Diagn Interv Radiol 2026; DOI: 10.4274/dir.2025.253325

ABDOMINAL IMAGING

ORIGINAL ARTICLE

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Magnetic resonance T1ρ relaxation in patients with liver fibrosis: a systematic review and meta-analysis

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PURPOSE

This study aimed to evaluate the diagnostic performance of T1ρ relaxation in distinguishing patients with liver fibrosis (LF) from those without.

METHODS

A systematic review was conducted using PubMed, EMBASE, Cochrane, and Web of Science databases up to February 2025 to identify studies assessing T1ρ for LF diagnosis.

RESULTS

Eleven studies involving 792 patients were included. T1ρ values were significantly higher in cirrhotic versus normal livers [weighted mean difference (WMD): 6.69, $P < 0.001$], and in fibrotic versus normal livers (WMD: 7.17, $P = 0.006$). Patients with Child–Pugh classes A, B, and C showed significantly higher T1ρ values compared with normal liver ($P < 0.001$). T1ρ values in LF stages F1–F3 were not significantly different from normal liver ($P = 0.18$), but stage F4 showed significant differences (WMD: 10.48, $P = 0.02$).

CONCLUSION

T1ρ relaxation differentiates high-grade LF from normal liver tissue.

CLINICAL SIGNIFICANCE

As a non-invasive imaging technique, T1ρ shows potential for use in the diagnosis and follow-up of LF and to optimize the assessment and management of chronic liver disease.

KEYWORDS

Liver fibrosis, cirrhosis, imaging biomarker, meta-analysis, T1ρ relaxation

Liver fibrosis (LF) progression occurs in almost all cases of chronic liver disease (CLD) and represents the most common consequence of these conditions.[1] During the healing process, excessive protein deposition in the extracellular matrix leads to scarring that connects the adjacent portal triad to the central vein, ultimately resulting in cirrhosis.[2,3] The main clinical manifestations of cirrhosis include impaired liver function, portal hypertension, and the development of hepatocellular carcinoma.[4-6] End-stage LF is typically considered irreversible, with limited effective treatment options; however, complications of early or intermediate stages are often treatable.[2,7-9] Therefore, early LF detection and accurate staging are crucial for therapeutic decisions and prognosis determination.

Currently, liver biopsy serves as the gold standard for LF diagnosis, but its clinical adoption is limited due to its highly invasive nature, variability in patient and physician acceptance, risk of serious complications, and potential sampling errors.[10-12] Consequently, non-invasive imaging techniques such as magnetic resonance (MR) elastography and ultrasound elastography have been developed to assess hepatic fibrosis.[13-15] However, MR elastography requires specific hardware and software, and ultrasound elastography is operator-dependent and less repro-

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Received 06 March 2025; revision requested 18 May 2025; last revision received 11 June 2025; accepted 28 June 2025.

Epub: 22.09.2025

Publication date: 02.01.2026

DOI: 10.4274/dir.2025.253325

You may cite this article as: Liu X, Wang Y, Xu C, Li Y, Lei J. Magnetic resonance T1ρ relaxation in patients with liver fibrosis: a systematic review and meta-analysis. *Diagn Interv Radiol.* 2026;32(1):16-24.

ducible.[14-17] Therefore, there is a clear clinical need for a simpler, more objective method to non-invasively assess LF staging.

T1ρ refers to the spin-lattice relaxation time (ms) constant in the rotating coordinate frame, which describes the decay of transverse magnetization under a spin-locked radiofrequency field.[18,19] As T1ρ is sensitive to the macromolecular components of the tissue, T1ρ MR imaging shows potential for evaluating LF.[20-24] This meta-analysis aims to assess the diagnostic value of T1ρ in patients with CLD.

Methods

This systematic evaluation followed the Preferred Reporting Items for Systematic Evaluation and Meta-Analysis (PRISMA) guidelines[25,26] and was registered with PROSPERO (ID: CRD42024498897). Ethics approval and informed consent were not required, as systematic reviews synthesize and summarize existing literature rather than directly involving human or animal participants.

