Iranian Heart Journal; 2021; 22 (3)

Original Article

The Safety of Direct-Acting Antiviral Treatment for Hepatitis C Virus in Egyptian Patients With Ischemic Heart Disease and Mildly Impaired Systolic Function

Mahmoud A. Abouomar[1*], MD; Mohamed Yousef[2], MD; Ayman Elsheikh[1], MD

ABSTRACT

Background: Hepatitis C virus (HCV) infection is considered a public health problem in Egypt. The use of direct-acting antivirals (DAAs) in patients infected with HCV has been shown to be effective. The cardiac safety of these antivirals remains uncertain, however. This study aimed to assess the safety of the use of DAAs in patients suffering from ischemic heart disease (IHD) with mildly impaired systolic function.

Method: This prospective cohort study was performed on 200 patients with chronic HCV infection scheduled for DAA use. The patients were divided into 2 groups: Group I comprised 96 patients with IHD and mildly impaired systolic function and Group II comprised 104 patients without IHD and with normal left ventricular ejection fractions. Both groups received sofosbuvir (400 mg) and daclatasvir (60 mg) daily for 12 weeks. Electrocardiography and echocardiography were performed prior to the start, during, and after 12 weeks of treatment.

Result: At the end of the treatment period, no changes were observed in the patients' cardiac symptoms and signs. No significant changes were also detected in electrocardiographic parameters, including the QTc interval in Group I (P =0.60) or Group II (P =0.63). Moreover, no changes were recorded in both groups regarding left ventricular systolic and diastolic functions (ie, the dimension, the ejection fraction, the transmitral E/A ratio, the E/E' ratio, and the deceleration time), the tricuspid annular plane systolic excursion, right ventricular systolic pressure, and the mean pulmonary artery pressure.

Conclusions: The use of DAAs to treat Egyptian patients infected with HCV was safe in those suffering from IHD with mildly impaired systolic function. The treatment with DAAs exerted no effects on the QTc interval and the function of the left and right ventricles.
(Iranian Heart Journal 2021; 22(3): 13-22)

KEYWORDS: Hepatitis C virus, Ischemic heart disease, Direct-acting antiviral, ECG, Echocardiography

[1] Department of Cardiology, Tanta University, Tanta, Egypt.
[2] Department of Tropical Medicine, Tanta University, Tanta, Egypt.

***Corresponding Author:** Mahmoud A Abouomar, MD; Department of Cardiology, Tanta University, Tanta, Egypt.
Email: maabouomar@gmail.com **Tel:** +2 01096085665

Received: January 7, 2021 **Accepted:** Mach 28, 2021

Hepatitis C virus (HCV) infection is an important cause of chronic liver disease worldwide and is considered a health problem in Egypt. The long-term influence of infection with HCV ranges from minimally histological changes in liver cells to extensive liver fibrosis and/or cirrhosis, and it may result in hepatocellular carcinoma. [1] Although HCV primarily affects liver cells, it may lead to extrahepatic manifestations. HCV has been isolated from the myocardium of patients with myocarditis and cardiomyopathy; therefore, it is regarded as a cardiotropic virus that causes cardiomyopathy. [2] Up to 50% of patients with advanced liver cirrhosis are likely to have cardiac dysfunction, a condition often called "cirrhotic cardiomyopathy". Such patients have increased or normal cardiac output at rest with a blunted response to exercise. They may also have a prolonged QT interval and chronotropic incompetence. [3] The therapy of chronic HCV-infected patients developed with time from interferon-based therapy to highly effective direct-acting antivirals (DAAs). Sofosbuvir represents the first principle step in the new era in the treatment of chronic HCV since it is the first approved DAA with good tolerability, appropriate pharmacokinetic profile, limited drug interactions, effective antiviral activities, and a high genetic barrier against all HCV genotypes. Sofosbuvir has become commercially available in combination with ribavirin, which achieves high-sustained virological response rates after 12 to 24 weeks of therapy. [4] DAAs have received breakthrough therapy status by the Food and Drug Administration (FDA); nonetheless, post-marketing reports, case reports, and retrospective studies have suggested possible deleterious effects on the heart such as toxic cardiomyopathy and bradyarrhythmia. [5, 6] On the other hand, oral antiviral treatment for patients with HCV induces cardiac adverse effects. Indeed, a previous investigation reported 3 cases of severe bradyarrhythmia, which occurred during treatment among 415 HCV-infected patients taking sofosbuvir plus daclatasvir, simeprevir, or ribavirin. Reports have also focused on the possibility of the cardiotoxic effect of sofosbuvir when combined with amiodarone. The occurrence of syncopal attacks was reported in 2 cases a few days after the administration of sofosbuvir. [8]

