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A Diagnostic Score (DS) in the Difficult Diagnosis of Non-specific Abdominal Pain (NSAP)

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Abstract. *Background/Aim: The diagnostic scores (DSs) for patients with non-specific abdominal pain (NSAP) have been rarely evaluated. Patients and Methods: In the NSAP study group there were 614 patients (268 females and 346 males) versus 719 patients in the non-NSAP group including 368 females and 351 males. The clinical symptoms (n=22), signs and tests (n=14) and laboratory analyses (n=3) were recorded in each patient. Meta-analytical techniques were used to detect the summary sensitivity (Se) and specificity (Sp) estimates for each data set (symptoms, signs and tests as well as DS models). Results: In receiver operating characteristic (ROC) analysis, the area under curve (AUC) values for i) symptoms ii) signs and tests and iii) DS were as following: i) AUC=0.542 (95% CI=0.512-0.572); ii) AUC=0.625 (95% CI=0.550-0.700), and iii) AUC=0.874 (95% CI=0.850-0.898). The differences between these AUC values are as following: between i and ii, p=0.097; between i and iii, p<0.0001 and between ii and iii, p<0.0001. Conclusion: This is the first study to provide evidence that DS may help in the difficult diagnosis of NSAP.*

Acute abdominal pain (AAP) is one of the most common diseases seen among patients at the emergency unit (EU), accounting for about 6-10% of all EU visits (1, 2). Non-specific abdominal pain (NSAP) is the commonest cause of AAP, of less than a week duration accounting for 30-51% of all AAP patients (3-5). The incidence of NSAP has remained stable in adult patients (4) and the differential diagnosis of AAP and NSAP depends on optimal clinical assessment including history-taking and detecting signs and tests (6). Ravn-Christensen *et al*. (7) collected 1,474 AAP patients including 390 (26%) NSAP patients, of which 16% were re-admitted during three months to EU for AAP. In their previous study, Meklin *et al*. (8) pointed out the difficulty of differential diagnosis between AAP *versus* NSAP. Although, the rate of emergency surgery in NSAP has decreased (2), the high incidence of NSAP cases prompted us to try to enhance the diagnostic performance of NSAP by detecting i) symptoms, ii) signs and tests, as well as iii) the DS in confirming NSAP.

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Key Words: Non-specific abdominal pain, symptoms, signs, tests, diagnostic score, HSROC, diagnostic accuracy.

Patients and Methods

Patients. In the NSAP study group there were 614 patients (268 females and 346 males) *versus* 719 patients in the non-NSAP group including 368 females and 351 males. The clinical symptoms (n=22), signs and tests (n=14) and laboratory analyses (n=3) were recorded in each patient. The diagnosis of NSAP was confirmed by considering all clinical history-taking details, clinical findings and results of the laboratory tests together and following the diagnostic criteria of AAP and NSAP.

DS models. A multivariate logistic (stepwise) regression analysis (SPSS Statistics 26.0.0.1; IBM, Armonk, NY, USA) was used to disclose the variables with an independent predictive value. All the variables of symptoms as well as signs and tests presented in Tables I and II were included in the analysis as binary data *e.g*., NSAP=1 and other diagnosis of AAP=0. Using the coefficients of the regression model, a DS was built and its predictive value for NSAP was studied. The coefficient of the multivariate analysis shows the

Table I. *The clinical history of non-specific abdominal pain (NSAP) versus any other cause of acute abdominal pain.*

Clinical history variable	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Location of initial pain	Upper, central or lower midline	Other	343	271	369	350
2. Location of pain at diagnosis	Upper, central or lower midline	Other	260	354	211	508
3. Duration of pain at diagnosis	≤12 hours	>12 hours	217	397	241	475
4. Intensity of abdominal pain	Subjectively moderate or weak pain	Intolerable pain	537	77	580	139
5. Progression of pain from onset to diagnosis	Weaker or subjectively same pain than at the onset	Worse pain	478	136	468	251
6. Type of pain	Steady pain	Colicky or intermitted pain	313	301	418	301
7. Aggravating factors	No aggravating factors	Movement, coughing, respiration, food or other	204	410	152	567
8. Relieving factors	No	Yes	233	381	201	518
9. Previous similar pain	Yes	No	210	397	237	475
10. Vertigo	No	Yes	588	23	701	17
11. Nausea	Yes	No	326	288	440	279
12. Vomiting	No	Yes	403	211	355	364
13. Appetite	Normal appetite	No appetite	207	407	149	570
14. Previous indigestion	No	Yes	504	108	548	171
15. Jaundice	No	Yes	609	5	691	28
16. Bowels	Normal	Diarrhea, constipation, blood, mucus or white stools	472	142	543	176
17. Micturition	Normal	Abnormal	581	33	666	53
18. Drugs for abdominal pain	No	Yes	589	25	689	29
19. Previous abdominal surgery	No	Yes	477	137	522	196
20. Previous abdominal diseases	No	Yes	516	98	582	136
21. Use of alcohol	No	Yes	581	33	684	34
22. Gender	Female	Male	268	346	368	351

FN: False negative; FP: false positive; TN: true negative; TP: true positive.

relative risk of a patient with a given symptom and sign and test to have NSAP.

The DS formula for NSAP was: 0.22 × Gender (female=1, male=0) - 0.02 × Age (years) - 0.47 × Location of initial pain (PE=1, NE=0) + 0.53 × Location of pain at diagnosis (PE=1, NE=0) + 0.45 × Progression of pain (PE=1, NE=0) + 0.29 × Relieving factors (PE=1, NE=0) - 0.38 × Previous similar pain (PE=1, NE=0) + 0.70 × Vertigo (PE=1, NE=0) + 1.63 × Jaundice (PE=1, NE=0) + 0.47 × Mood (PE=1, NE=0) + 0.99 × Distension (PE=1, NE=0) + 2.34 × Mass (PE=1, NE=0) + 0.55 × Rebound (PE=1, NE=0) + 0.76 × Guarding (PE=1, NE=0) + 2.90 × Rigidity (PE=1, NE=0) + 1.49 × Murphy (PE=1, NE=0) + 0.59 × Bowel sounds (PE=1, NE=0) + 1.02 × Leucocyte count (PE=1, NE=0) + 3.36 × Urine (PE=1, NE=0) – 13.77. PE=positive endpoint and NE=negative endpoint (Table III).

