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Association of exercise participation levels with cardiometabolic health and quality of life in individuals with hepatitis C

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ABSTRACT

Objective Hepatitis C virus (HCV) infection is associated with an increased risk of cardiovascular disease (CVD) and reduced health-related quality of life (HRQoL). Although physical activity (PA)/exercise has been shown to reduce CVD risk and improve HRQoL in patients with liver disease, there is limited data in HCV. We aimed to explore the association between PA/exercise levels, CVD risk and HRQoL in patients with HCV and assess individuals' attitudes to PA/exercise.

Design Cross-sectional observational study recruiting consecutive patients with HCV from viral hepatitis clinics. Data were collected on CVD risk factors, anthropometry, HRQoL and the Exercise Benefits and Barriers Scale (EBBS).

Results 86 patients were recruited (71% men, 94% white, age 52±13 years); 49% of the cohort self-reported to be currently active. Although HRQoL was reduced across the cohort, patients that were regularly 'active' reported significantly higher HRQoL scores across Short-Form 36v2 domains compared with their inactive counterparts ($p<0.05$). Metabolic and cardiovascular characteristics were no different between groups stratified by PA/exercise status ($p>0.05$). EBBS scores were similar in the 'active' versus 'inactive' groups, however, patients categorised as 'active' scored significantly higher on the psychological outlook and social interaction subscales ($p<0.05$) than those that were 'inactive'. There were significant associations between EBBS scores and HRQoL ($p<0.05$).

Conclusions PA/exercise is associated with increased HRQoL in patients with HCV irrespective of clinical parameters. Addressing specific motivators/barriers to exercise for patients will be key to designing effective PA/exercise interventions in this patient population to ensure maximum uptake and adherence.

Summary box

What is already known about this subject?

- Individuals with hepatitis C virus (HCV) have an increased risk of cardiovascular disease and reduced health-related quality of life (HRQoL) compared with the general population.

What are the new findings?

- Individuals with HCV who engage in regular moderate or vigorous physical activity (PA) have significantly better HRQoL compared with inactive individuals.
- Active individuals have higher scores for psychological outlook and social interaction subscales of the Exercise Benefits and Barriers Scale.
- There were significant associations between attitude to exercise and HRQoL in individuals with HCV.

How might it impact on clinical practice in the foreseeable future?

- Exercise/PA could be an important tool for improving HRQoL in patients with HCV.
- Addressing specific motivators and barriers to exercise will be key in designing effective exercise interventions in this population to maximise uptake and adherence.

INTRODUCTION

Hepatitis C virus (HCV) infection is a major cause of chronic liver disease affecting an estimated 71 million people worldwide.[1] The disease causes numerous extrahepatic manifestations resulting in a high burden of comorbidity, including increased risk of cardiovascular disease (CVD)[2–7] and neuropsychiatric disorders and depression[8–10] even after successful antiviral treatment. Health-related quality of life (HRQoL) is also significantly reduced compared with non-HCV infected individuals.[11 12]

Recently, we developed a holistic care bundle to identify and target modifiable clinical parameters and health behaviours in individuals with HCV in order to improve overall health status and clinical prognosis.[7] A central component of this work was the assessment of exercise participation levels, which showed that fewer individuals with HCV meet current physical activity (PA) recommendations than the general population.[13] We also showed

that sedentary behaviour was associated with reduced HRQoL.

Although others have previously shown PA/exercise to improve HRQoL in patients with liver disease,[14–16] few studies have assessed the strength of this association in patients with HCV, or explored individual's attitudes to PA/exercise. This information is fundamental for developing effective strategies for engaging individuals with HCV identified as sedentary in lifestyle improvement programmes. Therefore, we aimed to explore the association between sedentary behaviour and HRQoL and assess individuals' attitudes to PA/exercise using the Exercise Benefits and Barriers Scale (EBBS). Our specific aims were to: (1) determine whether individuals with HCV who engage in regular PA/exercise have fewer cardiometabolic risk factors than sedentary individuals; (2) define the perceived benefits and barriers to PA/exercise in this cohort; (3) determine whether there is a relationship between attitudes to PA/exercise and HRQoL in this cohort.

METHODS

Study design

This cross-sectional, observational study recruited consecutive patients with HCV (treated or untreated) attending the viral hepatitis clinics at The Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK. This was a substudy of the previously reported ENHANCE study[7] and included 86 patients (out of 100) who had complete EBBS data. Unfortunately, 14 of the patients did not complete the EBBS survey or did not complete is fully so were excluded from the analysis. Their clinical and demographic data was similar to the main cohort.

