

Original Article



Impact of COVID-19 Pandemic Lockdown in Decompensated Heart Failure Hospitalizations

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Received: Jan 14, 2021 Revised: Mar 2, 2021 Accepted: Mar 5, 2021

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Conflict of Interest

The authors have no financial conflicts of interest.

ABSTRACT

Background and Objectives: Coronavirus disease 2019 (COVID-19) pandemic lockdown may have collaterally affected the care of patients with acute decompensated heart failure (ADHF). We aimed to evaluate the impact of lockdown pandemic on hospitalizations for ADHF.

Methods: We conducted a single-center study, performing a retrospective analysis of prospectively collected data. We included consecutive adult patients with a primary diagnosis of ADHF admitted to a cardiovascular disease specialized hospital. We compared those patients admitted between March–June of 2019 (before COVID-19 [BC]) and 2020 (after COVID-19 [AC]), during mandatory lockdown.

Results: A total 79 corresponding to BC period and 60 to AC period were included, representing a decrease of 25% (interquartile range [IQR], 11–33). During the BC period, 31.6% of patients were referred from other centers compared to 15% during the pandemic (p=0.02). In the AC period patients were older (median age, 81[IQR, 73–87] years vs. 77 [IQR, 64–84] years, p=0.014). The etiology of HF, cause of decompensation, left ventricular function, and laboratory parameters were similar in both periods. The use of mechanical ventilation (13.9% vs. 3.3%, p=0.03) and circulatory support (7.6% vs. 0%, p=0.02) was higher in the BC period. During the BC period, 5 emergency heart transplants were performed, and none in AC, (p=0.004). In-hospital mortality was similar in both periods (3.8% vs. 3.3%; p=0.80).

Conclusions: We observed a reduction in the number of hospitalizations and referral of patients for ADHF during COVID-19 pandemic.

Keywords: Heart failure; Coronavirus; COVID-19; Hospitalization; Mortality

INTRODUCTION

Early on during the pandemic of coronavirus disease 2019 (COVID-19) health authorities declared the preventive and compulsory social isolation with the aim of slowing the spread of the disease. As a consequence COVID-19 spread was reduced compared with predictions based on data from other countries. However, a collateral adverse consequence of the lockdown was a problematic access to the health system facilities, affecting care of both acute



Author Contributions

Conceptualization: Burgos LM, Villalba L, Botto F, Diez M; Data curation: Burgos LM, Villalba L, Miranda RPM; Formal analysis: Burgos LM, Villalba L, Miranda RPM; Investigation: Burgos LM, Miranda RPM; Methodology: Burgos LM, Ramírez AG; Project administration: Burgos LM; Resources: Botto F; Software: Burgos LM, Miranda RPM, Ramírez AG; Supervision: Botto F, Diez M; Validation: Botto F, Diez M; Visualization: Burgos LM, Ramírez AG, Botto F, Diez M; Writing - original draft: Burgos LM, Villalba L, Miranda RPM, Ramírez AG, Botto F, Diez M; Writing - review & editing: Burgos LM, Botto F, Diez M.

and chronic cardiovascular disease.²⁾ This phenomenon has been reported by many hospitals that demonstrated a decrease in admissions for acute coronary syndrome³⁻⁶⁾ with a higher inhospital mortality and complications rate.⁶⁾

Recently, 2 studies reported a decrease in hospitalizations for acute decompensated heart failure (ADHF).⁷⁻⁹⁾ Delaying medical assistance until symptoms become critical could theoretically lead to fewer admissions but with a higher severity.

Since little is known about the impact of the compulsory social isolation on the clinical characteristics and in-hospital outcomes of patients with ADHF, we conduct a study to assess the impact of the COVID-19 pandemic during the strict isolation period on the number of hospitalizations for ADHF compared to the same period of the previous year. The secondary objectives were to determine the clinical profile, severity and in-hospital mortality of patients hospitalized for ADHF in each period.