Statistical analysis. STATA/SE version 16.1 (StataCorp, College Station, TX, USA) was used for analysis. The statistical tests presented were two-sided, and *p*-Values <0.05 were considered statistically significant. Using 2×2 tables, sensitivity (Se) and specificity (Sp) with 95% confidence intervals (95% CI) for each clinical history-taking variable, finding or test was determined. A meta-analytical technique (metaprop) was used to create separate forest plots for Se and Sp for each set of data, including each diagnostic variable. We calculated the summary estimates of Se and Sp, positive (LR+) and negative likelihood ratio (LR–) and diagnostic odds ratio, using a random effects bivariate model and fitted the summary hierarchical receiving operating characteristic (HSROC) curves using the NSAP endpoint. Roccomp test (STATA) was used to compare the AUC values of HSROC tests between the 3 diagnostic sets (history-taking, clinical signs, DSs).

Results

Patient data of the study. In the NSAP study group, 614 patients (268 females and 346 males) were included, and in the non-NSAP group, there were 719 patients (368 females and 351 males) with the following AAP diagnoses: acute appendicitis (n=271), acute cholecystitis (n=124), acute renal colic (n=59), acute small bowel obstruction (n=53), non-organic dyspepsia (n=50) and other AAP patients (n=160), with the mean (SD) age of 37.5 (21.7) years.

The clinical symptoms in NSAP. The overall sensitivity of the clinical symptoms for detecting NSAP was 69% (95% CI=58-80%) (Figure 1). The Se was higher than 69% for 11 of the symptoms. The five most sensitive clinical history-taking variables (vertigo, jaundice, micturition, drugs for abdominal pain and use of alcohol) showed 95-99% Se in

Table II. *The clinical signs and investigations of non-specific abdominal pain (NSAP) versus any other cause of acute abdominal pain.*

Clinical signs and investigations	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Mood	Normal	Distressed or anxious	537	77	569	150
2. Colour	Normal	Jaundiced, pale, flushed or cyanosed	556	58	625	94
3. Abdominal movement	Normal	Poor/nil	594	20	645	73
4. Scar	No	Yes	469	145	517	201
5. Distension	No	Yes	596	18	640	75
6. Tenderness	Upper, central or lower midline	Other	184	422	133	585
7. Mass	No	Yes	612	2	687	32
8. Rebound	No	Yes	434	180	268	451
9. Guarding	No	Yes	413	201	213	506
10. Rigidity	No	Yes	602	11	436	283
11. Murphy's positive	No	Yes	601	13	607	111
12. Bowel sounds	Normal	Abnormal	571	43	573	146
13. Renal tenderness	No	Yes	496	118	476	243
14. Rectal digital tenderness	Normal	Abnormal	467	145	502	216
15. Body temperature	≤37.1˚C	>37.1˚C	352	210	354	316
16. Leucocyte count (LC)	<10 000/mm^3	≥10 000/mm^3	357	136	252	336
17. Urine	Normal	Abnormal	520	6	522	66

FN: False negative; FP: false positive; TN: true negative; TP: true positive.

Table III. *Diagnostic score (DS) for the non-specific abdominal pain (NSAP) model. The DS model is shown at six different cut-off levels of symptoms, signs and tests. Cut-off levels: DS I=0.48, DS II=0.50, DS III=0.53, DS IV=0.54, DS V=0.55 and DS VI=0.58.*

Logistic DS model	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. DS I	NSAP	Other cause of abdominal pain	523	91	176	543
2. DS II	NSAP	Other cause of abdominal pain	516	98	169	550
3. DS III	NSAP	Other cause of abdominal pain	503	111	150	569
4. DS IV	NSAP	Other cause of abdominal pain	500	114	145	574
5. DS V	NSAP	Other cause of abdominal pain	495	119	142	577
6. DS VI	NSAP	Other cause of abdominal pain	480	134	130	589

FN: False negative; FP: false positive; TN: true negative; TP; true positive. *DS: 0.22 × Gender (female=1, male=0) - 0.02 × Age (years) - 0.47 × Location of initial pain (PE=1, NE=0) + 0.53 × Location of pain at diagnosis (PE=1, NE=0) + 0.45 × Progression of pain (PE=1, NE=0) + 0.29 × Relieving factors (PE=1, NE=0) - 0.38 × Previous similar pain (PE=1, NE=0) + 0.70 × Vertigo (PE=1, NE=0) + 1.63 × Jaundice (PE=1, NE=0) + 0.47 × Mood (PE=1, NE=0) + 0.99 x Distension (PE=1, NE=0) + 2.34 × Mass (PE=1, NE=0) + 0.55 × Rebound (PE=1, NE=0) + 0.76 × Guarding (PE=1, NE=0) + 2.90 × Rigidity (PE=1, NE=0) + 1.49 × Murphy (PE=1, NE=0) + 0.59 × Bowel sounds (PE=1, NE=0) + 1.02 × Leucocyte count (PE=1, NE=0) + 3.36 × Urine (PE=1, NE=0) – 13.77. PE: Positive endpoint; NE: negative endpoint.

diagnosis of NSAP (Figure 1). The overall specificity of the history-taking for detecting NSAP was only 35% (95% CI=24-48%) (Figure 2). Altogether, 11 symptoms showed Sp higher than 35%. The five most specific symptoms of NSAP (location of pain at diagnosis, aggravating factors, relieving factors, previous similar pain and appetite) showed Sp values of 67-79% (Figure 2).

