

REVIEW ARTICLE

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

Khazar Garjani^{1,3}, Elnaz Vahidi¹, Mehrad Aghili¹, Amir Abbas Azimi

Nezhad¹, Parinaz Dadlani^{2*}, Hadi Mirfazaelian^{1,3}

1. Emergency Medicine Department, Tehran University of Medical Sciences, Tehran, Iran.
2. Department of Emergency Medicine, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3. Prehospital and Hospital Emergency Research Center, Tehran University of Medical Sciences, Tehran, Iran.

Abstract:

Background: 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

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 $\geq 250/\text{mL}$, 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 ascites. 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 (QUADAS 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 I^2 . 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 (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 ($PCT \times (ESR + CRP)$) (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 ($\leq 100,000$ 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 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 established 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. 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.

7.2. Conflict of interest

None.

7.3. Funding

None.

ACCEPTED MANUSCRIPT

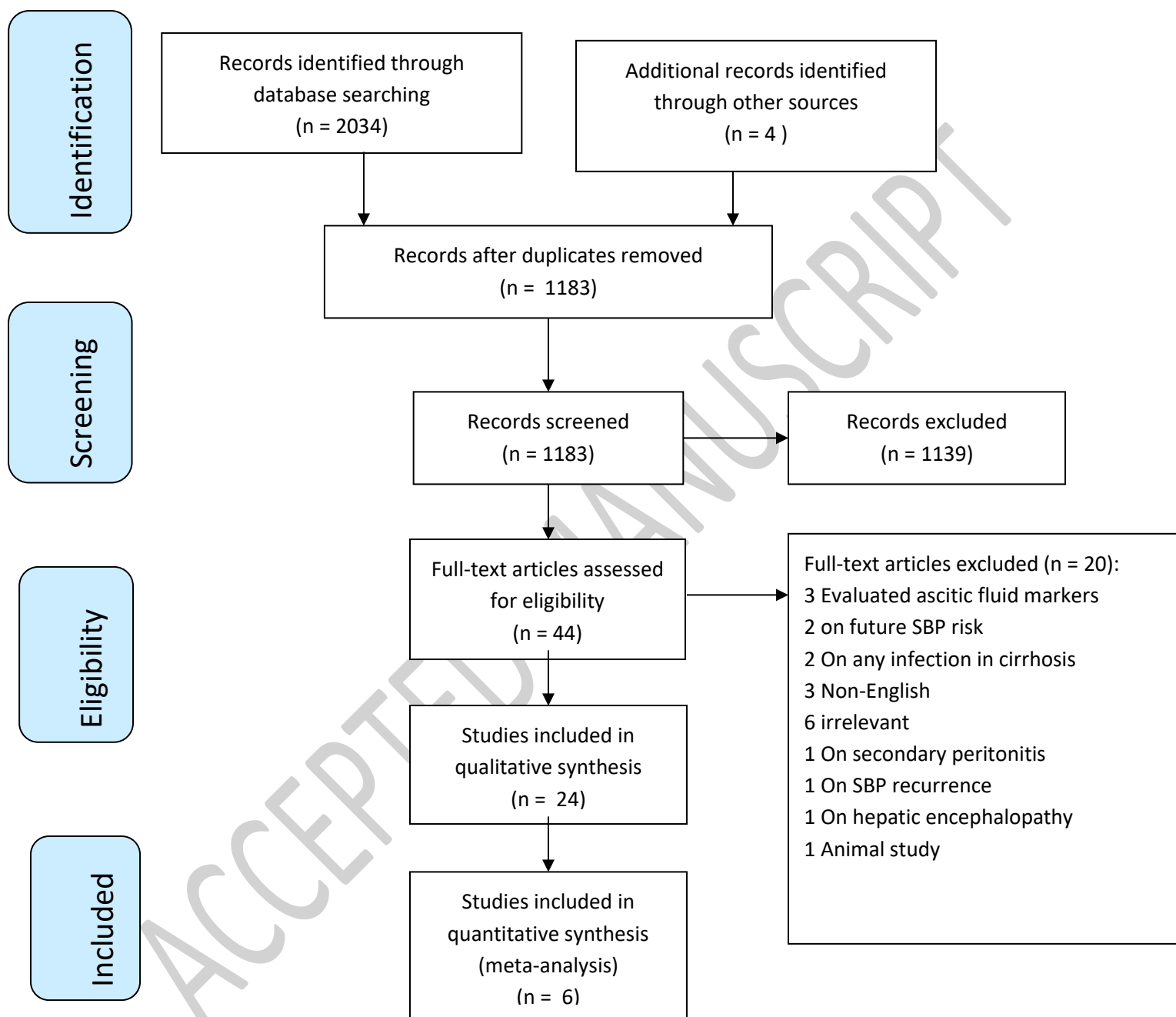






















































Figure 1 Flow diagram of the study

ACCEPTED MANUSCRIPT

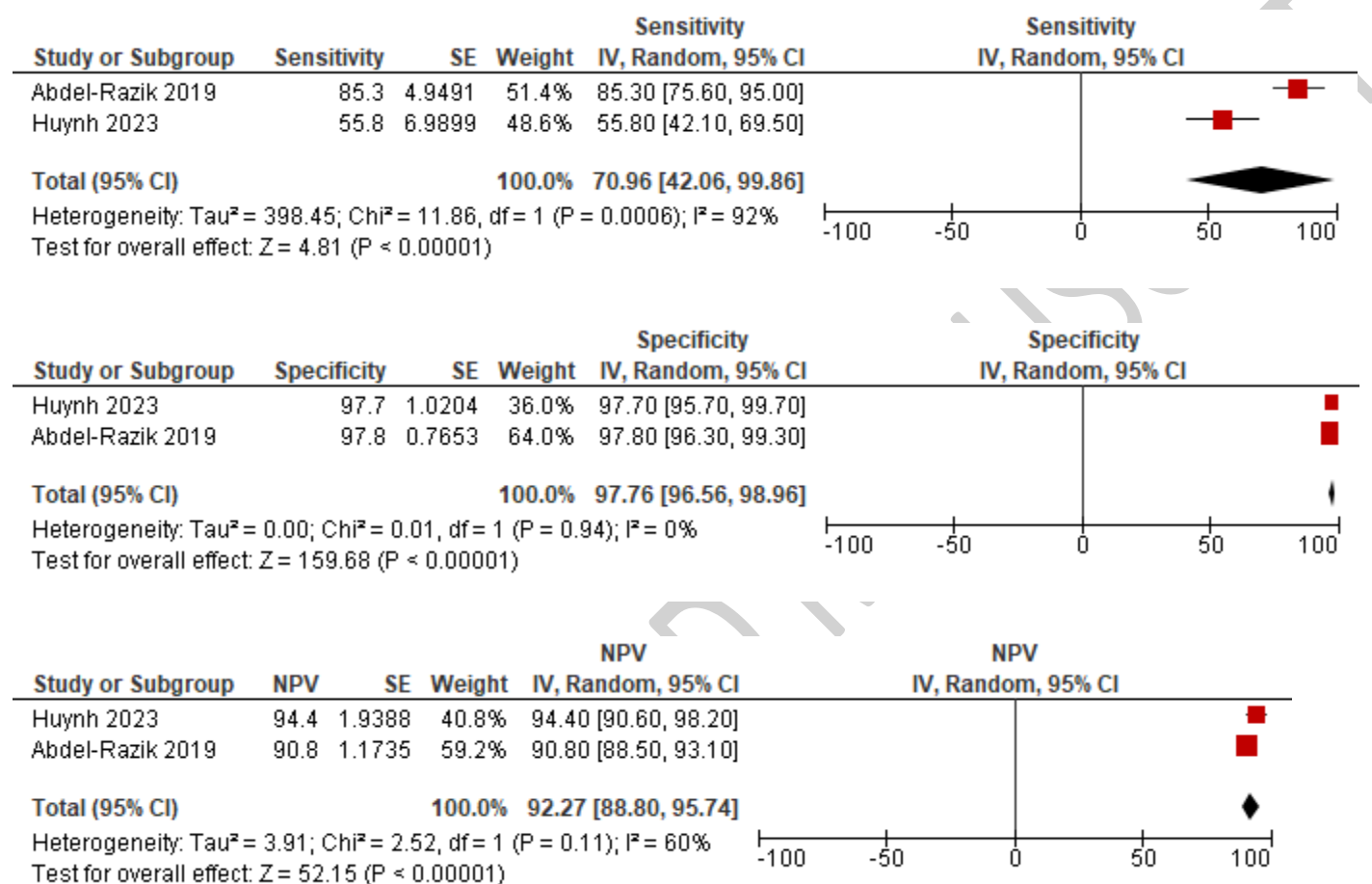
Figure 2 Risk of bias assessment using quality assessment of diagnostic accuracy studies version 2 (QUADAS-2)