Our study aimed to assess the effects of the treatment of chronic HCV-infected patients with DAAs on electrocardiographic (ECG) parameters, including the corrected QT interval (QTc), and the function of the left ventricle (LV) and the right ventricle (RV) according to transthoracic echocardiography.

METHODS

The present prospective cohort study was conducted on 200 treatment-naïve adult patients (≥ 18 years old) suffering from chronic HCV infection confirmed by a polymerase chain reaction test for HCV (genotype 4). The patients were randomly selected from the Tanta University Tropical Medicine Clinic for HCV-infected patients in the period from September 2018 through September 2020. The local research committee approved the study following the Declaration of Helsinki. All the patients gave written informed consent. The exclusion criteria were as follows: a history of cardiac arrhythmias; current cardiac arrhythmias; significant valvular heart disease; New York Heart Association (NYHA) functional class III or IV or a left ventricular ejection fraction (LVEF) of less than 40%; bradycardia (heart rate <60 bpm); uncontrolled hypertension; a history of treatment for chronic HCV; concomitant infection with either hepatitis B virus, human immunodeficiency virus (HIV) or

bilharziasis; decompensated liver cirrhosis (ie, ascites, encephalopathy, and bleeding varices); an estimated glomerular filtration rate of less than 30 mL/min; pregnancy; any form of autoimmune diseases; a history of malignancy; and the use of medications known to be cardiotoxic or to have a negative chronotropic or antiarrhythmic effect. The patients were assigned to 2 groups: Group I comprised 96 patients with ischemic heart disease (IHD) and mildly impaired systolic function (LVEF =40%–50%), and Group II consisted of 104 control patients without IHD and with normal systolic function (LVEF >55%). All the patients were treated according to the national protocol for the management of chronic HCV infection as follows: they were all given a combination of sofosbuvir (400 mg) daily and daclatasvir (60 mg) daily for 12 weeks and they were all easy to treat (ie, naïve, total serum bilirubin <1.2, the international normalized ratio [INR] <1.2, the platelet count >150000, and serum albumin >3.5 g/dL). [9, 10]

Detailed patient history was taken, especially to define the Child–Pugh score [11] and to assess for the presence of the exclusion criteria. Height in centimeters and weight in kilograms were measured to estimate the body surface area (BSA) in square meters. The BSA was calculated using the Mosteller formula (BSA =square root of height in cm × weight in kg/3600). [12]

Venous blood samples were obtained from all the patients to measure the complete blood picture, serum albumin, total bilirubin, the prothrombin time, the partial thromboplastin time, the INR, liver enzymes, the rapid ELISA testing of HCV antibodies and hepatitis B surface antigens, serum creatinine, serum urea, the lipid profile, blood sugar, and glycosylated hemoglobin. Additionally, the quantitative polymerase chain reaction of HCV antibodies was assessed before the start of treatment, at 4 weeks, at the end of treatment, and 12 weeks after the end of treatment. Abdominal ultrasonography was done at the commencement of treatment to examine liver cirrhosis criteria with the FibroScan to assess liver stiffness/scaring.

