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ORIGINAL ARTICLE

Management of HCV-related decompensated cirrhosis with direct-acting antiviral agents: who should be treated?

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Abstract

Background Medical treatment of decompensated cirrhosis due to hepatitis C virus (HCV) remains a clinical challenge even in the era of direct-acting antiviral drugs (DAAs). We evaluated the efficacy and safety of DAAs in the management of HCV genotype 4-related decompensated cirrhosis.

Methods The study included a treatment group ($n=160$) composed of HCV patients with decompensated cirrhosis who received DAAs for 3 months and a matched control group ($n=80$) who preferred not to receive DAAs, follow-up was for 24–31 months.

Results In treatment group; there were improvements in platelet count, albumin, CTP ($p=0.001$) and MELD scores ($p=0.03$), a significant reduction in the frequency of hepatic encephalopathy (HE). SVR was achieved in 90%. Hepatocellular carcinoma (HCC) developed in 10% ($n=18$) within 6.8 ± 2.5 months after DAAs, survival was higher in the treated vs. the control group (28.9 ± 0.95 vs. 11.4 ± 2.2 months, $p=0.001$). Liver volume by ultrasound at a cutoff 495 ml was predictive of complications after DAAs therapy mainly HCC and reduced survival with sensitivity 93.2%, specificity 72%.

Conclusion HCV with decompensated cirrhosis and adequate liver volume had a 90% SVR with improved CTP&MELD and survival. Clinical trial: (NCT03547895).

Keywords HCV · Decompensated cirrhosis · DAAs · Liver volume

Introduction

The treatment varieties for patients with HCV-related decompensated cirrhosis remain a challenge. With the introduction of oral direct-acting antiviral (DAAs), SVR had been achieved in more than 90% with reduced risk of decompensation that needs liver transplantation. [1].

Reduced rates of SVR in decompensated cirrhosis were explained by the extensive porto-systemic collaterals and advanced fibrotic parenchyma which provides dormant foci for viral reactivation [2]. Achieving SVR is expected to improve portal hemodynamics and hepatic venous pressure gradient [3].

DAAs may induce rapid loss of anti-HCV immune responses with re-differentiation of memory T cell, T-lymphocyte deactivation, and normalization of NK-cell function leading to loss of immunological barrier against carcinogenesis [4]. SVR achieved by DAAs in decompensated cirrhosis may approach the rates that were achieved in non-cirrhotic patients. [5].

Viral clearance is expected to be associated with reduced morbidity and mortality rates [6]; however, the important question that should be asked is SVR beneficial in reversing the functional hepatic impairment although it appears that they reached a point of no return.

The current study aimed to evaluate the efficacy and safety of DAAs in managing HCV patients with decompensated cirrhosis and the impact of achieving sustained virological response on improving the quality of life, short term survival and if viral eradication would stepdown CTP, MELD scores.

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Methods

Study design and patients selection

The study was conducted from the first of June 2015 till June 2018 in the Hepatology clinic of Zagazig University hospitals (a tertiary referral center) in Egypt.

Out of 502 patients who were presented with decompensated cirrhosis due to HCV, 342 patients were excluded (Fig. 1 supplementary). Finally, 160 patients with decompensated cirrhosis were selected to receive DAAs. Patients were included if HCV-related decompensated cirrhosis was proved by the positivity of HCV RNA, elevated transaminases, difficult to treat- ascites or frequent attacks of hepatic encephalopathy, CTP score >9, MELD score ≥ 15 but <29 as above this cut off value; the 3 months mortality is 52.6% [7].

Patients were excluded if they had compensated cirrhosis; exposure to previous antiviral therapy; hepatocellular carcinoma; grade III, IV hepatic encephalopathy; other causes of liver diseases, previous liver transplantation; patients with cardiomyopathy (left ventricular ejection fraction less than 50%).