METHODS

We conducted a single-center cohort study, performing a retrospective analysis of prospectively collected data. It is a national referral center, specialized in cardiovascular disease, located in a metropolitan city and accounts with 24-hour cardiac catheterization lab, surgery and availability of every kind of physiology procedures as well as the use of advance circulatory mechanical assist devices and heart transplantation. Adult patients consecutively admitted to the hospital with a primary diagnosis of ADHF (acute or acute on chronic) were evaluated by a member of the heart failure (HF) team and registered in a dedicated database.

For the present report we compared patients admitted between March and June 2019 with those admitted in the same period of 2020, while strict lockdown was mandatory. We named the periods before COVID-19 (BC) and after COVID-19 (AC).

Study population: eligible patients were patients over 18 years of age hospitalized for ADHF.

Inclusion criteria: hospitalization of 24 hours or more for decompensated HF, defined as new symptoms or worsening of previous symptoms (including orthopnea, deterioration of dyspnea to CF to III–IV, bendopnea, fatigue) or signs of volume overload. Presence on physical examination of jugular engorgement, hepatojugular reflux, edema in the lower limbs and/or signs of pulmonary congestion. Findings on chest radiograph of signs consistent with congestion.

Exclusion criteria: Those patients with HF secondary to other diagnosis, such as acute myocardial infarction, sepsis or cardiac arrest were excluded.

Demographic data, etiology, cause of decompensation, clinical presentation, comorbidities and laboratory (peak values during hospitalization) and echocardiographic parameters were collected. All HF subtypes were considered for the analysis, including HF with reduced ejection fraction (HFrEF), preserved ejection fraction and mid-range ejection fraction (subtypes were defined by an echocardiogram performed during the index hospitalization or 3 months before).



In addition, we evaluated the proportion of patients who were referred to our center in both periods from other non-specialized cardiovascular hospitals.

Outcomes

The primary outcome was the rate of hospitalization for ADHF. Secondary outcomes were number of referred patients, length of stay, requirement of vasoactive medication (inotropic/vasodilator), renal replacement therapy (RRT), invasive and non-invasive mechanical ventilation, mechanical circulatory assistance, heart transplant and in-hospital mortality.

Statistical analysis

Continuous variables were expressed as mean and standard deviation or median and interquartile range (IQR) according to the observed distribution. Kolmogorov-Smirnov or Shapiro-Wilk test according to the sample size was used to determine distribution. To compare continuous variables, the Student's t-test or the Mann-Whitney U test was used, depending on the distribution. Categorical variables were expressed as numbers and percentages. Comparisons between proportions were performed using the χ^2 test or Fisher's exact test, according to the frequency of expected values. Two-tailed p values <0.05 were considered statistically significant. SPSS statistics, version 23.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis.

Ethical considerations

The study was approved by the institutional research and ethics board (approval number 1596), and was registered on the PRIISA.BA platform of Buenos Aires city Ministry of Health. The study was a retrospective investigation with de-identified data, according to national regulations for requesting informed consent. At the time of hospitalization, patients signed consent for the transfer of personal data for scientific purposes.

The study was carried out in accordance with national and international standards for the protection of research subjects such as the Declaration of Helsinki, Resolution of the Ministry of National Health 1480/2011, Ciudad de Buenos Aires law 3301, ANMAT resolution 6677/10 and amendments 4008 and 4009.

RESULTS

A total of 139 patients with primary diagnosis of ADHF were included, 79 corresponding to BC period and 60 to AC period, which represents a 25% (IQR, 11–33) decrease in hospitalizations during the pandemic lockdown. During the BC period, 31.6% of patients were referred from other centers compared to 15% during the pandemic (p=0.02).

Patient's baseline characteristics according to the exposure group are shown in **Table 1**. Compared to the BC period, in the AC period patients were older (median age, 81[IQR, 73–87] years vs. 77 [IQR, 64–84] years, p=0.014), and there was a trend towards a higher number of men, 70% vs. 54.4% (p=0.06). We found no differences in the rest of comorbidities. No patient was diagnosed positive for COVID-19.

The HF clinical findings of patients were similar regarding systemic venous congestion, acute pulmonary edema, low cardiac output and cardiogenic shock (p=0.2) (**Table 2**).

