Decreased Quality of Life is Significantly Associated with Body Composition in Patients with Nonalcoholic Fatty Liver Disease

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Abbreviations: BMI- Body Mass Index; NAFLD- nonalcoholic fatty liver disease; SF-36 - 36 Item Short Form Health Survey; QOL- the quality of life

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Abstract

Background & Aims: We studied impaired quality of life (QOL) and its determinants among individuals with nonalcoholic fatty liver disease (NAFLD).

Methods: We collected data from 341 patients with NAFLD who completed the short form 36 (SF-36) questionnaire. Body composition and liver fibrosis were assessed in patients with NAFLD using bioelectrical impedance and transient elastography, respectively. Advanced fibrosis was defined as liver stiffness measurements (LSMs) of 12.1 kPa or greater. SF-36 scores of patients with NAFLD were compared with SF36 scores of individuals with chronic medical illnesses and the general population obtained from the published literature.

Results: Among patients with NAFLD, percent body fat was negatively associated with scores from all 8 SF-36 scales, whereas lean body mass was positively associated with scores from 5 of 8 SF-36 scales. On multivariable analysis, SF-36 PF scores were negatively associated with type 2 diabetes, body mass index, and LSM and positively associated with lean body mass and level of alanine aminotransferase. Patients with NAFLD, and even those without advanced fibrosis, had significantly lower mean QOL scores than the control group or the general population.

Conclusions: Individuals with NAFLD, even those without advanced fibrosis, have lower QOL than controls. Body composition associates with QOL in patients with NAFLD; both of the modifiable factors independently associated with QOL are related to body composition. Further studies are needed to investigate if interventions to improve body composition can increase QOL for patients with NAFLD.

Keywords: BMI, overweight, obesity, steatosis

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of liver disease in the US and it is rapidly becoming one of the leading causes for liver related morbidity and mortality. [1–3] There is growing interest in better understanding the relationship between NAFLD and patient reported outcomes such as quality of life (QOL). Over the last decade, a number of studies have emerged in the literature describing reduced QOL in patients with NAFLD. [4–6] While these studies significantly advanced our understanding of QOL in NAFLD and NASH, they have largely included select subgroups of patients (e.g., biopsy proven NASH) participating in randomized clinical trials or observational studies. [4–6] These studies have utilized both the Short form 36 (SF-36) [4] and the Chronic Liver Disease Questionnaire (CLDQ). [5,6] The CLDQ was developed for measuring QOL in patients with various types of chronic liver disease and is widely utilized in various research settings. [5,7–9] However, this tool does not allow for comparisons to chronic medical conditions other than chronic liver disease or to general population. The SF-36 questionnaire, while not specifically designed for liver disease population, has long been used to estimate QOL in many different populations and it allows for comparing QOL among different populations including general population.[10–15]

When measuring QOL in patients with NAFLD, it is important to account for the impact of coexisting morbidities (e.g., obesity, diabetes, hypertension, etc) on their QOL as each of these comorbidities has been associated with reduced QOL. [12,16–24] In this regard, it is important to compare the QOL of NAFLD patients to another group of individuals without known liver disease but enriched with metabolic comorbidities. In

other disease states, it is well recognized that body composition is an important correlate for poor quality of life.[25–27] There are no studies to date examining the impact of body composition on reduced QOL in patients with NAFLD.

To further advance of our understanding of QOL in patients with NAFLD, we conducted a prospective, clinic based study of unselected patients with well characterized NAFLD to examine the relationship between (a) body composition and QOL in NAFLD and (b) QOL and NAFLD-related clinical variables, including liver stiffness and fibrosis. As an exploratory aim, we compared the QOL of this cohort of patients with NAFLD to a cohort of patients with chronic medical illnesses and to the United States general population.

Methods

Consecutive patients with NAFLD referred to Indiana University NAFLD Clinic who completed SF-36 questionnaire were included in this analysis. This study was approved by the Institutional Review Board and all participants signed an informed consent.

