Accuracy of prognostic serological biomarkers in predicting liver fibrosis severity in people with metabolic dysfunction-associated steatotic liver disease: a meta-analysis of over 40,000 participants.

Sergio M. López Tórrez, Camila O. Ayala, Paula Bayer Ruggiro, Caroline Abud Drumond Costa, Mario B Wagner, Alexandre Vontobel Padoin, Rita Mattiello*

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Supplementary Table 1. PRISMA-DTA Checklist Item

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2 to 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	3 to 5
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5 to 6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	6
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	6
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	7
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	7 to 8
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	5 to 8
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and	8 to 9

		comparing tests, f) handling of different reference standards	

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	8 to 9
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	8 to 9
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	10 to 12
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	12
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	13 to 18
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	13 to 18
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	19
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	19 to 22
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	22
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	23
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	25

Supplementary Text 1. Electronic search strategy.

MEDLINE/PubMed

#1. "Fatty liver" [MeSH]
#2. liver, Fatty* [Title/Abstract]
#3. Steatohepatitis* [Title/Abstract]
#4. Steatohepatitides* [Title/Abstract]
#5. Steatosis of Liver* [Title/Abstract]
#6. Liver Steatosis*[Title/Abstract]
#7. Liver Steatoses* [Title/Abstract]
#8. Steatoses, Liver* [Title/Abstract]
#9. Steatosis, Liver* [Title/Abstract]
#10. Hepatosteatosis* [Title/Abstract]
#11. #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10
#12. "Non-alcoholic Fatty Liver Disease" [MeSH]
#13. Non alcoholic Fatty Liver Disease* [Title/Abstract]
#14. Nonalcoholic Fatty Liver Disease* [Title/Abstract]
#15. Fatty Liver, Nonalcoholic* [Title/Abstract]
#16. Fatty Livers, Nonalcoholic* [Title/Abstract]
#17. Liver, Nonalcoholic Fatty* [Title/Abstract]
#18. Livers, Nonalcoholic Fatty* [Title/Abstract]
#19. Nonalcoholic Fatty Liver* [Title/Abstract]
#20. Nonalcoholic Fatty Livers* [Title/Abstract]
#21. Nonalcoholic Steatohepatitis* [Title/Abstract]
#22. Steatohepatitis, Nonalcoholic* [Title/Abstract]
#23. NALFD* [Title/Abstract]
#24. NASH* [Title/Abstract]
#25. Metabolic-Associated Fatty Liver Disease* [Title/Abstract]
#26. MAFLD* [Title/Abstract]
#27. #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26
#28. #11 OR #27
#29. "Biopsy" [MeSH]
#30. Biopsies* [Title/Abstract]
#31. #29 OR #30
#32. "Liver Cirrhosis" [MeSH]
#33. Hepatic Cirrhosis* [Title/Abstract]
#34. Hepatic Cirrhoses* [Title/Abstract]
#35. Cirrhosis, Hepatic* [Title/Abstract]
#36. Cirrhosis, Liver* [Title/Abstract]
#37. Cirrhoses, Liver* [Title/Abstract]
#38. Fibrosis, Liver* [Title/Abstract]
#39. Fibroses, Liver* [Title/Abstract]
#40. Liver Fibrosis* [Title/Abstract]
#41. Liver Fibroses* [Title/Abstract]
#42. Cirrhosis* [Title/Abstract]
#43. #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42
#44. "Prognosis" [MeSH]
#45. Prognoses* [Title/Abstract]
#46. Predict* [Title/Abstract]

#47. Course* [Title/Abstract]
#48. “ROC curve” [MeSH]
#49. Curves, ROC* [Title/Abstract]
#50. Receiver Operating Characteristic* [Title/Abstract]
#51. Stratification* [Title/Abstract]
#52. Discrimination* [Title/Abstract]
#53. c-statistic* [Title/Abstract]
#54. Area under the curve* [Title/Abstract]
#55. Curve, Area Under* [Title/Abstract]
#56. AUC* [Title/Abstract]
#57. “Calibration” [MeSH]
#58. Indices* [Title/Abstract]
#59. Algorithm* [Title/Abstract]
#60. #44 OR #45 OR #46 OR #47 OR #48 OR #49 #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59
#61 FibroTest
#62. FibroMeter
#63. Enhanced liver fatty
#64. ELF
#65. NAFLD fibrosis score
#66. FIB-4 index
#67. BARD score
#68. APRI
#69. Hepascore
#70. FORN score
#71. FIBROSpect test
#72. #61 OR #62 OR #63 OR #64 OR #65 OR #65 OR # 66 OR #67 OR #68 OR #69 OR #71 OR #72
#73. #28 AND #31 AND #43 AND #60 AND #72

EMBASE

#1. ‘Fatty liver’
#2. ‘liver, Fatty’
#3. ‘Steatohepatitis’
#4. ‘Steatohepatitides’
#5. ‘Liver Steatosis’
#6. ‘Liver Steatoses’
#7. ‘Steatosis, Liver’
#8. ‘Hepatosteatosis’
#9. OR/ #1 - #9
#10. ‘nonalcoholic fatty liver’
#11. ‘NAFLD (nonalcoholic fatty liver disease)’
#12. ‘non alcoholic fatty liver disease’
#13. ‘non alcoholic hepato-steatosis’
#14. ‘non alcoholic liver steatosis’
#15. ‘non alcoholic steatotic hepatopathy’
#16. ‘nonalcoholic hepatosteatosis’
#17. ‘non-alcoholic FLD’
#18. ‘nonalcoholic FLD’
#19. ‘metabolic fatty liver’
#20. ‘MAFLD (metabolic associated fatty liver disease)’

#21. OR/ #10 - #20
#22. OR/ #9 - #21
#23. ‘Biopsy’
#24. ‘Bioptic diagnosis’
#25. ‘Bioptical diagnosis’
#26. OR/ #23 – #25
#27. ‘Liver cirrhosis’
#28. ‘Cirrhosis’
#29. ‘Cirrhosis hepatis’
#30. ‘Cirrhosis, liver’
#31. ‘Hepatic cirrhosis’
#32. OR/ #27 – #31
#33. ‘Prognosis’
#34. ‘Prognoses’
#35. ‘Predict’
#36. ‘Course’
#37. ‘receiver operating characteristic’
#38. ‘receiver operating characteristic curve’
#39. ‘ROC curve’
#40. ‘ROC analysis’
#41. ‘Stratification’
#42. ‘Discrimination’
#43. ‘area under the curve’
#44. ‘area under curve’
#45. ‘AUC’
#46. ‘AUC (area under the curve)’
#47. ‘Calibration’
#48. ‘Indices’
#49. ‘Algorithm’
#50. OR/ #33 – #49
#51. ‘FibroTest’
#52. ‘FibroMeter’
#53. ‘Enhanced liver fatty’
#54. ‘ELF’
#55. ‘NAFLD fibrosis score’
#56. ‘FIB-4 index’
#57. ‘BARD score’
#58. ‘APRI’
#59. ‘Hepascore’
#60. ‘FORN score’
#61. ‘FIBROSpect test’
#62. OR/#51 - #61
#63. #22 AND #26 AND #32 AND #50 AND #62

LILACS

Fatty liver OR liver, Fatty OR Steatohepatitis OR Steatohepatitides OR Steatosis of Liver OR Liver Steatosis OR Steatoses, Liver OR Steatosis, Liver OR Hepatosteatosis OR Non-alcoholic Fatty Liver Disease OR Nonalcoholic Fatty Liver Disease OR Nonalcoholic Fatty Liver Disease

Nonalcoholic Steatohepatitis OR Steatohepatitis, Nonalcoholic OR NALFD OR NASH OR Metabolic-Associated Fatty Liver Disease OR MAFLD

AND

Biopsy OR Biopsies

AND

Liver Cirrhosis OR Hepatic Cirrhosis OR Cirrhosis, Hepatic OR Cirrhosis, Liver OR Fibrosis, Liver OR Liver Fibrosis OR Liver Fibroses OR Cirrhosis

AND

Prognosis OR Prognoses OR Predict OR Course OR Receiver Operating Characteristic OR ROC curve OR Curves, ROC OR Stratification OR Discrimination OR c-statistic OR Area under the curve OR Curve, Area Under OR Calibration OR Indices OR Algorithm

AND

FibroTest OR FibroMeter OR Enhanced liver fatty OR ELF OR NAFLD fibrosis score OR FIB-4 index OR BARD score OR APRI OR Hepascore OR FORN score OR FIBROSpect test

CINAHL

Fatty liver
OR
liver, Fatty
OR
Steatohepatitis
OR
Steatohepatitides
OR
Steatosis of Liver
OR
Liver Steatosis
OR
Liver Steatoses
OR
Steatoses, Liver
OR
Steatosis, Liver
OR
Hepatosteatosis
AND
Non-alcoholic Fatty Liver Disease
OR
Non alcoholic Fatty Liver Disease
OR

Nonalcoholic Fatty Liver Disease
OR
Fatty Liver, Nonalcoholic
OR
Fatty Livers, Nonalcoholic
OR
Liver, Nonalcoholic Fatty
OR
Livers, Nonalcoholic Fatty
OR
Nonalcoholic Fatty Liver
OR
Nonalcoholic Fatty Livers
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Metabolic-Associated Fatty Liver Disease
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OR
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OR
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OR
Liver Fibrosis
OR
Liver Fibroses
OR
Cirrhosis
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Course

OR
Receiver Operating Characteristic
OR
ROC curve
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OR
FIBROSpect test

Cochrane Hepato-Biliary Group Diagnostic Test Accuracy Studies Register

Title, abstract, keyword: Fatty liver OR liver, Fatty OR Steatohepatitis OR Steatohepatitides OR Steatosis of Liver OR Liver Steatosis OR Steatoses, Liver OR Steatosis, Liver OR Hepatosteatosis OR Non-alcoholic Fatty Liver Disease OR Nonalcoholic Fatty Liver Disease OR Nonalcoholic Fatty Liver Disease OR Fatty Liver, Nonalcoholic OR Fatty Livers, Nonalcoholic ORLiver, Nonalcoholic Fatty OR Livers, Nonalcoholic Fatty OR Nonalcoholic Fatty Liver OR Nonalcoholic Fatty Livers OR Nonalcoholic Steatohepatitis OR Steatohepatitis, Nonalcoholic OR NALFD OR NASH Metabolic-Associated Fatty Liver Disease OR MAFLD

AND

Title, abstract, keyword: Biopsy OR Biopsies

AND

Title, abstract, keyword: Liver Cirrhosis OR Hepatic Cirrhosis OR Cirrhosis, Hepatic OR Cirrhosis, Liver OR Fibrosis, Liver OR Liver Fibrosis OR Liver Fibroses OR Cirrhosis AND prognosis OR Prognoses OR Predict OR Course OR Receiver Operating Characteristic OR ROC curve OR Curves, ROC OR Stratification OR Discrimination OR c-statistic OR Area under the curve OR Curve, Area Under OR Calibration OR Indices OR Algorithm

AND

Title, abstract, keyword: FibroTest OR FibroMeter OR Enhanced liver fatty OR ELF OR NAFLD fibrosis score OR FIB-4 index OR BARD score OR APRI OR Hepascore OR FORN score OR FIBROSpect test

Web of Science

1. TS= (Fatty liver)
2. TS= (liver, Fatty)
3. TS= (Steatohepatitis)
4. TS= (Steatohepatitides)
5. TS= (Steatosis of Liver)
6. TS= (Liver Steatosis)
7. TS= (Liver Steatoses)
8. TS= (Steatoses, Liver)
9. TS= (Steatosis, Liver)
10. TS= (Hepatosteatosis)
11. OR/ 1 – 10
12. TS= (Non-alcoholic Fatty Liver Disease)
13. TS= (Non alcoholic Fatty Liver Disease)
14. TS= (Nonalcoholic Fatty Liver Disease)
15. TS= (Fatty Liver, Nonalcoholic)
16. TS= (Fatty Livers, Nonalcoholic)

17. TS= (Liver, Nonalcoholic Fatty)
18. TS= (Livers, Nonalcoholic Fatty)
19. TS= (Nonalcoholic Fatty Liver)
20. TS= (Nonalcoholic Fatty Livers)
21. TS= (Nonalcoholic Steatohepatitis)
22. TS= 9Steatohepatitis, Nonalcoholic)
23. TS= (NALFD)
24. TS= (NASH)
25. TS= (Metabolic-Associated Fatty Liver Disease)
26. TS= (MAFLD)
27. OR/ 12 – 26
28. OR/ 11 – 27
29. TS= (Biopsy)
30. TS= (Biopsies)
31. OR/ 29 – 30
32. TS= (Liver Cirrhosis)
33. TS= (Hepatic Cirrhosis)
34. TS= (Cirrhosis, Hepatic)
35. TS= (Cirrhosis, Liver)
36. TS= (Fibrosis, Liver)
37. TS= (Liver Fibrosis)
38. TS= (Liver Fibroses)
39. TS= (Cirrhosis)
40. OR/ 32 – 39
41. TS= (Prognosis)
42. TS= (Prognoses)
43. TS= (Predict)
44. TS= (Course)
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53. TS= (AUC)
54. TS= (Calibration)
55. TS= (Indices)
56. TS= (Algorithm)
57. OR/ 41 – 56
58. TS= (FibroTest)
59. TS= (FibroMeter)
60. TS= (Enhanced liver fatty)
61. TS= (ELF)
62. TS= (NAFLD fibrosis score)
63. TS= (FIB-4 index)
64. TS= (BARD score)
65. TS= (APRI)
66. TS= (Hepascore)
67. TS= (FORN score)
68. TS= (FIBROSpect test)

69. OR/ 58-68
70. 28 AND 31 AND 40 AND 57 AND 69

SciELO

Fatty liver OR liver, Fatty OR Steatohepatitis OR Steatohepatitides OR Steatosis of Liver OR Liver Steatosis OR Steatoses, Liver OR Steatosis, Liver OR Hepatosteatosis OR Non-alcoholic Fatty Liver Disease OR Nonalcoholic Fatty Liver Disease OR Nonalcoholic Fatty Liver Disease OR Fatty Liver, Nonalcoholic OR Fatty Livers, Nonalcoholic ORLiver, Nonalcoholic Fatty OR Livers, Nonalcoholic Fatty OR Nonalcoholic Fatty Liver OR Nonalcoholic Fatty Livers OR Nonalcoholic Steatohepatitis OR Steatohepatitis, Nonalcoholic OR NALFD OR NASH OR Metabolic-Associated Fatty Liver Disease OR MAFLD

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AND

FibroTest OR FibroMeter OR Enhanced liver fatty OR ELF OR NAFLD fibrosis score OR FIB-4 index OR BARD score OR APRI OR Hepascore OR FORN score OR FIBROSpect test

Supplementary Text 2. Characteristic description of the studies in Table 1

The characteristics of the included studies of the systematic review were published between 2004(1) and 2021 (2–4). Of these, the majority were cross-sectional (68%) (2,3,5–86). The period of execution of the study varied from 1995 (4) to 2019 (84), regarding the number of institutions involved, 71% of the studies were carried out in only one intuition (1–3,6–10,12,13,15,17,18,21–25,27–31,33–37,39–44,46,47,49,50,52,53,55–58,60,62–66,68,69,72–74,77,80–86,88,89,92,94–96,100,101,103–113,115–122) and the remaining 39% were varied institutions (4,5,11,14,16,19,20,26,32,38,48,51,54,59,61,67,70,71,75,76,78,87,90,91,93,97–99,102,114,123–126).

In relation to race, most of the studies were carried out in the Caucasian population 56.11% (1,4,5,7–9,11,13–17,19,21–24,26,28,31,34–36,38,40–42,45,47–51,55,57,59,61,62,65,67,70,71,73,75,76,80,82,83,85,86,88–102,113,115–117,119–121,123,124,127–130) followed in the Asian population 28% (6,14,20,25,27,30,33,39,43,44,46,53,54,56,58,60,64,66,69,71,72,74,77,78,84,103–110,131–133) Hispanic 10.7% (3,10,12,18,32,41,52,63,68,70,71,75,81,134) African 1.43 % (125,129).

Regarding the components of the metabolic syndrome, at least one of these was registered in 55.40% of the studies (6,7,9,11–14,16–18,20–22,25,26,28–35,38,41,42,44,48,49,51–53,55,56,58–62,64–67,70,71,74–78,80,83,85,86,88,90,91,95,97,99,105,108–110,113,118,123,127,129,130,132,134–137), systemic arterial hypertension in 40% of the studies in the range was (15.8% (33)-89.1% (132)), (6,7,13,14,17,20,21,28–30,33,35,44–46,48,52,53,55,58,60,62,64,66,67,70,74,75,77,78,82–87,95,110,113,115,118,127,132,134–138) diabetes mellitus type 2 in 61.80% in the range was (8.4 (23)-100% (85,88)), (3,4,6,7,9,11–14,16–18,21–23,25,26,28–35,38,41–49,51–53,55,56,58,60–62,65–68,70,71,74–78,80,82–88,90,95,97,99,105,108–110,112,113,115,118,123,127,129,132,134,136–138) and dyslipidemia in 26.60% in the ranged was (9 to 96%) (6,21,28,34,48,52,58,66,70,87,105,113,115,127,130,132,135,136). AST was reported in 60.40%

(84) of the studies, (2,3,6,7,9,12,13,16,19,21–23,26–29,31–34,36,38–43,45,46,48,51–55,58,60–62,64–67,70–75,80–84,86,87,90,94,95,105,118,123,127,129–132,134,136–138) mean and standard deviation values ranged from (22.3±9 (52) to 79.6±58 (19)), alanine transaminase was evaluated in 62.50% of the studies, (2–4,6,7,9,12–14,16,18,19,21–23,25,27–29,31–34,36,38–43,45–49,51–56,59–62,64–67,69–78,80,82,84–87,90,94,95,105,109,110,118,122,123,127,129–132,134,136–138) with mean and standard deviation values ranged from (23.9±12 (52) to 135.5±96 (36)), the aspartate aminotransferase/alanine aminotransferase ratio was evaluated in 46% of the studies, (2,3,6,7,13,16,18,20–23,25,26,28,29,31,33,34,36,38–42,45,47–49,51,55,56,58,60–62,64–66,71–78,80,82,84–87,94,105,110,118,127,130,132,136–138) with mean and standard deviation values ranged from (0.48±0.37 (118) to 1±0.9 (109)), the platelets was evaluated in 56.80% of the studies, (2,3,6,16,21,22,27,28,33,34,39–43,48,51,52,58,66,67,71,72,80,87,90,105,118,127,130,131,134,136,137) with mean and standard deviation values ranged from (153±65 (27) to 305±90 (86)), in the glycoxylated hemoglobin registered in the 7.20% of the studies,(7,13,23,28,39,41,42,56,64,65,67–71,82–85,95,109,123,129,132,136) with mean and standard deviation values ranged from (0.4±0.37 (118) to 14 ±5(7)), glycemia was reported in the 28.70% of the studies, (6,13,14,16,21,23,28,32,33,38,39,41,42,45,48,49,55,56,59,62,69,73–75,78,82–87,95,105,110,123,127,131,132,136,138) with mean and standard deviation values ranged from (85.4±20 (23) to 148±42 (123)), in the triglycerides was reported in the 40% of the studies, (6,7,9,14,16,21,23,27,29,31,33,36,38,41–46,48,49,53,56,58,59,62,64,65,69,73,78,81–87,95,105,109,110,127,129,131,132,134,136–138) with mean and standard deviation values ranged from (85.07±123 (14) to 239±1.94 (9)), and finally cholesterol was evaluated in the 31.60% of the studies, (6,7,9,14,21,23,27,29,31,33,38,39,41–46,48,49,54,56,58,62,65,69,74,78,82–87,105,109,110,127,129,131,132,136–138) with mean and standard deviation values ranged from (228±58 (87) to 92.6±58 (110)).

