Hepat Mon. 2022 December; 22(1):e124229. doi: 10.5812/hepatmon-124229.
Published online 2022 May 31. **Research Article**

Relationship Between Cardiovascular Disease Risk Factors and Quality of Life in Patients with Metabolic-Associated Fatty Liver Disease

Raika Jamali [1, 2, *], Soroush Veisi [1], Arsia Jamali [3] and Mehdi Yaseri [4]

[1] Research Development Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran
[2] Digestive Disease Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[3] Department of Internal Medicine, Eisenhower Medical Center, California, USA
[4] Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran

[*] *Corresponding author*: Research Development Center, Sina Hospital, Tehran University of Medical Sciences, Tehran, Iran. Email: raika.jamali@gmail.com

Received 2022 March 27; **Revised** 2022 May 19; **Accepted** 2022 May 20.

Abstract

Background: Metabolic-associated fatty liver disease (MAFLD) is a common cause of liver-related mortality and morbidity worldwide. However, there is a paucity of literature on the relationship between cardiovascular disease (CVD) risk factors and quality of life (QoL) in patients with MAFLD.

Objectives: This study aimed to examine the association between QoL and CVD risk factors in an Iranian MAFLD population.

Methods: This study was conducted on MAFLD patients, referred to the gastroenterology clinic of a general hospital from September 2017 until September 2018. The QoL and Framingham Risk Score (FRS) were determined using the WHOQOL-BREF questionnaire and an online web calculator, respectively. A hierarchical multiple linear regression model was developed to evaluate the association between QoL and FRS after adjusting for the sociodemographic characteristics.

Results: This study was performed on 200 participants. All domains of QoL were associated with older age, hypertension, smoking, diabetes mellitus, higher systolic blood pressure, and lower high-density lipoprotein levels in the univariate regression analysis ($P < 0.05$ for all). Meanwhile, FRS was adversely correlated with the total QoL score (correlation coefficient: -0.49; 95% CI: -0.61, -0.35; $P < 0.001$). After adjusting for the sociodemographic variables, the results of the hierarchical multiple linear regression model showed that age, smoking, diabetes mellitus, hypertension, and FRS were correlated with the overall QoL score ($P < 0.05$ for all). Hypertension was the main predictor of the total QoL score ($B = -5.51$, 95% CI: -7.18, -3.68; $P < 0.05$). A higher FRS was inversely associated with the physical domain of QoL ($B = -0.05$, 95% CI: -0.09, -0.01; $P < 0.05$), the environment domain of QoL ($B = -0.04$, 95% CI: -0.09, -0.01; $P < 0.05$), and the total score of QoL ($B = -0.04$, 95% CI: -0.08, -0.02; $P < 0.05$).

Conclusions: According to the results of this study, a higher risk of developing CVD may reduce QoL in patients with MAFLD. Hypertension, diabetes mellitus, and smoking were the key predictive determinants of QoL in this population. Further studies are suggested to determine if modification of the mentioned risk factors can improve QoL in MAFLD patients.

Keywords: Quality of Life, Cardiovascular Disease Risk Factors, Metabolic-Associated Fatty Liver Disease, Fatty Liver

1. Background

Metabolic-associated fatty liver disease (MAFLD) is the leading cause of chronic liver disease worldwide. The burden of this disease is increasing due to the rising prevalence of metabolic syndrome (1). Similarly, the incidence of MAFLD in the Iranian population has increased in recent years (2). Considering the increasing burden of this disease, it is important to investigate its impact on the patients' health-related quality of life (QoL). Besides, modification of factors that are related to QoL can improve the patients' well-being.

A national survey in China showed that MAFLD impaired QoL (3). It could cause fatigue, depression, agitation, cognitive impairments, limited physical activity, and reduced well-being (4). Besides, obesity and diabetes mellitus (DM) decreased QoL, while achieving the appropriate body weight increased QoL in MAFLD patients (5, 6). Generally, QoL is adversely affected by lobular inflammation and advanced fibrosis, according to the histological examination of MAFLD (7-10). These findings suggest that QoL in MAFLD is correlated with disease severity and the associated metabolic disorders.

MAFLD is associated with cardiovascular disease (CVD) (11). Evidence suggests that the liver fat content, as a marker of visceral adiposity, is related to the development of CVD in MAFLD (12). CVD affects physical activity and may

decrease QoL. Meanwhile, according to previous research, patients with at least one CVD risk factor, such as hypertension (HTN), DM, or high levels of cholesterol, are likely to describe their QoL as "less than good" (13). Overall, it seems reasonable to define CVD risk factors that impact QoL in MAFLD. Modification of these risk factors not only reduces the CVD morbidity and mortality, but also improves QoL in these patients.

So far, limited research has investigated the effect of single CVD risk factors on disability and QoL (14). There is also a paucity of literature on the relationship between multiple CVD risk factors and QoL in MAFLD. Notably, there is a lack of data addressing this phenomenon in the Iranian population.

2. Objectives

The current study aimed to evaluate the association between a panel of CVD risk factors [Framingham Risk Score (FRS)] and the main domains of QoL in a cohort of Iranian MAFLD patients.

3. Methods

3.1. Study Design

This cross-sectional, prospective cohort study was conducted on MAFLD patients, referred to the gastroenterology clinic of Sina Hospital, affiliated to Tehran University of Medical Sciences (Tehran, Iran), from September 2017 until September 2018.