The control group included 80 patients, who were selected from patients who refused treatment with DAAs ($n=147$), they fulfilled the inclusion criteria and were age, sex, CTP and MELD scores-matched, they preferred to be managed conservatively avoiding treatment by DAAs by themselves ($n=43$) or by their relatives ($n=37$) as they were concerned about the possible higher risk of liver cancer after DAAs, although we clarified to them that DAAs were not proved to be carcinogenic and this effect was noticed mainly in patients with previous history of HCC or already had HCC, but not diagnosed yet.

The study and control patients were collected from June 2015 till October 2015, the last patient successfully terminated DAAs on 24th of May 2016, and then the period follow-up was extended till 24th June 2018.

A complete history taking and meticulous clinical examination were done for all of the patients to document features of liver cirrhosis and decompensation.

Baseline laboratory investigation

- Investigations preliminary to antiviral therapy: liver and kidney function tests, HBA1c if diabetic and serum AFP. CTP and MELD scores were calculated.
- Quantitative assessment of HCV load in the serum by real time Quantitative PCR just before the study in both groups and after the first month, at the end of treatment and 3 months, 6 months post-treatment to detect SVR 12th, 24th in DAAs treated group.
- Genotyping for HCV using INNO-LiPA II, based on genotype-specific oligonucleotides from the 5′ UTR that are immobilized on a nitrocellulose strip [8].

Abdominal ultrasonography (USG)

The patients were evaluated by a single expert operator using (Sonoscape A6 ultrasound machine) for criteria of decompensated cirrhosis and to exclude HCC.

Manual appreciation of liver volume by USG as a predictor of functional hepatic reserve using the standard ellipsoid formula (max. length × max. width × max. depth × 0.523) which is used for estimating the volume of irregularly shaped organs [9], normal liver volume for adults is 18 ml/kg body weight [10] (Fig. 1).

After treatment termination; USG was done every 6 months for a period of 24 months.

Treatment exposure and outcome

Medications

The treated patients were given sofosbuvir 400 mg, ribavirin 400–600 mg, and daclatasvir 60 mg daily for 3 months. Ribavirin was added at a low dose to avoid the occurrence of drug-induced anemia. In addition they were given supportive therapy which included silymarin 420 mg daily, branched chain amino acids and diuretics for ascites. Post-treatment evaluation included sustained virological response (SVR), development of complications and impact of SVR on frequency of hepatic encephalopathy (HE), ascites control and short-term survival defined as a survival that extends more than 1 year after termination of DAAs.

The control group was given supportive treatment in the form of branched chain amino acids composed of valine, leucine, and isoleucine, silymarin 420 mg daily, diuretics for ascites and oral vitamin K1 10 mg for bleeding tendency. They were followed up for the planned period to record the occurrence of complications as hepatic encephalopathy, variceal bleeding, and complications due to ascites as spontaneous bacterial peritonitis or hepatorenal syndrome and death.

Monitoring

- All the patients had regular bi-weekly visits in the first 6 months, then every 2 months for 24 months. Patients' evaluation in every visit included a full history taking, clinical examination and routine laboratory investigations.
- Serious complications which required hospital admission during treatment were recorded such as life-threatening infections, gastrointestinal bleeding, hepatic encephalop-

