Journal of Microbiology, Immunology and Infection 55 (2022) 643—650

Available online at www.sciencedirect.com

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journal homepage: www.e-jmii.com

Original Article

Improvement of patient-reported outcomes in patients achieving sustained virologic response with direct-acting antivirals for hepatitis C virus infection

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Received 8 December 2021; received in revised form 16 March 2022; accepted 28 April 2022
Available online 17 May 2022

KEYWORDS
Quality of life;
HCV;
DAA

Abstract *Background:* Patient-reported outcome (PRO) in patients with chronic hepatitis C virus (HCV) infection (CHC) after successful direct-acting antiviral (DAA) therapy remains elusive. The study aimed to investigate the impact of DAA therapy on health-related quality of life (HRQoL). We also assess the associated factors predictive of HRQoL change after sustained virologic response (SVR) to HCV therapy.
Methods: CHC patients receiving DAA therapy were prospectively recruited. They completed paired HRQoL assessments which included Short-Form-36 (SF-36), Pittsburgh Sleep Quality

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https://doi.org/10.1016/j.jmii.2022.04.011

Index (PSQI) score, Taiwanese Depression Questionnaire score, and State Trait Anxiety Inventory (STAI) score before treatment and at Week 12 off-treatment. Clinical data and characteristics were compared in a paired manner.
Results: A total of 158 patients achieved SVR (SVR rate: 96.6%) were enrolled into the final analysis. Improvement of depression, anxiety, digestive symptoms, and SF-36 items of vitality, body pain, physical functioning, emotional functioning, social functioning, and mental health were demonstrated among SVR patients. Sleep quality, or other SF-36 items were not significantly changed after the treatment. Multivariate analysis revealed that improvement of sleep quality, depression, and anxiety were associated with better HRQoL.
Conclusion: SVR to HCV therapy by DAA significantly improved PROs including HRQoL.

Introduction

Chronic hepatitis C virus (HCV) infection (CHC) is a global health issue, leading to cirrhosis, hepatic decompensation and hepatocellular carcinoma.[1] More than 70 million people in the world have suffered from chronic HCV infections and the prevalence of HCV infection is in 1.8%—5.5% of the population in Taiwan.[2–5] Besides liver injury, the extrahepatic manifestations are not uncommon in CHC patients such as type 2 diabetes mellitus (T2DM), hyperlipidemia, cryoglobulinemia, lymphoma, atherosclerosis, ischemic heart, glomerulonephritis and autoimmune disorders.[6–9] Therefore, the successful HCV treatment is based on the depletion of both hepatic and extrahepatic insults. Interferon (IFN)-free direct-acting antivirals (DAAs) have now become the mainstream of treatment because of the extremely high efficacy, short treatment duration, and excellent tolerability.[10–12] Eradication of HCV improves the long-term hepatic outcomes, decreases the development of liver-related events, and amelioration of extra-hepatic manifestations.[13–16]

HCV-infected patients carry a lower health-related quality of life (HRQoL) compared to the general population and patients with chronic hepatitis B.[17–19] The impairment in HRQoL is presented either in physical or psychological manifestations such as fatigue, persistent flu-like symptoms, joint pain, itching, sleep disturbances, appetite changes, nausea and depression. The change of HRQoL subsequent to a sustained virologic response (SVR) after DAA therapy remains elusive and the results from the cumulative studies were not conclusive.[20–25] Evaluating the HRQoL in CHC patients is a clinical challenge largely due to the asymptomatic presentation.

Consequently, we aimed to investigate the impact of DAA therapy on HRQoL of various directions. We also aimed to elucidate the clinical factors predicting the improvement in HRQoL after DAA therapy.

Methods

Subjects and study design

The Research Ethical Committee of Hualien Tzu Chi Hospital approved this multi-center, prospective study before it was performed. The study was performed in accordance with the principles of the Declaration of Helsinki. The prospective study was conducted at a medical center hospital, a regional hospital, and primary care centers in Eastern Taiwan. Written informed consent for an interview, anthropomorphic measurements, and medical record review were obtained from subjects prior to enrollment. Age, gender, and major comorbidities were recorded using standardized techniques.

