Vibration-controlled transient elastography for non-invasive screening of liver fibrosis and steatosis in Turkish patients with psoriasis: A cross-sectional study

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Abstract

Background and Aim: The prevalence of fibrosis and steatosis in patients with psoriasis, as determined by vibration-controlled transient elastography (VCTE), has not been evaluated in Turkiye to date. The present cross-sectional study aims to present the first systematic screening results, focusing on two primary objectives: 1) establishing the prevalence of fibrosis and steatosis, and 2) identifying independent predictors for liver stiffness measurement (LSM) and controlled attenuation parameter (CAP) values in this patient population.

Materials and Methods: Patients were eligible for inclusion if they had a confirmed diagnosis of psoriasis by a qualified dermatologist based on characteristic signs and symptoms and histopathological examination, and had undergone VCTE for LSM and CAP measurements.

Results: The diagnosis of severe fibrosis and cirrhosis – identified by LSM values of 10.0−13.9 and ≥14.0 kPa, respectively – was significantly prevalent (7.0% and 10.1%, respectively) among a sizeable cohort of relatively young Turkish patients with psoriasis (n=328; mean age: 49.5±12.7 years). Additionally, severe steatosis, as diagnosed by VCTE and characterized by a CAP value exceeding 290 dB/m, was identified in up to 43.3% of patients. Although body mass index (BMI) was the only variable found to be independently associated with LSM, multivariable linear regression analysis failed to identify any statistically independent predictor of CAP values.

Conclusion: The prevalence of hepatic fibrosis and steatosis in Turkish patients with psoriasis is far from negligible, with BMI identified as an independent risk factor for fibrosis.

Keywords: Fibrosis; psoriasis; steatosis; transient elastography; vibration-controlled.

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Introduction

Psoriasis is a chronic, immune-mediated inflammatory skin disease that persists over an individual's lifetime.[1] This condition is linked to the development of several comorbidities, including psoriatic arthropathy, cardiovascular disease, metabolic syndrome, obesity, diabetes mellitus, dyslipidemia, and hepatic disorders.[2] Several studies have uncovered a substantial association between psoriasis and non-alcoholic fatty liver disease (NAFLD).[3–5] Remarkably, individuals with psoriasis have been observed to have a two-fold increased likelihood of developing liver fibrosis and hepatic steatosis, even after considering other established risk factors.[6] Individuals with moderate-to-severe psoriasis seem to be disproportionately impacted, an effect that may be intensified by the use of systemic immunomodulators like methotrexate, which carry a potential risk of hepatotoxicity.[6,7] As a result, it is crucial to detect fibrosis and steatosis at an early stage in individuals with psoriasis to minimize the potential for liver-related complications.[8]

Vibration-controlled transient elastography (VCTE) is a non-invasive diagnostic technique that evaluates liver stiffness by examining the velocity of a shear wave generated inside the liver.[9,10] The liver stiffness measurement (LSM) serves as a marker for hepatic fibrosis.[11,12] Concurrently, VCTE obtains the controlled attenuation parameter (CAP), an indicator of hepatic steatosis, by assessing the extent of ultrasound signal attenuation as it passes through the liver parenchyma.[13,14] Therefore, VCTE has the potential to function as a comprehensive screening tool that can assess both fibrosis and steatosis, making it an ideal diagnostic option for individuals at risk of liver disease. In a recent systematic review and meta-analysis, Marsh and colleagues examined fifteen studies from 2007 to 2019 that investigated the application of VCTE in psoriasis for evaluating hepatic fibrosis and steatosis.[15] The combined data included 1,536 patients diagnosed with either psoriasis or psoriatic arthritis. The researchers concluded that VCTE may serve as a practical and non-invasive method for detecting fibrosis and steatosis in this particular patient group.[15] Furthermore, regarding methotrexate-related hepatic fibrosis, VCTE exhibited a high level of specificity and negative predictive value.[15]

Presently, there exists a scarcity of published data on the link between psoriasis and liver disease in Turkiye. However, in a study conducted on a cohort of 518 patients, Tula et al.[16] reported that the leading causes of abnormal liver enzymes in Turkish patients with psoriasis were medications (57%) and NAFLD (22%). The prevalence of fibrosis and steatosis in patients with psoriasis, as determined by VCTE, has not been

evaluated in Turkiye to date. In light of this, the present cross-sectional study aims to present the first systematic screening results, focusing on two primary objectives: 1) establishing the prevalence of fibrosis and steatosis, and 2) identifying independent predictors for LSM and CAP values in this patient population.