3.2. Patient Enrolment Protocol

All patients with a persistent increase in aminotransferase levels above the normal range (40 U/L) and evidence of fatty liver on abdominal ultrasonography were enrolled in this study. The exclusion criteria were as follows: known chronic hepatitis (alcoholic fatty liver disease, viral disease, autoimmune disease, Wilson's disease, and hemochromatosis); use of hepatotoxic medications; intravenous drug abuse; congestive heart failure; chronic kidney disease; chronic obstructive pulmonary disease; cirrhosis; and any known cancer, except skin cancer. MAFLD was diagnosed based on evidence of any fatty change on liver ultrasonography and ruling out other causes of a persistent increase in aminotransferase levels.

3.3. Sociodemographic Data Registry

The participants were interviewed, and their sociodemographic information, such as age, sex, marital status, education level, annual income, and smoking status, was registered. According to the poverty threshold defined by the research department of the Iranian Islamic Council, annual income was classified as low, low-intermediate, high-intermediate, and high (15). History of medical conditions, including HTN and DM, and history of receiving antihypertensive agents, oral hypoglycemic agents, or insulin were documented; this information was self-reported in the initial interview. The researcher examined the report validity by reviewing the participants' medical records. Height (meter) and weight (kg) were measured, and the body mass index (BMI) was also calculated. BMI was categorized according to the World Health Organization (WHO) classification. A BMI of 18.5 to < 25 kg/m^2 indicates a healthy range; a BMI of ≥ 25 to 30 kg/m^2 represents the overweight range; a BMI of ≥ 30 to 35 kg/m^2 represents the group of class 1 obesity; a BMI of ≥ 35 to 40 kg/m^2 represents the group of class 2 obesity; and a BMI of ≥ 40 kg/m^2 represents the group of class 3 obesity. Also, systolic blood pressure (SBP) at rest was recorded (cmHg) for each patient.

3.4. Laboratory Measurements

All laboratory measurements, including serum aspartate aminotransferase (AST, U/L), alanine aminotransferase (ALT, U/L), alkaline phosphatase (ALP, U/L), fasting blood sugar (FBS, mg/dL), triglyceride (TG, mg/dL), cholesterol (CHOL, mg/dL), low-density lipoprotein (LDL, mg/dL), and high-density lipoprotein (HDL, mg/dL), were performed based on the instructions of the manufacturers' kits. These measurements were performed in the standard environment of the hospital medical laboratory. Laboratory values were defined based on the ELISA method, using a Roche 704 Automated Chemistry Analyzer. Also, Pars Azmun Reagent Kits (Tehran, Iran) were used for laboratory assessments, which were performed based on the manufacturer's instructions described in our previous studies. To understand the measurement details and standard reporting units, readers are invited to study our previous research (16, 17).

3.5. Abdominal Ultrasonography Method

Transabdominal ultrasound was performed using a Hitachi EUB 405 apparatus, equipped with a 3.5 MHz convex probe to diagnose fatty liver. The radiologist compared the echogenicity of the right kidney (void of fat) with the right liver lobe in a sagittal view. The criteria for diagnosis and staging of fatty liver have been described in our previously published study (12).

3.6. CVD Risk Assessment

The sex-specific FRS was calculated for each participant, using a web-based FRS calculator

(https://www.qxmd.com/calculate/calculator_-252/framingham-risk-score-2008). This model uses age, smoking, diabetes, total cholesterol, HDL, HTN, and systolic blood pressure to estimate 10-year total coronary heart disease events (18). The results of calculations are expressed as percentage. The scores were classified as follows: < 10% as low-risk, 10 - 19% as intermediate risk, and ≥ 20% as high risk, according to the American Heart Association (AHA) CVD risk assessment guidelines (19, 20).

3.7. Health-Related QoL Evaluation

The QoL was evaluated using the Persian version of the WHOQOL-BREF questionnaire, validated in Iran (21). The WHOQOL-BREF is a tool, containing 26 items. Twenty-four items of the questionnaire distinguish physical health, psychological health, social relationships, and environment, and the last two items evaluate general health. The score for each domain and the overall score were recorded for each patient (22).

3.8. Ethical Considerations

The research goals were fully explained to patients who were willing to participate in this study, and a written informed consent form was obtained before enrollment. The Ethics Committee of Tehran University of Medical Sciences approved the protocol of this study (registration ID: IR.TUMS.DDRI.REC.1397.001).

3.9. Sample Size Calculation

At an alpha level of 0.05 ($Z\alpha = 1.96$) and power of 80% ($Z\beta = 0.84$), the biostatistician estimated the sample size based on the following formula:

$$\left[\frac{Z\alpha + Z\beta}{0.5} \times ln\left(\frac{1+r}{1-r}\right)\right]^2 + 3$$

The expected correlation coefficient (clinically significant) was set at a minimum level of 0.2. The sample size was estimated at 200.