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Abdo et al 2023	?	😊	😊	😊	😊	😊	😊
Huynh et al 2023	😊	😊	😊	😊	😊	😊	😊
Wehmeyer et al 2014	😊	😊	😊	😊	😊	😊	😊
Du et al 2023	😊	😊	😊	😊	😊	😊	😊
Xiang et al 2021	😊	😊	😊	😊	😊	😊	😊
Wurstle et al 2022	😊	😊	😊	😊	😊	😊	😊
Popoiag et al 2021	😊	😊	😊	😊	😊	😊	😊
Shi et al 2012	😊	😊	😊	😊	😊	😊	😊
Yin et al 2024	😊	😊	😊	😊	😊	😊	😊
Zhou et al 2022	😊	😊	😊	😊	😊	😊	😊
Hu et al 2021	😊	😊	😊	😊	😊	😊	😊
elsadek 2020	😊	😊	😊	😊	😊	😊	😊
Abdel et al 2019	😊	😊	😊	😊	😊	😊	😊
Wang et al 2018	😊	😊	😊	😊	😊	😊	😊
Obstein et al 2007	😊	😊	😊	😊	😊	😊	😊
Kamal et al 2024	😊	😊	😊	😊	😊	😊	😊
Popoiag et al 2021	😊	😊	😊	😊	😊	😊	😊

Mousa et al 2018							
Silvey et al 2024							
Cai et al 2015							
Gayatri et al 2007							
Kraja B et al							
Abudeif et al 2023							
Ehendawy R et al 2023							
 Low risk  High risk  Unclear risk							

ACCEPTED MANUSCRIPT

Figure 3 Diagnostic performance of Mansoura scoring system



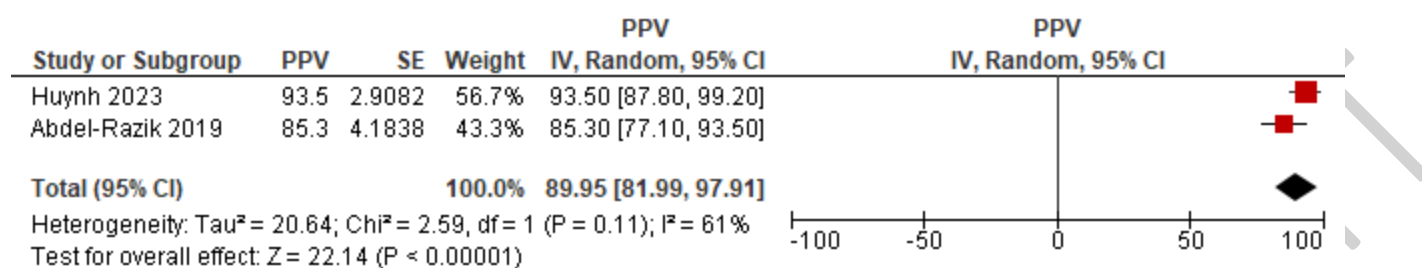
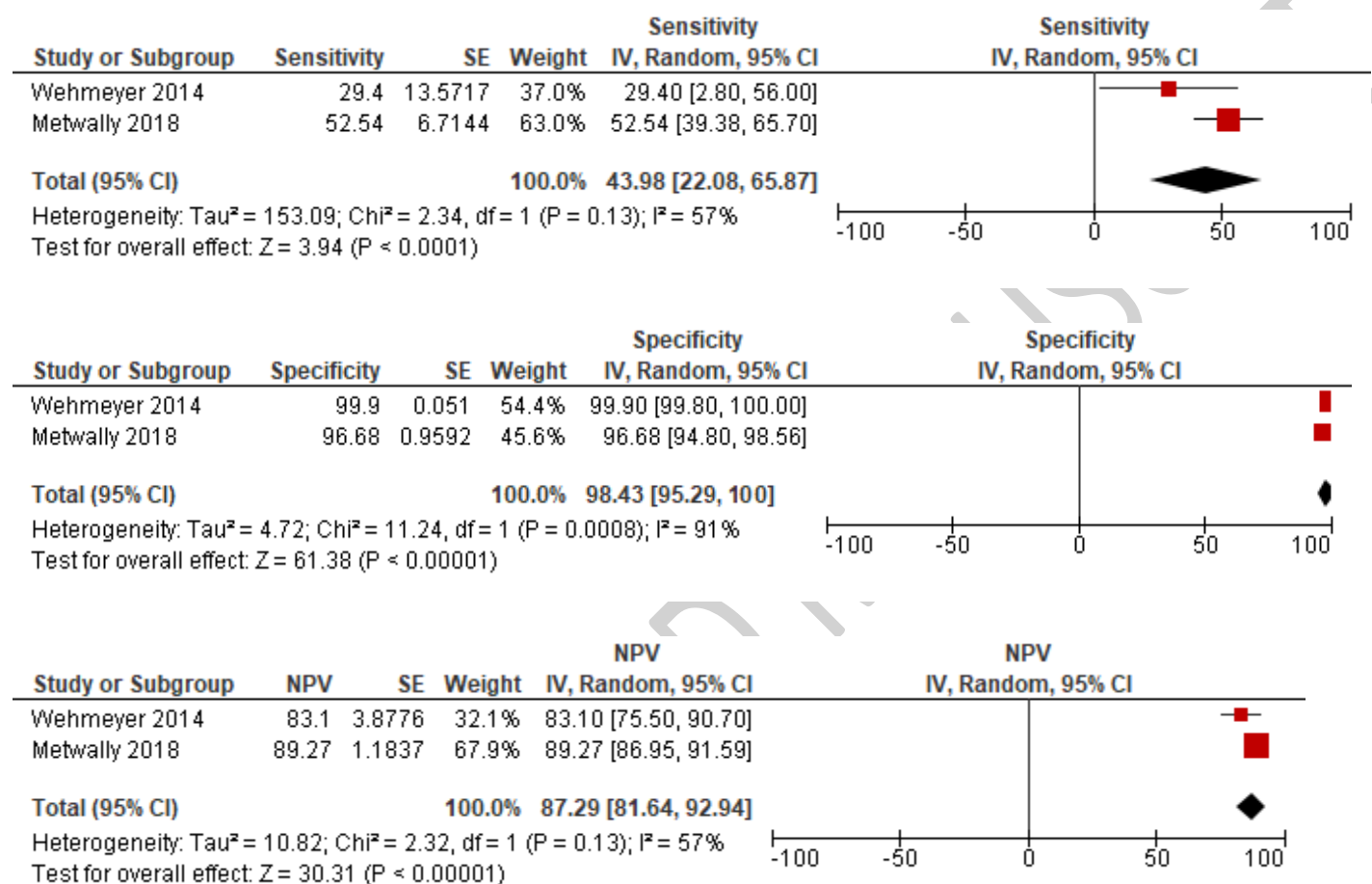


