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A Diagnostic Score (DS) Is a Powerful Tool in Diagnosis of Acute Appendicitis in Elderly Patients With Acute Abdominal Pain

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Abstract. *Background/Aim: Although acute appendicitis (AA) in elderly patients is different from AA in younger patients, the accuracy of diagnostic scores (DSs) in detecting AA is rarely considered. Patients and Methods: A cohort of 470 AAP (acute abdominal pain) patients older than 50 years, including 224 women (53.7%) and 193 men (46.3%), were included in the study. The most significant diagnostic predictors were used to construct DS formulas for AA diagnosis with (Tax+) and without body temperature (Tax–). Meta-analytical techniques were used to calculate the summary Se and Sp estimates for each data sets (history-taking, findings, and DS formulas). Results: In SROC analysis, the AUC values for i) symptoms ii) signs and tests iii)* DS_{Tax-} *and iv)* DS_{Tax+} *were as follows: i) AUC=0.658 (95%CI=0.601-0.709); ii) AUC=0.751 (95%CI=0.701-0.800), iii) AUC=0.977 (95%CI=0.942-1.000), and for iv) AUC=0.980 (95%CI=0.956-1.000). Using roccomp analysis for these AUC values, the differences were significant as follows: between i) and ii) p=0.0358; between i) and iii) p<0.0001; between i) and iv) p<0.0001; between ii) and iii) p<0.0001; between ii) and iv) p<0.0001; and between iii) and iv) p=0.682. Conclusion: Similar to younger AA patients, the DS formula was superior to both the clinical history-taking and findings, and therefore, the use of DS should be an important part of the diagnostic decision tree of AA also in the elderly patients presenting with AAP.*

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Key Words: Acute appendicitis, acute abdominal pain, elderly patients, diagnostic score, body temperature, ROC, HSROC, diagnostic accuracy.

Acute appendicitis (AA) in elderly patients is in many respects different from AA in younger patients with acute abdominal pain (AAP). AA among elderly patients might have lower diagnostic accuracy, longer delay from onset of symptoms to admission, and therefore, higher AA perforation rate leading to higher complication and mortality rate. Ceresoli *et al*. (1) analysed an AA cohort of 16,544 patients and showed, that after adolescence, the incidence of AA decreases along with increasing age (1). In their study on AAP patients, Kraemer *et al*. (2) reported that 15% of the patients older than 50 years of age had a final diagnosis of AA, as compared to nearly 30% of AA among younger patients (2). However, along with the aging of the Western populations, AA among the elderly is likely to be more common in the future (1).

The lack of commonly accepted guidelines and diagnostic scoring (DS) specified for elderly patients with AA (3) encouraged us to evaluate the accuracy of the clinical diagnosis of AA among elderly patients. We designed the present study to assess the relative accuracy of i) a clinical history-taking, ii) clinical findings, as well as iii) the DS without body temperature (Tax–) and iv) the DS with body temperature (Tax+) in detecting clinically confirmed AA among the elderly patients with AAP.

Patients and Methods

Included in the present study were 470 elderly patients older than 50 years, of whom 224 were women (53.7%) and 193 were men (46.3%). The diagnosis of AA was confirmed by considering all clinical history-taking details, clinical findings and results of the laboratory tests together and following the diagnostic criteria of AA as previously described (4-8) (Tables I and II).

Table I. *The clinical history of the elderly patients (≥50 years) with acute appendicitis versus other cause of abdominal pain.*

Clinical history variable	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Location of initial pain	Upper left or right quadrants of abdomen	Other quadrants of abdomen	18	35	134	230
2. Location of pain at diagnosis	Right lower quadrant of abdomen	Other quadrants of abdomen	46	7	51	313
3. Duration of pain: Duration of pain at diagnosis	≤48 hours	>48 h	39	14	228	136
4. Intensity of abdominal pain	Subjectively weak/moderate pain	Intolerable pain	46	7	289	75
5. Progression of pain from onset to diagnosis	Subjectively same or worse pain	Weaker pain than at the onset	37	16	247	117
6. Type of pain	Intermitted pain	Colicky or steady pain	7	46	37	327
7. Aggravating factors	No aggravating factors	Movement, coughing, respiration, food or other	48	5	235	129
8. Relieving factors	No relieving factors or lying still	Vomiting, food or antacids	46	1	283	49
9. Previous similar pain	No	Yes	45	7	212	150
10. Vertigo	No	Yes	53	0	344	18
11. Nausea	No	Yes	26	27	122	242
12. Vomiting	No	Yes	33	20	171	190
13. Appetite	No appetite	Normal appetite	43	10	282	82
14. Previous indigestion	No	Yes	44	9	231	132
15. Jaundice	No	Yes	53	0	344	20
16. Bowels	Normal	Constipation, diarrhea, blood, mucus, white or normal stools	45	8	242	122
17. Micturition	Normal	Abnormal	50	3	328	36
18. Drugs for abdominal pain	No	Yes	53	0	336	28
19. Previous abdominal surgery	No	Yes	43	10	182	182
20. Previous abdominal diseases	No	Yes	45	8	249	115
21. Use of alcohol	No	Yes	53	0	353	11

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

Identifying the DS models. In the computation of the diagnostic score (DS), 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 presented in Tables I and II were included in the analysis as binary data, *e.g.* AA=1 and other diagnosis of AAP=0. Using the coefficients of the regression model, a DS was built and its predictive value for AA was studied. The coefficient of the multivariate analysis showed the relative risk ($RR=e^n$, $n=\beta$) of a patient with a given history-taking detail, clinical findings or test to have an AA.

The formula without body temperature count (Tax–). The formula without Tax in hierarchical summary receiving operating characteristic (HSROC) analysis is; DS_{Tax-}=2.40× location of pain at diagnosis (positive endpoint=1, negative endpoint=0) + 3.67× tenderness (positive endpoint=1, negative endpoint=0) + 2.93× rigidity (positive endpoint=1, negative endpoint=0) –6.54 (Table III).

The formula with body temperature count (Tax+). The formula with Tax is; DS_{Tax+}=1.95× location of pain at diagnosis (positive endpoint=1, negative endpoint=0) + 1.25× previous abdominal surgery (positive endpoint=1, negative endpoint=0) + 4.07× tenderness (positive endpoint=1, negative endpoint=0) + 2.96× rigidity (positive endpoint=1, negative endpoint=0) + 1.31× body temperature (positive endpoint=1, negative endpoint=0) – 8.12 (Table IV).