The presence of NAFLD was defined based on the AASLD guidelines where there was evidence of hepatic steatosis, either by imaging or histology, and lack of secondary causes of hepatic fat accumulation such as significant alcohol consumption, long-term use of a steatogenic medication, or monogenic hereditary disorders. [28] After enrollment, participants were offered to undergo body composition analysis and complete a SF-36 questionnaire in addition to clinical evaluation, which included laboratories, vibration controlled transient elastography (VCTE), and where clinically indicated, a liver biopsy.

The SF-36 is a health survey, which measures QOL of individuals equal to or greater than 18 years of age, in eight dimensions: physical functioning (PF), role limitations due to physical health (RLPF), emotional well-being (EW), role limitations due to emotional problems (RLE), energy/fatigue (EF), social functioning (SF), pain, and general health (GH). Each scale of SF-36 was transformed to a continuous scale ranging between 0 - 100, and scores were calibrated in such a way that 50 is the average. [29] SF-36 questionnaire version 1 was chosen to assess health-related QOL for this study due to select strengths of this questionnaire over disease-specific instruments. [30] First, it is used widely in the literature in many disease states with well-established interpretive methodology and normative data. Second, as one of our primary outcomes was to compare how QOL in NAFLD compares to individuals with non-liver related chronic medical illnesses, it was crucial to utilize an instrument that was validated in both general population and in those with multiple chronic medical illnesses. Lastly, in addition to its performance in the general population, metabolic syndrome, chronic medical illnesses, SF-36 performed well in the NAFLD population. [31]

The SF-36 questionnaires were scored based on their responses, as indicated in the RAND webpage. [30] The score for each scale would be the proportion of the total score that is possible. Blank items were not taken into account for the total score, and scales represent the average of all items answered by individuals. SF-36 scores from previously published cohorts with multiple chronic medical illnesses [11] and the general population in the United States [29] were used for comparative purposes. The cohort with chronic medical illnesses (N = 3445) had mean age of 54 years, 61.7% female, 76.2%

White with 52% who graduated from high school, and a minority who were poor (7.3%). The chronic medical illness burden of this population included hypertension (60.6%), diabetes (18.1%), congestive heart failure (6.3%), myocardial infarction (3.1%), clinical depression (14.6%), and symptomatic depression (22.8%). [11] *Fibroscan@ Touch 502* was used to measure liver stiffness measurement (LSM) and continued attenuation parameter (CAP) as surrogates for liver fibrosis and liver steatosis, respectively. Medium probe was used in 18% and XL probe was used in 82%. A liver biopsy was performed where clinically indicated. Among those who had a liver biopsy before enrollment in the study, histology slides were requested and reviewed by our dedicated liver pathologists. Liver histology was scored based on the NASH CRN scoring system.[28]

The body composition was measured using InBody 570 (InBody, Seoul, Korea), which utilizes bioelectrical impedance technology.[32] Dry lean mass is a measure of protein and mineral content, while lean body mass is a measure of everything in the body except fat and includes dry lean mass and total body water. Body fat mass is a measure of total body fat (subcutaneous and visceral), and percent body fat is the ratio of body fat mass to the total weight. The skeletal muscle mass is the total weight of skeletal muscle.

Statistical Analysis

Continuous variables were expressed as mean ± Standard deviation or median with ranges as appropriate. Categorical variables were expressed as percentages or proportions. Comparisons across categories are based on the Chi-square test (or Fisher's Exact test) for categorical variables, and comparisons for continuous variables

are based on ANOVA or Wilcoxon (Normal Approximation). Pearson correlation coefficient was used to analyze correlations between scales of SF-36 and patient and disease-specific variables. Univariate analysis was performed to understand the relationship between variables and SF-36 scales. Variables that were related to SF-36 scales at or below p-value of 0.05 were included in multivariable analysis. If multiple metabolic syndrome features or multiple co-linear laboratory parameters were associated at or below p-value of 0.05, one of the metabolic syndrome features or co-linear laboratory values were chosen in the multivariable model to minimize multi co-linearity. We removed variables that had excessive missingness rate. SF-36 scales and LSM were analyzed as continuous variables for univariate analysis. Additionally, LSM was also categorized into those with and without advanced fibrosis. Advanced fibrosis was defined as LSM > 12.1 kPa, which had 90% specificity for excluding stage 3 and 4 fibrosis. [33] Radar chart was designed using charts function on excel spreadsheet.