3.10. Statistical Analysis Method

Demographic and clinical data are described as frequency (percentage) for categorical variables and as mean ± standard deviation (SD) for continuous variables. The normal distribution of variables was evaluated using Kolmogorov–Smirnov test, which indicated the non-normal distribution of all variables. Therefore, Mann–Whitney U test and Spearman's correlation test were used to analyze the associations between CVD risk factors and QoL in a univariate model. After adjusting for factors affecting QoL, a multiple linear regression analysis was performed to distinguish CVD risk factors, which were independently related to the QoL domains. The bootstrapping method was also applied by calculating the bias-corrected and accelerated (BCa) confidence intervals (CIs) with 1000 replications.

A two-step hierarchical multiple linear regression model was developed to determine the effect of each CVD risk factor on QoL while controlling for independent sociodemographic variables. In the first step, marital status, education level, income, geographical distribution, and BMI were entered in the model. In the second step, statistically significant variables ($P < 0.05$), including age, smoking, DM, HTN, and HDL, were entered into the model. Multicollinearity was assessed using the variance inflation factor (VIF) and tolerance for the variables. The tolerance values ranged from 0.108 to 0.959, and the VIF values ranged from 1.043 to 9.220; these findings revealed that multicollinearity was not a problem in the analyses. IBM SPSS Version 20 was used for data analysis. The significance level was set at $P \leq 0.05$, and clinically significant correlations were set at ≥ 0.2. Also, regression coefficients with 95% CIs were reported for each regression model.

4. Results

4.1. Patient Enrollment Process

The eligibility of 254 patients, who were referred to our hospital for the evaluation of MAFLD during the study, was examined. Forty-one candidates did not meet the inclusion criteria, and seven candidates accepted the study protocol, but refused to sign the informed consent form. Of the remaining patients (n = 206), six did not complete the interviews or measurements; the participation rate was estimated at 97%.

4.2. Clinical and Sociodemographic Characteristics

This study was performed on 200 individuals (54% male; 46% female). The participants' mean age was 51.64 ± 2.69 years (range: 40 - 65 years). Considering the geographical distribution, 26 (13%) patients resided in rural areas. The majority of the participants were married (71%, n = 142). In terms of education level, almost half of the participants had a master's degree (49%, n = 98). Low income (11.5%, n = 23) and low-middle income (47.5%, n = 95) had the highest frequencies in the study population, respectively. The BMI was normal in 5 (5.5%) cases, overweight in 58 (29%) cases, and obese in 131 (94.5%) cases. The majority of the patients had DM (82%, n = 163) or HTN (77%, n = 154). The prevalence of smoking was 52 (26%). The participants' mean systolic blood pressure was 14.19 ± 0.54 cmHg, with a range of 13 - 16 cmHg.

4.3. Laboratory Measurements, FRS Scores, and QoL Domain Scores

The mean serum cholesterol level was 182.25 ± 35.91 mg/dL (range: 107 - 387 mg/dL), and the mean serum HDL level was 34.55 ± 3.63 (range: 27 - 55 mg/dL). Based on the FRS, there were 20 (10%) individuals with a low risk of CVD development, 25 (12.5%) individuals with an intermediate risk, and 155 (77.5%) individuals with a high risk of CVD development. The mean FRS was 33.24% ± 15.91, with a range of 3.77% to 78.16% in the study population. The mean normalized QoL score of the participants was 43.55 ± 9.27, according to the WHOQOL-BREF questionnaire. The mean score of the physical domain was 44.79 ± 9.40; the mean score of the psychological domain was 40.40 ± 7.45; the mean score of the social relationship domain was 42.63 ± 14.62; and the mean score of the environmental domain was 45.17 ± 8.88. Table 1 presents the sociodemographic characteristics, clinical characteristics, QoL, and FRS scores in the study population.

4.4. Univariate Regression Analysis to Determine the Relationship Between QoL and CVD Risk Factors

There was no significant difference in terms of QoL between men and women. However, the mean total QoL score and the mean score of each QoL domain were slightly higher in men than in women ($P > 0.05$). The univariate regression analysis showed a significant negative correlation between the overall QoL score and the FRS, age, smoking, DM, HTN, and SBP ($P < 0.05$). Moreover, a significant negative relationship was found between the mentioned CVD risk factors and all QoL domains in this analysis ($P < 0.05$). Meanwhile, the mean HDL level had a significant positive association with the overall QoL score and the scores of all QoL domains ($P < 0.05$). Table 2 presents the results of the univariate regression analysis for determining the relationship between QoL and CVD risk factors.

4.5. Hierarchical Multiple Linear Regression Model to Determine the Effect of Each CVD Risk Factor on QoL

Table 3 presents the results of adjusted regression models for defining the association of QoL scores with the CVD risk (model 1) and FRS (model 2). There was a significant negative association between the overall QoL score and age (B = -0.21; 95% CI: -0.41, -0.02; $P < 0.05$), smoking (B = -2.44; 95% CI: -3.73, -1.11; $P < 0.05$), DM (B = -2.44, 95% CI: -3.87, -1.28; $P < 0.05$), HTN (B = -5.51; 95% CI: -7.18, -3.68; $P < 0.05$), and FRS (B = -0.04; 95% CI: -0.08, -0.02; $P < 0.05$). HTN was the main predictor of the total QoL score. Smoking, DM, and HTN were the key determinants of all domains of QoL. Age was inversely associated with the phycological domain of QoL (B = -0.18; 95% CI: -0.35, -0.01; $P < 0.05$), social relationships domain (B = -0.36; 95% CI: -0.69, -0.03; $P < 0.05$), and environmental domain (B = -0.24; 95% CI: -0.47, -0.05; $P < 0.05$). A higher FRS score was inversely associated with the physical domain of QoL (B = -0.05; 95% CI: -0.09, -0.01; $P < 0.05$) and the environment domain of QoL (B = -0.04; 95% CI: -0.09, -0.01; $P < 0.05$).