Supplementary Table 2. Characteristics of studies included

First author (year of publication) [ref]	Study design	Period of Study	Institution	Race %	HTN%	DM (%)	DLD (%)	MetS	AST(SD)	ALT(SD)	AST/ALT ratio (SD)	Platelet (SD)	HbA1C (%)	Glycemia (SD)	Triglycerides	Cholesterol
Abe M, 2014(131)	Cross-sectional	2003-2013	Multiple	Asian	?	?	?	?	61.4±48	85.5±68	?	189±68	?	115±38	144.4±77	195.4±41
Adams L, 2008(112)	?	?	One	?	?	32	?	?	?	?	?	?	?	?	?	?
Adams L, 2011(16)	Cross-sectional	?	Multiple	Caucasian	?	24.8	?	Yes	37±54	66.5±88	0.55	233.6±76	?	97±79	141±20	?
Ahmed Z, 2016(37)	Cross-sectional	?	One	?	?	?	?	?	?	?	?	?	?	?	?	?
Aida Y, 2015(39)	Cross-sectional	2008-2013	One	Asian	?	?	?	?	42±8.5	52±12.5	0.8	200±24	6.2±1	106.5±7.8	?	197±41
Alkhouri N, 2015(111)	?	?	One	?	?	?	?	?	?	?	?	?	?	?	?	?
Anam M, 2017(118)	?	?	One	?	49.8	54.9	?	Yes	28±5.5	58±12	0.48	238±21	?	?	?	?
Angelidi A, 2017(88)	?	?	One	Caucasian	?	100	?	Yes	?	?	?	?	?	?	?	?
Angulo P, 2014(127)	Cross-sectional	2003-2011	Multiple	Caucasian 91.6	35.7	29.3	53.4	Yes	55±1	81±2	0.8±0.02	237±3	?	114±2	194±4	209±2
Angulo P, 2007(48)	Cross-sectional	2000-2003	Multiple	Caucasian	30	30.5	60	Yes	60±50	87±72	0.94±0.9	235±84	?	116±50	211±161	209±50
Anstee Q, 2019(71)	Cross-sectional	?	Multiple	Caucasian 67, Asian 26, Hispanic 27	?	54.5	?	Yes	37.5±9.7	42±10.5	0.79	227±38	6±1.8	?	?	?
Amernia B, 2021(2)	Cross-sectional	2019	One	?	?	?	?	?	44.7±22.5	51.5±43.3	0.92±0.25	236.6±91.8	?	?	?	?
Arora S, 2016(113)	?	?	One	Caucasian 81	58	48	37	Yes	?	?	?	?	?	?	?	?
Aykut U, 2014(34)	Cross-sectional	?	One	Caucasian	?	19.3	24	Yes	53±31	84±56	0.63	224±194	?	121±55	?	?
Balakrishnan M, 2018(10)	Cross-sectional	2015-2018	One	Hispanic	?	?	?	?	?	?	?	?	?	?	?	?
Balakrishnan M, 2021(3)	Cross-sectional	2010-2014	One	Hispanic	?	53.5	?	?	68.8±57.6	102.6±80	0.75±0.44	235.9±72.5	?	?	?	?
Barritt A, 2019(11)	Cross-sectional	?	Multiple	Caucasian 87	?	60	?	Yes	?	?	?	?	?	?	?	?
Boursier J, 2016(51)	Cross-sectional	2003-2014	Multiple	Caucasian	?	48	?	Yes	48±30	69±49	0.69	217±70	?	?	?	?
Boursier J, 2017(89)	?	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Boursier J, 2019(90)	?	2004-2017	Multiple	Caucasian	?	51.1	?	Yes	39±6.2	56±11.3	?	222±70	?	?	?	?
Brandman D, 2017(124)	Longitunal	?	Multiple	Caucasian 83	?	?	?	?	?	?	?	?	?	?	?	?
Bril F, 2020(123)	Cross-sectional	?	Multiple	Caucasian 58	?	100	?	Yes	41±26	57±390	?	?	7.1±1.1	148±42	?	?
Broussier T, 2020(80)	Cross-sectional	2014-2017	One	Caucasian	?	38.1	?	Yes	33±7.5	42±10	0.76	238±43	?	?	?	?

Cales P, 2009(5)	Cross-sectional	2001-2006	Multiple	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Cales P, 2010(8)	Cross-sectional	2001-2006	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Cebreiros I, 2014(21)	Cross-sectional	2012-2013	One	Caucasian	47.4	24.6	64.9	Yes	24.1±12.3	31.9±26	0.75	248±60.8	?	87	141±55.5	175.1±41.3
Cengiz M, 2015(40)	Cross-sectional	?	One	Caucasian	?	?	?	?	38.5±3.6	53±5.8	0.72	230±76.8	?	?	?	?
Chan W, 2014(132)	Cross-sectional	2012-2014	One	Asian	89.1	52.4	94.6	Yes	41±9.2	71±9.2	0.57	?	6.5±1.5	108	153.2±62	192.5±420
Chowdhury S, 2013(27)	Cross-sectional	2008-2010	One	Asian	?	?	?	?	57±38	74±44	?	153±65	?	?	146±94	153±50
Cichoz-Lach H, 2012(22)	Cross-sectional	?	One	Caucasian	?	23	?	Yes	68±51	97±61	0.72±0.3	276±80	?	?	?	?
Cui J, 2015(41)	Cross-sectional	2012-2014	One	Caucasian 52, Hispanic 28.4	?	25.5	?	Yes	42.3±35	58±56	0.82±0.31	246±62	6.1±0.9	108±33	153.9±75	181±38
de Carli M, 2020(134)	Cross-sectional	2013-2015	One	Hispanic	45.9	27.6	?	Yes	33.8±17.4	50.1±33.7	?	264.5±66	6.3±1.6	?	164.5±79.9	?
de Cleva R, 2016(52)	Cross-sectional	2005-2013	One	Hispanic	64.2	36.4	23.8	Yes	22.3±9	23.9±12	?	271±71	?	?	?	?
Demir M, 2011(24)	Cross-sectional	1998-2009	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Demir M,2013(28)	Cross-sectional	1998-2009	One	Caucasian	41	10	25	Yes	43.1±38	69±64	0.62	247±71	?	103±30	?	?
Dincses E, 2015(42)	Cross-sectional	?	One	Caucasian	?	36.5	?	Yes	61±38	89±58	0.7	229±91	?	128±42	199±91	221±59
Drolz A, 2017(35)	Cross-sectional	?	One	Caucasian	53	30	?	Yes	?	?	?	?	?	?	?	?
Dvorak K, 2014(36)	Cross-sectional	2010-2013	One	Caucasian	?	?	?	?	77.1±42	135.5±96	0.65±0.2	?	?	?	159.4	?
Eddowes P, 2019(114)	?	?	Multiple	?	?	?	?	?	?	?	?	?	?	?	?	?
Fagan K, 2015(115)	Cohort	1999-2013	One	Caucasian 72.6	16.1	10.3	12.8		?	?	?	?	?	?	?	?
Francque S, 2012(23)	Cross-sectional	2005-2010	One	Caucasian	?	8.4	?	?	31±14	43.3±22	0.75±0.18	?	5.6±0.5	85.4±20	148±83	203±40
Fujii H, 2009(6)	Cross-sectional	1998-2007	One	Asian	46	44	62	Yes	72±74	106±86	0.67	192±85	?	124±45	123±121	209±42
Fujii H, 2009(135)	Cross-sectional	2009	One	Asian	32.5	41	68	Yes	?	?	?	?	?	?	?	?
Gallego-Duran R, 2012(91)	?	?	Multiple	Caucasian	?	?	?	Yes	?	?	?	?	?	?	?	?
Guha I, 2008(59)	Cross-sectional	2002-2006	Multiple	Caucasian	?	?	?	Yes	?	77.3	?	239	?	113	221.4	?
Guillaume M, 2019(130)	Cross-sectional	2010-2017	Multiple	Caucasian	60.7	48.2	37.6	Yes	45±33	63±38	0.71	228±67	?	?	?	?
Guturu P, 2008(119)	?	1998-2006	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Harrison S, 2008(70)	Cross-sectional	2001-2005	Multiple	Caucasian 68, Hispanic 24, African	60	35	42	Yes	48	69	0.7	?	5.9	?	?	?

Hagström H, 2019(87)	Retrospective cohort	1971 - 2009	Multiple	?	30	14	9	?	40±20.7	73±46.6	0.58±0.20	243±62.9	?	95±26	177±98.5	228±58
Huang C, 2019(103)	?	?	?	Asian	?	?	?	?	?	?	?	?	?	?	?	?
Inadomi C, 2020(136)	?	2016-2019	Multiple	Asian	64.5	50.3	66.5	Yes	46±23	59.5±32.5	0.77	204 ±81	6.3±1.6	113±32	131±101	188±61
Isgro M, 2014(50)	Cross-sectional	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Itoh Y, 2018(66)	Cross-sectional	2013-2015	One	Asian	42	38	47	Yes	46	63	0.73	206	?	?	?	?
Joo S, 2017(104)	?	?	One	Asian	?	?	?	?	?	?	?	?	?	?	?	?
Joo, S 2015(92)	?	2013-2014	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Jouness R, 2016(93)	?	?	Multiple	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Kao W, 2020(105)	Prospective cohort	2016-2018	One	Asian	?	26.8	16.9	Yes	38.2 ± 32.2	55.0 ± 42.2	0.69	292.0±71.4	?	119.4 ± 57.8	161.9 ± 112.5	190.0 ± 37.6
Kawamura, 2015(43)	Cross-sectional	1990-2011	One	Asian	?	27.7	?	?	65.7±61	108.1±65	?	196.3±86	?	?	131.8±42	200.8
Kim D, 2011(106)	?	2002-2009	One	Asian	?	?	?	?	?	?	?	?	?	?	?	?
Kim D, 2013(137)	Cross-sectional	2007-2010	One	?	45.1	27.5	?	Yes	47.2±31	60.4±55	0.78	216±79	?	?	143.4±77	172.3±40
Kobayashi N, 2017(58)	Cross-sectional	1999-2013	One	Asian	45	46.4	51.4	Yes	60	85	0.7	235	?	?	152.6	203.3
Kolhe K, 2019(72)	Cross-sectional	2012-2013	One	Asian	?	?	?	?	46.1±28	52.1±24.1	0.88	220±75	?	?	?	?
Kosick H, 2019(116)	?	2010-2018	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Kruger F, 2008(120)	?	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Kruger F, 2011(125)	?		Multiple	African 69%	?	?	?	?	?	?	?	?	?	?	?	?
Kumar R, 2013(33)	Cross-sectional	2009-2011	One	Asian	15.8	16.6	?	Yes	45±93	62.5±74	0.72	186±111	?	99.1	165.6±77	180±48
Labenz C, 2018(67)	Cross-sectional	?	Multiple	Caucasian	54.4	29.9	37.5	Yes	48±55	60±75	?	234±104	7.1	?	?	?
Lambrecht J, 2019(94)	?	?	One	Caucasian	?	?	?	?	37±10.7	45.5±9	0.79±0.27	?	?	?	?	?
Lang S, 2020(83)	Cross-sectional	2015-2018	One	Caucasian	74.6	39	?	Yes	46.5±23	47.8±38.5	?	193±81	5.7	111.5±35.6	154±125	176±51.7
Lardi L, 2020(139)	?	?	One	Hispanic	?	?	?	?	?	?	?	?	?	?	?	?
Lassailly G, 2011(17)	Cross-sectional	2006-2009	One	Caucasian	60.4	31.9	58	Yes	?	30.8	?	?	?	?	?	?
Le P, 2018(128)	?	2004-2008	Multiple	Caucasian 80	?	?	?	?	?	?	?	?	?	?	?	?
Lee T, 2013(29)	Cross-sectional	2002-2006	One	?	49	32.7	28.9	Yes	55±11.2	63±19	0.90±0.62	?	?	?	157±35	183.5±21
Liu W, 2020(84)	Cross-sectional	2017-2019	One	Asian	35	31.5	?	?	47.9±31.8	80.5±76.4	0.59	242.1 ± 58.8	6.1 ± 1.2	100±27	201±131	194±73

Loaeza-del-Castillo, 2008(81)	Cross-sectional	?	One	Hispanic	?	?	?	?	72 ±171	?	?	262 ±65	?	?	150	?
Loong T, 2017(60)	Cross-sectional	2006-2013	One	Asian	49.8	54.9	?	Yes	28±5.5	58±12	0.48	238±21	?	?	?	?
Luger M, 2016(95)	Randomized controlled trial	2014-2015	One	Caucasian	52	26	48	Yes	28±13	36.4±20	?	281±64	6±1.3	108±36.6	198±46	?
Mahadeva S, 2013(30)	Cross-sectional	2009-2010	One	Asian	48.1	47.3	60.3	Yes	?	?	?	?	?	?	?	?
Marella H, 2019(129)	Cross-sectional	2006-2016	One	Caucasian, Africanamerican	?	34.1	?	Yes	40±37	52±51	?	266±88	6.4±1.9	?	184.4±202.3	181.1±52.8
McPherson S, 2010(9)	Cross-sectional	2003-2009	One	Caucasian	?	50.3	?	Yes	63±44	94±63	?	255±91	?	?	239.1±194	208.8±54
McPherson S, 2017(61)	Cross-sectional	?	Multiple	Caucasian	?	45.6	?	Yes	49.8±4.5	73.4±9.8	0.67	246	?	?	?	?
McPherson, 2013(31)	Cross-sectional	1999-2009	One	Caucasian	?	43	?	Yes	43.5	61.5	0.7	244	?	?	203.5	208.4
Meneses D, 2020(82)	Cross-sectional	?	One	Caucasian	52	26	28	Yes	21±3	25±4.25	0.84	274±65	5.7	101±5	140±25	183.7±42
Miao C, 2010(117)	?	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Miele L, 2015(96)	?	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Miele L, 2017(62)	Prospective	?	One	Caucasian	34.2	15.8	?	Yes	38±19.5	57±27.7	0.66	222±61	?	91±26.5	126±67.5	201±43.5
Miller A, 2019(57)	Cross-sectional	?	One	Caucasian 87	?	?	?	?	?	?	?	?	?	?	?	?
Miller M, 2010(15)	Cross-sectional	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Munteanu M, 2016(97)	Cohort	2005-2014	Multiple	Caucasian	?	22.7	?	Yes	?	?	?	?	?	?	?	?
Nascimbeni, 2015(98)	Cohort	?	Multiple	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Nassif AT, 2017(63)	Cross-sectional	2012-2013	One	Hispanic	?	?	?	?	?	?	?	?	?	?	?	?
Okajima A, 2017(64)	Cross-sectional	2013-2015	One	Asian	36.8	?	57.1	Yes	53±34	73±52	0.72	222±66	6.4±1.1	?	180±132	?
Pastor-Ramirez, 2017(99)	?	?	Multiple	Caucasian	?	30	?	Yes	?	?	?	?	?	?	?	?
Pathik P, 2015(44)	Cross-sectional	2011-2012	One	Asian	16.9	49	?	Yes	?	?	?	243±8.2	?	?	220±11	223±7
Peleg N, 2017(65)	Cross-sectional	2005-2012	One	Caucasian	?	34.6	?	Yes	59.7	69.8	0.85	188.8	6.59	?	150	171
Pérez-Gutiérrez O, 2013(32)	Cross-sectional	2005-2011	Multiple	Hispanic	?	21.5	?	Yes	57.6±58	73±82	?	238±95	?	107±25	?	?
Petta S, 2015(45)	Cross-sectional	?	One	Caucasian	24	19.5	?	?	43.9±28	78±49	0.56	225±65	?	98.5±26	151±93	205±46
Petta S, 2017(138)	Cross-sectional	2009	Multiple	?	43.4	54.7	?	?	47.4±40.2	77.3±58.8	0.61	229±70.3	?	111±41.3	161.2±102.4	201.8±46.9
Pimentel S, 2010(12)	Cross-sectional	?	One	Hispanic	?	16	?	Yes	30±17	38±29	?	279±73	?	?	?	?
Polyzos S, 2019(73)	Cross-sectional	2008-2010	One	Caucasian	?	?	?	?	38.3±5.6	56.2±10.5	0.68	226±16.5	?	104±6	180.5±24	?
Prasad S, 2020(107)	?	?	One	Asian	?	?	?	?	?	?	?	?	?	?	?	?

Qureshi K, 2008(86)	Cross-sectional	2002-2007	One	Caucasian 86	67	35	50	Yes	25±11	29±16	0.86	305	?	115±38	156±92	198±39
Raszeja-Wyszomirska J, 2010(13)	Cross-sectional	2006-2009	One	Caucasian	29.7	17.8	68.9	Yes	51.5±34	80.8±55	0.79	223±62	6.2±1	102.4±23	?	?
Rath M, 2016(53)	Cross-sectional	2011-2013	One	Asian	26.6	16.7	62	Yes	41.5±18	60±43.5	?	215±42	?	?	170±113	?
Ratziu C, 2006(26)	Cross-sectional	2001-2004	Multiple	Caucasian	23.5	34	39	Yes	47.5	75	0.63	?	?	?	?	?
Ratziu V, 2004(1)	?	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Ruffillo G, 2011(18)	Cross-sectional	?	One	Hispanic	?	23.1	65.9	Yes	?	69	0.57	235	?	?	?	?
Saez E, 2017(100)	?	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Sebastiani G, 2011(19)	Cross-sectional	2003-2008	Multiple	Caucasian	?	?	?	?	79.6±58	72.3±47	?	251±81	?	?	?	?
Seth A, 2016(68)	Cross-sectional	2010-2014	One	Hispanic 77	?	50	?	?	?	?	?	?	7.5	?	?	?
Shah A, 2009(7)	Cross-sectional	?	One	Caucasian 74	44	19	?	Yes	43	63	0.68	241	14	?	148	120
Shaheen A, 2016(121)	Cohort	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Shima T, 2019(74)	Cross-sectional	2013-2016	One	Asian	60.4	58.6	76.6	Yes	56.4±35.4	81.7±56.8	0.69	210±64	?	113.3 ± 39.1	?	200.5 ± 38.8
Shoji H, 2016(54)	Cross-sectional	?	Multiple	Asian	?	?	?	?	48±57	66±12	?	198±83	?	?	?	193±20
Shukla A, 2015(46)	Cross-sectional	?	One	Asian	17.6	19.6	?	?	59.3±46	51.5±38	?	216±70	?	?	154.2±70	175±51
Siddiqui M, 2016(55)	Cross-sectional	2006-2013	One	Caucasian 86	58	39.3	49.3	Yes	62.3±43	80.7±53	0.77	254±96	?	122±53	?	?
Siddiqui M, 2019(75)	Cross-sectional	2004-2009	Multiple	Caucasian 73, Hispanic 13	58	39	62	Yes	51.2±36.7	69.8±50.6	0.73	236±69.8	?	110.6±38.4	?	?
Simo K, 2014(38)	Cross-sectional	2005-2011	Multiple	Caucasian 67.1	?	29.3	?	Yes	27.8±17.3	31.2±24.3	0.98±0.28	298.9±66.8	?	111.2±46.9	163.3±97.5	196.5±41.7
Singh A. 2020(85)	Cross-sectional	2000-2015	One	Caucasian	75.9	100	70.8	Yes	27±5.5	28±18-45	0.96	217.6±83	6.7±1.5	110±12	124±24	167.8±43.6
Singh T, 2018(126)	Cohort	2006-2015	Multiple	?	?	?	?	?	?	?	?	?	?	?	?	?
Sjowall C, 2015(47)	Cross-sectional	?	One	Caucasian	?	51	?	?	39±16	66.2±40	0.59	231±66	?	?	?	?
Stauber R, 2018(101)	Cohort	?	One	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?
Staufer K, 2019(76)	Cross-sectional	2011-2016	Multiple	Caucasian	?	30	?	Yes	41±7.2	55±12	0.74	223±89	?	?	?	?
Subasi C, 2015(49)	Cross-sectional	?	One	Caucasian	?	16.9	?	Yes	58±36	91±61	0.63	226±84	?	124±47	194±95	211±53
Sumida Y, 2012(20)	Cross-sectional	2002-2008	Multiple	Asian	32	42	?	Yes	43±9.5	69±17	0.62±0.7	227±67	?	?	147±25	209±40
Takeuchi H, 2018(69)	Cross-sectional	2010-2015	One	Asian	?	?	?	?	59.5±52.70	87.9±90.3	?	223±82.4	7.1±1.8	127.4±51.2	155±81	185.5±39.3
Tanwar S, 2006(102)	?	?	Multiple	Caucasian	?	?	?	?	?	?	?	?	?	?	?	?