Results

Three hundred and ninety-eight individuals were enrolled in the study from July 2017 to September 2019, of whom 341 participants completed the SF-36 questionnaire. Of these, 299 (88%) had transient elastography, 112 (33 %) had a liver biopsy, and 279 (82%) had body composition analysis.

Baseline characteristics of the NAFLD cohort

Three hundred and forty-one individuals with nonalcoholic fatty liver disease (NAFLD) who completed the SF-36 questionnaire constituted our study cohort. The mean age of the cohort was 52.5 years, 96% were White, and 60% were females, 85% were obese,

48% had type 2 diabetes, and 55% had hypertension. Median LSM was 8.5 kPa (range, 2.1 KPa – 75 KPa). Detailed characteristics of the study cohort are listed in **Table 1**.

Body Composition and SF-36

Correlation coefficients between body composition parameters (body mass index (BMI), body fat mass, percent body fat, lean body mass, dry lean mass, and skeletal muscle mass) and SF-36 scales are listed in **Table 2**. Physical and mental summary component score were positively correlated with lean body, dry lean and skeletal muscle mass. Additionally, physical summary component score was negatively correlated with BMI, body fat mass and percent body fat. Individual scales of each summary score followed similar trends. Notably, percent body fat was the only variable that was significantly negatively associated with all eight scales of SF-36.

Demographic and clinical variables of NAFLD patients associated with SF-36 scores

Results from univariate and multivariable analysis of factors associated with the PF scale are shown in **Table 3**. PF scores were univariately negatively associated with age, BMI, type 2 diabetes, hypertension, LSM and, ballooned hepatocytes and fibrosis on histopathology, and positively associated with male gender, ALT, and lean body mass. On multivariable analysis, type 2 diabetes, LSM, and BMI were negatively associated with PF score, whereas ALT and lean body mass were positively associated with PF score. Univariate and multivariable analyses of the other seven SF-36 scales are shown in **Supplementary Table 1**, where we observe general trends of a positive association

of male gender and negative association of BMI and LSM with most of the SF-36 scales.

SF-36 scales in individuals with NAFLD with and without advanced fibrosis

Characteristics of individuals with NAFLD with and without advanced fibrosis are listed in Table 1. The QOL in the NAFLD cohort was significantly different between those with and without advanced fibrosis. Details of these differences are shown in **Table 4**. SF-36 scores for PF, RLPF, EW, RLE, and EF were significantly lower among those with advanced fibrosis compared to those without advanced fibrosis. When advanced fibrosis was defined based on stage 3 and 4 fibrosis on histopathology, similar trends were seen. Additionally, SF and pain scores were also significantly lower in those with advanced fibrosis. The differences in SF-36 scales based on histopathology are detailed in **Supplementary Table 2**.

QOL in the subgroup of NAFLD without advanced fibrosis

The factors associated with SF-36 PF scale in NAFLD without advanced fibrosis are shown in **Table 5**. The associations with other seven SF-36 scales are listed in **Supplementary Table 3**. On univariate analysis, male gender, lean body mass, and ALT were positively associated, while age and BMI were negatively associated with the PF scale in the subgroup without advanced fibrosis. Lean body mass, ALT continued to be positively associated, and BMI negatively associated with PF scale on multivariable analysis. As seen in the entire cohort, age and male gender no longer had significant association on multivariable analysis. Among individuals without advanced fibrosis, the LSM or fibrosis staging by histopathology were not associated with the SF-36 PF scale.