Statistical analysis. The other statistical analyses were performed using STATA/SE version 16.1 (StataCorp, College Station, TX, USA). Statistical tests presented were two-sided, and *p*-value <0.05 was considered statistically significant. Using 2×2 tables, we calculated sensitivity (Se) and specificity (Sp) with 95% confidence intervals (95%CI) for each clinical history-taking detail, finding or test, and using meta-analytical technique (metaprop) separate forest plots for Se and Sp were created for each set of data, including each diagnostic variable (as equivalent to "study ID"). We calculated the summary estimates of Se and Sp, positive (LR+) and negative likelihood ratio (LR–) and diagnostic odds ratio (DOR), using a random effect bivariate model and fitted the HSROC curves, including all diagnostic variables in the DS_{Tax-} and DS_{Tax+} models, using the AA endpoint.

Results

Diagnostic performance of the clinical history-taking. The overall Se of the clinical history-taking for detecting AA was 83% (95%CI=72-92%). Se was higher than 83% for 11 diagnostic symptoms. The five best clinical history-taking variables (relieving factors, vertigo, jaundice, drugs for abdominal pain and use of alcohol) showed 98-100% Se in diagnosis of AA (Figure 1). The overall Sp of the history-taking for detecting AA was 34% (95%CI=22-46%) (Figure 2). Altogether, 10 symptoms showed Sp higher than 34%.

Table II. *The clinical signs and investigations of elderly patients (≥50 years) with acute appendicitis versus other cause of abdominal pain.*

Clinical signs and investigations	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Mood	Normal	Distressed or anxious	47	6	294	70
2. Colour	Normal or flushed	Jaundiced, pale or cyanosed	52	1	328	36
3. Abdominal movement	Poor/nil	Normal	6	47	34	329
4. Scar	No	Yes	42	11	178	185
5. Distension	No	Yes	49	4	293	69
6. Tenderness	Right lower quadrant of abdomen	Other quadrants of abdomen	50	3	49	315
7. Mass	No	Yes	53	0	338	26
8. Rebound	Yes	No	48	5	146	218
9. Guarding	Yes	No	49	4	199	165
10. Rigidity	Yes	No	39	14	78	286
11. Murphy's positive	No	Yes	50	3	292	72
12. Bowel sounds	Normal	Abnormal	51	2	274	90
13. Renal tenderness	No	Yes	37	16	242	122
14. Rectal digital tenderness	Abnormal	Normal	26	27	45	318
15. Body temperature	≥37.1˚C	<37.1˚C	32	21	88	233
16. Leucocyte count (LC)	≥10,000/mm^3	<10,000/mm^3	31	16	104	165
17. Urine	Normal	Haematuria or bacteriuria	47	0	281	22

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

Table III. *Diagnostic score for acute appendicitis (AA) in elderly patients (≥50 years) without body temperature in the DS model shown at five different cut-off levels: DS I=–3.60, DS II=–1.21, DS III=–0.47, DS IV=DS values between –4.14 and –0.47 excluded, n=128 patients, DS V=DS values between –1.21 and –0.47 excluded, n=43 patients.*

Diagnostic score (DS)	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Logistic model DST- I	AA	Other cause of AAP	50	3	54	310
2. Logistic model DST- II	AA	Other cause of AAP	49	4	38	326
3. Logistic model DST- III	AA	Other cause of AAP	37	16	7	357
4. Logistic model DST- IV	AA	Other cause of AAP	37	1	4	244
5. Logistic model DST- V	AA	Other cause of AAP	37	4	7	326

TP: True positive; FN: false negative; FP: false positive; TN: true negative; AAP: acute abdominal pain. Formula for DS: 2.40 × location of pain at diagnosis (positive endpoint=1, negative endpoint=0) + 3.67 × tenderness (positive endpoint=1, negative endpoint=0) + 2.93 × rigidity (positive endpoint=1, negative endpoint=0) -6.54.

Table IV. *Diagnostic score for acute appendicitis (AA) in elderly patients (≥50 years) with body temperature in the DS model shown at five different cut-off levels: DS VII=–1.97, DS VIII=–1.09, DS IX=–0.66, DS X=DS values between –1.97 and –0.66 excluded, n=29 patients, DS XI=DS values between –1.97 and 0.46 excluded, n=43 patients.*

Diagnostic score (DS)	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Logistic model DST+ VII	AA	Other cause of AAP	50	3	29	292
2. Logistic model DST+ VIII	AA	Other cause of AAP	49	4	27	294
3. Logistic model DST+ IX	AA	Other cause of AAP	41	12	9	312
4. Logistic model DST+ X	AA	Other cause of AAP	41	3	9	292
5. Logistic model DST+ XI	AA	Other cause of AAP	34	3	2	292

TP: True positive; FN: false negative; FP: False positive; TN: True negative; AAP: acute abdominal pain. Formula for DS: 1.95 × location of pain at diagnosis (positive endpoint=1, negative endpoint=0) + 1.25 × previous abdominal surgery (positive endpoint=1, negative endpoint=0) + 4.07 × tenderness (positive endpoint=1, negative endpoint=0) + 2.96 × rigidity (positive endpoint=1, negative endpoint=0) + 1.31 × body temperature (positive endpoint=1, negative endpoint=0) – 8.12.

