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MASLD Is Associated With Decreased General Health Perception, Quality of Life and Work Productivity in a Low Fibrosis Population

L. J. M. Heyens[1,2,3,4] | C. Van Steenkiste[5,6] | M. Struyve[4] | S. M. Francque[6,7] | G. H. Koek[2,8] | G. Robaeys[1] | the MASLD Research Group

[1]Faculty of Health and Life Sciences/LCRC, Hasselt University, Diepenbeek, Belgium | [2]School of Nutrition and Translational Research in Metabolism, NUTRIM, Maastricht University, Maastricht, the Netherlands | [3]Department of Future Health, LCRC(-MHU), Ziekenhuis Oost-Limburg, Genk, Belgium | [4]Department of Gastroenterology, Ziekenhuis Oost-Limburg, Genk, Belgium | [5]Department of Gastroenterology and Hepatology, AZ Maria Middelares, Gent, Belgium | [6]Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium | [7]Laboratory of Experimental Medicine and Paediatrics, University of Antwerp, Antwerp, Belgium | [8]Department of Gastroenterology and Hepatology, Maastricht University Medical Centre—MUMC+, Maastricht, the Netherlands

Correspondence: L. J. M. Heyens (l.heyens@maastrichtuniversity.nl)

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ABSTRACT

Background: Data on quality of life in a low fibrosis prevalence metabolic dysfunction-associated steatotic liver disease (MASLD) cohort are scarce, as previous research has focused on advanced fibrosis and cirrhosis. This study examined the association between steatosis and general and mental health, as well as productivity in patients in primary care and a diabetes population.

Methods: Three cohort studies were conducted in Belgian and Dutch primary care and a Belgian hospital. Liver stiffness (>12 kPa) and steatosis (>275 dB/m) were measured using vibration-controlled transient elastography and controlled attenuation parameter (CAP). Participants completed questionnaires measuring anxiety (GAD-7), depression (PHQ-9), work productivity (WPAI-SHP), and general health (SF-36), and data were analysed with Spearman correlation.

Results: Of 311 participants, 142 (45.7%) and 15 (4.7%) had steatosis and fibrosis. Individuals with steatosis had a higher BMI (30.5 kg/m^2 vs. 25.5 kg/m^2, $p<0.001$), increased liver stiffness (5.7 kPa vs. 4.6 kPa, $p<0.001$), lower general health scores (SF-36, $p<0.001$) and physical functioning (SF-36, $p=0.024$) compared to those without. No significant differences were found for depression ($p=0.955$) or anxiety ($p=0.557$). Absenteeism was more prevalent in the steatosis group ($p=0.016$), though the reasons for absenteeism were mostly unrelated to steatosis. Higher CAP values were negatively correlated with physical functioning ($r=-0.193$, $p<0.001$), energy/fatigue ($r=-0.112$, $p=0.049$), and general health ($r=-0.235$, $p<0.001$) in the total cohort.

G. H. Koek and G. Robaeys contributed equally to this study.

MASLD Research Group: Y. Kockaerts, Department of Endocrinology, Ziekenhuis Oost-Limburg, Genk, Belgium; I. Lowyck, Department of Endocrinology, Ziekenhuis Oost-Limburg, Genk, Belgium; K. Stinkens, Department of Endocrinology, Ziekenhuis Oost-Limburg, Genk, Belgium; H. Van Leeuwen-Wintjens, Department of Endocrinology, Ziekenhuis Oost-Limburg, Genk, Belgium; L. Vernijns, Huisartsenbox, Genk, Belgium; J. Germaux, Huisartsenpraktijk Medi-Mine, Genk, Belgium; T. Meyers, Groepspraktijk Luce, Genk, Belgium; J. Gyselaers, Gezondheidscentrum Sirona vzw, Genk, Belgium; S. Pietermans, Groepspraktijk De Dam, Maasmechelen, Belgium; R. Bollen, W-Care Hoeselt, Hoeselt, Belgium; A. Robaeys, Huisartsen Termolen, Zonhoven, Belgium; C. Gilio, Huisarts Gilio, Maasmechelen, Belgium; R. Remmen, Maatschappelijke Gezondheidszorg en Eerstelijnzorg, University of Antwerp, Wilrijk, Belgium; J. Muris, Department of General Practice, CAPHRI Care and Public Health Research Institute, UM, the Netherlands; M. Uitterhoeve-Prins, Dokters van Hier, Maastricht, the Netherlands; M. Bremers, Huisartsenspraktijk Bandkeramiek, Elsloo, the Netherlands; L. van Bokhoven, CAPHRI Care and Public Health Research Institute, UM, the Netherlands; K. de Munck, Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium; E. Rubens, Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium; K. Joris, Department of Gastroenterology and Hepatology, Antwerp University Hospital, Antwerp, Belgium

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Conclusion: Steatosis does not appear to affect anxiety or depression, but does negatively affect general health perception and physical activity. Further investigation is needed to determine whether a potential relationship between work productivity and steatosis exists.

1 | Introduction

Metabolic dysfunction-associated steatotic liver disease (MASLD, formerly known as non-alcoholic fatty liver disease; NAFLD [1]) has become the most frequent cause of chronic liver disease worldwide and is rapidly becoming the first indication for liver transplantation [2, 3]. MASLD is defined by a hepatic lipid accumulation in more than 5% of the hepatocytes or diagnosed on imaging, combined with metabolic risk factors like dyslipidaemia, hypertension, and diabetes. Other causes of steatogenesis (e.g., alcohol and steatogenic drugs) can co-exist but are not part of the MASLD definition [4]. It represents a broad spectrum of clinical entities ranging from isolated steatosis to inflammation or metabolic dysfunction-associated steatohepatitis (MASH), liver fibrosis, cirrhosis, and advanced liver disease with hepatic failure and hepatocellular carcinoma (HCC) [5]. MASLD is also related to the development of metabolic disturbances (e.g., incident diabetes) and is associated with an increased risk for cardiovascular disease (CVD), non-liver malignancy, and other health problems [6–9].

Regardless of the severity and the presence of co-morbidities, people with MASLD have an impaired quality of life (QoL) and social life [10]. The literature currently available concerning QoL is mainly concentrated on the more severe stages, for example, liver fibrosis, cirrhosis, or HCC, due to the fact that it was first thought that MASLD was asymptomatic [11]. However, there is increasing evidence that MASLD is associated with nonspecific symptoms like fatigue, anxiety, and depression, but also reduced physical fitness [12]. The latter can substantially impact QoL. Furthermore, they could also influence productivity at work, and the latter also has a societal impact [13].

Consequently, QoL was recently included as a secondary or exploratory endpoint in clinical trials. In the future, it will become an even more critical endpoint in trials and a vital decision-making element when determining an individual's treatment plan. In addition, the association of MASLD with obesity and T2DM augments the long-term impact on the QoL and puts tremendous strain on healthcare systems worldwide [13]. In this study, we sought to investigate the relationship between MASLD and (i) general health, (ii) QoL subdivided into anxiety, depression, physical functioning, energy and fatigue levels, emotional well-being, pain, and social functioning, and finally, (iii) work productivity. The possible relationship was investigated in a primary care and T2DM population with predominantly early-stage MASLD, as research for this population is lacking.