Literature search

Databases searched included PubMed, Cochrane Library, Web of Science, and Embase initially up to October 2023, using the search terms "liver" OR "hepatic" OR "hepar" AND "T1rho mapping" OR "T1rho relaxation" OR "T1ρ mapping" OR "T1ρ relaxation" (Supplementary file 1). Reference lists of all eligible studies were also screened for additional relevant publications. The search was updated in February 2025 in the same databases, and the results were screened according to the inclusion criteria.

Study selection

Eligible studies included English-language publications reporting liver T1ρ relaxation times and featuring at least two participant groups, one of which had cirrhosis or LF. Specific inclusion criteria were 1) patients with a definitive diagnosis of cirrhosis or hepatic fibrosis via pathological or clinical evaluation, 2) reported liver T1ρ values, and 3) a control group consisting of healthy individuals or patients without hepatic fibrosis. Exclusion criteria were 1) articles lacking valid data, 2) duplicate publications, 3) non-original research, and 4) non-English language literature. Two reviewers independently screened all titles and abstracts identified by the search. Articles judged eligible by at least one reviewer were retrieved as full-text manuscripts for further evaluation. Articles meeting the inclusion criteria after full-text review were included in the review. Conflicts of opinion at any stage were resolved through consensus.

Main points

- This study constitutes a pioneering advancement as the first systematic review and meta-analysis assessing the diagnostic efficacy of magnetic resonance imaging T1ρ relaxation for liver fibrosis (LF).
- This meta-analysis concludes that T1ρ can identify LF in patients with chronic liver disease, providing a new idea for non-invasive assessment of LF.
- Differences and limitations should be noted when using biomarker imaging to diagnose disease.

Data extraction

Two investigators independently extracted the following data from the included literature: T1ρ relaxation times for cirrhosis and LF (combined if liver function grading or pathological stage grading was reported separately for cirrhosis), authors, year of publication, study design type, number of patients, mean age, MR imaging (MRI) hardware, pulse sequence and parameters, Child–Pugh classification[27] or pathological stage grading, T1ρ relaxation time, and standard deviation. When data were unclear or unavailable, the original authors were contacted via email. If no response was received, data were extracted from charts, if available.

Quality assessment

Two researchers evaluated the quality of the included literature using the Newcastle–Ottawa Scale (NOS)[26] quality assessment tool for observational studies as recommended in the Cochrane Handbook. The NOS scale includes two scales for assessing cohort and case–control study quality, covering study population selection, comparability, and exposure or outcome assessment. Each study was scored on a scale from 0 to 9. A score of ≥6 was considered indicative of high quality, whereas studies scoring ≤3 were regarded as low quality and were excluded from the analysis due to critical methodological limitations. Higher scores reflected higher study quality. Any disagreement between the two investigators was resolved through discussion, with a third researcher acting as final arbiter if necessary.

Statistical analysis

Statistical analysis was performed using Review Manager 5.4 (Cochrane), and the results were compared using pooled estimates of weighted mean differences (WMDs) and 95% confidence intervals (CIs) for the MRI component data, with $P < 0.05$ deemed statistically significant. Sensitivity analyses and publication bias assessments were performed using Stata 15.0 (StataCorp LLC). In calculating the combined effect sizes, we weighted all WMDs according to the sample size of the respective studies. For the T1ρ relaxation time, WMD was calculated as the difference between a normal liver and patients with cirrhosis or LF divided by the pooled standard deviation. The heterogeneity of the results was verified using the Q-test and I^2 statistic.[28] $P \geq 0.01$ and $I^2 < 50\%$ indicated low statistical heterogeneity among study results, warranting the use of a fixed-effects model for meta-analysis; conversely, higher statistical heterogeneity supported a random-effects model. Potential sources of heterogeneity (methodological, statistical, or clinical) were analyzed, with subgroup analyses conducted as appropriate. Descriptive analysis was used if the heterogeneity between groups was too large or not easily combined clinically. Positive values indicated patients with prolonged T1ρ relaxation times. Publication bias was assessed using Egger's test, with $P > 0.1$ suggesting no significant bias. The robustness of the pooled results was tested with leave-one-out sensitivity analyses: each study was sequentially excluded from the meta-analysis, and the pooled WMD and I^2 were recalculated. The results were considered stable if the recalculated WMD remained within the 95% CI of the overall effect estimate, and the I^2 value did not fluctuate by more than 10% compared with the original value.

