CANCER DIAGNOSIS & PROGNOSIS
1: 265-274 (2021) doi: 10.21873/cdp.10034

History-taking, Clinical Signs, Tests and Scores for Detection of Non-organic Dyspepsia (NOD) Among Patients With Acute Abdominal Pain (AAP)

MAARET ESKELINEN[1*], JANNICA MEKLIN[1*], TUOMAS SELANDER[2], KARI SYRJÄNEN[3,4] and MATTI ESKELINEN[1]

[1]*Department of Surgery, Kuopio University Hospital and School of Medicine, University of Eastern Finland, Kuopio, Finland;*
[2]*Science Service Center, Kuopio University Hospital and School of Medicine, University of Eastern Finland, Kuopio, Finland;*
[3]*Molecular Oncology Research Center, Barretos Cancer Hospital, Barretos, Brazil;*
[4]*SMW Consultants Ltd., Kaarina, Finland*

Abstract. *Background/Aim: The diagnostic accuracy of history-taking, clinical signs and tests and diagnostic scores (DSs) for patients with non-organic dyspepsia (NOD) have been rarely evaluated. Patients and Methods: A cohort of 1333 patients presenting with acute abdominal pain (AAP) were studied, including 50 patients with confirmed NOD. The most significant diagnostic variables (in multivariate logistic regression analysis) were used to construct six different DS models and their diagnostic accuracy was compared with clinical symptoms and signs and tests. 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 hierarchical summary receiver operating characteristic (HSROC) analysis, the area under curve (AUC) values for i) symptoms ii) signs and tests iii) DS were as follows: i) AUC=0.608 [95% confidence interval (CI)=0.550-0.666]; ii) AUC=0.621 (95% CI=0.570-0.672) and iii) AUC=0.877 (95% CI=0.835-0.919). The differences between these AUC values (roccomp analysis) are as follows: between i) and ii) p=0.715; between i) and iii) p<0.0001; between ii) and iii) p<0.0001. Conclusion: The present study is the first to provide evidence that the DS could be used in diagnosis of NOD. The major advantage of our DS is that this model does not need radiology or endoscopy to reach high diagnostic accuracy.*

This article is freely accessible online.

*These Authors contributed equally to this study.

Correspondence to: Matti Eskelinen, MD, Ph.D., School of Medicine, University of Eastern Finland, P.O. Box 100, FI-70029 KYS, Finland. Tel: +358 17173311, Fax: +358 17172611, GSM: +358 400969444, e-mail: matti.eskelinen@kuh.fi

Key Words: Non-organic dyspepsia, symptoms, signs, tests, diagnostic score, HSROC, diagnostic accuracy.

Non-organic dyspepsia (NOD), also known as functional dyspepsia, is "a collection of symptoms" without evidence of an organic disease that could explain the symptoms (1, 2). NOD is estimated to affect about 15-40% of the general population in Western countries (3, 4). The symptoms of NOD are non-specific including location of pain at upper abdomen, pain duration over 12 hours, similar pain and indigestion previously, poor appetite and vomiting (5). According to previous analyses, the patients with upper abdominal pain (AAP) and previous history of indigestion tended to be at risk for NOD (5). The diagnostic accuracy of the clinical findings in NOD have rarely been investigated and the few studies performed include gastroscopy referral patients (6). To circumvent this type of bias we investigated the diagnostic accuracy of clinical findings in NOD among patients with AAP.

Although, the diagnostic performance of clinical symptoms, signs and tests have been investigated earlier in acute appendicitis (AA) (7-11), acute cholecystitis (AC) (12) and in acute small bowel obstruction (13), there is very little data on the diagnostic accuracy of history-taking, clinical signs, tests and diagnostic score (DS) for NOD; this prompted us to re-evaluate the accuracy of the clinical diagnosis of NOD. The present study evaluated the relative accuracy of i) symptoms, ii) signs and tests, as well as iii) the DS in confirming NOD among the patients with AAP.