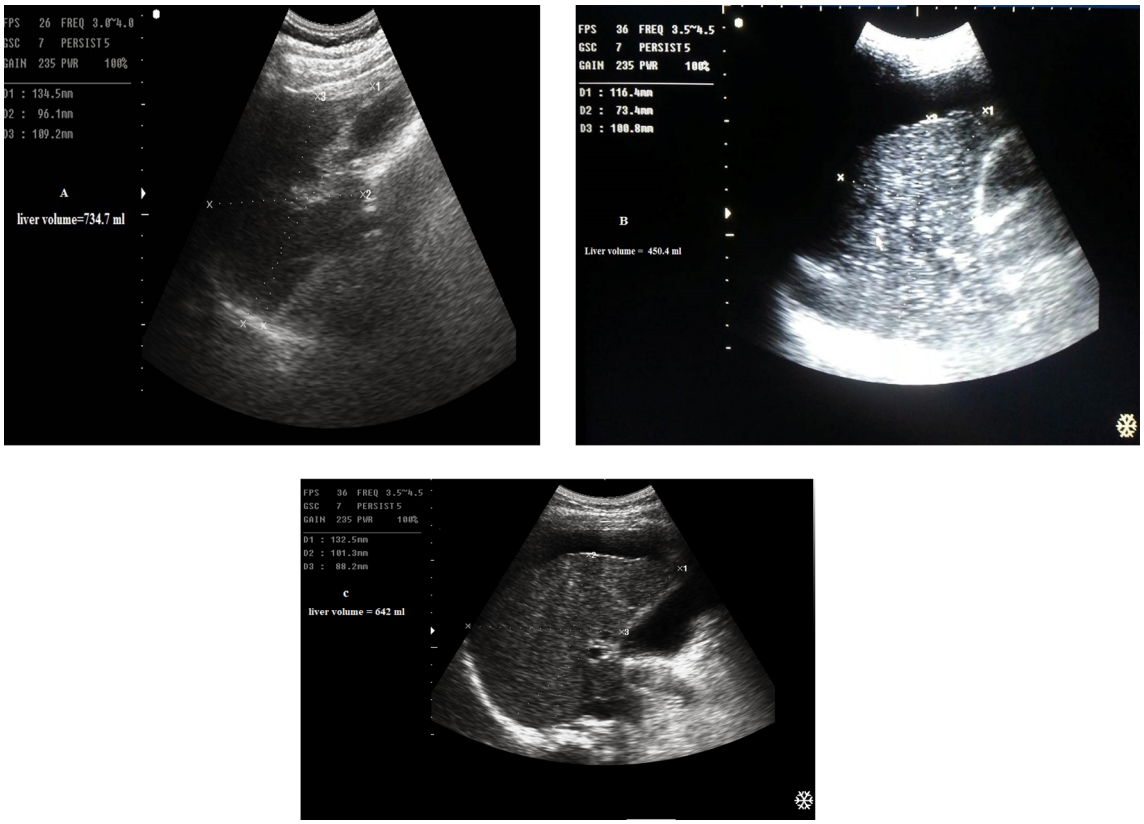

Fig. 1 manual liver assessment by ultrasound (max. length × max. width × max. depth × 0.523) **a** Liver volume = 734.7 ml, **b** shrunken liver with a volume of 450.4 ml, **c** cirrhotic liver with ascites and a liver volume of 642 ml

athy, difficult-to-treat ascites, hepatocellular carcinoma, and death.

- Difficult-to-treat ascites was defined as ascites that rapidly recurs after paracentesis or cannot be completely mobilized despite sodium restriction of less than 2 g/day with maximal dose of furosemide (160 mg) or spironolactone (400 mg) or inability to reach maximum diuretic dose due to emergence of side effects, and after confirming compliance with sodium restrictions proved by the 24-h urine sodium < 78 mEq.
- All the patients who had hepatic encephalopathy type C [11] were graded according to The West Haven semi-quantitative criteria [12].

Outcome evaluation

- The primary outcome was achievement of SVR 12th and 24th defined as undetectable HCV RNA by real time Quantitative PCR at 12 and 24 weeks, respectively after end-of treatment.
- Secondary outcomes included intra-group improvement of the liver synthetic function, improvement in frequency or grading of hepatic encephalopathy and ascites control defined by significant weight loss > 10% with reduction or complete disappearance of ascites by ultrasonography, change in MELD score, and the occurrence of side effects during the period of study or death.

Statistical analysis

- All data were analyzed using SPSS 20.0 for windows (SPSS Inc., Chicago, IL, USA). Results were expressed as mean ± SD. The sample size was determined according to an equation which utilized population size, confidence level (%) and margin of error (%).Categorical variables were analyzed using the χ^2 test and continuous variables were analyzed using the Student's t test. Correlation analysis to detect variables associated with SVR using Pearson's correlation coefficient (r). $p < 0.05$ was considered to be statistically significant.
- Survival analysis was performed using Kaplan–Meier test; the significance of the curves was assessed using Log rank, Breslow and Tarone–Ware tests. Cox proportional hazard analysis was used to estimate the hazard ratio of liver related adverse events and death. Survival difference was done after adjusting for age, gender, ascites severity, cause of cirrhosis, previous prophylaxis

of variceal bleed, and prophylaxis of spontaneous bacterial peritonitis.

