The Use of Transient Elastography and FibroTest for Monitoring Hepatotoxicity in Patients Receiving Methotrexate for Psoriasis

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IMPORTANCE There is a need for noninvasive tools to monitor hepatotoxicity in patients with psoriasis who are receiving methotrexate sodium.

OBJECTIVE To evaluate the use of transient elastography (TE) and FibroTest (FibroSURE in the United States), an indirect serum marker of fibrosis, in this population.

DESIGN, SETTING, AND PARTICIPANTS Patients receiving methotrexate therapy for psoriasis between January 2008 and September 2009 were recruited from a dermatology outpatient department. Transient elastography and FibroTest were performed, and patients with abnormal results were considered for liver biopsy. Serial procollagen III peptide (PIIINP) results were recorded.

INTERVENTIONS Transient elastography uses pulse-echo ultrasonography to measure liver stiffness, and this result is an indirect measure of hepatic fibrosis. FibroTest is an indirect serum marker of hepatic fibrosis.

MAIN OUTCOMES AND MEASURES Procollagen III peptide, TE, and FibroTest results, as well as the need for liver biopsy in this cohort.

RESULTS Seventy-seven patients (41 male [53%]) were included. Fifty (65%) patients had a valid TE assessment, and 9 (18%) had an abnormal result (range, 7.1-11.3 kPa). Being overweight or obese increased the possibility of obtaining an invalid TE result significantly (P = .01). On univariate analysis body mass index (r = 0.40, P = .005) and age (r = 0.52, P = .005) were correlated with abnormal TE results. Seventy-one patients received a FibroTest and 11 of 70 analyzed (16%) had an abnormal result (METAVIR score >F1). Age (r = 0.31, P = .009), cumulative methotrexate dose (r = 0.31, P = .01), and duration of methotrexate therapy (r = 0.36, P = .002) were correlated with abnormal FibroTest results. There was no correlation between PIIINP levels and TE results or between PIIINP levels and FibroTest results. Steatosis was demonstrated in all 5 patients who received liver biopsies during the study. Two patients had hepatic fibrosis, with 1 showing a sinusoidal pattern of fibrosis attributed to steatohepatitis.

CONCLUSIONS AND RELEVANCE Transient elastography and FibroTest are effective noninvasive tools for monitoring hepatotoxicity in patients receiving methotrexate for psoriasis. We propose that the need for liver biopsy could be reduced if abnormalities in at least 2 tests (serial PIIINP, TE, or FibroTest) are required before biopsy is considered. This strategy should be evaluated in prospective studies.

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Methotrexate sodium is used frequently as monotherapy in the long-term management of severe psoriasis and is likely to remain popular because of its long-established safety profile and favorable cost profile. Liver fibrosis is the main disadvantage, although studies vary on the prevalence of methotrexate-induced liver injury in patients with psoriasis. Frequent evaluation of liver enzyme levels and procollagen III peptide (PIIINP) levels as well as periodic liver biopsies have been recommended during therapy.

The 2009 American Academy of Dermatology guidelines suggest consideration of liver biopsy in low-risk patients who have persistent abnormal liver function test results during treatment or after a total cumulative methotrexate sodium dose of 3.5 to 4.0 g. Liver biopsy is the criterion standard for diagnosing liver fibrosis, but it may be associated with significant morbidity and mortality of up to 0.33%, thereby limiting its use.

Patients with psoriasis may have comorbidities related to obesity, alcohol intake, and diabetes mellitus. These conditions increase the risk of liver disease and adverse effects related to the liver biopsy procedure. In addition, the histologic accuracy of a liver biopsy may be affected by sampling error, pathologist inconsistency in observations, and discontinuous and semiquantitative histologic scoring systems.

Although serial monitoring of PIIINP has reduced the need for liver biopsy considerably, some patients with high PIIINP values who proceed to biopsy do not have fibrosis or cirrhosis. Psoriatic arthritis occurs in approximately one-third of patients with psoriasis. Serum PIIINP levels may be a less reliable marker of liver fibrosis in these patients because elevated levels may be related to active joint disease.