The clinical signs and tests in NSAP. The overall sensitivity of the signs and tests for NSAP was 86% (95% CI=76-93%) (Figure 3), and 9 signs and tests had Se exceeding 86%. The six most accurate signs and tests (abdominal movement, distension, mass, rigidity, Murphy's positive and urine) showed 97-100% Se (Figure 3). The overall specificity of the signs and tests was only 31% (95% CI=20-43%) (Figure 4), while 7 signs and tests showed Sp higher than 31%. The five most specific signs and tests (tenderness, rebound, guarding, body temperature and leucocyte count), however, showed 47-81% Sp (Figure 4).

The DS in NSAP. The most significant predictors of NSAP in multivariate analysis were gender, age (years), location of

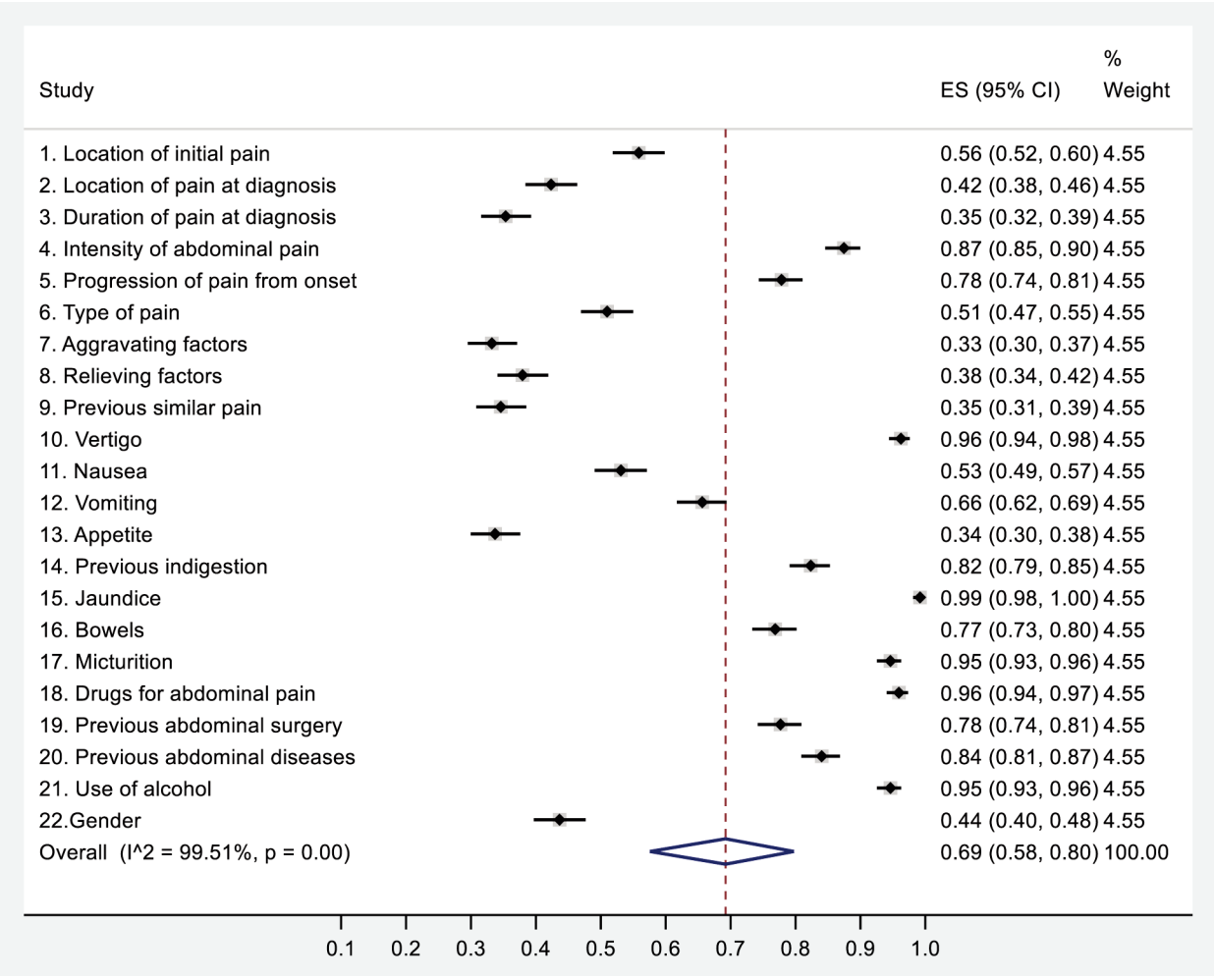

Figure 1. *Sensitivity values of history-taking in non-specific abdominal pain (NSAP) (random-effects model). ES: Estimated sensitivity; CI: confidence interval.*

initial pain, location of pain at diagnosis, progression of pain, relieving factors, previous similar pain, vertigo, jaundice, mood, distension, mass, rebound, guarding, rigidity, Murphy, bowel sounds, leucocyte count and urine. The best diagnostic level for DS model [DS IV; Se=81%, Sp=80%, efficiency (Eff)=81%] was reached at a cut-off level of 0.54 for DS (Figures 5 and 6). The DS model was tested at six different cut-off levels to disclose the highest diagnostic accuracy (Figures 5 and 6). The overall Se and Sp of these six DS models were 82% (95% CI=80-84%) and 79% (95% CI=77-81%), respectively (Figures 5 and 6). Three of these models showed Se ≥82% and four models had Sp ≥79%.