Results

Treatment group

The first patient who had received DAAs was on June 2015 and the last patient who had terminated treatment was on 24th of May 2016, they were followed till June 2018; the period of strict observation and follow-up was 29.3 ± 1.9 months (24-31 months). Table 1 shows the baseline characteristics of the treated patients and controls.

Outcome of the study

Treated group

One hundred and sixty patients (124 males, 36 females) showed difficult to treat cirrhotic ascites. 116 (72.5%) patients experienced chronic recurrent episodes of hepatic encephalopathy grade II (2.1 ± 0.6 episodes/2.9 ± 0.9 months).

After 3 months, all the patients had completed the course of therapy without any reported major complications. There was a significant improvement in the baseline laboratory parameters as shown in Table 2. Before starting DAAs treatment, all patients (100%) were eligible for liver transplantation listing, having MELD score > 18 [20.6 ± 2.04] (Table 2). After DAAs therapy, more than 80 patients (55.5%) had MELD score less than 18 and only 12 (8.3%) of the treated patients had improved MELD score to less than 15 (14.1 ± 1.1).

116 patients (72.5%) had experienced chronic episodic hepatic encephalopathy before initiation of DAAs, but during the period of treatment and till the end of follow-up, a significant reduction in the number of patients who experienced hepatic encephalopathy was noted; only 32/116 still experiencing HE ($\chi^2 > 14.312$, $p = 0.002$). Additionally, the frequency of episodes was significantly reduced from 2.1 ± 0.6 to 1.4 ± 0.2 episodes/2.9 ± 0.9 months, ($p = 0.003$).

Ascites was prevalent in all the patients before DAAs (100%). After treatment, it became completely controlled in 40 patients (25%), partially controlled in 92 patients (57.5%) and still poorly controlled in 28 patients (17.5%) (Table 3).

47 (29.4%) patients gave previous history of variceal bleeding with regular endoscopic surveillance aiming for variceal eradication; 29 patients showed grade I–II non-risky esophageal varices (EV) and followed up every 4–6 months, ten patients had obliterated EV and followed up every 9 months, eight patients had gastric varices that were secured with amacrylate before DAAs treatment and followed every 6 months. During the period of treatment and follow-up no patient had experienced any attack of variceal bleeding with no recorded deaths (Table 4).

Table 1 Baseline characteristics of the treated and controls groups

Variable	Treated group ($n = 160$)	Control group ($n = 80$)	p value
Age	51.4 ± 6.3	49 ± 5.8	0.6
M/F	124/36	63/17	0.37
Genotype	4a (96), 4c (60), mixed (4)	4a (42), 4c (35), mixed (3)	0.12
BMI (kg/m^2)	28.5 ± 1.5	27.9 ± 2.4	0.4
ALT (IU/L)	66 ± 16	76 ± 8	0.01
AST (IU/L)	77.4 ± 22.4	69.4 ± 12.5	0.02
Albumin (gm/dl)	2.5 ± 0.4	2.4 ± 0.52	0.17
T. bilirubin (mg/dl)	2.1 ± 0.5	1.9 ± 0.2	0.055
WBC's	3.3 ± 0.9	3.5 ± 0.7	0.1
Hemoglobin (gm/dl)	10.9 ± 0.9	10.4 ± 0.5	0.06
Platelets (10^3/ul)	85.9 ± 15.5	81.8 ± 11.1	0.17
PC%	66.7 ± 3.6	61.2 ± 2.7	0.7
INR	1.6 ± 0.24	1.55 ± 0.2	0.3
Creatinine (mg/dl)	1.1 ± 0.3	1.2 ± 0.5	0.24
AFP (ng/ml)	17.8 ± 10.8	16.4 ± 8.3	0.07
Serum sodium (mEq/L)	130 ± 3.7	128.5 ± 4.3	0.12
CTP	11.2 ± 1.2	11.4 ± 0.98	0.35
MELD	20.6 ± 2.04	21.8 ± 1	0.51
HCV-RNA (KIU/ml)	460.8 ± 62.5	325 ± 90.3	0.01
Liver volume (ml)	880 ± 302	702 ± 189	0.083