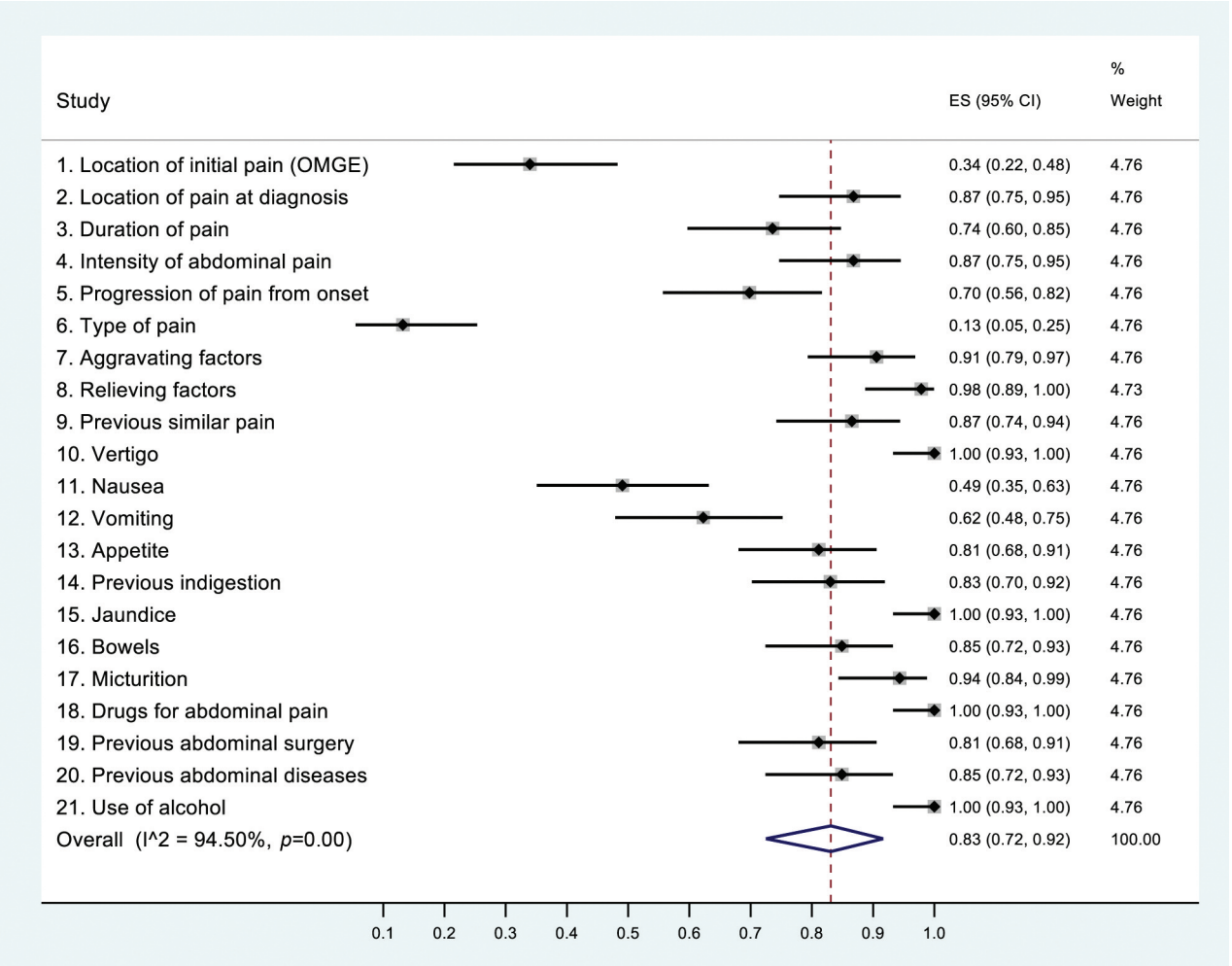

Figure 1. *Sensitivities of the history-taking in acute appendicitis (random-effects model). ES: Estimated sensitivity; CI: confidence interval.*

The five best symptoms of AA (location of initial pain, location of pain at diagnosis, type of pain, nausea, and vomiting) showed 53-90% Sp (Figure 2).

Diagnostic performance of the clinical findings and tests. The overall Se of the diagnostic findings for detecting AA was 84% (95%CI=72-93%) (Figure 3), and 10 findings had Se exceeding 84%. The five most accurate findings (colour, tenderness, mass, bowel sounds and urine) showed 94-100% Se (Figure 3). The overall Sp of the findings was 45% (95%CI=29-61%) (Figure 4), while 8 findings showed Sp higher than 45%. The five most accurate findings (abdominal movement, tenderness, rigidity, rectal digital tenderness, and body temperature) showed 73-91% Sp (Figure 4).

Diagnostic performance of the DS without body temperature (DS_{Tax-}). The most important predictors of AA without Tax (n=417) were location of pain at diagnosis, tenderness and rigidity, and used to construct the DS_{Tax-} formula for AA diagnosis; DS_{Tax-}=a patient is admitted to the emergency room with abdominal pain; at diagnosis the pain was localized at the right lower quadrant of the abdomen (RLQ) (1 point × 2.40); clinical examination showed RLQ tenderness (1 point × 3.67), rigidity (1 point × 2.93) – constant value 6.54. The best diagnostic performance level for DS_{Tax-} formula (DS IV; Se=97%, S*p*=98%) was reached when the patients with a DS_{Tax-} value between -4.14 and -0.47 were considered as "undefined" patients for whom follow-up is required before the decision to operate (n=128) (Figure 5). The DS model was tested at five different cut-off levels to disclose the best diagnostic performance in elderly patients (Figure 5). The Se and Sp of these five DS_{Tax-} formulas were 90% (95%CI=80-97%) and 95% (95%CI=89-99%), respectively (Figures 5 and 6). Three of these