Transient elastography (TE) using pulse-echo ultrasonography measures the propagation and velocity of the wave in the liver in one dimension, correlating with tissue stiffness and serving as an indirect measure of fibrosis. A meta-analysis of 9 studies involving TE for diagnosing fibrosis showed a sensitivity of 87% and specificity of 91%. The ability to differentiate mild from advanced fibrosis was not as good, which may be explained in part by a lack of uniformity of stiffness cutoff values among the studies evaluated.

FibroTest (BioPredictive), known as FibroSURE in the United States, is a patented artificial intelligence algorithm that has been validated as an indirect serum marker of fibrosis in patients with hepatitis C. It is a fibrosis index that uses input values of 5 serum markers (γ-glutamyltransferase, bilirubin, haptoglobin, apolipoprotein A-I, and α2-macroglobulin) and is corrected for age and sex, leading to a composite value between 0 and 1 to determine the presence of liver fibrosis. In a systematic review of 9 studies evaluating use of FibroTest in hepatitis C-related fibrosis, the specificity and sensitivity of FibroTest were 90% (range, 87%-92%) and 47% (range, 35%-59%), respectively. METAVIR is a scoring system used to quantify the degree of inflammation (A0-A4) and fibrosis (F0-F4) in a liver biopsy, where a score of F2 or more represents fibrosis. The combined use of TE and FibroTest in patients with hepatitis C virus demonstrated that when both results were in agreement, liver biopsy confirmed the results in 84% of the cases with scores of F2 or above, 95% of the cases with F3 or F4, and 94% of the cases with F4

There have been few studies investigating the role of TE and FibroTest in patients with psoriasis treated with methotrexate. The aim of our study was to define the role of these tests in monitoring our patients receiving methotrexate for treatment of psoriasis.

Methods

One hundred eleven patients were receiving methotrexate therapy for psoriasis between January 1, 2008, and September 30, 2009, according to the departmental database. They were contacted in September 2009, and 77 patients participated. Patient demographics; comorbid diseases, including diabetes mellitus; medications; risk factors for liver disease, including current alcohol consumption; body mass index (BMI [calculated as weight in kilograms divided by height in meters squared]); and evidence of chronic viral hepatitis were recorded. Patients are advised not to drink alcohol after starting methotrexate therapy. The results of standard blood tests that are used to monitor methotrexate, including serial liver function tests (alanine aminotransferase (ALT), aspartate aminotransferase, alkaline phosphatase, bilirubin, and albumin) and serum PIIINP, were reviewed. The laboratory reference ranges for PIIINP are 1.2 to 4.2 μg/L, and 3 serial values greater than 4.2 μg/L in 1 year or 2 values greater than 8 μg/L are considered abnormal and require review to determine the need for liver biopsy. The cost of PIIINP is €39 (US $54) per sample. All patients were asked to receive TE (FibroScan, Echosens). We obtained funding in 2011 to investigate these patients to detect hepatic fibrosis with FibroTest. The medical records of patients with abnormal TE or FibroTest results were reviewed by a consultant hepatologist who considered the need for liver biopsy. Approval for the study was granted by the St Vincent’s University Hospital ethics and medical research committee. Patients provided written informed consent and received no financial compensation.

Histologic Methods

Liver biopsies were performed using ultrasonography guidance. The results of the liver biopsies were reviewed by a consultant histopathologist with an interest in liver disease to define fibrosis and progression of hepatic damage (Roenigk grade 3a and above). In patients younger than 70 years without complications, the cost for an elective inpatient liver biopsy is €837 (National Health Service Tariff 2007-2008 [US $1161]).