Table 2 Comparison between the baseline laboratory characteristics of the treated and control groups and at the end of the study

	Before DAAs	After DAAs	*p*
Treated group			
Platelet count ($\times 10^3$/ul)	85.9 ± 15.5	90.6 ± 13.9	0.01
S. Albumin (gm/dl)	2.5 ± 0.4	2.9 ± 0.13	0.02
T. bilirubin (mg/dl)	1.7 ± 0.5	1.4 ± 0.2	0.034
Serum AFP (ng/ml)	17.8 ± 10.8	10.3 ± 4.4	0.001
Serum creatinine (mg/dl)	1.1 ± 0.3	0.95 ± 0.23	0.09
Serum sodium (meq/l)	130 ± 3.7	132.4 ± 1.4	0.13
INR	1.6 ± 0.24	1.4 ± 0.15	0.09
CTP score	11.2 ± 1.2	7.8 ± 0.9	0.001
MELD score	20.6 ± 2.04	17.1 ± 1.2	0.03
Control group			
Platelet count ($\times 10^3$ cell/ul)	81.8 ± 11.1	71.6 ± 9.4	0.001
S. Albumin (gm/dl)	2.4 ± 0.52	2.3 ± 0.2	0.1
T. bilirubin (mg/dl)	1.9 ± 0.2	2.2 ± 0.5	0.01
INR	1.55 ± 0.2	1.8 ± 0.2	0.02
Serum AFP (ng/ml)	16.4 ± 8.3	28.4 ± 5.1	0.003
Serum sodium	128.5 ± 4.3	118 ± 6.2	0.001
Creatinine (mg/dl)	1.2 ± 0.5	1.4 ± 0.3	0.042
CTP	11.4 ± 0.98	12.3 ± 1.01	0.001
MELD	21.8 ± 1.8	26.4 ± 1.6	0.034

SVR was achieved in 144 patients (90%). Sixteen patients (10%) were non-responders. All of the non-responders showed viral clearance after 1 month of therapy, 12/16 patients achieved end of treatment response (ETR) then experienced relapse 3 months post-treatment ($n = 8/12$) or 6 months post-treatment ($n = 4/12$). The baseline characteristics of the non-responder vs. SVR patients were shown in (Table 5); a highly significant difference was noted regarding transaminases, AFP levels which were higher in the non-responders, liver volume was significantly lower in the non-responders with significantly higher HCC frequency.

Liver volume appreciated by a single experienced radiologist through bed-side abdominal USG had a significant impact on the result of therapy, complications and survival as shown in Table 4.

HCC had developed 6.8 ± 2.5 months after treatment termination ($n = 18$, 10%), odds ratio 2.25, 95% CI 0.72–7.01, 10/18 patients had achieved SVR, all of them had reduced liver volume (490 ± 58 ml) when compared to non-HCC group (800.4 ± 263 ml) ($p = 0.001$).

Variables correlated with SVR were: sex ($r = 0.419$, $p = 0.007$), AST ($r = -0.455$, $p = 0.003$), ALT ($r = -0.537$, $p = 0.000$), AFP ($r = -0.597$, $p = 0.000$) and liver volume ($r = 0.377$, $p = 0.001$).

Variables correlated with HCC were: AST ($r = 0.194$, $p = 0.014$), ALT ($r = 0.209$, $p = 0.008$), AFP ($r = 0.342$, $p = 0.001$), SVR ($r = -0.409$, $p = 0.001$) and liver volume ($r = -0.319$, $p = 0.001$). It appeared that liver volume is an important variable that determines the outcome of DAAs in decompensated cirrhosis.