Thanapirom K, 2017(122)	?	2016	One	?	?	?	?	?	32.9±23.2	50.4±45.2	?	272±62	?	?	?	?
Tomeno W, 2019(77)	Cross-sectional	2014-2017	One	Asian	47.1	31.1	56.1	Yes	29±20.3	30±30.3	0.94±0.33	188±39	?	?	?	?
Treeprasertsuk S, 2016(56)	Cross-sectional	2009-2012	One	Asian	?	38	?	Yes	38±39	56±47	0.67	267±64	7.3±8.7	112±33	146±60	198±46
Uy D, 2011(108)	?	2007-2010	One	Asian	?	16.4	?	Yes	?	?	?	?	?	?	?	?
Wong V, 2010(14)	Cross-sectional	2003-2009	Multiple	Caucasian 52, Chinese 48	40.2	36.2	?	Yes	?	75±54	?	?	?	115±46	85.07±123	208.8±50.2
Xun Y, 2012(25)	Cross-sectional	2005-2010	One	Asian	?	32.2	?	Yes	61±41	100±74	0.61	200±56	?	?	?	?
Yang M, 2019(78)	Cross-sectional	2012-2017	Multiple	Asian	34.8	30.2	?	Yes	74.1±35.6	135.1±48.9	0.69±0.37	240.1±66.5	?	96.5±24.1	188.1±81.3	191.8±80
Yoneda M, 2013(109)	Cross-sectional	2002-2011	One	Asian	?	46	63.8	Yes	24.7±10	23.7±7	1	211±69	5.9±0.9	?	140±72	202.6
Younes R, 2021(4)	Multicenter Cohort	1995 - 2015	Multiple	Caucasian	?	28.2	?	?	37±26	59±34.8	?	225±83	?	?	?	?
Zhou Y, 2019(110)	?	2016-2018	One	Asian	42	51	96	Yes	45.7±32.3	49±20.8	0.8±0.4	249.9±58	?	110±30	442±106	92.6±58
Zou C, 2019(133)	?	?	One	Asian	?	?	?	?	?	?	?	?	?	?	?	?

ALT Alanine aminotransferase AST; Aspartate aminotransferase; DM Diabetes Mellitus; DLD Dyslipidemia; HTN Hypertension; HbA1c glycated hemoglobin; MetS Metabolic syndrome, SD Standards Deviation, ? not responded

Supplementary Table 3. Characteristics of the studies included in the systematic review according to the serological biomarkers in predicting liver fibrosis severity in people with MASLD

		Number studies from severity				
Score Models	**Number of participants**	**Any fibrosis**	**Significant fibrosis**	**Advanced fibrosis**	**Cirrhosis**	**Total**
APRI	29 136	3	34	40	3	80
FIB-4	36 357	5	37	43	4	89
NFS	31 538	5	36	43	3	87
BARD score	18 869	1	20	29	2	52
FibroMeter	4 206	2	4	12	1	17
FibroTest	2 079	0	4	6	2	11
ELF	2 403	2	2	6	0	14
Forns score	1 045	0	1	1	1	3
Hepa score	2 122	0	2	2	0	4

APRI aspartate aminotransferase to platelet ratio index; ELF enhanced liver fibrosis; FIB-4 fibrosis index-4; NFS Non-alcoholic fatty liver disease fibrosis score.

Supplementary Table 4. Cut-off values of serological biomarkers from the studies included in predicting liver fibrosis severity in people with MASLD

First author (year of publication) [ref]	FIB-4	APRI	NFS	BARD Score	FibroMeter	FibroTest	ELF	Hepascore	Forns score
Abe M, 2014[20]	?	?	?	NA	NA	NA	NA	NA	NA
Adams L, 2008[21]	NA	?	NA	NA	NA	?	NA	?	NA
Adams L, 2011[57]	SF: 1.45 AF: 1.54 Cirrhosis: 1.92	SF: 0.43 AF: 0.54 Cirrhosis: 1.92	NA	SF: 2.00 AF: 2.00 Cirrhosis: 3.00	SF: 0.34 AF: 0.47 Cirrhosis: 0.57	SF: 0.34 AF: 0.47 Cirrhosis: 0.57	NA	SF: 0.44 AF: 0.37 Cirrhosis: 0.70	NA
Ahmed Z, 2016[35]	?	?	NA	NA	NA	NA	NA	NA	NA
Aida Y, 2015[31]	AF: 2.09	AF: 0.67	NA	NA	NA	NA	NA	NA	NA
Alkhouri N, 2015[95]	?	?	?	NA	NA	NA	NA	NA	NA
Anam M, 2017[38]	?	?	?	?	?	NA	NA	NA	NA
Angelidi A, 2017[66]	SF: 1.00	SF: >0.23	SF: >-1.44	SF: 2.50	NA	NA	NA	NA	NA
Angulo P, 2014[96]	?	?	AF: >0.67	?	NA	NA	NA	NA	NA
Angulo P, 2007[97]	NA	NA	AF: 0.67	NA	NA	NA	NA	NA	NA
Anstee Q, 2019[98]	AF: 2.67	NA	AF: 0.68	NA	NA	NA	AF: 11.30	NA	NA
Amernia B, 2021[99]	AF: 1.19	AF: 0.70	NA	NA	NA	NA	NA	NA	NA
Arora S, 2016[62]	AF: 1.10	?	?	?	NA	NA	NA	NA	NA
Aykut U, 2014[30]	NA	NA	?	NA	AF: 0.82	NA	NA	NA	NA
Balakrishnan M, 2018[100]	AF: 1.45	AF: 1.00	SF: 1.43 AF: 1.43	AF: 2.00	NA	NA	NA	NA	NA
Balakrishnan M, 2021[101]	AF: 1.30	AF: 1.00	AF: 0.67 AF: -1.45	AF: 2.00	NA	NA	NA	NA	NA
Barritt A, 2019[74]	NA	AF: 1.30	AF: 0.67	NA	NA	NA	NA	NA	NA
Boursier J, 2016[63]	AF: 1.52	AF: 0.56	AF: 1.04	AF: 2.00	AF: 0.31	AF: 0.32	NA	AF: 0.32	NA
Boursier J, 2017[39]	NA	NA	?	NA	?	NA	NA	NA	NA
Boursier J, 2019[44]	AF: <1.30	NA	AF: <-1.45	NA	AF: <0.46	?	NA	?	NA
Brandman D, 2017[40]	Cirrhosis: 1.67	Cirrhosis: 0.54	Cirrhosis: 0.28	Cirrhosis: 3.00	NA	NA	NA	NA	NA
Bril F, 2020[102]	NA	NA	NA	NA	NA	AF: 0.35	NA	NA	NA
Broussier T, 2020[103]	AF: <1.30	NA	NA	NA	AF: <0.46	NA	NA	NA	NA
Cales P, 2009[104]	NA	?	?	NA	SF: 0.29	NA	NA	NA	NA
Cales P, 2010[105]	NA	NA	?	NA	NA	?	NA	NA	NA
Cebreiros I, 2014[106]	NA	NA	NA	NA	AnF: 2.75	NA	AF: 8.72	NA	NA
Cengiz M, 2015[107]	?	?	NA	NA	NA	NA	NA	NA	NA

Chan W, 2014[108]	NA	NA	AF: >-1.45	NA	NA	NA	NA	NA	NA
Chowdhury S, 2013[59]	NA	AF: 1.00	NA	NA	NA	NA	NA	NA	NA
Cichoz-Lach H, 2012[109]	NA	NA	AF: >0.67	AF: ≥0.8	NA	NA	NA	NA	NA
Cui J, 2015[110]	AF: 1.30	?	?	?	NA	NA	NA	NA	NA
de Carli M, 2020[75]	AF: 2.67	AF: >0.98	AF: >0.67	AF: ≥ 2	NA	NA	NA	NA	NA
de Cleva R, 2016[111]	NA	AF: 0.44	NA	NA	NA	NA	NA	NA	NA
Demir M, 2011[24]	NA	NA	AF: 0.67	?	NA	NA	NA	NA	NA
Demir M,2013[112]	SF: 1.45 AF: 3.25	NA	SF: 1.46 AF: 0.67	SF: 0-1 AF: 2-4	NA	NA	NA	NA	NA
Dincses E, 2015[113]	NA	NA	?	NA	?	NA	NA	NA	NA
Drolz A, 2017[114]	?	?	?	?	NA	NA	NA	NA	NA
Dvorak K, 2014[115]	SF: 1.24	SF: 0.65	SF: 2.16	AF: 0.71	NA	NA	?	NA	NA
Eddowes P, 2019[45]	AF: 3.25	NA	AF: 0.67	NA	AF: 0.71	NA	NA	NA	NA
Fagan K, 2015[60]	NA	NA	NA	NA	NA	NA	AF: ≥9.8	NA	NA
Francque S, 2012[116]	?	?	AF: >2.14	?	NA	NA	NA	NA	?
Fujii H, 2009[47]	NA	AF: >2.00	NA	NA	NA	NA	NA	NA	NA
Fujii H, 2009[117]	NA	NA	NA	?	NA	NA	NA	NA	NA
Gallego-Duran R, 2012[27]	NA	NA	?	NA	NA	AF: <0.58	NA	NA	NA
Guha I, 2008[89]	NA	NA	NA	NA	NA	NA	AF: -1.24	NA	NA
Guillaume M, 2019[118]	NA	NA	NA	NA	AF: 0.43	NA	AF: 9.3	NA	NA
Guturu P, 2008[119]	NA	SF: <0.44	NA	?	NA	NA	NA	NA	NA
Harrison S, 2008[120]	NA	NA	NA	AF: >2.00	NA	NA	NA	NA	NA
Hagström H, 2019[80]	?	?	AF: 1.00	AF: 1.45	NA	NA	NA	NA	NA
Huang C, 2019[121]	?	?	?	?	?	NA	NA	NA	NA
Inadomi C, 2020[122]	SF: 2.67 AF: 2.67	NA	NA	NA	NA	NA	SF: 9.86 AF: 10.36	NA	NA
Isgro M, 2014[123]	NA	NA	NA	NA	NA	NA	?	NA	NA
Itoh Y, 2018[124]	NA	NA	NA	NA	NA	NA	AF: 9.2	NA	NA
Joo S, 2017[125]	?	NA	?	?	NA	NA	NA	NA	NA
Joo, S 2015[32]	?	NA	NA	NA	NA	NA	NA	NA	NA
Jouness R, 2016[36]	?	NA	?	NA	NA	NA	NA	NA	NA
Kao W, 2020[81]	SF: 0.66	AF: 0.40	SF: 1.90	NA	NA	NA		NA	NA
Kawamura, 2015[126]			NA	NA	NA	NA	NA	NA	NA

Kim D, 2011[49]	?	?	?	?	NA	NA	NA	NA	NA
Kim D, 2013[127]	AF: 3.25	AF: 1.50	AF: 0.68	AF: 2.00	NA	NA	NA	NA	NA
Kobayashi N, 2017[128]	SF: 0.85	AF: 0.45	NA	NA	NA	NA	NA	NA	NA
Kolhe K, 2019[76]	SF: 1.45	SF: 0.45	NA	NA	NA	NA	NA	NA	NA
Kosick H, 2019[77]	?	?	?	?	NA	NA	NA	NA	NA
Kruger F, 2008[129]	NA	AF: 0.98	AF: -1.30	NA	NA	NA	NA	NA	NA
Kruger F, 2011[130]	NA		AF:1.31	NA	NA	NA	NA	NA	NA
Kumar R, 2013[28]	?	?	?	?	NA	NA	NA	NA	NA
Labenz C, 2018[131]	?	?	?	NA	NA	NA	NA	NA	NA
Lambrecht J, 2019[46]	SF: 1.50	SF: 0.49	NA	NA	NA	NA	NA	NA	NA
Lang S, 2020[83]	AnF: 1.3	NA	AnF: 0.68	NA	NA	NA	NA	NA	NA
Lardi L, 2020[132]	NA	NA	NA	NA	NA	?	NA	NA	NA
Lassailly G, 2011[25]	NA	NA	NA	NA	NA	?	NA	NA	NA
Le P, 2018[42]	AF: 1.64	AF: 0.59	NA	?	NA	NA	NA	NA	NA
Lee T, 2013[51]	?	NA	?	?	?	NA	NA	NA	NA
Liu W, 2020[84]	SF: 0.87	NA	NA	SF: 1.00	NA	NA	NA	NA	NA
Loaeza-del-Castillo, 2008[133]	NA	SF: <0.2 Cirrhosis: <0.5	NA	NA	NA	NA	NA	NA	NA
Loong T, 2017[67]	NA	NA	NA	NA	AF: 0.82	NA	NA	NA	NA
Luger M, 2016[37]	?	NA	?	NA	NA	NA	NA	NA	NA
Mahadeva S, 2013[134]	NA	?	?	NA	NA	NA	NA	NA	NA
Marella H, 2019[86]	AF: 2.67	AF: 1.50 Cirrhosis: 1.50	AF:0.67 Cirrhosis: 0.67	AF: 2.00	NA	NA	NA	NA	NA
McPherson S, 2010[135]	AF: 1.30	AF: 1.00	AF: 1.45	?	NA	NA	NA	NA	NA
McPherson S, 2017[68]	AF: 2.67	?	AF: 0.68	NA	NA	NA	NA	NA	NA
McPherson, 2013[93]	AF: 3.25	NA	AF: 1.45	AF: 2.00	NA	NA	NA	NA	NA
Meneses D, 2020[82]	SF: 2.67	SF: 0.98	SF: 0.68	SF: 3.00	NA	NA	NA	NA	?
Miao C, 2010[136]	?	NA	?	?	NA	NA	NA	NA	NA
Miele L, 2015[137]	NA	NA	NA	NA	NA	NA	AF: 9.80	NA	NA
Miele L, 2017[138]	NA	NA	NA	NA	NA	NA		NA	NA
Miller A, 2019[139]	AF: >3.25	AF: >2.00	AF: 0.67	NA	NA	NA	NA	NA	NA
Miller M, 2010[23]	?	NA	?	?	NA	NA	NA	NA	NA
Munteanu M, 2016[64]	?	NA	?	?	NA	Cirrhosis: 0.74	NA	NA	NA

Nascimbeni, 2015[33]	?	?	?	?	NA	NA	NA	NA	NA
Nassif AT, 2017[69]	NA	NA	NA	AF: >2.00	NA	NA	NA	NA	NA
Okajima A, 2017[70]	AnF: 1.44	AnF: 0.49 SF: 0.69 AF: 0.78	AnF: 1.85 SF: 1.94 AF: 0.11	NA	NA	NA	NA	NA	NA
Pastor-Ramirez, 2017[140]	?	?	?	?	NA	NA	NA	NA	NA
Pathik P, 2015[34]	NA	AF: 0.68	AF: 1.00	NA	NA	NA	NA	NA	NA
Peleg N, 2017[141]	AF: 1.30	AF: 1.00	NA	NA	NA	NA	NA	NA	NA
Pérez-Gutiérrez O, 2013[142]	AF: ≥3.25	AF: ≥1.00	AF: ≥0.67	AF: ≥2.00	NA	NA	NA	NA	NA
Petta S, 2015[143]	AF: >2.67	NA	AF: >0.67	NA	NA	NA	NA	NA	NA
Petta S, 2017[71]	AF: 2.67	NA	AF: 0.68	NA	NA	NA	NA	NA	NA
Pimentel S, 2010[55]	NA	NA	AF: >0.67	NA	NA	NA	NA	NA	NA
Polyzos S, 2019[144]	?	SF: 0.50	?	NA	NA	NA	SF: 9.00	NA	NA
Prasad S, 2020[85]	AF: 2.02	AF: 1.09	AF: 0.24	NA	NA	NA	NA	NA	NA
Qureshi K, 2008[22]	NA	NA	SF: 0.67 AF: 0.67	NA	NA	NA	NA	NA	NA
Raszeja-Wyszomirska J, 2010[48]	NA	NA	NA	SF: 2.00	NA	NA	NA	NA	NA
Rath M, 2016[145]	NA	AF: 0.56	AF: 1.46	?	NA	NA	NA	NA	NA
Ratziu C, 2006[146]	NA	NA	NA	NA	NA	AF: 0.70	NA	NA	NA
Ratziu V, 2004[53]	NA	NA	NA	NA	NA	SF: 0.30	NA	NA	NA
Ruffillo G, 2011[147]	NA	NA	AF: 0.67	AF: >2.00	NA	NA	NA	NA	NA
Saez E, 2017[41]	NA	SF: 0.45	SF: 0.36	?	NA	NA	NA	NA	NA
Sebastiani G, 2011[148]	NA	SF: 1.50	NA	NA	NA	SF: 0.48	NA	NA	NA
Seth A, 2016[149]	?	?	?	?	NA	NA	NA	NA	NA
Shah A, 2009[150]	AF: 2.67	NA	NA	NA	NA	NA	NA	NA	NA
Shaheen A, 2016[65]	AnF: 1.87	?	?	NA	NA	NA	NA	NA	NA
Shima T, 2019[78]	AF: 1.87	AnF: 0.39 AF: 0.55	AnF: 1.54 AF: 0.58	NA	NA	NA		NA	NA
Shoji H, 2016[151]	SF: 1.37 AF: 2.25	SF: 0.75 AF: 0.88	SF: 1.10 AF: 0.53	?	NA	NA	NA	NA	NA
Shukla A, 2015[152]	AF: 2.64	NA	NA	NA	NA	NA	NA	NA	NA
Siddiqui M, 2016[153]	SF: 1.31 AF: 1.96	AF: 0.71	AF: 0.16	AnF: 2.00 AF: 4.00	AnF: 0.15	NA	NA	NA	NA
Siddiqui M, 2019[90]	AF: 1.37	AnF: 0.74 SF: 0.84	AnF: 1.51 SF: 0.80	NA	NA	NA	NA	NA	NA

		AF: 0.84	AF: -0.76						
Simo K, 2014[154]	NA	NA	SF: 0.68	NA	NA	NA	NA	NA	NA
Singh A. 2020[155]	AF: 2.67	AF: 1.50	AF: 0.68	NA	NA	NA	NA	NA	NA
Singh T, 2018[156]	AF: >2.67	AF: >1.5	AF: >0.67	NA	NA	NA	NA	NA	NA
Sjowall C, 2015[61]	NA	?	?	?	NA	NA	NA	NA	NA
Stauber R, 2018[43]	NA	NA	NA	NA	NA	NA	AF: 9.10	NA	NA
Staufer K, 2019[157]	SF: 1.30 AF: 1.30	NA	NA	NA	SF: 0.31	NA	SF: 9.10 AF: 9.80	NA	NA
Subasi C, 2015[158]	AF: 3.00	AF: 3.00	AF: 3.00	AF: 3.00	?	NA	NA	NA	NA
Sumida Y, 2012[50]	AF: 1.45	AF: 1.00	AF: 1.45	AF: 2.00	NA	NA	NA	NA	NA
Takeuchi H, 2018[73]	SF: 1.72 AF: 1.41	NA	NA	NA	NA	NA	NA	NA	NA
Tanwar S, 2006[54]	?	?	?	?	NA	NA	?	NA	NA
Thanapirom K, 2017[72]	?	?	NA	NA	NA	NA	NA	NA	NA
Tomeno W, 2019[159]	AF: 3.25	NA	NA	NA	NA	NA	NA	NA	NA
Treeprasertsuk S, 2016[160]	AF: 1.30	NA	AF: 1.46	AF: 2.00	NA	NA	NA	NA	NA
Uy D, 2011[26]	?	?	NA	?	NA	NA	NA	NA	NA
Wong V, 2010[56]	AF: 0.50	AF: 1.30	AF: 1.46	AF: 2.00	NA	NA	NA	NA	NA
Xun Y, 2012[58]	AF: 1.30	AF: 0.50	AF: 1.46	AF: 2.00	NA	NA	NA	NA	NA
Yang M, 2019[161]	AF: 2.67	AF: 0.98	AF: 0.675	AF: 2.00	?	NA	NA	NA	?
Yoneda M, 2013[29]	AF: 2.67	NA	AF: 0.73	AF: 3.00	NA	NA	NA	NA	NA
Younes R, 2021[162]	?	?	?	?	NA	NA	NA	?	NA
Zhou Y, 2019[79]	?	?	?	?	NA	NA	NA	NA	NA
Zou C, 2019[19]	?	?	?	?	NA	NA	NA	NA	NA

AF advanced fibrosis, AnF any fibrosis; APRI aspartate aminotransferase to platelet ratio index; BARD score body mass index, aspartate aminotransferase/alanine aminotransferase ratio, diabetes score; ELF enhanced liver fibrosis; FIB-4 fibrosis index-4; NFS Non-alcoholic fatty liver disease fibrosis score; NA not applicable, SF significant fibrosis;? not responded

Supplementary Table 5. Risk of bias assessment of included studies using the QUADAS 2 tool.