HSROC and AUC values. HSROC curves were used to visualise the pooled overall accuracy of the symptoms (Figure 7), signs and tests (Figure 8) and different DS models (Figure 9) in detecting NSAP. In SROC analysis, the AUC values for i) symptoms ii) signs and tests as well as iii) DS were as follows: i) AUC=0.542 (95% CI=0.512-0.572); ii) AUC=0.625 (95% CI=0.550-0.700), and iii) AUC=0.874 (95% CI=0.850-0.898). The differences between these AUC values (roccomp analysis) are as following: between i and ii, p=0.097; between i and iii, p<0.0001 and between ii and iii, p<0.0001.

Discussion

Prompted by the difficulty of NSAP diagnosis among the AAP patients and the lack of diagnostic accuracy studies on DS with HSROC analysis, we designed the present study to assess the diagnostic performance of i) symptoms, ii) signs and tests, as well as iii) the DS in confirming NSAP.

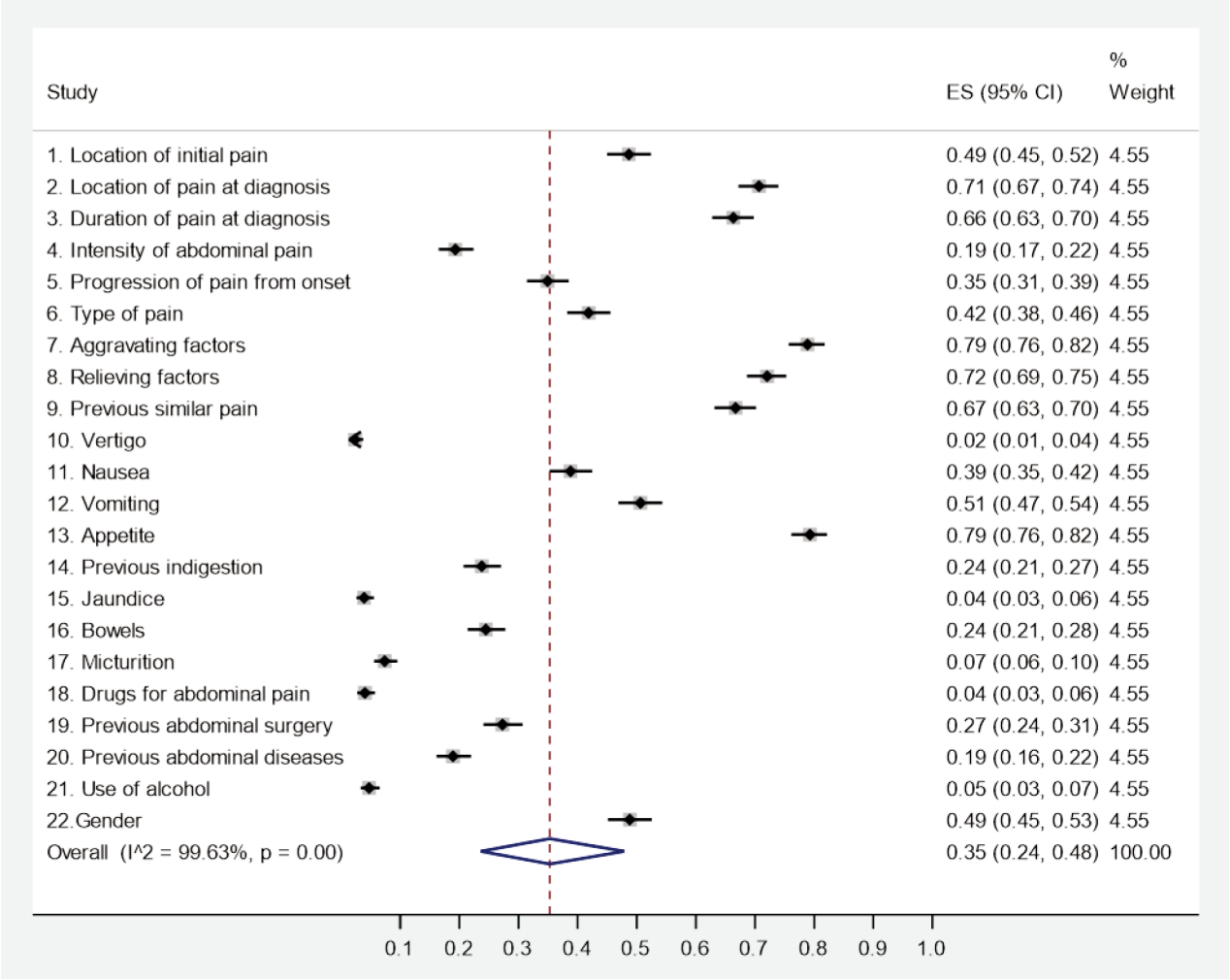

Figure 2. *Specificity values of history-taking in non-specific abdominal pain (NSAP) (random-effects model). ES: Estimated specificity; CI: confidence interval.*

The clinical symptoms and signs and tests investigated in the AAP patients follow the diagnostic criteria shown in the Research Committee of the World Organization of Gastroenterology (OMGE) (9-16). Here we refer the most important clinical features in making the distinction between NSAP and AA. Nausea and vomiting are usually reported to be in favour of AA, however, the diagnostic accuracy of these symptoms has not been considered in detail before. In our study, 53% of the NSAP patients had nausea and 34% had vomiting. Special attention is paid to the location of pain, which in AA moves from midline to right lower quadrant (RLQ). Instead, in NSAP the pain is diffuse or remains in RLQ. At physical examination, it is necessary to record the abdominal tenderness, rebound tenderness, guarding, abdominal rigidity and Murphy's sign. Location of tenderness in AA is mostly focal RLQ tenderness, whereas in NSAP, the location of tenderness is usually described to localize at midline or being more diffuse. In our study, 30% of the patients with NSAP had abdominal tenderness at the midline of the abdomen (Se of 0.30 and Sp of 0.81). Rebound tenderness and guarding are usually reported to be negative in NSAP patients, but the diagnostic accuracy of these tests has rarely been assessed in NSAP. In the present series, 33% of the NSAP patients had a negative guarding test (Se of 0.67 and Sp of 0.70) and 29% had positive rebound tenderness (Se of 0.71 and Sp of 0.63). Both clinical tests, when absent and correctly assessed, exclude intra-abdominal inflammation and peritoneal irritation. The abdominal rigidity test is usually shown to be negative in NSAP patients and in our cohort, 98% (11/613) of the NSAP patients had a negative abdominal rigidity test result (Se of 0.98 and Sp of 0.39).