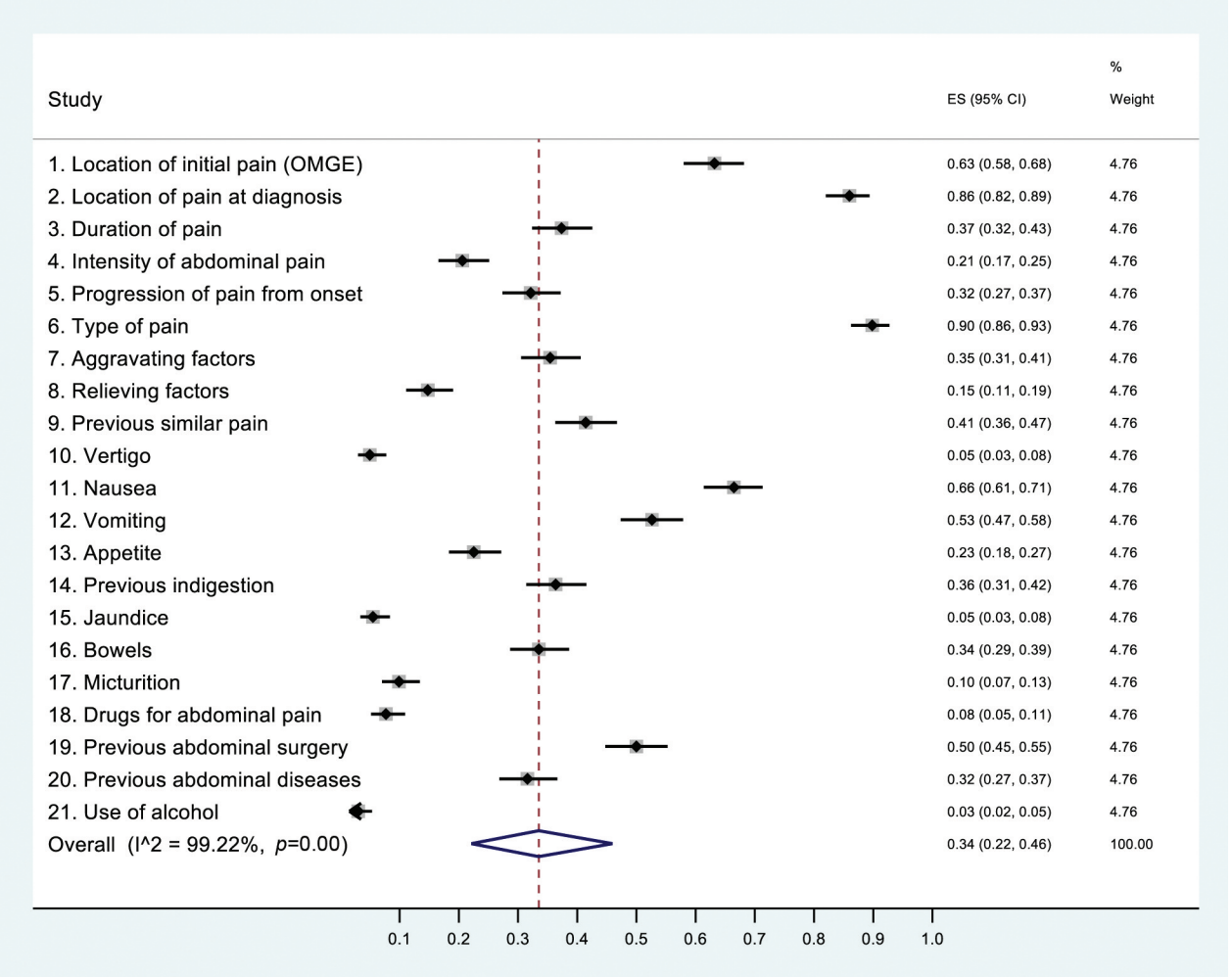

Figure 2. *Specificities of the history-taking in acute appendicitis (random-effects model). ES: Estimated specificity; CI: confidence interval.*

formulas showed Se >90% and three formulas had Sp >95%. The best diagnostic DS_{Tax-} formula in these elderly patients (formula DS IV, Figures 5 and 6) showed Se of 97% (95%CI=86-100%) and Sp of 98% (95%CI=96-100%).

Diagnostic performance of the DS with body temperature (DS_{Tax+}). The significant independent predictors were used to build up the five different DS_{Tax+} models. The Se and Sp of these five DS_{Tax+} models were 90% (95%CI=84-95%) and 96% (95%CI=92-98%), respectively (Figures 7 and 8). Four formulas showed Se >90% and three formulas Sp over 96%. The DS_{Tax+} (formula DS IX, Figures 7 and 8) showed Se of 93% (95%CI=81-99%) and Sp of 97% (95%CI=94-99%) (Figures 7 and 8).

HSROC and comparison of the AUC values . STATA (metandiplot) was used to draw the HSROC curves to visualise the pooled overall diagnostic performance of the different DS formulas in detecting AA in elderly patients (Figures 9 and 10). In SROC analysis, the AUC values for i) clinical history-taking ii) diagnostic findings and tests iii) DS_{Tax-} (Figure 11) and iv) DS_{Tax+} (Figure 12) were as follows: i) AUC=0.658 (95%CI=0.601-0.709); ii) AUC=0.751 (95%CI=0.701-0.800), iii) AUC=0.977 (95%CI=0.942-1.000), and for iv) AUC=0.980 (95%CI=0.956-1.000). In roccomp analysis for the AUC values, the differences were significant as follows: between i) and ii) p=0.0358; between i) and iii) p<0.0001; between i) and iv) p<0.0001; between ii) and iii) p<0.0001; between ii) and iv) p<0.0001; and between iii) and iv) p=0.682.

Discussion

The clinical history-taking and findings in elderly versus younger AA patients. Our interest was to compare the

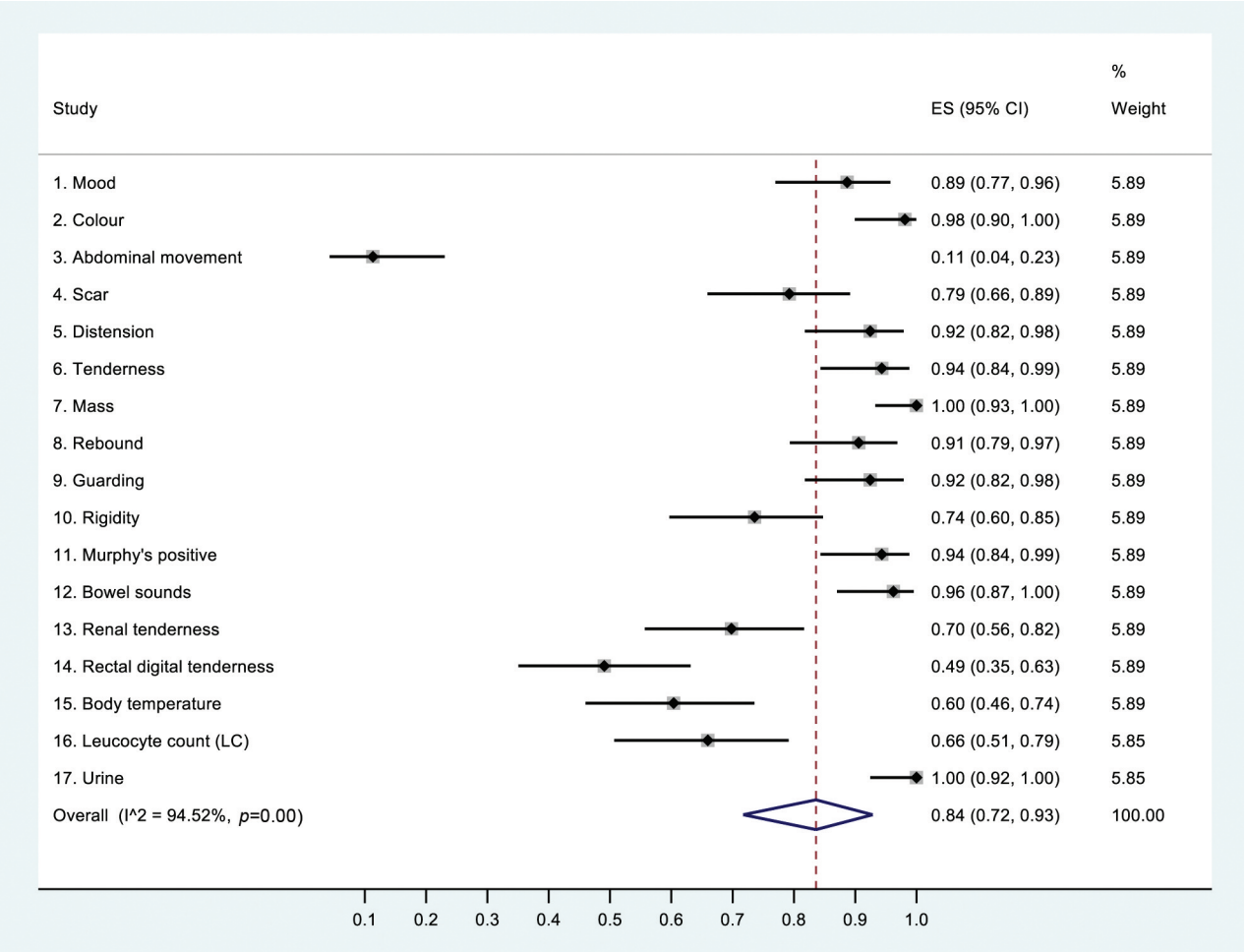

Figure 3. *Sensitivities of the signs and tests in acute appendicitis (random-effects model). ES: Estimated sensitivity; CI: confidence interval.*