2 | Materials and Methods

2.1 | Study Design

Three cross-sectional prospective cohort studies were conducted from September 2019 to February 2024 in nine primary care practices (PCP) throughout Belgium (NCT04647409), five PCP practices in the Netherlands (NCT04918732), and the endocrinology department of Ziekenhuis Oost-Limburg (NCT04999124). The study protocol was conducted according to the Helsinki Declaration after approval by the Ethics Committee of Hasselt University CME2020 019, University Hospital Antwerp 19/44/495, the Medical Ethical Committee of Maastricht University/Maastricht University Medical Centre NL73265.068.20, and the Committee Medical Ethics of Ziekenhuis Oost-Limburg CTU2020015. Good clinical practice (GCP) guidelines were followed throughout the study.

2.2 | Participants

The general practitioner (GP) recruited participants on an incoming basis, or e-mails were sent through the electronic patient file system used in the PCP. Additionally, flyers and posters were available in the waiting room. People with T2DM were recruited by their endocrinologists.

Participants were eligible for inclusion if they were older than 18 years old, able to understand Dutch, and had no excessive alcohol use (more than 2 or 3 glasses of alcohol per day for women or men, respectively). Individuals with a known history of other liver diseases, i.e., hepatitis B virus, hepatitis C virus, autoimmune hepatitis, primary biliary cirrhosis, hemochromatosis, Wilson's disease, or Alpha 1 antitrypsin deficiency, were excluded. Other exclusion criteria were secondary causes of steatosis or drug-induced liver injury, which included the use of medications such as amiodarone, tamoxifen, and methotrexate.

2.3 | Data Collection

Anthropometric data, such as waist circumference, weight, height, blood pressure, but also smoking status, alcohol usage, and demographic data, were collected on the day of evaluation. Laboratory data, medical history, and medication usage were collected retrospectively from electronic patient records (EPD). A body mass index (BMI) of <25, 25–30, and $>30\,\text{kg/m}^2$ was considered as normal weight, overweight, and obesity, respectively [14, 15]. Furthermore, metabolic syndrome (MetS) diagnosis was based on the International Diabetes Federation consensus [16].

2.4 | Non-Invasive Tests

As a surrogate for liver fibrosis, liver stiffness was measured by Vibration Controlled Transient Elastography (VCTE) and steatosis by Controlled Attenuation Parameter (CAP). VCTE and CAP were measured utilising a FibroScan 430+ mini (Echosens, Paris, France) in the right liver lobe by intercostal approach. Subjects were asked to be in fasting conditions for at least 3 h before the examination and were placed in a supine position with arms in maximal abduction. For screening, the M probe (3.5 MHz) or the XL probe (2.5 MHz) was selected depending

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Key Points

- MASLD-related cirrhosis has a detrimental effect on quality of life (QoL); however, in people with early-stage MASLD, i.e., simple steatosis, it remains scarcely investigated.
- Our research showed that even in early-stage MASLD, patients experience lower physical functioning and general health perception compared to those without steatosis, regardless of comorbidities.
- Unlike MASH or cirrhosis, this early-stage cohort showed no significant relationship between steatosis and mental health disorders.
- Individuals with steatosis exhibited higher levels of absenteeism and overall work impairment. While a direct causal link should be investigated, the data suggest that early-stage MASLD carries a socioeconomic burden.

on the indication from the device. VCTE and CAP values were considered reliable when the interquartile range (IQR) was equal to or less than 30% of the median LSM value (IQR/med), and at least ten measurements were performed. A CAP value of > 275 dB/m was considered as having steatosis [17]. A VCTE value of ≥ 8 or ≥ 12 kPa was considered as having significant or advanced fibrosis, respectively [18]. To detect at-risk MASH, the FibroScan-AST (FAST) score was used [18, 19]. A FAST value of > 0.67 was considered as having at-risk MASH [18].

2.5 | Questionnaires

After consent, participants self-administered a questionnaire assessing general health, QoL, work productivity, and demographic characteristics like income and educational status. Income was categorised as low or high based on the poverty boundary of Belgium. Educational status was categorised into low (no school or elementary school), mid (high school), or high (college or university). The following validated non-disease-specific questionnaires were used to assess general health, QoL, and work productivity: General Anxiety Disorder (GAD-7), Patient Health Questionnaire (PHQ-9), Workers Productivity and Activity Impairment (WPAI) questionnaire, and Short Health Form-36 (SF-36) [20–24]. To measure anxiety and depressive feelings, the GAD-7 and the PHQ-9 questionnaires were used, respectively. Higher scores indicated greater feelings of anxiety or depression. A score of < 5 for the GAD-7 and ≤ 4 for the PHQ-9 scores indicated no anxiety or depressive feelings, with a maximum score of 21 and 27, respectively [25, 26]. Productivity at work or in one's spare time was measured with the WPAI questionnaire, as was proposed by Younossi and colleagues [27]. The WPAI yielded four types of scores: (i) absenteeism, expressed as work time missed; (ii) presenteeism, expressed as reduced on-the-job effectiveness; (iii) work productivity loss, expressed as overall work impairment; and (iv) activity impairment, which was expressed as impairment during daily activities outside work. Results of items one to three were limited to those who worked at the time of the study. WPAI outcomes are expressed as impairment percentages, with higher numbers indicating greater impairment and less productivity, i.e., worse outcomes [20]. The presence of absenteeism or presenteeism was defined as having a value larger than zero in the absence of validated cut-off values. Finally, general well-being was measured with the SF-36 (RAND 36-Item Health Survey version 1.0). The SF-36 was used to assess eight domains: (i) general health perceptions, (ii) physical functioning, (iii) bodily pain, (iv) role limitations due to physical health problems, (v) role limitations due to personal or emotional problems, (vi) emotional well-being, (vii) social functioning, and (viii) energy/fatigue. A higher score indicated a better outcome, and the scores ranged from 0 to 100 [28].

2.6 | Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) (Version 29.0, Armonk, New York, IBM Corp). Categorical variables were presented as absolute values with percentages. The Shapiro–Wilk or Kolmogorov–Smirnov test was used to test for the normality of continuous variables. All skewed numeric variables are presented as median with interquartile range (IQR). The nonparametric Mann–Whitney *U* and Kruskal–Wallis tests were used to compare two or more groups for continuous variables with a non-normal distribution. As a post-hoc analysis, the Dunn's test (Bonferroni correction for multiple testing) was performed for the Kruskal–Wallis test. To compare discrete and categorical variables, the Chi-Square or Fisher's Exact test was used. The Fisher's Exact test was only used if the expected count was less than five in the cells. To test the correlation between CAP and QoL, a Pearson or Spearman's rho analysis was performed depending on the normality of the variable. A binomial logistic regression analysis was used to test the relationship between CAP and QoL with the following variables included: age, sex, smoking behaviour (never smoked, ex-smoker, smoker), alcohol use (yes/no), T2DM (yes/no) and BMI. The number of subjects included in every analysis is designated by '*n*'. A *p*-value ≤ 0.05 and ≤ 0.001 is anticipated as statistically significant and highly statistically significant.