Patients

Individuals aged 18 years or older were included if they had chronic HCV infection (defined as HCV RNA detectable in blood for >6 months) or had achieved sustained virological response (SVR=cure of infection) 3 months after antiviral treatment. Exclusions were: currently on antiviral treatment for HCV or within 3 months post-treatment; coinfection with hepatitis B or HIV; history of hepatocellular carcinoma; liver transplantation; decompensated cirrhosis (Child-Pugh Score ≥7); or were unable to give informed consent.

Clinical and laboratory data

All clinical and laboratory data were collected at the time of enrolment including age, gender, ethnicity, weight, waist circumference, waist to hip ratio and body mass index. Body composition was measured using 8-point Bioelectrical Impendence Analysis (SECA BIA mBCA 525 Machine, SECA, UK). Blood tests were taken including: full blood count, liver enzymes, HbA1c, lipids, glucose, vitamin D, thyroid stimulating hormone and HCV RNA, which were analysed in an accredited NHS clinical laboratory. A detailed medical history, including a list of current prescribed medications, was recorded and cross-referenced with information from primary care. Details about each individual's history of HCV infection was also collected including: suspected route of infection, previous antiviral treatment and outcomes, and current status (active HCV viraemia or SVR). Stage of liver fibrosis was assessed using transient elastography and cirrhosis was defined as a liver stiffness measurement >12.5 kPa, liver biopsy demonstrating cirrhosis or imaging evidence of cirrhosis with portal hypertension.

Details of any history of CVD including ischaemic heart disease, cerebrovascular disease, peripheral vascular disease or atrial fibrillation were recorded. We used the QRISK3 (www.qrisk.org) to determine an individual's estimated risk of a major cardiovascular event in the next 10 years. Smoking history was documented as never smoked, current smoker or previous smoker (for >1 year). The metabolic syndrome and its individual features were defined according to the International Diabetes Federation criteria.[17] Information on past or current history of mental health disorders was also collected. A history of 'significant' mental health disorder was defined as one where pharmacological treatment was used for its treatment.

HRQoL was determined using the Hepatitis Quality of Life Questionnaire (HQLQv2), a survey constructed to assess the functional health and well-being of patients with HCV, using the Short-Form 36v2 (SF36v2) Health Survey and 15 additional hepatitis-specific questions relevant in assessing the impact of hepatitis.[18] SF36v2 scores presented in this study were normalised to the US general population to have a mean of 50 and SD of 10.[19] Therefore, SF36v2 scores below 50 were considered reduced HRQoL in this study. Scores were normalised to US data because this is more recent than UK data, by 12 years and there has been a marked change in HRQoL over that time. US and UK populations have similar HRQoL. For the hepatitis specific scores, the Hepatitis Distress scale (HD), Positive Wellbeing (PWB), Hepatitis Specific Limitations scale (HLIM) and Hepatitis Specific Health Distress scale (HHD), scores ranged from 0 to 100 (not normalised to the US population) with higher scores indicating better HRQoL.

Details about each patients' current self-reported PA/exercise levels were recorded as sedentary, engaging in regular moderate PA/exercise (≥150 min/week of activity that leads to faster breathing, increased heart rate and feeling warmer (eg, walking 3–4 m/hour and household tasks, like mowing the lawn or vacuuming)) or regular vigorous PA/exercise (≥75 min/week of activity that leads to very hard breathing, shortness of breath, rapid heartbeat and should leave a person unable to maintain a conversation comfortably (eg, running at 6–8 m/hour or cycling 12–14 m/hour)). Patients completed the EBBS which provides a measurement of the perceived benefits and barriers to participating in PA/exercise, and has been demonstrated to be a valid tool in a range of clinical cohorts in adults with chronic diseases.[20] The

EBBS contains 43 statements pertaining to 'ideas about exercise' and is scored on a Likert-scale with responses ranging from 4 (strongly agree) to 1 (strongly disagree). Twenty-nine statements relate to perceived benefits of exercise and 14 relate to perceived barriers. Scores for the total instrument range from 43 to 172 with higher scores representing a more positive attitude towards PA/exercise.

A measure of socioeconomic status/deprivation was assessed by mapping the home postcode for each patient onto the English Indices of Deprivation using the Index of Multiple Deprivation (IMD).[21] The lower layer super output area (LSOA) was calculated for each individual patient postcode. The LSOA with a rank of 1 is the most deprived and the LSOA with a rank of 32 844 is the least deprived. Deciles for the IMD are calculated by ranking the 32 844 LSOAS in England into 10 equal groups (1 being the most deprived area decile and 10 the least deprived).

