**REVIEW ARTICLE** **DOI:** https://doi.org/10.18502/fem.v9i4.20868

# Decision tools for diagnosing spontaneous bacterial peritonitis: a systematic review and meta-analysis

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*Published online: 2025-09-05*

**Abstract:** **Backgound:** Approximately one-third of the spontaneous bacterial peritonitis (SBP) are missed due to the absence of paracentesis, and any delay in antibiotic initiation significantly increases mortality. Clinical decision tools may help to rule out or rule in the diagnosis without paracentesis. This study systematically reviewed the performance of available decision tools for diagnosing SBP in adult patients with cirrhosis.

**Methods:** We included all original studies that evaluated clinical decision tools for SBP diagnosis. Search was conducted in MEDLINE, Embase, Scopus, and Web of Science Core Collection from inception to September 2024. Study quality was evaluated using Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS 2).

**Results:** From 2038 records, 44 articles were scrutinized in full text. Twenty-four studies ultimately met eligibility criteria. Most of the studies were at low risk of bias. Several tools relied on laboratory findings with clinical features. In meta-analysis the Mansoura scoring system (cut-off of 4) showed a pooled sensitivity of 70.96% (95% CI: 42.06%,99.86%) and a negative predictive value 92.27% (95% CI: 88.80%,95.74%). The Wehmeyer's scoring system achieved pooled specificity and positive predictive value of 98.43% (95% CI: 95.29,101.58%) and 90.26% (95% CI: 70.28,110.23%). A MELD score >15 yielded had pooled sensitivity of 83.85% (95% CI: 78.50%,89.20%) and negative predictive value of 87.56% (95% CI: 81.29%,93.84%).

**Conclusion:** Several decision tools, particularly laboratory-based (e.g. procalcitonin) tools, showed high sensitivity to potentially rule out SBP. Some other tools (e.g. Mansoura, Wehmeyer rules) can reliably rule in the diagnosis. However, tools all the tools need further validation before widespread adoption.

**Keywords:** Cirrhosis; Decision Tool; Diagnosis; Spontaneous Bacterial Peritonitis

Cite this article as: Garjani K, Vahidi E, Aghili M, Azimi Nezhad AA, Dadlani P, Mirfazaelian H . Decision tools for diagnosing spontaneous bacterial peritonitis: a systematic review and meta-analysis. Front Emerg Med. 2025;9(4):e33.

## 1. Introduction

Infections are the most frequent complications among cirrhotic patients with spontaneous bacterial peritonitis (SBP), representing one of the most common and serious forms (1). SBP is defined as ascetic fluid neutrophil count ≥250/mL, with or without a positive culture, in the absence of findings suggestive of secondary peritonitis (2). This condition carries a high mortality, with each hour of delayed diagnosis increasing mortality by 3.3% (3). Therefore, timely paracentesis is crucial in all cirrhotic patients with ascites and suspected SBP (4).

Despite this, an observational study in the US showed that more than 30% of eligible patients do not undergo paracentesis (5). Barriers to paracentesis may include low clinical suspicion, overestimation of bleeding risk in patients with coagulopathy, crowded emergency departments, and patient discomfort (6). Clinical decision tools are increasingly used in various medical conditions to improve diagnostic accuracy and guide timely management. In cirrhosis, both clinical and laboratory parameters (e.g., variceal hemorrhage, elevated CRP (6,7) have been associated with increased SBP risk. Decision tools with high specificity or positive likelihood ratio could help physicians identify high-risk patients earlier, guide diagnostic paracentesis, and reduce delays in treatment. At the other end, highly sensitive tools are able to rule out SBP and omit unnecessary paracentesis.

This systematic review aimed to evaluate the performance of existing decision tools for diagnosing SBP in adults with cirrhosis.

## 2. Methods

We included original studies that introduced or evaluated the performance of a scoring system or a clinical decision tool for diagnosing SBP in patients with cirrhosis and as-

cites. For this review, we defined a clinical decision tool as any combination of at least two parameters. We excluded case series, case reports, animal studies and non- English publications. No restriction was applied with regard to study location or publication year. The study protocol was registered in PROSPERO CRD42024594802; available at: (https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42024594802)

### *2.1. Search strategy*

A medical librarian assisted in directing the search strategy. We used the following keywords: "liver cirrhosis", "patients with ascites", "clinical decision rule", "clinical scoring tool"," clinical prediction rule", "paracentesis", "abdominocentesis", "spontaneous bacterial peritonitis", and "infectious peritonitis". Searches were conducted in Ovid MEDLINE (R), Embase (embase.com), Scopus, and Web of Science Core Collection (SCIE, SSCI, and ESCI) from database inception to September 2024. The search strategy is provided in the supplementary file.

### *2.2. Study selection and Data extraction*

Two reviewers screened the titles and abstracts of potentially relevant articles independently using the online platform, Rayyan. Full texts of potentially eligible studies were assessed independently by the same reviewers with any conflicts resolved by a third reviewer. In the next step, the citations of selected studies and their references were screened. If we were not able to obtain full-text articles online, we tried to contact the authors.

For each study we extracted: first author, publication year, country, sample size, sex distribution, exclusion criteria, study design, reference standard for SBP diagnosis, decision tool components and outcome measures (sensitivity, specificity, predictive values, and likelihood ratios). If we were not able to obtain the required data from the manuscript, we contacted the corresponding authors.

### *2.3. Quality assessment*

The quality of the studies included was assessed using the quality assessment of diagnostic accuracy studies version 2 (QAUDAS 2) tool. This tool assesses the quality of primary diagnostic accuracy studies and evaluates four key domains: patient selection, index test, reference standard, and flow/timing (i.e., time interval between index test and reference standard). Each domain was rated as "low," "high", or "unclear" risk of bias, the first three domains were also rated for applicability. If a study is judged as "low" on all domains relating to bias or applicability, then it is appropriate to have an overall judgment of "low risk of bias" or "low concern regarding applicability" for that study. If a study is judged "high" or "unclear" in 1 or more domains, then it may be judged "at risk of bias" or as having "concerns regarding applicability." (8)

### *2.4. Data synthesis and analysis*

For each study, we extracted or calculated true positives, false positives, false negatives, and true negatives to construct 2×2 tables. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (PLR), and negative likelihood ratio (NLR) were derived whenever possible. When raw figures were unavailable, we used reported indices with their confidence intervals. Meta-analyses were performed using inverse variance methods with the random effects model due to anticipated high heterogeneity. The statistical heterogeneity was quantified by I2. Analysis were conducted in Review Manager Version 5.4. The results were reported at a 95% confidence interval (CI). QUADAS-2 assessments were visualized using the ROBVIS tool (9).

## 3. Results

### *3.1. Study selection*

The initial search identified 2038 records. After removing the duplicates, 1183 records remained. Of these, 1139 were excluded based on the title and/or abstract by the authors. Forty-four full texts were reviewed and 20 were excluded for the following reasons: evaluation of ascitic fluid markers (n=3), assessment of future rather than current SBP risk (n=2), predictors of non-SBP infections (n=2), non-English studies (n=3), irrelevant (n=7), focus on secondary peritonitis (n=1), SBP recurrence (n=1), and SBP in hepatic encephalopathy (n=1). Ultimately, 24 studies were included. [10-33] The PRISMA flow diagram is presented in figure 1.

### *3.2. Study characteristics*

Across the 24 studies, 18974 patients were included, all of which were published after 2007. Eight studies were conducted in China, seven in Egypt, two in the United States, and the remainder across Asia and Europe. Ten studies were retrospective, nine were prospective, three were cross- sectional. Two used a retrospective derivation with prospective validation design. Key study characteristics are summarized in the supplementary file.

### *3.3. Risk of bias*

Using the QUADAS-2 tool, most of the studies were rated as low risk of bias. Two studies were classified as unclear because the method for selecting SBP-negative patients was not specified (18,31) (Figure 2).