Results

Study selection and article screening

An initial search was conducted in October 2023 and updated in February 2025 by two researchers who each developed a search strategy. The initial search yielded 231 potentially eligible documents. After removing 99 duplicates, 132 titles and abstracts were screened, and 45 of these were excluded. After full-text review, another 76 documents were excluded (22 reviews, commentaries, or editorials; 39 animal experiments; 12 irrelevant articles; and 3 with no available data). The updated search did not identify any additional eligible publications. Ultimately, 11 articles[29-39] with a total of 792 participants were included. The literature screening flowchart is shown in Figure 1.

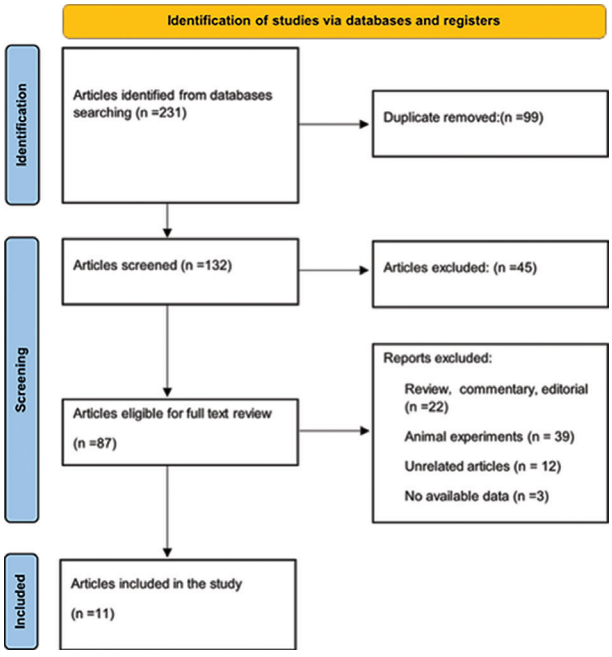

Figure 1. The PRISMA flowchart quantifies the studies accepted and rejected within the different review stages and explains the reasons for the different review stage.

Study characteristics

The characteristics of all included studies are shown in Tables 1 and 2. T1ρ values were reported as outcome metrics in all 11 studies, with six assessing T1ρ values in patients with cirrhosis, six in patients with fibrosis, and one reporting both Child–Pugh scores and T1ρ values corresponding to their pathological classifications.

Quality assessment

All 11 articles included were case–control studies. Six were high-quality articles and five were medium-quality articles, as shown in Supplementary Table 1.

Descriptive analysis

Of the 11 studies, nine observed a significant increase in T1ρ relaxation times in patients with fibrosis or cirrhosis compared with normal liver. Specifically, all six studies evaluating cirrhosis reported significantly longer T1ρ relaxation times, and four of the six studies assessing patients with LF reported significantly longer T1ρ relaxation times. Supplementary Table 2 provides the individual *P* values and Z-scores derived from forest plots.

Meta-analysis

Data on T1ρ values from patients with cirrhosis or LF were collected, and the combined WMD forest plots are shown in Figures 2 and 3, respectively. The differences between the two groups were statistically significant: cirrhosis group WMD: 6.69 [95% CI (4.14, 9.25); $P < 0.001$; Figure 2] and LF group WMD: 7.17 [95% CI (2.08, 12.26); $P = 0.006$; Figure 3].

Subgroup analysis

Two subgroup analyses were performed to assess the impact of disease severity. Statistically significant differences in T1ρ values were observed in patients with cirrhosis with different Child–Pugh scores when compared with controls: Child–Pugh stage A WMD 4.73 [95% CI (2.26, 7.20); $P < 0.001$], Child–Pugh stage B WMD 9.17 [95% CI (7.21, 11.13); $P < 0.001$], and Child–Pugh stage C WMD 15.97 [95% CI (9.30, 22.64); $P < 0.001$] (Figure 4). Comparison of T1ρ values of patients with different fibrosis stages showed no significant difference for stages F1–F3 [WMD: 4.38; 95% CI (−2.04, 10.80); $P = 0.18$]. However, stage F4 showed a significant increase [WMD: 10.48; 95% CI (1.61, 19.36); $P = 0.02$] (Figure 5). We also analyzed the difference in T1ρ values between patients with stage F1 fibrosis and healthy controls. Although the mean T1ρ values were higher in the F1 group, the difference was not statistically significant [WMD: 3.06, 95% CI (−1.39, 7.51); $P = 0.18$].