Table 1. Baseline characteristics of patients hospitalized for acute decompensated heart failure

Demographic characteristics	Before COVID-19 (n=79)	After COVID-19 (n=60)	p value
Age	77 (64-84)	81 (73-87)	0.014
Male (sex)	43 (54.4)	42 (70.0)	0.06
Hypertension	19 (24.1)	20 (33.3)	0.2
Diabetes	19 (24.1)	20 (33.3)	0.2
Dyslipidemia	46 (58.2)	40 (66.7)	0.3
Smoker	5 (6.3)	3 (5.0)	0.7
Atrial fibrillation	34 (43.0)	24 (40.0)	0.7
Coronary artery disease	34 (43.0)	19 (31.7)	0.1
Moderate-severe VHD	37 (46.8)	27 (45.0)	0.8
Chronic kidney failure	13 (16.5)	10 (16.7)	0.3
Stroke	3 (3.8)	4 (6.7)	0.5
COPD	14 (17.7)	7 (11.7)	0.9
PVD	9 (11.4)	9 (15.0)	0.4
Referred from other center	25 (31.6)	9 (15.0)	0.02

Values are presented as median (interquartile range) or number (%).

COPD = chronic obstructive pulmonary disease; COVID-19 = coronavirus disease 2019; PVD = peripheral vascular disease; VHD = valvular heart disease.

Table 2. HF clinical profile of patients hospitalized in each period

HF clinical profile	Before COVID-19 (n=79)	After COVID-19 (n=60)	p value
HF etiology			0.2
Hypertensive	10 (12.7)	1 (1.7)	
CAD	29 (36.7)	23 (38.3)	
Idiopathic	5 (6.3)	4 (6.7)	
Valvular heart disease	13 (16.5)	17 (28.3)	
Hypertrophic/infiltrative	5 (6.3)	3 (5.0)	
Viral myocarditis	3 (3.8)	1 (1.7)	
Other*	14 (17.7)	11 (18.3)	
Previous HF hospitalization	19 (24.1)	16 (26.7)	0.7
HFrEF	32 (41.0)	22 (40.0)	0.9
ADHF clinical profile			0.2
Systemic venous congestion	60 (75.9)	51 (85.0)	
Pulmonary edema	11 (13.9)	3 (5.0)	
LCOS/cardiogenic shock	8 (10.0)	6 (10.0)	
Cause of decompensation			0.8
Infection	12 (15.2)	7 (11.7)	
No medication compliance	6 (7.6)	5 (8.3)	
No diet adherence	10 (12.7)	7 (11.7)	
Bradyarrhythmia	0 (0.0)	1 (1.7)	
Supraventricular tachyarrhythmia	9 (11.4)	6 (10.0)	
Pulmonary embolism	0 (0.0)	1 (1.7)	
Other	12 (15.2)	10 (16.7)	
No identified/disease progression	21 (26.6)	20 (33.3)	
NA	7 (8.9)	3 (5.0)	

Values are presented as number (%).

ADHF = acute decompensated heart failure; CAD = coronary artery disease; COVID-19 = coronavirus disease 2019; HF = heart failure; HFrEF = heart failure with reduced ejection fraction; LCOS = low cardiac output syndrome; NA = not available.

The etiology of HF and cause of decompensation did not differ in both periods, and the rate of previous hospitalization for ADHF and diagnosis of HFrEF was similar.

Before the pandemic, the mean sodium at admission was lower (p=0.03), without finding significant differences in the rest of the laboratory parameters between both periods (**Table 3**).

^{*}Other: chagas disease, congenital heart defect, pulmonary hypertension, tachycardia-induced cardiomyopathy, peripartum cardiomyopathy and cardiac toxicity due to chemo- or radiotherapy.