### *3.4. Performance of diagnostic tools*

The tools with their performances have been presented in table 2 and the supplementary file. Two studies designed a nomogram, one with laboratory data only (14) and the other used clinical manifestations and laboratory findings (17). Three studies developed machine learning models that included several factors such as current medications, comorbidities, patient clinical examination, and laboratory data

**Table 1** Included studies characteristics

| Study | Year | country | Study design | Sample size | Male (%) | Exclusion criteria | Reference standard | Predictors | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Obstein KL et al. | 2007 | US | Retrospective | 111 | 78 (70.2) | Immunosuppressed patients due to HIV infection or prior transplantation/ antibiotic administration within 2 weeks prior to paracentesis/ potential confounding etiology for ascites unrelated to cirrhosis such as congestive heart failure or a malignancy with metastasis to the liver/prior history of SBP | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | Bilirubin, Cr, INR | It is on MELD score system. Diagnostic paracentesis within 5 days of admission |
| Gayatri AA et al. | 2007 | Indonesia | Prospective | 62 | 50 (80.7) | DIC/ infection of abdominal wall/ poor cooperative patients/ intestinal obstruction and history of abdominal surgery | PMN count > 250 cells/mm3 in AF or positive AF culture | Bilirubin, Cr, INR | It is on MELD score system. |
| Shi KQ et al. | 2011 | China | Retrospective in derivation and prospective in validation | 676 (derivation phase) 198 (validation phase) | 493 (72.9) (derivation phase) 145 (73.2) (validation phase) | Gastrointestinal hemorrhage/ previous history of gastrointestinal hemorrhage or SBP/ liver cancer/ antibiotic administration within 2 weeks before admission/ potential confounding etiology for ascites unrelated to cirrhosis (peritoneal carcinomatosis, pancreatitis,..)/ fever, abdominal pain, or hepatic encephalopathy/ nosocomial-acquired SBP | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | Serum Cr, TB, WBCs count, PT | Paracentesis within 48 h of admission prospectively CART tree stratifies patients into high, intermediate, and low risk |
| Kraja B et al. | 2012 | Albania | Cross-sectional | 256 | 199 | Antibiotic or PPI treatment/upper GI bleeding/ ascitis unrelated to their cirrhosis/ HCC | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | Bilirubin, Cr, INR | It is on MELD score system. |
| Wehmeyer M et al. | 2014 | Germany | Prospective | 220 (derivation phase) 76 (validation phase) | 145 (65.9) (derivation phase) 49 (64.5) (validation phase) | Prior antibiotics use/ hemorrhagic ascites/ malignant ascites/ secondary peritonitis | PMN count > 250 cells/mm3 in AF | PLT, age, CRP | |
| Cai Z et al. | 2015 | China | Retrospective | 129 | 82 (63.5) | Liver failure/ liver cancer/ fungal infection/ serious heart, lung, or brain insufficiency or a mental illness | Abdominal pain and/or fever (>37.5°C), and/or abdominal and rebound tenderness (excluding secondary peritonitis) Ascites fluid leukocytes count ≥250/mm3 and/or bacterial culture positivity | PCT, WBC/PLT | |
| Metwally K et al. | 2018 | Egypt | Prospective | 300 | 180 (60) | Malignancy/hemorrhagic ascites/ secondary peritonitis/ antibiotic treatment at the time of paracentesis with other systemic infections related to respiratory or urinary tract infection | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | PLT, age, CRP | Wehmeyer's and modified Wehmeyer's scoring system with a different cut-off of CRP |

**Table 1** Included studies characteristics (continued)

| Study | Year | country | Study design | Sample size | Male (%) | Exclusion criteria | Reference standard | Predictors | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Wang H et al. | 2018 | China | Prospective | 259 | 162 (62.5) | Lack of clinical data/ infections other than ascitic fluid infection/ antibiotics use prior to admission/ malignant ascites | Culture positive SBP: ascitic fluid PMN > 0.25 × 109 cells/L with positive bacterial culture<br>Culture negative SBP: PMNL>0.25 ×109cells/L, with negative Gram stain and bacterial culture<br>Bacterascites: PMNL <0.25 × 109 cells/L with positive bacterial culture<br>Sterile ascites: PMNL<0.25 × 109 cells/L with negative bacterial culture | PCT, dCHC, sNFI | |
| Mousa N et al. | 2018 | Egypt | Prospective | 180 | 108 (60) | Ascites without cirrhosis/ immunocompromised state/ sepsis/ secondary peritonitis/ prophylactic antibiotics for SBP/ diabetes mellitus/ hyperlipidemia/ clinically overt hypo- or hyperthyroidism/ peripheral vascular disease/ hypertension or heart failure and major cardiac problems/ autoimmune diseases or neoplastic disorders/ hematological disorders on anticoagulants/ unrelated infection that may influence the levels of blood WBC or CRP | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | NLR, CRP | |
| Abdel-Razik A et al. | 2019 | Egypt | Retrospective | 966 | 610 (65.59) | Antibiotic and/or prophylaxis for SBP, NSAID, OCP before admission/ ascites due to noncirrhotic reasons/ hematological diseases/ surgical abdominal interference within 3 months of study entry/ antiplatelet medications before admission/ bone marrow transplantation, chemotherapy or radiotherapy 1 month before admission/ pregnancy/ secondary peritonitis/ immunocompromised patients/ bacterial infection other than SBP/ conditions associated with increased MPV/ recent hemorrhage/ platelet or blood transfusion before admission | PMN≥250 cells/ml in AF | Age, MPV, NLR, CRP | |
| Elsadek H.M. et al. | 2020 | Egypt | Prospective | 178 | 93 (52) | Infections other than AF infection/HCC/antibiotics use 10 days prior to admission/bacterascites | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | PCT, ESR, CRP | PEC index = PCT× (ESR + CRP). |
| Hu Y et al. | 2021 | China | Retrospective | 1399 | 684 (48) | Malignancy/ acquired immunodeficiency syndrome/ nosocomial acquired SBP/ antibiotics use within 3 months before admission/ previous SBP/ confounding etiologies for SBP/ infection other than SBP/ incomplete clinical data | Abdominal pain and/or fever (T> 37.5 °C) and/or abdominal tenderness and rebound tenderness (excluding secondary peritonitis)<br>Ascites polymorphonuclear cells count≥250/mm3 and/or positive ascites bacteria culture | Total protein, CRP, prothrombin activity, cholinesterase, lymphocyte ratio, apolipoprotein A1 | Machine learning model |

**Table 1** Included studies characteristics (continued)

| Study | Year | country | Study design | Sample size | Male (%) | Exclusion criteria | Reference standard | Predictors | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Popoiag RE et al. | 2021 | Romania | Retrospective | 216 | 142 (65.7) | Intra abdominal surgical causes of peritonitis or other infectious causes | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | NLR, ESR | |
| Xiang S et al. | 2022 | China | Retrospective | 3837 | 2,587 (67.42) | < 18 years/ acquired immunodeficiency syndrome/ tumors/secondary peritonitis/ tuberculous peritonitis/ Indicators with a missing rate >30% | Two of the following: fever, abdominal pain, abdominal tenderness, rebound pain, and other abdominal cavity symptoms and signs of internal infection OR WBC >0.5 × 109 /L or Neutrophils >0.25 × 109 /L in ascites fluid OR Positive bacterial culture of ascites | MCHC, PT, lymphocyte percentage, prealbumin, TB, abnormal CRP level, abnormal PCT level | This study had internal and external validation phases. A nomogram has been constructed |
| Würstle S et al. | 2022 | Germany | Retrospective | 700 | - | Ascites for hemorrhage, malignancy, pancreatitis, tuberculous, chylous ascites/ continuous ambulatory peritoneal dialysis peritonitis | PMN≥250 cells/ml and/or leukocyte count ≥500/mm3 in AF | CRP, previous hydropic decompensation, WBC count, organ failure, fever, acute gastrointestinal bleeding, PPI medication, previous SBP, Charlson Comorbidity Index > 6, no propranolol or carvedilol medication, MELD-Na score > 24.9, Child-Pugh class C | SBP and secondary peritonitis patients were not excluded. A machine learning approach was conducted in this study to differentiate infected from non-infected ascites in patients. |
| Zhou Z et al. | 2022 | China | Prospective | 90 | 66 (73) | Upper gastrointestinal bleeding/intake of antibiotic therapy in the previous 2 weeks/HCC/other associated causes of ascites/severe cardiopulmonary or renal complications | PMN count > 250 cells/mm3 in AF OR Positive ascites culture | OTU-based biomarkers | Based on the change in the structure and composition of the gut microbiota between the SBP and nSBP groups |
| Huynh NC et al. | 2023 | Vietnam | Prospective | 121 | 86 (71.1%) | Antibiotics use in the previous two weeks or prophylaxis for SBP before admission/ascites without portal hypertension/ hemorrhage into ascites/ secondary peritonitis/infections other than SBP/malignancy/hematologic disease/antiplatelet, non-steroidal anti-inflammatory drugs use/platelet or blood transfusion before admission/diseases associated with increased MPV | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | Age, NLR, CRP, MPV | External validation of Mansoura scoring system |