CHC patients eligible for and receiving DAA therapy (elbasvir/grazoprevir, glecaprevir/pibrentasvir, sofosbuvir/velpatasvir, or sofosbuvir/ledipasvir) were prospectively recruited according to the national treatment guidelines of Taiwan from April 2019 to December 2020. The treatment regimens and strategies conformed to the regulations of the Health and Welfare Department of Taiwan and regional guidelines.[26,27] CHC was defined as having a detectable HCV antibody and serum HCV RNA for $\geq$6 months. A SVR12 was defined as the lack of detectable HCV RNA ($<$12 IU/mL) 12 weeks after treatment completion (end-of-follow-up, EOF). Roche's cobas® system was utilized for HCV RNA detection and HCV genotypes identification. Patients need for ribavirin or not achieved SVR were excluded.

Patient-reported outcomes

All patients completed assessments at baseline and at SVR12, including Short-Form-36 (SF-36), Pittsburgh Sleep Quality Index (PSQI) score,[28] Taiwanese Depression Questionnaire score (TDQ),[29] State Trait Anxiety Inventory (STAI) score,[30] Gastrointestinal Symptom Rating Scale (GSRS).[31]

We used SF-36 as a tool to survey HRQoL upon their outpatient-based visits. The SF-36 Health Survey is a 36-item, patient-reported survey of patient health. The SF-36 is a measure of health status and has been widely used globally with confident performance. The SF-36 consists of eight scaled scores, which are the weighted sums of the questions in their section. Each scale is directly transformed into a 0—100 scale on the assumption that each question carries equal weight. The lower the score shows the more disability. The eight sections consist physical component summary (PCS) and mental component summary (MCS). The sleep quality was evaluated according to self-reported questionnaire PSQI over a recent month. Patients with global score (sum of seven components, 0—3 scale) more than five were considered to have sleep disturbance. Patients were guided to finish 18 questions (0—3 scale) of culture-based TDQ. In our study, depression

was defined as global score more than 18. Anxiety was diagnosed by global score of STAI more than 40. STAI is composed of 20 items for trait anxiety and 20 items for state anxiety, scores of each item range from 1 to 4. The GSRS is a disease-specific instrument of 15 items combined into five symptom clusters depicting reflux, abdominal pain, indigestion, diarrhea, and constipation. The GSRS has a seven-point graded Likert-type scale where 1 represents absence of troublesome symptoms and 7 represents very troublesome symptoms.

Statistical analysis

The data were expressed as frequencies, proportions, or mean ± standard deviations, according to the characteristics of each item. Data were compared between the baseline and the end of the therapy. Paired sample t-test was adopted to determine whether the mean difference between the parameters at baseline and after receiving therapy was significant from zero. Factors associated with changes of SF-36 scores were evaluated by multiple linear regression multivariate analysis (Model 1: adjusted for all covariates; Model 2: only adjusted for age, sex, and covariates with $P < 0.10$ in crude analysis). Statistically significant differences were defined as $P < 0.05$. All of the statistical analyses were performed using SPSS software version 21.0 (IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.)

Results

Patient characteristics

After excluding 11 patients need for ribavirin and 6 patients not achieved SVR, a total of 158 CHC patients (aged 60.20 ± 11.70 years, 54.4% females) achieved SVR (SVR rate: 96.6%) were enrolled into the final analysis (Fig. 1). The patient characteristics were summarized in Table 1. The percentage of medications prescribed for DAA therapy were 17.7% for elbasvir/grazoprevir, 15.4% for glecaprevir/pibrentasvir, 21.7% for sofosbuvir/velpatasvir, and 45.1% for sofosbuvir/ledipasvir. Nine (5.5%) patients had liver cirrhosis, Child-Pugh score A, 23 (14.6%) patients had chronic kidney disease (CKD), and 58 (36.7%) patients had diabetes mellitus (DM).