TE Methods

Transient elastography assessments were performed according to the manufacturer’s standard operating procedure, all by the same physician (M.L.). Measurements were performed on the right lobe of the liver. The transducer was placed in the intercostal space while the patients were supine with their arms in maximal abduction behind their heads. Assessments were performed between October 9, 2009, and April 26, 2010. Each patient received a series of 10 validated electrographic measurements. The results are expressed in kilopascals. A cutoff value of 7.1 kPa was chosen to identify patients with signifi-

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cant fibrosis (METAVIR ≥F2). Previous TE studies of patients with chronic hepatitis C demonstrated that when TE results were compared with liver biopsy results, a cutoff value of 7.1 kPa corresponded with a fibrosis stage of F2 or higher. Transient elastography assessments with 10 validated measurements and a success rate of at least 60% were deemed to be reliable. These guidelines are advised by the manufacturer and have been used in prior studies. The cost of a TE machine is €89 500 (US$124 160) (plus value-added tax).

**FibroTest Methods**

The 5 serum markers were analyzed for FibroTest, leading to a composite value ranging from 0 to 1.00 to determine the presence of significant liver fibrosis. A score of 0 indicates minimal or no fibrosis. A cutoff value of 0.31 was chosen to identify patients with significant fibrosis (≥F1). FibroTests were performed between February 14 and June 10, 2011, and cost €177 (US$246) per sample.

**Statistical Analysis**

The χ² test was used for comparison of dichotomous variables, and the Mann-Whitney test was used for nonnormally distributed continuous variables. Data were analyzed using SPSS, version 20.0 for Windows (SPSS Inc). The cutoff value for significance was set at \( P = .05 \).

### Results

**Demographics and Liver Disease Risk Factor Profiles**

Seventy-seven patients (41 male [53%]) were included in the study. The Table reports the demographic and clinical characteristics of the study population. Seventy patients (91%) had chronic plaque psoriasis and 7 (9%) had palmoplantar pustulosis. Fifty patients (65%) were overweight (BMI >25) and 24 (31%) were obese (BMI >30). Twenty patients (26%) had psoriatic arthritis and 4 (5%) had diabetes mellitus. The median alcohol consumption during the study was low (0.06 U/wk). Ten patients (13%) had nonalcoholic steatosis demonstrated on previous liver biopsy. Two patients (3%) had grade 3a Roenigk changes demonstrated on previous liver biopsy. Forty-five patients (58%) were still receiving methotrexate for psoriasis, and 32 (42%) individuals had discontinued methotrexate during the previous 20 months. Methotrexate therapy was discontinued based on suboptimal response or adverse effects including hepatic fibrosis in 2 (3%) patients. The median cumulative methotrexate sodium dose in 77 patients was 2.6 g (range, 0.13-19.1 g) and the median cumulative duration of methotrexate treatment was 2.8 years (range, 0.3-20.6 years). Six (8%) patients had persistently elevated ALT levels (elevated in at least 5 of 9 readings, with ALT <2 times the upper limit of normal in all patients). Seventy-one of the 77 patients (92%) who had TE assessments agreed to receive a FibroTest. Reasons for trial discontinuation are outlined in the Figure.

**Transient Elastography**

Fifty patients (65%) had a valid TE assessment, 18 patients (23%) had an unreliable reading due to a success rate of less than 60%, and 9 patients (12%) had an invalid test (eTable 1 in Table. Demographics of 77 Patients With Psoriasis Receiving Methotrexate

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, No. (%)</td>
<td>41 (53)</td>
</tr>
<tr>
<td>Age, y</td>
<td>51 (22-85)</td>
</tr>
<tr>
<td>Mean</td>
<td>51.4</td>
</tr>
<tr>
<td>Type of psoriasis, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Chronic plaque psoriasis</td>
<td>70 (91)</td>
</tr>
<tr>
<td>Palmoplantar pustulosis</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>20 (26)</td>
</tr>
<tr>
<td>BMI, median (range)</td>
<td>27.7 (19.8-63.6)</td>
</tr>
<tr>
<td>Overweight, BMI &gt;25, No. (%)</td>
<td>50 (65)</td>
</tr>
<tr>
<td>Obese, BMI &gt;30, No. (%)</td>
<td>24 (31)</td>
</tr>
<tr>
<td>Morbidly obese, BMI &gt;40, No. (%)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Alcohol consumption, median (range), U/wk</td>
<td>0.06 (0-24)</td>
</tr>
<tr>
<td>Diabetes mellitus, No. (%)</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Cigarette smoking, No. (%)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>27 (35)</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Hepatitis B or C test result negative, No. (%)</td>
<td>25 (32)*</td>
</tr>
<tr>
<td>Methotrexate therapy</td>
<td></td>
</tr>
<tr>
<td>Cumulative dose, median, (range), g</td>
<td>2.6 (0.13-19.1)</td>
</tr>
<tr>
<td>Cumulative dose, mean, g</td>
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<tr>
<td>Duration, median, (range), y</td>
<td>2.8 (0.3-20.6)</td>
</tr>
<tr>
<td>Duration, mean, y</td>
<td>5.1</td>
</tr>
</tbody>
</table>