Cardiac Investigations: The following cardiac investigations were performed at baseline, at 6 weeks after treatment, and at 1 week after the end of treatment. Twelve-lead surface ECG was performed to assess the heart rate, the presence of any grade of heart block, the QTc, the presence of significant ST, T-wave changes suggestive of IHD, rhythms, the P-wave size, the QRS duration and axis, and voltage. Echocardiography was performed using a GE Vivid 7 echocardiographic machine with a 2.5 MHz transducer to obtain the LV end-diastolic and end-systolic diameters via the M-mode from the short-axis parasternal view at the level of the papillary muscles, the LV end-diastolic and end-systolic volumes, the LVEF via the modified Simpson method, [13] and the indexed LV end-diastolic and end-systolic volumes according to the BSA. In addition, the indexed left atrial volume was measured using the biplane Simpson method from the apical 4- and 2-chamber views. [13] The LV diastolic function was evaluated by estimating the transmitral E/A and the E/E' ratio, the deceleration time, and the lateral mitral annular early diastolic myocardial velocity (E'). The RV function was assessed by estimating the mean pulmonary artery pressure, the RV systolic pressure, and the tricuspid annular plane systolic excursion (TAPSE). [14]

Statistical Analysis

The data were statistically analyzed using Prism 5, version 5. Categorical variables were expressed as numbers and percentages and analyzed using the χ^2 test. Continuous variables were expressed as the mean ± the standard deviation (SD) and analyzed using

the Student *t* test for the variables that passed normality tests and the Mann–Whitney *U* test for those that did not pass normality tests. Correlations were analyzed using the Pearson correlation coefficient (*r*). A probability *P*-value of less than 0.05 was considered statistically significant, and a *P*-value of less than 0.0001 was considered highly significant.

RESULTS

The baseline demographic and clinical characteristics, as well as the results of the assessment of liver status by abdominal ultrasonography and the FibroScan, are shown in Table 1. The patients suffering from IHD with impaired systolic function (Group I) were older than the patients without IHD and with normal LVEFs (Group II) (56.2 ± 6.4 vs 54.1 ± 8.2 y; *P* =0.046). No statistically significant differences were noted as regards the patients' sex (*P* = 0.75). There was a higher percentage of diabetes and hypertension in Group I than in Group II (40 [41.6%] vs 35 [33.6%]; *P* =0.014 and 46 [47.9%] vs 38 [36.5%]; *P* =0.0022, respectively). The patients in Group I were more likely to be obese (body mass index =26.80 ± 2.80 vs 25.60 ± 2.70; *P* =0.0023). Regarding cardiac drug therapy, the rates of the consumption of anti-ischemic and anti-heart failure drugs (ie, beta-blockers, ACEI/ARBS, diuretics, mineralocorticoids, statins, antiplatelets, and digoxin) were higher in Group I than in Group II (Table 1).

Concerning biochemical markers, there were no statistically significant differences between the 2 groups except that in Group I, hemoglobin was low and glycosylated hemoglobin was high by comparison with Group II (Table 1). Baseline clinical examinations were done as regards shortness of breath, cough, palpitation, chest pain, fatigue, and headache. The same factors were then reassessed at the end of treatment. Some patients' complaints of fatigue and headache during treatment (side effects of drugs) disappeared after finishing the course, and no differences were observed between the 2 groups in this regard. With respect to liver disease status, the incidence of more advanced liver disease in Group I was higher than that in Group II; nevertheless, no clinically and statistically significant differences were detected between the 2 groups (Table 1).

The effects of treatment on ECG parameters, the heart rate, the PR interval, the QRS duration, and the QTc interval showed no statistically significant differences between the 2 study groups after treatment when compared with their values before treatment. There were no significant changes in the ST-segment and the T wave or arrhythmias between the groups at the start, during, and at the end of the treatment course.

The use of DAAs in the patients had no effects on the systolic and diastolic functions of the LV and the RV (Table 3).