Table 3. Laboratory parameters of patients hospitalized for acute decompensated heart failure in each period

Laboratory measurement	Before COVID-19 (n=79)	After COVID-19 (n=60)	p value
Sodium	135±4.80	138±4.90	0.003
Urea (mg/dL)	63 (47.00-88.00)	66 (55.00-92.00)	0.1
Creatinine (mg/dL)	1.36 (1.06-1.84)	1.36 (1.15-1.91)	0.7
GOT	25 (18.00-30.00)	25 (20.00-32.00)	0.9
GPT	20 (14.00-40.00)	20 (15.00-33.00)	0.8
Hemoglobin (g/dL)	12.1 (10.70-13.80)	12 (10.80-13.30)	0.7
Hs-TnT	31 (19.00-60.00)	35 (22.00-53.00)	0.4

Values are presented as mean ± standard deviation or median (interquartile range).

The reported values represent the peak values during hospitalization index.

COVID-19 = coronavirus disease 2019; GOT = aspartate aminotransferase; GPT = alanine aminotransferase; Hs-TnT = high sensitive troponin T.

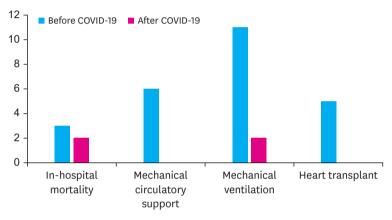


Figure 1. In-hospital outcomes of patients hospitalized for acute decompensated heart failure in each period. COVID-19 = coronavirus disease 2019.

Table 4. In-hospital outcomes of patients hospitalized for acute decompensated heart failure in each period

In-hospital outcomes	Before COVID-19 (n=79)	After COVID-19 (n=60)	p value
Length of stay in days	4 (3-7)	4 (3-7)	
Inotropic use	7 (8.9)	5 (8.3)	0.9
IV vasodilatador use	31 (39.7)	23 (38.3)	0.9
RRT	2 (2.5)	0 (0.0)	0.2
Mechanical ventilation	11 (13.9)	2 (3.3)	0.03
MCS	6 (7.6)	0 (0.0)	0.02
Heart transplant	5 (6.3)	0 (0.0)	0.04
In-hospital mortality	3 (3.8)	2 (3.3)	0.8

Values are presented as median (interquartile range) or number (%).

COVID-19 = coronavirus disease 2019; IV = intravenous; MCS = mechanical circulatory support; RRT = renal replacement therapy.

The use of invasive and non-invasive mechanical ventilation (13.9% vs. 3.3% p=0.03) and mechanical circulatory support (7.6% vs. 0%, p=0.02) was higher in the BC period. During the BC period, 5 emergency heart transplants surgeries were performed, and none in AC, being this difference statistically significant (6.3% vs. 0%, p=0.004). In-hospital mortality rate was similar (3.8% vs. 3.3%; p=0.80) between both periods (**Figure 1**). Length of stay was the same in BC and AC period. Regarding in-hospital outcomes, requirement of vasoactive medication (inotropic/intravenous vasodilators) was similar in both groups. The requirement of RRT was similar in both periods (**Table 4**).



DISCUSSION

Our observations from a specialized cardiovascular hospital indicate that there was a marked decline in ADHF hospitalizations during the COVID-19 pandemic, and a reduction in the number of patients referred from other centers.

The hospitalized patients in the BC period were more severely ill. Strikingly during the lockdown we did not use intraaortic balloon pump counterpulsation or extracorporeal membrane oxygenation support or performed emergency heart transplants. Although fewer patients with advanced HF were admitted in the BC period, mortality was similar in both periods.

Unlike the reports about the impact of COVID-19 pandemic on patients with acute myocardial infarction⁶⁾⁽⁰⁾ that arrived with more severe clinical presentations and showed a higher inhospital mortality rate, our sample of patients with primary diagnosis of ADHF did not show a greater severity or mortality, contrarily to our initial hypothesis.

The reason could be probably related to the low rate of national referrals of patients with advanced HF who required more advanced treatments during COVID-19 pandemic. Our center is a third level national reference site, and is located in the city of Buenos Aires, the area that concentrates the largest number of COVID-19 cases in the country. Therefore, it could be probably difficult referring patients in this context due to barriers in accessibility generated by the lockdown.