SF-36 scales in the NAFLD cohort compared to chronic medical illness cohort and the United States general population

Details of the chronic medical illness cohort are described in the methods section. **Figure 1** shows a radar chart of the eight SF-26 scales in the NAFLD cohort compared to the chronic medical illness cohort and the US general population. Mean scores of the eight scales of SF-36 in the NAFLD cohort, subgroup of NAFLD without advanced fibrosis, chronic medical illness, and the general population in the US are listed in Supplementary **Table 4.** NAFLD cohort had significantly low scores across all eight scales compared to the US general population and in six of eight scales (PFing, EF, SF, pain, and GH and RLE) compared to chronic medical illness cohort. The QOL in the subgroup of NAFLD without advanced fibrosis was significantly lower than the US general population across all SF-36 scales, except for EW and RLE and significantly lower than with chronic medical illness cohort in all SF-36 scales, except for PFing and EW.

Discussion

In this clinic-based study, we confirm that QOL in individuals with NAFLD is significantly lower among those with advanced fibrosis. A novel observation of our study is that body composition parameters are significantly associated with reduced QOL. In fact, body composition parameters are the only two modifiable factors that significantly associated with low QOL in NAFLD. Our exploratory analysis shows that QOL in a well-characterized cohort with NAFLD was not only lower than that reported for the US general population but also lower than QOL reported in chronic medical illness cohort.

Percent body fat correlated negatively with all SF-36 scales in the NAFLD cohort. Lean body mass, dry lean mass, and skeletal muscle positively correlated with PF, RLPF, EW, RLE, and SF scales. BMI and body fat mass negatively correlated with PF, RLPF, EF, pain, and GH scales. Lean body mass was significantly positively associated with PF score in the NAFLD cohort and the subgroup without advanced fibrosis, after adjusting for multiple other factors.

In our study, five of eight SF-36 scales (PF, RLPF, EW, RLE and EF) were significantly lower in NAFLD with advanced fibrosis. These findings remained consistent even when liver histology was used for defining advanced fibrosis. These results are different from a previously published study in a well-characterized NAFLD cohort, where only PF scale was found to be different between those with and without cirrhosis. [4] Our study cohort had a high proportion with advanced fibrosis, 34% based on LSM, and also based on histopathology (39% vs. 28%), and higher prevalence of comorbidities, such as type 2 diabetes (48% vs. 27%), compared to previously published study.

After adjustment for other factors, BMI, presence of type 2 diabetes, and LSM were negatively, while lean body mass and ALT were positively associated with PF score. Previously published studies in the general population reported a negative association of BMI [12,16,17,24] and age with the SF-36 PF scale. [34] In the subgroup of patients without advanced fibrosis, lean body mass and ALT were positively associated, while BMI was negatively associated with the PF score. Although the male gender was positively associated with PF score on univariate analysis in the entire cohort and the subgroup

without advanced fibrosis, the association lost significance on multivariable analysis after adjusting for age, BMI, lean body mass, presence of type 2 diabetes, ALT and LSM. Our findings highlight the important role of body composition in influencing QOL in individuals with NAFLD.

In our exploratory analysis, we observed that QOL in the NAFLD cohort was significantly lower than that reported for the US general population and chronic medical illness cohort. These differences were evident even with the subgroup of NAFLD without advanced fibrosis. This was intriguing because chronic medical conditions such as obesity and hypertension by themselves are associated with diminished QOL. SF-36 PF scores were significantly lower in severely obese, obese and overweight (63.5 ± 0.9, 74.1 ± 0.7, and 80 ± 0.5) compared to normal weight (85.9 ± 0.4) in post-menopausal women.[13] As a reference, SF-36 PF score in our NAFLD cohort was 68.3 ± 27.8. Presence of hypertension reduced QOL (SF-36 PF - 70.9 ± 27.4 vs.89.2 ± 18.6) in the Swedish population based study.[22] We admit that our control groups likely have undiagnosed NAFLD in some proportion, thus making our interpretations challenging.

Several limitations of our study deserve further discussion. While our participants were a “real-world” sample of NAFLD patients, they were enrolled at a single tertiary care center. Fibrosis in our cohort was determined based on LSM on transient elastography. While LSM has been proven to be a valid estimation of liver fibrosis, liver histology was only available in 33% of our cohort. Notwithstanding this limitation, our study is one of the first studies to evaluate the association between QOL and LSM, which is used more commonly in daily practice than a liver biopsy to determine the severity of fibrosis.