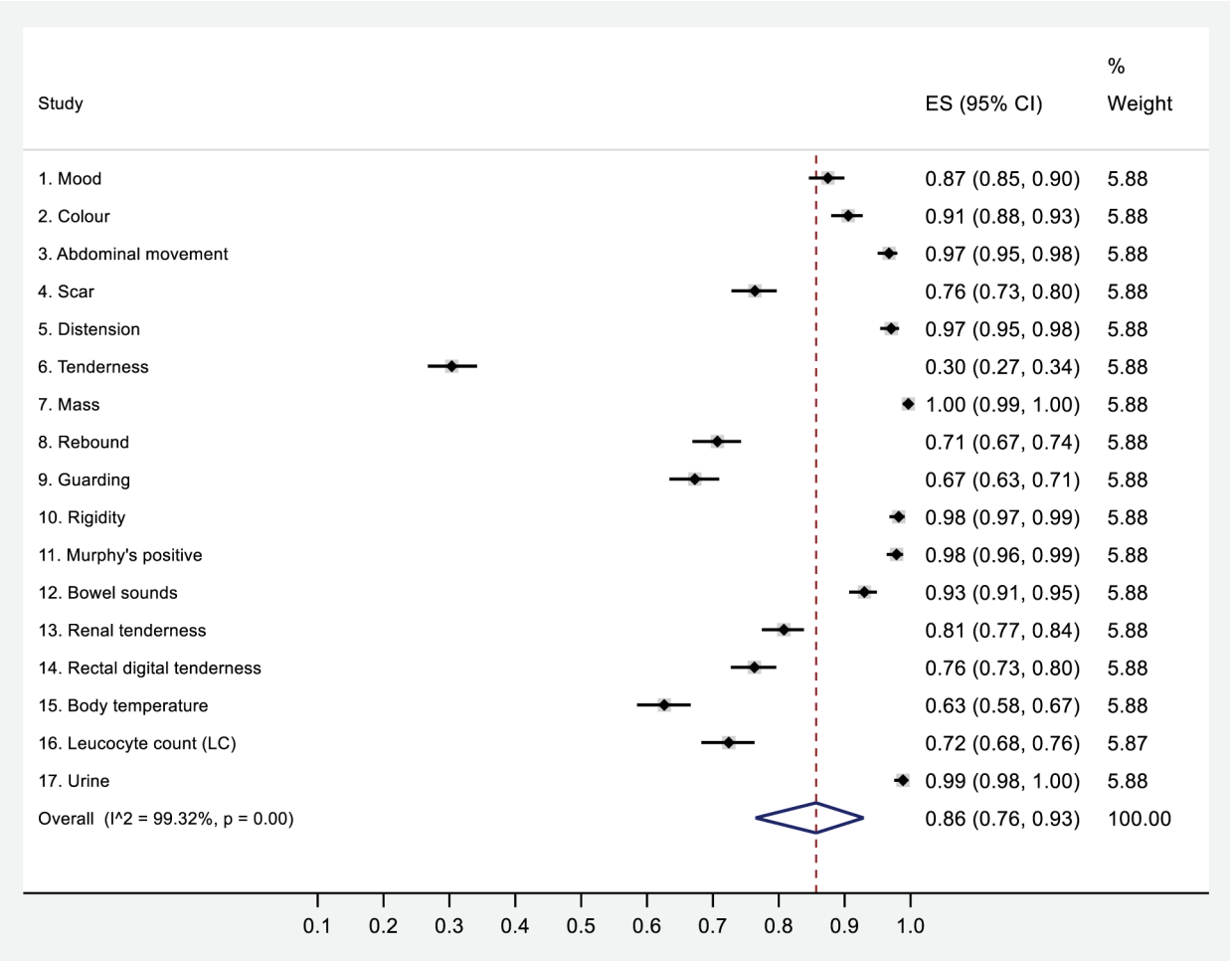

Figure 3. *Sensitivity values of signs and tests in non-specific abdominal pain (NSAP) (random-effects model). ES: Estimated sensitivity; CI: confidence interval.*

Acute appendicitis (AA) is a reason of similar symptoms and signs than that in NSAP and therefore the AA is an important differential diagnostic disease in confirming NSAP. Meklin *et al.* (8) reported the overall Se of the symptoms in AA; 80% (95% CI=67-90%), which was higher than that in NSAP patients in this study; 69% (95% CI=58-80 %). However, the Sp of the symptoms in NSAP in this study was slightly higher than that in AA patients in Meklin *et al.* (8) study; 35% (95% CI=24-48%) *versus* 30% (95% CI=19-42%). The overall Se of the signs and tests in detecting NSAP in this study was 86% (95% CI=76-93%), which was similar to that of the AA patients in Meklin *et al.* (8) study; 86% (95% CI=79-92%). However, the pooled Sp of the signs & tests in detecting NSAP in this study was slightly lower than that of the AA patients in Meklin *et al.* (8) study; 31% (95% CI=20-43%) *versus* 34% (95% CI=20-50%).