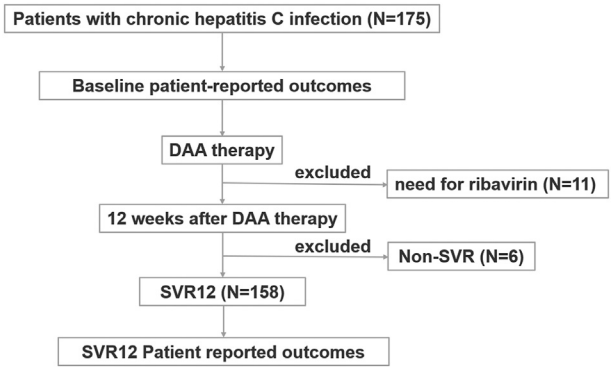

Figure 1. Flow diagram for study inclusion and exclusion.

Table 1 Demographics of patients with chronic HCV achieved SVR.

Demographics	Total
N	158
Age	60.20 ± 11.70
Gender	—
Male	72 (45.6%)
Female	86 (54.4%)
Medication	—
sofosbuvir/velpatasvir	73 (46.2%)
elbasvir/grazoprevir	27 (17.1%)
glecaprevir/pibrentasvir	27 (17.1%)
sofosbuvir/ledipasvir	31 (19.6%)
BMI	25.55 ± 4.99
HCV genotype	—
1a	6 (3.8%)
1b	75 (47.5%)
2	61 (38.6%)
3	2 (1.3%)
6	12 (7.6%)
Unclassified	2 (1.3%)
HCV viral load	3964457.29 ± 6376006.35
AST (U/L)	57.88 ± 59.92
ALT (U/L)	73.42 ± 120.54
Platelet (1000/μL)	201.89 ± 69.79
CKD (%)	23 (14.6%)
DM(%)	58 (36.7%)
Cirrhosis (%)	8 (5.1%)
Child pugh score A	8 (5.1%)
Child pugh score B	0 (0.0%)
Child pugh score C	0 (0.0%)

BMI, body mass index; HCV, hepatitis C virus; SVR, sustained virologic response; AST, aspartate aminotransferase; ALT, alanine aminotransferase; CKD, chronic kidney disease; DM, diabetes mellitus.
Data are presented as n or mean ± standard deviation.

Changes in PRO from the baseline to EOF

Comparisons of PRO scores between the baseline and post-treatment were demonstrated in Table 2. Improvement of aspartate aminotransferase (AST) level (−31.06 U/L), alanine aminotransferase (ALT) level (−50.48 U/L), depression (-1.94, TDQ), anxiety (-0.92, STAI), digestive symptoms (-3.02, GSRS), and SF-36 items of physical role functioning, bodily pain, vitality, social role functioning, emotional role functioning and mental health were noted among patients who had SVR after DAA therapy However, anxiety, or SF-36 items of physical functioning as well as general health perceptions were not significantly changed after the treatment.

Multivariable models for changes of HRQoL from the baseline to post-treatment

Regarding the baseline conditions, multivariate analysis didn't find any clinical or demographic characteristics that was associated with improvements in HRQoL except that baseline depression level was positively correlated with

Table 2 Comparisons of PRO scores between the baseline and post-treatment for SVR patients (n = 158).