5. Discussion

The present study evaluated the association between QoL and CVD risk factors in a cohort of Iranian MAFLD patients. The CVD risk factors were prevalent in the study population. The FRS score was inversely associated with QoL. The results of the univariate regression analysis revealed significant correlations between six out of eight factors present in the FRS equation and the score of QoL. After controlling for confounding factors affecting QoL, the results of the hierarchical multiple linear regression model showed that four of these factors had significant effects on QoL. HTN was the best predictor of QoL in all domains, as well as the overall QoL. DM and smoking were the second and third best predictors of QoL in this study, respectively. The strength of the current study was the simultaneous evaluation of a panel of CVD risk factors while adjusting for the main factors influencing QOL.

The methodological differences in the sociodemographic characteristics of the participants in earlier studies might have produced conflicting results regarding the association between CVD and QoL. Using the WHOQOL-BREF questionnaire, Blay et al. found that age was not associated with QoL in any of the four domains (23). On the other hand, Garcia-Campayo et al. used the short-form health survey (SF-36) and concluded that age significantly affected the mental aspect of QoL; however, it was not possible to determine the association between the physical aspect of QoL and age (24). In the present study, age played a significant role in predicting the environmental QoL score, as well as the total score of QoL in patients with MAFLD. Although this study did not include a wide age range, the results showed that attention must be paid to the environmental factors in the elderly as their age advances. Meanwhile, sex was not significantly associated with the QoL scores in our survey, which is consistent with the results of previous research (23, 25).

Among clinical characteristics, HTN was the most important factor in determining QoL in the present study. Similarly, a systematic review by Trevisol et al. showed that both physical and mental health domains of QoL were inversely related to HTN (26). This meta-analysis compared QoL between hypertensive and normotensive individuals by extracting the data of 20 eligible studies. Lower scores

Table 1. Sociodemographic Characteristics, Clinical Characteristics, Quality of Life, and Framingham Risk Score in the Study Population

Characteristics	N = 200	Percentage/Range
Age (y)	51.64 ± 2.69	40 - 65
Sex		
Male	108	54.00
Female	92	46.00
BMI		
Normal	5	5.50
Overweight	58	29.00
Obesity I	86	43.00
Obesity II	32	16.00
Obesity III	13	6.50
Geographical distribution		
Rural	26	13.00
Urban	174	87.00
Marital status		
Single	29	14.50
Married	142	71.00
Divorced	23	11.50
Widowed	6	3.00
Education level		
Under high school diploma	31	15.50
High school diploma	65	32.50
Master's degree	98	49.00
PhD	6	3.00
Income status		
Low	23	11.50
Low-middle	95	47.50
High-middle	65	32.50
High	17	8.50
Smoking		
Yes	52	26.00
No	148	74.00
DM		
Yes	163	82.00
No	37	18.00
HTN		
Yes	154	77.00
No	46	23.00
SBP (cmHg)	14.19 ± 0.54	13 - 16
Total cholesterol (mg/dL)	182.25 ± 35.91	107 - 387
HDL (mg/dL)	34.55 ± 3.63	27 - 55
FRS score	33.24% ± 15.91	3.77 - 78.16
Low risk (< 10%)	20	10.00
Intermediate risk (10 - 19%)	25	12.50
High risk (≥ 20%)	155	77.50
QoL score	43.55 ± 9.27	20 - 55
Physical domain	44.79 ± 9.40	25 - 57
Psychological domain	40.40 ± 7.45	21 - 50
Social relationships domain	42.63 ± 14.62	0 - 58
Environmental domain	45.17 ± 8.88	22 - 56

Abbreviations: BMI, body mass index; cmHg, centimeter mercury; DM, diabetes mellitus; FRS, Framingham risk score; HDL, high-density lipoprotein; HTN, hypertension; mg/dL, milligram/deciliter; Qol; quality of life; SBP, systolic blood pressure.

[a] Values of quantitative variables are reported as mean ± SD.

[b] BMI is categorized according to the World Health Organization (WHO) classification. Healthy BMI range: 18.5 to < 25 kg/m^2, overweight: ≥ 25 to 30 kg/m^2; obese class I: ≥ 30 to 35 kg/m^2, obese class II: ≥ 35 to 40 kg/m^2, obese class III: ≥ 40 kg/m^2.