Statistical analysis

Descriptive information for each variable was derived and the distribution assessed to determine normality. Metric and normally distributed variables are reported as mean±SD, non-normally distributed variables are reported as median and IQR, and categorical variables are reported as frequency (percentage) unless otherwise stated. The cohort was stratified according to activity level ('inactive' vs engaging in moderate or vigorous PA/exercise (termed 'active')), with differences between dichotomised variables assessed using independent t-tests, Mann-Whitney U tests or Fisher's exact tests. Differences between EBBS scores were assessed using a general linear model with multiple comparisons adjusted using Bonferroni correction. Multiple linear regression models were used to investigate the associations between clinical characteristics and EBBS scores. Models were fit to estimate associations with sequential adjustment for age, gender and participation in exercise. Data analysis was performed with SPSS (IBM SPSS Statistics V.25, IBM Corp) with statistical significance inferred at a two-tailed $p<0.05$; 95% CIs and β coefficients are presented where relevant.

RESULTS

Baseline clinical characteristics

A total of 86 patients (42 active and 44 inactive) were included in the analysis. The clinical characteristics of all patients are presented in tables 1 and 2. The gender, ethnicity and socioeconomic status distributions were similar between active and inactive patients (table 1; $p>0.05$). Metabolic and cardiovascular characteristics, as well as blood biochemistry, were also similar between patient groups stratified by PA/exercise status (table 2). The prevalence of a psychological comorbidity was high

Table 1 Patients demographic and anthropometric characteristics

		Exercise status		
	All patients	Inactive	Active	P value
Demographic characteristics				
n	86	44	42	–
Age (years)	52±13	51±14	53±11	0.432*
Male (%)	71	68	71	0.639†
White (%)	94	93	95	0.998 †
IMDR	10 239±8869	9429±8256	11 087±9495	0.391*
IMDD	3 (4)	3 (4)	3 (5)	0.789†
Current or previous IDU (%)	70	68	53	0.025†
Current or previous heavy alcohol intake (%)	44	42	46	0.687†
Anthropometry				
Weight (kg)	82.56±19.73	84.42±21.34	80.65±17.99	0.381*
BMI (kg/m^2)	27.69±6.02	28.45±6.42	26.90±5.56	0.240*
Waist circumference (cm)	95.30±15.03	96.40±14.78	94.10±15.40	0.494*
Hip circumference (cm)	101.69±13.34	103.81±15.22	99.57±10.94	0.173*
Waist-to-hip ratio	0.93 (0.1)	0.92 (0.1)	0.95 (0.1)	0.483‡
Fat mass (%)	29.06±10.20	28.39±11.85	29.73±8.40	0.634*

Metric and normally distributed variables are reported as mean±SD; non-normally distributed variables are reported as median and IQR, and categorical variables are reported as frequency (percentage).
*independent t-test.
†Fisher's exact test.
‡Mann-Whitney U test.
BMI, body mass index; IDU, injecting drug use; IMDD, Index of Multiple Deprivation Decile; IMDR, Index of Multiple Deprivation Rank.

Table 2 Metabolic and cardiovascular characteristics, and blood biochemistry

	All patients	Exercise status		
		Inactive	Active	P value
Metabolic and cardiovascular characteristics				
Cirrhosis (%)	35	39	30	0.602*
Sustained virological response (%)	72	71	71	0.998*
SBP (mm Hg)	134±19	130±21	137±17	0.104†
DBP (mm Hg)	83 (13)	78 (11)	86 (15)	0.496‡
Hypertensive (%)	62	55	66	0.180*
Metabolic syndrome (%)	27	30	25	0.620*
Metabolic syndrome features	2 (2)	2 (2)	2 (2)	0.359*
Dyslipidaemia (%)	17	16	18	0.376*
Diabetes (%)	15	16	14	1.000*
CVD (%)	9	11	7	0.713*
CKD (%)	2	5	0	0.494*
Depression (%)	50	57	41	0.281*
Smoking (%)	48	55	39	0.226*
QRISK3	11.69±11.32	11.57±12.62	11.82±9.97	0.922†
Biological age (years)	60±13	59±14	62±12	0.255†
Blood biochemistry				
Platelets (10^9/L)	229.68±94.48	225.07±87.08	234.40±102.35	0.652†
White cell count (10^9/L)	7.55±2.41	7.63±2.81	7.48±1.94	0.771†
Albumin (g/L)	45.92±3.23	44.93±3.01	46.95±3.15	0.004†§
Bilirubin (µmol/L)	7.50 (6.25)	7.00 (7.00)	8.00 (6.00)	0.388‡
ALP (µL/L)	82.26±27.11	86.77±31.11	77.54±21.55	0.119†
ALT (U/L)	28.00 (28.25)	28.00 (33.00)	28.00 (19.00)	0.417‡
GGT (U/L)	40.00 (61.00)	45.00 (100.00)	33.00 (53.00)	0.619‡
AST (U/L)	27.00 (19.75)	26.50 (27.00)	27.50 (17.35)	0.588‡
HbA1c (mmol/mol)	38.00 (6.00)	38.50 (6.00)	38.00 (5.50)	0.493‡
Vitamin D (nmol/L)	45.00 (42.50)	37.00 (32.50)	53.00 (36.50)	0.580‡
Total cholesterol (mmol/L)	4.42±1.12	4.19±1.18	4.65±1.01	0.549†
Triglycerides (mmol/L)	1.40 (0.95)	1.69 (1.17)	1.30 (1.00)	0.611‡
HDL (mmol/L)	1.40 (0.50)	1.40 (0.53)	1.30 (0.55)	0.837‡
Cholesterol/HDL ratio (mmol/L)	3.20 (1.49)	2.95 (1.25)	3.50 (1.41)	0.604‡
LDL (mmol/L)	3.07±1.08	2.85±1.13	3.30±1.00	0.062†
TSH (mU/L)	1.74 (1.16)	1.75 (1.19)	1.74 (0.41)	0.410‡