We face a pandemic caused by a virus against which still do not have specific therapies or vaccines. We need to trust classical public health measures such as isolation and quarantine, social distancing and containment of the community to curb the pandemic. ¹¹⁾ All these traditional tactics were used in China on an unprecedented massive scale. ¹²⁾¹³⁾ These are essential measures to contain COVID-19 infection, but could difficult health care access, limit referral, consultation and medical follow-up for patients with cardiovascular diseases such as HF. "Stay-at-home" slogan may potentially lead patients to delay or defer hospital admission for acute cardiovascular conditions. ¹⁴⁾ Recent evidence has demonstrated marked reductions in the rates of hospitalization for acute coronary syndrome³⁻⁶, ¹⁰, ¹⁰, ¹⁰, and aortic dissection. ¹⁷⁾ In addition, a decrease in hospitalizations for ADHF was reported. ⁷⁻⁹⁾ Unlike our study, in a recently published analysis, ⁹⁾ patients admitted during the COVID-19 pandemic had more severe symptoms at admission. However, the treatment for advanced HF, such as mechanical circulatory assistance and heart transplantation, was not evaluated.

In our analysis we only included patients with primary diagnosis of ADHF, and those with acute myocardial infarction (e.g. Killip B, C and D) were excluded, thus the already known decrease in the incidence of acute coronary syndrome during the pandemic would not explain this decline in ADHF hospitalizations.

The cause of the reduction of ADHF hospitalizations is probably multifactorial and may include patient's fears of contagion and the conduct of waiting for the pandemic to subsides to seek medical care and underdiagnosis by the emergency services, due to overload of the health system. The decline in ambulatory cardiovascular visits, outpatient testing, and deferral of elective procedures may have also contributed to the lower rate of hospitalizations, as these often may serve as points of referral for in-patient hospitalization.¹⁴⁾



Alternatively, one should consider the idea that ADHF hospitalization declined due to decrease in exacerbations. In the best scenario, patients staying home could have improved self-care and achieved greater adherence to hygienic, dietary and pharmacological measures. Those are fundamental pillars in treatment because it is known that transgressions in diet and low adherence to medications are the main triggers for ADHF. In addition, the adoption of more accessible forms of communication between patients and their providers, including virtual visits, may have been able to avert certain exacerbations.

We must mention that it is a retrospective study with the inherent limitations of this type of design. In the analyzed and compared periods, there could have been other variables not valued that had an impact on the results. It is important to mention that the months prior to the pandemic were not compared, since the seasonal variation that ADHF hospitalization have in both volume and severity in their presentation is already known. ¹⁹⁾²⁰⁾

Public health departments, emergency medical services, and hospitals must maintain the highest standards of infection control to gain the trust of the community. In addition, mass public education efforts should assure patients that health care services remain operational and safe for use. It should be the responsibility of health care professionals, authorities and scientific societies to educate the population to avoid unnecessary consultation in emergencies, and at the same time, to emphasized on alarm symptoms of serious diseases that need prompt evaluation and treatment. It is also important to detect changes in attention of severe pathologies, such as ADHF in order to establish measures early.

Further urgent attention is needed to understand and mitigate these patterns, including plans to promote referral policies to achieve the timely referrals of patients with complex cardiovascular disease. Especially those with advanced HF, so that they can be evaluated by a HF team and receive appropriate treatment, with mechanical circulatory support or emergency heart transplantation when appropriate.

In conclusion, our specialized cardiovascular hospital we observed a reduction in the number of hospitalizations and referral of patients for ADHF during COVID-19 pandemic. In the before COVID-19 period, patients required more frequently respiratory and circulatory mechanical assistance and emergency heart transplantation, however mortality in both periods was similar.

The change in hospitalizations for less severe ADHF during the pandemic could be multifactorial but probably driven by a decrease in the number of patients referred from other hospitals to receive more advanced therapies.

REFERENCES

- Ministerio de Salud. Reporte diario nuevo coronavirus 2019 [Internet]. Santiago: Ministerio de Salud; 2021 [cited 2021 Feb 28]. Available from https://www.argentina.gob.ar/coronavirus/informe-diario.
- Bozovich GE, Alves De Lima A, Fosco M, et al. Collateral damage of COVID-19 pandemic in private healthcare centres of Argentina. Medicina (B Aires) 2020;80 Suppl 3:37-41.