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared). * Only 25 patients were tested; all had negative results.

![Table. Demographics of 77 Patients With Psoriasis Receiving Methotrexate](http://archderm.jamanetwork.com/)

**Figure. Transient Elastography and FibroTest Trial Flow Diagram**

- 111 Patients assessed for eligibility
- 34 Excluded
  - 1 Did not meet inclusion criteria (patient had not received methotrexate treatment for 4 years)
  - 33 Declined to participate
- 77 Participants
- 51 Had serial PIIINP monitoring before transient elastography
- 71 Underwent FibroTest
- 34 Had serial PIIINP monitoring before FibroTest
- 6 Declined to have FibroTest
- 77 Included in analysis of transient elastography
- 70 Included in analysis of FibroTest
- 1 Excluded because of abnormal haptoglobin

Recruitment and enrollment of patients for transient elastography and FibroTest. PIIINP indicates procollagen III peptide.
FibroTest results. Three patients had persistently elevated within the reference range; 2 of these patients had abnormal measurements in the year before FibroTest had PIIINP results had failed or invalid TE assessments. One of 9 patients (11%) with an abnormal TE result had a persistently elevated ALT of 59 IU/L (reference range, 0–50 IU/L [to convert ALT to microkatal per liter, multiply by 0.0167]). A BMI greater than 25 predicted an invalid TE result (P = .01).

On univariate analysis, BMI (r = 0.40, P = .005) and age (r = 0.52, P = .005) were correlated with abnormal TE results. The duration of methotrexate treatment, cumulative methotrexate dose, alcohol consumption, and sex showed no significant correlation with abnormal TE results. Thirty-seven of 41 patients (90%) with normal TE results had FibroTests done and the results of 5 (14%) of the FibroTests were abnormal.

FibroTest
Seventy-one patients received a FibroTest; the score could not be calculated in 1 patient owing to an abnormal haptoglobin level. Eleven (16%) patients had an abnormal FibroTest value of greater than F1 (eTable 2 in the Supplement). Procollagen III peptide levels were normal in 3 patients (27%) with abnormal FibroTest results, persistently abnormal in 1 patient (9%), and were not recorded in 7 patients (64%) because they were no longer receiving methotrexate. Previous levels were within the reference range in all but 1 of these 7 patients. Age (r = 0.31, P = .009), cumulative methotrexate dose (r = 0.31, P = .01), and methotrexate duration (r = 0.36, P = .002) correlated with abnormal FibroTest results.

Procollagen III Peptide Level
Fifty-one patients received serial PIIINP level monitoring in the 12 months before TE assessment because other patients did not have levels measured once they discontinued methotrexate. Nine (18%) patients had at least 3 abnormal PIIINP results, all of whom had chronic plaque psoriasis; only 1 patient had psoriatic arthritis (eTable 1 in the Supplement). Eight of 9 patients (89%) were receiving methotrexate at the time of the TE assessment.

Five of 9 patients (56%) with persistently elevated PIIINP levels had a TE result within the reference range; 4 of these patients (44%) were receiving methotrexate. The other patient was receiving an alternative treatment because of persistently elevated PIIINP levels and patient preference not to proceed to liver biopsy. These 4 patients receiving methotrexate should have been considered for liver biopsy based on the British Association of Dermatologists guidelines. A normal TE assessment in each case would have avoided liver biopsy. However, only 2 of the 4 patients with persistently abnormal PIIINP levels and normal TE assessments while receiving methotrexate underwent biopsy, which demonstrated Roenigk grade 1 changes in both patients. Two patients with persistently elevated PIIINP levels had abnormal TE results and 2 patients had failed or invalid TE assessments.