Table 2. The Results of Univariate Regression Analysis for Determining the Correlation Between the Quality of Life and Cardiovascular Disease Risk Factors

Characteristics	Physical Health	Psychological	Social Relationships	Environment	Overall QoL
Sex					
Male	45.9 ± 8.5	41.5 ± 6.3	44.6 ± 12.8	46.3 ± 7.8	44.8 ± 8.1
Female	43.7 ± 10.1	39.3 ± 8.3	40.7 ± 16.1	44.0 ± 9.8	42.3 ± 10.2
P-value	0.18	0.10	0.14	0.16	0.15
Smoking					
Yes	54 ± 5.0	46.9 ± 3.7	55.5 ± 5.7	53.5 ± 4.1	52.3 ± 4.3
No	41.7 ± 8.5	38.2 ± 7.1	38.3 ± 14.4	42.4 ± 8.3	40.6 ± 8.6
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
DM					
Yes	42.1 ± 8.5	38.4 ± 7.0	39.9 ± 14.0	42.7 ± 8.2	41.0 ± 8.6
No	55.5 ± 2.8	48.2 ± 2.3	57.7 ± 2.2	54.9 ± 2.1	53.8 ± 2.2
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
HTN					
Yes	41.3 ± 8.6	37.9 ± 6.9	37.9 ± 13.8	42.1 ± 8.1	40.3 ± 8.4
No	55.1 ± 2.6	47.8 ± 2.3	56.8 ± 3.2	54.5 ± 2.1	53.3 ± 2.2
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Age					
Correlation coefficient	-0.29	-0.30	-0.28	-0.30	-0.29
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
95% CI					
Lower	-0.42	-0.42	-0.41	-0.42	-0.42
Upper	-0.16	-0.16	-0.13	-0.16	-0.15
SBP					
Correlation coefficient	-0.24	-0.23	-0.24	-0.26	-0.25
P-value	0.001	0.001	0.001	< 0.001	< 0.001
95% CI					
Lower	-0.38	-0.37	-0.38	-0.39	-0.39
Upper	-0.09	-0.07	-0.09	-0.10	-0.10
Total cholesterol					
Correlation coefficient	0.03	0.03	0.01	0.02	0.02
P-value	0.67	0.71	0.89	0.75	0.74
95% CI					
Lower	-0.11	-0.11	-0.14	-0.13	-0.12
Upper	0.18	0.18	0.17	0.19	0.18
HDL					
Correlation coefficient	0.18	0.18	0.19	0.19	0.19
P-value	0.013	0.009	0.006	0.008	0.008
95% CI					
Lower	0.01	0.03	0.04	0.02	0.02
Upper	0.31	0.32	0.34	0.31	0.32
FRS					
Correlation coefficient	-0.49	-0.45	-0.48	-0.50	-0.49
P-value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
95% CI					
Lower	-0.60	-0.57	-0.60	-0.61	-0.61
Upper	-0.34	-0.32	-0.34	-0.36	-0.35

Abbreviations: DM, diabetes mellitus; FRS, Framingham risk score; HDL, high-density lipoprotein; HTN, hypertension; Qol; quality of life; SBP, systolic blood pressure.

Table 3. Adjusted Multiple Linear Regression Models for Determining the Correlation Between Quality of Life and Cardiovascular Disease Risk Factors

Variables	Physical Health	Psychological Health	Social Relationships	Environment	Overall
Model 1 (QoL and CVD Risk)					
Age					
Regression coefficient	-0.13	-0.18	-0.36	-0.24	-0.21
95% CI	(-0.27, 0.01)	(-0.35, -0.01)	(-0.69, -0.03)	(-0.47, -0.05)	(-0.41, -0.02)
P-value	0.07	0.04	0.03	0.02	0.02
Smoking					
Regression coefficient	-2.64	-2.3	-2.74	-2.26	-2.44
95% CI	(-4.87, -0.54)	(-3.41, -1.07)	(-5.32, -0.81)	(-3.36, -1.09)	(-3.73, -1.11)
P-value	0.005	0.001	0.01	0.002	0.001
DM					
Regression coefficient	-1.62	-2.41	-4.7	-2.35	-2.44
95% CI	(-3.05, -0.48)	(-3.78, -1.28)	(-7.66, -1.64)	(-4.11, -1.03)	(-3.87, -1.28)
P-value	0.009	0.001	0.002	0.002	0.001
HTN					
Regression coefficient	-6.78	-3.71	-5.66	-5.67	-5.51
95% CI	(-9.38, -4.61)	(-5.12, -2.29)	(-9.46, -2.29)	(-7.41, -3.82)	(-7.18, -3.68)
P-value	0.001	0.001	0.003	0.001	0.001
HDL					
Regression coefficient	0.01	0.01	0.01	0.04	0.01
95% CI	(0.01, 0.03)	(-0.01, 0.02)	(-0.01, 0.04)	(0.00, 0.03)	(0.00, 0.02)
P-value	0.29	0.26	0.23	0.08	0.1
Model 2 (QoL and FRS)					
FRS					
Regression coefficient	-0.05	-0.02	-0.05	-0.04	-0.04
95% CI	(-0.09, -0.01)	(-0.05, 0.02)	(-0.11, 0.02)	(-0.09, -0.01)	(-0.08, -0.02)
P-value	< 0.01	0.42	0.19	0.04	0.04

Abbreviations: CVD, cardiovascular Disease; DM, diabetes mellitus; FRS, Framingham risk score; HDL, high-density lipoprotein; HTN, hypertension; Qol; quality of life.

of the physical and mental domains were reported based on FS-36 in the hypertensive group. Moreover, Uchmanowicz et al. found that lower QoL was associated with reduced adherence to therapeutic recommendations (27). Their study on 186 hypertensive elderly patients showed that QoL scores dramatically decreased in patients with low compliance regarding "appointment keeping" and "medication taking", which in turn exacerbated the disease over time and led to an even lower QoL.

