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INPLASY

Clinical application of serum Mac-2 binding protein glycosylation isomers in the diagnosis of liver fibrosis: a meta-analysis

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Chen, JH; Wang, CC; Tzeng, IS.

Corresponding author:
I-Shiang Tzeng

istzeng@gmail.com

Author Affiliation:
Taipei Tzu Chi Hospital.

ADMINISTRATIVE INFORMATION

Support - Taipei Tzu Chi Hospital.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 September 2025 and was last updated on 20 September 2025.

INTRODUCTION

Review question / Objective P – Patient, problem, or population: Patients with chronic liver diseases
Patients at different stages of liver fibrosis (F1-F4)

I – Intervention:
Mac-2 binding protein glycosylation isomer (M2BPGi) testing/measurement
Using M2BPGi as a diagnostic biomarker

C – Comparison, control, or comparator:
Likely compared against reference standard methods for diagnosing liver fibrosis (though not specified here)
May include comparison between different fibrosis stages or healthy controls

O – Outcome(s):
Primary outcome: Diagnostic accuracy of M2BPGi for liver fibrosis detection
Sensitivity: 72.4% (95% CI 63.2% to 80.0%)
Specificity: 72.9% (95% CI 66.8% to 78.2%)
Area under the curve: 0.7238
Optimal cut-off value: 1.307

Clinical outcome: Early prediction of poor chronic liver disease progression.

Rationale Clinical Need and Problem

Early detection challenge: Chronic liver diseases progress through different fibrosis stages (F1-F4), and early detection is crucial for timely intervention and better patient outcomes
Current limitations: Traditional methods for assessing liver fibrosis may be invasive (liver biopsy), expensive, or have limited accessibility
Disease burden: Chronic liver diseases represent a significant global health burden requiring reliable, non-invasive diagnostic tools

Scientific Rationale for M2BPGi

Biological relevance: Mac-2 binding protein glycosylation isomer is associated with liver fibrosis pathogenesis and reflects changes in glycosylation patterns during liver damage
Non-invasive approach: Offers a potentially safer, more accessible alternative to invasive procedures
Quantifiable biomarker: Can be measured with a specific cut-off value (1.307) for clinical decision-making

Research Justification

Evidence synthesis need: Multiple individual studies existed but required systematic evaluation through meta-analysis to determine overall diagnostic performance
Clinical translation: Need to establish pooled diagnostic accuracy metrics (sensitivity 72.4%, specificity 72.9%) to guide clinical implementation
Standardization: Determining optimal cut-off values across different populations and studies

Clinical Impact

Early intervention: Enables earlier identification of patients at risk for disease progression
Resource optimization: Could reduce unnecessary invasive procedures while maintaining diagnostic accuracy
Personalized care: Supports risk stratification and tailored treatment approaches.

Condition being studied

Primary Condition:
Liver Fibrosis - specifically the progression of chronic liver diseases through different fibrosis stages (F1-F4)
Clinical Context:

Chronic liver diseases with associated fibrotic changes
Liver fibrosis staging from early (F1) to advanced (F4) stages
Progressive hepatic scarring that can lead to cirrhosis and liver failure

Disease Characteristics:

Pathophysiology: Excessive accumulation of extracellular matrix proteins leading to scarring of liver tissue
Progressive nature: Advances through distinct stages (F1-F4) with increasing severity
Clinical significance: Can progress to cirrhosis, portal hypertension, and liver failure if undetected/untreated

Diagnostic Challenge:

Asymptomatic early stages: Patients may not show symptoms until advanced stages
Need for staging: Accurate assessment of fibrosis stage is crucial for treatment decisions
Monitoring requirement: Regular assessment needed to track disease progression

Study Focus:
The research specifically examines the diagnostic accuracy of M2BPGi in:

Detecting presence of liver fibrosis
Distinguishing between different fibrosis stages
Early identification of patients at risk for disease progression
Predicting poor outcomes in chronic liver disease patients.

METHODS

Search strategy

Databases Searched:

Ovid Medline - Primary medical literature database
Ovid EMBASE - European biomedical database
Ovid Cochrane - Cochrane Library for systematic reviews
WHO Clinical Trials Registry - International clinical trials database
Google Scholar - Broader academic search engine
PubMed - US National Library of Medicine database
ScienceDirect - Elsevier's scientific database

Search Period:

Through March 31, 2024 - Comprehensive search up to this date

Search Strategy Characteristics:
Comprehensive Coverage:

Multiple databases ensure broad literature capture
Mix of medical and general academic sources for complete coverage
Trial registries included to identify ongoing/unpublished studies

Database Selection Rationale:

Ovid platforms - Gold standard for systematic reviews (Medline, EMBASE, Cochrane)
PubMed - Additional MEDLINE coverage with unique indexing
ScienceDirect - Publisher-specific content not always indexed elsewhere
Google Scholar - Grey literature and broader academic content

WHO Clinical Trials Registry - Unpublished trial data and ongoing studies

Likely Search Terms (Not explicitly stated):
Based on the topic, searches likely included combinations of:

"Mac-2 binding protein"
"M2BPGi"
"Glycosylation isomer"
"Liver fibrosis"
"Chronic liver disease"
"Diagnostic accuracy"

Search Limitations:

Language restrictions - Not specified in abstract
Study design filters - Not mentioned
Grey literature - Partially addressed through Google Scholar.

Participant or population
Patients with chronic liver diseases
Patients at different stages of liver fibrosis (F1-F4).

Intervention
Mac-2 binding protein glycosylation isomer (M2BPGi) testing/measurement
Using M2BPGi as a diagnostic biomarker.