performance of the clinical history-taking variables, findings and laboratory tests between the elderly AA patients and younger adult AA patients reported in our recent study (9), to examine whether the common clinical variables differ in elderly and younger adults. The Se of the history-taking in detecting AA in elderly 83% (95%CI=72-92%) was slightly higher than that detecting AA in younger female and male patients; 80% (95%CI=67-90%) and 81% (95%CI=66-92%), respectively. In addition, the overall Sp of the clinical history-taking in diagnosis of AA in elderly (34%; 95%CI=22-46%) was slightly higher than that in younger adult female and male patients; 30% (95%CI=19-42%) and 31% (95%CI=20-43%), respectively. Instead, the overall Se of the findings and tests in detecting AA in the elderly was 84% (95%CI=72-93%), which was slightly lower than that among the younger adult female and male patients; 86% (95%CI=79-92%) and 88% (95%CI=82-94%), respectively. However, the Sp of the clinical history-taking in diagnosis of AA in the elderly (45%; 95%CI=29-61%) was significantly higher than that of the younger female and male patients; 34% (95%CI=20-50%) and 34% (95%CI=20-51%), respectively.

When the performance of the DS models was compared between elderly and younger adult AA patients, the trend was similar. The pooled Se of the DS models in diagnosis of AA in the elderly (90%; 95%CI=80-97%) and in the younger female and male patients was very similar; 90% (95%CI=85-95%) and 93% (95%CI=88-96%), respectively. Although, Se and Sp usually behave reciprocally, it was a surprise to find that the Sp of the DS in the elderly (95%; 95%CI=89-99%) was significantly higher than that in the younger adult female and male patients; 85% (95%CI=74-94%) and 84% (95%CI=74-92%), respectively. In spite of that, the AUC values based on HSROC analysis of the DS_{Tax-} and DS_{Tax+}

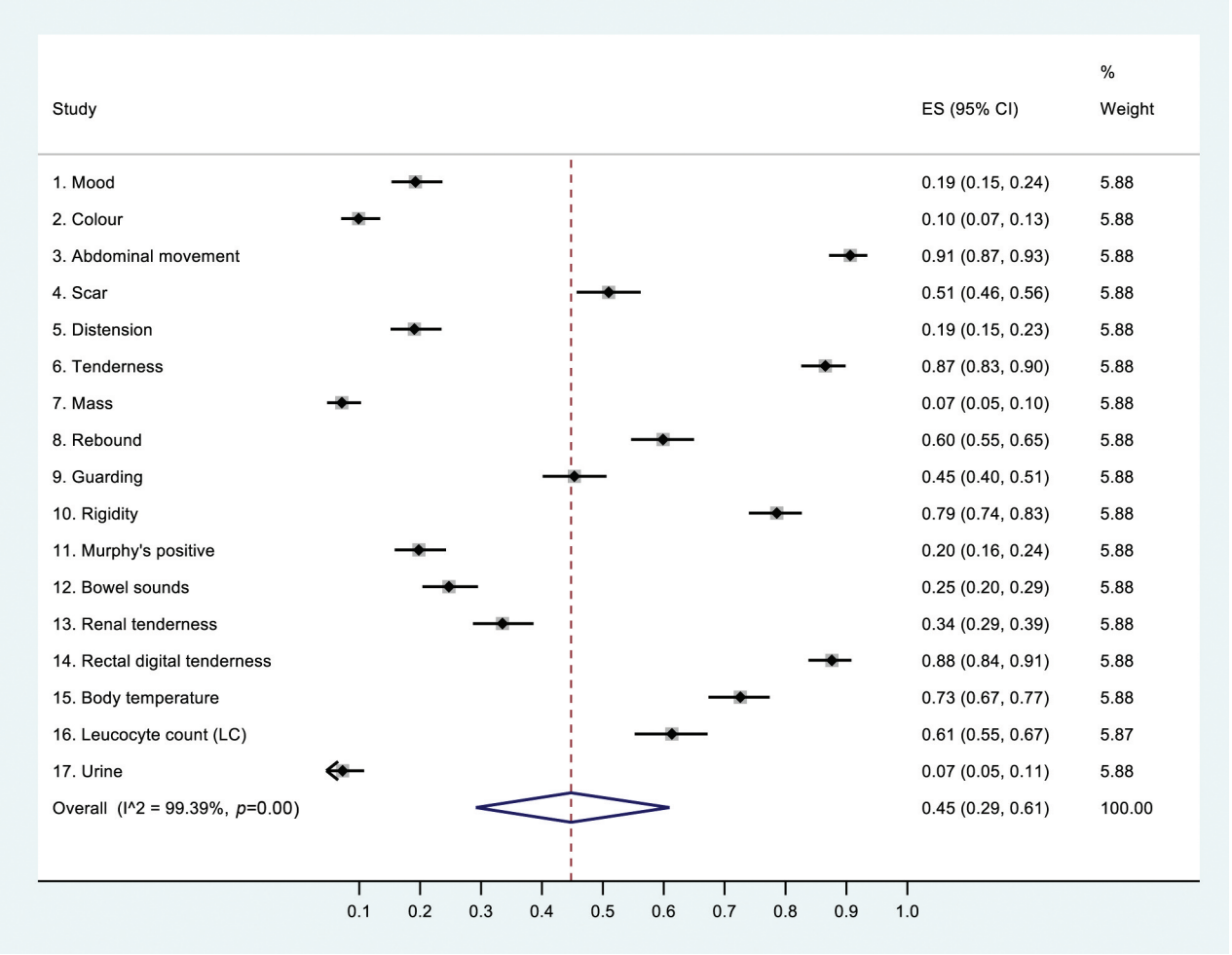

Figure 4. *Specificities of the clinical signs and tests in acute appendicitis (random-effects model). ES: Estimated specificity; CI: confidence interval.*

in the elderly [AUC=0.977 (95%CI=0.942-1.000) and AUC=0.980 (95%CI=0.956-1.000), respectively], and those in younger female [0.953 (95%CI=0.923-0.969)] and male patients [0.956 (95%CI=0.930-0.969)] (9) were very similar, with no significant difference in the roccomp analysis.