Liver volume at a cut off value 495 ml was predictive of complications after DAAs, mainly HCC and reduced survival (Fig. 2), AUC 0.92, $p = 0.001$, 95% CI 0.879–0.964, sensitivity 93.2%, specificity 72%.

The control group

The baseline characteristics are shown in Table 1. All had poorly controlled ascites, 68 patients (85%) gave previous history of recurrent episodes of hepatic encephalopathy (2.3 ± 0.5 episodes/2.83 ± 1.03 months).They were given the planned treatment and in the complicated cases, upper GI endoscopy for bleeding esophageal varices was done and were managed by endoscopic band ligation ($n = 37$, 46.3%) or amacrylate injection for gastric varices ($n = 7$, 8.8%).

At the end of the follow-up (Table 2), a highly significant statistical difference was noted when compared to the baseline data with worsening of MELD score and a step up of their CTP score.

Hepatic encephalopathy persisted in 34 patients, (42.5%) which was significantly lower than pretreatment patients' number but still significantly lower than that achieved in the DAAs group ($p = 0.001$). Ascites was poorly controlled in 64 (80%), partially controlled in 14 (17.5%) and completely controlled in two patients (2.5%) and that was significantly lower when compared to the treated group ($p = 0.001$). Death was recorded in 18 patients (22.5%) due to spontaneous

Table 3 Impact of SVR on the occurrence of hepatic encephalopathy and ascites control

	Before DAAs	After DAAs	*p*
Hepatic encephalopathy			
Prevalence ($n =$, %)	116 patients, (72.5%)	32 patients, (20%)	0.002
Frequency of episodes	2.1 ± 0.6	1.4 ± 0.2	0.003
Ascites	160 patients (100%)	120 patients (75%)	0.004
Poorly controlled	160 (100%)	28 (17.5%)	0.001
Partially controlled	0	92 (57.5%)	0.000
Completely controlled	0	40 (25%)	0.000

Table 4 Impact of liver volume as a predictor of hepatic reserve on the outcome of the patients under study

	Treated patients	Control	*p*
SVR (*n*, ml)			
Positive	(*n* = 144) 980.4 ± 287.6	–	
Negative	(*n* = 16) 541.3 ± 38.3		
p value	0.001, *t* = 6.07		
Hepatic encephalopathy (*n*, ml)			
Absent	(*n* = 128), 936 ± 308	(*n* = 12), 745 ± 182	0.036
Present	(*n* = 32), 658 ± 116	(*n* = 68), 650 ± 168	0.8
p value	0.001, *t* = 5.12	0.08, *t* = 1.7	
Ascites control (*n*, ml)			
Completely controlled	(*n* = 40), 1020 ± 302	(*n* = 2), 925 ± 49	0.66
Partially controlled	(*n* = 92), 886 ± 287	(*n* = 14), 724 ± 227	0.046
Poorly controlled	(*n* = 28), 661 ± 248	(*n* = 64), 650 ± 153	0.79
p value	0.001, *f* = 13.2	0.034, *f* = 3.51	
Death	(*n* = 0), -	(*n* = 18), 482 ± 139	–
Survival	(*n* = 160), 880 ± 302	(*n* = 62), 724 ± 129	0.001
p value	–	0.0001, *t* = 6.6	

Table 5 Baseline characteristics and frequency of HCC in non-responder vs. SVR patients