 PUBMED
- De Filippo O, D'Ascenzo F, Angelini F, et al. Reduced rate of hospital admissions for ACS during COVID-19 outbreak in Northern Italy. N Engl J Med 2020;383:88-9.
 PUBMED | CROSSREF



4. Metzler B, Siostrzonek P, Binder RK, Bauer A, Reinstadler SJ. Decline of acute coronary syndrome admissions in Austria since the outbreak of COVID-19: the pandemic response causes cardiac collateral damage. Eur Heart J 2020;41:1852-3.

PUBMED | CROSSREF

- Garcia S, Albaghdadi MS, Meraj PM, et al. Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. J Am Coll Cardiol 2020;75:2871-2.

 PURMED I CROSSREE
- 6. De Rosa S, Spaccarotella C, Basso C, et al. Reduction of hospitalizations for myocardial infarction in Italy in the COVID-19 era. Eur Heart J 2020;41:2083-8.

PUBMED I CROSSREF

7. Hall ME, Vaduganathan M, Khan MS, et al. Reductions in heart failure hospitalizations during the COVID-19 pandemic. J Card Fail 2020;26:462-3.

PUBMED | CROSSREF

8. Burgos LM, Diez M, Villalba L, et al. Impact of the COVID-19 pandemic on heart failure hospitalizations. MEDICINA (B Aires) 2020;80:315-6.

PUBMED

9. Bromage DI, Cannatà A, Rind IA, 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. Eur J Heart Fail 2020;22:978-84.

PUBMED | CROSSREF

- 10. Candiello A, Lasave L. Impact of COVID-19 pandemic on ST-elevation myocardial infarction [Internet]. [place unknown]: Stent Save a Life; 2020 [cited 2021 Feb 28]. Available from http://stentsavealife.com.ar.
- 11. Wilder-Smith A, Freedman DO. Isolation, quarantine, social distancing and community containment: pivotal role for old-style public health measures in the novel coronavirus (2019-nCoV) outbreak. J Travel Med 2020;27:taaa020.

PUBMED | CROSSREF

 McCloskey B, Heymann DL. SARS to novel coronavirus - old lessons and new lessons. Epidemiol Infect 2020;148:e22.

PUBMED | CROSSREF

13. Du Z, Wang L, Cauchemez S, et al. Risk for transportation of 2019 novel coronavirus disease from Wuhan to other cities in China. Emerg Infect Dis 2020;26:1049-52.

PUBMED | CROSSREF

- Bhatt AS, Moscone A, McElrath EE, et al. Declines in hospitalizations for acute cardiovascular conditions during the COVID-19 pandemic: a multicenter tertiary care experience. J Am Coll Cardiol 2020;20:35393-6.
- 15. Solomon MD, McNulty EJ, Rana JS, et al. The COVID-19 pandemic and the incidence of acute myocardial infarction. N Engl J Med 2020;383:691-3.

PUBMED | CROSSREF

- Romaguera R, Ribera A, Güell-Viaplana F, et al. Decrease in ST-segment elevation myocardial infarction admissions in Catalonia during the COVID-19 pandemic. Rev Esp Cardiol (Engl Ed) 2020;73:778-80.
- 17. El-Hamamsy I, Brinster DR, DeRose JJ, et al. The COVID-19 pandemic and acute aortic dissections in New York: a matter of public health. J Am Coll Cardiol 2020;76:227-9.
- Corradi L, Pérez G, Costabel JP, et al. Insuficiencia cardíaca descompensada en la Argentina: registro CONAREC XVIII. Rev Argent Cardiol 2014;82:519-28.
- 19. Gallerani M, Boari B, Manfredini F, Manfredini R. Seasonal variation in heart failure hospitalization. Clin Cardiol 2011;34:389-94.

PUBMED | CROSSREF

 Akintoye E, Briasoulis A, Egbe A, et al. Seasonal variation in hospitalization outcomes in patients admitted for heart failure in the United States. Clin Cardiol 2017;40:1105-11.
 PUBMED | CROSSREF