Figure 4 Diagnostic performance of Wehmeyer's scoring system



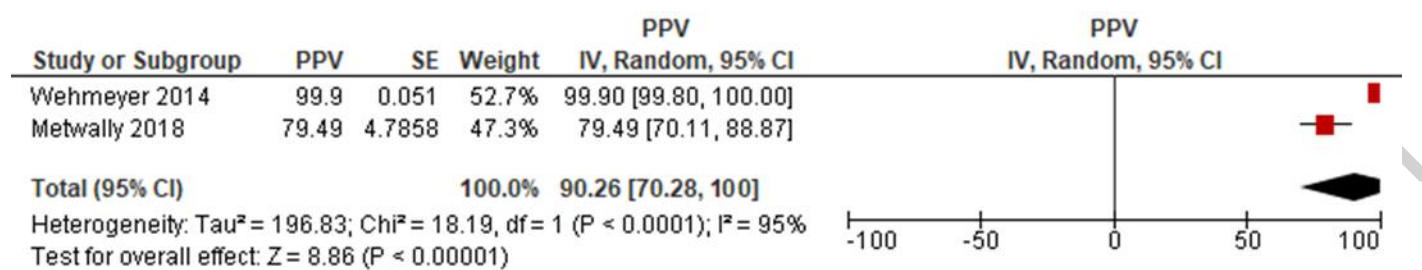


Figure . Diagnostic performance of MELD score at cut-off of <15 (left), and ≥ 25 (right)