The majority of patients with HTN either had a high risk of CVD or had already developed CVD. The results of a trial on 207 hypertensive individuals revealed that HTN management not only reduced the CVD risk, but also improved the QoL (28). Similar to our findings, Oza et al. found that SBP was negatively associated with QoL (29). This study included 269 hypertensive patients and assessed QoL using the WHOQOL-BREF and MINICHAL scales. On the other hand, Katsi et al. described that stage and awareness of hypertension did not affect physical and mental health (30). This survey used SF-36 for the evaluation of QoL and included 189 hypertensive patients. The controversial results of the mentioned research could be attributed to differences in the study population regarding the socioeconomic factors and the type of questionnaire used for QoL evaluation.

Similarly, DM was another determinant of QoL among the participants, which influenced all domains of QoL and the overall score of QoL. Consistent with the results of our survey, Trikkalinou et al. found that DM affected major components of QoL. They proposed that DM comorbidi-

ties and psychological burden caused limitations in their communication with friends and social ties (31). It is noteworthy that in the present study, DM affected social relationships more than any other domain. Additionally, Goldenberg et al., in a meta-analysis evaluating 54 studies, reported that smokers had an impaired QoL in their lifetime. The extent of this negative association was related to the number of cigarettes smoked per day (32). This finding is consistent with our results, which showed that smoking had negative effect on QoL.

To the best of our knowledge, there is no information in the literature regarding the relationship between dyslipidemia and QoL in MAFLD patients. However, there are controversies considering the association of QoL with dyslipidemia in non-MAFLD cohorts (33, 34). A survey by Zhang et al. on 756 post-myocardial infarction patients showed that lipid control could improve QoL; they measured the EQ-5D score for the assessment of QoL (33). On the contrary, Souto et al. showed that familial hypercholesterolemia (FH) was not associated with QoL (34). This study included individuals with a high risk of FH, undergoing genetic screening. The QoL was measured using SF-12 before molecular tests. The mean QoL scores were not significantly different between affected and non-affected cases of FH. Neither the presence of mutations, nor pharmacological treatments were related to QoL; however, a history of CVD was negatively related to QoL. Meanwhile, no significant association was found between QoL and HDL or total cholesterol in a sample of MAFLD patients with a moderate CVD risk. The discrepancy between the results of previous research might be related to differences in the study population characteristics regarding the CVD risk and determinants of QoL.

There are some limitations to the present study. First, this was a cross-sectional study; therefore, it was not possible to infer any causality or directionality. Second, due to the use of convenience sampling, the results may not be generalizable to all MAFLD patients. Third, some gathered data was self-reported in this study, which might result in recall (reporting) bias. Finally, some clinical features (anxiety state or depressive mood) that might influence QoL were not assessed in the current study. To overcome these limitations, multicenter cohort studies with a larger sample size are recommended while considering the participants' moods and emotions.

5.1. Conclusion

According to the current results, HTN, DM, and smoking were the main predictors of QoL in a cohort of Iranian MAFLD patients. Based on the results, control of the mentioned risk factors in these patients would not only improve the QoL, but also reduce the CVD mortality and morbidity.

Footnotes

Authors' Contribution: Jamali, R. and Jamali, A. conceived of the study and designed it; Veisi, S. enrolled the participants; Jamali, R. diagnosed non-alcoholic fatty liver disease; Jamali, R. and Veisi, S. collected the data; Yaseri, M. and Veisi, S. performed the statistical analysis and interpreted the data; and Veisi, S., Jamali, R., and Jamali, A. prepared the draft of the manuscript. All authors read and approved the final version of the manuscript.

Conflict of Interests: Raika Jamali is the reviewer of the journal. The author was completely excluded from all review processes of the manuscript.

Data Reproducibility: The data presented in this study were uploaded during submission as a supplementary file and are openly available for readers upon request.

Ethical Approval: The Ethics Committee of Tehran University of Medical Sciences approved the protocol of this study (ethics.research.ac.ir/ProposalCertificateEn.php?id=20949).

Funding/Support: This study was financially supported by Tehran University of Medical Sciences, with the grant number, 9111215333.

Informed Consent: The study goals were fully explained to willing patients, and a written informed consent form was obtained before enrollment.

References

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016;**64**(1):73–84. doi: 10.1002/hep.28431. [PubMed: 26707365].
2. Motamed N, Khoonsari M, Panahi M, Rezaie N, Maadi M, Safarnezhad Tameshkel F, et al. The Incidence and Risk Factors of Non-Alcoholic Fatty Liver Disease: A Cohort Study from Iran. *Hepat Mon*. 2020;**20**(2). e98531. doi: 10.5812/hepatmon.98531.
3. Huang R, Fan JG, Shi JP, Mao YM, Wang BY, Zhao JM, et al. Health-related quality of life in Chinese population with non-alcoholic fatty liver disease: a national multicenter survey. *Health Qual Life Outcomes*. 2021;**19**(1):140. doi: 10.1186/s12955-021-01778-w. [PubMed: 33962617]. [PubMed Central: PMC8106221].
4. Golabi P, Otgonsuren M, Cable R, Felix S, Koenig A, Sayiner M, et al. Non-alcoholic Fatty Liver Disease (NAFLD) is associated with impairment of Health Related Quality of Life (HRQOL). *Health Qual Life Outcomes*. 2016;**14**:18. doi: 10.1186/s12955-016-0420-z. [PubMed: 26860700]. [PubMed Central: PMC4746896].
5. Funuyet-Salas J, Perez-San-Gregorio MA, Martin-Rodriguez A, Romero-Gomez M. Quality of Life and Coping in Nonalcoholic Fatty Liver Disease: Influence of Diabetes and Obesity. *Int J Environ Res Public Health*. 2021;**18**(7). doi: 10.3390/ijerph18073503. [PubMed: 33800585]. [PubMed Central: PMC8036804].