First author (year publication) [ref]	Patients' selection	Index test	Reference standard	Flow and timing
Abe M, 2014(131)	Unclear	Unclear	Low	Unclear
Adams L, 2008(112)	Unclear	Low	Low	Unclear
Adams L, 2011(16)	Low	Low	Unclear	Low
Ahmed Z, 2016(37)	Unclear	Unclear	Low	Unclear
Aida Y, 2015(39)	Unclear	Low	High	Unclear
Alkhouri N, 2015(111)	Unclear	Low	High	Low
Anam M, 2017(118)	Unclear	Unclear	Low	High
Angelidi A, 2017(88)	Low	Low	Unclear	Unclear
Angulo P, 2014(127)	Low	Low	High	Low
Angulo P, 2007(48)	Low	Low	Low	Unclear
Anstee Q, 2019(71)	Unclear	Low	Low	Low
Amernia B, 2021(2)	Low	Low	Low	Low
Arora S, 2016(113)	Low	Unclear	Unclear	Unclear
Aykut U, 2014(34)	Unclear	Low	Low	Unclear
Balakrishnan M, 2018(10)	Low	Low	Low	High
Balakrishnan M, 2021(3)	Low	Low	Low	Low
Barritt A, 2019(11)	Unclear	Low	Unclear	Low
Boursier J, 2016(51)	Low	Low	Unclear	Low
Boursier J, 2017(89)	Unclear	Low	Low	Unclear
Boursier J, 2019(90)	Unclear	Low	Low	Unclear
Brandman D, 2017(124)	Unclear	Low	Low	Unclear
Bril F, 2020(123)	Unclear	Low	Low	Low
Broussier T, 2020(80)	Low	Low	Low	Low
Cales P, 2009(5)	Low	High	Low	Unclear
Cales P, 2010(8)	Low	Low	High	Unclear
Cebreiros I, 2014(21)	Low	Unclear	Low	Unclear
Cengiz M, 2015(40)	Unclear	Low	Low	Low
Chan W, 2014(132)	Unclear	Unclear	Low	Low
Chowdhury S, 2013(27)	Low	Low	Unclear	Low
Cichoz-Lach H, 2012(22)	Low	Low	Low	Low
Cui J, 2015(41)	Unclear	Unclear	Low	Low
de Carli M, 2020(134)	Unclear	Low	Unclear	Low
de Cleva R, 2016(52)	Low	Low	Low	Low
Demir M, 2011(24)	Unclear	Low	Low	Unclear
Demir M,2013(28)	Low	Low	Low	Low
Dincses E, 2015(42)	Low	Low	Low	Low
Drolz A, 2017(35)	Unclear	Low	Low	Low
Dvorak K, 2014(36)	Unclear	Unclear	Low	Low
Eddowes P, 2019(114)	Unclear	Low	Low	High
Fagan K, 2015(115)	High	Low	Unclear	High
Francque S, 2012(23)	Low	Unclear	Low	Low

Fujii H, 2009(6)	Unclear	Low	Unclear	Low
Fujii H, 2009(135)	Low	Low	Unclear	Low
Gallego-Duran R, 2012(91)	Unclear	High	Low	Unclear
Guha I, 2008(59)	Unclear	Low	Low	Low
Guillaume M, 2019(130)	Low	Low	Low	Unclear
Guturu P, 2008(119)	Low	High	Low	Unclear
Harrison S, 2008(70)	High	Low	Unclear	High
Hagström H, 2019(87)	Low	Low	Low	Low
Huang C, 2019(103)	Unclear	Low	Low	Unclear
Inadomi C, 2020(136)	Low	Low	Low	Unclear
Isgro M, 2014(50)	Unclear	Low	Low	Low
Itoh Y, 2018(66)	Unclear	Low	Low	Low
Joo S, 2017(104)	Low	Low	High	Low
Joo, S 2015(92)	Unclear	Unclear	Low	Unclear
Jouness R, 2016(93)	Unclear	Low	Low	High
Kao W, 2020(105)	Low	Low	Unclear	Low
Kawamura, 2015(43)	Low	Unclear	Low	Low
Kim D, 2011(106)	Unclear	Unclear	Low	Low
Kim D, 2013(137)	Low	Unclear	Low	Unclear
Kobayashi N, 2017(58)	Low	Low	High	Low
Kolhe K, 2019(72)	Low	Low	Unclear	Low
Kosick H, 2019(116)	Unclear	Low	Unclear	Low
Kruger F, 2008(120)	Low	Low	Low	Low
Kruger F, 2011(125)	Low	Low	Low	High
Kumar R, 2013(33)	Unclear	High	Low	Unclear
Labenz C, 2018(67)	Low	Low	Low	Low
Lambrecht J, 2019(94)	Unclear	Low	Low	High
Lang S, 2020(83)	Low	Low	Unclear	Low
Lardi L, 2020(139)	Low	Low	Low	Low
Lassailly G, 2011(17)	Unclear	Low	Low	Unclear
Le P, 2018(128)	Unclear	Unclear	Low	High
Lee T, 2013(29)	Unclear	Low	Low	Low
Liu W, 2020(84)	Low	Low	Unclear	Low
Loaeza-del-Castillo, 2008(81)	Low	Low	Low	Unclear
Loong T, 2017(60)	Low	Low	Unclear	Low
Luger M, 2016(95)	Unclear	Low	Low	High
Mahadeva S, 2013(30)	Unclear	High	Low	Low
Marella H, 2019(129)	Unclear	Low	Low	Low
McPherson S, 2010(9)	Low	Low	Low	Unclear
McPherson S, 2017(61)	Low	Unclear	Low	Low
McPherson, 2013(31)	Low	Low	Unclear	Low
Meneses D, 2020(82)	Low	Low	Unclear	Low
Miao C, 2010(117)	Low	Low	Low	Unclear
Miele L, 2015(96)	Low	Low	Low	Unclear
Miele L, 2017(62)	Low	Low	Low	Low
Miller A, 2019(57)	Low	Low	Low	Unclear
Miller M, 2010(15)	Unclear	High	Low	Unclear
Munteanu M, 2016(97)	Low	Low	Unclear	Unclear
Nascimbeni, 2015(98)	Unclear	Low	Unclear	Unclear
Nassif AT, 2017(63)	Low	Low	Unclear	Unclear

Okajima A, 2017(64)	Low	Low	Unclear	Low
Pastor-Ramirez, 2017(99)	Low	Low	Low	Low
Pathik P, 2015(44)	Unclear	Low	Low	Unclear
Peleg N, 2017(65)	Low	Low	Low	Unclear
Pérez-Gutiérrez O, 2013(32)	Low	Unclear	Low	Unclear
Petta S, 2015(45)	Unclear	Low	Low	Low
Petta S, 2017(138)	Low	Low	Unclear	Low
Pimentel S, 2010(12)	Unclear	Low	Unclear	Low
Polyzos S, 2019(73)	Low	Low	Low	Low
Prasad S, 2020(107)	Low	Low	Unclear	Low
Qureshi K, 2008(86)	Unclear	Low	Low	Unclear
Raszeja-Wyszomirska J, 2010(13)	Unclear	Low	Low	Low
Rath M, 2016(53)	Low	Low	Low	Unclear
Ratziu C, 2006(26)	Low	Unclear	Unclear	Unclear
Ratziu V, 2004(1)	Low	Low	Low	Low
Ruffillo G, 2011(18)	Low	Low	Low	Low
Saez E, 2017(100)	Unclear	Low	Low	High
Sebastiani G, 2011(19)	Low	Low	Low	Unclear
Seth A, 2016(68)	Unclear	Low	Low	Low
Shah A, 2009(7)	Unclear	Unclear	Low	Low
Shaheen A, 2016(121)	Low	Low	Unclear	Unclear
Shima T, 2019(74)	Low	Low	Unclear	Low
Shoji H, 2016(54)	Unclear	Low	High	Low
Shukla A, 2015(46)	Low	Low	Low	Unclear
Siddiqui M, 2016(55)	Low	Low	Low	Low
Siddiqui M, 2019(75)	Low	Low	High	Unclear
Simo K, 2014(38)	Unclear	Unclear	Low	Low
Singh A. 2020(85)	Low	Low	Low	Low
Singh T, 2018(126)	Unclear	Low	Low	Low
Sjowall C, 2015(47)	Low	Low	Unclear	Low
Stauber R, 2018(101)	Unclear	Low	Low	Unclear
Staufer K, 2019(76)	Low	Low	Low	Low
Subasi C, 2015(49)	Low	Low	Low	Unclear
Sumida Y, 2012(20)	Unclear	Low	Unclear	Low
Takeuchi H, 2018(69)	Low	Low	Unclear	Unclear
Tanwar S, 2006(102)	Low	Low	Unclear	High
Thanapirom K, 2017(122)	Low	Low	Unclear	Low
Tomeno W, 2019(77)	Low	Low	Low	Low
Treeprasertsuk S, 2016(56)	Low	Low	Low	Low
Uy D, 2011(108)	Unclear	Low	Low	Unclear
Wong V, 2010(14)	Low	Unclear	Unclear	Low
Xun Y, 2012(25)	Low	Low	Unclear	Unclear
Yang M, 2019(78)	Low	Low	Low	Low
Yoneda M, 2013(109)	Low	Low	Low	Low
Younes R, 2021(4)	Unclear	Low	Low	Unclear
Zhou Y, 2019(110)	Low	Low	Unclear	Low
Zou C, 2019(133)	Unclear	Low	Low	Unclear

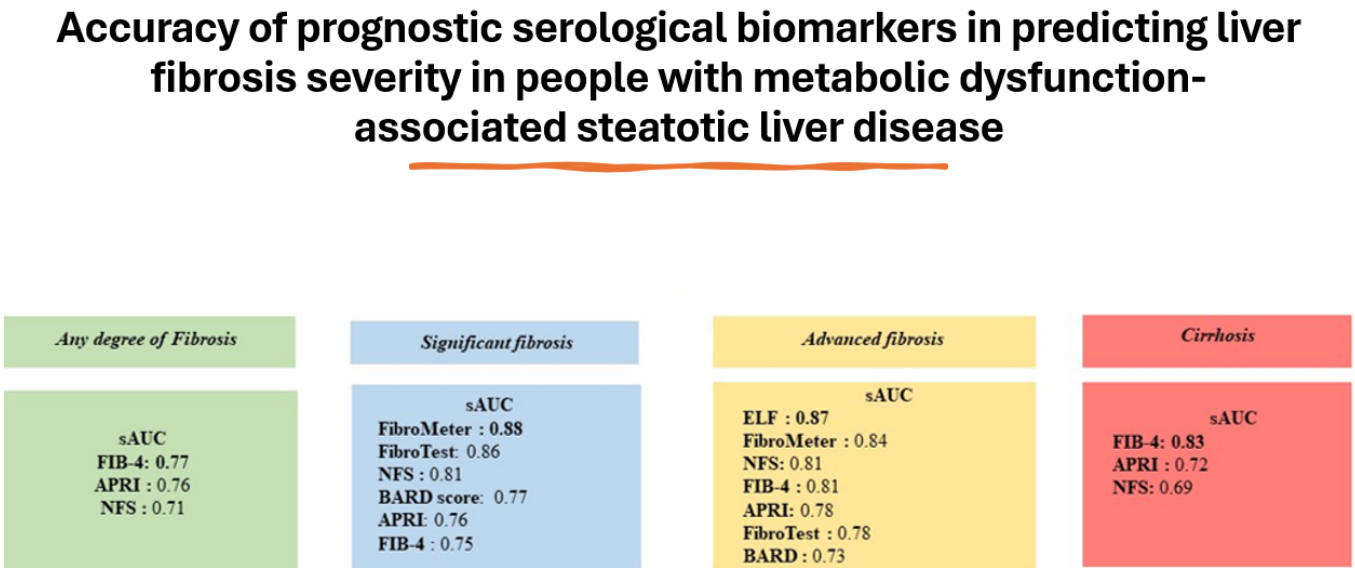
Supplementary Table 6. Assessment of the applicability concerns of the included studies using

First author, (year publication) [ref]	Patient selection	Index test	Reference standard
Abe M, 2014(131)	Unclear	Low	Unclear
Adams L, 2008(112)	Unclear	Low	Low
Adams L, 2011(16)	Unclear	Low	Low
Ahmed Z, 2016(37)	Unclear	Unclear	High
Aida Y, 2015(39)	Low	Low	Unclear
Alkhouri N, 2015(111)	Unclear	High	Low
Anam M, 2017(118)	Unclear	Low	Low
Angelidi A, 2017(88)	Low	Unclear	High
Angulo P, 2014(127)	Low	Low	Unclear
Angulo P, 2007(48)	Low	Unclear	Low
Anstee Q, 2019(71)	Unclear	Unclear	Low
Amernia B, 2021(2)	Low	Low	Low
Arora S, 2016(113)	Low	Unclear	Low
Aykut U, 2014(34)	Low	Unclear	Low
Balakrishnan M, 2018(10)	Unclear	Unclear	Low
Balakrishnan M, 2021(3)	Low	Low	Low
Barritt A, 2019(11)	Low	Low	Low
Boursier J, 2016(51)	Low	Low	Unclear
Boursier J, 2017(89)	Unclear	High	Low
Boursier J, 2019(90)	Low	Low	Unclear
Brandman D, 2017(124)	Low	Low	Unclear
Bril F, 2020(123)	Unclear	Unclear	Low
Broussier T, 2020(80)	Low	Low	Unclear
Cales P, 2009(5)	Unclear	High	Low
Cales P, 2010(8)	Low	Low	Low
Cebreiros I, 2014(21)	Unclear	Low	Low
Cengiz M, 2015(40)	Low	Low	Unclear
Chan W, 2014(132)	Low	Low	Unclear
Chowdhury S, 2013(27)	Low	Unclear	Low
Cichoz-Lach H, 2012(22)	Unclear	Low	Low
Cui J, 2015(41)	Low	Unclear	Low
de Carli M, 2020(134)	Unclear	Low	Unclear
de Cleva R, 2016(52)	Unclear	Low	Low
Demir M, 2011(24)	Unclear	Unclear	Low
Demir M,2013(28)	Low	Low	Low
Dincses E, 2015(42)	Low	Low	Unclear
Drolz A, 2017(35)	Unclear	Low	Low
Dvorak K, 2014(36)	Low	Unclear	Low

Eddowes P, 2019(114)	Unclear	Low	Low
Fagan K, 2015(115)	High	Low	Unclear
Francque S, 2012(23)	Unclear	Low	Low
Fujii H, 2009(6)	Low	Low	Low
Fujii H, 2009(135)	Unclear	Low	Low
Gallego-Duran R, 2012(91)	Unclear	High	Low
Guha I, 2008(59)	Low	Low	Low
Guillaume M, 2019(130)	Low	Low	Unclear
Guturu P, 2008(119)	Low	High	Low
Harrison S, 2008(70)	High	Low	High
Hagström H, 2019(87)	Low	Low	Unclear
Huang C, 2019(103)	Unclear	Low	Unclear
Inadomi C, 2020(136)	Unclear	Low	Unclear
Isgro M, 2014(50)	Unclear	Low	High
Itoh Y, 2018(66)	Unclear	Low	Low
Joo S, 2017(104)	Unclear	Low	Unclear
Joo, S 2015(92)	Unclear	Unclear	Low
Jouness R, 2016(93)	Unclear	Low	Unclear
Kao W, 2020(105)	Unclear	Low	Low
Kawamura, 2015(43)	Unclear	High	Low
Kim D, 2011(106)	Unclear	Unclear	Low
Kim D, 2013(137)	Unclear	Unclear	Low
Kobayashi N, 2017(58)	Low	Low	Unclear
Kolhe K, 2019(72)	Low	Low	Unclear
Kosick H, 2019(116)	Unclear	Unclear	Low
Kruger F, 2008(120)	Low	Low	Low
Kruger F, 2011(125)	Unclear	Low	Unclear
Kumar R, 2013(33)	Low	Unclear	High
Labenz C, 2018(67)	Low	Low	Low
Lambrecht J, 2019(94)	Low	Low	Low
Lang S, 2020(83)	Low	Low	Low
Lardi L, 2020(139)	Low	Low	Low
Lassailly G, 2011(17)	Unclear	Low	Low
Le P, 2018(128)	Unclear	Low	Unclear
Lee T, 2013(29)	Unclear	Low	Low
Liu W, 2020(84)	Low	Low	Low
Loaeza-del-Castillo, 2008(81)	Unclear	High	Low
Loong T, 2017(60)	Low	Low	Unclear
Luger M, 2016(95)	High	Low	Unclear
Mahadeva S, 2013(30)	Unclear	High	Low
Marella H, 2019(129)	Unclear	Low	Low
McPherson S, 2010(9)	Low	Low	Low
McPherson S, 2017(61)	Unclear	Low	Low
McPherson, 2013(31)	Low	Low	Low

Meneses D, 2020(82)	Low	Low	Unclear
Miao C, 2010(117)	Low	Low	Low
Miele L, 2015(96)	Low	Low	Unclear
Miele L, 2017(62)	Low	Low	Low
Miller A, 2019(57)	Unclear	Unclear	Low
Miller M, 2010(15)	Unclear	Unclear	Low
Munteanu M, 2016(97)	Low	Low	High
Nascimbeni, 2015(98)	Unclear	Low	High
Nassif AT, 2017(63)	Low	Low	High
Okajima A, 2017(64)	Low	Low	Unclear
Pastor-Ramirez, 2017(99)	Low	Unclear	Low
Pathik P, 2015(44)	Unclear	Low	Low
Peleg N, 2017(65)	Low	Low	Low
Pérez-Gutiérrez O, 2013(32)	Low	Unclear	Low
Petta S, 2015(45)	Unclear	Low	Unclear
Petta S, 2017(138)	Low	Low	Unclear
Pimentel S, 2010(12)	Unclear	Low	Low
Polyzos S, 2019(73)	Low	Low	Low
Prasad S, 2020(107)	Low	Low	Low
Qureshi K, 2008(86)	Low	Low	Low
Raszeja-Wyszomirska J, 2010(13)	Unclear	Unclear	Low
Rath M, 2016(53)	Low	Low	Low
Ratziu C, 2006(26)	Low	Unclear	Unclear
Ratziu V, 2004(1)	Low	Unclear	Low
Ruffillo G, 2011(18)	Low	Low	Low
Saez E, 2017(100)	Unclear	Low	High
Sebastiani G, 2011(19)	Unclear	Low	Low
Seth A, 2016(68)	Low	Low	Unclear
Shah A, 2009(7)	Low	Low	Low
Shaheen A, 2016(121)	Low	Unclear	Low
Shima T, 2019(74)	Low	Low	Unclear
Shoji H, 2016(54)	Unclear	Low	High
Shukla A, 2015(46)	Low	Unclear	Low
Siddiqui M, 2016(55)	Low	Low	Low
Siddiqui M, 2019(75)	Low	Low	High
Simo K, 2014(38)	Unclear	Unclear	Low
Singh A. 2020(85)	Low	Low	Low
Singh T, 2018(126)	Unclear	Low	Low
Sjowall C, 2015(47)	Low	Low	Unclear
Stauber R, 2018(101)	Low	Low	Low
Staufer K, 2019(76)	Low	Low	Low
Subasi C, 2015(49)	Low	Low	Low
Sumida Y, 2012(20)	Low	Low	Low

Takeuchi H, 2018(69)	Low	Unclear	Unclear
Tanwar S, 2006(102)	Unclear	Low	Unclear
Thanapirom K, 2017(122)	Unclear	Low	Low
Tomeno W, 2019(77)	Unclear	Unclear	Low
Treeprasertsuk S, 2016(56)	Low	Low	Low
Uy D, 2011(108)	Unclear	Low	Low
Wong V, 2010(14)	Low	Unclear	Low
Xun Y, 2012(25)	Unclear	Low	Unclear
Yang M, 2019(78)	Low	Low	Low
Yoneda M, 2013(109)	Unclear	Low	Low
Younes R, 2021(4)	Low	Low	Low
Zhou Y, 2019(110)	Low	Low	Unclear

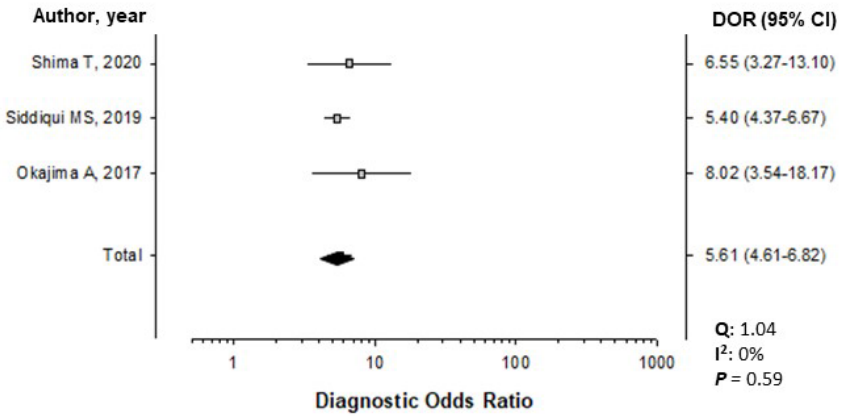


Supplementary Figure 1. Algorithm of the prognostic accuracy of serological biomarkers in predicting liver fibrosis severity in people with MASLD