**Between group difference at p<0.01; ***between group difference at p<0.001.
Metric and normally distributed variables are reported as mean±SD; non-normally distributed variables are reported as median and IQR, and categorical variables are reported as frequency (percentage).
*Fisher's exact test.
†Independent t-test.
‡Mann-Whitney U test.
§Between group difference at p<0.05.
ALP, Alkaline Phosphatase; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; CKD, Chronic Kidney Disease; CVD, cardiovascular disease; DBP, Diastolic Blood Pressure; GGT, Gamma Glutamyl Transferase; HDL, High Density Lipoprotein; LDL, Low Density Lipoprotein; SBP, Systolic Blood Pressure; TSH, thyroid stimulating hormone.

in both groups and greatest in those characterised as inactive (inactive: 57% vs active 41%, p=0.031).

Self-reported exercise participation and EBBS scores

Self-reported exercise participation and EBBS scores are presented in table 3. From our sample of 86 patients, 49% (n=42) of the cohort self-reported to be currently active, of which 14% (n=12) self-reported regular participation in vigorous PA/exercise. Of those patients classified with cirrhosis (n=30, (35%)), 43% (n=13) were physically active, compared with 52% (n=29) of those classified as non-cirrhotic. Of those patients with active viraemia (28%, (n=24)), 50% were classified as physically active;

