Patients hospitalised with heart failure across different waves of the COVID-19 pandemic show consistent clinical characteristics and outcomes

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A B S T R A C T

Background: During the first wave of the COVID-19 pandemic, admissions for cardiovascular disease, including Heart Failure (HF), were reduced. Patients hospitalised for HF were sicker and with increased in-hospital mortality. So far, whether following waves had a different impact on HF patients is unknown.
Methods: All consecutive patients hospitalised for acute heart failure during three different COVID-19 related national lockdowns were analysed. The lockdown periods were defined according to Government guidelines as 23/3/2020 to 4/7/2020 (First Lockdown), 4/11/2020 to 2/12/2020 (Second Lockdown) and 5/1/2021 to 28/2/2021 (Third Lockdown).
Results: Overall, 184 patients hospitalised for HF were included in the study, 95 during the 1st lockdown, 30 during the 2nd lockdown and 59 during the 3rd lockdown. Across the three groups had comparable clinical characteristics, comorbidities and cardiovascular risk factors. Specialist in-hospital care was uninterrupted during the pandemic showing comparable mortality rates ($p = 0.10$). Although medical therapy for HF was comparable between the three lockdowns, a significantly higher proportion of patients received Angiotensin Receptor-Neprilysin Inhibitors (ARNI) in the second and third lockdowns ($p < 0.001$).
Conclusions: Although public health approaches changed throughout the pandemic, the clinical characteristics and outcomes of HF patients were consistent across different waves. For patients hospitalised in the subsequent waves, a more rapid optimization of medical therapy was observed during hospitalization. Particular attention should be devoted to prevent collateral cardiovascular damage during public health emergencies.

1. Introduction

The COVID-19 pandemic is an unprecedented medical emergency. The SARS-CoV-2 infection is associated with a severe pneumonia caused by abnormal lung syncytia and enhanced inflammasome [1,2]. Although a direct cardiac infection from the virus is still debated, the effect of the pandemic on patients with cardiovascular disease has been massive and required a significant repurposing of medical services [3,4]. During the COVID-19 pandemic, there has been a significant reduction in the number of patients presenting with common medical emergencies like acute myocardial infarction, ischemic stroke and subarachnoid hae-morrhage [5].However, those who were admitted were sicker and had a

higher cardiovascular mortality, independent of SARS-CoV-2 infection [6]. For patients with acute heart failure (HF) there was a 47% reduction in admissions to hospitals across the UK during the first COVID-19 wave, with reciprocally increased HF-related mortality both in the community and in-hospital [6–8]. The combination of fewer patients presenting with HF and an increased rate of HF-related mortality in the community was consistent globally [3,9]. Indeed, acute HF admissions in Italy reduced by 49% from February to April 2020 when compared with the same period in 2019 [9] Similarly, in the USA, there was an estimated decline of 60% in acute HF admissions during the first wave [10], and patients were sicker [7].

However, most such studies have focused on the first wave of the

pandemic. Whether subsequent waves had a different impact on HF admissions is unknown and we hypothesised that an incremental return to pre-lockdown conditions would be observed with each successive lockdown, as healthcare systems adapted. The aim of this study is to describe trends and characteristics of acute heart failure admissions during the subsequent waves of the COVID-19 pandemic in the UK, as compared to the first wave.

2. Methods

2.1. Study design and population

This is a retrospective analysis of all consecutive patients hospitalised for acute heart failure at King's College Hospital, London during three different COVID-19 related national lockdowns. To investigate the different characteristics and outcomes across different phases of the pandemic, especially with the changes in public health messages, we analysed the admissions across the three lockdown periods in the UK. The lockdown periods were defined according to Government guidelines as 23/3/2020 to 4/7/2020 (First Lockdown), 4/11/2020 to 2/12/2020 (Second Lockdown) and 5/1/2021 to 28/2/2021 (Third Lockdown). The first lockdown occurred during the first wave of the COVID-19 pandemic, while the other two lockdown occurred in the second wave. As previously described, the Heart Failure Unit operated normally during the whole pandemic period, allowing capture of all patients with a diagnosis of HF that were referred to the service [11,12]. All patients were admitted to the hospital via the Emergency Department or as direct admissions from the Outpatient Department.