Publication bias

Egger's test showed no significant publication bias for either the cirrhosis or fibrosis meta-analyses.

Sensitivity analysis

Leave-one-out sensitivity analyses showed that removing individual studies did not significantly impact the results, affirming the stability and reliability of the random-effects calculations. In addition, I^2 values varied by no more than 5% across all recalculated models, indicating that no single study exerted undue influence on the overall results. Detailed results are presented in Supplementary Figures 1 and 2, and the corresponding I^2 values are shown in Supplementary Tables 3, 4.

Table 1. Description of studies included in the systematic review

Study	Country	Duration of patient recruitment	Age (mean/range)	Gender	Study design	Reference standard	Disease spectrum
Chen et al.[35] 2018	China	2014.03–2016.11	Patient: 51 (28–75) Control: 38 (23–64)	16 F/17 M 9 F/24 M	Prospective	Clinical	HBV, HCV, ALD
Allkemper et al.[29] 2014	Germany	2012.07–2013.07	Patient: 59.7 (28–74) Control: 49 (29–76)	12 F/22 M 9 F/16 M	Prospective	Pathology	HCV, ALD, NASH, AIH, unknown
Takayama et al.[39] 2022	Japan	2015.10–2018.07	73.8 (22–86)	29 F/53 M	Retrospective	Pathology	HBV, HCV, ALD, NASH, AIH, glycogenosis, Non-B/C hepatitis, unknow
Singh et al.[31] 2015	India	NA	Patient: 40–70 Control: 27–65	NA	Prospective	Pathology	HCV

Table 1. Continued

Study	Country	Duration of patient recruitment	Age (mean/range)	Gender	Study design	Reference standard	Disease spectrum
Takayama et al.[32] 2014	Japan	2012.05–2013.07	65.2 (35–86)	18 F/35 M	Retrospective	Pathology	HBV, HCV, ALD, NAFLD, AIH, NASH, PBC, unknow
Xie et al.[34] 2017	China	2015.07–2016.03	Patient: 41.7 (21–63) Control: 51.8 (35–74)	5 F/13 M 5F/13 M	Prospective	Clinical	HBV
Hou et al.[38] 2022	China	2019.04–2019.10	58	NA	Retrospective	Pathology	NAFLD
Suyama et al.[37] 2021	Japan	2016.07–2017.01	Patient: 68 (36–87) Control: 30 (26–46)	NA	Prospective	Clinical	HBV, HCV, AIH, NAFLD, ALD
Rauscher et al.[30] 2014	Germany	2012.01–2012.11	Patient: 56.6 (23–80) Control: 42.7 (27–65)	NA 6 F/4 M	NA	Clinical	HBV, HCV, ALD
Yang et al.[33] 2016	China	2014.03–2015.11	Patient: 48.47 (34–70) Control: 41.44 (22–64)	3 F/14 M 19 F/21 M	NA	Pathology	HBV, HCV, ALD
Stief 2019	Germany	2016.05–2017.03	65.2 (23–88)	129 F/84 M	Retrospective	Clinical	NA

HBV, hepatitis B virus; HCV, hepatitis C virus; ALD, alcoholic liver disease; NAFLD, non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis; AIH, autoimmune hepatitis; PBC, primary biliary cholangitis; F, female; M, male; NA, not available.