Table 3 Self-report Exercise Benefit and Barrier Scale (EBBS) scores

	All patients	Exercise status		
		Inactive	Active	P value
Total EBBS score	122.69±16.46	117.66±15.91	127.95±15.52	0.416*
Combined benefit items score	83.24±13.67	79.61±14.96	87.05±11.13	0.189*
Combined barrier items score	39.44±6.34	38.05±6.06	40.90±6.37	0.744*
Perceived benefit items				
Life enhancement subscale				
25: My disposition is improved by exercise	2.85±0.66	2.77±0.77	2.93±0.51	0.253*
26: Exercising helps me sleep better at night	2.85±0.69	2.75±0.78	2.95±0.58	0.110*
29: Exercise helps me decrease fatigue	2.62±0.72	2.50±0.79	2.74±0.63	0.290*
32: Exercise improves my self-concept	2.92±0.65	2.77±0.68	3.07±0.60	0.175*
34: Exercising increases my mental alertness	2.90±0.69	2.77±0.74	2.02±0.60	0.302*
35: Exercise allows me to carry out normal activities without becoming tired	2.81±0.64	2.73±0.62	2.90±0.66	0.649*
36: Exercise improves the quality of my work	2.71±0.63	2.64±0.69	2.79±0.56	0.137*
41: Exercise improves overall body function	2.93±0.66	2.86±0.70	3.00±0.62	0.315*
Standardised subscale score	2.82±0.51	2.72±0.55	2.93±0.44	0.653*
Physical performance subscale				
7: Exercise increases my muscle strength	3.08±0.72	2.98±0.73	3.19±0.71	0.262*
15: Exercises increases my level of physical fitness	3.12±0.71	3.05±0.71	3.19±0.71	0.696*
17: My muscle tone is improved with exercise	3.06±0.64	2.89±0.69	3.24±0.53	0.035* †
18: Exercising improves functioning of my cardiovascular system	3.06±0.62	2.86±0.67	3.26±0.50	0.020* †
22: Exercise increases my stamina	3.14±0.65	3.02±0.73	3.26±0.54	0.330*
23: Exercise improves my flexibility	3.09±0.71	3.02±0.79	3.17±0.62	0.449*
31: My physical endurance is improved by exercise	3.03±0.66	2.91±0.68	3.17±0.62	0.214*
43: Exercise improves the way my body looks	2.99±0.68	2.93±0.76	3.05±0.58	0.452*
Standardised subscale score	3.07±0.52	2.96±0.57	3.19±0.45	0.795*
Psychological outlook subscale				
1: I enjoy exercise	2.80±0.78	2.50±0.85	3.12±0.55	0.001* ‡
2: Exercise decreases feelings of stress and tension for me	2.85±0.78	2.66±0.83	3.03±0.70	0.136*
3: Exercise improves my mental health	2.77±0.75	2.57±0.76	2.98±0.68	0.018* †
8: Exercise gives me a sense of personal accomplishment	2.90±0.85	2.73±0.90	3.07±0.78	0.257*
10: Exercising makes me feel relaxed	2.83±0.69	2.66±0.78	3.00±0.54	0.095*
20: I have improved feelings of well-being from exercise	2.93±0.73	2.80±0.79	3.07±0.64	0.283*
Standardised subscale score	2.84±0.62	2.65±0.69	3.05±0.46	0.024* †
Social interaction subscale				
11: Exercising lets me have contact with friends and persons I enjoy	2.49±0.72	2.30±0.73	2.69±0.64	0.032* †
30: Exercising is a good way for me to meet new people	2.70±0.63	2.61±0.65	2.79±0.61	0.200*
38: Exercise is good entertainment for me	2.76±0.77	2.68±0.83	2.83±0.70	0.539*
39: Exercise increases my acceptance by others	2.40±0.74	2.39±0.84	2.40±0.63	0.252*
Standardised subscale score	2.58±0.52	2.49±0.54	2.68±0.49	0.017* †
Preventive health subscale				
5: I prevent heart attacks by exercising	2.93±0.70	2.82±0.72	3.05±0.66	0.505*
13: Exercising increases my levels of physical fitness	2.91±0.57	2.77±0.60	3.05±0.49	0.148*
27: I will live longer if I exercise	2.85±0.69	2.68±0.77	3.02±0.56	0.114*
Standardised subscale score	2.90±0.52	2.76±0.55	3.04±0.44	0.339*
Perceived barrier items				

Continued

Table 3 Continued

	All patients	Exercise status		
		Inactive	Active	P value
Exercise milieu subscale				
9: Places for me to exercise are too far away	3.00±0.75	2.91±0.77	3.10±0.73	0.124*
12: I am too embarrassed to exercise	2.99±0.75	2.84±0.86	3.14±0.65	0.215*
14: It costs too much to exercise	2.98±0.74	2.91±0.83	2.05±0.62	0.411*
16: Exercise facilities do not have convenient schedules for me	2.87±0.72	2.84±0.71	2.90±0.73	0.821*
28: I think people in exercise clothes look funny	2.97±0.76	2.86±0.77	3.07±0.75	0.643*
42: There are too few places for me to exercise	2.77±0.78	2.61±0.81	2.93±0.71	0.160*
Standardised subscale score	2.93±0.52	2.83±0.50	3.03±0.53	0.319*
Time expenditure subscale				
4: Exercising takes too much of my time	2.86±0.74	2.77±0.80	2.95±0.66	0.226*
24: Exercise takes too much time from family relationships	3.15±0.62	3.09±0.60	3.21±0.65	0.253*
37: Exercise takes too much time from my family responsibilities	3.10±0.63	3.00±0.65	3.21±0.61	0.179*
Standardised subscale score	3.04±0.52	2.95±0.54	3.13±0.49	0.447*
Physical exertion subscale				
6: Exercise tires me out	2.09±0.71	1.98±0.66	2.21±0.75	0.465*
19: I am fatigued by exercise	2.35±0.75	2.30±0.82	2.40±0.66	0.371*
40: Exercise is hard work for me	2.28±0.82	2.18±0.90	2.38±0.73	0.149*
Standardised subscale score	2.24±0.61	2.15±0.64	2.33±0.56	0.248*
Family discouragement subscale				
21: My spouse (or significant other) does not encourage exercising	3.03±0.80	2.91±0.80	3.17±0.79	0.491*
33: My family members do not encourage me to exercise	3.00±0.80	2.84±0.86	3.17±0.70	0.214*
Standardised subscale score	3.02±0.69	2.88±0.67	3.17±0.69	0.059*

***Between group difference at p<0.001.
Scores for benefit subscale items are interpreted as higher values=greater benefits; barrier subscale items are interpreted as lower values=greater barriers.
Data presented mean±SD.
*Fisher's exact test.
†Between group difference at p<0.05.
‡Between group difference at p<0.01.
§Independent t-test.
¶Mann-Whitney U test.

of those patients without active viraemia (72% (n=62)), 51% were classified as physically active.