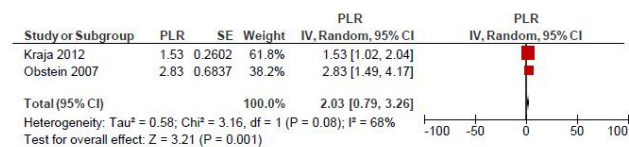
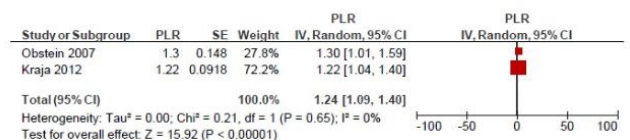
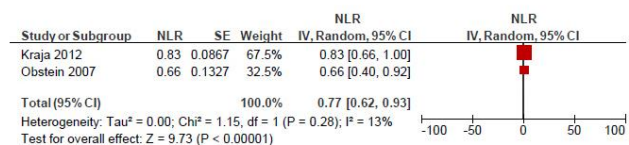
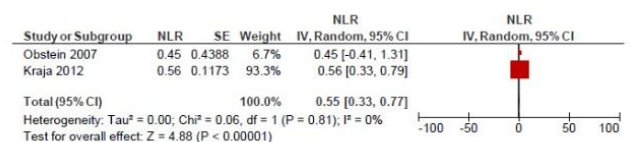
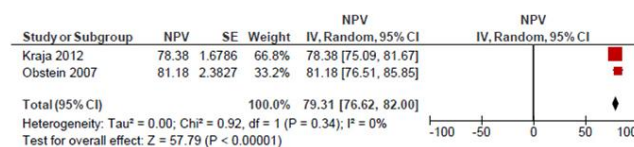
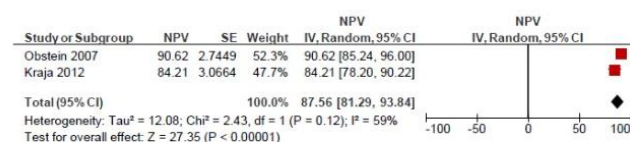
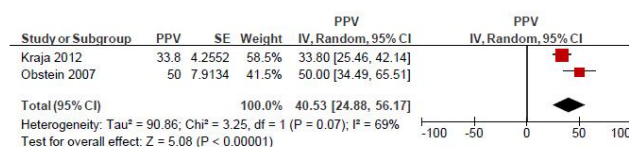
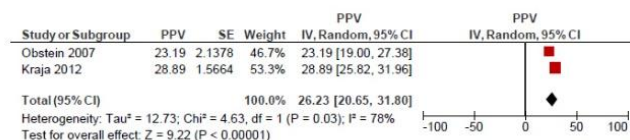
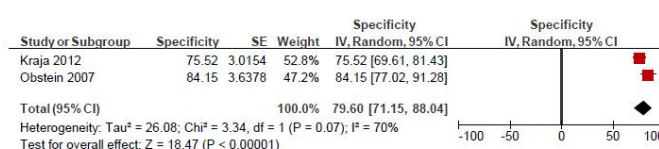
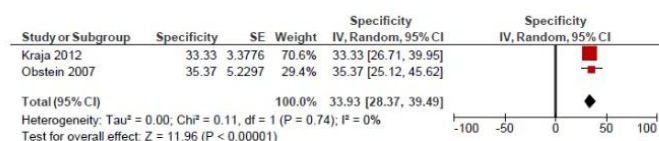
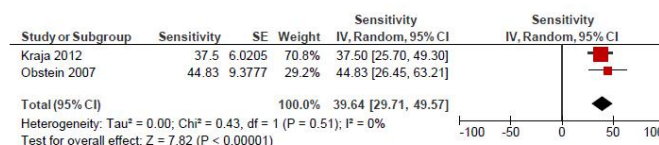
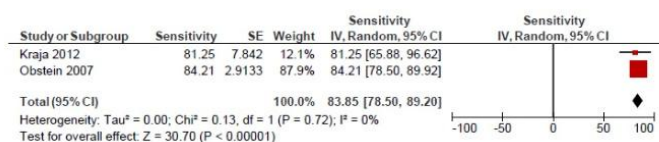


Table 2 Diagnostic performance of the tools

Tools name	Study	Sensitivity (CI 95%)	Specificity (CI 95%)	NPV (CI 95%)	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) ^ø	35.37 (25.12,46.70) ^ø	90.62 (76.67,96.60) ^ø	23.19 (19.00, 27.98) ^ø	0.45 (0.15,1.31) ^ø	1.30 (1.01,1.68) ^ø	NA	44.55 (34.66,54.78) ^ø
	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) ^ø	33.33 (26.71, 40.48) ^ø	84.21 (75.51, 90.22) ^ø	28.89 (25.82, 32.16) ^ø	0.56 (0.33, 0.97) ^ø	1.22 (1.04, 1.42) ^ø	NA	45.31 (39.10,51.63) ^ø
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(88.5 0,91.05)	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 (45.91,72.9 8)	94.29 (80.52, 98.50)	76.60 (70.26,81.9 3)	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 (0.7216,0.95 49)	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 (73.36,88.0 4)	74.05 (68.05,79.2 6-	77.55(69.8 9,83.71)	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 curve; NA: Not applicable; ø: cut-off of <15; *: cut-off = <17; NA: not applicable