Table 2. Description of studies included in the systematic review

Study	Scanner	TSL/frequency	Coil	TR/TE	Slices of T1ρ sequence	Shape of ROIs	Location of ROIs	Breath-control technique
Chen et al.[35] 2018	3.0 T Philips	0, 10, 20, 40, 60/500	16-Ch sense XL Torso	5.1/2.55	NA	NA	Eight functionally independent segments	Respiratory-triggered 3D whole-liver coverage sequence
Allkemper et al.[29] 2014	1.5T Philips	10, 20, 40, 80/500	16-Ch Torso	9.1/4.6	26	Circle	Liver parenchyma	Respiratory belt
Takayama et al.[39] 2022	3.0 T Philips	0, 20, 40, 60/500	32-Ch Torso-cardiac phased-array	1.6/5.4	3	Polygonal regions	Liver parenchyma	Breath-hold
Singh et al.[31] 2015	1.5T Siemens	0, 10, 20, 30/500	Body and spine array	5.1/2.4	1	NA	Liver parenchyma	Breath-hold
Takayama et al.[32] 2014	3.0 T Philips	1, 20, 40, 60/500	32-Ch Torso-cardiac phased-array	2.1/0.98	3	Circle; oval	Right lobe or segment IV of the left lobe	Breath-hold
Xie et al.[34] 2017	3.0 T Philips	1,10, 20, 30, 40, 50/500	16-Ch phased-array	3.8/1.82	8		Left lobes; right lobes	Breath-hold
Hou et al.[38] 2022	3.0 T Philips	0, 10, 30, 50/NA	Invivo 32-Ch cardiac	2000/20	3	NA	Liver parenchyma	Breath-hold
Suyama et al.[37] 2021	3.0 T Philips	0, 10, 20, 40, 60/1000	32-Ch torso	4.3/2.2	11	Focal	Right lobe	Breath-hold
Rauscher et al.[30] 2014	1.5T Siemens	4, 8, 16, 32, 48/NA	body and spine matrix	3/1.31	1	Circle/irregular	Right lobe	Breath-hold
Yang et al.[33] 2016	3.0 T Philips	1, 27, 54/500	16-Ch sense XL torso	2.1/1.02	3	Oval	NA	Breath-hold
Stief et al.[36] 2019	1.5T Siemens	0, 10, 20, 30, 40, 50/500	One-Ch body coil and 8-Ch surface coils	5.1/2.4	2	Circle	Right lobe	NA

TSL, time of spin-lock; TR, repetition time; TE, echo time; Ch, channel; ROI, region of interest; NA, not available.

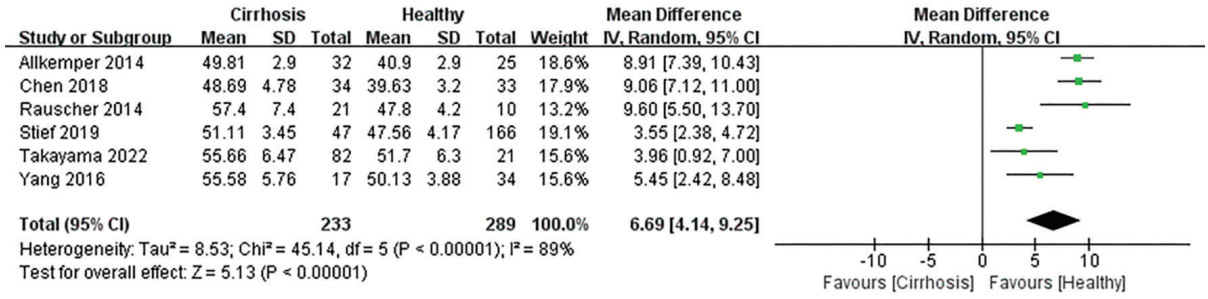

Figure 2. Forest plot showing individual differences and pooled mean standard deviation of T1ρ relaxation times (ms) in healthy controls and patients with cirrhosis. CI, confidence interval; SD, standard deviation; IV, inverse variance.