Items	Baseline	Post-treatment	Diff.	*P*-value
AST (U/L)	57.88 ± 59.92	26.82 ± 15.11	−31.06 ± 59.43	<0.001*
ALT (U/L)	73.42 ± 120.54	22.94 ± 16.00	−50.48 ± 120.52	<0.001*
Platelet (1000/μL)	201.89 ± 69.79	1331.01 ± 13575.85	1129.13 ± 13571.92	0.316
GSRS	4.70 ± 6.57	1.68 ± 4.95	−3.02 ± 6.13	<0.001*
PSQI	9.51 ± 2.94	9.72 ± 3.23	0.20 ± 2.72	0.350
Depression	6.47 ± 6.97	4.53 ± 5.28	−1.94 ± 6.22	<0.001*
Anxiety	36.42 ± 7.68	35.50 ± 6.58	−0.92 ± 5.71	0.044*
Physical quality of life				
PF	25.85 ± 5.58	25.82 ± 5.73	−0.03 ± 4.06	0.922
RP	6.98 ± 1.67	7.28 ± 1.47	0.30 ± 1.58	0.019*
BP	10.97 ± 1.57	11.27 ± 1.28	0.30 ± 1.30	0.005*
GH	17.33 ± 3.88	17.63 ± 4.18	0.30 ± 3.31	0.251
Mental quality of life				
VT	17.97 ± 3.91	18.5 ± 3.37	0.53 ± 3.29	0.047*
SF	9.28 ± 1.28	9.49 ± 0.94	0.21 ± 1.33	0.049*
RE	5.69 ± 0.87	5.84 ± 0.61	0.15 ± 0.89	0.041*
MH	23.98 ± 4.06	24.75 ± 3.40	0.77 ± 3.14	0.002*

PRO, patient-reported outcome; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PSQI, Pittsburgh Sleep Quality Index; GSRS, Gastrointestinal Symptom Rating Scale; PF, Physical Functioning; RP, Role Physical; BP, Bodily Pain; GH, General Health; VT, Vitality; SF, Social Functioning; RE, Role Emotional; MH, Mental Health.
Data are presented as n or mean ± standard deviation. **P*-value<0.05 was considered statistically significant after test.

improvements in SF-36 items of mental quality of life in both models (β = 0.23, model 1; β = 0.23, model 2) (Table 3).

Regarding alteration of conditions, multivariate analysis revealed that improvement of sleep quality (β = 0.61, model 1; β = 0.60, model 2), depression (β = −0.20, model 1; β = −0.20, model 2), and anxiety (β = −0.23, model 1; β = −0.23, model 2)were associated with improvement of physical quality of life in both models; improvement of depression (β = −0.41, model 1; β = −0.38, model 2) and anxiety (β = −0.25, model 1; β = −0.26, model 2)were associated with improvement of mental quality of life in both models. However, age, gender, changes of AST, ALT, platelet count, or digestive symptoms was not associated with improvements in either physical or mental quality of life (Table 4).

Discussion

This study investigated the impact of DAA therapy on HRQoL and other clinical characteristics in patients with chronic HCV infection. The clinical factors leading to the change in HRQoL were also determined. This work was accomplished by prospectively analyzing HRQoL, and psychological distress before and EOF in the in a clinical setting. The study demonstrated that SVR to HCV therapy by DAA provided the significant improvement of hepatis, psychological distress and HRQoL. Further multivariable analysis revealed that the significant improvement of HRQoL was in parallel with the improvement of psychological distress.

HRQoL is a critical segment in the assessment of any helpful mediation. It might be arguably more important than length of life, since patients are habitually more worried about quality and inability than about life span.[32] A few examinations have effectively explored the adjustments of HRQoL after HCV eradication with the new IFN-free regimen.[24,25,33–35] Specifically, the study by Ng et al. showed that HCV treatment with elbasvir/grazoprevir brought about a critical improvement of PROs as compared with the regimen using sofosbuvir/Peg-IFN/ribavirin.[34] Another study from Brazil assessed the adjustments of HRQoL evaluated with SF-36 in a cohort of 56 HCV patients treated with various DAAs regimens and they tracked down a better HRQoL after HCV eradication.[35] Furthermore, Nardelli et al. included 39 patients with chronic HCV infection, in which all patients achieved SVR and achieved improvement in neuropsychological symptoms and all domains of HRQoL, except for role limitation physical and bodily pain.[24] More recently, a large US multicenter observational study revealed that 1346 patients who were cured of hepatitis C experienced improvements in fatigue, sleep disturbance, and functional well-being, and trends for improved pain and depression.[25] We conducted a multicenter cohort of 158 patients with chronic HCV infection with similar results that successful DAA therapy improved patient's depression, digestive symptoms, and all domains of HRQoL except for physical functioning and general health. According to the current evidence, DAA treatment that cures HCV infection also improves patient's HRQoL.