Variable	Non-responders (*n* = 16)	Responders (*n* = 144)	*p* value
Age	51.7 ± 5.4	48.5 ± 5.2	0.32
M/F	10/6	114/30	0.13
Genotype	4a (7), 4c (5), mixed (3)	4a (89), 4c (55), mixed (1)	0.16, 0.59, 0.001
BMI (kg/m^2)	28.9 ± 1.7	27.4 ± 1.9	0.4
ALT (IU/L)	90 ± 8	74 ± 19	0.001
AST (IU/L)	97 ± 23	64 ± 14	0.001
Albumin (gm/dl)	2.3 ± 0.4	2.45 ± 0.5	0.24
T. bilirubin (mg/dl)	2.1 ± 0.6	1.97 ± 0.5	0.33
WBC's	3.2 ± 1.1	3.4 ± 0.95	0.4
Hemoglobin (gm/dl)	10 ± 0.76	10.3 ± 0.9	0.2
Platelets (10^3/ul)	83.3 ± 9.4	85.8 ± 15.9	0.53
PC%	64 ± 5.2	62 ± 3.7	0.06
INR	1.5 ± 0.1	1.6 ± 0.2	0.062
Creatinine (mg/dl)	1.3 ± 0.4	1.23 ± 0.32	0.4
AFP (ng/ml)	47.8 ± 5.2	19.4 ± 7.2	0.001
Serum sodium (mEq/L)	127 ± 5.7	132 ± 3.9	0.21
CTP	11.1 ± 0.94	11.2 ± 0.88	0.6
MELD	21.6 ± 1.4	20.7 ± 1.1	0.1
HCV-RNA (KIU/ml)	530.8 ± 54	472.6 ± 85	0.07
Liver volume (ml)	541.3 ± 38.3	918.2 ± 294.3	0.001
HCC (*n*, %)	8 (50%)	10 (6.9%)	0.001

bacterial peritonitis and hepatorenal syndrome ($n = 4$), hepatic encephalopathy ($n = 6$), gastrointestinal bleeding ($n = 8$).

The impact of adding antiviral therapy on survival and occurrence of major events as death was analyzed by Kaplan–Meier survival curve after a follow-up period of 24–31 months started from the first day of therapeutic intervention (Fig. 3); the mean survival time was significantly longer in decompensated cirrhotic patients who were treated with DAAs (28.9 ± 0.95 months [95% CI 28.7–29.8]) compared with those who were treated with supportive therapy (11.4 ± 2.2 months [95% CI

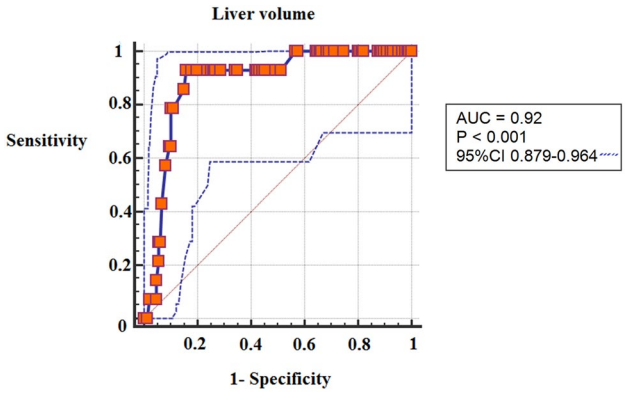

Fig. 2 Cut off value of liver volume as a predictive of complications after DAAs therapy mainly HCC and reduced survival, AUC 0.92, $p=0.001$

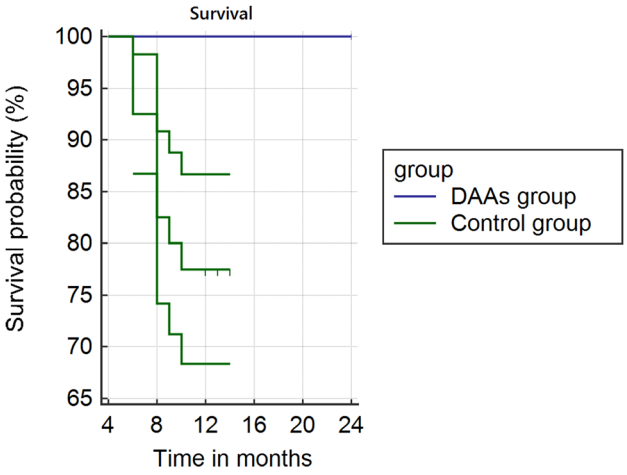

Fig. 3 Kaplan–Meier survival curve to show the impact of adding antiviral therapy on survival in the treated and control patients

10.86–11.84]; $p<0.001$). Cox's proportional hazard analysis revealed that decompensated cirrhotic patients who were not given DAAs for HCV eradication had a hazard ratio of death (HR): 5.4 with a shorter survival time [95% CI 3.51–8.15].