Table I. *Clinical history of the patients with non-organic dyspepsia (NOD) vs. other causes of abdominal pain. TP: True positive; FN: false negative; FP: false positive; TN: true negative.*

Clinical history variable	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Location of initial pain	Right or left upper abdomen	Other	39	11	452	831
2. Location of pain at diagnosis	Right or left upper abdomen	Other	37	13	425	858
3. Duration of pain: Duration of pain at diagnosis	>12 hours	≤12 hours	42	8	830	453
4. Intensity of abdominal pain	Subjectively moderate or weak pain	Intolerable pain	42	8	1,075	208
5. Progression of pain from onset to diagnosis	Weaker or subjectively same pain than at the onset	Worse pain	33	17	913	370
6. Type of pain	Steady pain	Colicky or intermitted pain	27	23	704	579
7. Aggravating factors	Movement, coughing, respiration, food or other	No aggravating factors	14	36	342	941
8. Relieving factors	Yes	No	37	13	862	421
9. Previous similar pain	Yes	No	33	17	414	855
10. Vertigo	No	Yes	47	2	1,242	38
11. Nausea	Yes	No	19	31	548	735
12. Vomiting	Yes	No	30	20	545	738
13. Appetite	No appetite	Normal appetite	43	7	934	349
14. Previous indigestion	Yes	No	22	28	257	1,024
15. Jaundice	No	Yes	47	3	1,253	30
16. Bowels	Diarrhea, constipation, blood, mucus or white stools	Normal	16	34	302	981
17. Micturition	Normal	Abnormal	48	2	1,199	84
18. Drugs for abdominal pain	Yes	No	8	42	46	1,236
19. Previous abdominal surgery	Yes	No	28	22	305	977
20. Previous abdominal diseases	Yes	No	22	28	211	1,070
21. Use of alcohol	No	Yes	47	3	1,218	64
22. Gender	Male	Female	32	18	604	679

Patients and Methods

In the NOD study group there were 50 patients (18 females and 32 males) *versus* 1283 patients in the non-NOD group including 679 females and 604 males. The clinical symptoms (n=22), signs and tests (n=14) and laboratory analyses (n=3) were recorded in each patient. The diagnosis of NOD 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 NOD.

Identifying the 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, signs and tests presented in Tables I and II were included in the analysis as binary data e.g., NOD=1 and other diagnosis of AAP=0. Using the coefficients of the regression model, a DS was built and its predictive value for NOD was studied. The coefficient of the multivariate analysis shows the relative risk (RR=en, n=ß) of a patient with a given symptom, sign or test of having NOD.

The DS formula derived for NOD. The DS: 1.43 × gender (female=0, male=1) + 0.82 × location of initial pain (PE=1, NE=0) + 1.08 × location of pain at diagnosis (PE=1, NE=0) + 1.23 × duration of pain (PE=1, NE=0) + 0.96 × previous similar pain (PE=1, NE=0) + 0.73 × appetite (PE=1, NE=0) + 1.10 × drugs for abdominal pain (PE=1, NE=0) - 0.86 × use of alcohol (PE=1, NE=0) + 1.16 × rigidity (PE=1, NE=0) + 0.49 × guarding (PE=1, NE=0) + 0.82 × leucocyte count (PE=1, NE=0) – 9.17.

Statistical analysis. STATA/SE version 16.1 (StataCorp, College Station, TX, USA) was used for further statistical analyses. The statistical tests presented were two-sided, and *p*-values under 0.05 were considered statistically significant. Using 2×2 tables, sensitivity and specificity with 95% confidence intervals (95% CI) for each clinical history-taking variable, finding or test were determined. A meta-analytical technique (metaprop) was used to create separate forest plots for sensitivity and specificity for each set of data, including each diagnostic variable. We calculated the summary estimates of sensitivity and specificity, positive and negative likelihood ratios and diagnostic odds ratio, using a random- effects bivariate model and fitted the summary hierarchical receiving operating characteristic (HSROC) curves, including all diagnostic variables in the DS model, using NOD as an 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 NOD study group, there were 50 patients (18 females and 32 males) *versus* 1283 patients in the non-NOD group (679 females and 604 males) including the following AAP patients: non-specific abdominal pain (n=616), acute appendicitis (n=271), acute