Currently, the mechanisms underlying for HRQoL improvement after DAA therapy have not fully determined. Study from Nardelli et al. demonstrated that neuropsychological symptoms strongly influenced HRQoL in 39 HCV patients with SVR. This study further indicated that neuropsychological symptoms strongly influenced HRQoL in HCV patients.[24] In our cohort, multivariate analysis demonstrated that improvement of physical quality of life was associated with improvement of sleep quality,

Table 3 Factors associated with change of SF-36 questionnaire score for SVR patients (n = 158).

Items	Physical quality of life						Mental quality of life					
	Crude		Model 1		Model 2		Crude		Model 1		Model 2	
	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value	β (95% CI)	*P*-value
Age	0.05 (-0.04, 0.14)	0.266	0.07 (-0.04, 0.18)	0.232	0.06 (-0.03, 0.15)	0.216	−0.03 (-0.12, 0.06)	0.539	0.01 (-0.10, 0.12)	0.860	0.01 (-0.09, 0.10)	0.895
Sex (M to F)	0.47 (-1.62, 2.57)	0.656	1.66 (-0.76, 4.08)	0.176	1.18 (-0.91, 3.27)	0.265	0.41 (-1.68, 2.50)	0.699	1.12 (-1.26, 3.50)	0.352	0.82 (-1.24, 2.88)	0.435
Medication												
sofosbuvir/ velpatasvir	1.04 (-1.84, 3.92)	0.478	0.29 (-3.16, 3.75)	0.867	1.14 (-1.71, 3.98)	0.432	0.24 (-2.72, 3.21)	0.871	−0.01 (-3.41, 3.39)	0.996		
elbasvir/ grazoprevir	0.59 (-2.89, 4.07)	0.737	−0.42 (-4.57, 3.73)	0.842	0.15 (-3.28, 3.58)	0.932	−0.15 (-3.73, 3.43)	0.935	0.58 (-3.50, 4.66)	0.779		
glecaprevir/ pibrentasvir	Ref.		Ref.		Ref.		Ref.		Ref.			
sofosbuvir/ ledipasvir	−3.45 (-6.81, −0.08)	0.045*	−3.92 (-7.85, 0.01)	0.050	−3.18 (-6.49, 0.14)	0.060	−0.14 (-3.60, 3.32)	0.936	−0.65 (-4.52, 3.21)	0.739		
Cirrhosis (Y to N)	0.40 (-4.37, 5.17)	0.868	−0.30 (-5.26, 4.67)	0.907			2.21 (-2.52, 6.94)	0.358	2.38 (-2.50, 7.26)	0.337		
CKD (Y to N)	−0.71 (-3.67, 2.25)	0.637	−2.63 (-6.32, 1.05)	0.160			0.97 (-1.98, 3.91)	0.517	0.85 (-2.77, 4.48)	0.643		
DM (Y to N)	0.29 (-1.88, 2.46)	0.791	0.00 (-2.50, 2.51)	0.997			0.41 (-1.74, 2.57)	0.705	−0.42 (-2.89, 2.04)	0.734		
Baseline AST	−0.01 (-0.03, 0.004)	0.116	0.01 (-0.04, 0.06)	0.656			0.00 (-0.02, 0.02)	0.973	−0.02 (-0.06, 0.03)	0.392		
Baseline ALT	−0.01 (-0.02, 0.00)	0.041*	−0.01 (-0.03, 0.01)	0.341	−0.01 (-0.01, 0.00)	0.167	0.00 (-0.01, 0.01)	0.635	0.01 (-0.01, 0.04)	0.233		
Baseline Platelet	0.00 (-0.02, 0.02)	0.942	0.00 (-0.02, 0.01)	0.632			−0.01 (-0.02, 0.01)	0.489	−0.01 (-0.03, 0.01)	0.425		
Baseline GSRS	0.12 (-0.04, 0.28)	0.133	0.03 (-0.15, 0.22)	0.730			0.03 (-0.13, 0.19)	0.692	−0.08 (-0.27, 0.10)	0.382		
Baseline PSQI	−0.05 (-0.41, 0.31)	0.790	−0.07 (-0.53, 0.38)	0.753			0.33 (-0.02, 0.69)	0.062	0.22 (-0.23, 0.67)	0.331	0.10 (-0.28, 0.48)	0.603
Baseline Depression	0.10 (-0.05, 0.25)	0.211	−0.02 (-0.23, 0.19)	0.845			0.30 (0.16, 0.44)	<0.001*	0.23 (0.03, 0.44)	0.027*	0.22 (0.03, 0.41)	0.025*
Baseline Anxiety	0.16 (0.03, 0.30)	0.017*	0.19 (0.00, 0.38)	0.050	0.16 (0.02, 0.29)	0.022*	0.23 (0.10, 0.36)	0.001*	0.12 (-0.07, 0.30)	0.211	0.11 (-0.06, 0.27)	0.210