Materials and Methods

Study Design and Participants

This study entails a cross-sectional examination of data collected prospectively over a decade-long period, spanning from 2013 to 2022. The patient group was identified at Department of Gastroenterology, Marmara University a renowned tertiary care center located in the metropolitan area of Istanbul, Turkiye. Patients were eligible for inclusion if they had a confirmed diagnosis of psoriasis by a qualified dermatologist based on characteristic signs and symptoms and histopathological examination, and had undergone VCTE. The identification of patients treated with methotrexate was conducted through a thorough review of their clinical charts. Individuals who had hepatitis B, hepatitis C, primary biliary cirrhosis, primary sclerosing cholangitis, hepatocellular carcinoma, or hereditary metabolic liver disease were excluded. The study was conducted in adherence to the principles set forth in the Declaration of Helsinki and received approval from the local ethics committee (reference number 09.2022.609). Given the cross-sectional nature of the study and the de-identification of data for analysis, the need for obtaining informed consent from participants was deemed unnecessary and subsequently waived by the ethics committee.

Vibration-Controlled Transient Elastography

An experienced operator (YY) performed the VCTE assessments using the FibroScan® 502 Touch device (Echosens SA, Paris, France), adhering to the guidelines provided by the manufacturer. Prior to the examination, patients with psoriasis fasted for at least three hours. The selection of the probe was carried out using an automated selection tool, choosing either the M (frequency: 3.5 Hz) or XL (frequency: 2.5 Hz) probe as required.[11,12] To determine LSM for each patient, a series of 10 consecutive valid measurements were taken (interquartile range-to-median ratio ≤0.3), and the median value was recorded.[11,12] The CAP is an algorithm that relies on the attenuation of ultrasound waves and is accessible through the FibroScan® system.[13,14] In each patient, CAP values were obtained concurrently with LSM values. The cutoff values for CAP and LSM were obtained from existing literature. Specifically, for fibrosis staging, the following ranges were used: F0: ≤6.0 kPa, F1: 6.1–7.0 kPa, F2: 7.1–9.9 kPa, F3: 10.0–13.9 kPa, F4: ≥14.0 kPa.[12] For steatosis grading, the ranges were: S0: <238 dB/m (<5%), S1: 238–258 dB/m (5%–33%), S2: 259–289 dB/m (34%–66%), S3: >290 dB/m (>66%).[12]

Statistical Analysis

Participants' general characteristics were summarized using descriptive statistics. Before conducting further analysis, relevant variables with skewed data distribution were subjected to a log-transformation to improve data normality. To identify independent predictors of LSM and CAP, multivariable stepwise linear regression analyses were conducted, wherein all variables listed in Table 1 were included as potential predictors/covariates. SPSS for Windows (version 20.0; IBM, Armonk, NY, USA) was utilized for all calculations, and statistical significance was determined by two-tailed p<0.05.

Table 1. General characteristics and VCTE parameters of patients with psoriasis included in the study

Variable	
Number of patients	328
Age, years	49.5±12.7
Male sex	163 (49.7%)
BMI, kg/m²	31.8±5.9
International normalized ratio	1.05±0.25
Creatinine, mg/dL	0.75±0.17
AST, U/L	35.8±33.1
ALT, U/L	54.7±44.2
Platelet count, 10⁹/L	260±74
Bilirubin, mg/dL	0.73±0.44
Total cholesterol, mg/dL	205±43
LDL cholesterol, mg/dL	155±62
Use of methotrexate	286 (87.1%)
LSM, kPa	8.54±8.48
CAP, dB/m	278.96±60.54

BMI: Body mass index; VCTE: Vibration-controlled transient elastography; BMI: Body mass index; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDL: Low-density lipoprotein; LSM: Liver stiffness measurement; CAP: Controlled attenuation parameter.

Results

Patients

A total of 328 Turkish patients with psoriasis (165 women and 163 men; mean age: 49.5±12.7 years; age range: 14–84 years) were included in the study (Table 1). Out of the total participants, 286 (87.1%) used methotrexate. The mean LSM was recorded at 8.54±8.48 kPa, with the lowest and highest values being 2.7 and 75.0 kPa, respectively. Additionally, the mean CAP was 278.96±60.54 dB/m, with a range of values between 100 and 400 dB/m.

Distribution and Predictors of Liver Stiffness Measurement

Fibrosis stage distribution among the 328 patients with psoriasis was determined based on LSM cutoff values reported in the literature.[12] Of these, 162 (49.4%) showed no evidence of fibrosis (F0), while 47 (14.3%) exhibited mild fibrosis (F1), 63 (19.2%) had moderate fibrosis (F2), 23 (7.0%) presented with severe fibrosis (F3), and 33 patients (10.1%) had cirrhosis (F4). Body mass index (BMI) was the only independent predictor of LSM values (beta=0.45, t=2.53, p=0.02) in multivariable linear regression analysis.

