heart failure during the peak of the pandemic [6, 7]. However, the impact of the pandemic on the optimisation of GDMT is unknown.

In the UK, heart failure nurse specialists supervise the titration and optimisation of GDMT for patients proven to have HFrEF. The majority of these specialist nurses are independent prescribers and many have additional qualifications in advanced practice. In many regions, including ours, the pandemic resulted in the re-deployment of nurse specialists, especially those working in hospital settings away from heart failure services to manage the burden of COVID-19. Perhaps in response to this, the number of consultations with community heart failure nurse specialists increased, albeit with a transition to telephone consultations.

For patients with newly diagnosed HFrEF, the optimisation of GDMT was less during the COVID-19 pandemic compared to the previous year, especially the up-titration of inhibitors of the renin-angiotensin system, despite an overall *higher* number of consultations. The reasons for this may firstly be due to carers being less comfortable with dose escalation of medications which usually require an assessment of blood pressure and kidney function between dosing increments. Prior to the pandemic, usual practice was to require blood tests for renal function after two weeks, with regular follow-up appointments to titrate dosing according to blood pressure and heart rate. Whilst during the pandemic, the majority of patients had access to blood pressure monitors (provided by primary care or purchased), the access to routine blood testing was reduced. Hence, given the more directly clinically obvious effects of β-blockers and thereby more straightforward monitoring of side effects or complications of therapy, may have meant carers were more comfortable to up-titrate these agents. Additionally, the re-deployment of hospital heart failure nurse specialists away from heart failure services is likely to have an impact on the optimisation of GDMT, because of their key role in patient education and ongoing care.

We have previously shown that even small increments in dosing of disease modifying therapies are associated with favourable outcomes in HFrEF [8]. We explored rates of heart failure hospitalisations and all-cause mortality, and although observed outcomes were similar, this might have been due to small numbers of patients a low event rate, and it is feasible that at a population level, the COVID-19 pandemic might have resulted in worse long-term outcomes for

Table 1. Baseline clinical characteristics of patients between study periods.

	All patients (n = 114)	COVID-19 (n = 60)	Previous year (n = 54)	p-value
Demographics				
Age (years)	74.7 ± 1.2	74.3 ± 1.6	75.2 ± 1.7	0.72
Male sex [n (%)]	70 (61.4)	35 (58.2)	35 (64.8)	0.48
Medical history				
Ischaemic aetiology [n (%)]	36 (32.4)	15 (25.4)	21 (40.4)	0.093
Hypertension [n (%)]	61 (53.5)	33 (55.0)	28 (51.9)	0.74
Diabetes mellitus [n (%)]	44 (38.6)	20 (33.3)	24 (44.4)	0.22
Atrial fibrillation [n (%)]	47 (41.2)	25 (41.7)	22 (40.7)	0.92
Stroke [n (%)]	11 (9.6)	3 (5.0)	8 (14.8)	0.076
Chronic kidney disease [n (%)]	25 (21.9)	12 (20.0)	13 (24.1)	0.60
COPD [n (%)]	14 (12.3)	6 (14.8)	8 (10.0)	0.43
NYHA class				
I	8 (7.0)	6 (10.0)	2 (3.7)	
II	66 (57.9)	36 (60.0)	30 (55.6)	0.27
III	40 (35.1)	18 (30.0)	22 (40.7)	
Blood tests				
Haemoglobin (g/L)	128.7 ± 1.8	129.5 ± 2.2	127.8 ± 3.0	0.64
Creatinine (μmol/L)	100.1 ± 3.6	98.4 ± 5.0	102.0 ± 5.3	0.61
Albumin (g/L)	35.7 ± 0.4	35.5 ± 0.6	35.9 ± 0.6	0.66
HbA1c (mmol/mol)	47.7 ± 1.4	46.0 ± 1.4	49.7 ± 2.5	0.21
NT-pro-BNP (ng/L)	6577.9 ± 681.6	6620.6 ± 856.7	6526.1 ± 1103.7	0.95
Electrocardiogram				
Heart rate (beats/min)	83.2 ± 1.9	85.1 ± 2.5	81.3 ± 2.9	0.33
QRS (ms)	109.5 ± 2.5	105.5 ± 3.3	113.6 ± 3.7	0.10
PR (ms)	181.1 ± 5.4	174.4 ± 7.6	188.8 ± 7.6	0.19
LBBB [n (%)]	15 (13.5)	7 (12.3)	8 (14.8)	0.46
Echocardiogram				
LVEF (%)	33.1 ± 1.1	33.8 ± 1.5	32.4 ± 1.7	0.54
LVEDd (mm)	54.4 ± 0.9	53.1 ± 1.1	56.1 ± 1.6	0.13
RV impairment [n (%)]	57 (50.4)	32 (54.2)	25 (46.3)	0.40
RWMA [n (%)]	70 (61.4)	32 (53.3)	38 (70.4)	0.062
Baseline medical therapy				
Beta-blocker [n (%)]	80 (70.2)	42 (70.0)	38 (70.4)	0.97
Bisoprolol dose (mg)	3.5 ± 0.3	3.2 ± 0.4	3.8 ± 0.5	0.35
ACEi/ARB [n (%)]	73 (64.0)	36 (60.0)	37 (68.5)	0.34
Ramipril dose (mg)	2.9 ± 0.3	2.7 ± 0.4	3.1 ± 0.4	0.56
Loop diuretic [n (%)]	75 (65.8)	42 (70.0)	33 (61.1)	0.32
Furosemide dose (mg)	38.0 ± 4.5	40.7 ± 6.8	35.0 ± 6.0	0.54
MRA [n (%)]	24 (21.1)	15 (25.0)	9 (16.7)	0.28
Ivabradine	5 (4.4)	1 (1.7)	4 (7.4)	0.14
SGLT2i [n (%)]	12 (10.5)	7 (11.7)	5 (9.3)	0.68
Antiplatelet [n (%)]	41 (36.0)	20 (33.3)	21 (38.9)	0.54
Anticoagulant [n (%)]	34 (29.8)	20 (33.3)	14 (25.9)	0.39