Across the whole cohort, the highest scoring exercise benefit subscale was physical performance, and the social interaction subscale was scored lowest (tables 3 and 4). Preventive health, psychological outlook and life enhancement subscales were largely comparable (tables 3 and 4). Physical performance was negatively associated with social interaction (r=−0.251; p=0.020). The highest scoring individual benefit item *was* 'exercise improves my flexibility' and the lowest was 'exercise increases my acceptance by others'. Family discouragement and time expenditure were rated similarly as the main overarching barriers to exercise (tables 3 and 4), with patients scoring 'exercise takes too much time from family relationships' as the highest individual barrier item. The lowest scoring barrier subscale was physical exertion, with patients scoring 'exercise tires me out' as the lowest individual barrier item. Overall, the perceived benefits (mean±SD: 2.87±0.47) and barriers (mean±SD: 2.82±0.45) to exercise were equally weighted (p=0.386) in a 1:1 ratio. Mean scores for all benefits and barriers were between 2 and 3, which, equated to between 'agree' and 'disagree' on the EBBS scoring scale. Stratification by PA/exercise status did not reveal statistically significant between-group differences in overall EBBS scores, however, patients categorised as active scored significantly higher on the psychological outlook and social interaction subscales (table 3). Specifically, active patients scored 'Exercise improves my mental health' and 'Exercise lets me have contact with friends and persons I enjoy' significantly greater than inactive patients (table 3).

Relationship between HRQoL and PA

HRQoL was reduced with mean scores for all SF36v2 domains below that of the general population (data shown

Table 4 Standardised perceived benefit and barrier subscale multiple comparison matrix

	1	2	3	4	5
Perceived benefit items					
1: Life enhancement	–	<0.001***	0.984	<0.001***	0.994
2: Physical performance		–	<0.001***	<0.001***	<0.001***
3: Psychological outlook			–	0.002***	0.957
4: Social interaction				–	<0.001***
5: Preventive health					–
Perceived barrier items					
1: Exercise milieu	–	0.952	<0.001***	0.957	
2: Time expenditure		–	<0.001***	0.996	
3: Physical exertion			–	<0.001***	
4: Family discouragement				–	

*Between item difference at p<0.05; **between item difference at p<0.01; ***between item difference at p<0.001; post-hoc comparisons adjusted using Bonferroni corrections.

previously[7]). However, patients categorised as active demonstrated significantly higher HRQoL scores (signifying better HRQoL) across SF36v2 domains, including: Physical Functioning (41±11 vs 48±11, p=0.031), General Health (37±11 vs 45±11, p=0.001), Vitality (39±10 vs 48±12, p<0.001), Social Functioning (35±14 vs 46±13, p=0.003), Mental Health (37±14 vs 48±11, p=0.003), Physical Component Score (41±12 vs 47±10, p=0.003), Mental Component Score (36±15 vs 46±33, p=0.003), Hepatitis Distress (42±33 vs 65±33, p=0.005), Physical Wellbeing (40±28 vs 64±23, p=0.017), for inactive versus active individuals, respectively.

Relationship between EBBS scores and HRQoL

Table 5 shows results from linear regression analyses between EBBS scores with self-report HRQoL. Significant associations were observed between total EBBS score, combined benefit item score and combined barrier item score with Physical Component Score and Mental Component Score, as well as all HCV specific components (table 5). Associations remained robust following adjustment for confounders and further adjustment for activity status (table 5). Further, significant associations were observed between Life Enhancement, Physical Performance, Psychological Outlook, Preventative Health and Exercise Milieu EBBS subscales with Physical Component Score (p<0.05), and, Preventative Health, Exercise Milieu, and Physical Exertion EBBS subscales with Mental Component Score (p<0.05); these associations remained significant following adjustment for confounders and activity status.

DISCUSSION

Our findings show that patients with a history of HCV infection (treated or untreated) who regularly undertake PA/exercise report significantly higher HRQoL scores compared with their inactive counterparts, irrespective of CVD risk and comorbidity. Collectively, these findings suggest that PA/exercise should be promoted as a potential therapeutic tool to improve HRQoL in patients with HCV, even if participation may not result in improved cardiometabolic and biochemical parameters.