3 | Results

3.1 | Cohort Characteristics

In total, 870 people were screened, of whom 619 (71.1%) met the inclusion criteria. Of the 619 participants, 449 (72.5%) received the questionnaire, and 311 (69.2%) filled it out completely (Figure 1). Participants who partially filled out the questionnaire had a lower educational level ($p = 0.012$) than those who completed the questionnaire (Table S1). Almost half of the predominantly White cohort was male (47.3%), with a median age of 61 [52–67] years. A median BMI of 27.8 [24.6–31.4] kg/m^2 was measured, and 85 (27.3%) of the participants had T2DM and 153 (49.2%) MetS (Table 1). Steatosis was found in 142 (45.7%) participants; 5 (2.6%) had MASH based on the FAST score, and 15 (4.8%) had advanced fibrosis. Characteristics were compared and significant differences between people with or without steatosis were found between sex distribution (55.6% vs. 40.2% males, $p = 0.007$), ALAT (26.0 [19.0–44.0] vs. 20.0 [15.0–27.0] U/L, $p < 0.001$) and VCTE (5.7 [4.3–8.1] vs. 4.6 [3.8–5.7] kPa, $p < 0.001$) (Table 1). Next, 59

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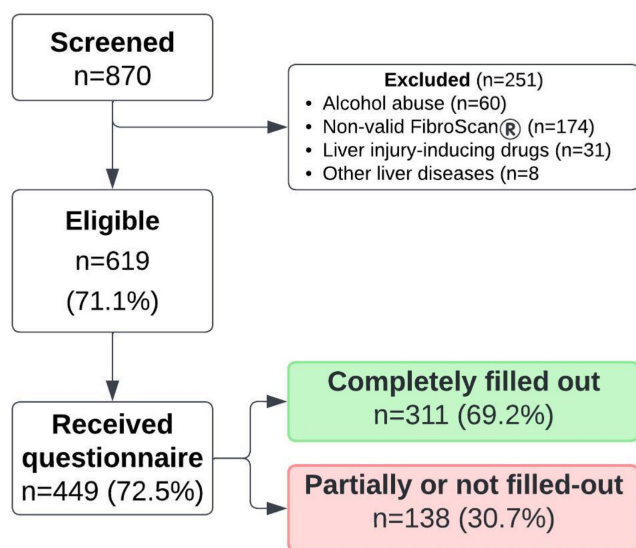

FIGURE 1 | Flowchart of the inclusion process.

(41.5%) individuals with steatosis had T2DM compared to 25 (14.8%) in the group without steatosis ($p<0.001$). People with diabetes and with steatosis had an average diabetes duration of 7 [3–15] years; 14 (23.7%) had a history of cardiovascular disease, of whom 4 (28.6%) had a myocardial infarction (data not shown).

3.2 | Income and Degree of Education

Of the total cohort, 270 (86.8%) had a normal or high income. When comparing the income between those with or without steatosis, no significant difference was found ($p=0.808$) (Table 1). For educational status, 34 (11.0%) had a low degree, 123 (39.5%) had a moderate degree, and 154 (49.5%) had a higher degree (Table 1). No significant difference in educational status was found between people with or without steatosis ($p=0.090$). When comparing people without steatosis to those with steatosis but without diabetes, a significant difference was observed in educational status ($p=0.005$).

3.3 | General Health Perception

The overall score for general health perception, as measured by the SF-36, was 40.4 [30.6–45.4] (Table 2). Significant differences were observed between all subgroups (with or without steatosis ($p<0.001$), no steatosis and people with steatosis and T2DM ($p=0.012$), and no steatosis versus steatosis without T2DM ($p<0.001$)). Also, after stratification by sex, the difference in general health perception remained significant in both men and women (Table S2). Negative correlations were observed between CAP and general health perception ($r=-0.235$, $p<0.001$) in the total study cohort (Table 3). Logistic regression analysis controlling for age, sex, smoking behaviour, alcohol use, BMI, and T2DM showed a decreased odds ratio for general health perception of 0.969 (95% CI 0.943–0.995, $p=0.019$) when having steatosis. Similarly, when also adding corrections for income and degree of education to the previous regression model, the odds for general health perception decreased to 0.970 (95% CI 0.944–0.996, $p=0.026$) (Table 4).

3.4 | Quality of Life

The overall scores of the following SF-36 items, physical functioning, limitations of physical health, and emotional health were 85.0 [70.0–95.0], 100.0 [50.0–100.0], and 100.0 [100.0–100.0], respectively (Table 2). For energy and fatigue, emotional well-being, social functioning, and pain, the scores were 65.0 [50.0–80.0], 80.0 [64.0–88.0], 87.5 [75.0–100.0], and 77.5 [57.5–100.0], respectively (Table 2). Physical functioning was lower in the group with steatosis compared to those without (85 [70.0–95.0] vs. 90 [70.0–100.0] ($p=0.024$)). For emotional well-being and limitations of emotional health, no difference in scores was observed between people without steatosis and those with steatosis and T2DM, though there were differences between the other subgroups (Table 2). When stratified by sex, no significant differences in SF-36 items between people with or without steatosis were observed for men or women (Table S2). Negative correlations were observed between CAP and physical functioning ($r=-0.193$ ($p<0.001$)), energy and fatigue ($r=-0.112$ ($p=0.049$)), and pain ($r=-0.116$ ($p=0.040$)) in the total study cohort (Table 3). In the subgroup of people without steatosis, a negative correlation was found between CAP and physical functioning ($r=-0.221$, $p=0.004$) and a positive correlation between VCTE and emotional well-being ($r=0.154$, $p=0.046$). The latter correlation was also found in the group of people with steatosis ($r=0.191$, $p=0.023$). No correlations were found between CAP or VCTE among people with steatosis and with or without T2DM (Table 3). Furthermore, the correlation analysis was repeated, but without MASH or advanced fibrosis (≥12 kPa) participants. The observed correlations were similar to those seen with MASH and advanced fibrosis participants included (data not shown). Additionally, the FAST score showed no correlations with any of the items of the SF-36 questionnaire (Table S7). Logistic regression analysis showed that items of the SF-36, except for general health, were not associated with the presence of steatosis (Table 4).

Scores for depression and anxiety were 4.0 [1.0–7.5] and 2.0 [0.0–5.5], respectively, for the total cohort (Table 2). A significant result was found when comparing anxiety scores between participants without steatosis and those with both diabetes and steatosis (2.0 [0.0–5.0] vs. 1.0 [0.0–4.0], $p=0.049$). No correlations were found between depression and anxiety scores and CAP (Table S3) or the FAST score (Table S7). Next, the correlation analysis was repeated after omitting the participants with MASH or advanced fibrosis (≥12 kPa). Again, no correlations were observed between depression and anxiety scores and CAP (data not shown). Furthermore, logistic regression analysis showed that neither anxiety nor depression was associated with the presence of steatosis (Table 4).