COPD, chronic obstructive pulmonary disease; NYHA, New York Heart Association; HbA1c, glycosylated haemoglobin; NT-pro-BNP, N-terminal pro-brain natriuretic peptide; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVEDd, left ventricular end-diastolic diameter; RV, right ventricular; RWMA, regional wall motion abnormality; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; MRA, mineralocorticoid receptor antagonist; SGLT2i, sodium-glucose co-transporter 2 inhibitor.

patients with HFrEF and this warrants further investigation. Another explanation might be due to a reluctance to seek medical attention, as evidenced by the lower rate of attendances for worsening heart failure observed during the COVID-19 pandemic [6, 9].

The principal limitations of this study are the small sample size and short duration of follow-up. Despite this, we were able to show a less successful optimisation of medical therapies during the COVID-19 pandemic. This study was conducted in a single centre in the UK, and so may not be generalisable to other healthcare systems. We included patients who
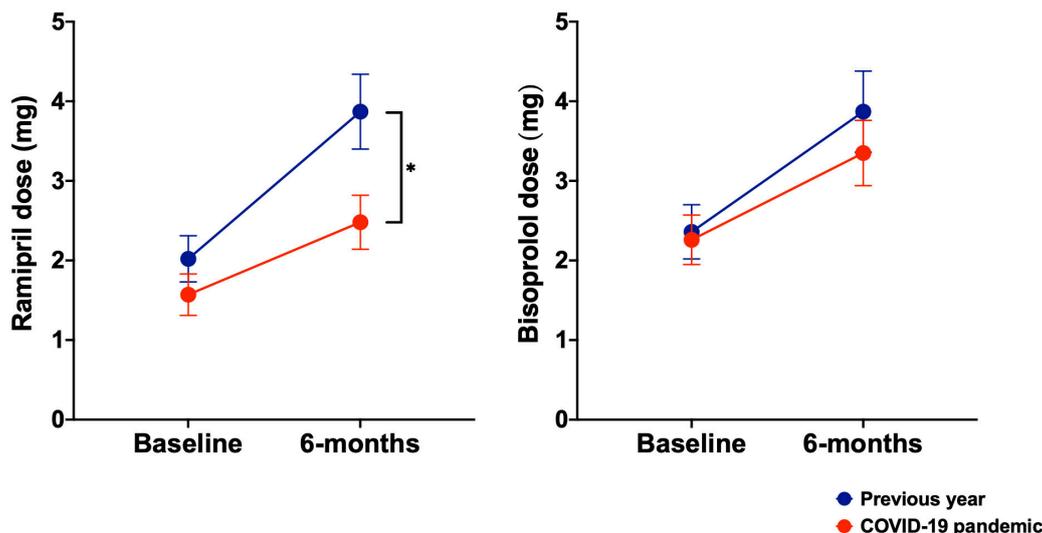
Fig. 2. Plots of the change in equivalent dosing of ramipril and bisoprolol between baseline and 6-months, excluding patients who were receiving maximum licensed doses at baseline. Description: The change in dosing was lower for patients whose period of dose optimisation was during the COVID-19 pandemic. * $p < 0.05$.