DISCUSSION

HCV infection is considered a major cause of liver cirrhosis and chronic liver disease worldwide and is regarded as a health problem, especially in Egyptian patients. It is associated with many hepatic and extrahepatic manifestations, including heart problems. [1, 2] Regarding DAAs, the FDA has announced a change in labeling for hepatitis C antiviral ledipasvir/sofosbuvir (Harvoni) and sofosbuvir (Sovaldi) after the manufacturers reported the occurrence of bradycardia, needing pacemaker insertion, and even death in patients who took these medications with amiodarone. [15]

Table 1. Baseline clinical and demographic characteristics of both groups

Characteristics	IHD With Low EF (n =96)	Not Ischemic With Normal EF (n =104)	*P*-value
Age (y): mean ± SD	56.2 ±6.4	54.1 ±8.2	0.046*
Sex, No. (M/F) (N/%)	60/36	74/30	0.75
BMS (kg/m) mean ± SD	26.80±2.80	25.60±2.70	0.0023*
Hypertension (N/%)	46 (47.9%)	38 (36.5%)	0.0022
Diabetes mellitus (N/%)	40 (41.6%)	35 (33.6%)	0.014
Smoker (N/%)	50 (53.2%)	52 (50%)	0.59
Dyslipidemia (N/%)	30 (31.25%)	30 (28.8%)	1.00
Liver Assessment by Abdominal Ultrasound at Baseline			**0.846**
Normal	44 (45.83%)	56 (53.84%)	
Parenchymatous liver disease	31 (32.29%)	30 (28.84%)	
Cirrhotic liver disease	21 (21.87%)	18 (17.30%)	
FibroScan Assessment at Baseline			**0.876**
F0	25(26.0%)	30(28.8%)	
F1	48(50%)	50(48.08%)	
F2	20 (20.08%)	20 (19.23%)	
F3	3(3.12%)	6(5.7%)	
F4	0(0%)	0(0%)	
Biochemical Indicators			
Hemoglobin , g/dL	12.30±2.40	13.10±2.34	0.018*
Albumin, mg/dL	4.0±1.2	4.2±1.1	0.220
ALT, mg/dL	57.90±11.20	55.00±12.800	0.090
AST, mg/dL	42.00±10.30	40.40±11.80	0.310
Glycosylated hemoglobin%,	6.0±2.20	5.4±2.00	0.044*
Creatinine, mg/dL	0.9±0.6	1.00±0.80	0.321
eGFR, mL/min	73.2±29.6	72.4±30.0	0.84
TC, mg/dL	180.20±10.80	178.50±12.40	0.304
LDL-C ,mg/dL	119.20±8.10	120.400±6.800	0.256
Cardiac Drug History			
ACEI/ARBS (%)	90 (93.75%)	20(19.2%)	< 0.0001
Beta-blockers (%)	80 (83.3%)	28 (26.9%)	< 0.0001
Diuretics (%)	42 (43.75%)	15 (14.4%)	< 0.0001
Mineralocorticoids inhibitors (%)	24 (25%)	4 (3.8%)	<0.0001
Antiplatelets(ASA and/or clopidogrel)	60 (62.5%)	24 (23.0%)	<0.0001
Statins	36 (39.5%)	26 (25%)	<0.0001
Digoxin (%)	10 (10.4%)	0 (0%)	<0.0001

IHD, Ischemic heart disease; eGFR, Estimated glomerular filtration rate; LDL-C, Low-density lipoprotein cholesterol; TC, Total cholesterol; M/F, Male/female

* significant *P*-value

Table 2. Comparison of ECG and echocardiographic variables in patients with no IHD and with normal EF before and after treatment

Characteristics	Group II With Normal EF (n =104) Before Treatment	Group II With Normal EF (n =104) After Treatment	*P*-value
ECG Parameters			
Heart rate (b/m)	84.50 ±12.14	82.42 ±11.62	0.52
P-R interval (ms)	140.20 ±18.13	142.68 ±17.82	0.33
QRS duration (ms)	98.10 ±8.20	96.88 ±8.23	0.29
QTc, ms	414.92±28.30	412.86±27.46	0.60
Echo-Doppler Parameters			
LVEDD, mm	49.18±2.94	48.80±2.64	0.32
LVEDS, mm	31.02±2.48	30.82±2.18	0.53
LVEDV, ml	95.24±18.78	96.42±19.64	0.65
LVESV, ml	32.09±6.80	31.94±6.01	0.86