**Table 1** Included studies characteristics (comtinued)

| Study | Year | country | Study design | Sample size | Male (%) | Exclusion criteria | Reference standard | Predictors | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Abdo G et al. | 2023 | Israel | Retrospective | 229 | 146 (63.8) | Secondary ascites unrelated to cirrhosis/ creatinine > 5 mg/dl due to dialysis dependency | Positive culture of AF | NLR, CRP, TB | |
| Du T et al. | 2023 | China | Retrospective | 413 | 336 (81.4) | Pregnancy/secondary peritonitis/ peritoneal dialysis associated peritonitis/chronic liver disease without cirrhosis | One or more of the following symptoms or signs occur: fever, abdominal pain, abdominal tenderness or rebound tenderness, refractory ascites<br>One or more of the following results on laboratory tests are positive: ascites bacteria culture, absolute ascites PMN cell counts≥0.25× 109/L, and PCT>0.5 ng/ml<br>Infection of other sites is excluded | FNR, Albumin, NLR | |
| Abudeif A et al. | 2023 | Egypt | Cross sectional | 332 | 223 (67.2) | Immunosuppression/ heart Failure/ clinically and laboratory-evident autoimmune Diseases/ hematological disorders/ peripheral vascular Disease/ severe infections other than SBP/ antibiotic treatment before hospitalization/ NSAIDs, anticoagulants, or oral contraceptives use | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | NLR MPV | |
| Elhendawy RI et al. | 2023 | Egypt | Retrospective | 60 | 36 (60) | Exudative ascites/ immunocompromised or sepsis cases/ antibiotics for SBP prophylaxis for at least one month before hospitalization/ hematological disorders on anticoagulant medications | PMN count > 250 cells/mm3 in AF | NLR CRP | |
| Yin X et al. | 2024 | China | Cross-sectional | 1081 (training and internal validation)<br>367 (external validation) | 824 (76.22) (training and internal validation)<br>296 (80.7) (external validation) | Antibiotic, nonsteroidal anti-inflammatory drugs or contraceptives use/ SBP prophylaxis/ ascites without cirrhosis/ abdominal surgery within the past 3months/ vomiting/diarrhea/ abdominal diseases (such as gastritis, enteritis, or intestinal obstruction)/chemotherapy or radiation therapy within the past 1 month/ pregnancy/ secondary peritonitis/ bacterial infections other than SBP/recent bleeding/ other causes of fever, other infections or diseases that may affect the blood, white blood cell (WBC) count or C-reactive protein (CRP) levels, or other diseases that can cause elevated LDH level | Positive AF culture and/or PMN ≥250/mm3 in ascites without any other intraperitoneal source of infection or other cause of increased ascitic neutrophils | Abdominal pain, diarrhea, WBC count, percentage of neutrophils, PCT, LDH, blood sugar, MELD | This study has introduced a nomogram for predicting SBP |

**Table 1** Included studies characteristics (continued)

| Study | Year | country | Study design | Sample size | Male (%) | Exclusion criteria | Reference standard | Predictors | Comments |
|---|---|---|---|---|---|---|---|---|---|
| Silvey S et al. | 2024 | US | Retrospective (building a model by machine learning and internal validation) Prospective (external validation) | 9643 (model building) 2826 (internal validation) 276 (external validation) | 9920 (97.20) (model building) 2910 (97.10) (internal validation) 463 (59.60) (external validation) | Patients with HIV or prior organ transplants | PMN≥250 cells/ml in AF /positive ascites bacterial or fungal culture/ validated ICD-9/ICD-10 SBP code | WBC count, PLT count, AST, ALP, INR, neutrophil percentage, blood glucose, BUN, temperature, BMI, albumin, DBP, GFR, eosinophil percentage, HB, CO2, SBP, K | Machine learning model |
| Kamal A et al. | 2024 | Egypt | Prospective | 124 | 79 (63) | Secondary bacterial peritonitis/ tuberculous and malignant, pancreatic ascites/ trauma/surgery/cancer/ any concurrent infections affecting WBC or CRP levels (such as urinary tract or pulmonary infections) | PMN count > 250 cells/mm3 in AF regardless of the results of ascitic culture | NLR, CRP | Index: NLR x CRP |