REFERENCES

1. Ekpanyapong S, Reddy KR. *Infections in Cirrhosis*. Curr Treat Options Gastroenterol. 2019. **17**(2):254-70.
2. European Association for the Study of the Liver. EASL clinical practice guidelines on the management of ascites, spontaneous bacterial peritonitis, and hepatorenal syndrome in cirrhosis. *J Hepatol*. 2010;**53**(3):397-417.
3. Deutsch-Link S, Campbell PT, Shah ND. PRO: ascitic fluid cell count should be routinely sent with every therapeutic paracentesis to assess for spontaneous bacterial peritonitis. *Clin Liver Dis (Hoboken)*. 2023;**22**(4):140-142.
4. Long B, and Gottlieb M. *Emergency medicine updates: spontaneous bacterial peritonitis*. Am J Emerg Med. 2023;**70**:84-9.
5. Orman ES, Hayashi PH, Bataller R, Barritt AS 4th. Paracentesis is associated with reduced mortality in patients hospitalized with cirrhosis and ascites. *Clin Gastroenterol Hepatol*. 2014;**12**(3):496-503.e1..
6. Alhumaid S, Al Mutair A, Al Alawi Z, et al. Proton pump inhibitors use and risk of developing spontaneous bacterial peritonitis in cirrhotic patients: a systematic review and meta-analysis. *Gut Pathog*. 2021;**13**(1):17.7. Thalheimer U, Triantos CK, Samonakis DN, Patch D, Burroughs AK. Infection, coagulation, and variceal bleeding in cirrhosis. *Gut*. 2005;**54**(4):556-63.
8. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011;**155**(8):529-36.
9. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. *Res Synth Methods*. 2021;**12**(1):55-61.
10. Abdel-Razik A, Mousa N, Abdel-Aziz M, et al. Mansoura simple scoring system for prediction of spontaneous bacterial peritonitis: lesson learnt. *Eur J Gastroenterol Hepatol*. 2019;**31**(8):1017-24.
11. Abdo G, Nir U, Rawajdey R, et al. A novel score-based approach by using routine laboratory tests for accurate diagnosis of spontaneous bacterial peritonitis (SBP) in cirrhotic patients. *EJIFCC*. 2023;**34**(4):297-304.
12. Huynh NC, Vo TD. Validation of a new simple scoring system to predict spontaneous bacterial peritonitis in patients with cirrhosis and ascites. *BMC Gastroenterol*. 2023;**23**(1):272.
13. Wehmeyer MH, Krohm S, Kastein F, Lohse AW, Lüth S. Prediction of spontaneous bacterial peritonitis in cirrhotic ascites by a simple scoring system. *Scand J Gastroenterol*. 2014;**49**(5):595-603.
14. Xiang S, Tan J, Tan C, et al. Establishment and validation of a non-invasive diagnostic nomogram to identify spontaneous bacterial peritonitis in patients with decompensated cirrhosis. *Front Med (Lausanne)*. 2022;**8**:797363..
15. Würstle S, Hapfelmeier A, Karapetyan S, et al. A novel machine learning-based point-score model as a non-invasive decision-making tool for identifying infected ascites in patients with hydropic decompensated liver cirrhosis: a retrospective multicentre study. *Antibiotics (Basel)*. 2022;**11**(11):1610.
16. Shi KQ, Fan YC, Ying L, et al. Risk stratification of spontaneous bacterial peritonitis in cirrhosis with ascites based on classification and regression tree analysis. *Mol Biol Rep*. 2012;**39**(5):6161-9.
17. Yin X, Qin E, Song R, et al. Diagnostic model for spontaneous bacterial peritonitis in cirrhotic patients with ascites: a multicenter cohort study. *Eur J Gastroenterol Hepatol*. 2024;**36**(11):1319-28.