6. Jamali R, Moghtadaie A, Miratashi Yazdi SA, Moghtadaie H. Impact of standard treatment on the quality of life of non-alcoholic fatty liver disease patients. *J Taibah Univ Med Sci*. 2021;**16**(5):755–60. doi: 10.1016/j.jtumed.2021.03.010. [PubMed: 34690658]. [PubMed Central: PMC8498682].
7. Huber Y, Boyle M, Hallsworth K, Tiniakos D, Straub BK, Labenz C, et al. Health-related Quality of Life in Nonalcoholic Fatty Liver Disease Associates With Hepatic Inflammation. *Clin Gastroenterol Hepatol*. 2019;**17**(10):2085–92. doi: 10.1016/j.cgh.2018.12.016. [PubMed: 30580090].
8. McSweeney L, Breckons M, Fattakhova G, Oluboyede Y, Vale L, Ternent L, et al. Health-related quality of life and patient-reported outcome measures in NASH-related cirrhosis. *JHEP Rep*. 2020;**2**(3):100099. doi: 10.1016/j.jhepr.2020.100099. [PubMed: 32435754]. [PubMed Central: PMC7229498].
9. Gronkjaer LL, Lauridsen MM. Quality of life and unmet needs in patients with chronic liver disease: A mixed-method systematic review. *JHEP Rep*. 2021;**3**(6):100370. doi: 10.1016/j.jhepr.2021.100370. [PubMed: 34805816]. [PubMed Central: PMC8585663].
10. Sayiner M, Stepanova M, Pham H, Noor B, Walters M, Younossi ZM. Assessment of health utilities and quality of life in patients with non-alcoholic fatty liver disease. *BMJ Open Gastroenterol*. 2016;**3**(1). e000106. doi: 10.1136/bmjgast-2016-000106. [PubMed: 27648297]. [PubMed Central: PMC5013331].
11. Ashraf H, Karbalai S, Jamali R. Nonalcoholic fatty liver disease and cardiovascular concerns: The time for hepatologist and cardiologist close collaboration. *World J Meta-Anal*. 2021;**9**(2):164–75. doi: 10.13105/wjma.v9.i2.164.
12. Jamali R, Pourhassan S, Maghbouli N, Ashraf H, Sohrabpour AA. Liver fat content might be an appropriate measure for estimation of cardiovascular disease risk in non-alcoholic steatohepatitis patients. *Med J Islam Repub Iran*. 2020;**34**:135. doi: 10.34171/mjiri.34.135. [PubMed: 33437731]. [PubMed Central: PMC7787026].
13. Li C, Ford ES, Mokdad AH, Balluz LS, Brown DW, Giles WH. Clustering of cardiovascular disease risk factors and health-related quality of life among US adults. *Value Health*. 2008;**11**(4):689–99. doi: 10.1111/j.1524-4733.2007.00307.x. [PubMed: 18194400].
14. Daviglus ML, Liu K, Pirzada A, Yan LL, Garside DB, Feinglass J, et al. Favorable cardiovascular risk profile in middle age and health-related quality of life in older age. *Arch Intern Med*. 2003;**163**(20):2460–8. doi: 10.1001/archinte.163.20.2460. [PubMed: 14609782].
15. Arian Shahbazian MA, Einian M, Kaviani Z. *[Poverty threshold estimation during the first six month of 2018]*. Tehran, Iran: Islamic Consultative Assembly (Parliament); 2018. Persian.
16. Jamali R, Razavizade M, Arj A, Aarabi MH. Serum adipokines might predict liver histology findings in non-alcoholic fatty liver disease. *World J Gastroenterol*. 2016;**22**(21):5096–103. doi: 10.3748/wjg.v22.i21.5096. [PubMed: 27275102]. [PubMed Central: PMC4886385].
17. Razavizade M, Jamali R, Arj A, Matini SM, Moraveji A, Taherkhani E. The effect of pioglitazone and metformin on liver function tests, insulin resistance, and liver fat content in nonalcoholic Fatty liver disease: a randomized double blinded clinical trial. *Hepat Mon*. 2013;**13**(5). e9270. doi: 10.5812/hepatmon.9270. [PubMed: 23930133]. [PubMed Central: PMC3736624].
18. D'Agostino RS, Vasan RS, Pencina MJ, Wolf PA, Cobain M, Massaro JM, et al. General cardiovascular risk profile for use in primary care: the Framingham Heart Study. *Circulation*. 2008;**117**(6):743–53. doi: 10.1161/CIRCULATIONAHA.107.699579. [PubMed: 18212285].
19. Jahangiry L, Farhangi MA, Rezaei F. Framingham risk score for estimation of 10-years of cardiovascular diseases risk in patients with metabolic syndrome. *J Health Popul Nutr*. 2017;**36**(1):36. doi: 10.1186/s41043-017-0114-0. [PubMed: 29132438]. [PubMed Central: PMC5682637].