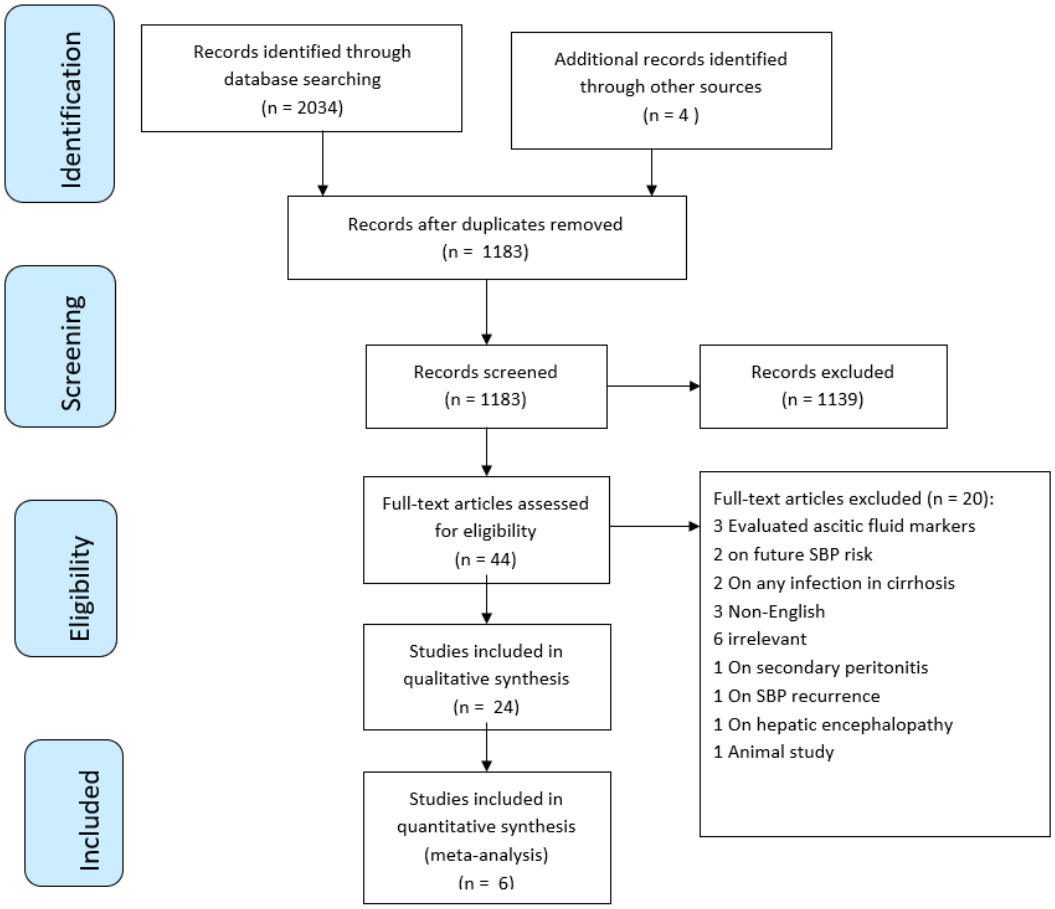


**Figure 1** Flow diagram of the study.

**Table 2** Diagnostic performance of the tools

| Tools name | Study | Sensitivity (CI 95%) | Specificity (CI 95%) | NPV (CI 95%) | PPV PPV (CI 95%) | NLR (CI 95%) | PLR (CI 95%) | AUC (CI 95%) | Accuracy (CI 95%) |
|---|---|---|---|---|---|---|---|---|---|
| Mansoura scoring system | Huynh NC et al. | 85.3 (68.9,95.0) | 97.7 (91.9,99.7) | 94.4 (87.5,98.2) | 93.5 (78.6,99.2) | NA | NA | 0.89 | NA |
| | Abdel Razik A et al. | 55.8 (41.3,69.5) | 97.8 (95.0,99.3) | 90.8 (87.9,93.1) | 85.3 (70.2,93.5) | NA | NA | 0.795 (0.645,0.833) | NA |
| Wehmeyer's scoring system | Wehmeyer M et al. | 29.4 (10.3,56.0) | 100 (93.9,100) | 83.1 (71.9,90.6) | 100 (46.3,100) | NA | NA | 0.68 (0.511,0.848) | NA |
| | Metwally K. et al. | 52.54 (39.12,65.70) | 96.68 (93.56,98.56) | 89.27 (86.40,91.59) | 79.49 (65.28,88.87) | 0.49 (0.37,0.64) | 15.83 (7.68,32.62) | NA | 88.00 (83.78,91.45) Ø |
| MELD score | Obstein KL et al. | 84.21 (60.42, 96.62)∂ | 35.37 (25.12,46.70)∂ | 90.62 (76.67,96.60)∂ | 23.19 (19.00, 27.98)∂ | 0.45 (0.15,1.31)∂ | 1.30 (1.01,1.68)∂ | NA | 44.55 (34.66,54.78)∂ |
| | Gayatri AA et al. | 47.37 (24.45,71.14) ♣ | 83.72 (69.30, 93.19) ♣ | 78.26 (69.73,84.91) ♣ | 56.25 (35.99,74.62) ♣ | 0.63 (0.40, 0.98) ♣ | 2.91 (1.27,6.65) ♣ | NA | 72.58 (59.77,83.15) ♣ |
| | Kraja B et al. | 81.25 (69.54, 89.92) ∂ | 33.33 (26.71, 40.48) ∂ | 84.21 (75.51, 90.22) ∂ | 28.89 (25.82, 32.16) ∂ | 0.56 (0.33,0.97) ∂ | 1.22 (1.04, 1.42) ∂ | NA | 45.31 (39.10,51.63) ∂ |
| CART model | Shi K et al. | 50.33 (42.14,58.50) | 96.00 (94.01, 97.48) | 87.42 (85.54,89.08) | 77.78 (69.30,84.44) | 0.52 (0.44,0.61) | 12.58 (8.11, 19.51) | 0.924 (0.878,0.957) | 0.881 |
| PEC index | Elsadek H.M. et al. | 98.33 | 96.67 | NA | NA | NA | NA | 0.977 (0.940,0.996) | NA |
| Other | Kamal A et al. | 94.0 (83.5,98.7) | 94.59 (86.7, 98.5) | 95.9 (88.6,98.6) | 92.2 (81.9, 96.8) | NA | NA | 0.979 (0.935, 0.996) | 94.4 |
| | Du T et al. | 20.00 (10.03,33.72) | 97.52 (95.35, 98.86) | 89.85 (88.50,91.05) | 52.63 (32.19, 72.23) | 0.82 (0.71,0.94) | 8.07 (3.45, 18.89) | 0.808 | NA |
| | Popoiag R et al. | NA | NA | NA | NA | NA | NA | 0.990 (0.965,0.999) | NA |
| | Mousa N at al. | 95.1 | 96.3 | 89.7 | 98.4 | NA | NA | 0.97±0.02 | 95.6 |
| | Cai Z et al. | 97.30 (90.58,99.67) | 60.00 (45.91,72.98) | 94.29 (80.52, 98.50) | 76.60 (70.26,81.93) | 0.05 (0.01,0.19) | 2.43 (1.76,3.37) | 87.50 (79.18,93.37) | NA |
| | Zhou Z et al. | NA | NA | NA | NA | NA | NA | 0.8383 (0.7216,0.9549) | NA |
| | Wang H et al. | 92.6 | 95.3 | 90.5 | 94.7 | 0.11 | 18.6 | 0.937 (0.901,0.994) | NA |
| | Abdo G et al. | 69.09 (59.57,77.55) | 81.51 (73.36,88.04) | 74.05 (68.05,79.26- | 77.55 (69.89,83.71) | 0.38 (0.28,0.51) | 3.74 (2.51, 5.56) | NA | 75.55 (69.45,80.97) |
| | Xiang S et al. | 73.9 | 62.2 | NA | NA | NA | NA | 0.745 | NA |
| | Abudeif A et al. | 79 | 81 | 69 | 88 | NA | NA | 0.892 (0.854,0.931) | 80 |
| | Elhendawy RI et al. | 96 (87.4,96) | 92 (85.4,90) | 90 | 92 | NA | NA | 0.89 (0.78,1.85) | 95 (88.4,100) |
| | Yin X et al. | NA | NA | NA | NA | NA | NA | 0.90 (0.87,0.94) | NA |
| | Hu Y et al. | 92.7 | 45.7 | 90.4 | 53.2 | NA | NA | 0.822 (0.783,0.856) | NA |
| | Scott S et al. | 98.3 | 8.0 | 94.5 (86.5,98.5) | 15.9 | NA | NA | 72.9 (70.0,75.8) | NA |
| | Würstle S et al. | 94.7 | 42.3 | 98.1 | 85.1 | NA | NA | 0.87 | NA |

NPV: Negative predictive value; PPV: Positive predictive value; PLR: Positive likelihood ratio; NLR: Negative likelihood ratio; AUC: Area under the cure; NA: Not applicable; ∂: cut-off of <15; ♣: cut-off =<17; NA: not applicable