Discussion

The benefits of eradicating HCV virus in decompensated liver disease may be greater than doing so in other patients. The results of oral DAAs in the management of HCV-related liver disease are undoubted [12], however, their use in patients with decompensated cirrhosis is challenging especially in those who may frequently experience worsening of hepatic decompensation. [13].

The current study evaluated the impact of DAAs on patients with decompensated cirrhosis regarding outcome and survival and utilized manual liver volume appreciated by abdominal ultrasound as a novel prognostic factor in this special category of HCV patients. In our study, liver volume less than 495 ml was associated with reduced survival and higher incidence of HCC even if SVR was achieved by DAAs and thus, the latter should be discouraged.

The rate of SVR in the current study was 90% and treatment was well tolerated without discontinuation or non-compliance. A non-randomized study showed that SVR was higher in patients who received daclatasvir compared to ledipasvir. [14].

The treated group showed an improvement in MELD and CTP scores, suggesting the benefits of therapy in this category of patients and that was supported by a study which reported that even in non-responders to antiviral therapy; there was a modest improvement in MELD [15], in addition, 8.3% of the treated patients had improved MELD score to less than 15 (14.1 ± 1.1) and became deferred completely from consideration for liver transplantation at the end of follow-up period and this finding shed light on an overlooked advantage of DAAs therapy in decompensated cirrhosis.

Patients who achieved SVR showed a significant reduction in the frequency of hepatic encephalopathy episodes, improvement in the management of ascites. No recorded mortality among the treated patients during the follow-up when compared to the control group.

In studies which enrolled patients with decompensated cirrhosis due to HCV as SOLAR-1, SOLAR-2; SVR rates were lower when liver disease was progressive being 96% in patients without cirrhosis or 60–75% in patients with severe hepatic impairment [16]. In SOLAR-2, though a few patients infected with HCV genotype 4 were enrolled; it showed that DAAs were safe and well tolerated. [17].

The ALLY-1 study evaluated the administration of sofosbuvir, daclatasvir and ribavirin in patients with advanced cirrhosis or post-transplant HCV recurrence involving all of the genotypes. 83% of the patients achieved SVR12. SVR in HCV-G4 in this study was 100%; however, the number of patients was small (4/4). Treatment was well tolerated, with no adverse events. [18].

The use of sofosbuvir with daclatasvir or ledipasvir in decompensated cirrhosis was associated with improvement in CTP and MELD scores and synthetic liver function [19, 20] and that was supported also by The meta-analysis of Guarino et al. [21].

In conclusion, this real-life study had enrolled an adequate number of patients with HCV genotype 4-related decompensated cirrhosis. Treatment of decompensated cirrhotic patients with CTP >9, MELD ≥ 15 but <29 by a 3-month course of DAAs had led to SVR in 90% with improvement in CTP and MELD scores and a significant reduction in hepatic

encephalopathy episodes with better control of ascites and improved short-term survival mainly in patients with adequate liver volume which is a novel prognostic factor in this category of patients and we do not recommend giving this treatment to patients with a liver volume less than 495 ml unless it is a preliminary step before an imminent liver transplantation. Clinical trial: (NCT03547895).

Author contribution Amr Shaaban Hanafy was responsible for the study concept and design and he is the Guarantor of the article. Mohamed Bassiony was responsible for data acquisition and recording, Mohammad Abd Alkhalik supervised radiological investigations. All authors had full access to all data in the study, and take responsibility for the integrity of the data and the accuracy of the analysis. Amr Hanafy wrote the manuscript and performed statistical analysis. All authors were responsible for the critical review and had approved the final draft submitted.

Compliance with ethical standards

Conflict of interest Amr Shaaban Hanafy, Mohamed A. Bassiony and Mohammad Abd Alkhalik Basha declare that they have no conflict of interest.

Ethical approval The study was approved by Zagazig university institutional research committee at the 3rd of May 2015. Written, informed consent was obtained from each patient included in the study. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

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