The clinical picture of HCV and recovery from treatment is characterised by a highly comorbid state coupled with reduced life expectancy. We have previously shown a high prevalence of cardiometabolic risk in this cohort of patients with HCV,[7] however, the finding that increased cardiometabolic risk is ubiquitous within this patient group irrespective of PA/exercise participation was somewhat unexpected. Participation in regular PA/exercise is widely recognised to reduce cardiometabolic risks in both the general population and those with chronic disease.[22–24] Our observational data would suggest that PA/exercise participation may have little impact on cardiometabolic characteristics in HCV, although in a relatively small sample size. However, it is worth noting that within our 'active' HCV cohort, rates of statin and antihypertensive prescribing were low (14% and 32%, respectively), and smoking rates were very high (39% current smokers vs 14% in the UK general population[25]), which collectively, may have negated the potential benefits of regular PA/exercise participation on cardiometabolic parameters. It is important to note however, that we investigated the associations between clinical parameters and self-reported PA/exercise participation at a single time point, and therefore longitudinal and interventional studies are required to fully establish whether PA/exercise has a therapeutic role in modifying cardiometabolic risk in this patient group. It is widely accepted that PA/exercise is an important and effective therapy for improving the pathology and symptoms related to specific liver diseases[26–32] with studies demonstrating that moderate PA is beneficial in maintaining functional capacity, improving body composition, glucose homoeostasis, dyslipidaemia and hypertension,[33 34] as well as reducing hepatic steatosis and improving liver

Table 5 Linear regression analysis between EBBS scores with self-report hepatitis quality of life scores

	Model 1		Model 2		Model 3	
	β (95% CI)	P value	β (95% CI)	P value	β (95% CI)	P value
Total EBBS score						
PCS	0.242 (0.097 to 0.387)	0.001**	0.255 (0.113 to 0.396)	0.001**	0.213 (0.067 to 0.359)	0.005**
MCS	0.295 (0.111 to 0.480)	0.002**	0.287 (0.102 to 0.471)	0.003**	0.216 (0.029 to 0.403)	0.024*
HD	0.892 (0.468 to 1.316)	<0.001***	0.884 (0.466 to 1.303)	<0.001***	0.747 (0.321 to 1.173)	0.001**
PWB	0.633 (0.282 to 0.984)	0.001**	0.615 (0.264 to 0.967)	0.001**	0.446 (0.099 to 0.794)	0.012**
HLIM	0.783 (0.438 to 1.128)	<0.001***	0.793 (0.444 to 1.142)	<0.001***	0.737 (0.372 to 1.102)	<0.001***
HHD	0.422 (–0.006 to 0.849)	0.053	0.406 (–0.084 to 1.044)	0.094	0.358 (–0.099 to 0.806)	0.116
Combined benefit item score						
PCS	0.220 (0.041 to 0.399)	0.016*	0.222 (0.047 to 0.398)	0.013*	0.171 (–0.007 to 0.348)	0.059
MCS	0.233 (0.004 to 0.463)	0.046*	0.232 (0.004 to 0.460)	0.046*	0.147 (–0.079 to 0.374)	0.200
HD	0.762 (0.231 to 1.294)	0.005**	0.458 (–0.110 to 1.026)	0.112	0.605 (0.083 to 1.127)	0.024*
PWB	0.635 (0.202 to 1.067)	0.005**	0.629 (0.198 to 1.060)	0.111	0.429 (0.009 to 0.849)	0.046*
HLIM	0.811 (0.383 to 1.239)	<0.001***	0.813 (0.380 to 1.246)	<0.001***	0.735 (0.286 to 1.183)	0.002**
HHD	0.234 (–0.303 to 0.771)	0.338	0.253 (–0.281 to 0.787)	0.349	0.172 (–0.374 to 0.732)	0.521
Combined barrier item score						
PCS	0.601 (0.223 to 0.979)	0.002**	0.678 (0.310 to 1.045)	<0.001***	0.594 (0.226 to 0.961)	0.002**
MCS	0.898 (0.429 to 1.366)	<0.001***	0.853 (0.379 to 1.326)	0.001**	0.721 (0.254 to 1.187)	0.003**
HD	2.363 (1.276 to 3.448)	<0.001***	2.274 (1.188 to 3.360)	<0.001***	1.998 (0.929 to 3.068)	<0.001***
PWB	1.423 (0.452 to 2.394)	0.005**	1.331 (0.345 to 2.317)	0.009**	1.017 (0.087 to 1.948)	0.033*
HLIM	1.631 (0.653 to 2.608)	0.001**	1.703 (0.706 to 2.700)	0.001**	1.554 (0.551 to 2.556)	0.003**
HHD	1.772 (0.716 to 2.829)	0.001**	1.641 (0.562 to 2.721)	0.003**	1.562 (0.446 to 2.678)	0.007**