Table II. *Clinical signs and investigations of patients with non-organic dyspepsia (NOD) versus other causes of abdominal pain. TP: True positive; FN: false negative; FP: false positive; TN: true negative.*

Clinical signs and investigations	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Mood	Distressed or anxious	Normal	10	40	227	1,066
2. Color	Normal	Jaundiced, pale, flushed or cyanosed	44	6	1,137	146
3. Abdominal movement	Normal	Poor/nil	47	3	1,192	90
4. Scar	Yes	No	28	22	318	964
5. Distension	No	Yes	46	4	1,190	89
6. Tenderness	Right or left upper abdomen	Other	30	19	281	994
7. Mass	No	Yes	50	0	1,249	34
8. Rebound	No	Yes	36	14	666	617
9. Guarding	No	Yes	33	17	593	690
10. Rigidity	No	Yes	47	3	991	291
11. Murphy's positive	No	Yes	46	3	1,162	121
12. Bowel sounds	Normal	Abnormal	42	8	1,102	181
13. Renal tenderness	No	Yes	39	11	933	350
14. Rectal digital tenderness	Normal	Abnormal	47	3	922	358
15. Body temperature	≤37.2˚C	>37.2˚C	22	11	523	594
16. Leucocyte count (LC)	≤8200/mm^3	>8,200/mm^3	18	10	402	651
17. Urine	Normal	Abnormal	36	0	1,060	72

Table III. *Diagnostic score for non-organic dyspepsia (NOD) patients. The DS model is shown at six different cut-off levels of symptoms, signs and tests. Cut-off levels: DS I=0.045, DS II=0.05, DS III=0.055, DS IV=0.06, DS V=0.065 and DS VI=0.07.*

Diagnostic score (DS)	Positive endpoint	Negative endpoint	TP	FN	FP	TN
1. Logistic model DS I	NOD	Other cause of abdominal pain	40	10	215	1,068
2. Logistic model DS II	NOD	Other cause of abdominal pain	39	11	203	1,080
3. Logistic model DS III	NOD	Other cause of abdominal pain	39	11	185	1,098
4. Logistic model DS IV	NOD	Other cause of abdominal pain	38	12	179	1,104
5. Logistic model DS V	NOD	Other cause of abdominal pain	34	16	160	1,123
6. Logistic model DS VI	NOD	Other cause of abdominal pain	33	17	152	1,131

TP: True positive; FN: false negative; FP: false positive; TN: true negative; PE: positive endpoint; NE: negative endpoint; DS: 1.43 × gender (female=0, male=1) + 0.82 × location of initial pain (PE=1, NE=0) + 1.08 × location of pain at diagnosis (PE=1, NE=0) + 1.23 × duration of pain (PE=1, NE=0) + 0.96 × previous similar pain (PE=1, NE=0) + 0.73 × appetite (PE=1, NE=0) + 1.10 x drugs for abdominal pain (PE=1, NE=0) - 0.86 × use of alcohol (PE=1, NE=0) + 1.16 × rigidity (PE=1, NE=0) + 0.49 × guarding (PE=1, NE=0) + 0.82 × leucocyte count (PE=1, NE=0) – 9.17.

cholecystitis (n=124), acute renal colic (n=59), acute small bowel obstruction (n=53) and other AAP patients (n=160), with the mean (SD) age of 37.5 (21.7) years.

The clinical symptoms of NOD. The overall Se of the clinical symptoms for detecting NOD was 67% (95% CI=56-77%) (Figure 1).The Se was higher than 67% for ten of the symptoms. The five most sensitive clinical history-taking variables (vertigo, appetite, jaundice, micturition and use of alcohol) showed 86-96% Se in diagnosis of NOD (Figure 1). The Sp of the history-taking for detecting NOD was only 46% (95% CI=32-61%) (Figure 2). Altogether, 11 symptoms showed Sp higher than 46%. The five most specific symptoms of NOD (previous indigestion, bowels, drugs for abdominal pain, previous abdominal surgery and previous abdominal diseases) showed 76-96% Sp (Figure 2).