Thirty-one of 34 patients (91%) with serial PIIINP measurements in the year before FibroTest had PIIINP results within the reference range; 2 of these patients had abnormal FibroTest results. Three patients had persistently elevated PIIINP levels; 2 of these patients had normal FibroTest results (eTable 2 in the Supplement). There was no significant correlation between PIIINP results and TE results or between PIIINP and FibroTest results.

Liver Biopsies
Liver biopsies were done because of persistently elevated PIIINP levels (eTables 1 and 2 in the Supplement), and 5 of 10 patients (50%) were selected according to age, comorbid disease, and patient preference. The liver biopsies demonstrated steatosis in all 5 patients, which was of moderate severity in 2 patients (40%). One of the 5 patients had portal fibrosis (Roenigk grade 3a), and another patient had sinusoidal fibrosis (Roenigk grade 3b) attributed to steatohepatitis. The patient with portal fibrosis had an abnormal TE result (9.9 kPa), persistently elevated ALT level (59 IU/L), and persistently elevated PIIINP levels. A FibroTest was done in that patient 12 months after methotrexate was discontinued and the result was within the reference range. The patient with sinusoidal fibrosis had an invalid TE result, liver enzyme levels within the reference range, and persistently elevated PIIINP levels. The FibroTest result after methotrexate was discontinued was abnormal (F1–F2). Three of the 5 patients without hepatic fibrosis demonstrated on liver biopsy had normal TE results, as well as liver enzyme levels and FibroTest results within the reference range (1 patient had a failed TE assessment). Liver biopsy could have been avoided in these 3 patients based on normal TE or FibroTest results. Two of the 5 patients who had liver biopsies continued receiving methotrexate, and 3, including 2 patients with hepatic fibrosis, received alternative systemic or biologic therapies.

Five patients did not have liver biopsies; alternative systemic therapies were instituted in 4 of these patients, and a clinically based decision was made for the fifth patient to continue methotrexate because it was the best option to control his psoriasis (eTable 3 in the Supplement). Three of these 5 patients had normal TE results, 1 patient had an abnormal TE assessment, and the other patient had a failed TE assessment. Two of these 5 patients had an abnormal FibroTest result.

Discussion
Seventy-seven patients were investigated, and liver biopsy was considered for 10 patients based on persistently abnormal PIIINP results before TE or FibroTest was performed. The results of liver function tests were satisfactory in these patients. Five of the 10 patients had liver biopsies and liver fibrosis was observed in 2 of these patients. Based on normal TE or FibroTest results within the reference range, 3 liver biopsies could have been avoided. We decided not to perform a liver biopsy in 1 patient because of his age, and 4 patients preferred to switch to alternative therapy rather than undergo a liver biopsy. There was no significant correlation between the PIIINP and TE results or between the PIIINP and FibroTest results in our study, and the small number of patients with abnormal test results may account for this lack of correlation. It is reassuring that the results of TE in 2 patients with hepatic...
fibrosis were abnormal. There may be a selection bias, with people who were concerned about the possibility of liver disease more likely to participate in the study, although the participation rate was high.

Two studies9,22-28 compared TE with and without FibroTest with liver biopsy in patients with psoriasis treated with methotrexate. Berends et al19 compared TE and FibroTest with liver biopsy results in 24 patients with psoriasis treated with methotrexate. Transient elastography values ranged between 3.3 and 18.4 kPa and correctly identified 88% of the patients without significant liver fibrosis. Transient elastography was less effective in detecting significant liver fibrosis (sensitivity was 50%). FibroTest correctly identified patients with significant fibrosis in 83% of the cases. Bray et al20 reported on 21 patients with psoriasis who were receiving methotrexate for more than 6 months. Elevated PIIINP levels met the criteria for liver biopsy in these patients, and all had undergone biopsy within 12 months of TE assessments. The investigators stated that TE and PIIINP level monitoring could have prevented 7 of 21 liver biopsies.