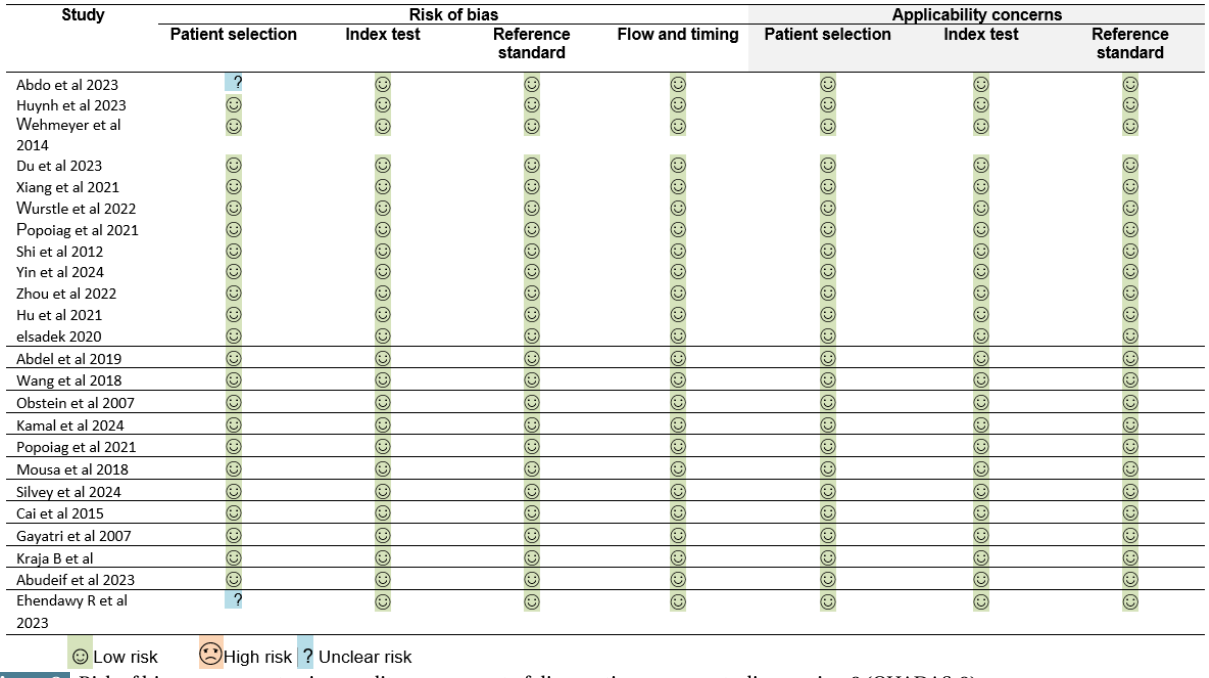


**Figure 2** Risk of bias assessment using quality assessment of diagnostic accuracy studies version 2 (QUADAS-2)

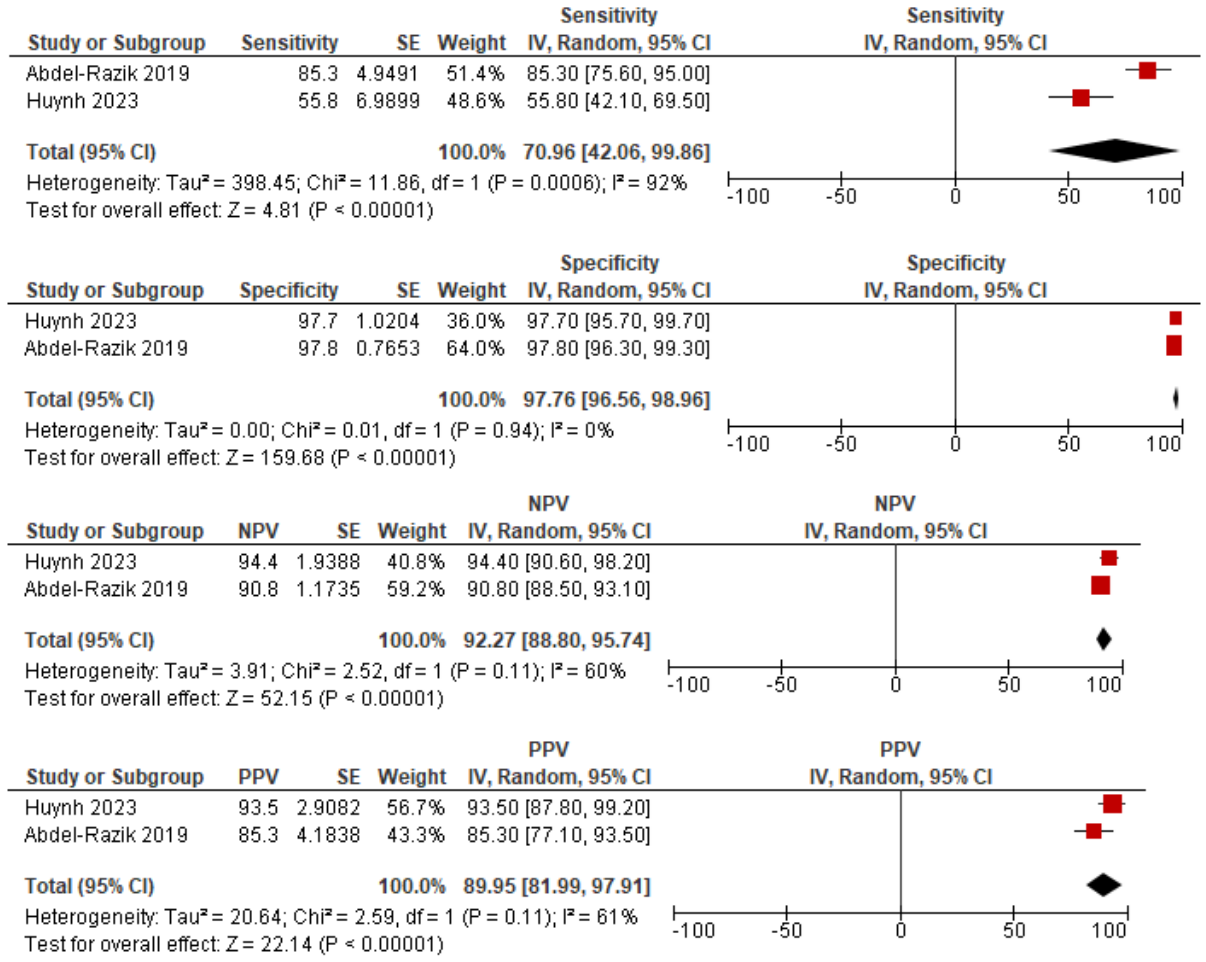


**Figure 3** Diagnostic performance of Mansoura scoring system.

(15,19,26).

***3.4.1. Laboratory-based tools***

Several studies have developed diagnostic tools based on laboratory parameters only. These included values such as ferritin to neutrophil ratio, neutrophil to lymphocyte ratio, and white blood cell to platelet ratio. Three studies incorporated procalcitonin (PCT) which consistently demonstrated high sensitivity and low NLR. For example, the combination of PCT and WBC/PLT ratio yielded an NLR of 0.05 (27). On the other hand, some other laboratory-based tools showed high specificity with variable sensitivity. A study by Shi K et al. (16) classified patients into low, moderate, and high-risk groups based on serum creatinine, total bilirubin, prothrombin time, and white blood cell count, achieving a specificity of 96.00% (95% CI: 94.01%,97.48%). The PEC index (PCT × (ESR + CRP) (20), showed a specificity of 96.67%. However, PLRs were presented by a few studies and were 12.58 (95% CI: 8.11,19.51) in the CART tool, another laboratory-based tool (16). (Table 2)

***3.4.2. Clinical and laboratory combined tools***

Four studies integrated clinical variables with laboratory findings. The Mansoura scoring system, evaluated in two studies, assigns points for age (>55 years), CRP (>40 milligrams/liter (mg/L), mean platelet volume (> 8.5 fl), and neutrophil to lymphocyte ratio) (10,12). Each item had a score of one, except CRP that scored 2. At a cut-off score of 4, pooled sensitivity was 70.96% (95% CI: 42.06%,99.86%) and NPV 92.27% (95% CI: 88.80%,95.74%) while pooled specificity and PPV were 97.76% (95% CI: 96.56,98.96%) and 89.95 % (95% CI: 81.99%,97.91%), respectively (Figure 3).

***3.4.3. Wehmeyer's scoring system***

Two studies assessed the Wehmeyer's scoring system. This tool combines thrombocytopenia (≤100,000 cells/microL), age>60 years, and CRP (>60 mg/L), (13,28). In this scoring system, thrombocytopenia and age had 1 point each and CRP 2 points. At a cut-off of ≥3, pooled sensitivity and specificity were 43.98% (95% CI: 22.08%,65.87%) and 98.43% (95% CI: 95.29%,101.58%), respectively. Pooled PPV was 90.26% (95% CI: 70.28%,110.23%) and NPV was 87.29% (95% CI: 81.64%,92.94%) (Figure 4). The NLR and PLR were reported by only one of the studies as 0.49 ( 95% CI: 0.37,0.64) and 15.83 ( 95% CI: 7.68,32.62), respectively (28). One other study reported the area under the receiver operating characteristic curve (ROCAUC), which was 0.68 (95% CI: 0.511,0.848) (13). It is notable that a study modified the Wehmeyer's scoring system by reclassifying the CRP into three levels with different scores. By this modification, about 20% (58 out of 300) of the patients were stratified as low risk with no SBP (28).