Table 2. Frequency of follow-up consultations during the study periods.

	COVID-19	Previous year	*p*-value
Hospital nurse face-to-face	0	28	**0.001**
Hospital nurse telephone	1	3	0.26
Community nurse face-to-face	122	110	0.50
Community nurse telephone	185	53	**0.008**
Physician face-to-face	61	76	**0.003**
Physician telephone	21	0	**<0.001**

had LVEF 40–49% who might be regarded as having heart failure with mid-range ejection fraction according to guidelines [1]. Despite there being less clear-cut evidence of benefit of medical therapy for such patients, it is usual practice that those presenting with signs and symptoms of heart failure, with raised NT-proBNP and evidence of LV systolic dysfunction to be treated with an ACEi/ARB and beta-blocker.

5. Conclusions

Our study adds to the growing literature of the impact of the COVID-19 pandemic on the care for patients with chronic heart failure [6]. Our data suggest that a transition towards telephone consultations and reduction in appointments with hospital heart failure nurses was associated with less successful optimisation of GDMT compared to usual care involving face-to-face clinics, with implications for service design during subsequent waves of the pandemic and beyond.

Author contributions

JJ and BN collected the data. SS and JJ analysed the data. MM and SS drafted the manuscript. JG and KKW provided critical revision. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Approval was given following institutional governance review following submission to the Clinical Audit Database at Leeds Teaching Hospital National Health Service Trust. The study was conducted in accordance with the principles outlined in the Declaration of Helsinki. In view of the retrospective nature, individual consent was waived as appropriate data protection safeguards were in place.

Conflict of interest

KKW has received speakers' fees and honoraria from Medtronic, Cardiac Dimensions, Novartis, Abbott, BMS, Pfizer, Bayer and has received an unconditional research grant from Medtronic. JG has received honoraria from Abbott, Medtronic and Microport and has received an unrestricted research grant from Medtronic. SS is funded by a British Heart Foundation Clinical Research Training Fellowship. None of the other authors have any disclosures.

References

[1] Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, *et al*. 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. European Heart Journal. 2016; 37: 2129–2200.

[2] Harkness A, Ring L, Augustine DX, Oxborough D, Robinson S, Sharma V, *et al*. Normal reference intervals for cardiac dimensions and function for use in echocardiographic practice: a guideline from the British Society of Echocardiography. Echo Research and Practice. 2020; 7: G1–G18.

[3] Chatrath N, Kaza N, Pabari PA, Fox K, Mayet J, Barton C, *et al*. The effect of concomitant COVID-19 infection on outcomes in patients hospitalized with heart failure. ESC Heart Failure. 2020; 7: 4443–4447.

[4] Raad M, Gorgis S, Dabbagh M, Parikh S, Cowger J. Characteristics and Outcomes of Patients with Heart Failure Admitted with Covid-19 in a Cohort Study from Southeast Michigan. Journal of Cardiac Failure. 2020; 26: S74.

[5] Sankaranarayanan R, Hartshorne-Evans N, Redmond-Lyon S, Wilson J, Essa H, Gray A, *et al*. The impact of COVID-19 on the management of heart failure: a United Kingdom patient questionnaire study. ESC Heart Failure. 2021; 8: 1324–1332.

[6] Bromage DI, Cannatà A, Rind IA, Gregorio C, Piper S, Shah AM, *et al*. 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. European Journal of Heart Failure. 2020; 22: 978–984.

[7] 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. Journal of Cardiac Failure. 2020; 26: 464–465.

[8] Straw S, McGinlay M, Relton SD, Koshy AO, Gierula J, Paton MF, *et al*. Effect of disease-modifying agents and their association with mortality in multi-morbid patients with heart failure with reduced ejection fraction. ESC Heart Failure. 2020; 7: 3859–3870.

[9] Jiménez-Blanco Bravo M, Cordero Pereda D, Sánchez Vega D, del Prado Díaz S, Monteagudo Ruiz J, Zamorano Gómez J, *et al*. Heart Failure in the Time of COVID-19. Cardiology. 2020; 145: 481–484.