Transient elastography performed in patients receiving methotrexate demonstrated in several studies21-23 that the cumulative methotrexate dose was not associated with an abnormal TE result, suggesting that alternative factors play a significant role in patients developing hepatic fibrosis. A systematic review27 of liver toxicity in patients receiving methotrexate for psoriasis identified type 2 diabetes mellitus and obesity as factors associated with a significantly increased risk of hepatic fibrosis. Three studies22-25 examined the role of TE, with or without FibroTest, in defining risk factors for hepatotoxicity in patients receiving methotrexate.

Leonard et al21 reported that, in patients with psoriasis who were receiving methotrexate, 19 (40%) of 47 TE assessments failed because of obesity. Three (11%) of the remaining 28 patients had abnormal TE results. The cumulative dose of methotrexate, BMI, presence of diabetes, and alcohol excess did not correlate with median TE stiffness.21 Obesity was present in 31% of our patients. Higher BMI was associated with an abnormal TE result (P = .005) and also increased the risk of TE failure (P = .01). This is a limiting factor in the use of TE. Laharie et al22 investigated patients receiving methotrexate for rheumatoid arthritis (149 [28.8%]), Crohn disease (124 [23.9%]), psoriasis (111 [21.4%]), and other inflammatory diseases. The authors reported that only 8.5% of 518 patients with inflammatory disease treated with or being considered for treatment with methotrexate had an abnormal TE and/or FibroTest result.22 Similar to the finding in our study, BMI greater than 28 was associated with abnormal TE results, but the investigators also related high alcohol consumption with abnormal TE results.

Barbero-Villares et al23 investigated 53 patients with TE who were receiving methotrexate for the management of rheumatoid arthritis, inflammatory bowel disease, or psoriasis and showed no associations between cumulative methotrexate dose or duration and fibrosis. We found that cumulative methotrexate dose and duration of methotrexate therapy did not correlate with TE but correlated with abnormal FibroTest results (P < .05).

Older age was associated with both abnormal TE (P = .005) and abnormal FibroTest results (P = .009). Older age has been associated with abnormal TE and/or FibroTest results in several studies.28-38 The significance of the association with age is not clear. A study39 of 152 patients without known liver disease found no statistically significant difference in mean liver stiffness in various age subgroups. Another study40 evaluated elderly inpatients without liver disease, elderly patients with liver disease, and healthy younger individuals serving as controls and found that an age greater than 85 years did not correlate with fibrosis. A study involving 1338 patients by Poynard et al41 demonstrated that age was associated with increased liver stiffness, but this association almost disappeared after adjustment for metabolic factors.

Nonalcoholic fatty liver disease is associated with psoriasis42 and nonalcoholic steatosis was found in 13% of patients in our study. Nonalcoholic steatosis is a significant cause of liver injury in patients with psoriasis and may be more important than cumulative dose or duration of methotrexate therapy. Using methotrexate in patients with preexisting risk factors for liver disease increases the possibility of hepatic fibrosis. Liver function in these patients requires frequent monitoring. In addition, methotrexate alone can cause a nonalcoholic steatohepatitis-like pattern of liver injury.43 Transient elastography and FibroTest are effective noninvasive tools to monitor patients with nonalcoholic steatohepatitis.44

FibroTest is a single cross-sectional measurement to detect hepatic fibrosis, whereas PIIINP requires serial monitoring. Procollagen III peptide level reflects extracellular matrix turnover or fibrogenesis, and extensive matrix deposition that is present in cirrhosis may not be detected by determining PIIINP levels when inflammation is minimal. In addition, PIIINP is not organ specific and may be elevated in patients with psoriatic arthritis owing to active joint disease. Psoriatic arthritis affects approximately one-third of patients with psoriasis, making abnormal PIIINP levels difficult to interpret in these patients. A study45 that evaluated a single PIIINP level in detecting fibrosis compared with liver biopsy demonstrated a sensitivity of 81% and a specificity of 62%. Based on a meta-analysis46 of 4 studies comparing PIIINP with liver biopsy in patients receiving methotrexate treatment for psoriasis, the sensitivity of PIIINP is 77.3% (95% CI, 66%-86%) and the specificity is 91.5% (88%-95%).

