



Effect of Successful Treatment of Hepatitis C Virus Infection Recurrence With Direct-Acting Antiviral Agents on Physical Performance in Liver Transplant Recipients

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ABSTRACT

Background. Hepatitis C virus (HCV) infection deregulates function of many organs and systems, affecting patient's daily functioning. The results of treatment of HCV infection recurrence after liver transplantation have improved significantly as a result of the introduction of direct-acting antiviral agents (DAA). This study was aimed at prospective assessment of the effect of HCV elimination with DAA on physical performance of liver transplant recipients.

Methods. Eight women and 21 men, median age 61.3 (range, 20.1–71.5) years, participated in the study. Assessment of serum total bilirubin, alanine and aspartate aminotransferase, muscle strength, body composition, and 6-minute walk test (6MWT) were performed before treatment and 12 weeks after the end of the treatment period.

Results. In the 6MWT test we observed significant subjective (dyspnea: 58.3% pretreatment vs 27.6% posttreatment, $P = .018$; fatigue: 96.6% pretreatment vs 51.7% posttreatment, $P = .0001$) and objective improvement (distance: 415.4 meters pretreatment vs 505.2 meters posttreatment, $P < .0000001$). We did not observe an increase in muscle mass nor improvement in blood biochemical parameters.

Conclusion. A significant objective and subjective improvement in physical performance was seen in liver transplant recipients after successful treatment of HCV infection with DAA.

ALTHOUGH hepatitis C virus (HCV) is a hepatotropic and lymphotropic RNA virus, HCV infection is associated with a variety of extrahepatic manifestations. Some of them are general symptoms that may interfere with patients' daily activities. Fatigue is one of the most frequent symptoms and is reported by almost 80% of HCV-infected patients [1–5]. Patients' physical activity is also influenced by musculoskeletal symptoms, including musculoskeletal pain (81%–86%), morning stiffness (58%), arthralgia (54%–86%), and muscle pain (50%) [1,4]. Many authors studying HCV infection have reported low health-related quality of life (HRQL) with physical functioning dimensions being the most affected [6–9]. Similar symptoms include the major side effects of antiviral therapy based on interferon (IFN) use, causing a further decrease of HRQL during treatment [10]. Physical impairment

observed in HCV-infected subjects may also be a consequence of malnutrition and lowered muscle mass resulting from chronic disease and inflammation [11,12].

At follow-up, 24 weeks after completion of pegylated IFN-based antiviral therapy, HRQL, as measured by the 36-item Short Form (SF-36) Health Survey, revealed significant improvements in some dimensions except for the physical functioning subscale [6]. In that study the authors also found that that female gender was associated with worse HRQL

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Table 1. Patients' Demographics and Results of Physical Performance Tests

Variable	Mean (SD)	Median (IQR)	N (%)
Age (years)	–	61.3 (53.9–67.1)	–
Time after LTx (months)	–	62.7 (52.9–94.5)	–
Before antiviral therapy			
BMI (kg/m ²)	26.28 (2.87)	–	–
Grip strength right hand (kg)	40 (11.67)	–	–
Grip strength left hand (kg)	36.9 (12.01)	–	–
Dyspnoea after 6MWT (Borg scale)	–	0.5 (0.0–0.5)	17 (58.62)
Fatigue after 6MWT (Borg scale)	–	0.5 (0.0–0.5)	28 (96.55)
6MWT distance (m)	415.35 (99.06)	–	–
BMR (kcal)	1764 (291)	–	–
Fat (%)	28.99 (9.74)	–	–
FFM (kg)	59.79 (10.16)	–	–
ALT (IU/L)	–	47 (31–79)	–
AST (IU/L)	–	33 (28–57)	–
T-bil (mg/dL)	–	0.88 (0.74–1.38)	–
12 weeks after antiviral therapy			
BMI (kg/m ²)	28.92 (5.09)	–	–
Grip strength right hand (kg)	40.17 (11.0)	–	–
Grip strength left hand (kg)	36.52 (12.68)	–	–
Dyspnea after 6MWT (Borg scale)	–	0.0 (0.0–0.5)	8 (27.59)
Fatigue after 6MWT (Borg scale)	–	0.5 (0.0–0.5)	15 (51.72)
6MWT distance (m)	505.24 (107.63)	–	–
BMR (kcal)	1772 (284)	–	–
Fat (%)	28.71 (9.37)	–	–
FFM (kg)	60.15 (9.91)	–	–
ALT (IU/L)	–	19 (15–28)	–
AST (IU/L)	–	21 (17–23)	–
T-bil (mg/dL)	–	1.19 (0.76–1.68)	–

Abbreviations: 6MWT, 6-minute walk test; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BMR, basal metabolic rate; FFM, fat-free mass; IQR, interquartile range; LTx, liver transplantation; T-bil, total bilirubin.

outcomes [6]. However, there is almost general agreement that successful HCV infection therapy is associated with improved HRQL [8]. The results of treatment with HCV infection have improved significantly after 2014 as a result of the introduction of direct-acting antiviral agents (DAAs), which have replaced previously used IFN-based therapeutic regimens. DAAs have also been used successfully in liver transplant recipients with HCV infection recurrence [13–15]. The aim of the present study was objective and subjective assessment of physical performance of LTx patients before and after successful HCV therapy.

MATERIALS AND METHODS

In this open, prospective, single-center study we assessed liver transplant (LTx) recipients with a recurrence of hepatitis C virus (HCV) infection. Between July and November 2016, 29 consecutive LTx patients who qualified for use of DAA therapy agreed to participate in the study and were included. There were 8 women (27.59%) and 21 men (72.41%) with a median age of 61.3 (range, 20.1–71.5) years and at a median of 62.7 (range, 43.7–218.6) months after LTx for post-HCV liver cirrhosis.

The study analyses were performed before the start of DAA therapy and 12 weeks after its discontinuation. Blood samples were withdrawn for hemoglobin, serum creatinine, urea, iron, and albumin. Physical performance assessment included measurement of muscle strength with a hand dynamometer

(Model 5030J1; Jamar Technologies, Hatfield, PA), 6-minute walk test (6MWT) with distance measurement and Borg scale assessment of dyspnea and fatigue, and body composition analysis (BC-41 Body Composition Analyzer; Tanita Corp, Arlington Heights, IL).

All data were analyzed using Statistica version 13.1 software (Dell, Round Rock, TX). The Shapiro-Wilk test was used for normality testing. Continuous variables are reported as mean \pm SD for normally distributed data and median and range for non-normally distributed data. Normally distributed data were subjected to parametric statistical analysis, and nonparametric methods were used to test non-normally distributed variables. $P < .05$ was considered significant.

RESULTS

Patients' demographic data and results of physical performance tests are presented in Table 1. Comparison of physical performance test results before and 12 weeks after successive HCV infection therapy revealed substantial improvement in terms of dyspnea, fatigue, and 6MWT distance (Fig 1). We observed a significant increase in body mass index (BMI) values. There were no statistically significant differences regarding grip strength of right and left hands, basal metabolic rate (BMR), fat percentage, and fat-free body mass (FFM). The results are presented in Table 2. Laboratory liver function tests revealed significant decreases

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