SF-36, Short-Form-36; SVR, sustained virologic response; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PSQI, Pittsburgh Sleep Quality Index; GSRS, Gastrointestinal Symptom Rating Scale; CKD, chronic kidney disease; DM, diabetes mellitus.

Dependent variable: change of SF-36 questionnaire score. Model 1: adjusted for all covariates listed above; Model 2: only adjusted for age, sex, and covariates with $P < 0.10$ in crude analysis. *P-value<0.05 was considered statistically significant after test.

Table 4 Factors associated with change of SF-36 questionnaire score for SVR patients (n = 158).

Items	Physical quality of life						Mental quality of life					
	Crude		Model 1		Model 2		Crude		Model 1		Model 2	
	β(95% CI)	*P*−value	β(95% CI)	*P*−value	β(95% CI)	*P*−value	β(95% CI)	*P*−value	β(95% CI)	*P*−value	β(95% CI)	*P*−value
Age	0.05 (−0.04, 0.14)	0.266	0.06 (−0.04, 0.16)	0.229	0.05 (−0.04, 0.14)	0.277	−0.03 (−0.12, 0.06)	0.539	0.02 (−0.08, 0.11)	0.691	−0.01 (−0.09, 0.07)	0.878
Sex (M to F)	0.47 (−1.62, 2.57)	0.656	1.47 (−0.80, 3.74)	0.202	1.14 (−0.90, 3.18)	0.273	0.41 (−1.68, 2.50)	0.699	0.77 (−1.41, 2.95)	0.485	0.69 (−1.19, 2.57)	0.472
Medication												
sofosbuvir/ velpatasvir	1.04 (−1.84, 3.92)	0.478	−0.02 (−3.22, 3.18)	0.990	0.64 (−2.09, 3.37)	0.644	0.24 (−2.72, 3.21)	0.871	−1.04 (−4.12, 2.04)	0.505		
elbasvir/ grazoprevir	0.59 (−2.89, 4.07)	0.737	−1.71 (−5.53, 2.11)	0.377	−1.06 (−4.44, 2.32)	0.536	−0.15 (−3.73, 3.43)	0.935	−1.03 (−4.70, 2.65)	0.582		
glecaprevir/ pibrentasvir	Ref.		Ref.		Ref.		Ref.		Ref.			
sofosbuvir/ ledipasvir	−3.45 (−6.81, −0.08)	0.045*	−3.54 (−7.19, 0.12)	0.058	−2.82 (−6.02, 0.39)	0.085	−0.14 (−3.60, 3.32)	0.936	−0.79 (−4.31, 2.72)	0.656		
Cirrhosis (Y to N)	0.40 (−4.37, 5.17)	0.868	−0.49 (−5.15, 4.17)	0.836			2.21 (−2.52, 6.94)	0.358	2.74 (−1.74, 7.23)	0.228		
CKD (Y to N)	−0.71 (−3.67, 2.25)	0.637	−2.18 (−5.47, 1.11)	0.192			0.97 (−1.98, 3.91)	0.517	1.38 (−1.78, 4.55)	0.388		
DM (Y to N)	0.29 (−1.88, 2.46)	0.791	−0.04 (−2.37, 2.29)	0.973			0.41 (−1.74, 2.57)	0.705	−0.81 (−3.05, 1.43)	0.476		
Change of AST	0.02 (−0.001, 0.03)	0.060	−0.03 (−0.08, 0.01)	0.182	−0.03 (−0.07, 0.01)	0.168	0.00 (−0.02, 0.02)	0.963	0.00 (−0.04, 0.04)	0.949		
Change of ALT	0.01 (0.001, 0.02)	0.023*	0.02 (0.00, 0.04)	0.054	0.02 (0.00, 0.04)	0.046*	0.00 (−0.01, 0.01)	0.745	0.00 (−0.02, 0.02)	0.791		
Change of Platelet	0.00 (0.00, 0.00)	0.743	0.00 (0.00, 0.00)	0.571			0.00 (0.00, 0.00)	0.355	0.00 (0.00, 0.00)	0.210		
Change of GSRS	−0.19 (−0.36, −0.02)	0.027*	−0.10 (−0.28, 0.08)	0.265	−0.10 (−0.26, 0.07)	0.256	−0.10 (−0.27, 0.07)	0.244	0.00 (−0.17, 0.17)	0.961		
Change of PSQI	0.45 (0.07, 0.83)	0.021*	0.61 (0.20, 1.02)	0.004*	0.60 (0.22, 0.98)	0.002*	−0.25 (−0.63, 0.13)	0.196	0.04 (−0.36, 0.43)	0.850		
Change of Depression	−0.24 (−0.41, −0.08)	0.004*	−0.20 (−0.39, −0.001)	0.049*	−0.20 (−0.38, −0.01)	0.035*	−0.50 (−0.65, −0.35)	<0.001*	−0.41 (−0.59, −0.22)	<0.001*	−0.38 (−0.55, −0.21)	<0.001*
Change of Anxiety	−0.26 (−0.44, −0.08)	0.004*	−0.23 (−0.44, −0.02)	0.032*	−0.23 (−0.43, −0.03)	0.026*	−0.46 (−0.63, −0.30)	<0.001*	−0.25 (−0.45, −0.05)	0.017*	−0.26 (−0.45, −0.08)	0.006*