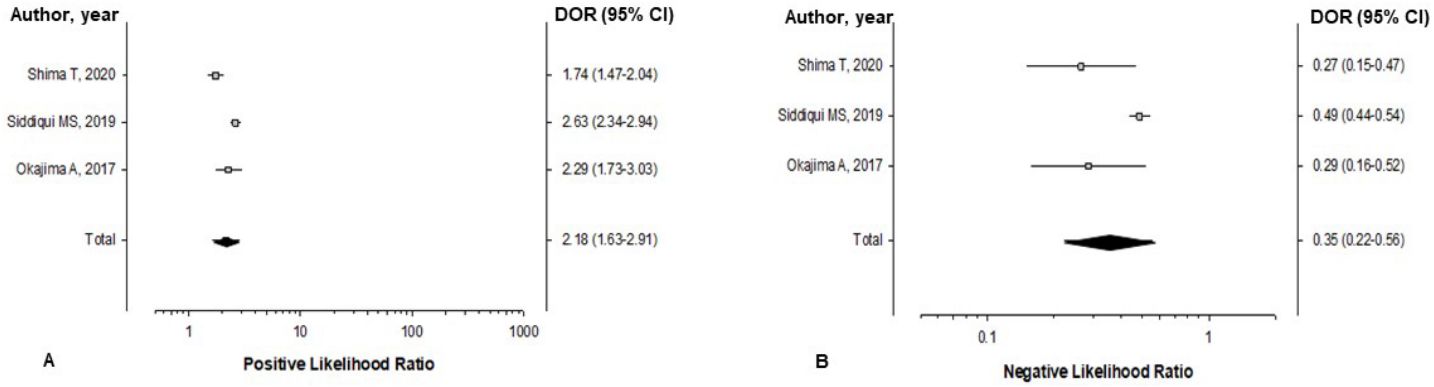
Meta-analysis figures

APRI

Diagnosis of any fibrosis (F0 vs F1-F4)

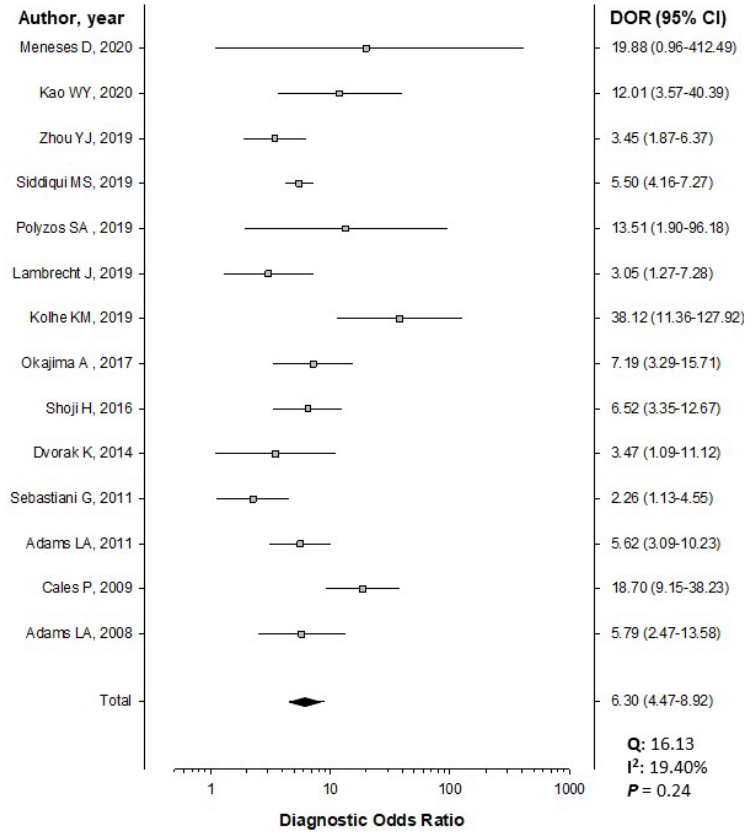


Supplementary Figure 2. Forest plot of meta-analysis of diagnostic odds ratio for APRI values in any fibrosis.

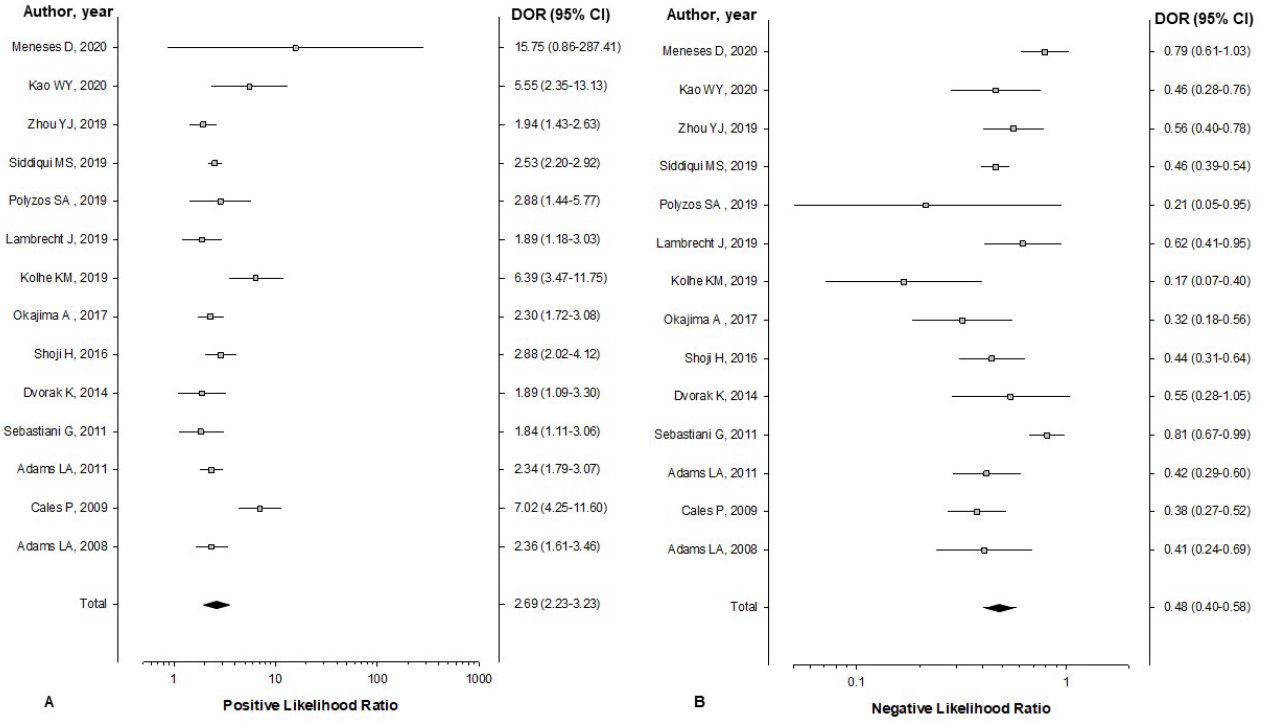


Supplementary Figure 3. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for APRI values in any fibrosis.

Diagnosis of significant fibrosis (F0-1 vs F2-4)

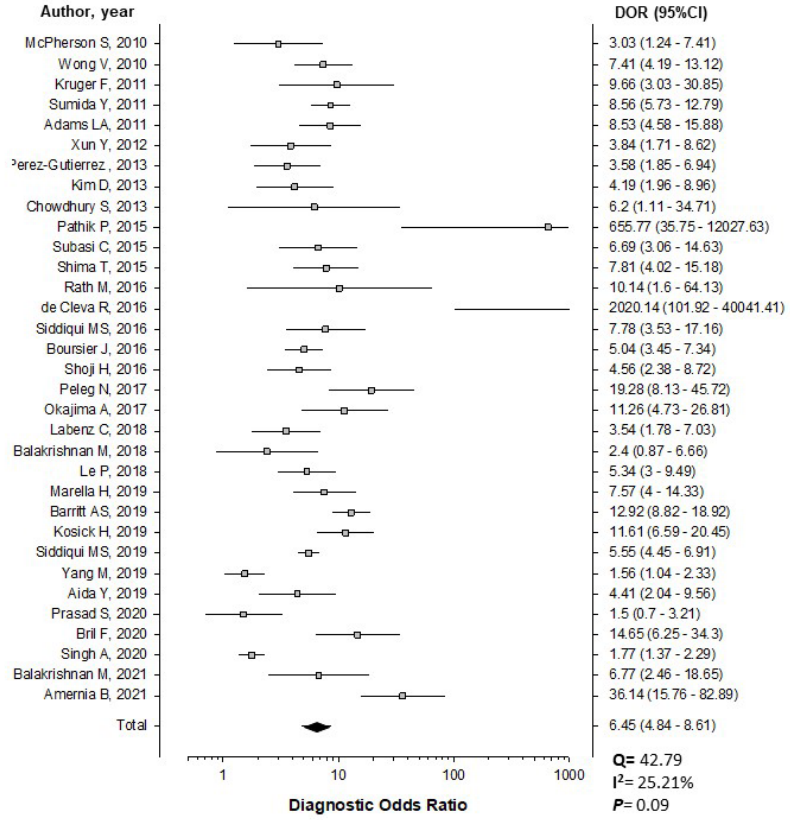


Supplementary Figure 4. Forest plot of meta-analysis of diagnostic odds ratio for APRI values in significant fibrosis.

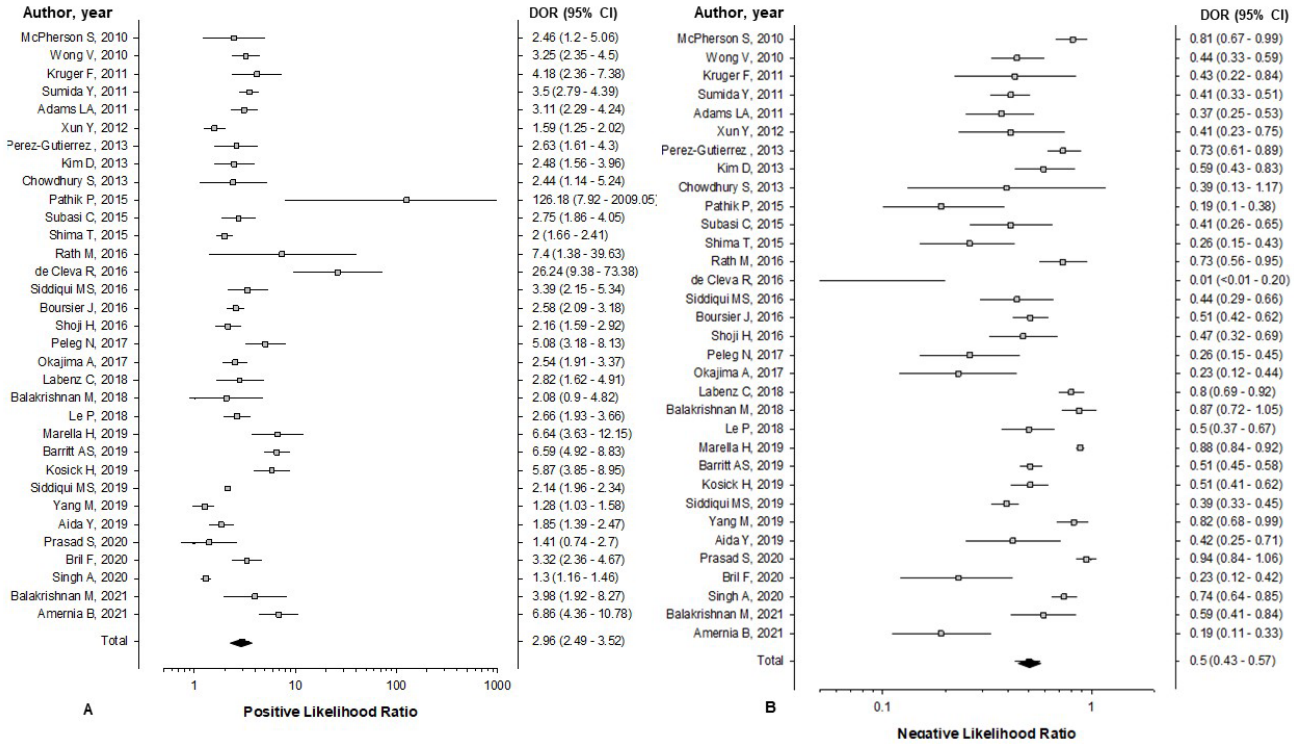


Supplementary Figure 5. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for APRI values in significant fibrosis.

Diagnosis of advanced fibrosis (F0-2 vs F3-4)

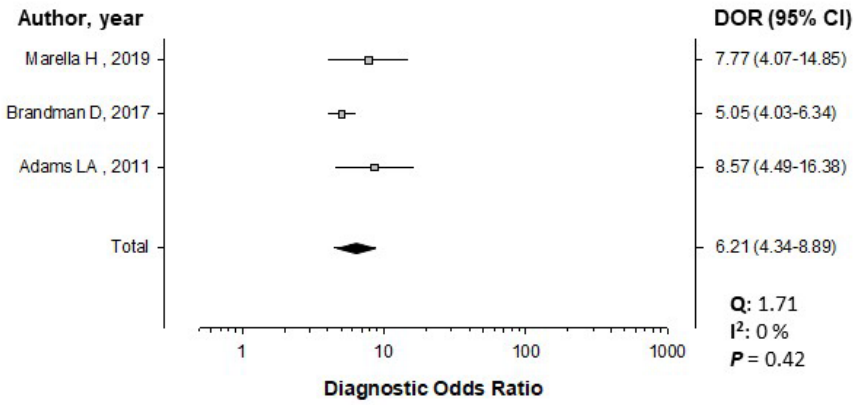


Supplementary Figure 6. Forest plot of meta-analysis of diagnostic odds ratio for APRI values in advanced fibrosis.

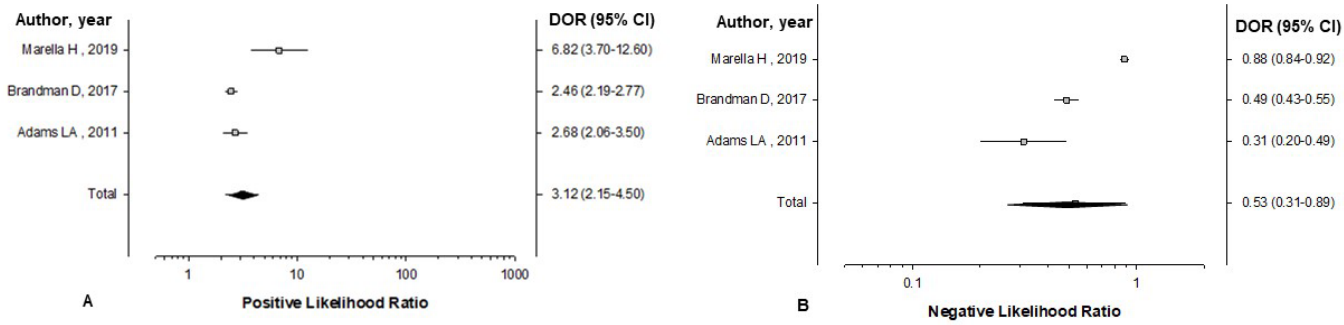


Supplementary Figure 7. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for APRI values in advanced fibrosis.

Diagnosis of cirrhosis (F0-3 vs F4)



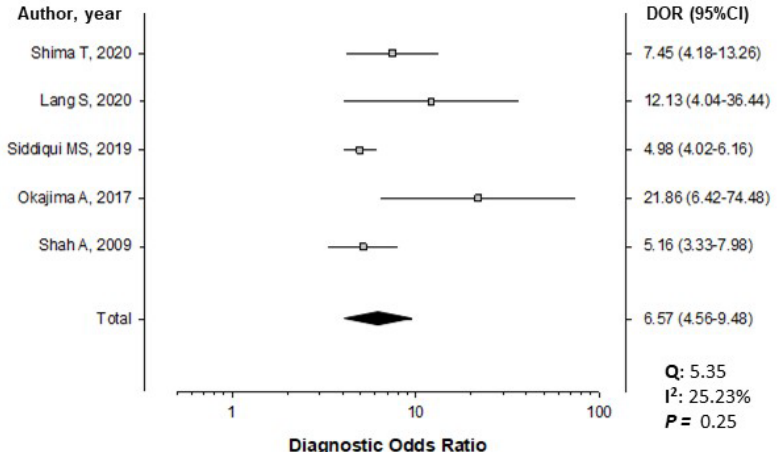
Supplementary Figure 8. Forest plot of meta-analysis of diagnostic odds ratio for APRI values in cirrhosis.



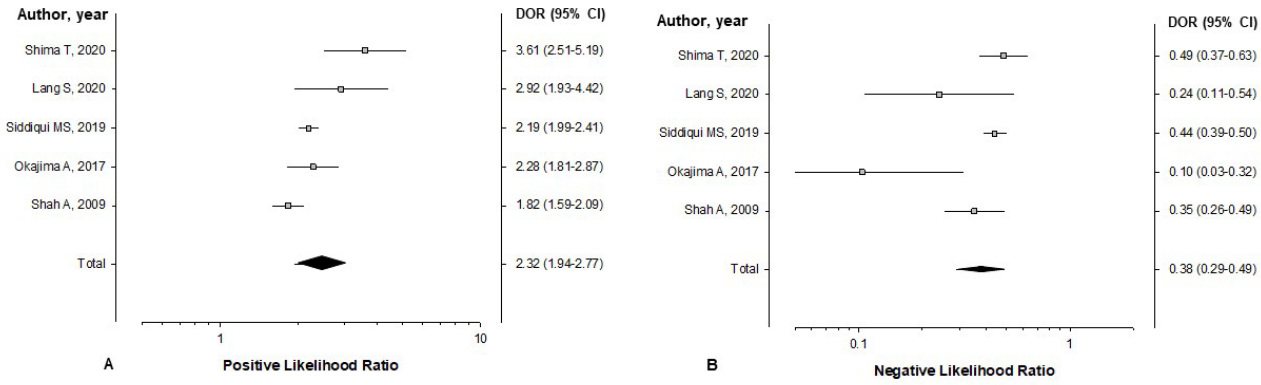
Supplementary Figure 9. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for APRI values in cirrhosis.

FIB-4

Diagnosis of any fibrosis (F0 vs F1-F4)

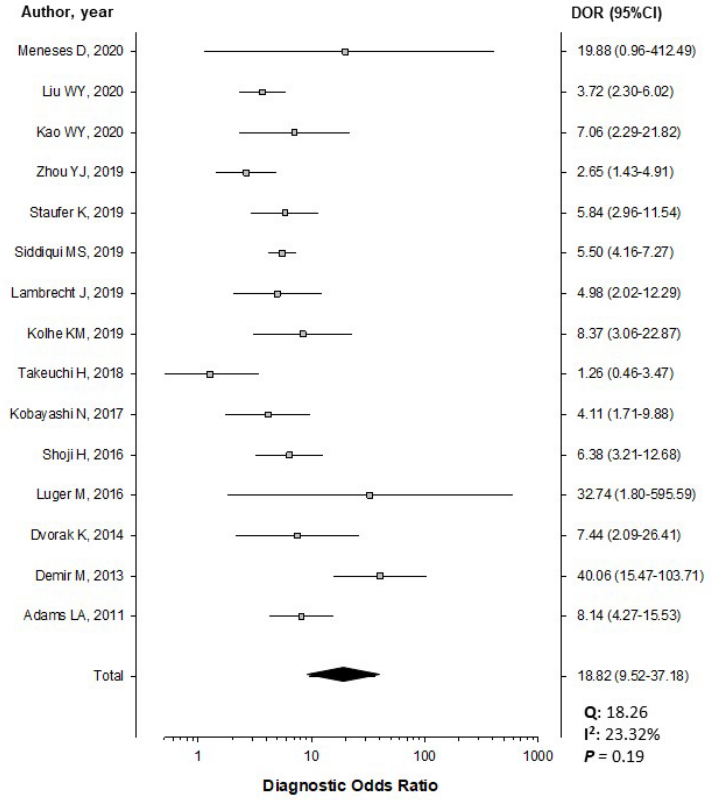


Supplementary Figure 10. Forest plot of meta-analysis of diagnostic odds ratio for FIB-4 values in any fibrosis.