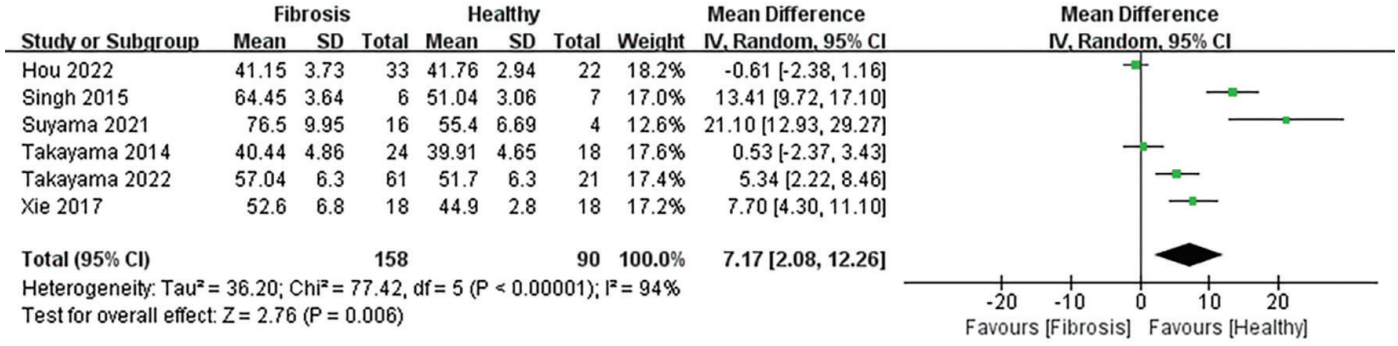

Figure 3. Forest plot showing individual differences and pooled mean standard deviation of T1ρ relaxation times (ms) for healthy controls and patients with fibrosis. CI, confidence interval; SD, standard deviation; IV, inverse variance.

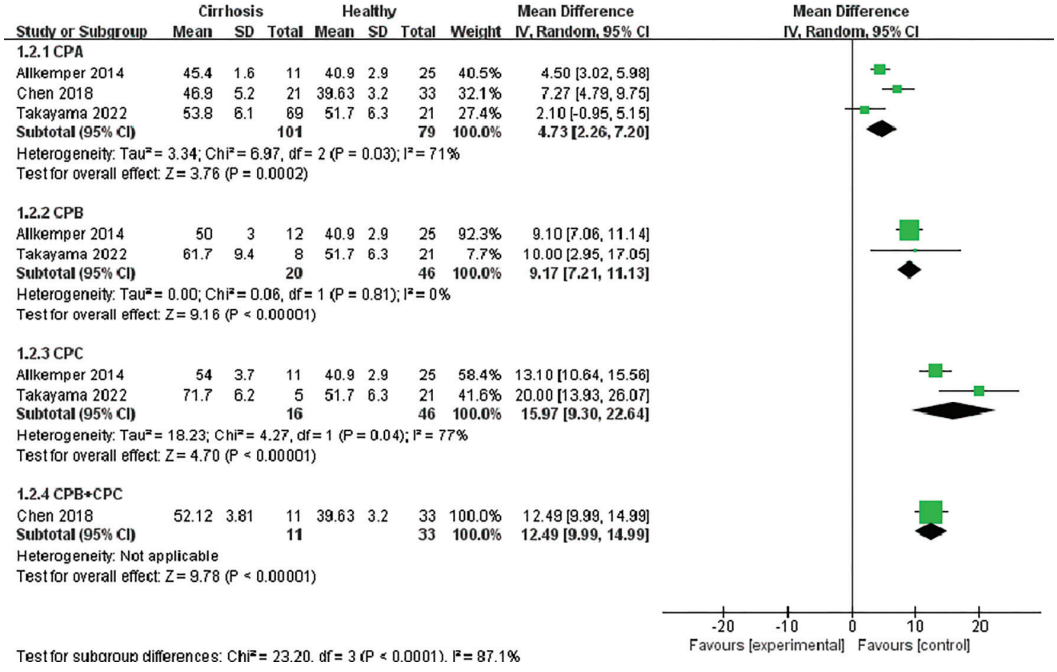

Figure 4. Forest plots showing individual differences in T1ρ relaxation times (ms) and pooled mean standard deviations for healthy controls and patients with cirrhosis with different Child–Pugh scores. SD, standard deviation; CI, confidence interval; CPA, Child–Pugh A; CPB, Child–Pugh B; CPC, Child–Pugh C; IV, inverse variance