Another limitation of our study cohort was the lack of diversity, with the majority of participants being Caucasian and a small representation from other race and ethnicity groups. The clinical relevance of various statistically significant numerical differences that we observed in our study is unclear and may be addressed in a larger study including individuals with NAFLD, chronic medical illnesses and general population where the independent relationship between levels of individual domain score and overall well-being can be investiged.

Despite these limitations, our study shows that individuals with NAFLD have poorer QOL than the US general population and chronic medical illness cohort and QOL is further diminished in NAFLD with advanced fibrosis. Interestingly, even patients without advanced fibrosis had worse QOL compared to general population and those with chronic medical illnesses, suggesting that factors other than fibrosis are behind their lower QOL. We also show that in NAFLD, body composition parameters (BMI and lean body mass) are associated with QOL after adjustment for multiple factors and in fact are the only two modifiable factors of the five associated with QOL. Further studies are needed to investigate if interventions improving the body composition in patients with NAFLD would positively impact their QOL.

In summary, in this study we show that (a) patients with NAFLD have worse QOL compared to the US general population and those with chronic medical illnesses; (b) body composition parameters are significantly associated with QOL in NAFLD and in fact they are the only modifiable factors (BMI and lean body mass) associated with QOL in this population; and (c) although advanced fibrosis is an important determinant of

QOL in patients with NAFLD, interestingly even those without advanced fibrosis had worse QOL compared to general population and those with chronic medical illnesses.

Figure Legend

Figure 1: Radar chart comparing the eight SF-36 scales of NAFLD cohort with chronic medical illness cohort and the US general population. Each spoke represents a SF-36 scale (0-100).

Table 1: Baseline characteristics of NAFLD cohort and those with and without advanced fibrosis

Variables	Overall Mean ± SD (N=341)	Non-advanced Fibrosis (< 12.1KPa) Mean ± SD (N=197)	Advanced fibrosis (> 12.1 KPa) Mean ± SD (N=102)	P-value¶
Age (years)	52.54 ± 13.26	49.79 ± 13.09	55.19 ± 12.30	0.0006
Sex: Female, %	60	60.0	63	0.37
Race, % Caucasian African American American Indian/Alaskan Native Asian More than one race	 95.9 1.8 0.3 1.8 0.3	 94 3 1 2 1	 98 0 0 2 0	
Ethnicity: Hispanic, %	2.4	2	3	0.21
BMI (kg/m^2)	36.07 ± 7.21	34.62 ± 6.89	38.28 ± 7.08	<0.0001
Weight (kg)	103.96 ± 23.51	99.26 ± 20.95	110.43 ± 24.66	<0.0001
Liver Stiffness Measurement (KPa)* (median(range))#	8.5 (5.95 - 16.30)	6.4 (6.0 - 8.5)	20.8 (15.2 - 27.9)	<0.0001
Continuous Attenuation Parameter (db/m)	327.81 ± 54.51	320.57 ± 53.61	341.77 ± 53.78	0.001
Risk Factors Associated with NAFLD				
Obesity, %	85	81	91	0.03
Type 2 Diabetes mellitus, %	48	38	66	<0.0001
Dyslipidemia, %	45	43	55	0.06
Hypertension, %	55	47	69	0.0005
Obstructive Sleep Apnea, %	26	23	30	0.15
Hypothyroidism, %	13	12	15	0.53
Laboratory Data				
ALT (U/L)	46.94 ± 35.83	48.49 ± 34.57	47.93 ± 41.42	0.90
AST (U/L)	38.27 ± 23.00	35.47 ± 22.55	43.37 ± 24.56	0.01
ALP (U/L)	84.03 ± 44.81	80.33 ± 47.23	82.03 ± 30.8	0.75
Total Bilirubin (mg/dl)	0.75 ± 0.58	0.65 ± 0.37	0.79 ± 0.74	0.04
Total Protein (gm/dl)	7.40 ± 0.49	7.45 ± 0.45	7.34 ± 0.51	0.06
Albumin (gm/dl)	4.29 ± 0.45	4.43 ± 0.33	4.19 ± 0.43	<.0001
Creatinine (mg/dl)	0.87 ± 0.25	0.86 ± 0.21	0.87 ± 0.29	0.75
WBC (cells/cumm)	7.21 ± 2.88	7.41 ± 3.08	7.19 ± 2.55	0.58
Hgb (g/dl)	14.05 ± 1.40	14.24 ± 1.18	14.04 ± 1.52	0.26
PLT (cells/cumm)	234.07 ± 93.35	261.94 ± 73.70	203.01 ± 103.46	<0.0001
INR	1.16 ± 0.27	1.08 ± 0.07	1.19 ± 0.24	<0.0001
Triglyceride (mg/dl) ^	164.13 ± 84.40	167.35 ± 86.79	166.36 ± 83.46	0.94
Cholesterol (mg/dl) ^	171.52 ± 42.21	175.14 ± 42.45	166.39 ± 37.93	0.18
HDL (mg/dl) ^	42.75 ± 12.56	42.46 ± 12.73	43.72 ± 12.52	0.53
LDL (mg/dl) ^	104.49 ± 57.77	106.11 ± 53.40	102.16 ± 65.43	0.67