LVEDVI, ml/m^2	53.84±10.02	54.26±9.80	0.76
LVESVI, ml/m^2	18.26±2.98	18.02±2.50	0.52
LVEF, %	64.26±3.16	65.08±3.04	0.28
LAVI, ml/m^2	26.64±4.08	25.14±3.96	0.15
LV Diastolic Function			
Transmitral E/A ratio	1.12±0.40	1.06±0.38	0.26
DT, ms	190.06±29.58	186.48±26.40	0.35
Lateral mitral E', cm/s	15.43±4.08	14.52±3.83	0.098
E/E' ratio	6.86±2.84	6.42±2.54	0.24
RV Function			
RVSP, mm Hg	25.82±6.10	24.97±7.08	0.35
Mean PAP, mm Hg	17.05±3.20	16.96±3.85	0.85
TAPSE, mm	23.06±3.40	22.98±3.08	0.85

LV, Left ventricle; RV, Right ventricle; LVEDD, Left ventricular end-diastolic dimension; LVESD, Left ventricular end-systolic dimension; LVEDV, Left ventricular end-diastolic volume; LVESV, Left ventricular end-systolic volume; QTc, Corrected QT interval; LVEDVI, Left ventricular end-diastolic volume index; LVESVI, Left ventricular end-systolic volume index; LVEF, Left ventricular ejection fraction; LAVI, Indexed left atrial volume; RVSP, Right ventricular systolic pressure; PAP, Pulmonary artery pressure; TAPSE, Tricuspid annular plane systolic excursion

* significant *P*-value

Table 3. Comparison of ECG and echocardiographic parameters in patients with IHD and with mildly impaired EF before and after treatment

Characteristics	IHD With Mildly Impaired EF (n =96) Before Treatment	IHD with Mildly Impaired EF (n =96) After Treatment	*P*-value
ECG Parameters			
Heart rate (b/m)	86.40 ±13.18	83.62 ±12.02	0.13
P-R interval (ms)	144.30 ±18.04	145.18 ±17.94	073
QRS duration (ms)	100.10 ±7.20	98.94 ±8.74	0.318
QTc, ms	418.82±30.60	416.80±28.48	0.638
Echo-Doppler Parameters			
LVEDD, mm	54.92±3.14	55.34±2.98	0.345
LVEDS, mm	38.01±3.08	38.14±2.97	0.76
LVEDV, ml	158.04±28.12	162.34±29.14	0.32
LVESV, ml	61.24±10.36	63.04±9.82	0.22
LVEDVI, ml/m^2	70.48±16.12	72.34±15.00	0.41
LVESVI, ml/m^2	33.13±5.08	34.02±4.98	0.224
LVEF, %	45.04±3.08	44.38±3.16	0.094
LAVI, ml/m^2	30.14±5.12	31.04±4.98	0.221
LV Diastolic Function			
Transmitral E/A ratio	0.80±0.10	0.77±0.12	0.061
DT, ms	230.16±30.18	234.50±29.80	0.319
Lateral mitral E', cm/s	13.2±1.42	12.80±1.43	0.053
E/E' ratio	11.98±4.23	12.05±4.56	0.912
RV Function			
RVSP, mm Hg	30.45±9.00	29.98±10.13	0.735
Mean PAP, mm Hg	20.24±4.80	22.05±5.06	0.116
TAPSE, mm	28.90±5.14	30.06±4.93	0.114