Elderly patients DS_{Tax-} and DS_{Tax+}. AUC values based on HSROC comparison test showed that the diagnostic performance of the clinical findings was slightly better than that of the clinical history-taking details only (p=0.0358). However, as measured by the AUC values, the DS model is superior to both i) the clinical history-taking and ii) findings and tests. Previous studies with a design similar to ours are scanty and only two retrospective studies have evaluated the applicability of the DS models in elderly AA population. Shchatsko *et al*. (9) used Alvarado score in 96 patients and suggested that elderly patients with Alvarado score between 5 and 10 had high risk of AA. Another retrospective study of 41 elderly patients (10) used Alvarado score with 0.969 AUC value. However, both these studies were retrospective (9, 10), and the lack of convincing evidence in elderly AA patients prompted the expert panel (3) not to recommend Alvarado score for diagnosis of AA in elderly patients.

The present study specifically focused on HSROC analysis and AUC value as the most important DS test characteristics. The main objective of the DS is to separate those elderly AA patients who do need urgent attention from those who don't need. Some previous studies (2, 9) have emphasized the value of Tax analysis in AA diagnosis, but Tax analysis has certain limitations, including i) variation in the definition of Tax cut-off, as well as ii) variations in the duration of abdominal pain in the time of Tax testing (2, 9). In earlier studies, the frequency of fever in the elderly patients with AA diagnosis has varied between 30-80% (2, 9). There is

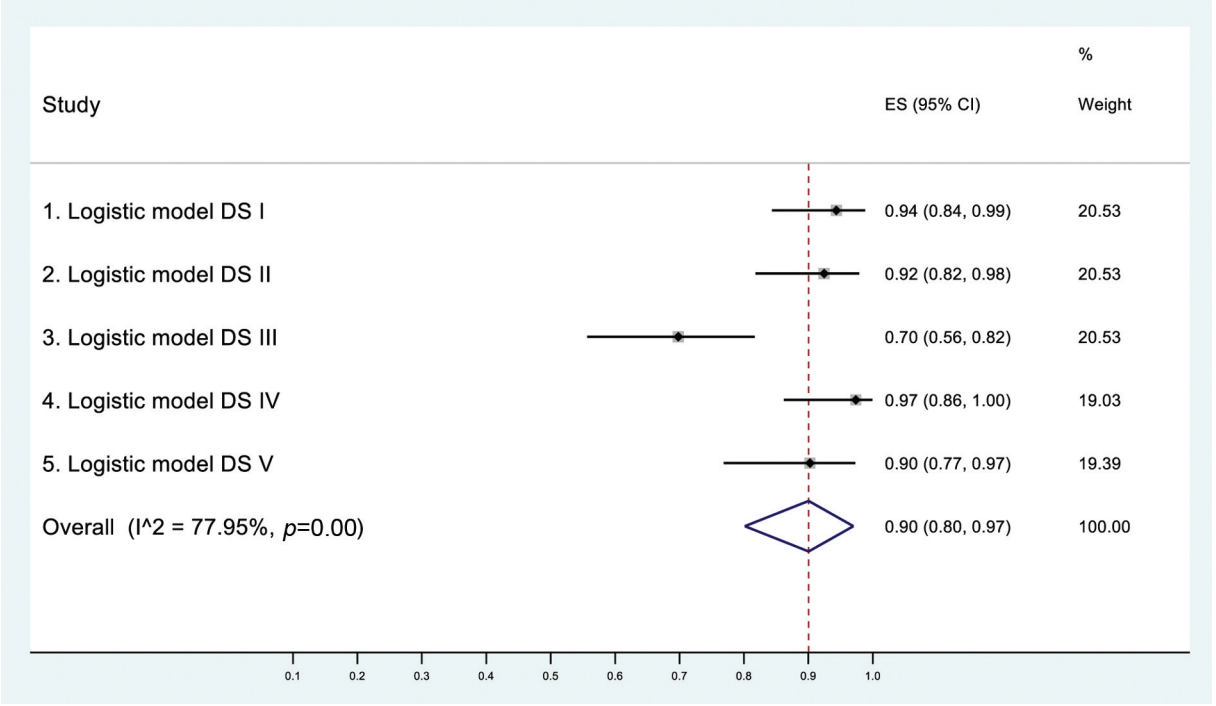

Figure 5. *Sensitivities of diagnostic scores without body temperature (DS_{Tax-}) at five different cut-off levels (DS I-V). ES: Estimated sensitivity; CI: confidence interval.*

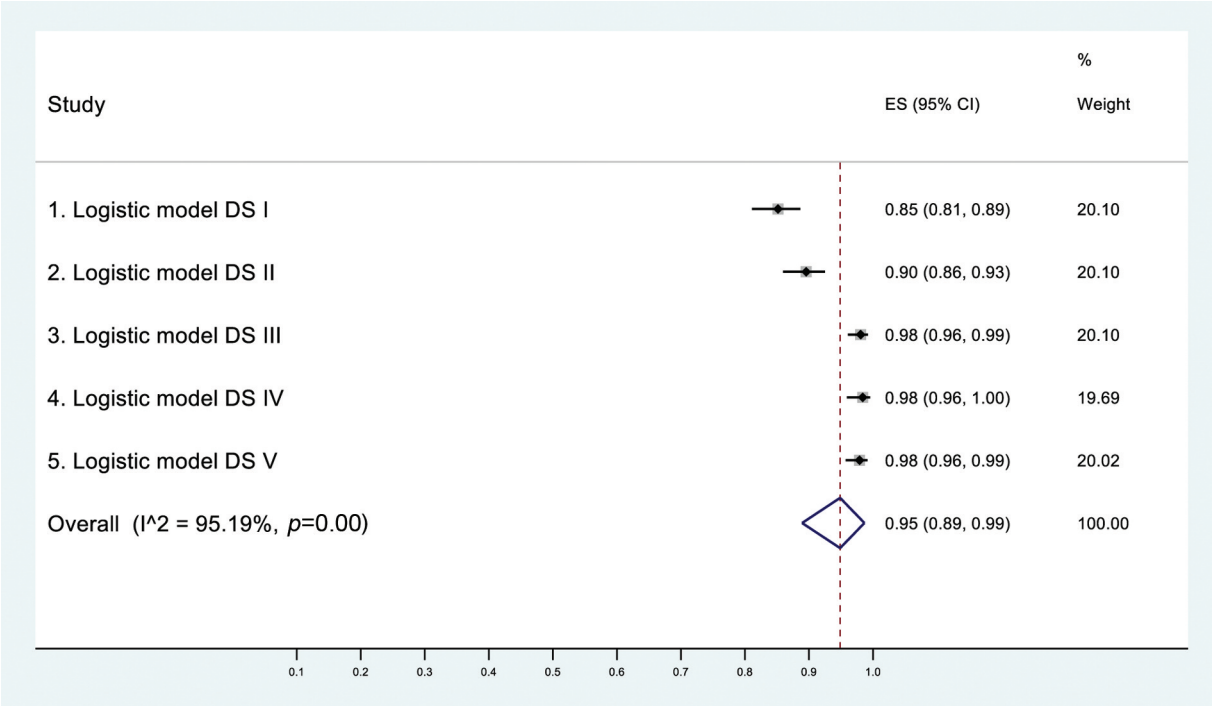

Figure 6. *Specificities of diagnostic scores without body temperature (DS_{Tax-}) at five different cut-off levels (DS I-V). ES: Estimated specificity; CI: confidence interval.*