SF−36, Short−Form−36; SVR, sustained virologic response; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PSQI, Pittsburgh Sleep Quality Index.
Dependent variable: changes of SF-36 questionnaire score; GSRS, Gastrointestinal Symptom Rating Scale; CKD, chronic kidney disease; DM, diabetes mellitus. Model 1: adjusted for all covariates listed above; Model 2: only adjusted for age, sex, and covariates with $P < 0.10$ in crude analysis. *P-value<0.05 was considered statistically significant after test.

depression, and anxiety; whereas improvement of mental quality of life was associated with improvement of depression and anxiety. Our findings suggest that both SVR to HCV therapy and decrease psychological burden may contribute to improvement HRQoL in HCV patients. It implicates that monitoring and management of psychological distress during DAA treatment may benefit HCV patients for better HRQoL.

There were some limitations in this study. Firstly, the assessment might not reflect the long-term outcomes following HCV clearance. In addition, there was no control group of general population included in this study for comparison. The difference between CHC and normal population in the aspects of HRQoL and/or PRO deserves further exploration.

In conclusion, our multi-center prospective real-world cohort study provided the evidence that SVR to HCV therapy by DAA significantly improved HRQoL and psychological distress. The improvement, in addition to the amelioration of liver-related events, awaits further investigation in a long-term.

Funding

This study was supported by a grant, TCRD109-74, from Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Hualien, Taiwan.

Declaration of competing interest

The authors declare that they have no competing interests.

Author contributions

CHY, MJB and CLC contributed to study concept and design, analysis and interpretation of data, drafting of the manuscript. JHW, MWW, TTL and WYL contributed to statistical analysis. SWL, LL, JSH, JFH and YCH contributed to the acquisition of data and research performance. We also thank Chung-Feng Huang for giving suggestions of the manuscript. All authors have approved the final version of the manuscript.

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