LV, Left ventricle; RV, Right ventricle; LVEDD, Left ventricular end-diastolic dimension; LVESD, Left ventricular end-systolic dimension; LVEDV, Left ventricular end-diastolic volume; LVESV, Left ventricular end-systolic volume; QTc, Corrected QT interval; LVEDVI, Left ventricular end-diastolic volume index; LVESVI, Left ventricular end-systolic volume index; LVEF, Left ventricular ejection fraction; LAVI, Indexed left atrial volume; RVSP, Right ventricular systolic pressure; PAP, Pulmonary artery pressure; TAPSE, Tricuspid annular plane systolic excursion

* significant *P*-value

Cardiovascular disorders and HCV infection have a high prevalence in the general population. Both have a high incidence in both middle-aged and old patients. HCV infection is a non-traditional risk factor for many cardiac diseases such as cardiomyopathies, coronary artery disease, and cardiac arrhythmias. Further, antiviral therapy could affect the heart. [16]

The prevalence of HCV in Egypt is high, and the treatment involving oral DAAs either with or without pegylated interferon is used extensively nowadays. Treatment with DAAs, targeting different steps in the HCV lifecycle, is effective in HCV-infected patients; however, the safety of DAAs in cardiac patients, especially those suffering from IHD, is still completely unknown. [6] In the current study, we aimed to assess the safety of the treatment of chronic HCV infection with DAAs according to the national protocol (the Egypt protocol) in patients suffering from IHD with mildly impaired systolic function using surface ECG and transthoracic echocardiography.

All our study patients were treatment-naïve. The study population comprised 96 patients suffering from IHD with mildly impaired systolic function (EF =40%–50%) and 104 patients without IHD.

The main findings of this study were that DAAs, used in the national Egyptian treatment protocol for HCV infection treatment, were safe in patients suffering from IHD with mildly impaired systolic function. DAAs had no effects on the dimensions, volumes, and systolic and diastolic functions of the LV and the RV as assessed by the various guideline-recommended measurements in patients with IHD and mildly impaired systolic function. Additionally, the treatment exerted no effects on ECG parameters (HR, PR, and QRS) including the QTc interval and ST-T wave changes.

In the present study, baseline clinical examinations were done to determine blood pressure; heart rate; jugular venous pressure; pallor; jaundice; cyanosis; ascites; lower limb edema; S3, S4, and any other murmurs; shortness of breath (NYHA functional class); cough; hemoptysis; palpitation; chest pain; and paroxysmal nocturnal dyspnea. All these factors were subsequently reassessed during and after the treatment course. We detected no statistically significant differences in cardiac symptoms and signs between the baseline and the post-treatment.

Baseline patient characteristics showed that the patients in the group with IHD and impaired systolic function were older and more obese. Additionally, hypertension and diabetes mellitus were more common in those with IHD (Table 1). These were risk factors of coronary artery disease.

The QTc interval did not change after treatment in this study. Biomy et al [17] studied the cardiac effects of DAAs in 170 patients infected with HCV. They divided their patients into 2 groups according to the line of treatment: Group I comprised 100 patients who received pegylated interferon-alpha, sofosbuvir, and ribavirin, while Group II consisted of 70 patients who were treated with sofosbuvir and simeprevir. After a follow-up period of 6 to 12 months, the authors found no change in the QTc interval, nor did they detect any cardiac arrhythmias in the treated patients throughout the study and during the follow-up visits. Durante-Mangoni et al [18] studied the ECG of 39 HCV-infected patients treated either with a sofosbuvir (n =26) or with a non-sofosbuvir-based treatment (n =13). ECG tracings were examined on the first day of treatment and then after 7, 14, and 28 days. They concluded that for the sofosbuvir group, the QTc interval significantly increased at 1 week (P =0.013) before it returned to the baseline values during therapy until the end of treatment.

Fontaine et al [7] reported 3 cases of significant bradyarrhythmia, which happened during treatment with sofosbuvir plus daclatasvir, simeprevir, or ribavirin among 415 patients treated for 1 year from January to the end of December, 2014. The results of the present study do not chime in with the results of that study, where there were no statistically significant differences in rhythms between the baseline and the post-treatment.