SF-36 scales				
Physical Component Summary Score (PCS)	40.52 ± 11.35	43.91 ± 10.21	35.92 ± 11.2	< 0.0001
Physical Functioning	68.34 ± 27.81	76.13 ± 24.96	59.74 ± 27.74	< 0.0001
Role Limitations due to Physical Health	58.06 ± 43.54	69.64 ± 41.41	43.07 ± 41.70	< 0.0001
Pain	58.32 ± 26.00	62.16 ± 26.07	53.36 ± 24.22	0.005
General Health	50.93 ± 22.46	56.10 ± 21.82	43.00 ± 20.65	< 0.0001
Mental Component Summary Score (MCS)	48.51 ± 10.66	48.40 ± 10.30	48.55 ± 10.99	0.91
Emotional Well-being	71.23 ± 19.27	71.47 ± 20.12	71.21 ± 18.55	0.91
Role Limitations due to Emotional Problems	74.26 ± 39.01	78.06 ± 37.14	69.64 ± 41.39	0.07
Energy/Fatigue	43.22 ± 22.50	45.97 ± 22.37	38.23 ± 22.35	0.005
Social Functioning	75.40 ± 27.50	78.05 ± 27.58	73.14 ± 25.82	0.13

Abbreviations: Body Mass Index (BMI); Alanine aminotransferase (ALT); Aspartate aminotransferase (AST); Alkaline Phosphatase (ALP); White Blood Cells (WBC); Hemoglobin (Hgb); Platelet (PLT); International Ionizes Ratio (INR); High Density Cholesterol (HDL): Low Density Cholesterol (LDL)

¶Comparing NAFLD patients with and without advanced fibrosis.

*****Vibration Controlled Transient Elastography data was available in 299 participants.

[#]Mean ± SD for Liver Stiffness Measurement was: Overall = 13.63 ± 13.09; Non-advanced fibrosis = 6.85 ± 2.27 and Advanced fibrosis = 24.75 ± 14.04.

^Lipid panel was available in 186 participants.

Table 2: Correlation between body composition parameters with the physical scale of SF-36 (N=274)