The clinical signs and tests in NOD. The overall Se of the signs and tests for NOD was 81% (95% CI=70-90%) (Figure 3), and 9 signs and tests had Se values exceeding 81%. The six most accurate signs and tests (abdominal movement, mass, rigidity, Murphy's positive, rectal digital tenderness and urine) showed 94-100% Se (Figure 3). The overall Sp of the signs and tests was only 32% (95% CI=18-47%) (Figure 4), while 7 signs and tests showed Sp higher than 32%. The five most specific signs and tests (mood, scar, tenderness, guarding and leucocyte count), however, showed 54-82% specificity (Figure 4).

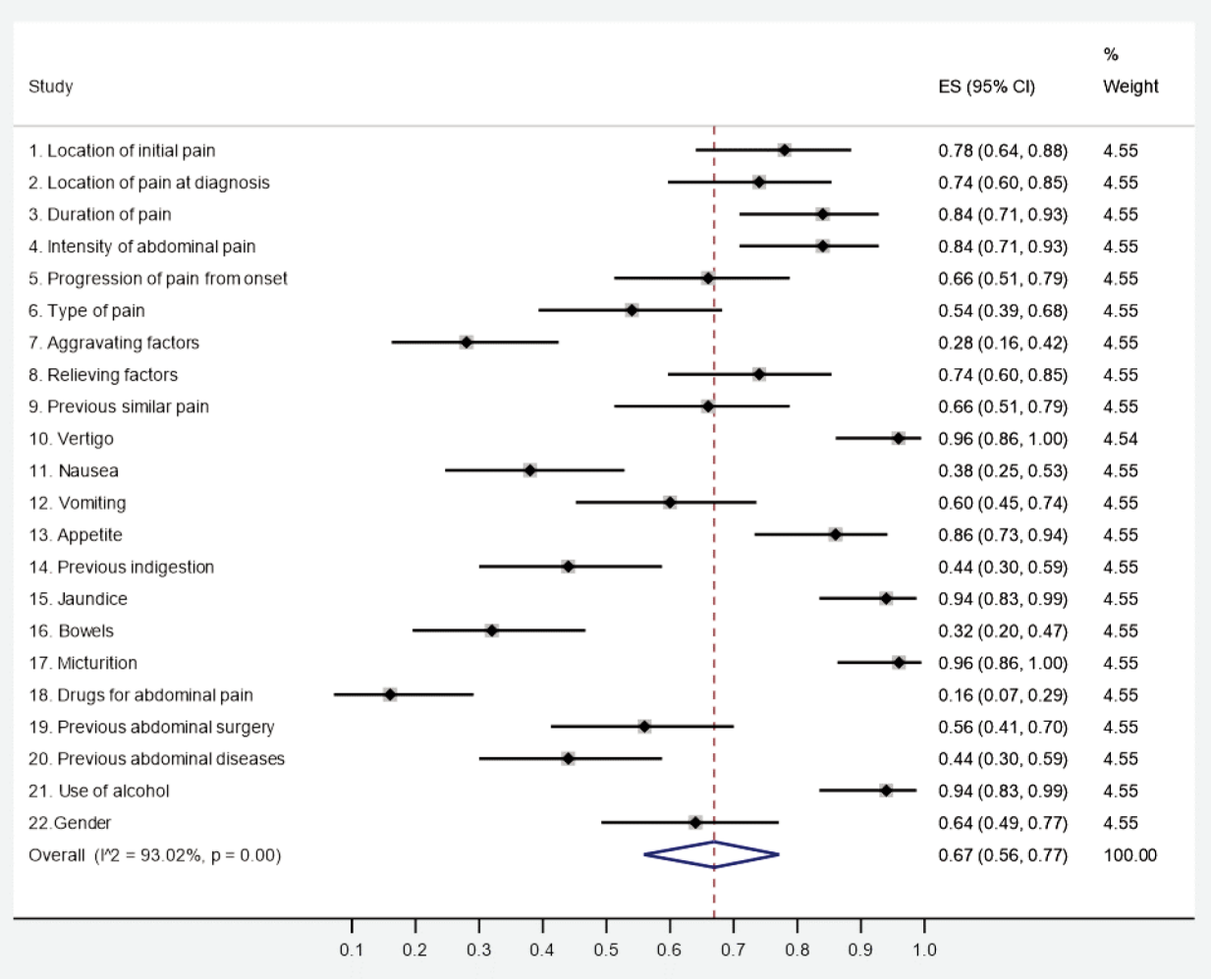

Figure 1. *Sensitivity of history-taking in non-organic dyspepsia (NOD) (random-effects model). ES: Estimated sensitivity; CI: confidence interval.*

Scoring in confirming NOD. The most important predictors of NOD were gender, location of initial pain, location of pain at diagnosis, duration of pain, previous similar pain, appetite, drugs for abdominal pain, use of alcohol, rigidity, guarding and leucocyte count. The best diagnostic level for DS model (DS III; Se=78%, S*p*=86%) was reached at a cut-off level of 0.055 for DS (Figures 5 and 6). The DS