3.5 | Work Productivity and Activity Impairment

In the total cohort, 139 (44.7%) worked at the time of the study visit. Absenteeism could be calculated in 128 (41.2%) of the study

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TABLE 1 | Characteristics of the study cohort.

	Total ($n = 311$)	No steatosis ($n = 169$)	Steatosis ($n = 142$)	Steatosis without T2DM ($n = 83$)	Steatosis and T2DM ($n = 59$)	P^1	P^2	P^3
Age (years)	61 [52–67]	60 [52–67]	61 [53–67.0]	60 [51–64]	63 ± 10	0.349	0.011*	0.501
Sex (male)	147 (47.3)	68 (40.2)	79 (55.6)	43 (51.8)	36 (61.10)	0.007*	0.006*	0.082
BMI (kg/m^2)	27.8 [24.6–31.4]	25.5 [23.5–28.3]	30.5 [28.1–34.6]	30.1 [27.5–34.3]	30.9 [29.4–35.0]	< 0.001*	< 0.001*	< 0.001*
Waist circumference (cm) ($n = 310$)	98.3 ± 15.0	91.0 ± 12.4	105.3 [97.5–114.0]	103.0 [94.0–114.0]	109.3 ± 10.0	< 0.001*	< 0.001*	< 0.001*
T2DM	85 (27.3)	25 (14.8)	59 (41.5)	0 (0)	59 (100)	< 0.001*	N.A.	N.A.
Metabolic syndrome ($n = 293$)	153 (49.2)	59 (36.9)	94 (70.7)	42 (53.8)	52 (94.5)	< 0.001*	< 0.001*	0.013*
Blood pressure ($n = 260$)								
SBP (mmHg)	131 [122.0–142.0]	129.0 [117–140]	136.0 [125–148.0]	136.2 ± 16.3	138.4 ± 12.9	< 0.001*	0.003*	0.011*
DBP (mmHg)	81 [77.0–88.0]	80.0 [74.5–86.0]	83.0 [79.0–90.0]	84.0 [80.0–90.0]	80.2 ± 11.5	0.005*	0.848	< 0.001*
Smoking status								
Never smoked	147 (47.2)	83 (49.1)	64 (44.4)	35 (42.2)	29 (49.2)	0.893	0.543	0.623
Ex-smoker	131 (42.1)	68 (40.2)	63 (44.4)	36 (43.4)	27 (45.8)			
Smoker	33 (10.6)	18 (10.7)	15 (10.6)	12 (14.5)	3 (5.1)			
Alcohol status								
Limited alcohol consumption[a]	215 (69.1)	120 (71.0)	95 (66.9)	62 (74.7)	32 (54.2)	0.840	0.111	0.531
Binge drinking[b]	17 (5.5)	7 (4.1)	10 (7.0)	9 (10.8)	1 (1.7)	0.081	0.295	0.046*
Weekly	10 (58.8)	2 (28.6)	8 (80.0)	7 (77.8)	1 (100)			
Monthly	7 (41.1)	5 (71.4)	2 (20.0)	2 (22.2)	0 (0)			
Ex-drinker	7 (2.3)	3 (1.8)	4 (2.8)	3 (3.6)	1 (1.7)			
Income								
Low	41 (13.2)	23 (13.6)	18 (12.7)	9 (10.8)	9 (15.3)	0.808	0.754	0.535
High	270 (86.8)	146 (86.4)	124 (87.3)	74 (89.2)	50 (84.7)			
Educational status								
Low	34 (11.0)	21 (12.4)	13 (9.1)	4 (4.8)	9 (15.3)	0.090	0.902	0.005*

(Continues)

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TABLE 1 | (Continued)

	Total ($n=311$)	No steatosis ($n=169$)	Steatosis ($n=142$)	Steatosis without T2DM ($n=83$)	Steatosis and T2DM ($n=59$)	P[1]	P[2]	P[3]
Mid	123 (39.5)	56 (33.1)	67 (47.1)	46 (55.4)	21 (35.6)			
High	154 (49.5)	92 (54.4)	62 (43.7)	33 (39.8)	29 (49.2)			
Laboratory values								
ASAT (U/L) ($n=269$)	22 [18.0–27.0]	21.0 [17–24.0]	23.0 [20–30.0]	23.0 [20.0–28.3]	23.0 [19.0–33.0]	0.001*	0.019*	0.004*
ALAT (U/L) ($n=281$)	22 [16.0–34.0]	20.0 [15.0–27.0]	26.0 [19.0–44.0]	24.0 [18.5–44.0]	29.0 [19.0–51.0]	<0.001*	<0.001*	<0.001*
GGT (U/L) ($n=281$)	24 [15.0–38.0]	20.0 [13–32]	28.0 [21–44.5]	26.0 [18.0–46.0]	31.0 [24.3–44.8]	<0.001*	<0.001*	0.002*
Thrombocytes ($*10^9$/L) ($n=284$)	250 [207.3–293.8]	251.0 [211.5–297.0]	246.5 [202.5–290.5]	251.0 [201.8–289.8]	242.0 [202.3–292.5]	0.543	0.672	0.587
Non-invasive tests								
VCTE (kPa)	5.1 [4.0–6.6]	4.6 [3.8–5.7]	5.7 [4.3–8.1]	5.4 [4.1–6.9]	6.6 [5.5–10.1]	<0.001*	<0.001*	0.009*
VCTE > 8 kPa	51 (16.4)	14 (8.3)	37 (26.1)	15 (18.1)	22 (37.3)	<0.001*	<0.001*	0.034*
VCTE > 12 kPa	15 (4.8)	3 (1.8)	12 (8.5)	4 (4.8)	8 (13.6)	0.006*	<0.001*	0.167
CAP (dB/m)	269.0 [230.0–317.0]	236.0 [204.0–256.0]	327.0 [301.0–357.0]	317.0 [292.0–353.0]	335.0 [56.0]	<0.001*	<0.001*	<0.001*
FAST score ($n=196$)	0.09 [0.04–0.19]	0.05 [0.03–0.10] ($n=109$)	0.18 [0.09–0.38] ($n=87$)	0.15 [0.09–0.34] ($n=61$)	0.23 [0.09–0.46] ($n=26$)	<0.001*	<0.001*	<0.001*
FAST ≥ 0.67	5 (2.6)	0	5 (5.7)	2 (3.3)	3 (11.5)	<0.001*	<0.001*	<0.001*
MASLD	141 (45.3)	0	141 (99.3)	82 (98.8)	59 (100)	<0.001*	<0.001*	<0.001*

Note: Data are presented as mean ± standard deviation, median [interquartile range], or number (%). P[1]: significant difference between steatosis and no steatosis, P[2]: no steatosis vs. steatosis with T2DM, P[3]: no steatosis vs. steatosis without T2DM. * indicates all significant results ($p<0.05$).

Abbreviations: ALAT, alanine aminotransferase; ASAT, aspartate aminotransferase; BMI, body mass index; CAP, controlled attenuation parameter; DBP, diastolic blood pressure; FAST, FibroScan-AST; GGT, gamma-glutamyl transpeptidase; MetS, metabolic syndrome; SBP, systolic blood pressure; T2DM, type 2 diabetes mellitus; VCTE, vibration-controlled transient elastography.