20. Bosomworth NJ. Practical use of the Framingham risk score in primary prevention: Canadian perspective. *Can Fam Physician*. 2011;**57**(4):417–23. [PubMed: 21626897]. [PubMed Central: PMC3076470].
21. Nejat SAHARNAZ, Montazeri A, Holakouie Naieni K, Mohammad KAZEM, Majdzadeh SR. The World Health Organization Quality of Life (WHOQOL-BREF) questionnaire: Translation and validation study of the Iranian version. *Journal of school of public health and institute of public health research*. 2006;**4**(4):1–12.
22. World Health Organization. *WHOQOL-BREF: introduction, administration, scoring and generic version of the assessment: field trial version, December 1996*. Geneva, Switzerland: World Health Organization; 1996.
23. Blay SL, Marchesoni MS. Association among physical, psychiatric and socioeconomic conditions and WHOQOL-Bref scores. *Cad Saude Publica*. 2011;**27**(4):677–86. doi: 10.1590/s0102-311x2011000400007. [PubMed: 21603751].
24. Garcia-Campayo J, Ayuso-Mateos JL, Caballero L, Romera I, Aragones E, Rodriguez-Artalejo F, et al. Relationship of somatic symptoms with depression severity, quality of life, and health resources utilization in patients with major depressive disorder seeking primary health care in Spain. *Prim Care Companion J Clin Psychiatry*. 2008;**10**(5):355–62. doi: 10.4088/pcc.v10n0502. [PubMed: 19158973]. [PubMed Central: PMC2629057].
25. Gonzalez-Blanch C, Hernandez-de-Hita F, Munoz-Navarro R, Ruiz-Rodriguez P, Medrano LA, Cano-Vindel A. The association between different domains of quality of life and symptoms in primary care patients with emotional disorders. *Sci Rep*. 2018;**8**(1):11180. doi: 10.1038/s41598-018-28995-6. [PubMed: 30046118]. [PubMed Central: PMC6060102].
26. Trevisol DJ, Moreira LB, Kerkhoff A, Fuchs SC, Fuchs FD. Health-related quality of life and hypertension: a systematic review and meta-analysis of observational studies. *J Hypertens*. 2011;**29**(2):179–88. doi: 10.1097/HJH.0b013e328340d76f. [PubMed: 21045726].
27. Uchmanowicz B, Chudiak A, Mazur G. The influence of quality of life on the level of adherence to therapeutic recommendations among elderly hypertensive patients. *Patient Prefer Adherence*. 2018;**12**:2593–603. doi: 10.2147/PPA.S182172. [PubMed: 30584283]. [PubMed Central: PMC6287422].
28. Arija V, Villalobos F, Pedret R, Vinuesa A, Jovani D, Pascual G, et al. Physical activity, cardiovascular health, quality of life and blood pressure control in hypertensive subjects: randomized clinical trial. *Health Qual Life Outcomes*. 2018;**16**(1):184. doi: 10.1186/s12955-018-1008-6. [PubMed: 30217193]. [PubMed Central: PMC6137925].
29. Oza BB, Patel BM, Malhotra SD, Patel VJ. Health related quality of life in hypertensive patients in a tertiary care teaching hospital. *J Assoc Physicians India*. 2014;**62**(10):22–9. [PubMed: 25906517].
30. Katsi V, Kallistratos MS, Kontoangelos K, Sakkas P, Souliotis K, Tsioufis C, et al. Arterial Hypertension and Health-Related Quality of Life. *Front Psychiatry*. 2017;**8**:270. doi: 10.3389/fpsyt.2017.00270. [PubMed: 29255431]. [PubMed Central: PMC5722974].
31. Trikkalinou A, Papazafiropoulou AK, Melidonis A. Type 2 diabetes and quality of life. *World J Diabetes*. 2017;**8**(4):120–9. doi: 10.4239/wjd.v8.i4.120. [PubMed: 28465788]. [PubMed Central: PMC5394731].
32. Goldenberg M, Danovitch I, IsHak WW. Quality of life and smoking. *Am J Addict*. 2014;**23**(6):540–62. doi: 10.1111/j.1521-0391.2014.12148.x. [PubMed: 25255868].
33. Zhang M, Chen P, Zhang Y, Su X, Chen J, Xu B, et al. Predictors of Quality of Life in Patients With Myocardial Infarction Combined With Dyslipidemia. *Front Public Health*. 2021;**9**:713480. doi: 10.3389/fpubh.2021.713480. [PubMed: 34692622]. [PubMed Central: PMC8528215].
34. Souto AC, Miname MH, Fukushima J, Jannes CE, Krieger JE, Hagger M, et al. Health related quality of life in individuals at high risk for familial hypercholesterolemia undergoing genetic cascade screening in Brazil. *Atherosclerosis*. 2018;**277**:464–9. doi: 10.1016/j.atherosclerosis.2018.05.036. [PubMed: 30270086].