When the NSAP patients in this study and the AA patients in Meklin *et al.* (8) are compared using the DS models, a similar trend can be seen. The overall Se of the DS models in NSAP is 82% (95% CI=80-84%) which is lower than that in AA patients (90%; 95% CI=85-95%). Although Se and Sp usually behave reciprocally, this was not the case with the overall Sp of the DS in NSAP patients, which was 79% (95% CI=77-81%), lower than that in AA (85%; 95% CI=74-94%).

ROC analysis has become popular to evaluate the diagnostic accuracy of various clinical methods and tests. The ROC analysis displays Se as a function of the false positive (FP) rate (1- Sp). Figure 7 shows the ROC analysis for clinical symptoms in NSAP detection and the curve closely parallels the diagonal reference line (AUC=0.500) with a low AUC value (AUC=0.542; 95% CI=0.512-0.572). The diagnostic accuracy of the signs and tests is slightly better than that of the clinical symptoms (AUC=0.625; 95% CI=0.550-0.700, Figure 8).

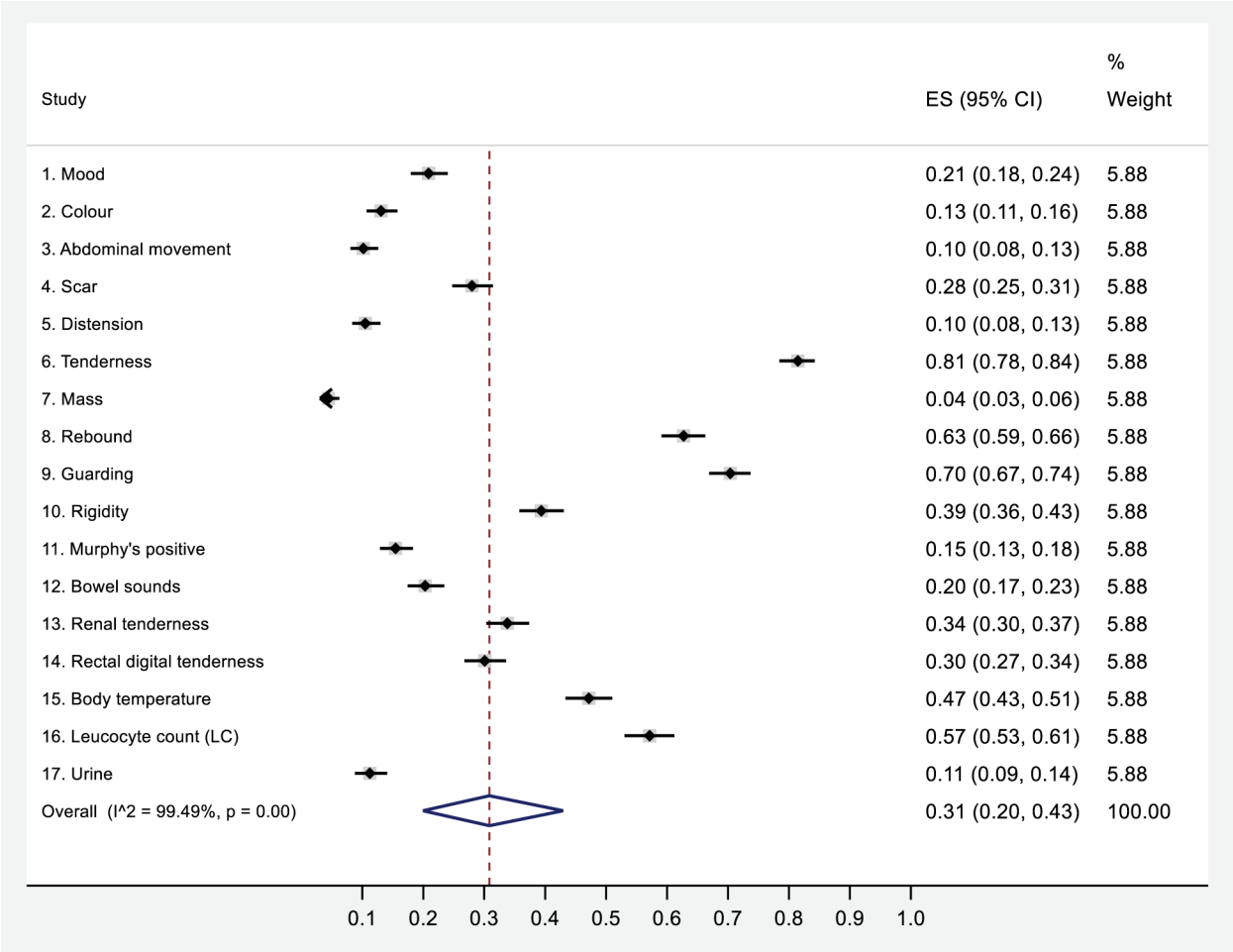

Figure 4. *Specificity values of clinical signs and tests in non-specific abdominal pain (NSAP) (random-effects model). ES: Estimated specificity; CI: confidence interval.*

Figure 9 shows the ROC analysis for the DS, with the curve moved towards the upper left corner, showing significantly better diagnostic performance in the NSAP patients than that of the clinical examination. The ROC analysis can also be used for test optimization by selecting various cut-off points for DS. The value of the clinical test could then be expressed by the Se and Sp for this particular cut-off point in ROC analysis and not for hypothetical situation, where the cut-off point is continuously changing. In the present series, however, the diagnostic accuracy of the DS (AUC=0.874; 95% CI=0.850-0.898) was lower for the NSAP patients than the AUC (AUC=0.953; 95% CI=0.923-0.969) obtained for the AA patients in the study by Meklin *et al*. (8).

Conclusion

Unfortunately, we could not perform direct comparisons to earlier clinical trials in NSAP, because this is the first study to provide evidence that DS could be used to assist in the difficult diagnosis of NSAP. Although the diagnostic accuracy of the DS is lower for the NSAP patients than that in AA patients, the major benefit of the DS is a possibility to avoid unnecessary laboratory analyses, endoscopy or radiological procedures to reach adequate diagnostic performance for NSAP.