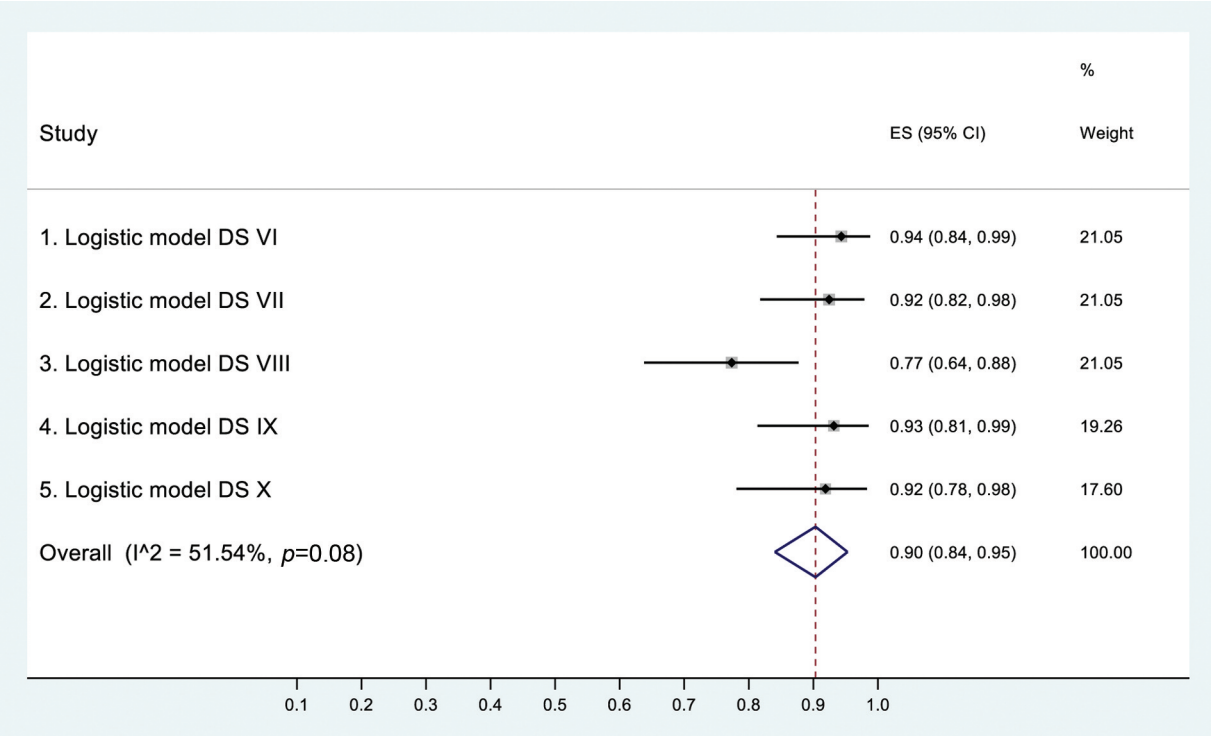

Figure 7. *Sensitivities of diagnostic scores with body temperature (DS_{Tax+}) at five different cut-off levels (DS VI-X). ES: Estimated sensitivity; CI: confidence interval.*

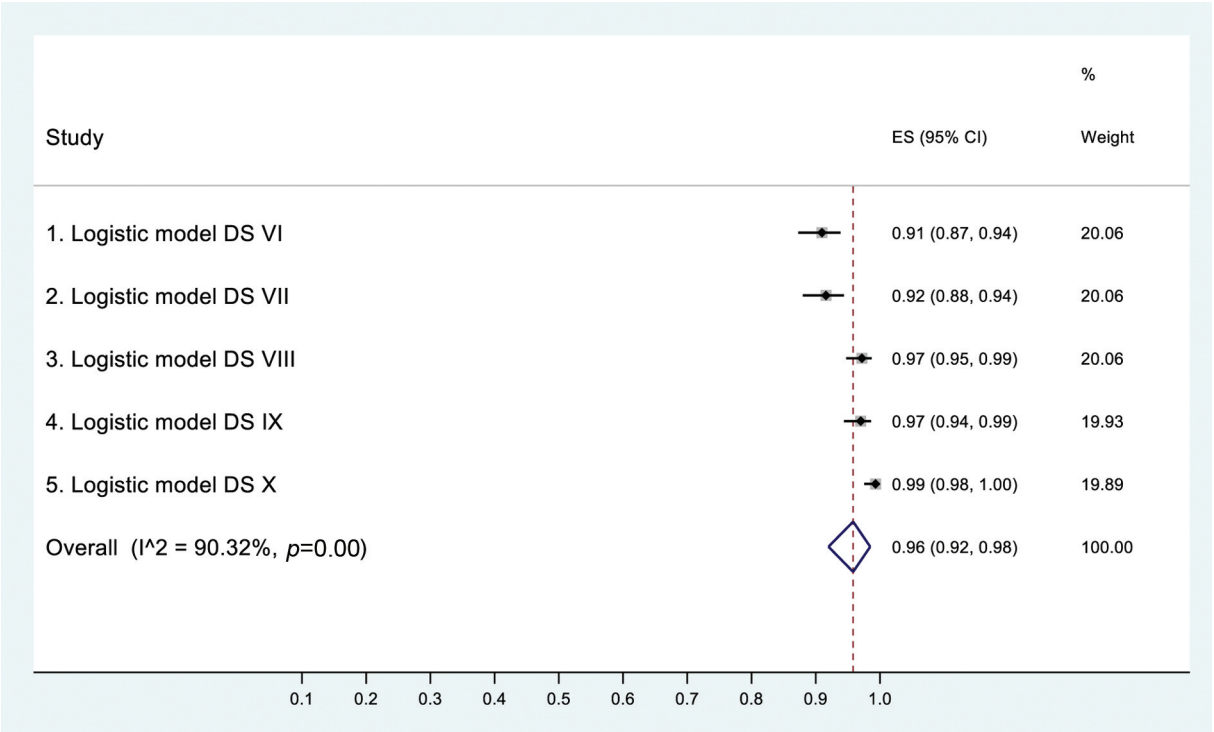

Figure 8. *Specificities of diagnostic scores with body temperature (DS_{Tax+}) at five different cut-off levels (DS VI-X). ES: Estimated specificity; CI: confidence interval.*