[a]Alcohol use was defined as the consumption of alcohol but without excessive alcohol usage (< 2/3E/day women/men) as those participants were excluded.

[b]Binge drinking is defined as drinking once per week or once per month, more than six units of alcohol on one occasion.

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TABLE 2 | Comparison of the quality of life questionnaires between people with or without steatosis and/or diabetes.

Questionnaire	Total ($n=311$)	No steatosis ($n=169$)	Steatosis ($n=142$)	Steatosis without T2DM ($n=83$)	Steatosis and T2DM ($n=59$)	P[1]	P[2]	P[3]
Depression (PHQ9)	4.0 [1.0–7.5]	4.0 [1.0–7.0]	3.0 [1.0–8.0]	4.0 [1.0–9.0]	3.0 [1.0–5.0]	0.955	0.322	0.477
Anxiety (GAD7)	2.0 [0.0–5.5]	2.0 [0.0–5.0]	1.0 [0.0–6.0]	3.0 [0.0–6.0]	1.0 [0.0–4.0]	0.557	0.049*	0.471
SF36						0.204	0.776	0.038*
Physical functioning	85.0 [70.0–95.0]	90 [70.0–100.0]	85 [70.0–95.0]	85.0 [70–95]	85.0 [70.0–95.0]	0.024*	0.084	0.057
Limitations physical health	100.0 [50.0–100.0]	100 [50.0–100.0]	100 [50.0–100.0]	100.0 [25.0–100]	100 [50.0–100.0]	0.856	0.739	0.599
Limitations of emotional health	100.0 [100.0–100.0]	100 [66.7–100.0]	100 [100.0–100.0]	100 [100.0–100.0]	100 [100.0–100.0]	0.175	0.035*	0.782
Energy and fatigue	65.0 [50.0–80.0]	65.0 [50.0–80.0]	62.5 [45.0–75.0]	60.0 [45–75]	65.0 [25.0]	0.157	0.548	0.116
Emotional well-being	80.0 [64.0–88.0]	80.0 [64.0–88.0]	82.0 [68–88]	80.0 [56–88]	88.0 [76.0–92.0]	0.213	0.002*	0.504
Social functioning	87.5 [75.0–100.0]	87.5 [75.0–100.0]	87.5 [75.0–100.0]	87.5 [62.5–100]	100.0 [87.5–100.0]	0.927	0.068	0.191
Pain	77.5 [57.5–100.0]	77.5 [67.5–100.0]	77.5 [57.5–90.0]	80.0 [57.5–90.0]	77.5 [57.5–90.0]	0.195	0.284	0.304
General health	40.4 [30.6–45.4]	40.6 [35.4–50.2]	35.6 [30.6–40.8]	35.6 [10.2]	35.8 [14.8]	< 0.001*	0.012*	< 0.001*
WPAI								
Absenteeism (%) ($n=128$)	0.0 [0.0–0.0]	0 [0–0]	0 [0–0]	0.0 [0.0–0.0]	0 [0.0–0.0]	0.016*	0.275	0.009*
Absenteeism present	14 (10.9)[a]	4 (5.3)[b]	10 (18.7)[c]	8 (21.6)[d]	2 (12.5)[e]	0.016*	0.294	0.009*
Presenteeism (%) ($n=81$)	0.0 [0.0–30.0]	10.0 [0.0–20.0]	10.0 [0.0–50.0]	10.0 [0.0–50.0]	5.0 [0.0–17.5]	0.276	0.790	0.118
Presenteeism present	45 (55.5)	23 (51.1)[b]	22 (61.1)[c]	17 (65.4)[d]	5 (50.0)[e]	0.368	1.000	0.243
Work productivity loss ($n=86$)	10.0 [0.0–50.0]	10.0 [0.0–30.0]	20.0 [0.0–61.3]	40.0 [0.0–70.0]	10.0 [0.0–47.5]	0.054	0.766	0.021*
Activity impairment	10.0 [0.0–50.0]	10.0 [0.0–50.0]	20.0 [0.0–50.0]	20.0 [0.0–50.0]	30.0 [0.0–50.0]	0.037*	0.132	0.068

Note: Data are presented as median [interquartile range], or number (%). P[1]: significant difference between steatosis and no steatosis, P[2]: no steatosis vs. steatosis with T2DM, P[3]: no steatosis vs. steatosis without T2DM. * indicates all significant results ($p<0.05$).

Abbreviations: CAP, controlled attenuation parameter; GAD-7, General Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9; SF-36, Short Health Form-36; VCTE, vibration controlled-transient elastography; WPAI, Workers Productivity and Activity Impairment.

[a] $n=128$ (absenteeism).
[b] $n=75$ (absenteeism) and $n=45$ (presenteeism).
[c] $n=53$ (absenteeism) and $n=36$ (presenteeism).
[d] $n=37$ (absenteeism) and $n=26$ (presenteeism).
[e] $n=16$ (absenteeism) and $n=10$ (presenteeism).

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TABLE 3 | Correlation analysis with VCTE and CAP for the total population.

	Total population ($n = 311$)				No steatosis ($n = 169$)				Steatosis ($n = 142$)			
	VCTE	*p*	CAP	*p*	VCTE	*p*	CAP	*p*	VCTE	*p*	CAP	*p*
Depression (PHQ9)	−0.071	0.215	0.007	0.906	−0.117	0.130	−0.006	0.935	−0.004	0.962	0.054	0.520
Anxiety (GAD7)	−0.110	0.054	−0.064	0.261	−0.085	0.270	−0.072	0.352	−0.105	0.215	−0.066	0.433
SF36												
Physical functioning	−0.068	0.234	−0.193	< 0.001*	−0.050	0.515	−0.221	0.004*	−0.004	0.966	−0.081	0.340
Limitations of physical health	0.035	0.542	−0.031	0.586	0.060	0.440	−0.095	0.220	0.002	0.977	0.027	0.747
Limitations of emotional health	0.082	0.149	0.047	0.413	−0.008	0.916	−0.117	0.130	0.138	0.101	0.079	0.351
Energy and fatigue	0.025	0.656	−0.112	0.049*	0.095	0.219	−0.091	0.240	0.015	0.859	−0.071	0.401
Emotional well-being	0.190	< 0.001*	0.094	0.099	0.154	0.046*	0.075	0.334	0.191	0.023*	0.041	0.627
Social functioning	0.109	0.054	0.012	0.837	0.093	0.231	−0.023	0.762	0.129	0.127	0.065	0.441
Pain	0.040	0.479	−0.116	0.040*	0.077	0.318	−0.124	0.107	0.043	0.608	−0.076	0.366
General health	−0.105	0.064	−0.235	< 0.001*	0.003	0.969	−0.134	0.081	−0.090	0.285	−0.015	0.858
WPAI												
Absenteeism ($n = 128$)	0.008	0.928	0.256	0.004*	−0.118	0.312	0.046	0.695	0.010	0.946	0.285	0.039*
Presenteeism ($n = 81$)	−0.112	0.318	0.117	0.298	−0.199	0.190	0.011	0.942	−0.141	0.413	0.041	0.815
Work productivity loss ($n = 86$)	−0.048	0.662	0.231	0.032*	−0.179	0.228	0.026	0.861	−0.088	0.596	0.212	0.194
Activity impairment	0.018	0.750	0.137	0.015*	−0.041	0.597	0.108	0.160	−0.004	0.958	0.023	0.784