Variables	Physical Component Summary Score (PCS)*	Physical Function	Role Limitations due to Physical Function	Pain	General Health	Mental Component Summary Score (MCS)*	Emotional	Role Limitations due to Emotional Problems	Social Function	Energy /Fatigue
	Correlation coefficient									
Body Mass Index	-0.13833	-0.247	-0.152	-0.209	-0.237	-0.05470	-0.087	-0.09	-0.093	-0.227
p-value	0.0220	<0.0001	0.012	0.0005	<0.0001	0.3670	0.149	0.161	0.126	0.0002
Body Fat Mass	-0.13833	-0.314	-0.172	-0.264	-0.267	-0.05390	-0.082	-0.1	-0.143	-0.241
p-value	0.0220	<0.0001	0.004	<0.0001	<0.0001	0.3741	0.176	0.088	0.018	<0.0001
Percent Body Fat	-0.13833	-0.417	-0.243	-0.338	-0.311	-0.16495	-0.184	-0.22	-0.257	-0.302
p-value	0.0220	<0.0001	<0.0001	<0.0001	<0.0001	0.0062	0.002	0.0002	<0.0001	<0.0001
Lean Body Mass	0.13833	0.182	0.122	0.099	0.065	0.15897	0.149	0.18	0.189	0.078
p-value	0.0220	0.002	0.044	0.101	0.286	0.0084	0.013	0.003	0.002	0.199
Dry Lean Mass	0.13833	0.209	0.141	0.116	0.076	0.15651	0.153	0.184	0.200	0.086
p-value	0.0220	0.0005	0.019	0.056	0.21	0.0095	0.011	0.002	0.0009	0.154
Skeletal Muscle Mass	0.13833	0.212	0.145	0.114	0.081	0.15647	0.152	0.185	0.203	0.087
p-value	0.0220	0.0004	0.016	0.060	0.182	0.0095	0.012	0.002	0.0007	0.149

*****PCS is a summary measure of physical function, role limitations due to physical function, pain and general health. MCS is a summary measure of emotional function, role limitations due to emotional problems, social function, energy/fatigue.

Table 3: Clinical factors associated with Physical Function Scale of SF-36 in the NAFLD cohort[¥]

	Univariate Analysis		Multivariable Analysis*[#]	
Variables	**Correlation Coefficient (95% CI)**	**p-value**	**Correlation Coefficient (95% CI)**	**p-value**
Age	-0.60 (-0.81 to -0.38)	**<0.0001**	-0.22 (-0.46 to 0.02)	0.07
Gender: Male	10.04 (4.10 to 15.98)	**<0.001**	-6.47 (-17.5 to 4.6)	**0.2**
Race: Caucasian vs rest	-9.90 (-24.74 to 4.94)	0.19		
BMI	-1.00 (-1.40 to -0.60)	**<0.0001**	-1.38 (-1.9 to -0.85)	<**0.0001**
Lean Body Mass	0.36 (0.11 to 0.60)	**0.004**	0.82 (0.3 to 1.27)	**0.0004**
Type 2 Diabetes mellitus	- 9.19 (-15.32 to -3.04)	**0.003**	-6.5 (-12.77 to -0.23)	**0.04**
Dyslipidemia	3.63(-2.61 to 9.88)	0.25		
Hypertension	-7.81 (-14.00 to -1.63)	**0.01**		
Alanine aminotransferase	0.23 (0.15 to 0.32)	**<0.0001**	0.16 (0.08 to 0.24)	**0.0001**
Aspartate aminotransferase	0.11 (-0.03 to 0.25)	0.12		
Liver Stiffness Measurement (KPa)	-0.54 (-0.79 to -0.29)	**<0.0001**	-0.37 (-0.61 to -0.12)	**0.002**
Histopathology: Fibrosis	-6.64 (-9.97 to -3.31)	**<0.0001**		
Histopathology: Steatosis	-0.43(-6.17 to 5.32)	0.89		
Histopathology: Ballooned Hepatocytes*	-9.10 (-15.33 to -2.86)	**0.004**		
Histopathology: Lobular Inflammation	2.78 (-4.92 to 10.47)	0.48		

Abbreviations: Body Mass Index: BMI

[¥]Values expressed as β-coefficients (95% CI)

*Variables with excessive missingness rate were not included in multivariable analysis.

[#]Multivariable model was based on an available sample size of 248 using listwise deletion due to missing data

Table 4: Differences in SF-36 scales in individuals with and without advanced fibrosis based on Transient elastography.[¥]

SF-36 Scales	Liver Stiffness Measurement < 12.1 KPa (n= 197)	Liver Stiffness Measurement ≥ 12.1KPa (n= 102)	P-value
Physical Functioning	76.13 ± 24.96	59.74 ± 27.74	<.0001
Role Limitations due to Physical Health	69.64 ± 41.41	43.07 ± 41.70	<.0001
Emotional Well-being	62.16 ± 26.07	53.36 ± 24.22	0.005
Role Limitations due to Emotional Problems	56.10 ± 21.82	43.00 ± 20.65	<.0001
Energy/Fatigue	45.97 ± 22.37	38.23 ± 22.35	0.005
Social Functioning	78.05 ± 27.58	73.14 ± 25.82	0.139
Pain	78.06 ± 37.14	69.64 ± 41.39	0.076
General Health	71.47 ± 20.12	71.21 ± 18.55	0.912

[¥]Values are shown as means ± standard deviation unless otherwise specified.