Data were extracted from local National Heart Failure Audit (NHFA). The NHFA collects data relating to HF hospitalizations from NHS Trusts in England and Health Boards in Wales. Patients were included in the audit if they had a diagnosis of AHF in the first diagnostic position, according to following ICD codes ([I11.0 Hypertensive heart disease with (congestive) heart failure; I25.5 Ischaemic cardiomyopathy; I42.0 Dilated cardiomyopathy; I42.9 Cardiomyopathy, unspecified; I50.0 Congestive heart failure; I50.1 Left ventricular failure; I50.9 Heart failure, unspecified]. Patients aged <18 years were excluded.

2.2. Data fields

Mandatory fields included demographics, signs and symptoms of HF, comorbidities, diagnostic tests, place of care, duration of stay, medications, and in-hospital mortality. The standard dataset used for the NHFA is available from NICOR (https://www.nicor.org.uk/national-cardiac-audit-programme/datasets).

2.3. Statistical analyses

Continuous variables were reported as means (standard deviation) or medians [interquartile range (IQR)], as appropriate. Categorical variables were reported as numbers (percentage). Categorical variables were compared using the Pearson Chi-square or the Fisher's exact test. For continuous variables the Mann–Whitney U test (non-parametric) or the one-way ANOVA for multiple comparisons were used. Normality of distribution was assessed by the Shapiro–Wilks test. Survival curves were estimated using the Kaplan-Meier estimator and adverse outcomes were compared using the log-rank test. Since the second and third lockdown might be considered as part of a unique "second wave", we performed a sensitivity analysis unifying the second and third lockdown periods and including the lifting periods. All analyses were conducted using SPSS statistics software, version 26.0 (IBM Corp., Armonk, NY, USA) and 'R' (R Project for Statistical Computing).

3. Results

During the three COVID-19 lockdown periods we observed a total of

184 hospitalizations for acute heart failure to King's College Hospital, London. Specifically, 95 during the 1st lockdown, 30 during the 2nd lockdown and 59 during the 3rd lockdown. Weekly admission rate was comparable between the three lockdown periods (Fig. 1, $p = 0.16$).

Baseline characteristics of patients are reported in Table 1. Age at admission was similar in all three groups (72 ± 15 years in 1st vs. 73 ± 12 years in 2nd vs. 72 ± 12 in 3rd lockdown, $p = 0.98$), as well as male sex (61% vs 57% vs 61% respectively, $p = 0.91$), and ethnicity (Caucasians 45% vs 47% vs 42% respectively, $p = 0.94$).

Overall, patients across the three groups had comparable comorbidities and cardiovascular risk factors (Table 1). The main clinical characteristics of the patients admitted with HF were also similar (Table 1). Nearly 90% of patients presented in NYHA class III or IV, although a significantly higher proportion of patients were in NYHA class IV during the second and third lockdown periods ($p < 0.001$). However, the degree of peripheral congestion was comparable throughout each lockdown ($p = 0.56$).

Two thirds of the admissions were for HF with reduced Ejection Fraction (HFrEF), and this was consistent throughout the three study periods (59% vs 63% vs 66% respectively, $p = 0.74$). Among those, the majority of patients with HFrEF presented with severe LV systolic impairment (LVEF <35%), which was similar in each period (83% vs 68% vs 82% respectively, $p = 0.51$).

Likewise, in-hospital management was similar during all three lockdowns. The majority of patients with acute heart failure were admitted to cardiology wards while the rest were admitted to medical wards ($p = 0.08$). Furthermore, more than two thirds of patients received heart failure specialist input, although a higher proportion was observed during the last lockdown (89% vs 77% vs 95% respectively, $p = 0.04$). This was possibly due to the change in approach by the National Health Service (NHS) to deal with conditions that carry high mortality like heart failure during the following waves of pandemic.

It is noteworthy that although evidence-based therapy for HFrEF on discharge was comparable between the three lockdown periods (Table 2), a significantly higher proportion of patients received Angiotensin Receptor-Neprilysin Inhibitors (ARNI) in the second and third study period (3% vs 24% vs 23% respectively, $p < 0.001$). In addition to this, there was no difference in the proportion of patients requiring a loop diuretic on discharge (91% vs 100% vs 91%, $p = 0.26$). Finally, comparable mortality rates were observed over a median follow-up of 38 [IQR 24–63] weeks from admission ($p = 0.10$) (Fig. 2). Although patients admitted during the third lockdown showed lower mortality, this did not reach statistical significance ($p = 0.04$; non-significant after Bonferroni's correction). Results were consistent both considering together the second and third lockdowns (Supplementary Table 1) and including the lifting periods (Supplementary Table 2).