A normal TE result makes the probability of liver fibrosis unlikely and is a better predictor of the absence of fibrosis than a positive TE result is a predictor of fibrosis.19 We used serial TE results to monitor patients with abnormal PIIINP levels to minimize the need for liver biopsy in older patients. A single FibroTest score was particularly useful in those who had a failed TE. Transient elastography and FibroTest are useful screening tools in patients with psoriatic arthritis.

FibroTest has limitations. There is a risk of false negatives in acute inflammation and false positives in hemolysis and Gilbert syndrome,47 which has been shown when FibroTest results were compared with liver biopsy results.37 One patient in our study had a liver biopsy demonstrating grade 3 hepatic fibrosis but a FibroTest result within the reference range. FibroTest has a sensitivity of 83%, indicating that it is a good screening test.
Another hepatic fibrosis index combines the prothrombin time, γ-glutamyltranspeptidase level, and serum apolipoprotein A-I level (PGA index) and has not been evaluated in patients with psoriasis. One study\(^5\) compared the PGA index with PIIINP levels in patients with alcoholic liver disease, primary biliary cirrhosis, chronic hepatitis B virus, and healthy age-matched individuals serving as controls. For the detection of cirrhosis the PGA index was 91% sensitive and 81% specific and, when combined with PIIINP, had a sensitivity of 85% and a specificity of 93%. Therefore, the combined use of screening tests makes sense and may overcome the individual drawbacks of each investigation.

Our study has some limitations but reflects our experience in clinical practice and so adds to the limited reported results on the use of TE and FibroTest in patients with psoriasis. A small group of patients were analyzed and some data were missing. Not all patients were evaluated with PIIINP levels or FibroTest. There was an interval between the TE and FibroTest assessments. However, patients who received a FibroTest had their demographics and investigations reanalyzed when FibroTest data were obtained to ensure accurate interpretation of the results. Select patients had liver biopsies as deemed clinically appropriate; therefore, not all abnormal TE and FibroTest data could be compared with liver biopsy findings. Nevertheless, these noninvasive tools allow an opportunity to monitor patients over time for hepatic fibrosis and compare assessments.

Conclusions

Transient elastography and FibroTest are screening tools to determine the presence of hepatic fibrosis. In this setting the sensitivity of the tests is important to detect hepatic fibrosis and combining the results improves accuracy. An abnormal result in 2 of 3 tests (PIIINP, TE, and FibroTest) reduces the need for a liver biopsy in our population. This strategy should be evaluated in larger prospective studies.
Methotrexate-induced hepatotoxicity in patients with psoriasis occurs rarely and unpredictably. Although liver monitoring must occur, dermatologists currently lack a reliable test. Unfortunately, many of the current recommendations for the monitoring of patients with psoriasis are poorly substantiated by rigorous data. For example, cumulative methotrexate dosage appears to be irrelevant. In addition, the liver biopsy, considered the criterion standard, suffers from sampling error, intraobserver and interobserver variability, and procedural pain and morbidity, making it a poor test. Most relevant, approximately 50% of patients with moderate to severe psoriasis have nonalcoholic fatty liver disease, a condition that displays histopathologic features indistinguishable from those associated with methotrexate-induced toxicity. Therefore, the liver biopsy cannot distinguish between drug-induced and disease-associated liver disease. Furthermore, with increasing age, liver function changes, and the severity of hepatic fibrosis on account of chronic hepatitis C is more severe in HIV-positive than HIV-negative patients despite antiretroviral therapy.

Liver fibrosis on account of chronic hepatitis C is an important determinant in the progression of disease-induced liver injury. Furthermore, with increasing age, liver function changes, and the severity of hepatic fibrosis on account of chronic hepatitis C is more severe in HIV-positive than HIV-negative patients despite antiretroviral therapy.