Table 5: Factors associated with SF-36 in the NAFLD without advanced fibrosis[¥]

	Univariate Analysis		Multivariable Analysis*[#]	
Variables	**B-coefficient**	**p-value**	**B-coefficient**	**p-value**
Age	-0.38 (-0.64 to -0.12)	**0.005**	-0.24 (-0.50 to 0.03)	0.09
Gender	14.94 (8.14 to 21.76)	**<0.0001**	-2.14 (-15.04 to 10.76)	0.74
Race: Caucasian vs rest	0.76 (-13.78 to 15.30)	0.92		
BMI	-0.77 (-1.27 to 0.27)	**0.002**	-1.13 (-1.76 to -0.50)	**<0.001**
Lean Body Mass	0.57 (0.35 to 1.0)	**<0.0001**	0.71 (0.19 to 1.23)	**0.007**
DM-2	-4.20 (-11.51 to -3.11)	0.26		
Dyslipidemia	-1.32 (-8.51 to 5.87)	0.13		
Hypertension	-4.44 (-11.54 to 2.66)	0.22		
ALT	0.17 (0.07 to 0.28)	**0.001**	0.13 (0.04 to 0.24)	**0.007**
AST	0.08 (-0.08 to 0.24)	0.34		
Liver Stiffness Measurement (K Pa)	0.006 (-5.47 to 5.47)	1.00		
Histopathology: Fibrosis	0.58 (-0.96 to 2.12)	0.46		
Histopathology: Steatosis	0.75 (-6.45 to 7.94)	0.84		
Histopathology: Ballooned Hepatocytes	-5.92 (-13.32 to 1.48)	0.12		
Histopathology: Lobular Inflammation	-1.34 (5.08 to -11.31)	0.79		

Abbreviations: Body Mass Index: BMI
[¥]Values expressed as β-coefficients (95% CI)
*Variables with excessive missingness rate were not included in multivariable analysis.

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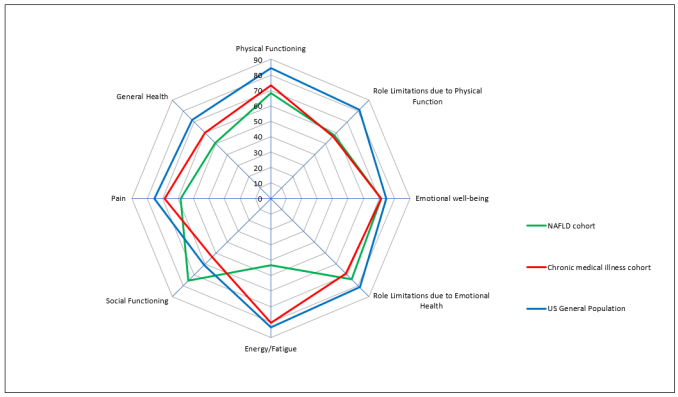
Physical Functioning
90
80
70
60
50
40
30
20
10
0
Role Limitations due to Physical Function
Emotional well-being
Role Limitations due to Emotional Health
Energy/Fatigue
Social Functioning
Pain
General Health
NAFLD cohort
Chronic medical illness cohort
US General Population

Need to Know

Background: Patients with nonalcoholic fatty liver disease (NAFLD) might have reduced quality of life (QOL).

Findings: Patients with NAFLD, even those without advanced fibrosis, have lower QOL than controls. Body composition associates with QOL in patients with NAFLD.

Implications for patient care: Improving body composition might increase QOL for patients with NAFLD.