4. Discussion

The COVID-19 pandemic has dramatically disrupted healthcare systems. During the first wave of the pandemic, significant resources
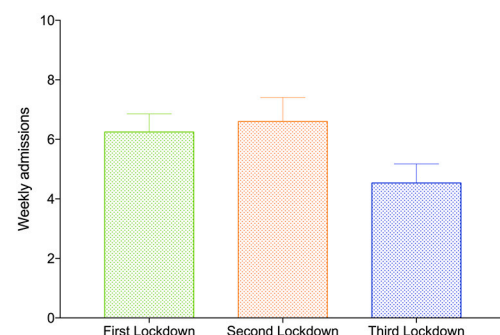

Fig. 1. Weekly admission rates.

Table 1
Baseline characteristics.

	First lockdown	Second lockdown	Third lockdown	p value
n = 184	95	30	59	
Age (years), mean (SD)	73 [63–84]	75 [67–83]	72 [66–81]	0.91
Male, n (%)	58 (61%)	17 (57%)	36 (61%)	0.91
Race, n (%)				
White	43 (45%)	14 (47%)	17 (42%)	
Black	39 (42%)	13 (43%)	20 (49%)	0.94
Other	12 (13%)	3 (10%)	4 (10%)	
Admission heart rate (bpm), median (IQR)	82 [70–100]	79 [65–86]	89 [75–109]	0.06
Admission rhythm, n (%)				
Sinus rhythm	41 (45%)	11 (41%)	26 (46%)	0.97
Atrial fibrillation	48 (52%)	15 (56%)	29 (52%)	
Admission systolic blood pressure (mmHg), median (IQR)	124 [109–148]	135 [116–148]	128 [111–150]	0.76
NYHA class, n (%)				
I	2 (2%)	0 (0%)	0 (0%)	
II	9 (10%)	2 (7%)	6 (10%)	<0.001
III	58 (64%)	9 (30%)	19 (33%)	
IV	22 (24%)	19 (63%)	33 (57%)	
NYHA Class III/IV, n (%)	80 (88%)	28 (93%)	52 (90%)	0.70
Severity of oedema, n (%)				
None	9 (10%)	3 (10%)	10 (17%)	
Mild	20 (21%)	9 (30%)	13 (22%)	0.56
Moderate	37 (39%)	12 (40%)	17 (29%)	
Severe	27 (30%)	6 (60%)	19 (32%)	
HF classification at admission, n (%)				
HFpEF	39 (41%)	11 (37%)	20 (34%)	0.74
HFrEF	57 (59%)	19 (63%)	38 (66%)	
↳ Severe LVSD	47 (83%)	13 (68%)	31 (82%)	0.51
Aetiology, n (%)				
Ischaemic	41 (45%)	15 (54%)	18 (31%)	0.09
Other	50 (55%)	13 (46%)	40 (69%)	
Comorbidities, n (%)				
Pre-existing valve disease	63 (66%)	10 (34%)	25 (42%)	0.001
HTN	64 (70%)	22 (73%)	35 (59%)	0.31
Diabetes	37 (39%)	12 (40%)	23 (39%)	0.99
COPD	17 (18%)	5 (17%)	9 (15%)	0.92
Device	22 (23%)	7 (25%)	8 (14%)	0.28

bpm: beats per minute; COPD: chronic obstructive pulmonary disease; HTN: hypertension; IHD: ischaemic heart disease; IQR: Interquartile Range; HFpEF: heart failure with preserved ejection fraction; HFrEF: heart failure with reduced ejection fraction; LVSD: Left ventricular systolic dysfunction; NYHA: New York Heart Association; SD: standard deviations.

Table 2
In-hospital and pharmacological management.