Conflicts of Interest

The Authors report no conflicts of interest or financial ties.

Authors' Contributions

All Authors contributed to the collection and analysis of data, drafting and revising the manuscript and read and approved the final article.

Acknowledgements

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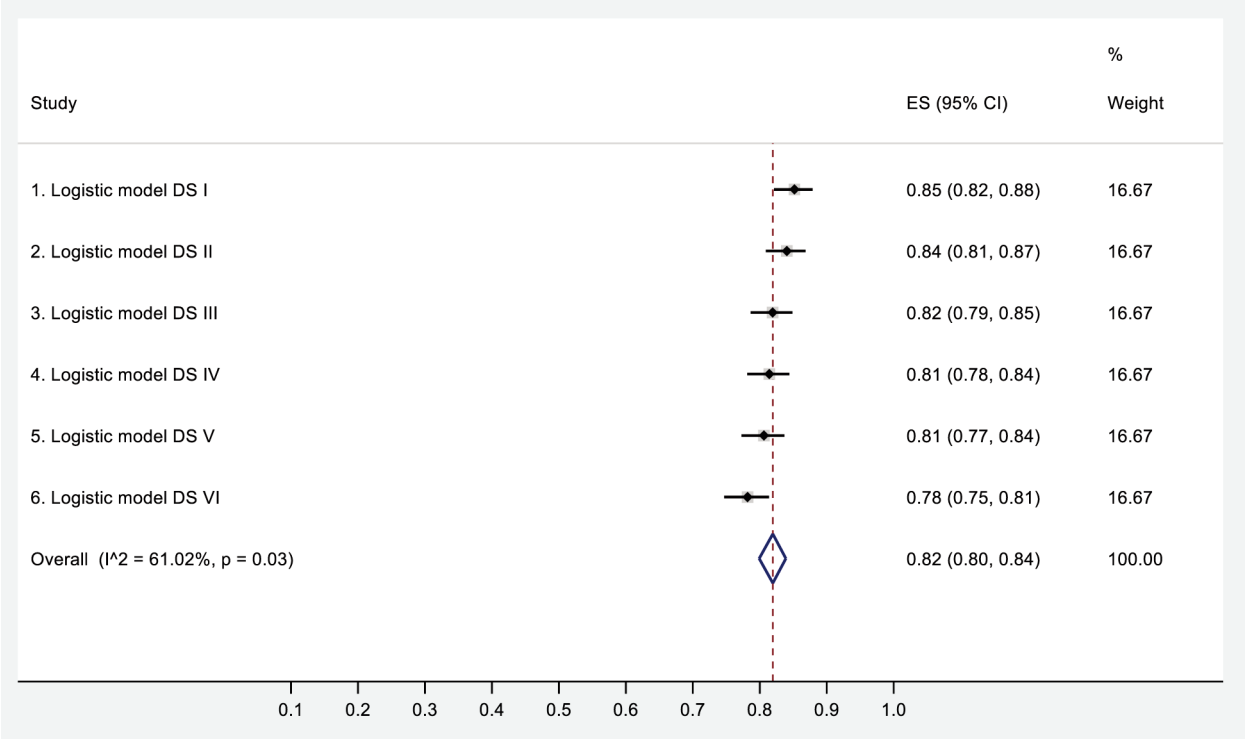

Figure 5. *Sensitivity values of diagnostic scores at six different cut-off levels (DS I-VI). ES: Estimated sensitivity; CI: confidence interval.*