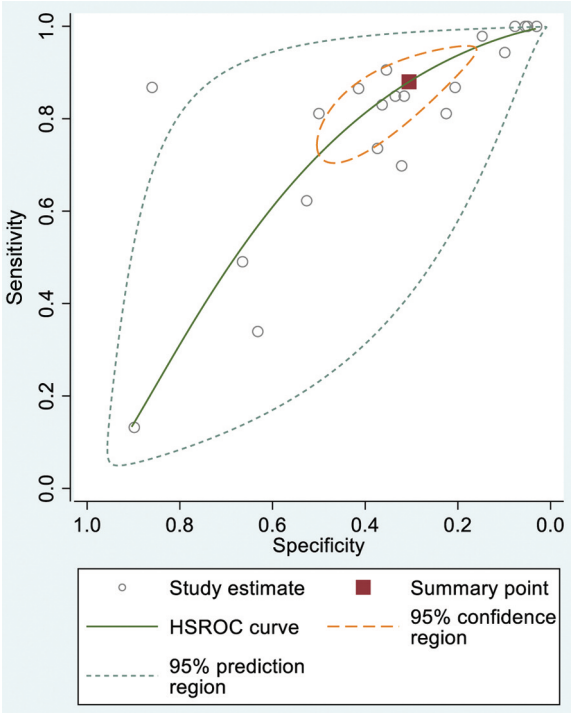

Figure 9. *Hierarchical summary receiver operating characteristic (HSROC) curve of the history-taking in acute appendicitis.*

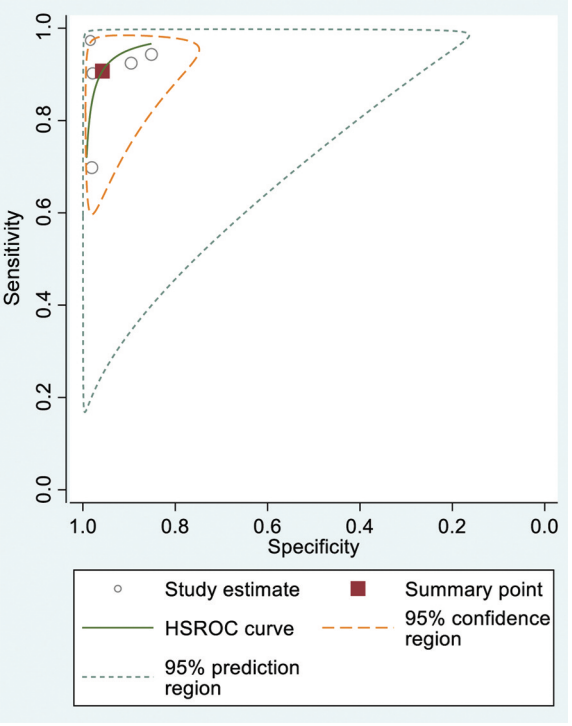

Figure 11. *Hierarchical summary receiver operating characteristic (HSROC) curve of the five* DS_{Tax-}.

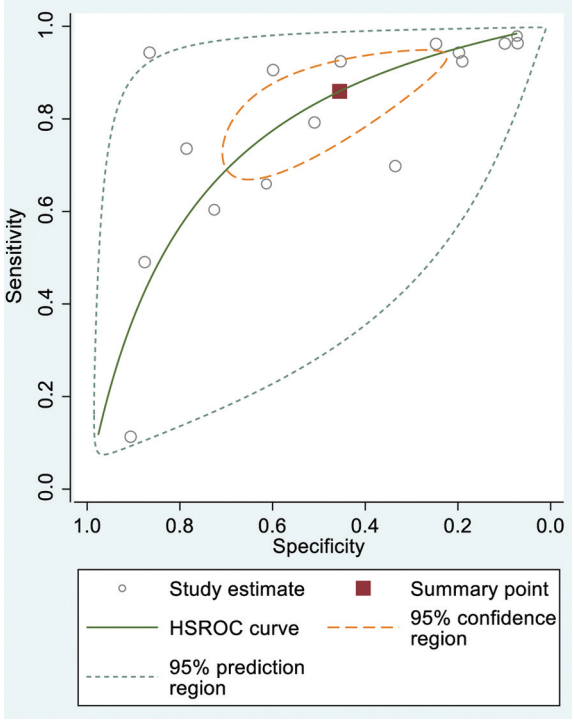

Figure 10. *Hierarchical summary receiver operating characteristic (HSROC) curve of the clinical signs and tests in acute appendicitis.*

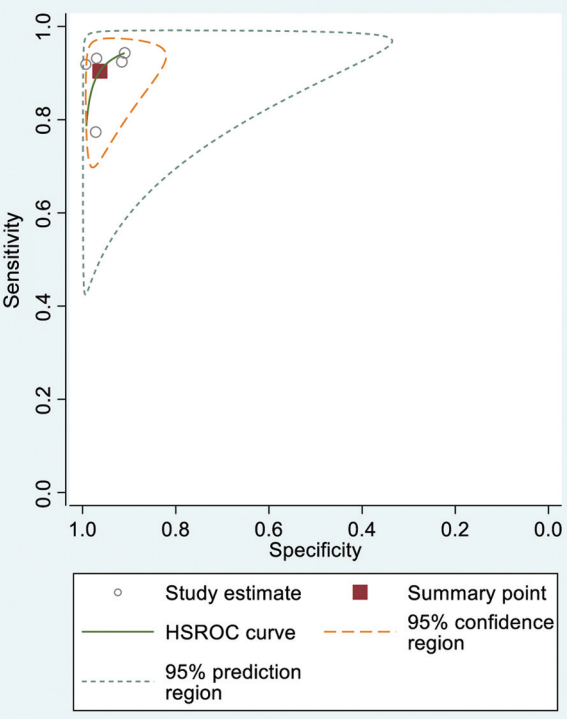

Figure 12. *Hierarchical summary receiver operating characteristic (HSROC) curve of the five* DS_{Tax+}.

still controversy, whether the elderly AA patients with presentation of fever differ significantly from those without fever. The present study favours the lack of any such difference, because no statistically significant difference was established in the HSROC analysis between DS_{Tax-} and DS_{Tax+} formulas in diagnosis of AA in these elderly patients.

Conclusion

Although, some previous studies (11, 12) have reported that the diagnostic accuracy of AA is lower in the elderly patients as compared to younger AA patients, the results of our study do not support this statement. In contrast, the AUC value of DS for AA in the elderly patients is slightly higher than that in younger AA patients. Similar to the younger patients (6), the DS formula is superior to both the clinical history-taking and findings, and therefore the use of DS (with or without body temperature) should be an important part of the diagnostic decision tree of AA also in the elderly patients presenting with AAP.

Conflicts of Interest

The Authors report no conflicts of interest or financial ties in relation to this study.

Authors' Contributions

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

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