	Steatosis without T2DM ($n = 83$)				Steatosis and T2DM ($n = 59$)			
	VCTE	*p*	CAP	*p*	VCTE	*p*	CAP	*p*
Depression (PHQ9)	−0.0219	0.793	0.119	0.282	0.111	0.403	−0.070	0.598
Anxiety (GAD7)	−0.050	0.653	−0.027	0.812	−0.073	0.583	−0.051	0.702
SF36								
Physical functioning	0.062	0.579	−0.078	0.482	−0.143	0.280	−0.066	0.619
Limitations of physical health	−0.002	0.988	0.039	0.729	−0.081	0.542	0.030	0.821
Limitations of emotional health	0.099	0.373	0.094	0.398	0.138	0.298	−0.029	0.829
Energy and fatigue	0.043	0.697	−0.070	0.530	−0.120	0.366	−0.107	0.419

(Continues)

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TABLE 3 | (Continued)

	Steatosis without T2DM ($n=83$)				Steatosis and T2DM ($n=59$)			
	VCTE	p	CAP	p	VCTE	p	CAP	p
Emotional well-being	0.161	0.147	−0.014	0.903	0.011	0.934	0.000	1.000
Social functioning	0.148	0.182	−0.021	0.850	−0.017	0.896	0.118	0.375
Pain	0.086	0.440	−0.029	0.796	−0.042	0.752	−0.132	0.320
General health	−0.114	0.303	0.023	0.835	−0.118	0.374	−0.067	0.614
WPAI								
Absenteeism ($n=128$)	−0.028	0.872	0.283	0.090	0.185	0.493	0.411	0.114
Presenteeism ($n=81$)	0.081	0.693	0.181	0.375	−0.662	0.037*	−0.190	0.599
Work productivity loss ($n=86$)	0.002	0.994	0.334	0.089	−0.275	0.388	0.129	0.691
Activity impairment	−0.125	0.259	0.025	0.825	0.222	0.090	0.009	0.944

Note: * indicates all significant results ($p<0.05$).
Abbreviations: CAP, controlled attenuation parameter; GAD-7, General Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9; SF-36, Short Health Form-36; VCTE, vibration controlled-transient elastography; WPAI, Workers Productivity and Activity Impairment.

participants, presenteeism in 81 (26.0%), and overall work impairment in 86 (27.7%) (Table 2).

Significant differences in absenteeism were seen between people with and without steatosis ($p=0.016$) and between people without steatosis and people with steatosis but without T2DM ($p=0.009$) (Table 2). Sex-stratified analyses showed no significant differences between the subgroups for absenteeism (Table S2). In the total cohort, a correlation was observed between CAP and absenteeism ($r=0.256$, $p=0.004$). Subgroup analysis showed a positive correlation between CAP and absenteeism ($r=0.285$, $p=0.039$) in people with steatosis (Table 3). People with absenteeism had a higher waist circumference ($p=0.001$), CAP value ($p=0.004$), more MASLD ($p=0.013$), and MetS ($p=0.022$) compared to those without absenteeism, respectively (Table S2). Next, people with absenteeism had higher scores for depression ($p=0.018$) and anxiety ($p=0.029$) and lower scores for physical functioning ($p=0.016$), emotional well-being ($p=0.032$), social function ($p<0.001$), and pain ($p=0.007$) (Table S2). A correlation analysis showed significant correlations for absenteeism with anxiety ($r=0.288$, $p=0.036$), emotional well-being ($r=-0.297$, $p=0.031$), and social functioning ($r=-0.382$) in participants with steatosis (Table S4). Absenteeism was present in 14 (10.9%) participants who worked. An in-depth search showed that absenteeism was not related to steatosis or obesity in four people (Table S5). Among the ten remaining participants with absenteeism, four had no accessible EPDs, three had no identifiable reason for absenteeism recorded in their EPDs, and for the final three participants, reasons were noted, but it was unclear whether the absenteeism was related to obesity or steatosis.

Presenteeism was observed in 45 (55.5%) of the participants who worked. No notable differences were identified between the subgroups (Table 2). People with presenteeism had no significant differences in clinical characteristics compared to those without presenteeism, though they had higher scores for depression and anxiety ($p<0.001$) and lower scores for physical functioning ($p=0.017$), energy and fatigue ($p<0.001$), emotional well-being ($p=0.002$), social functioning ($p<0.001$), pain ($p<0.001$), and general health ($p=0.028$) (Table S6). Correlations between presenteeism and the other QoL-related questionnaires were found but were not subgroup-specific (Table S4). The binomial logistic regression analysis for presenteeism (yes/no) with correction for age, smoking, alcohol use, sex, BMI, and T2DM yielded no significant results (β 1.001, 95% CI 0.982 to 1.050).

A percentage of 10.0 [0.0–30.0] work productivity loss was observed in the group of people with steatosis vs. 20 [0.0–61.3] in people without steatosis, leading to a borderline significant difference ($p=0.054$) (Table 2). The overall percentage of work productivity loss was highest in the non-diabetes steatosis group, 40.0 [0.0–70.0], compared to those without steatosis, 10.0 [0.0–30.0] ($p=0.021$) (Table 2). In the total group, a correlation was found between work productivity (0.231, $p=0.032$) and a higher CAP. Correlations between work productivity and the other QoL-related questionnaires were found, but were not subgroup-specific (Table S4). Logistic regression analysis showed a borderline significant odds ratio of 1.020 (95% CI 0.999–1.042, $p=0.057$) for work productivity independent of BMI, age, sex, T2DM, smoking, or alcohol, and a significant odds ratio of 1.023

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TABLE 4 | The binomial logistic regression analysis results with correction for age, sex, BMI, and T2DM.