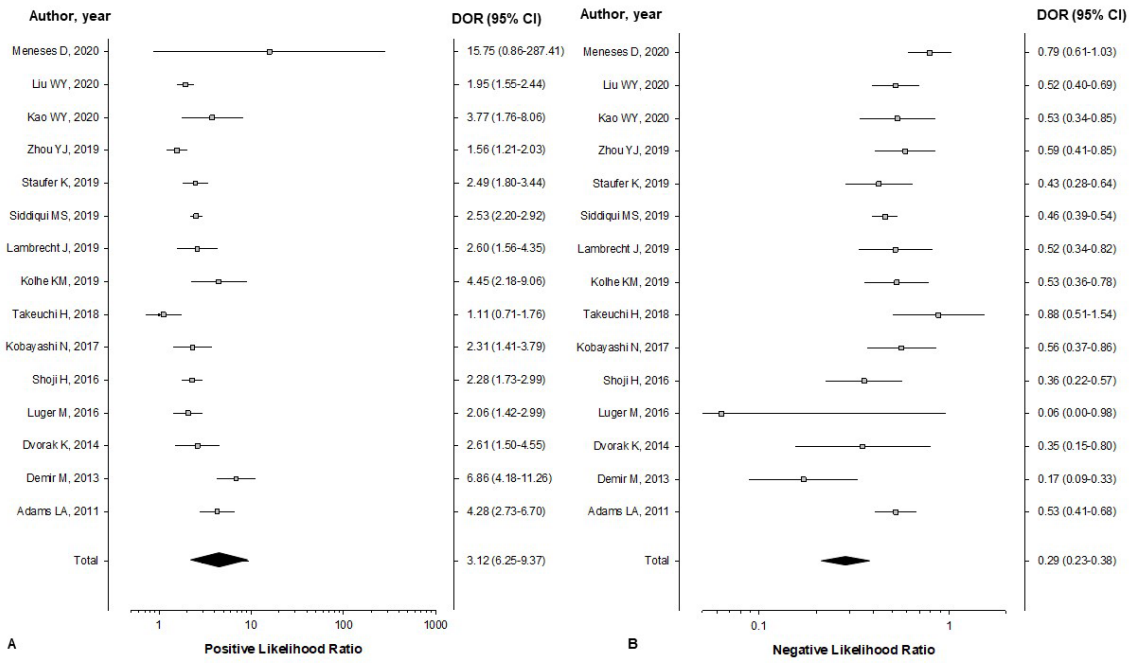


Supplementary Figure 11. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for FIB-4 values in any fibrosis.

Diagnosis of significant fibrosis (F0-1 vs F2-4)

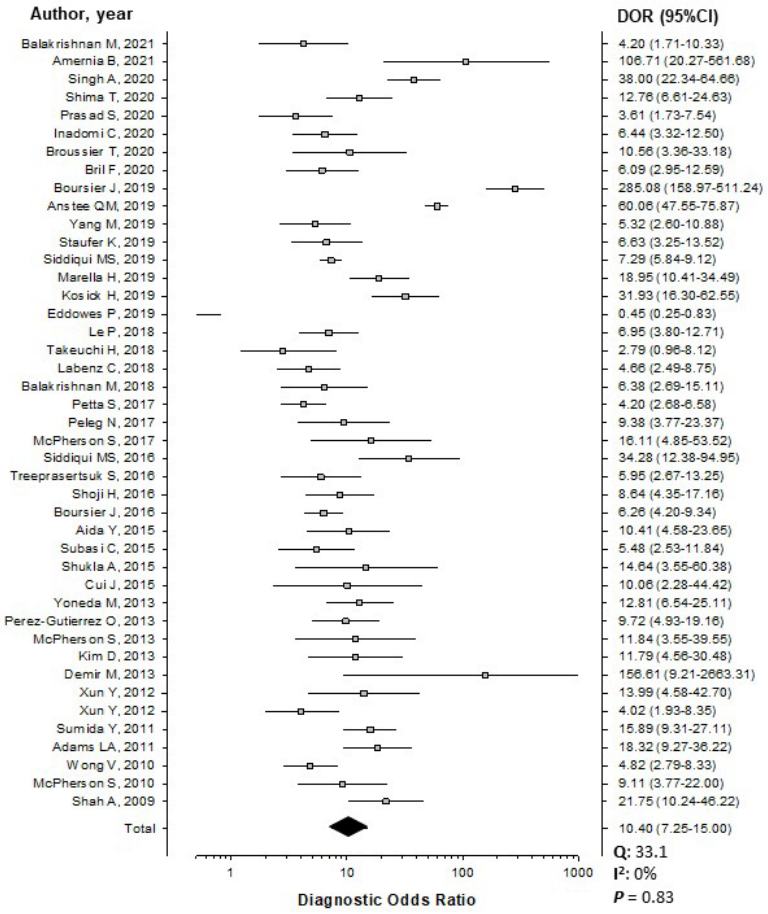


Supplementary Figure 12. Forest plot of meta-analysis of diagnostic odds ratio for FIB-4 values in significant fibrosis.

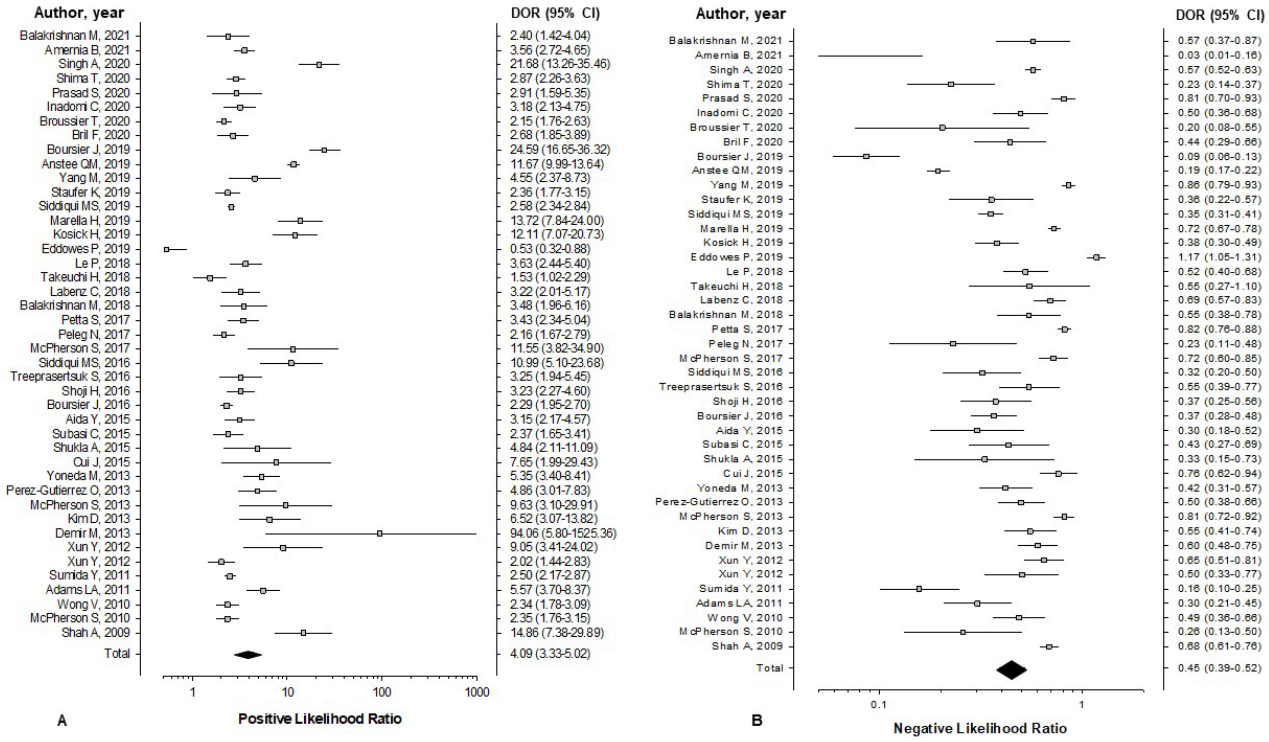


Supplementary Figure 13. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for FIB-4 values in significant fibrosis.

Diagnosis of advanced fibrosis (F0-2 vs F3-4)

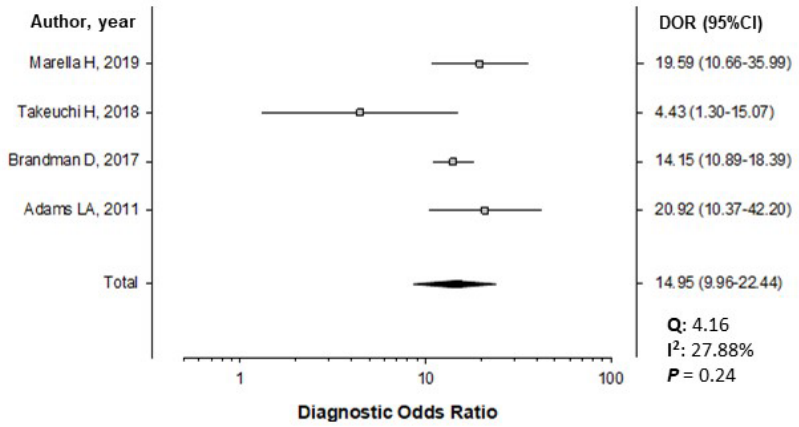


Supplementary Figure 14. Forest plot of meta-analysis of diagnostic odds ratio for FIB-4 values in advanced fibrosis.

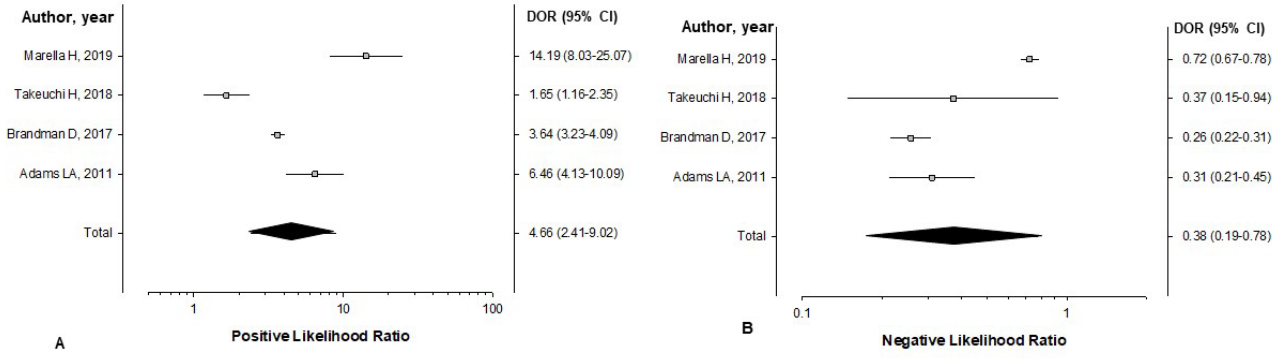


Supplementary Figure 15. (A) Forest plot of meta-analysis of positive likelihood and (B) negative likelihood ratio for FIB-4 values in advanced fibrosis.

Diagnosis of cirrhosis (F0-3 vs F4)



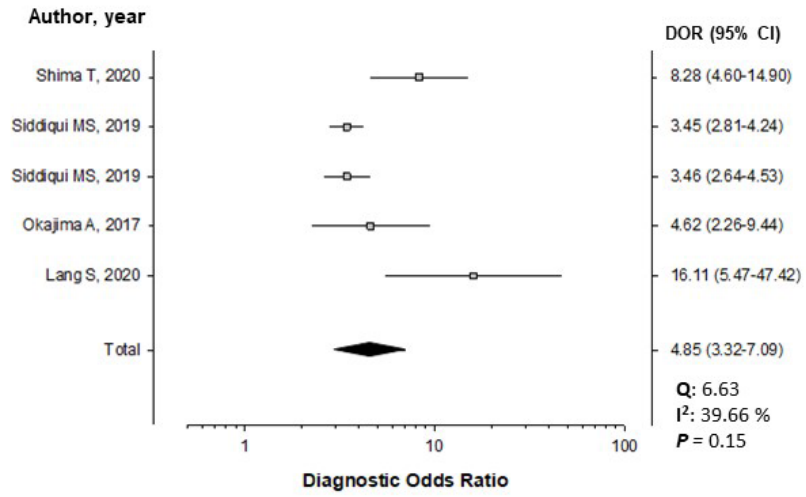
Supplementary Figure 16. Forest plot of meta-analysis of diagnostic odds ratio for FIB-4 values in cirrhosis.



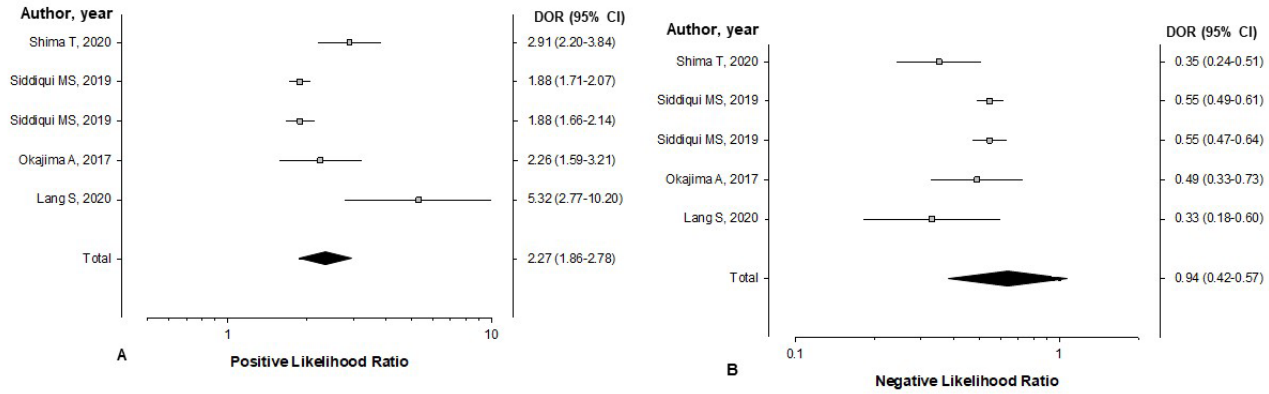
Supplementary Figure 17. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) Forest plot of meta-analysis of negative likelihood ratio for FIB-4 values in cirrhosis.

NFS

Diagnosis of any fibrosis (F0 vs F1-F4)

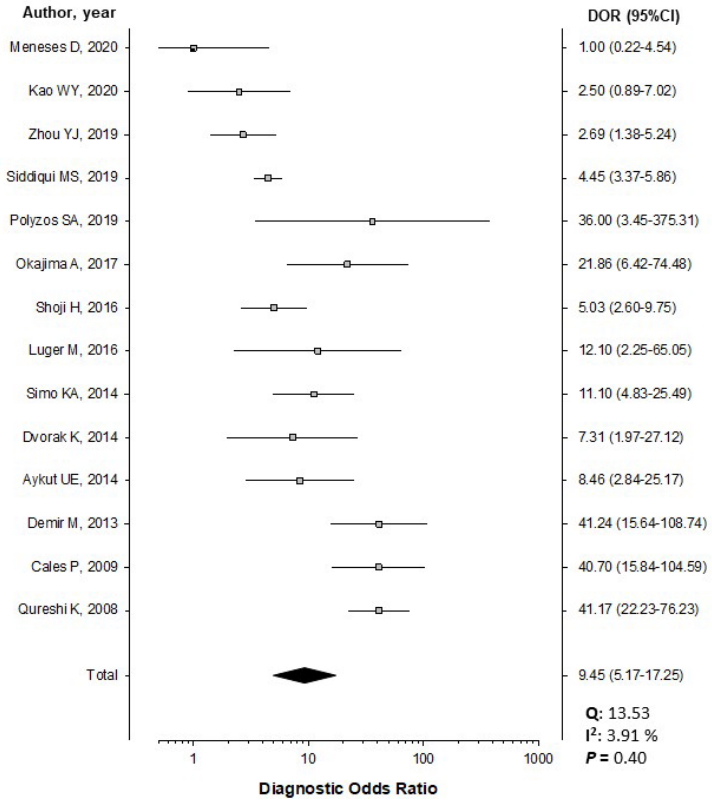


Supplementary Figure 18. Forest plot of meta-analysis of diagnostic odds ratio for NFS values in any fibrosis.

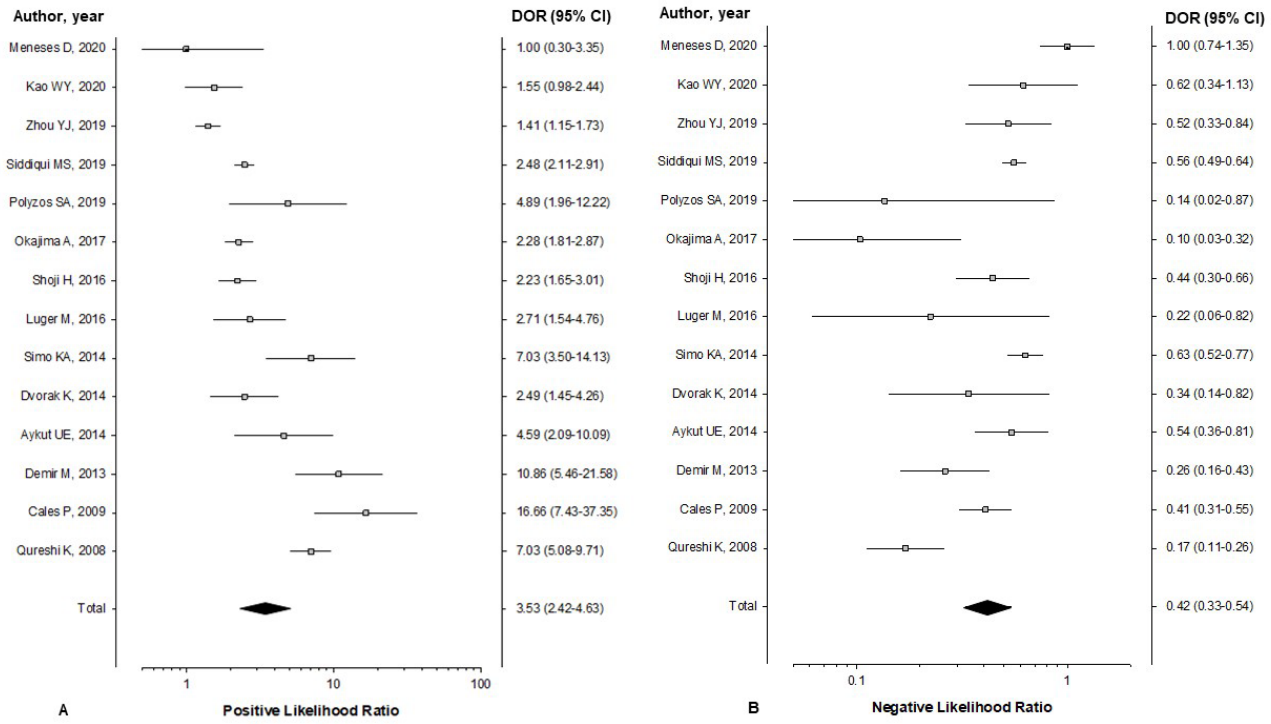


Supplementary Figure 19. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for NFS values in any fibrosis.

Diagnosis of significant fibrosis (F0-1 vs F2-4)

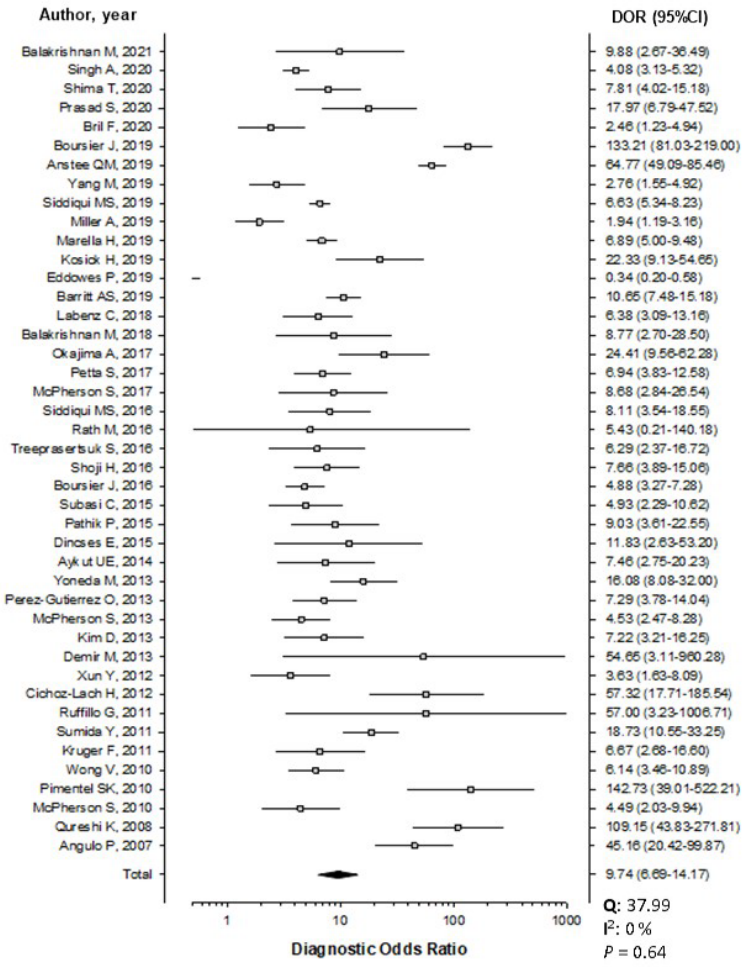


Supplementary Figure 20. Forest plot of meta-analysis of diagnostic odds ratio for NFS values in significant fibrosis.