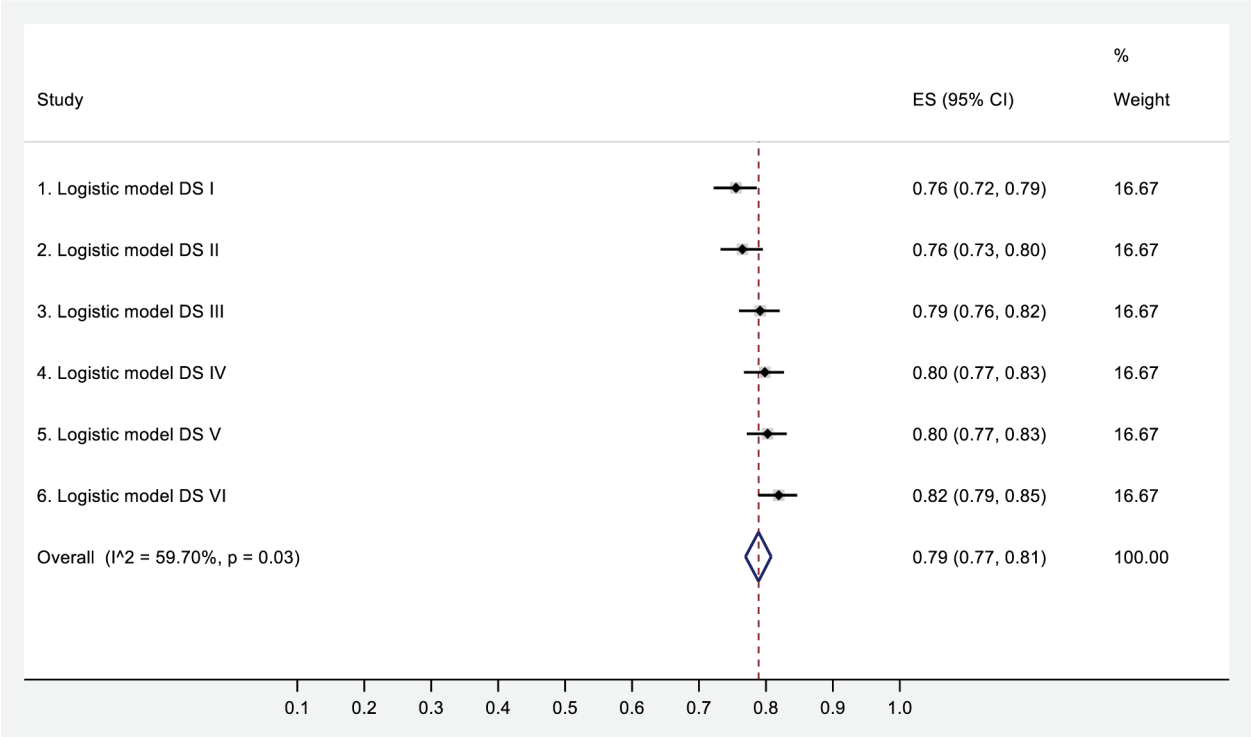

Figure 6. *Specificity values of diagnostic scores at six different cut-off levels (DS I-VI). ES: Estimated specificity; CI: confidence interval.*

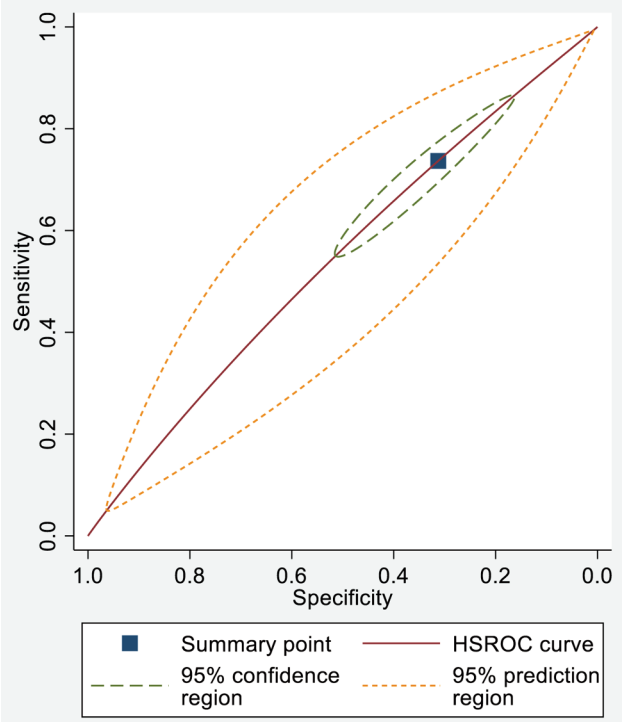

Figure 7. *Hierarchical summary receiver operating characteristic (HSROC) curve of the history-taking in non-specific abdominal pain (NSAP).*

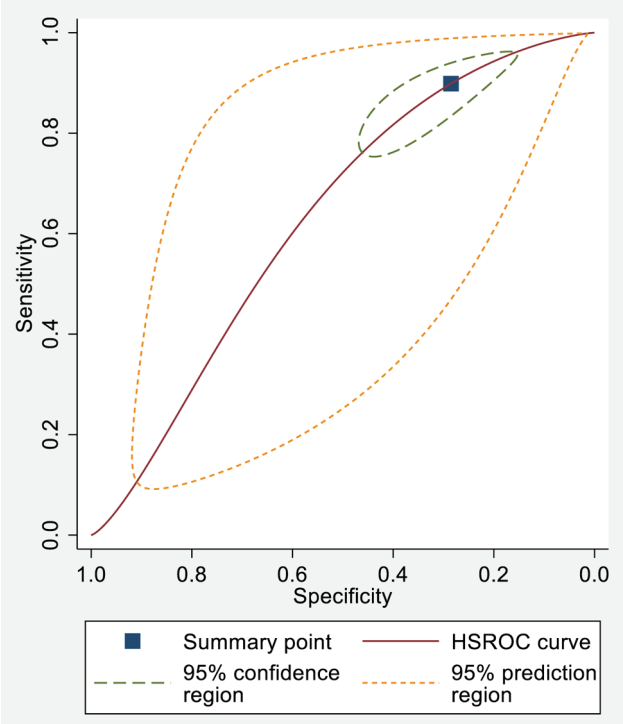

Figure 8. *Hierarchical summary receiver operating characteristic (HSROC) curve of the clinical signs and tests in non-specific abdominal pain (NSAP).*

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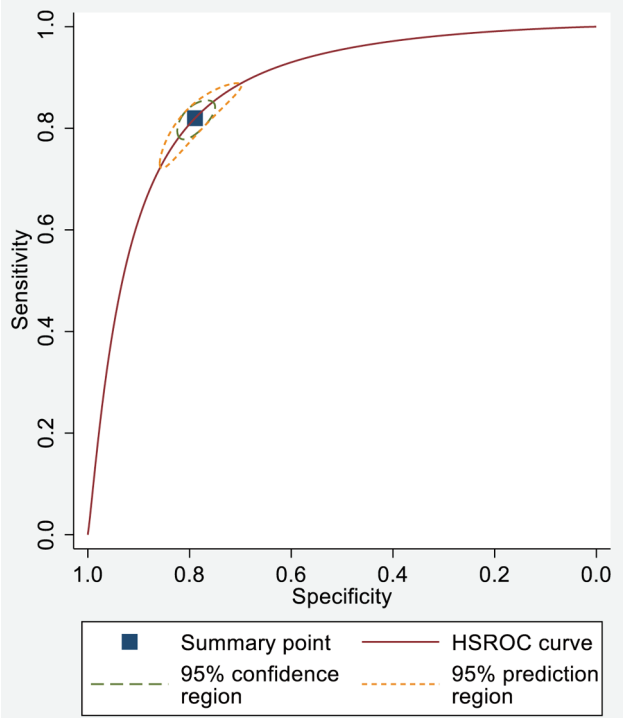

Figure 9. *Hierarchical summary receiver operating characteristic (HSROC) curve of the six diagnostic score models.*

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