	Model 1: Steatosis (yes (CAP > 275 dB/m) or no) with correction for age, smoking, alcohol use and sex		Model 2: Steatosis (yes (CAP > 275 dB/m) or no) with correction for BMI and T2DM		Model 3: Steatosis (yes (CAP > 275 dB/m) or no) with correction for age, smoking, alcohol use, sex, BMI and T2DM		Model 4: Steatosis (yes (CAP > 275 dB/m) or no) with correction for age, smoking, alcohol use, sex, BMI, T2DM, income and educational level	
	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p	Odds ratio (95% CI)	p
Depression (PHQ9)	1.006 (0.936–1.051)	0.795	0.972 (0.923–1.024)	0.292	0.979 (0.928–1.033)	0.436	0.975 (0.924–1.029)	0.357
Anxiety (GAD7)	0.996 (0.942–1.054)	0.894	0.988 (0.923–1.057)	0.719	0.994 (0.925–1.064)	0.852	0.988 (0.923–1.059)	0.798
SF36								
Physical functioning	0.992 (0.980–1.003)	0.150	1.010 (0.996–1.024)	0.160	1.009 (0.995–1.024)	0.204	1.010 (0.995–1.024)	0.189
Limitations physical health	0.999 (0.993–1.005)	0.671	1.001 (0.994–1.008)	0.768	1.000 (0.993–1.008)	0.910	1.000 (0.993–1.008)	0.925
Limitations emotional health	1.004 (0.997–1.010)	0.312	1.003 (0.995–1.011)	0.459	1.002 (0.994–1.010)	0.604	1.002 (0.994–1.010)	0.604
Energy and fatigue	0.989 (0.977–1.000)	0.052	0.998 (0.985–1.011)	0.783	0.995 (0.981–1.009)	0.479	0.996 (0.982–1.010)	0.595
Emotional well-being	1.002 (0.990–1.014)	0.747	1.004 (0.989–1.018)	0.622	1.003 (0.988–1.018)	0.723	1.003 (0.988–1.019)	0.658
Social functioning	0.998 (0.988–1.008)	0.722	1.001 (0.989–1.013)	0.876	0.999 (0.986–1.011)	0.842	0.999 (0.987–1.012)	0.935
Pain	0.994 (0.984–1.003)	0.188	1.005 (0.993–1.016)	0.409	1.003 (0.992–1.015)	0.589	1.004 (0.993–1.016)	0.488
General health	0.953 (0.931–0.975)	< 0.001*	0.970 (0.944–0.995)	0.021*	0.969 (0.943–0.995)	0.019*	0.970 (0.944–0.996)	0.026*
WPAI								
Absenteeism ($n = 128$)	1.017 (1.001–1.034)	0.040*	1.016 (0.996–1.036)	0.109	1.016 (0.995–1.037)	0.144	1.020 (0.999–1.041)	0.062
Presenteeism ($n = 81$)	1.018 (0.997–1.040)	0.101	1.016 (0.989–1.043)	0.245	1.022 (0.992–1.053)	0.150	1.020 (0.989–1.051)	0.206
Work productivity loss ($n = 86$)	1.017 (1.002–1.032)	0.025*	1.019 (1.000–1.039)	0.046*	1.020 (0.999–1.042)	0.057	1.023 (1.001–1.045)	0.037*
Activity impairment	1.009 (1.001–1.017)	0.023*	1.002 (0.993–1.012)	0.639	1.003 (0.994–1.012)	0.538	1.002 (0.993–1.012)	0.650

Note: * indicates all significant results ($p < 0.05$).
Abbreviations: BMI, body mass index; CAP, controlled attenuation parameter; GAD-7, General Anxiety Disorder-7; PHQ-9, Patient Health Questionnaire-9; SF-36, Short Health Form-36; T2DM, type 2 diabetes mellitus; WPAI, Workers Productivity and Activity Impairment.

(95% CI 1.001–1.045, $p = 0.037$) when also correcting for income and degree of education (Table 4).

In their free time, the total cohort experienced a 10.0 [0.0–50.0] percent impairment in activities outside of work. A significant difference was found when comparing those with or without steatosis ($p = 0.037$). When further stratified by sex, the significant difference in activity impairment between steatosis and no steatosis was observed in women ($p = 0.049$), but not in men (Table S2). In the total group, a positive correlation was found

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between free-time activity impairment ($r = 0.137$, $p = 0.015$) and a higher CAP. Correlations between activity impairment and the other QoL-related questionnaires were observed but were not subgroup-specific (Table S4).

Finally, the correlation analysis was repeated, omitting the participants without MASH or advanced fibrosis (≥12 kPa). The results of the correlation analysis remained similar (data not shown). Lastly, the FAST score showed no correlations with any of the items of the WPAI questionnaire (Table S7).

4 | Discussion

To our knowledge, this is the first prospective study concerning the influence of MASLD on general health perception, quality of life, and work productivity in an early-stage MASLD population with a low prevalence of advanced fibrosis (4.7%) and suspected MASH (2.6%) diagnosed using non-invasive tests.

Our analysis showed a significant difference in physical functioning and general health perception levels between individuals with steatosis and those without, as measured by the SF-36. This was also seen in the correlation analysis for the total cohort. Having T2DM did not change the results of the correlation. Logistic regression analysis confirmed a decreased odds ratio for general health in the case of steatosis, independent of age, sex, BMI, T2DM, smoking, alcohol use, income, and degree of education. Given the limited literature on MASLD, as it was only introduced in 2023, and QoL, we referenced available studies on NAFLD (which largely overlaps with (although is not identical to) MASLD, as long as MASLD is the only aetiology of steatosis) to contextualise our findings [27]. A small cohort study using the SF-36 performed by Sayiner et al. compared data from biopsy-proven cirrhotic MASLD ($n = 30$) and noncirrhotic MASLD ($n = 59$) patients [29]. Compared with our results, they found lower scores across all previously named domains, except general health perception, which was lower in our study cohort. The explanation for the difference is complex, as it could be expected that cirrhotic patients would have lower general health perception. Maybe the period during which our study took place, partly during the COVID-19 pandemic, skewed our study results, or physical differences like a higher BMI (39.9 ± 8.8 (Sayiner et al.) vs. 30.3 [27.7–34.3] kg/m^2), lay at the basis for the difference in general health. On the other hand, the small sample size ($n = 59$) of their study population [30] may be an explanation. In addition, Sayiner et al. performed a multiple regression analysis, adjusting for age, sex, and ethnicity, which showed no association between QoL measured with SF-36, BMI, and T2DM, findings comparable to ours [29]. In addition, sex-related differences in QoL were also investigated in our study cohort. Previous studies have shown, for example, that women experience more fatigue, but we did not observe these differences [13].

Although the association between anxiety and depression, and MASLD has been thoroughly described in literature [30–33], in our study cohort, depression and anxiety were absent in individuals with or without steatosis. Additionally, no associations were found between steatosis and anxiety or depression, suggesting that early-stage MASLD has no relationship with anxiety and depression. Furthermore, T2DM did not affect the relationship between depression and anxiety compared to individuals without T2DM. These conflicting findings, when compared to previous studies, could be attributed to variations in sample size and the socioeconomic backgrounds of participants. Additionally, differences in the prevalence of MASH and advanced fibrosis, which have been linked to depression and anxiety, may also contribute to these discrepancies [30, 31].

Within our study cohort, individuals with steatosis exhibited higher levels of absenteeism, which is associated with a loss in work productivity, compared to those without steatosis. Furthermore, a positive correlation was observed between increased steatosis severity, absenteeism, and overall work impairment across the total cohort. This trend persisted in subgroup analyses for individuals with steatosis. Nevertheless, these findings should be interpreted cautiously, as an in-depth search of the EPD revealed that in 28.5% of cases, no direct link between steatosis and absenteeism could be established. For the remaining participants, it remained uncertain whether absenteeism was attributable to steatosis or obesity.