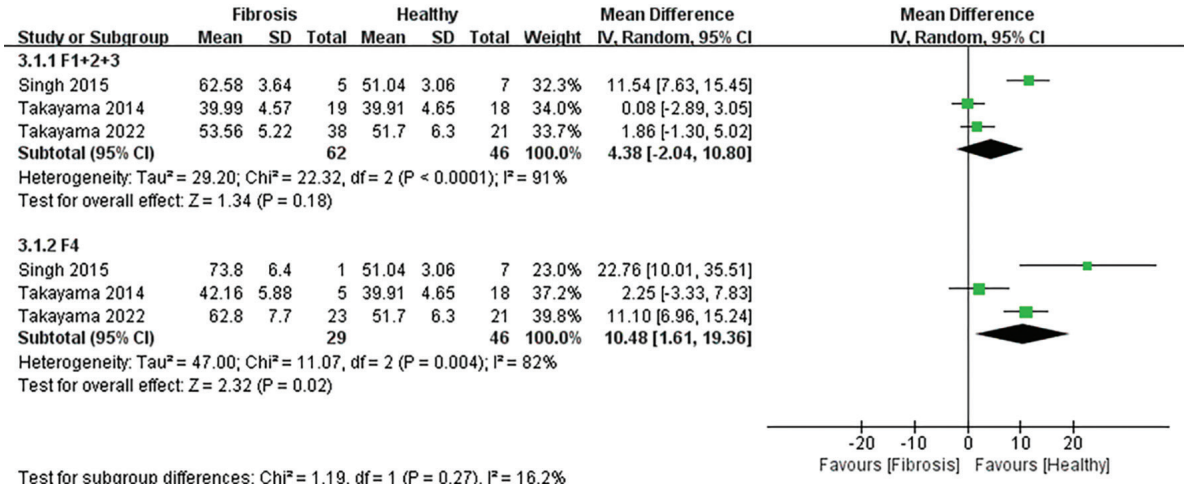

Figure 5. Forest plots showing individual differences in T1ρ relaxation times (ms) and pooled mean standard deviations for healthy controls and patients with different degrees of liver fibrosis. CI, confidence interval; IV, inverse variance; SD, standard deviation.

Discussion

Cirrhosis represents the advanced stage of various CLDs, and several imaging techniques facilitate direct diagnosis and staging of LF, including state or shear wave elastography, perfusion or dual-energy computed tomography, liver-specific contrast-enhanced MRI, diffusion-weighted MRI, and MR elastography.[40-45] T1ρ imaging, an emerging imaging technique, is currently used to detect macromolecular levels, and its diagnosis of LF may depend on the overall loss of macromolecule content and an increase in water fraction.[46] Our study, based on data from 11 studies involving 792 participants, showed that T1ρ relaxation time was effective in differentiating between normal livers and patients with LF. These findings align with previous animal studies[47-50] and underscore the potential of T1ρ values in reflecting the severity of LF.

The results of the subgroup analyses further indicated that T1ρ relaxation times showed a significant advantage in differentiating between varying degrees of cirrhosis as the disease progressed. Specifically, there was a significant difference between T1ρ values for cirrhosis across Child–Pugh stages compared with normal liver, and this difference increased with higher Child–Pugh scores. Furthermore, in the comparison of different fibrosis stages, although patients in stages F1–F3 did not show statistically significant differences, in stage F4 (i.e., advanced LF or cirrhosis), the difference in T1ρ values was statistically significant. Multiple subgrouping strategies were attempted—including by individual fibrosis stages and early (F1–2) versus advanced (F3–4) groupings—but most comparisons did not reach statistical significance due to limited data and high variability. Therefore, stages F1–3 were combined to examine overall T1ρ trends in early-to-moderate fibrosis.

The Child–Pugh classification for assessing liver reserve function in cirrhosis evaluates the overall functional status of the liver based on five clinical and biochemical parameters (bilirubin, albumin, coagulation time, ascites, and hepatic encephalopathy), whereas LF responds to histological alterations of the liver only. Previous studies have reported a negative correlation between T1ρ and liver iron concentration (LIC), suggesting that LIC may confound T1ρ measurements.[51,52] Moreover, changes in T1ρ values do not always directly reflect structural changes in hepatic tissues,[53,54] indicating that T1ρ values are sensitive to a wide range of biological and physical factors. T1ρ values may also be affected by unknown factors, such as inflammation, venous congestion, or lymphoedema, all of which could alter T1ρ signals, leading to increased differences in T1ρ signals in various regions of the liver, thus affecting fibrosis assessment. In addition, comorbidities such as diabetes and obesity may also interfere with the interpretation of the T1ρ signal, further increasing the variability of the signal. Therefore, more studies are needed to understand the effect of LF on liver T1ρ values.