Distribution and Predictors of Controlled Attenuation Parameter

Based on the CAP cutoff values described in the literature,[12] 91 (27.7%) patients with psoriasis showed no signs of steatosis (S0), while mild steatosis (S1) was observed in 37 (11.3%) patients, moderate steatosis (S2) in 58 (17.7%), and severe steatosis (S3) in 142 (43.3%) patients. The multivariable linear regression analysis did not identify any significant independent predictor of CAP values.

Discussion

Since NAFLD often exhibits no symptoms until it reaches advanced stages,[17] the importance of screening for fibrosis and steatosis in at-risk patients is steadily increasing. The findings of our research reveal that the diagnosis of severe fibrosis and cirrhosis—identified by LSM values of 10.0–13.9 and ≥14.0 kPa, respectively[12]—is significantly prevalent (7.0% and 10.1%, respectively) among a sizeable cohort of relatively young Turkish patients with psoriasis, as determined by VCTE. Of all the covariates analyzed, BMI stood out as the only predictor that exhibited an independent association with LSM values. Our study also revealed that severe steatosis (S3), as diagnosed by VCTE and characterized by a CAP value exceeding 290 dB/m, can be identified in up to 43.3% of patients with psoriasis. By examining data from Turkiye for the first time, this research provides additional evidence to support prior investigations conducted in diverse geographic and ethnic populations, which suggest that hepatic fibrosis and steatosis are frequently observed in psoriatic patients.[3–8] In addition, our data confirm the effectiveness of LSM and CAP assessments as valuable tools in detecting these conditions.[15]

Evidence suggests an alarmingly high prevalence of NAFLD among the Turkish population, reaching rates of 48.3%.[18] This disparity highlights a considerable public health concern in Turkiye compared to other countries. Consequently, early detection of liver fibrosis and steatosis has emerged as a vital focus in public health, especially for individuals with predisposing conditions such as psoriasis. However, the extensive implementation of VCTE screening for psoriatic patients necessitates a thorough evaluation of its cost-effectiveness. Further research is essential to ascertain the practicality and feasibility of this approach in addressing this critical issue. Fibrosis significantly impacts both hepatic and extrahepatic outcomes in patients with NAFLD.[19] In this study, we determined BMI to be the sole predictor of LSM, a non-invasive indicator of fibrosis, among our psoriatic patients. Our current findings are in line with those of a prior investigation by Brunner et al.,[20] which examined a sample of 52 Hungarian patients. Their findings indicated that patients with psoriasis and higher BMI values were more likely to exhibit elevated hepatic stiffness values, which is in agreement with the results of our study.[20] Additionally, we confirmed that methotrexate treatment does not represent an independent risk factor for liver fibrosis in patients with psoriasis,[20] as its predictive value is clearly overshadowed by the influence of BMI. However, we were unable to identify independent predictors of steatosis in our study group. The absence of any significant independent predictor of steatosis by multivariate analysis in the tested covariates may suggest that they are equally prevalent in patients with psoriasis who do not develop steatosis. Alternatively, it could indicate that the risk of steatosis is associated with psoriasis itself rather than specific characteristics of psoriatic patients.

There are several limitations to this study. First, liver biopsy, which is currently the reference standard for diagnosing liver fibrosis and steatosis, was not conducted due to ethical concerns and the known limitations associated with the procedure.[21] Second, including a control group could have yielded more relevant results by allowing us to examine the fibrogenic and steatogenic potential of psoriasis. Third, the present study was not intended to evaluate the accuracy of VCTE in comparison to other imaging techniques, such as ultrasound. While ultrasound is less sensitive than VCTE, it is also less costly. In future research, a thorough comparison of the cost-effectiveness between these two methods is necessary. Lastly, it should be noted that our research relied on a single measurement of LSM and CAP. In order to gain a more comprehensive insight into the progression and natural history of fibrosis and steatosis in psoriasis, it is highly recommended that future investigations utilize repeated or serial measurements of these parameters. This approach will not only provide a more accurate representation of the natural history of hepatic involvement in psoriasis but also contribute to the development of more effective treatment interventions.

Conclusion

The prevalence of hepatic fibrosis and steatosis in Turkish patients with psoriasis is far from negligible, with BMI identified as an independent risk factor for fibrosis. Nonetheless, the long-term consequences of these conditions on hepatic and extrahepatic outcomes in psoriatic patients warrant additional research. Future studies should strive to elucidate the factors leading to liver involvement in this patient population and investigate potential strategies to alleviate their negative impact and enhance clinical outcomes.

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