***3.4.4. MELD score***

Three studies assessed the model for end stage liver disease (MELD) score. It is calculated by using serum bilirubin, serum creatinine, and international normalized ratio (INR) (Supplementary file). At a threshold >15, pooled sensitivity and NPV of two studies (22,30) were 83.85% (95% CI: 78.50%,89.20%) and 87.56% (95% CI: 81.29%,93.84%), respectively. However, the specificity was at 34% (95% CI: 28-,39%) The Forest's plots of the other indices are illustrated in figure 5.

## 4. Discussion

Our study showed that some decision tools on laboratory values, especially on PCT can potentially rule out the SBP. Similarly, decision tools such as Mansoura and Wehmeyer's showed high specificity to rule in the diagnosis. Of note, tools such as the PEC index which showed high sensitivity and specificity the same time had low sample size and need further study before recommendation.

While various biomarkers have been investigated as potential diagnostic tools, no single laboratory study was approved for this mean. Multiple factors can explain their lack of usefulness as predictive tools. Many of these tests are nonspecific and rise due to various inflammatory conditions in addition to SBP. Additionally, it is essential to recognize that some of them (e.g., CRP) are also elevated due to compromised liver function in cirrhotic patients in the absence of any inflammation (34). To address this shortcoming, a combination of easily accessible serum biomarkers were tested to predict SBP. Some of these combined markers are based on the simple values of individual markers, while others utilize more complex mathematical formulas. Of note, there are studies that have used the neutrophil to lymphocyte ratio in their tool, an index specific for bacterial infection. A study demonstrated that (neutrophil to lymphocyte ratio) has a sensitivity of 94% and specificity of 94.59% (23). In addition, in terms of discriminatory ability, Mousa et al. study indicated that the summation of CRP values with the ratio exhibited excellent discriminative ability with the AUROC of 0.97±0.02 (25). Although had a small sample size, the combination of the ratio, FNR, and albumin represented an AUROC of 0.81, alongside a false positive rate of 2.53% (33). In addition, our findings suggested that serum PCT in combination with other laboratory studies may be valuable for excluding SBP for their high sensitivity. Of note, as proposed by Cai et al. (27) had a NLR of below 0.1 which is great property for a tool to be recommended for ruling out the SBP (35). In the PEC index, PCT multiplied by the sum of ESR and CRP. The result exhibited excellent diagnostic performance with the AUROC of 0.977 (95% CI: 0.940, 0.996) (19). In another study, PCT was combined with obtained from WBC count indices. As proposed by the authors, this score is particularly valuable for diagnosing culture-negative SBP (21). The PCT+WBC/PLT ratio, has been shown to significantly enhance the sensitivity of early detection of SBP when compared to the individual components of ratio (27).

Some other studies used sophisticated laboratory tests to make the diagnosis. For instance, alterations in gut microbiota are observed in patients with liver cirrhosis, and its correlation with the progression of the disease has been demonstrated (36,37). Zhou Z et al. explored gut microbiota as a diagnostic tool for SBP in cirrhosis patients. They identified