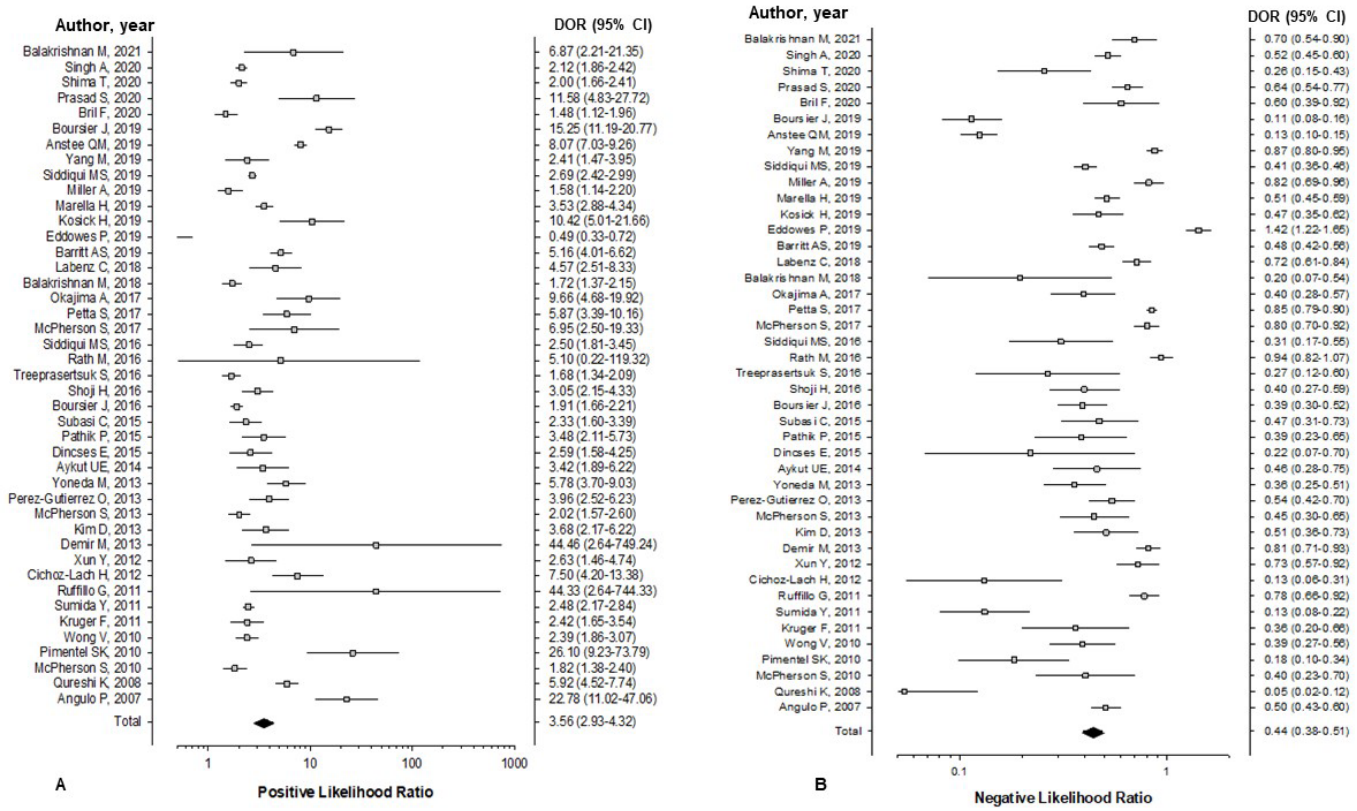


Supplementary Figure 21. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for NFS values in significant fibrosis.

Diagnosis of advanced fibrosis (F0-2 vs F3-4)

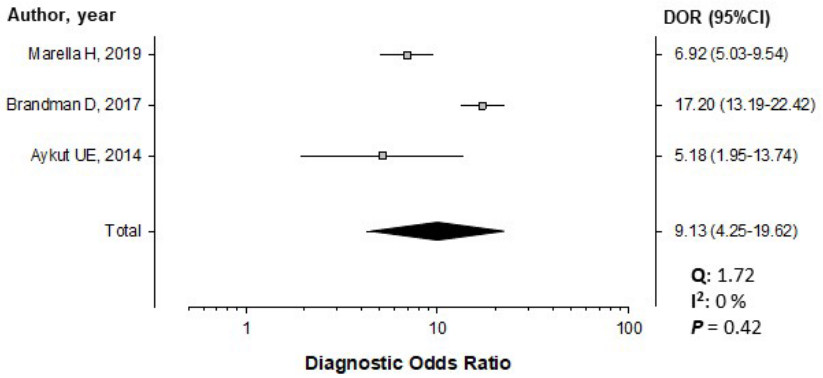


Supplementary Figure 22. Forest plot of meta-analysis of diagnostic odds ratio for NFS values in advanced fibrosis.

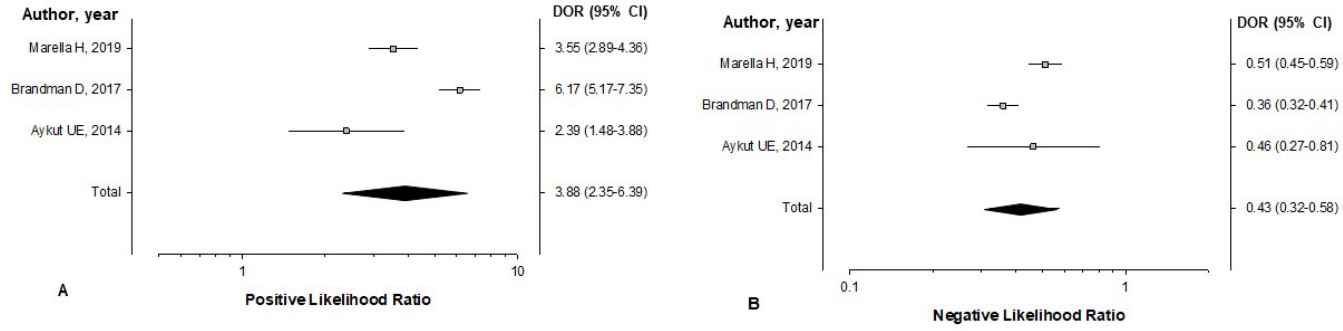


Supplementary Figure 23. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for NFS values in advanced fibrosis.

Diagnosis of cirrhosis (F0-3 vs F4)



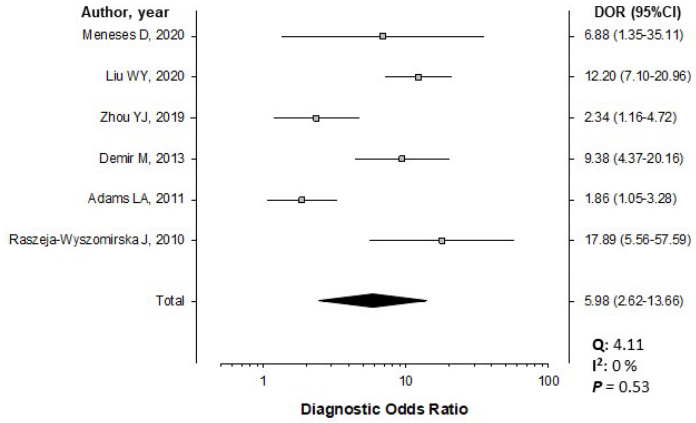
Supplementary Figure 24. Forest plot of meta-analysis of diagnostic odds ratio for NFS values in cirrhosis.



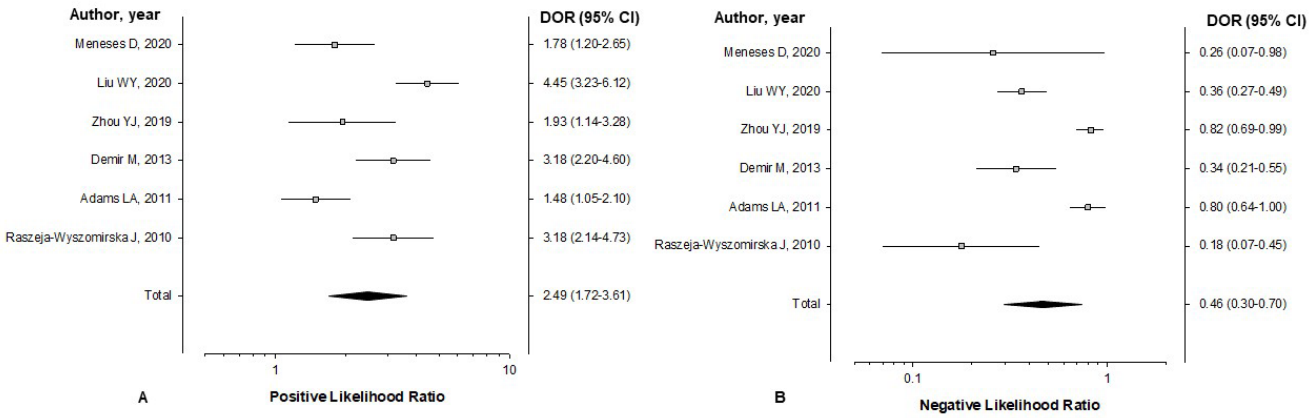
Supplementary Figure 25. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) Forest plot of meta-analysis of negative likelihood ratio for NFS values in cirrhosis.

BARD score

Diagnosis of significant fibrosis (F0-1 vs F2-4)

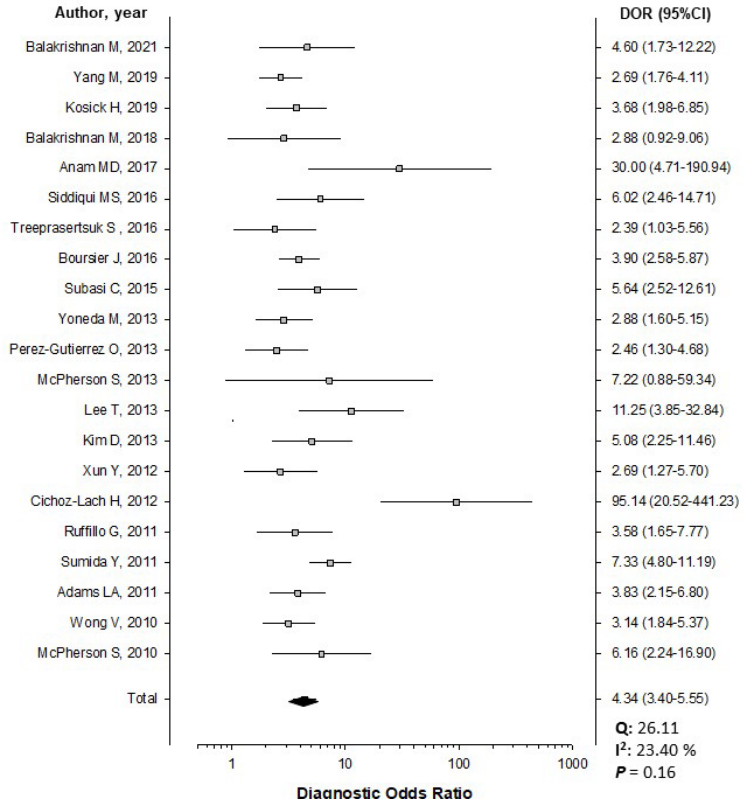


Supplementary Figure 26. Forest plot of meta-analysis of diagnostic odds ratio for BARD score values in significant fibrosis.

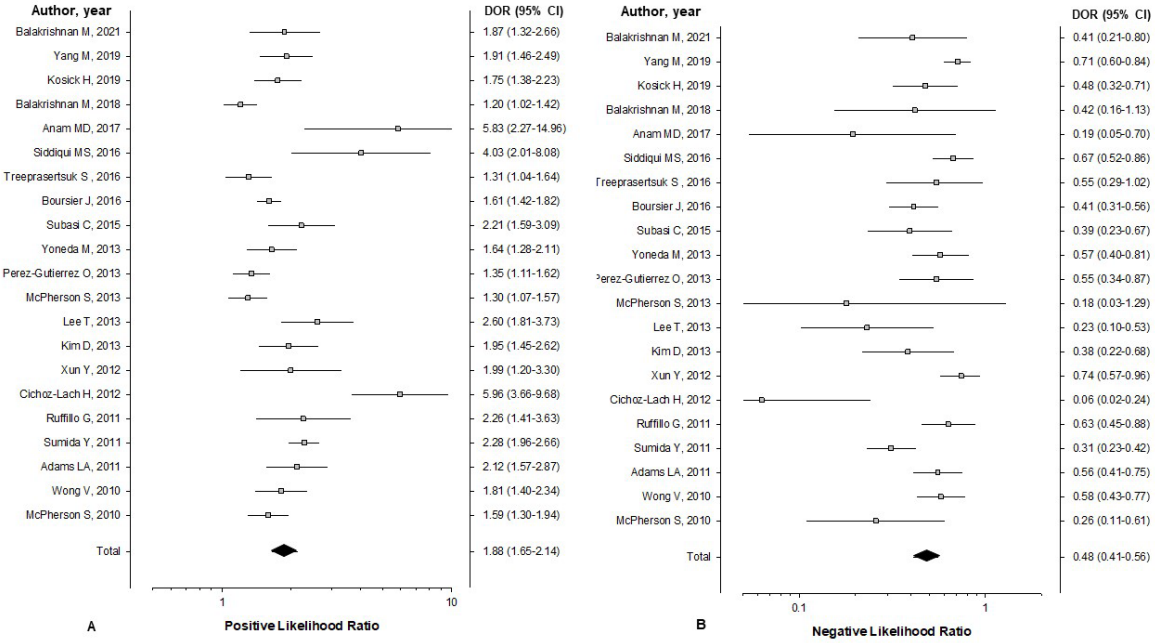


Supplementary Figure 27. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for BARD score values in significant fibrosis.

Diagnosis of advanced fibrosis (F0-2 vs F3-4)



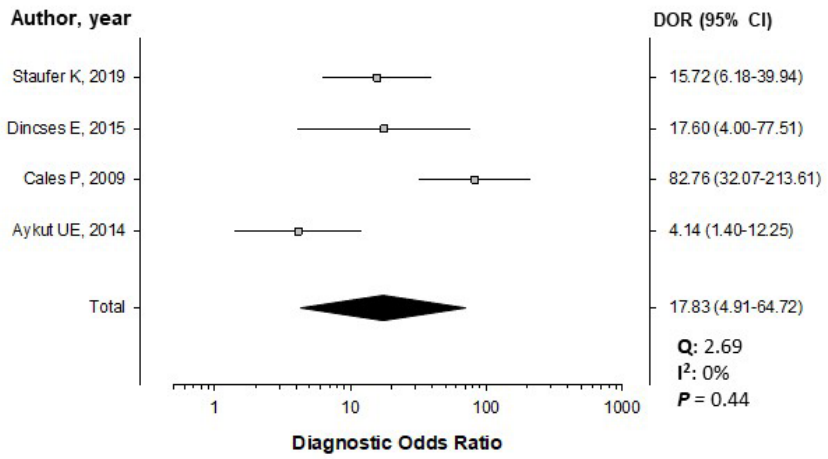
Supplementary Figure 28. Forest plot of meta-analysis of diagnostic odds ratio for BARD score values in advanced fibrosis.



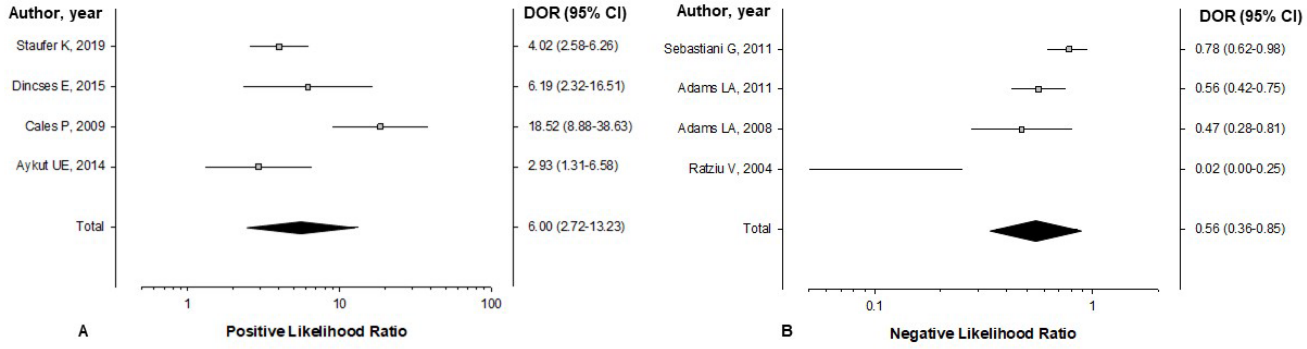
Supplementary Figure 29. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for BARD score values in advanced fibrosis.

FibroMeter

Diagnosis of significant fibrosis (F0-1 vs F2-4)

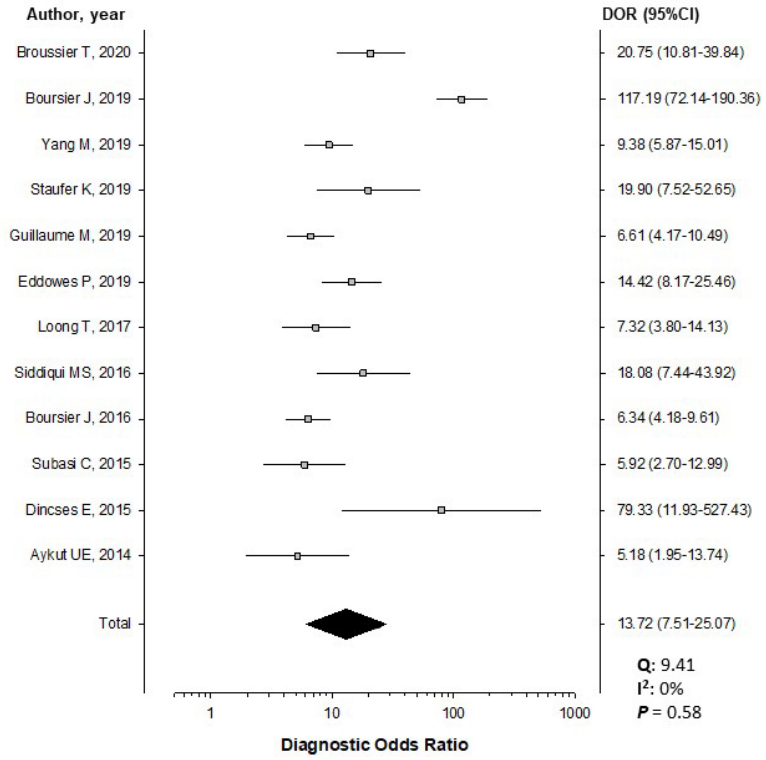


Supplementary Figure 30. Forest plot of meta-analysis of diagnostic odds ratio for FibroMeter values in significant fibrosis.