	First lockdown	Second lockdown	Third lockdown	p value
Place of care, n (%)				
Cardiology	42 (55%)	11 (41%)	29 (54%)	0.08
General medicine	28 (36%)	16 (59%)	24 (44%)	
Other	7 (9%)	0 (0%)	1 (2%)	
Specialist input, n (%)	83 (89%)	23 (77%)	55 (95%)	**0.04**
Creatinine at admission (μmol/L), median (IQR)	119 [93–165]	103 [91–159]	110 [89–164]	0.61
NT-proBNP at admission (pg/ml), median (IQR)	11,110 [4056–20,810]	3701 [2381–9734]	3628 [1707–8163]	**0.002**
Died in hospital, n (%)	9 (9%)	3 (10%)	3 (5%)	0.10
Pharmacological management for HFrEF, n(%)				
ARNI	3 (5%)	5 (33%)	12 (35%)	**0.001**
ACEi/ARBs/ARNI	36 (63%)	12 (75%)	28 (80%)	0.21
Beta-Blocker	44 (77%)	14 (82%)	32 (91%)	0.22
Diuretics	51 (90%)	17 (100%)	31 (89%)	0.35
MRAs	31 (54%)	13 (76%)	26 (74%)	0.08
ACEI or ARB or ARNI, beta blocker and MRA	24 (42%)	10 (53%)	21 (55%)	0.42

ACE: Angiotensin converting enzyme; ARB: angiotensin receptor blocker; ARNI: Angiotensin receptor-neprilysin inhibitor; HFrEF: Heart Failure with reduced Ejection Fraction; IQR: Interquartile Range; MRA: Mineralocorticoid receptor antagonist.
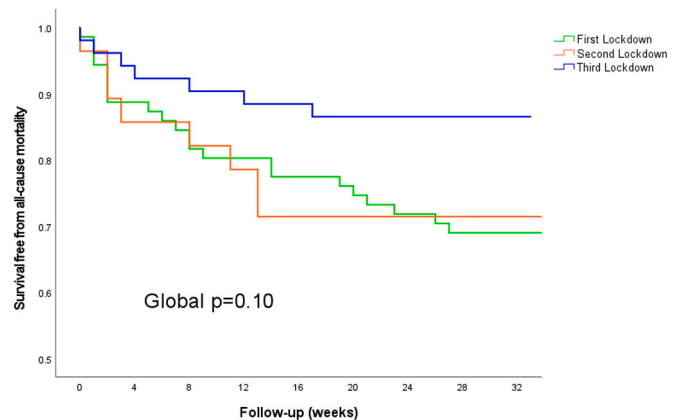

Fig. 2. Kaplan-Meier survival curves for in-hospital mortality across the three study periods.

were diverted towards caring for patients with SARS-CoV-2 infections. The reconfiguration of specialist cardiac services and public health messages resulted in a substantial reduction of patients being hospitalised for several conditions, including acute HF [7,13,14]. This quiescent admission period was followed by a rapid rebound in admissions after the peak of the pandemic [15]. Patients were generally sicker and in-hospital mortality was significantly increased irrespective of SARS-CoV-2 infection [6,16]. Although strategies were employed to reconfigure cardiovascular services to cope with the peak of the crisis, there was limited time for preparation, and substantial uncertainty. Hence, protocols that were developed hastily and with limited evidence may have contributed to adverse outcomes for patients with cardiovascular conditions, including HF [3]. With the lifting of the restrictions imposed during the first lockdown, more attention was paid to developing more rationalised and systematic approaches.

Despite the adaptation of healthcare systems and constant public health messages from NHS England [17] and the British Heart Foundation, which urged public to get care when they needed it during subsequent waves of the pandemic, a reduction of approximately 41% in heart failure admissions has been described [18]. This reduction in hospital admissions for HF and cardiovascular conditions was consistent

regardless of the comparator time period [6]. Similarly, in our analysis, the weekly admission rate for acute heart failure remained the same during the second wave of the COVID-19 pandemic (Fig. 1). This highlights how, despite the public health messages and healthcare reconfiguration, the admission rates have remained significantly reduced throughout the entire COVID pandemic, to date, with no differences between lockdown periods.

The clinical characteristics of acute heart failure admissions were comparable between the lockdown periods. Patients admitted during the COVID pandemic were severely symptomatic, although the percentage of patients with NYHA class IV was significantly higher following the first wave of the pandemic ($p < 0.001$). Several potential reasons might justify this observation. On one the hand, the reluctance of patients presenting to the hospital might have been more pronounced

during the subsequent waves of the pandemic. On the other hand, patients who survived the first wave presented with worse symptoms as the results of longer wait period. However, a comparable percentage of patients were admitted with severe symptoms (i.e. NYHA III/IV) across the three study periods. Further analysis might be warranted to shed light on this issue. Our analysis strengthens the reported evidence that patients admitted with HF during the pandemic were generally sicker compared to pre-pandemic periods [7,19]. Furthermore, pre-existing HF was associated with a higher risk of hospitalization for COVID during the first wave [20] and was more commonly associated with myocardial injury and worse outcomes [6,15,21].