model was tested at six different cut-off levels to disclose the highest diagnostic accuracy (Table III; Figures 5 and 6). The Se and Sp of these six DS models were 74% (95% CI=69-79%) and 86% (95% CI=84-87%), respectively (Table III; Figures 5 and 6). Four of these models showed Se >74% and three models had Sp >86%. The best diagnostic DS model in these NOD patients (DS III, Figures 5 and 6) showed Se of 78% (95% CI=64-88%) and Sp of 86% (95% CI=84-87%).

HSROC and comparison of the AUC values. STATA (metandiplot) was used to draw the HSROC curves to visualise the pooled overall accuracy of the symptoms (Figure 7), signs and tests (Figure 8) and different scoring models (Figure 9) in detecting NOD. In SROC analysis, the AUC values for i) symptoms ii) signs & tests iii) DS were as follows: i) AUC=0.608 (95% CI=0.550-0.666); ii) AUC=0.621 (95% CI=0.570-0.672) and iii) AUC=0.877 (95% CI=0.835-0.919). The differences between these AUC values (roccomp analysis) are as follows: between i) and ii) p=0.715; between i) and iii) p<0.0001; between ii) and iii) p<0.0001.

Discussion

Some years ago, the value of the history-taking in the diagnosis of NOD was reported, but at that time, the HSROC