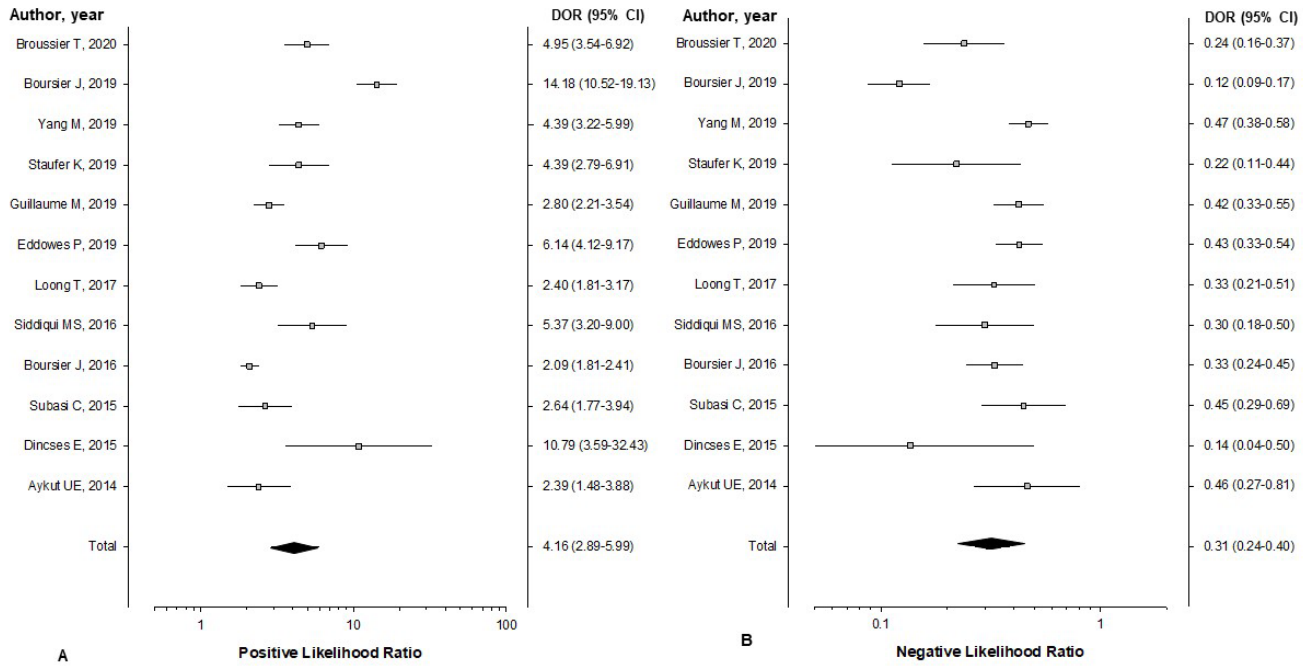


Supplementary Figure 31. (A) Forest plot of meta-analysis of positive likelihood and (B) negative likelihood ratio for FibroMeter values in significant fibrosis.

Diagnosis of advanced fibrosis (F0-2 vs F3-4)



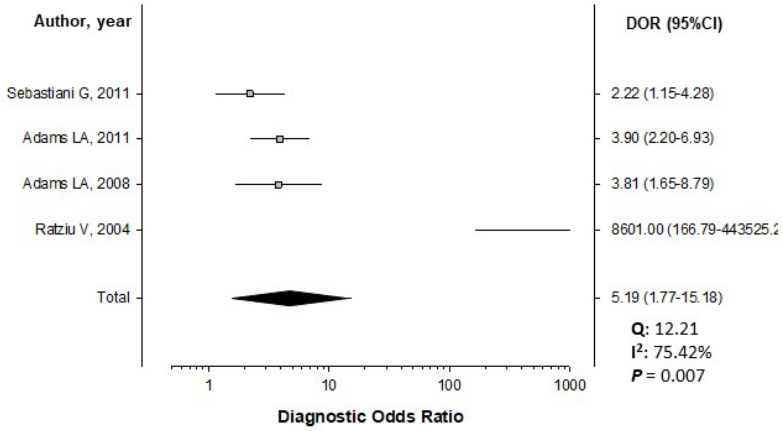
Supplementary Figure 32. Forest plot of meta-analysis of diagnostic odds ratio for FibroMeter values in advanced fibrosis.



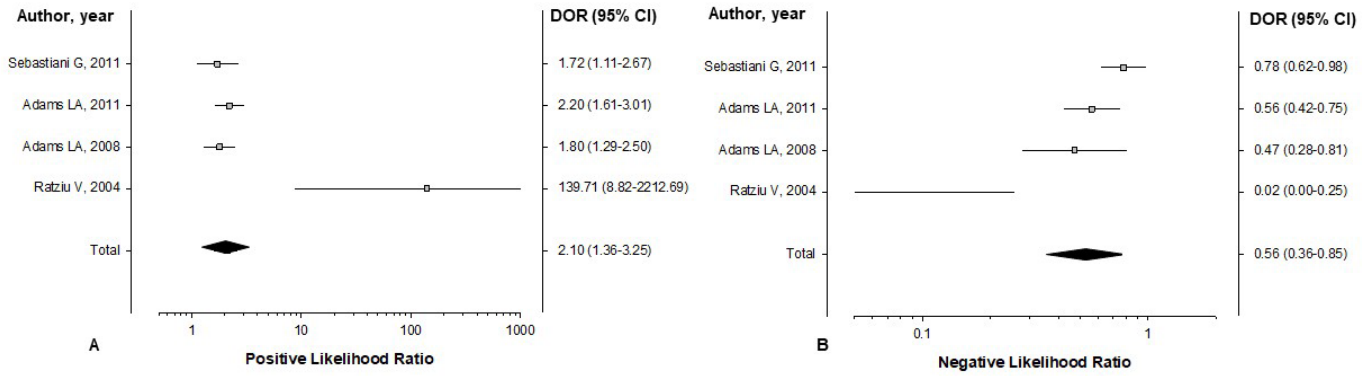
Supplementary Figure 33. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for FibroMeter values in advanced fibrosis.

FibroTest

Diagnosis of significant fibrosis (F0-1 vs F2-4)

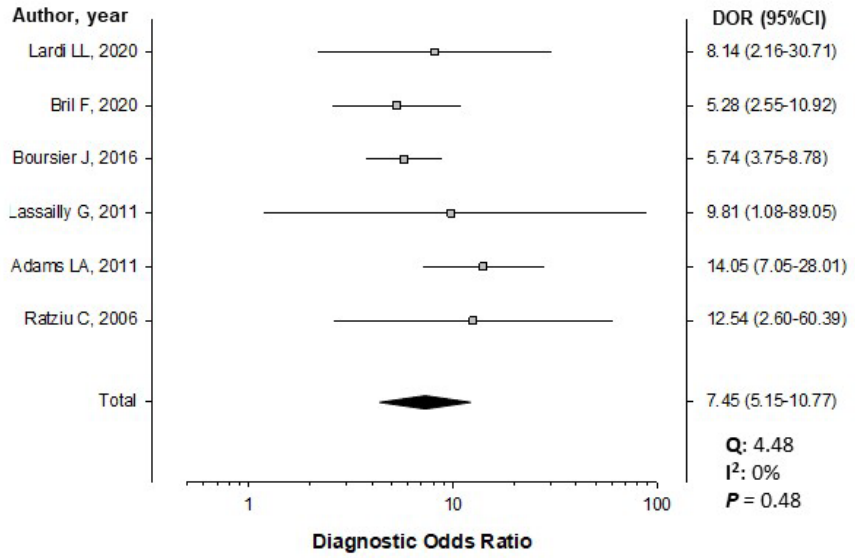


Supplementary Figure 34. Forest plot of meta-analysis of diagnostic odds ratio for FibroTest values in significant fibrosis.

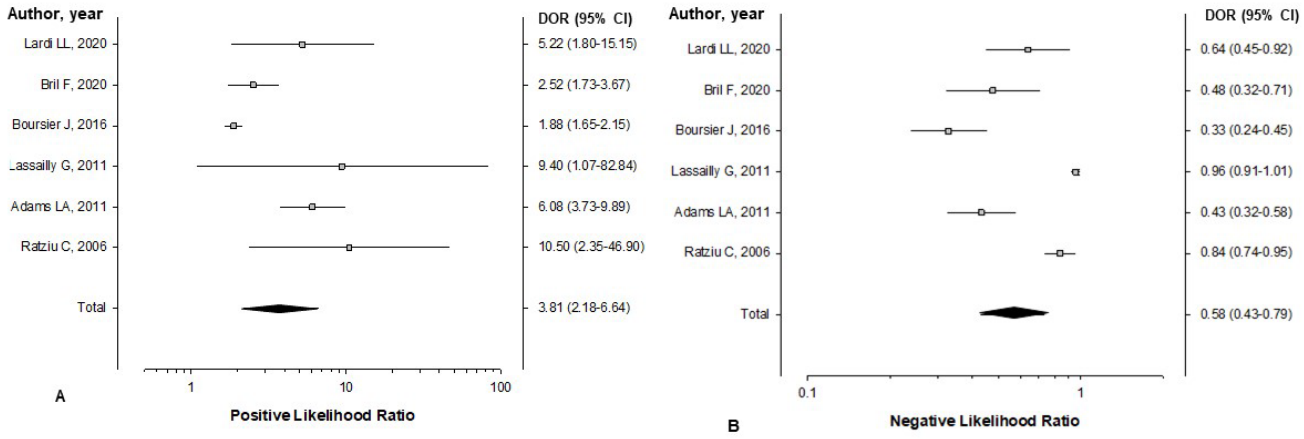


Supplementary Figure 35. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for FibroTest values in significant fibrosis.

Diagnosis of advanced fibrosis (F0-2 vs F3-4)



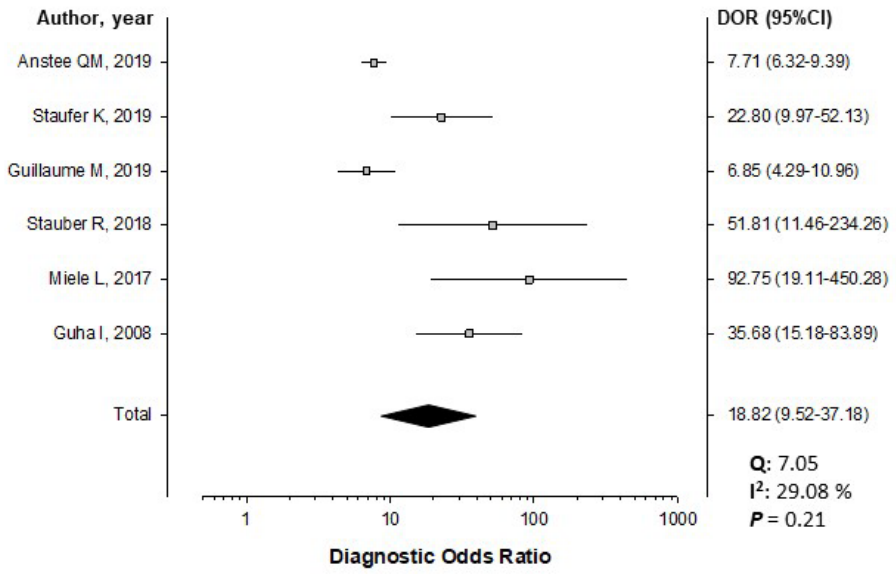
Supplementary Figure 36. Forest plot of meta-analysis of diagnostic odds ratio for FibroTest values in advanced fibrosis.



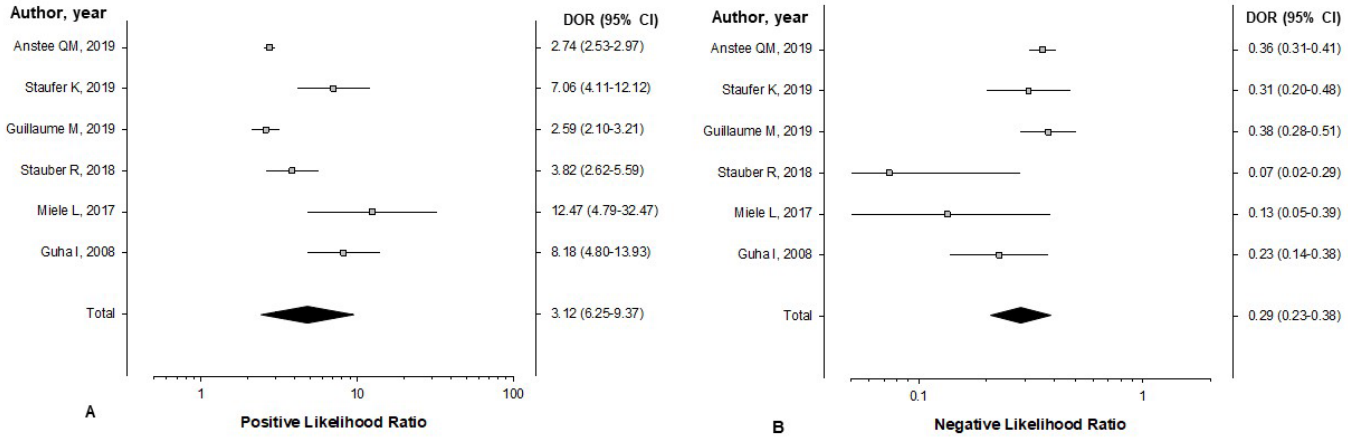
Supplementary Figure 37. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for FibroTest values in advanced fibrosis.

ELF

Diagnosis of advanced fibrosis (F0-2 vs F3-4)



Supplementary Figure 38. Forest plot of meta-analysis of diagnostic odds ratio for ELF values in advanced fibrosis.

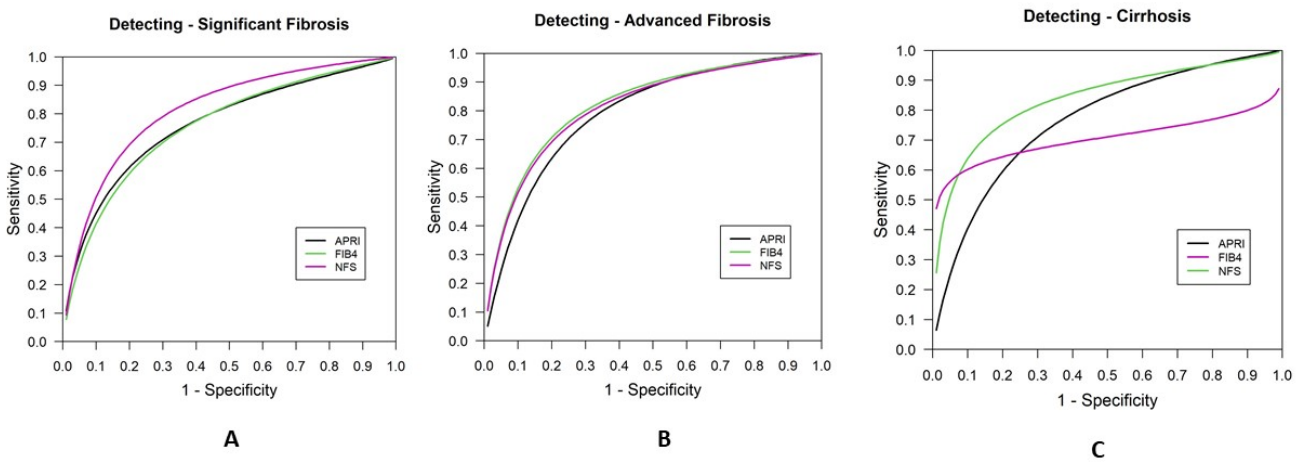


Supplementary Figure 39. (A) Forest plot of meta-analysis of positive likelihood ratio and (B) negative likelihood ratio for ELF values in advanced fibrosis.

Supplementary Table 7. Comparison of sAUC, sensitivity and specificity for serological biomarkers for in predicting liver fibrosis severity in people with MASLD.

Models	No. of studies/ patient*	AUC	Sensitivity rate % (95% CI)	Specificity rate % (95% CI)
APRI				
Any fibrosis	3 (1535)	0.76	77 (61-88)	64 (48-78)
Significant fibrosis	14 (4845)	0.76	63 (53-72)	79 (69-86)
Advanced fibrosis	33 (10341)	0.78	60 (50-69)	82 (76-87)
Cirrhosis	3 (2632)	0.72	47 (3-84)	87 (50-98)
FIB-4				
Any fibrosis	5 (2172)	0.77	77 (61- 87)	68 (57-78)
Significant fibrosis	15 (5222)	0.75	64 (52-74)	76 (66-84)
Advanced fibrosis	43 (16519)	0.81	60 (52-68)	87 (82-91)
Cirrhosis	4 (1886)	0.83	69 (43-86)	87 (57-97)
NFS				
Any fibrosis	5 (2725)	0.71	66 (62-70)	73 (64-81)
Significant fibrosis	14 (3031)	0.81	69 (56-79)	80 (71-88)
Advanced fibrosis	43 (17946)	0.81	62 (53-70)	85 (79-90)
Cirrhosis	3 (2478)	0.69	63 (58-68)	84 (73-91)
BARD score				
Significant fibrosis	6 (1275)	0.77	66 (45-82)	75 (65-83)
Advanced fibrosis	21 (4911)	0.73	72 (64-79)	63 (54-71)
FibroMeter				
Significant fibrosis	4 (651)	0.88	68 (48-82)	89 (80-95)
Advanced fibrosis	12 (3863)	0.84	74 (68-79)	82 (76-87)
FibroTest				
Significant fibrosis	4 (640)	0.86	72 (28-94)	85 (45-98)
Advanced fibrosis	6 (1620)	0.78	40 (15-72)	93 (73-99)
ELF				
Advanced fibrosis	6 (4200)	0.87	79 (68-87)	84 (75-90)

APRI aspartate aminotransferase to platelet ratio index; 95% CI confidence interval; ELF enhanced liver fibrosis; FIB-4 fibrosis index-4; MASLD metabolic dysfunction-associated steatotic liver disease; NFS Non-alcoholic fatty liver disease fibrosis score; sAUC summary area under curve.



Supplementary Figure 40. Sensitivity analysis with the most frequently used serological biomarkers and severities. (A) APRI, FIB-4, and NFS in detecting significant fibrosis, (B) APRI, FIB-4, and NFS in detecting advanced fibrosis, and (C) APRI, FIB-4, and NFS in detecting cirrhosis.

Supplementary Table 8. Results of the meta-analysis of the most frequent serological biomarkers used in predicting liver fibrosis severity in people with MASLD.

Serological biomarkers	No. of studies/ patient*	AUC	Sen rate % (95% CI)	Spe rate % (95% CI)	DOR (95% CI)	Cochran's Q	*p*	I^2	LR+ (95% CI)	LR- (95% CI)
APRI										
Significant fibrosis	14 (4845)	0.76	63 (53-72)	79 (69-86)	6.29 (4.47-8.92)	16.13	0.24	19.4	2.69 (2.23-3.23)	0.48 (0.40-0.58)
Advanced fibrosis	33 (10341)	0.78	60 (50-69)	82 (76-87)	6.45 (4.83-8.60)	42.78	0.009	25.21	2.96 (2.49-3.52)	0.50 (0.43-0.57)
Cirrhosis	3 (2632)	0.72	47 (3-84)	87 (50-98)	6.21 (4.34-8.89)	1.71	0.42	0	3.11 (2.15-4.50)	0.53 (0.31-0.89)
FIB-4										
Significant fibrosis	15 (5222)	0.75	64 (52-74)	76 (66-84)	5.75 (4.11-8.05)	18.26	0.19	23.33	2.51 (2.07-3.05)	0.50 (0.43-0.59)
Advanced fibrosis	43 (16519)	0.81	60 (52-68)	87 (82-91)	10.43 (7.25-15.02)	33.1	0.83	0	4.09 (3.33-5.02)	0.45 (0.39-0.52)
Cirrhosis	4 (1886)	0.83	69 (43-86)	87 (57-97)	14.95 (9.96-22.44)	4.16	0.24	27.88	4.66 (2.41-9.02)	0.38 (0.19-0.78)
NFS										
Significant fibrosis	14 (3031)	0.81	69 (56-79)	80 (71-88)	9.45 (5.17-17.5)	13.53	0.40	3.91	3.35 (2.42-4.63)	0.42 (0.33-0.54)
Advanced fibrosis	43 (17946)	0.81	62 (53-70)	85 (79-90)	9.74 (6.69-14.17)	37.99	0.64	0	3.56 (2.93-4.32)	0.44 (0.38-0.51)
Cirrhosis	3 (2478)	0.69	63 (58-68)	84 (73-91)	9.13 (4.25-19.62)	1.72	0.42	0	3.88 (2.35-6.39)	0.43 (0.32-0.58)

APRI aspartate aminotransferase to platelet ratio index; 95% CI confidence interval; ELF enhanced liver fibrosis; FIB-4 fibrosis index-4; NFS Non-alcoholic fatty liver disease fibrosis score; AUC, area under curve, Sen sensitivity Spe specificity, MASLD metabolic dysfunction-associated steatotic liver disease, I^2 heterogeneity; LR+ positive likelihood ratio; LR- negative likelihood ratio, p statistically significant value.

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