18. Zhou Z, Lv H, Lv J, et al. Alterations of gut microbiota in cirrhotic patients with spontaneous bacterial peritonitis: A distinctive diagnostic feature. *Front Cell Infect Microbiol.* 2022;12:999418.
19. Hu Y, Chen R, Gao H, et al. Explainable machine learning model for predicting spontaneous bacterial peritonitis in cirrhotic patients with ascites. *Sci Rep.* 2021;11(1):21639.
20. Elsadek HM, Elhawari SA, Mokhtar A. A novel serum index for accurate diagnosis of spontaneous bacterial peritonitis in cirrhotic patients without other infections. 2020.
21. Wang H, Li Y, Zhang F, et al. Combination of PCT, sNFI and dCHC for the diagnosis of ascites infection in cirrhotic patients. *BMC Infect Dis.* 2018;18(1):389.
22. Obstein KL, Campbell MS, Reddy KR, Yang YX. Association between model for end-stage liver disease and spontaneous bacterial peritonitis. *Am J Gastroenterol.* 2007;102(12):2732-6.
23. Kamal A. Evaluation of a novel index that incorporates both neutrophil- lymphocyte ratio and c-reactive protein for the detection of spontaneous bacterial peritonitis. The Egyptian Journal of Hospital Medicine. 2024; 94: 950-6 .
24. Popoiag RE, Suceveanu AI, Suceveanu AP, et al. Predictors of spontaneous bacterial peritonitis in Romanian adults with liver cirrhosis: Focus on the neutrophil-to-lymphocyte ratio. *Exp Ther Med.* 2021;22(3):983.
25. Mousa N, Besheer T, Abdel-Razik A, et al. Can combined blood neutrophil to lymphocyte ratio and C-reactive protein be used for diagnosis of spontaneous bacterial peritonitis?. *Br J Biomed Sci.* 2018;75(2):71-5.
26. Silvey S, Patel N, Liu J, et al. A Machine learning algorithm avoids unnecessary paracentesis for exclusion of sbp in cirrhosis in resource-limited settings. *Clin Gastroenterol Hepatol.* 2024;22(12):2442-50.e8.27. Cai ZH, Fan CL, Zheng JF, et al. Measurement of serum procalcitonin levels for the early diagnosis of spontaneous bacterial peritonitis in patients with decompensated liver cirrhosis. *BMC Infect Dis.* 2015;15:55.28. Metwally K, Fouad T, Assem M, Abdelsameea E, Yousery M. Predictors of Spontaneous Bacterial Peritonitis in Patients with Cirrhotic Ascites. *J Clin Transl Hepatol.* 2018;6(4):372-6.29. Gayatri AA, Suryadharma IG, Purwadi N, Wibawa ID. The relationship between a model of end stage liver disease score (MELD score) and the occurrence of spontaneous bacterial peritonitis in liver cirrhotic patients. *Acta Med Indones.* 2007;39(2):75-8.
30. Kraja B, Sina M, Mone I, et al. Predictive value of the model of end-stage liver disease in cirrhotic patients with and without spontaneous bacterial peritonitis. *Gastroenterol Res Pract.* 2012;2012:539059.
31. Elghoneimy, R.I.E.S.M. Predictive value of neutrophil to lymphocyte ratio combined with c-reactive protein for diagnosis of spontaneous bacterial peritonitis among cirrhotic patients. The Egyptian Journal of Hospital Medicine. 2023; 91: 4380-6.
32. Abudeif A, Elbadry MI, Ahmed NM. Validation of the diagnostic accuracy of neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) in cirrhotic patients with spontaneous bacterial peritonitis. *Egypt Liver Journal.* 2023;13. (2023).
33. Du T, Li QP, Jiang GX, et al. Systematically analysis of decompensated cirrhotic patients with spontaneous bacterial peritonitis to identify diagnostic and prognostic indexes. *BMC Infect Dis.* 2023;23(1):786.
34. Pieri G, Agarwal B, Burroughs AK. C-reactive protein and bacterial infection in cirrhosis. *Ann Gastroenterol.* 2014;27(2):113-20.
35. Deeks JJ, Altman DG. Diagnostic tests 4: likelihood ratios. *BMJ.* 2004;329(7458):168-9.
36. Qin N, Yang F, Li A, et al. Alterations of the human gut microbiome in liver cirrhosis. *Nature.* 2014;513(7516):59-64.

37. Lv LX, Fang DQ, Shi D, et al. Alterations and correlations of the gut microbiome, metabolism and immunity in patients with primary biliary cirrhosis. *Environ Microbiol.* 2016;18(7):2272-86..
38. Wiesner R, Edwards E, Freeman R, et al. Model for end-stage liver disease (MELD) and allocation of donor livers. *Gastroenterology.* 2003;124(1):91-6.

Search Strategy

Search Date: 24 Sep 2024

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

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

Supplementary table

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

Tool name	Study	Variables	Scores	Proposed cut-off
Mansoura	Abdel-Razik A et al. (1) and Huynh NC et al. (2)	Age \geq 55 years	1	NA
		MPV \geq 8.5 f	1	
		NLR \geq 2.5	1	
		CRP \geq 40 mg/l	2	
Wehmeyer	Wehmeyer M et al. (3)	Age >60 years	1	NA
		Platelet count \leq 100.000/ μ L	1	
		CRP >60 mg/L	2	
Modified Wehmeyer	Metwally K et al. (4)	Age >60 years	1	NA
		Platelet count \leq 100.000/ μ L	1	
		CRP (13.5 mg/L	0	
		13.5-30 mg/L	1	
		30-60 mg/L	2	
MELD score	Obstein KL et al. (5) and Kraja B et al. (6)	$0.957 \times \ln(\text{Cr}) +$ $0.378 \times \ln(\text{bilirubin}) +$ $1.120 \times \ln(\text{INR}) + 0.643$	NA	<15 16-24 \geq 25
	Gayatri AA et al. (7)			\leq 17 >18
PEC index	Elsadek H.M. et al. (8)	PCT \times (ESR + CRP)	NA	20
Other	Abdo G et al. (9)	TB \geq 2.375 mg/dl	1	NA
		NLR \geq 3.438	1	
		CRP \geq 30 mg/L	1	
	Kamal A et al. (10)	“NLR \times \sqrt 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 (WBC/PLT)≥0.25	NA	NA
	Wang H et al. (14)	PCT dCHC sNFI	NA	≥3.40
	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:

1. Abdel-Razik A, Mousa N, Abdel-Aziz M, Elsherbiny W, Zakaria S, Shabana W, et al. Mansoura simple scoring system for prediction of spontaneous bacterial peritonitis: lesson learnt. *Eur J Gastroenterol Hepatol*. 2019 Aug;31(8):1017–24.
2. Huynh NC, Vo TD. Validation of a new simple scoring system to predict spontaneous bacterial peritonitis in patients with cirrhosis and ascites. *BMC Gastroenterol*. 2023 Aug 9;23(1):272.
3. Wehmeyer MH, Krohm S, Kastein F, Lohse AW, Lüth S. Prediction of spontaneous bacterial peritonitis in cirrhotic ascites by a simple scoring system. *Scand J Gastroenterol*. 2014 May;49(5):595–603.
4. Metwally K, Fouad T, Assem M, Abdelsameea E, Yousery M. Predictors of Spontaneous Bacterial Peritonitis in Patients with Cirrhotic Ascites. *J Clin Transl Hepatol*. 2018 Sep 28;6(4):1–5.
5. Obstein KL, Campbell MS, Reddy KR, Yang YX. Association Between Model for End-Stage Liver Disease and Spontaneous Bacterial Peritonitis. *Am J Gastroenterol*. 2007 Dec;102(12):2732–6.
6. Kraja B, Sina M, Mone I, Pupuleku F, Babameto A, Prifti S, et al. Predictive Value of the Model of End-Stage Liver Disease in Cirrhotic Patients with and without Spontaneous Bacterial Peritonitis. *Gastroenterol Res Pract*. 2012;2012:1–5.
7. Gayatri AAAY, Suryadharma IGA, Purwadi N, Wibawa IDN. The relationship between a model of end stage liver disease score (MELD score) and the occurrence of spontaneous bacterial peritonitis in liver cirrhotic patients. *Acta Medica Indones*. 2007;39(2):75–8.
8. Elsadek HM, Elhawari SA, Mokhtar A. A novel serum index for accurate diagnosis of spontaneous bacterial peritonitis in cirrhotic patients without other infections. *Egypt Liver J*. 2020 Dec;10(1):10.
9. Abdo G, Nir U, Rawajdey R, Abu Dahoud W, Massalha J, Hajouj T, et al. A Novel Score-Based Approach by Using Routine Laboratory Tests for Accurate Diagnosis of Spontaneous Bacterial Peritonitis (SBP) in Cirrhotic Patients. *EJIFCC*. 2023 Dec;34(4):297–304.
- 10.
11. Popoiag RE, Suceveanu AI, Suceveanu AP, Micu S, Voinea F, Mazilu L, et al. Predictors of spontaneous bacterial peritonitis in Romanian adults with liver cirrhosis: Focus on the neutrophil-to-lymphocyte ratio. *Exp Ther Med*. 2021 Jul 12;22(3):983.
12. Mousa N, Besheer T, Abdel-Razik A, Hamed M, Deiab A, Sheta T, et al. Can combined blood neutrophil to lymphocyte ratio and C-reactive protein be used for diagnosis of spontaneous bacterial peritonitis? *Br J Biomed Sci*. 2018 Apr 3;75(2):71–5.
13. Cai ZH, Fan CL, Zheng JF, Zhang X, Zhao WM, Li B, et al. Measurement of serum procalcitonin levels for the early diagnosis of spontaneous bacterial peritonitis in patients with decompensated liver cirrhosis. *BMC Infect Dis*. 2015 Dec;15(1):55.
14. Wang H, Li Y, Zhang F, Yang N, Xie N, Mao Y, et al. Combination of PCT, sNFI and dCHC for the diagnosis of ascites infection in cirrhotic patients. *BMC Infect Dis*. 2018 Dec;18(1):389.

15. Abudeif A, Elbadry MI, Ahmed NM. Validation of the diagnostic accuracy of neutrophil to lymphocyte ratio (NLR) and mean platelet volume (MPV) in cirrhotic patients with spontaneous bacterial peritonitis. *Egypt Liver J.* 2023 Feb 13;13(1):9.
16. Elhendawy RI, Elghoneimy SM, Elnemr SA, Salem AA, Abdelkader AH. Predictive Value of Neutrophil to Lymphocyte Ratio Combined with C-Reactive Protein for Diagnosis of Spontaneous Bacterial Peritonitis among Cirrhotic Patients. *Egypt J Hosp Med.* 2023 Apr 1;91(1):4380–6.