Although it is uncertain whether the observed association with work productivity is caused by steatosis (the study lacked adequate power), several other studies have found a difference in work productivity between individuals with and without MASLD. For example, Balp et al. assessed the relationship between MASH and work productivity using data from the 2016 National Health and Wellness Survey, which was conducted in France, Germany, Italy, Spain, and the UK [32]. MASH patients ($n = 184$) exhibited worse WPAI scores with significantly more overall work impairment (49.2% vs. 30.8%) compared to the matched general population cohort ($n = 736$). Contrary to our findings, Balp et al. reported higher rates of all WPAI scores, which may be attributed to their use of a self-reported physician-diagnosed MASH cohort. In contrast, our study relied on a FibroScan-diagnosed MASLD cohort. Additionally, the lack of specific data on steatosis prevalence in the general population cohort of Balp et al. complicates direct comparisons. Nevertheless, it is also known that MASH is the more progressive form of the disease spectrum and has severe consequences on QoL, especially when significant or advanced fibrosis is present [33]. The differences in WPAI scores disappeared when the MASH cohort was compared to the matched T2DM cohort, indicating a similar burden of MASH on work and productivity as T2DM [32]. Analogue to our findings, WPAI scores for people with steatosis but with or without T2DM were similar. Geier and colleagues retrospectively analysed data from the Ipsos NASH-Atlas cohort (United States, France, and Germany) to assess the burden on QoL with the WPAI-SHP in a partially biopsy-confirmed MASH cohort ($n = 299$) with a high prevalence of advanced fibrosis (32.8%) [34]. Asymptomatic MASH patients experienced some degree of absenteeism (5.6%), presenteeism (4.4%), overall work impairment (9.0%), and activity impairment (14.2%) [34]. Although they analysed a MASH cohort, their results were very similar to our study cohort, with a comparable percentage of overall work impairment (10%) and activity impairment (20%). Data from the Global NAFLD/NASH Registry (GNR) in high-income countries also showed comparable results. They found an 8% work productivity impairment and a 15% activity impairment [35]. Moreover, in line with our findings, although a risk factor for MASLD, T2DM has been shown

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in several studies to have no additional effect on QoL compared to MASLD patients without T2DM [29, 36, 37]. The results of the current study, although requiring cautious interpretation, suggest, in conjunction with existing literature, a potential link between MASLD and reduced work productivity that warrants thorough investigation in future research, as this has significant socioeconomic implications.

The results of our study show that the association between early-stage MASLD and QoL seems to be limited to reduced physical fitness and general health. However, we hypothesise that the low-grade inflammation present in MASLD patients may be a driver of progression to more severe stages, which can affect QoL, a phenomenon not observed in the early stages of MASLD. This study did not investigate low-grade inflammation in relation to QoL. Still, the number of patients with fibrosis was low, suggesting that chronic inflammation was not prominent in this cohort. Gradual worsening over many years, as happens in MASLD, could lead to a noticeable decline in mental health, as seen in MASH and in people who have cirrhosis [38, 39]. This deterioration may, in turn, trigger psychological challenges, exacerbating workplace performance. These effects are thought to be mediated through the brain-liver axis [40, 41]. Although current evidence is suggestive rather than conclusive, these findings underscore the necessity for further prospective and longitudinal research to gain a clearer understanding of these relationships.

This study has several strengths that enhance its significance and reliability. The inclusion of a large population with a low prevalence of advanced fibrosis and MASH provides valuable insights into earlier stages of MASLD, which are often underrepresented in research. Additionally, the direct comparison between MASLD and non-MASLD populations allows for a deeper understanding of the associations with QoL. A strength of the study is its focus on work productivity, an often overlooked but critical aspect of the disease's burden. Furthermore, the investigation encompassed a broad spectrum of QoL parameters, including general health, depression, anxiety, etc., offering a comprehensive assessment of MASLD's association with daily living. Lastly, the well-characterised population ensures robust data quality, providing a solid foundation for the study's findings.

This study has several limitations. First, not all participants completed the questionnaires in full. Reminders were sent to participants at least twice, five and ten days after the initial email was sent with the link containing the questionnaire. However, some participants were unable to complete the questionnaire online, leading to the distribution of paper copies, which often resulted in missing answers since they were not required to complete every question before proceeding. Second, some of the participants were recruited during the COVID-19 pandemic. It is possible that the pandemic contributed to an overall dissatisfaction with life and, therefore, reduced QoL in the total study cohort unrelated to MASLD [42]. Also, the pandemic could have had an influence on absenteeism or work productivity, as people were required to stay at home if they had a positive COVID-19 test. Thirdly, the diagnosis of MASLD and MASH was based on FibroScan measurements and the FAST score, not on a liver biopsy, which remains the gold standard for MASLD and MASH diagnosis [43]. In addition, there is an ongoing debate regarding the optimal CAP cut-off value for diagnosing steatosis. While the 2021 guidelines recommend a threshold of 275 dB/m [17], the 2024 guidelines propose a lower cut-off of 248 dB/m [18]. The choice of cut-off can significantly influence prevalence estimates and study outcomes. Furthermore, the study utilised self-reported questionnaires, which are subject to recall and reporting bias, and alternative tools for detecting depression and anxiety might have been more sensitive in identifying subtle changes. The study lacked the power to fully investigate sex differences and work productivity, yielding correlation findings without robust regression results; therefore, the results of this analysis should be interpreted with care. Moreover, there is an oversampling of people with risk factors, for example, T2DM and obesity. Also, selection bias could not be completely avoided; flyers were distributed in the waiting rooms of endocrinology departments and primary care clinics, but these were mainly taken by older people, as children were excluded from the study. Additionally, some people were referred by their GP or endocrinologist based on deviant laboratory values. Finally, although some findings reached statistical significance, their clinical relevance remains uncertain, and the study has a cross-sectional design, and therefore, causal relationships cannot be made.

5 | Conclusion

Early-stage MASLD was associated with impaired general health and physical functioning in this prospective cohort study. However, no significant association was found between MASLD and depression or anxiety, even in individuals with T2DM. While steatosis appeared to contribute to work impairment, it remains unclear whether these effects are directly due to steatosis, obesity, or other unrelated factors, warranting a cautious interpretation. These findings highlight the importance of further research in larger and more diverse populations to clarify and expand upon these observations.

Author Contributions

L.J.M.H. contributed to the conception and design, participated in the acquisition of data, analysed and interpreted data, drafted the manuscript, revised the manuscript critically for important intellectual content, and provided final approval of the version to be published. L.J.M.H. is also the guarantor of this work and, as such, had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of the data analysis. The co-authors contributed to the conception and design, revised the manuscript critically for important intellectual content, and provided final approval of the version to be published.

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Ethics Statement

The study protocol was conducted according to the Helsinki Declaration after approval by the Ethics Committee of Hasselt University CME2020 019, University Hospital Antwerp 19/44/495, the Medical Ethical Committee of Maastricht University/Maastricht University Medical Centre NL73265.068.20, and the Committee Medical Ethics of Ziekenhuis Oost-Limburg CTU2020015.

Consent

All participants gave written consent.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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