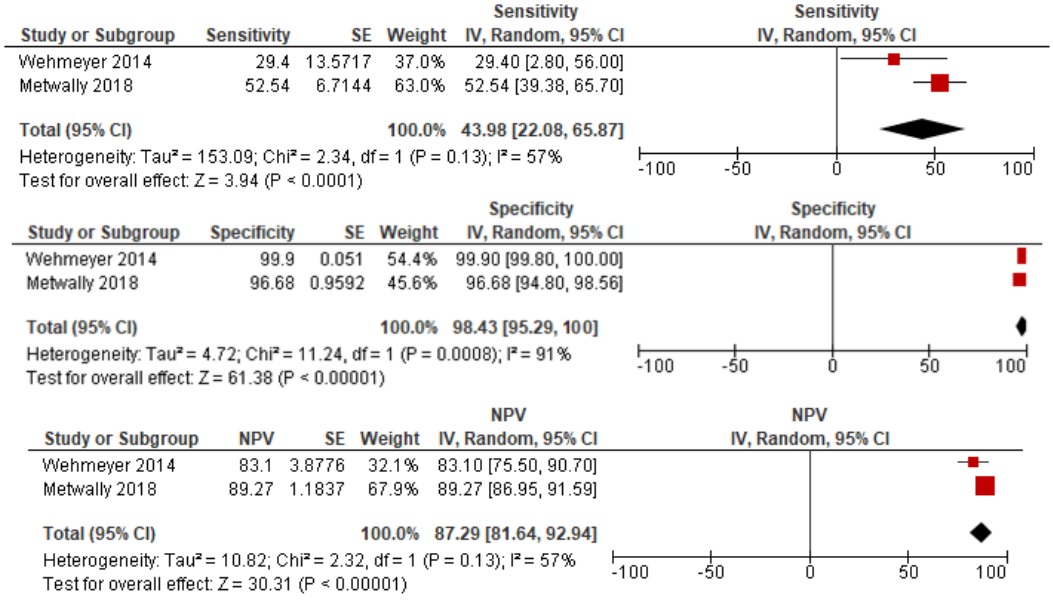


**Figure 4** Diagnostic performance of Wehmeyer's scoring system.

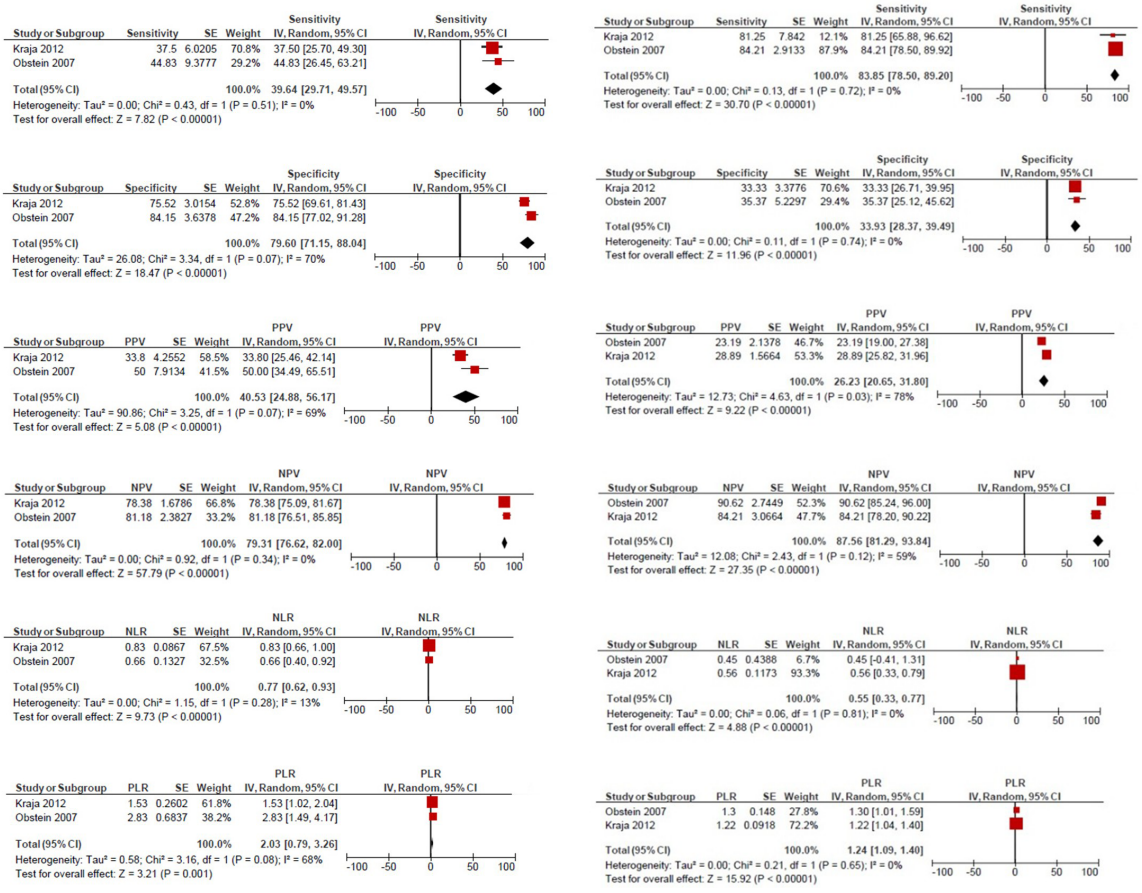


**Figure 5** Diagnostic performance of MELD score at cut-off of <15 (left), and ≥25 (right).

five operational taxonomic unit (OTU)-based biomarkers to develop a noninvasive diagnostic method for SBP (18). Currently, the implementation of this diagnostic tool may not be practical, particularly in clinical settings.

Among the other studies, the MELD score, initially established as a prognostic tool for assessing the survival of patients with cirrhosis, has also undergone evaluation for SBP diagnosis (38). Although it was shown that patients with higher MELD scores exhibited a higher risk of SBP, the predefined cut-offs used for cirrhotic patients (39); prognostication was not useful for the SBP diagnosis. Hence, other cut-offs were also tested. In our meta-analysis, the sensitivity and specificity of the MELD score was 83.85% (95% CI: 78.50%,89.20%) and 33.93% (95% CI: 28.37%,39.49%) for scores less than 15 and 39.64% (95% CI: 29.71%,49.57%) and 79.60% (95% CI: 71.15%,88.04%) for scores of 25 or greater, respectively. The Mansoura scoring system was developed through a methodologically sound study in 2019 (10) and subsequently externally validated in 2023 (12). In our meta-analysis, the pooled sensitivity and specificity for a cut-off of 4 were 70.96% (95% CI: 42.06%,99.86%) and 97.76% (95% CI: 96.56%,98.96%), respectively.

According to a study, at a cut-off of 5, the PPV was 100% (95% CI: 47.2%, 100%) and the specificity was 100% (95% CI: 98.9%,100%) (10). However, it should be highlighted that only 32 out of 121 patients were in the high-risk group. Wehmeyer's scoring system was also derived for diagnosing SBP in cirrhotic patients with ascites. According to the tool, patients with scores higher than 3 should be regarded as positive for SBP, thereby warranting the initiation of prophylactic antibiotic therapy. During the validation phase, only 2 out of 162 were false positive (13). A notable limitation is its inability exclude SBP in patients who score 1 or 2. In this study, the number of patients in the non-high-risk group is not specified, but it is noted that 12% of SBP patients had a score of 1 (13). In our meta-analysis, we found that the pooled sensitivity and specificity of Wehmeyer's scoring system are 43.98% (95% CI: 22.08%,65.87%) and 98.43% (95% CI: 95.29%,101.58%), respectively. Only one study (28) reported the PLR of 15.83, high above the 10 threshold which is an indicator for a tool for confirming the diagnosis (35). The modification of CRP, a predictor variable in this tool, helped to exclude SBP in all patients with 0 points; this accounted for 58 patients in a total study population of 300 (NPV for the 0-point patients in the original Wehmeyer's tool was 93.5%). However, the proportion of patients who were reclassified as low risk through this modification has not been presented in the study (28). In the modified Wehmeyer's scoring system, patients who receive scores of 4 or 5 are classified as high risk for SBP. It is noteworthy that only 15 out of a total of 300 patients classified as high scores. Furthermore, 2 of these high-risk patients tested negative for SBP. Consequently, the modified Wehmeyer's scoring system may prove to be a more effective tool to rule out the SBP than the original tool (28). The clinical implication of the review is showing tools with various tools with different properties, which can be used according to different clinical scenarios. Future studies can be aiming at validation of the tools with both high sensitivity and specificity. Furthermore, tools with well stablished properties can be combined with each other through sequential and parallel testing to enhance some of the features as needed.

## 5. Limitations

This study has several limitations. First, although we used random effect model for meta-analysis, inherent heterogeneity among included studies is a concern. Second, not all can be considered a formal decision tool as some studies just combined the laboratory results. Third, most of the laboratory parameters included in this review lack specificity as they may also be elevated in other infections, such as pneumonia and urinary tract infections.

## 6. Conclusion

In summary, multiple decision tools have been proposed for the diagnosis of SBP. Tools incorporating PCT, can potentially rule out SBP whereas Mansoura and Wehmeyer's scores are capable of ruling in the diagnosis. Further prospective, validation studies are needed before any single tool can be recommended for widespread clinical adoption.

## 7. Declarations

### *7.1. Acknowledgement*

None.

### *7.2. Authors' contribution*

Ideation and design: PD, HM; Data extraction: PD, KG, EV, MA, AAAN; Interpretation of the results: HM, PD, KG; Drafting the work: KG, PD; Revising draft critically for important intellectual content: All authors. The authors read and approved the final manuscript.

### *7.3. Conflict of interest*

None.

### *7.4. Funding*

None.

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**Supplementary 1** Ovid MEDLINE(R) ALL 1946 to September 23, 2024