One strength of this study is that it is the first meta-analysis of the effectiveness of T1ρ in differentiating normal liver from CLD-related fibrosis, conducted in accordance with established guidelines for systematic reviews and meta-analyses.[25] This included consensus among multiple reviewers at each step of the literature search, study selection, and data extraction; quality assessment of the studies; publication bias assessment and adjustment; and preplanned meta-analyses, including sensitivity analyses based on a priori assumptions in the event of substantial heterogeneity. However, the analysis encountered high heterogeneity among the included studies (>50% for the primary outcome), with the source of this heterogeneity remaining unidentified despite subgroup analyses. Moreover, the limited number of T1ρ studies on LF and small sample sizes further emphasize the need for additional research to strengthen confidence in the results.

Considerable variation was noted between MRI methods in the included studies, including scanners, coils, software, and pulse sequences, all of which can affect T1ρ relaxation. In this review alone, two brands of scanners, two magnet strengths, and seven different coils were identified (Table 2). Choice of pulse sequence can also significantly affect relaxation time, with a difference of as much as 10 ms observed across commonly used sequences.[55,56] Post-processing and segmentation can also affect T1ρ values, such as how the assessor defines the region of interest (ROI), differences in the ROI between studies, the number of slices included in the ROI,[57] the proximity of the border to other tissues, and partial volume effects.[58] Continued use of the recommended standardized terminology and ROI definitions will improve the comparability of ROIs across studies and study sites.[59] This study identified substantial differences in methods across testing sites, suggesting that considerable caution should be adopted when making comparisons across studies and highlighting

the limitations in the current state of T1ρ relaxation as an imaging biomarker.

Improving the reliability of compositional MRI as an imaging biomarker requires comparability across scanners and research institutions. The results of this study support current international efforts by researchers and vendors to improve sequencing, calibration, and standardization,[60] for example, the use of a calibration phantom to develop calibration functions to account for the different hardware and software used in different institutions.[60,61] Meanwhile, the findings from this study suggest that the future use of MRI component measurements as potential biomarkers would benefit from a deeper understanding of the impact of different testing methods and more standardization of data collection and analysis methods.[62,63]

Although this study provides a systematic analysis of the effectiveness of hepatic fibrosis detection with T1ρ by integrating the existing literature, there are still some limitations. First, the small number of original studies included limits our ability to draw more generalizable conclusions. Second, the different studies involved different groups of patients who varied in disease severity, LF etiology, age, and gender ratio, which may have affected T1ρ performance and thus the generalizability of the results. Third, the imaging parameters used in different studies (different settings of the T1ρ imaging sequence, different models of imaging equipment, different breathing control techniques, location of the ROIs, etc.) may have also contributed to the heterogeneity of the results.

The significant heterogeneity observed in the combined effect size of T1ρ relaxation times underscores the need for further investigation, particularly on the impact of different CLD stages. Subgroup analyses hint at varying degrees of heterogeneity across LF stages, suggesting the need for standardized assessment criteria and additional prospective studies to minimize bias and validate the diagnostic utility of T1ρ for LF staging. Although T1ρ values exhibited slight differences across fibrosis stages, they demonstrated limited ability to differentiate early-stage fibrosis from a normal liver, yet hold promise in differentiating F4 stage fibrosis from cirrhosis. This limitation is likely due to the subtle histological changes present in early-stage fibrosis, which may be below the detection threshold of T1ρ mapping techniques. At stages F1–F3, collagen deposition and extracellular matrix remodeling remain relatively limited, leading to only minor alterations in tissue macromolecular content and water interaction that may not significantly affect T1ρ relaxation times. This observation is consistent with prior studies using MR elastography and diffusion-weighted MRI, which have also demonstrated reduced sensitivity in differentiating early-stage LF.[64,65]

In conclusion, based on these results, hepatic T1ρ relaxation measurements show great potential in identifying LF in patients with CLD. This study provides a more plausible scientific basis for the validity of T1ρ for detecting LF and a new idea for the non-invasive assessment of LF.

Footnotes

Conflict of interest disclosure

The authors declared no conflicts of interest.

Acknowledgments

The authors thank all investigators and supporters involved in this study. This work was supported by the Health Industry Scientific Research Program of Gansu Province (GSWSKY2023-10).

Supplementary: https://d2v96fxpocvxx.cloudfront.net/51ec7646-9122-48c7-a1d9-90e9cb16981b/content-images/b0ff08a2-ecaa-4d23-bb16-25e503ca9f5a.pdf

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