Ahmad et al [19] assessed 34 patients who received interferon-free (Bristol-Myers Squibb) regimens (sofosbuvir-included regimens) and reported that 6 patients had LVEFs below 30%, 8 patients had LVEFs between 30% and 50%, and 11 patients required hospitalization for suspected cardiotoxicity. Of the patients with LVEFs below 50%, 6 had normalization of systolic function after a median of 20 days. T-wave inversions were the most sensitive predictor of LVEF dysfunction. These results are discordant with those reported in the present work, indicating that DAAs therapy did not induce any significant change in LV systolic and diastolic functions and that none of the patients developed new echocardiographic regional wall motion abnormalities at the end of the study period. Systolic function parameters showed nonsignificant changes over the study visits. Moreover, diastolic function parameters (ie, the E/A ratio, the deceleration time, the isovolumic relaxation time, and the E/e- ratio) showed no significant alterations between the beginning of the study and the follow-up visits.

Our 2 study groups showed no significant differences in cardiac symptoms and signs before and after treatment, which is concordant with the result reported by Biomy et al, [17] who detected no significant alterations in patient symptoms (shortness of breath, palpitations, and chest pain), signs (heart rate and blood pressure), or ECG recordings (arrhythmias, the QT interval, or ST-T wave changes) before and after oral antiviral treatment.

Renard et al [20] reported 3 cases of newly diagnosed or exacerbated severe pulmonary arterial hypertension in patients treated with sofosbuvir. Our study results indicated that DAA therapy did not induce any significant changes in pulmonary artery pressure. This could be because pulmonary arterial hypertension is associated with multiple factors besides DAA treatment.

In the present study, no diastolic parameters changed after treatment in both groups. This result disagrees with that reported by Novo et al, [21] who found that the lateral E' velocity decreased after treatment (P =0.001). The findings concerning diastolic parameters in our study are in line with those reported by Biomy et al, [17] who detected no changes in the E/A ratio, the deceleration time, and the E/E` ratio.

The current study showed no changes in LV volumes and EF after treatment in both patient groups with and without IHD. In concordance with the current study, studies by Novo et al [21] and Biomy et al [17] showed no differences in LV dimensions, volumes, and EF before and after treatment.

RV echocardiographic parameters such as TAPSE, the RV systolic pressure, and the mean pulmonary artery pressure showed no changes after treatment. Biomy et al [17] had similar findings, while Novo et al [21] reported similar results except for TAPSE, which was markedly reduced after treatment in their study (P <0.01).

Study Limitations

The present investigation is a single-center study with a small number of patients and only a 1-week follow-up period. The fact that patients with severely reduced LVEFs and patients with NYHA functional classes III and IV were not included is another

weakness of note. A longer follow-up period is needed in future studies to assess the long-term effects of DAAs.

CONCLUSION

The current national protocol of HCV infection treatment with DAAs, used in Egyptian patients, has a good cardiac safety profile. Such treatments have no effects on ECG parameters, including the QTc interval, nor do they exert any impacts on the functions of the LV and the RV. Additionally, they do not induce any significant changes in cardiac symptoms and signs during the treatment course. Further research on a larger number of patients with heart failure and a longer follow-up period is recommended.

Declaration
All the authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors. All the authors have approved the manuscript.

Ethics approval and consent to participate: The study protocol was reviewed and approved by the Ethics Committee (Tanta Faculty of Medicine). A written consent form was obtained from all the patients.

Consent to publish: Not applicable

Availability of data and martial: The data sets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Competing interests: The authors declare that they have no conflicts of interest concerning this paper.

Funding: No funding was obtained for this study.

Acknowledgments: We would like to thank our colleagues, nurses, and technicians in the Echocardiography Lab in the Cardiology Department and the Tropical Medicine Clinic in the Tana University Hospital for their assistance in collecting data and completing our study.

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