| | | |
|---|---|---|
| 1 | exp Liver Cirrhosis/ or exp Fibrosis/ or exp End Stage Liver Disease/ or exp Ascites/ | 235170 |
| 2 | (cirrho* or fibrosis).ti,ab,kf. | 359889 |
| 3 | ((chronic or "end stage" or acute) adj3 (liver or hepatic) adj3 (disease* or failure*)).ti,ab,kf. | 57010 |
| 4 | 1 or 2 or 3 | 487522 |
| 5 | exp Decision Support Techniques/ or exp Clinical Decision Rules/ | 83463 |
| 6 | (((diagnostic or decision* or predict* or prognostic) adj3 (rule* or scor* or value* or risk* or outcome* or index or model* or tool* or marker* or aid or aids)) or "non-Invasive Diagnos*").ti,ab,kf. | 942934 |
| 7 | (risk adj3 (assess* or evaluation or tool* or scor* or scal*)).ti,ab,kf. | 271035 |
| 8 | (decision adj3 ("Support Technique*" or modeling or Analys* or aid or aids)).ti,ab,kf. | 30374 |
| 9 | ((valid* or develop* or deriv* or perform*) adj3 (decision* or predict* or rule* or scor* or index or model* or tool* or algorithm)).ti,ab,kf. | 639163 |
| 10 | ((validation or derivation) adj3 (study or studies)).ti,ab,kf. | 32954 |
| 11 | 5 or 6 or 7 or 8 or 9 or 10 | 1721411 |
| 12 | (spontaneous adj3 bacterial adj3 peritonitis).ti,ab,kf. | 2808 |
| 13 | exp peritonitis/ or exp Ascitic Fluid/ | 41762 |
| 14 | 12 or 13 | 42942 |
| 15 | 4 and 11 and 14 | 525 |
| | **2. Embase (embase.com)** | |
| #1 | 'liver cirrhosis'/exp OR 'liver fibrosis'/exp OR 'end stage liver disease'/exp OR 'ascites'/exp | 338042 |
| #2 | cirrho*:ti,ab,kw OR fibrosis:ti,ab,kw | 593691 |
| #3 | ((chronic OR 'end stage' OR acute) NEAR/3 (liver OR hepatic) NEAR/3 (disease* OR failure*)):ti,ab,kw | 95531 |
| #4 | #1 OR #2 OR #3 | 759454 |
| #5 | 'decision support system'/exp OR 'clinical decision rule'/exp | 38214 |
| #6 | (((diagnostic OR decision* OR predict* OR prognostic) NEAR/3 (rule* OR scor* OR value* OR risk* OR outcome* OR index OR model* OR tool* OR marker* OR aid OR aids)):ti,ab,kw) OR 'non-invasive diagnos*':ti,ab,kw | 1349612 |
| #7 | (risk NEAR/3 (assess* OR evaluation OR tool* OR scor* OR scal*)):ti,ab,kw | 382313 |
| #8 | (decision NEAR/3 ('support technique*' OR modeling OR analys* OR aid OR aids)):ti,ab,kw | 40009 |
| #9 | ((valid* OR develop* OR deriv* OR perform*) NEAR/3 (decision* OR predict* OR rule* OR scor* OR index OR model* OR tool* OR algorithm)):ti,ab,kw | 857431 |
| #10 | ((validation OR derivation) NEAR/3 (study OR studies)):ti,ab,kw | 47430 |
| #11 | #5 OR #6 OR #7 OR #8 OR #9 OR #10 | 2329429 |
| #12 | (spontaneous NEAR/3 bacterial NEAR/3 peritonitis):ti,ab,kw | 5447 |
| #13 | 'bacterial peritonitis'/exp OR 'ascites fluid'/exp | 20533 |
| #14 | #12 OR #13 | 21302 |
| #15 | #4 AND #11 AND #14 | 1217 |
| #16 | #15 NOT 'conference abstract'/it | 729 |
| | **3. Scopus** | |
| #1 | TITLE-ABS-KEY(cirrho* OR fibrosis) | 553,856 |
| #2 | TITLE-ABS-KEY((chronic OR "end stage" OR acute) W/3 (liver OR hepatic) W/3 (disease* OR failure*)) | 93,886 |
| #3 | #1 OR #2 | 605,111 |
| #4 | TITLE-ABS-KEY(((diagnostic OR decision* OR predict* OR prognostic) W/3 (rule* OR scor* OR value* OR risk* OR outcome* OR index OR model* OR tool* OR marker* OR aid OR aids)) OR "non-Invasive Diagnos*") | 2,599,032 |
| #5 | TITLE-ABS-KEY(risk W/3 (assess* OR evaluation OR tool* OR scor* OR scal*)) | 1,266,454 |
| #6 | TITLE-ABS-KEY(decision W/3 ("Support Technique*" OR modeling OR Analys* OR aid OR aids)) | 136,357 |
| #7 | TITLE-ABS-KEY((valid* OR develop* OR deriv* OR perform*) W/3 (decision* OR predict* OR rule* OR scor* OR index OR model* OR tool* OR algorithm)) | 3,479,415 |
| #8 | TITLE-ABS-KEY((validation OR derivation) W/3 (study OR studies)) | 169,590 |
| #9 | #4 OR #5 OR #6 OR #7 OR #8 | 6,665,129 |
| #10 | TITLE-ABS-KEY(spontaneous W/3 bacterial W/3 peritonitis) | 3,349 |
| #11 | #3 AND #9 AND #10 | 584 |
| | **4. Web of Science Core Collection (SCIE, SSCI, and ESCI)** | |
| #1 | TS=(cirrho* OR fibrosis) | 467,153 |
| #2 | TS=((chronic OR "end stage" OR acute) NEAR/3 (liver OR hepatic) NEAR/3 (disease* OR failure*)) | 66,049 |
| #3 | #1 OR #2 | 504,983 |
| #4 | TS=(((diagnostic OR decision* OR predict* OR prognostic) NEAR/3 (rule* OR scor* OR value* OR risk* OR outcome* OR index OR model* OR tool* OR marker* OR aid OR aids)) OR "non-Invasive Diagnos*") | 1,747,951 |
| #5 | TS=(risk NEAR/3 (assess* OR evaluation OR tool* OR scor* OR scal*)) | 443,173 |
| #6 | TS=(decision NEAR/3 ("Support Technique*" OR modeling OR Analys* OR aid OR aids)) | 126,761 |
| #7 | TS=((valid* OR develop* OR deriv* OR perform*) NEAR/3 (decision* OR predict* OR rule* OR scor* OR index OR model* OR tool* OR algorithm)) | 2,089,444 |
| #8 | TS=((validation OR derivation) NEAR/3 (study OR studies)) | 53,605 |
| #9 | #4 OR #5 OR #6 OR #7 OR #8 | 3,826,117 |
| #10 | TS=(spontaneous NEAR/3 bacterial NEAR/3 peritonitis) | 4,141 |
| #11 | #3 AND #9 AND #10 | 466 |

**Supplementary 1** (continued)

| | | |
|---|---|---|
| 1 | Medline | 525 |
| 2 | Embase | 729 |
| 3 | Scopus | 584 |
| 4 | Web of Science Core Collection | 466 |
| Total | | 2304 |

**Supplementary 2** The variables in the decision tools for SBP diagnosis, their cut-offs and the scores

| Tools name | Study | Variables | Scores | Proposed cut-off |
|---|---|---|---|---|
| Mansoura | Abdel-Razik A et al. (1) | Age≥55 years | 1 | NA |
| | and | MPV ≥8.5 f | 1 | |
| | Huynh NC et al. (2) | NLR≥2.5 | 1 | |
| | | CRP≥40 mg/l | 2 | |
| Wehmeyer | Wehmeyer M et al. (3) | Age >60 years | 1 | NA |
| | | Platelet count ≤100.000/ µL | 1 | |
| | | CRP >60 mg/L | 2 | |
| Modified Wehmeyer | Metwally K et al. (4) | Age >60 years | 1 | NA |
| | | Platelet count ≤100.000/ µL | 1 | |
| | | CRP (13.5 mg/L | 0 | |
| | | 13.5-30 mg/L | 1 | |
| | | 30-60 mg/L | 2 | |
| | | ≥60mg/L) | 3 | |
| MELD score | Obstein KL et al. (5) | 0.957 × ln(Cr) + | NA | <15 |
| | and | 0.378 × ln(bilirubin) + | | 16-24 |
| | Kraja B et al. (6) | 1.120 × ln(INR) + 0.643 | | ≥25 |
| | Gayatri AA et al. (7) | | | ≤17 >18 |
| PEC index | Elsadek H.M. et al. (8) | PCT× (ESR + CRP) | NA | 20 |
| Other | Abdo G et al. (9) | TB≥ 2.375 mg/dl | 1 | NA |
| | | NLR≥ 3.438 | 1 | |
| | | CRP≥ 30 mg/L | 1 | |
| | Kamal A et al. (10) | "NLR x CRP" | NA | > 18.28 |
| | Popoiag R et al. (11) | ESR>33 mm/h | NA | NA |
| | | NLR>2.4 | | |
| | Mousa N et al. (12) | CRP>2.89 mg/L | NA | NA |
| | | NLR>11.3 | | |
| | Cai Z et al. (13) | PCT>2.0 ng/ml | NA | NA |
| | | (WBC/PLT)≥0.25 | | |
| Wang H et al. (14) | PCT | NA | ≥3.40 | |
| | dCHC | | | |
| | sNFI | | | |
| | Abudeif A et al. (15) | NLR + MPV | NA | >14.5 |
| | Elhendawy R et al. (16) | NLR+CRP | NA | >22.6 |

MPV: Mean platelet volume; NLR: Neutrophil to lymphocyte ratio; CRP: C-reactive protein; Cr: Creatinine; INR: International normalized ratio; PCT: Procalcitonin; ESR: Estimated sedimentation ratio; TB: Total bilirubin; WBC: White blood cell; PLT: Platelet; dCHC: difference in hemoglobin concentration between newly formed and mature red blood cells; sNFI: Mean fluorescence intensity of mature neutrophils; NA: Not applicable

## References (supplementary)


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