Models were fit to estimate associations with sequential adjustment for age and gender (model 2), and exercise status (model 3).
*Significant association at p<0.05; **significant association at p<0.01; ***significance association at p<0.001.
HD, Hepatitis Distress; HHD, Hepatitis-specific Health Distress; HLIM, Hepatitis-specific Limitations; MCS, Mental Health Component; PCS, Physical Health Component; PWB, Positive Wellbeing.

function.[35 36] Although such benefits are often assumed to apply to individuals with HCV, there is little available empirical evidence to support this. In addition, although it was beyond the scope of the present analysis, it would be of interest to assess the mediating impact of viraemic status as well as other prevalent clinical characteristics on PA levels given that recent data demonstrates that HCV increases fatigue[37] and that fatigue is improved following SVR.[38]

Our data support previous research highlighting patients with HCV have a significantly reduced HRQoL.[7 11 12] The present study extends this work, showing that patients with HCV who are regularly active report significantly higher HRQoL, across SF36v2 domains, compared with inactive counterparts. The main motivator for exercising was to improve physical performance, with those that exercised regularly indicating that improving muscle tone, stamina and cardiovascular fitness as being most important. This supports a rationale for practitioners to encourage patients with HCV to undertake regular PA/exercise as a way to improve HRQoL beyond simply targeting liver health. Furthermore, we show that individuals with HCV who were active report higher scores on the EBBS indicating a more positive perception towards PA/exercise, with psychological outlook and social interaction scoring significantly higher in those active compared with non-active HCV individuals. This is important given that a significant proportion of patients with HCV present with mental health disorders and would suggest that PA/exercise participation may be an effective tool to specifically address this within this cohort.

Overall, patients with HCV placed equal weighting on the perceived benefits and barriers to exercise. It is therefore important to acknowledge that this 'equipoise' may be unlikely to lead to behaviour change within the setting of current clinical practice, which focuses on simply promoting PA/exercise. It is therefore important for healthcare professionals (HCPs) to communicate to patients that the benefits of PA/exercise, extend beyond liver-health. Indeed, linking exercise participation to tangible improvements in HRQoL may be perceived as more important for patients with HCV than linking exercise participation to routine clinical biomarkers. Given that the benefits of PA/exercise need to be perceived as of high enough importance for patients to want to overcome the barriers of changing PA/exercise behaviours, HCPs also need to assess barriers in this population to enable the development of successful lifestyle interventions.

The greatest barriers to exercise were time, with patients in both groups indicating that taking time away from family for PA/exercise was prohibitive, and that family members discouraged PA/exercise. Both of these barriers need to be addressed to design a successful PA/exercise intervention for this patient population and thus future research should seek to establish the attitudes of family members early in the design stage. In the present study, other commonly perceived barriers such as cost and accessibility to PA/exercise were perceived no differently in those that did and did not exercise regularly. Although this is somewhat of a surprising finding, it is likely attributable to a lack of difference in socioeconomic status between the two groups with patients in this study.

Study limitations

The main limitations to the study are firstly the use of self-reporting to ascertain PA levels at a single time point, which lacks the precision of objective methods and may result in over-reporting or under-reporting of PA/exercise duration and intensity and may also not reflect historic activity levels. Future studies should seek to employ objective measures of PA (such as accelerometry) to provide a detailed description of 24-hour activity levels (including intensity) over a 7-day period. Second, the EBBS asks patients to 'score' their attitudes towards exercise on a scale of 1–4 but does not allow patients to elaborate on their responses. A more in-depth qualitative analysis of patient (and their families/friends) perceptions of benefits and barriers to exercise participation may be warranted prior to designing a targeted intervention for patients with HCV. Third, we were unable to ascertain whether the association between PA/exercise and reduced HRQoL was 'cause' or 'effect'. Fourth, the sample size was relatively small and consisted of predominately relatively older white men who were seen in secondary care which may limit generalisability and may be a factor accounting for our findings showing no association between PA/activity and cardiometabolic risk. Further larger studies in more diverse cohorts should be undertaking to confirm or refute these findings.

In conclusion, PA/exercise could be an important tool for improving HRQoL in patients with HCV irrespective of improvements in clinical parameters. Addressing specific motivators/barriers to exercise for patients will be key to designing effective PA/exercise interventions in this patient population to ensure maximum uptake and adherence.

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