During the pandemic, different working strategies were opted by the National Health Services (NHS). While hospital systems in the first wave were required to urgently reconfigure to manage the pandemic, this led to an unintentional interruption of pathways of care for important non-COVID conditions, such as cardiovascular and cancer, which led to higher excess mortality rates [3]. Initially, it included widespread redeployment of skilled workers to deal with COVID related admissions which resulted in cancellation of outpatient appointments and elective surgeries, then later in the pandemic NHS England implemented phase 3 of the NHS response which emphasized restoration of services. The lesson learnt from the COVID pandemic could allow better reconfiguration of healthcare services in similar emergency situations. The modification of cardiovascular services might be more phased and dynamic to avoid the sudden shock of complete cessation of routine work as effective continuation of cardiovascular services is essential to reduce the collateral damage [3,4].

Despite different strategies being used across the three lockdown periods, in-hospital management was comparable. More than half of HF patients were managed in cardiology wards and the vast majority received specialised HF input during their stay. Interestingly, despite comparable numbers of patients receiving guideline-directed medical therapy throughout the pandemic, we observed better in-hospital optimisation of therapy. In particular, we saw an increasing use of ARNI rather than ACEI suggesting better specialist input. Indeed, although a comparable number of admitted patients were on ARNI, the percentage of patients who initiated ARNI in-hospital was significantly higher during the second and third lockdown compared to the first wave of the pandemic. Interestingly, when second and third lockdowns were considered together, the more rapid uptitration was also confirmed by a higher percentage of patients receiving mineralocorticoid receptor antagonists in the later periods. This might reflect a more escalation of medical therapy with a preference for the in-hospital setting given the discontinuation of face-to-face follow-ups. The high percentage of patients receiving cardiology specialist input might have allowed a more tailored approach towards better in-hospital optimization of medical therapy.

In our study, the clinical characteristics of patients and in-hospital management were consistent throughout the three lockdowns, and this was associated with comparable outcomes (Fig. 2). However, during the first wave of the COVID pandemic, in-hospital mortality was significantly higher compared to previous years [6,15,19]. It is therefore reasonable to hypothesise that despite the different public health approaches over time, the impact of the COVID-pandemic was consistent throughout the entire period. Furthermore, the presence of subclinical cardiac dysfunction, especially in recovered COVID patients [22,23], might not be completely excluded and deserves further investigation.

4.1. Limitations

The results observed in this retrospective single centre analysis might be confounded by selection bias and might not be generalizable to other Heart Failure Units. Furthermore, despite the low number of missing variables, unmeasured residual confounding and unmeasured variables might have a potential impact on the results. Despite mortality rates being comparable across the three groups, regression models were not possible due to the low number of events. Lastly, we can only report associations rather than causal relationships, and further larger studies are needed to confirm these data.

5. Conclusion

The COVID-19 pandemic has dramatically disrupted continuity of care for patients with cardiovascular conditions. Despite the different public health approaches throughout the pandemic, the clinical characteristics, in-hospital management, and outcomes of patients admitted for acute heart failure were consistent across different waves. As COVID has potential for further surges, further attention should be afforded to prevention of collateral cardiovascular damage. For patients with acute HF, more rapid optimization of medical therapy during hospitalization might be one such approach. Further studies are required to confirm these results in larger populations with different healthcare approaches.

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CRediT authorship contribution statement

Irfan A. Rind: Conceptualization, Data curation, Writing – original draft, Writing – review & editing. **Antonio Cannata**: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Benedict McDonaugh**: Data curation, Methodology, Writing – original draft, Writing – review & editing. **Barbara Cassimon**: Data curation, Methodology, Writing – original draft, Writing – review & editing. **Clare Bannister**: Data curation, Methodology, Writing – original draft, Writing – review & editing. **Paul A. Scott**: Conceptualization, Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Susan Piper**: Conceptualization, Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Daniel I. Bromage**: Conceptualization, Data curation, Formal analysis, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Theresa A. McDonagh**: Conceptualization, Data curation, Methodology, Supervision, Writing – original draft, Writing – review & editing.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2021.12.042.

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