Comparator Likely compared against reference standard methods for diagnosing liver fibrosis (though not specified here).
May include comparison between different fibrosis stages or healthy controls

Study designs to be included Primary Study Design: Diagnostic Accuracy Studies - Studies evaluating the performance of M2BPGi as a diagnostic test for liver fibrosisLikely Included Study Types:Cross-sectional Studies:Studies comparing M2BPGi results against reference standard at single time pointMost common design for diagnostic accuracy researchCohort Studies: Prospective cohorts - Following patients forward to assess diagnostic performanceRetrospective cohorts - Using existing patient data to evaluate M2BPGi accuracyCase-control Studies:Comparing M2BPGi levels between patients with confirmed liver fibrosis.

Eligibility criteria Inclusion Criteria:
Study Design:

Diagnostic accuracy studies (cross-sectional, cohort, case-control)
Studies evaluating M2BPGi as diagnostic test for liver fibrosis
Studies providing sufficient data to calculate sensitivity and specificity

Population:

Patients with chronic liver diseases
Patients across liver fibrosis stages (F1-F4)
Adults (age restrictions not specified)
Any etiology of chronic liver disease (viral hepatitis, NASH, alcoholic liver disease, etc.)

Index Test:

M2BPGi measurement as the diagnostic test of interest
Studies reporting M2BPGi cut-off values
Quantitative M2BPGi results

Reference Standard:

Established methods for diagnosing/staging liver fibrosis
Likely includes:

Liver biopsy (histological assessment)
Transient elastography (FibroScan)
Other validated fibrosis assessment methods

Outcome Measures:

Studies reporting or allowing calculation of:

Sensitivity and specificity
Diagnostic accuracy metrics
Area under the ROC curve

Exclusion Criteria:
Study Design:

Case reports, case series
Review articles, editorials, commentaries
Conference abstracts without full data
Studies without appropriate control groups

Population:

Pediatric populations (likely excluded unless specified)
Acute liver conditions without chronic fibrosis component
Post-transplant patients (may be excluded due to different pathophysiology)

Data Quality:

Insufficient diagnostic data - Cannot extract 2x2 contingency table data
Poor methodological quality - Based on QUADAS-2 assessment
Duplicate publications - Same patient cohorts reported multiple times

Language and Publication:

Language restrictions - Not specified in abstract
Publication date - Through March 31, 2024
Publication status - Likely included published peer-reviewed studies

Additional Considerations:

Minimum sample size - Not specified but likely required adequate sample for statistical analysis
Clear diagnostic criteria - Studies must have well-defined fibrosis staging
Complete follow-up - For cohort studies, adequate follow-up duration.

Information sources
Primary Database Sources:
Medical Literature Databases:

Ovid Medline - Comprehensive biomedical literature database
Ovid EMBASE - European Medicines Agency database with international coverage
PubMed - US National Library of Medicine's biomedical database
ScienceDirect - Elsevier's full-text scientific database.

Systematic Review Database:

Ovid Cochrane - Cochrane Library containing systematic reviews and clinical trials.

Main outcome(s) Primary Diagnostic Accuracy Outcomes:
Sensitivity:

Pooled sensitivity: 72.4% (95% CI: 63.2% to 80.0%)
Measures M2BPGi's ability to correctly identify patients WITH liver fibrosis
True positive rate among patients with confirmed fibrosis

Specificity:

Pooled specificity: 72.9% (95% CI: 66.8% to 78.2%)
Measures M2BPGi's ability to correctly identify patients WITHOUT liver fibrosis
True negative rate among patients without fibrosis

Overall Diagnostic Performance:

Area under the ROC curve: 0.7238
Represents overall discriminatory ability of M2BPGi
Scale: 0.5 (no discrimination) to 1.0 (perfect discrimination)

Optimal Cut-off Value:

M2BPGi cut-off: 1.307
Threshold value that optimizes sensitivity and specificity balance
Clinical decision point for positive vs. negative test results

Clinical Significance:
Diagnostic Accuracy Interpretation:

Moderate diagnostic performance - Both sensitivity and specificity ~73%
Balanced accuracy - Similar sensitivity and specificity values
Clinical utility - AUC of 0.72 indicates fair to good discriminatory ability

Clinical Application:

Early prediction capability - Can identify patients at risk for poor chronic liver disease outcomes
Non-invasive screening - Alternative to more invasive diagnostic procedures
Risk stratification - Helps classify patients across different fibrosis stages (F1-F4)

Meta-analysis Methodology:

Linear mixed effects model used for pooling diagnostic accuracy measures
Pooled cut-off analysis - Determined optimal threshold across studies
Confidence intervals provided - Statistical precision of estimates.

Quality assessment / Risk of bias analysis
Data Quality:

Insufficient diagnostic data - Cannot extract 2x2 contingency table data
Poor methodological quality - Based on QUADAS-2 assessment
Duplicate publications - Same patient cohorts reported multiple times.

Strategy of data synthesis Linear mixed effects model used to pool diagnostic accuracy data.

Subgroup analysis This limits our ability to assess how M2BPGi performance may vary across different patient subgroups or disease etiologies.

Sensitivity analysis None.

Country(ies) involved Taiwan - Taipei Tzu Chi Hospital.

Keywords Mac-2 binding protein glycosylation isomer; Liver fibrosis; Threshold.

Contributions of each author

Author 1 - Jiann-Hwa Chen.
Email: cjhki.tiyi@msa.hinet.net
Author 2 - Chia-Chi Wang.
Email: uld888@yahoo.com.tw
Author 3 - I-Shiang Tzeng.
Email: istzeng@gmail.com