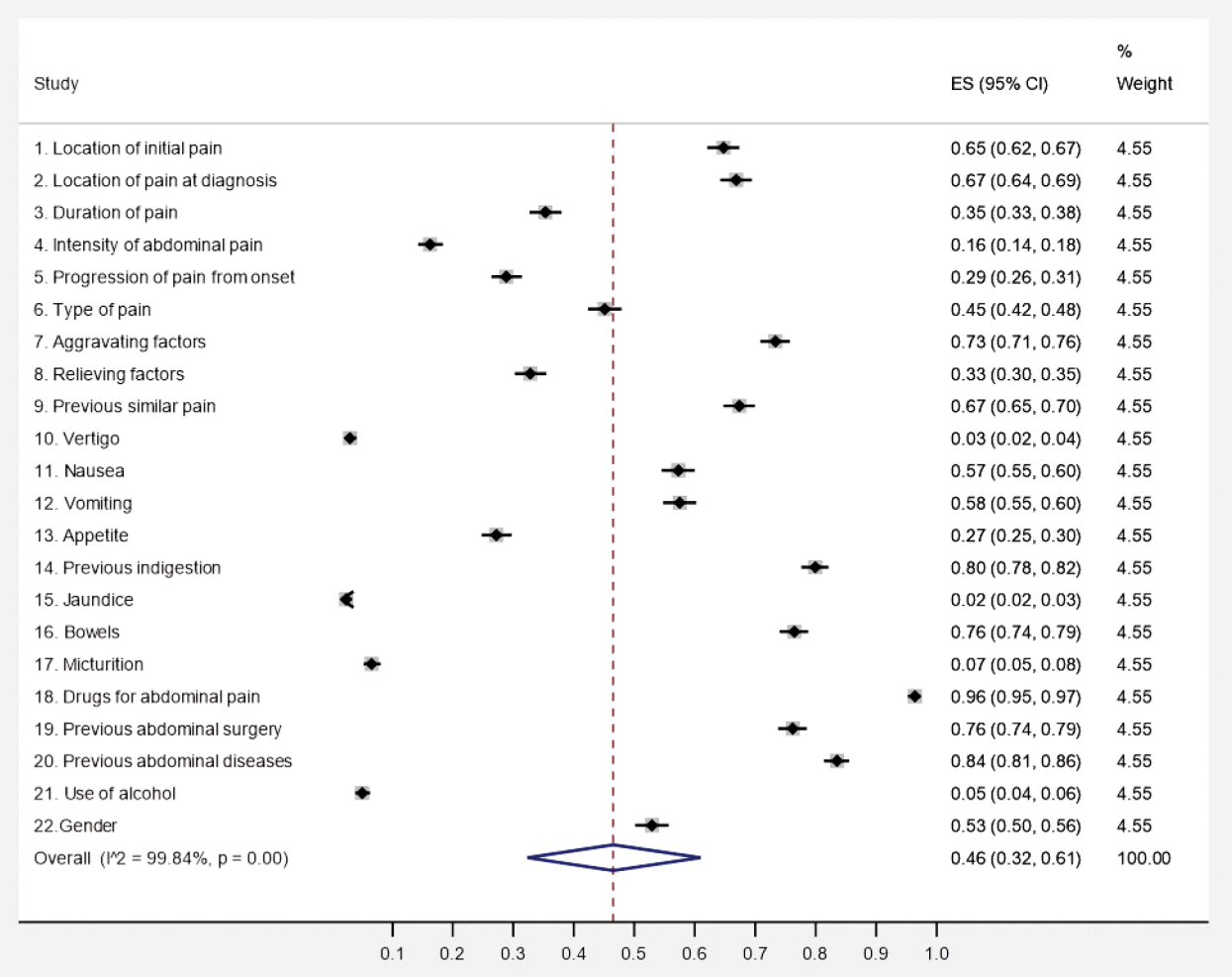

Figure 2. *Specificity of history-taking in non-organic dyspepsia (NOD) (random-effects model). ES: Estimated specificity; CI: confidence interval.*

and AUC analysis to confirm the diagnostic performance of clinical findings and scoring was not available (5). Prompted by the difficulty of NOD 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 scoring in confirming NOD among the patients with AAP.

The diagnosis of NOD could be made based on common clinical findings supported by signs and tests, ultrasound (US) and gastroscopy. One of the most difficult problems in detection of NOD is the lack of a golden standard (1, 2). To overcome this problem, we analysed the NOD diagnosis based on the final diagnosis of all AAP patients. Clinical findings of NOD include the location of initial pain and pain at diagnosis usually in the upper abdomen. Pajala *et al*. (14) reported the location of upper abdominal pain (UAP) in 77% of the patients with NOD. Similarly, in our study 78% of NOD patients had UAP initially and 74% had the UAP at diagnosis with a diagnostic efficiency (De) in NOD of 65% *versus* 67%, respectively. In patients with AAP, nausea, vomiting and poor appetite are usually regarded as NOD symptoms. In our study, only 38% of the NOD patients had nausea and 60% had vomiting, the De being in NOD of 57% *versus* 58%, respectively. The results of earlier investigations did not support a strong link between specific symptoms and NOD (5). However, patients with UAP, with a previous history of abdominal surgery and indigestion seem to be at risk for NOD and DS might help differentiate NOD from other causes of AAP.

Talley *et al*. (15) recruited 113 patients with upper-gastrointestinal symptoms and population-based subjects

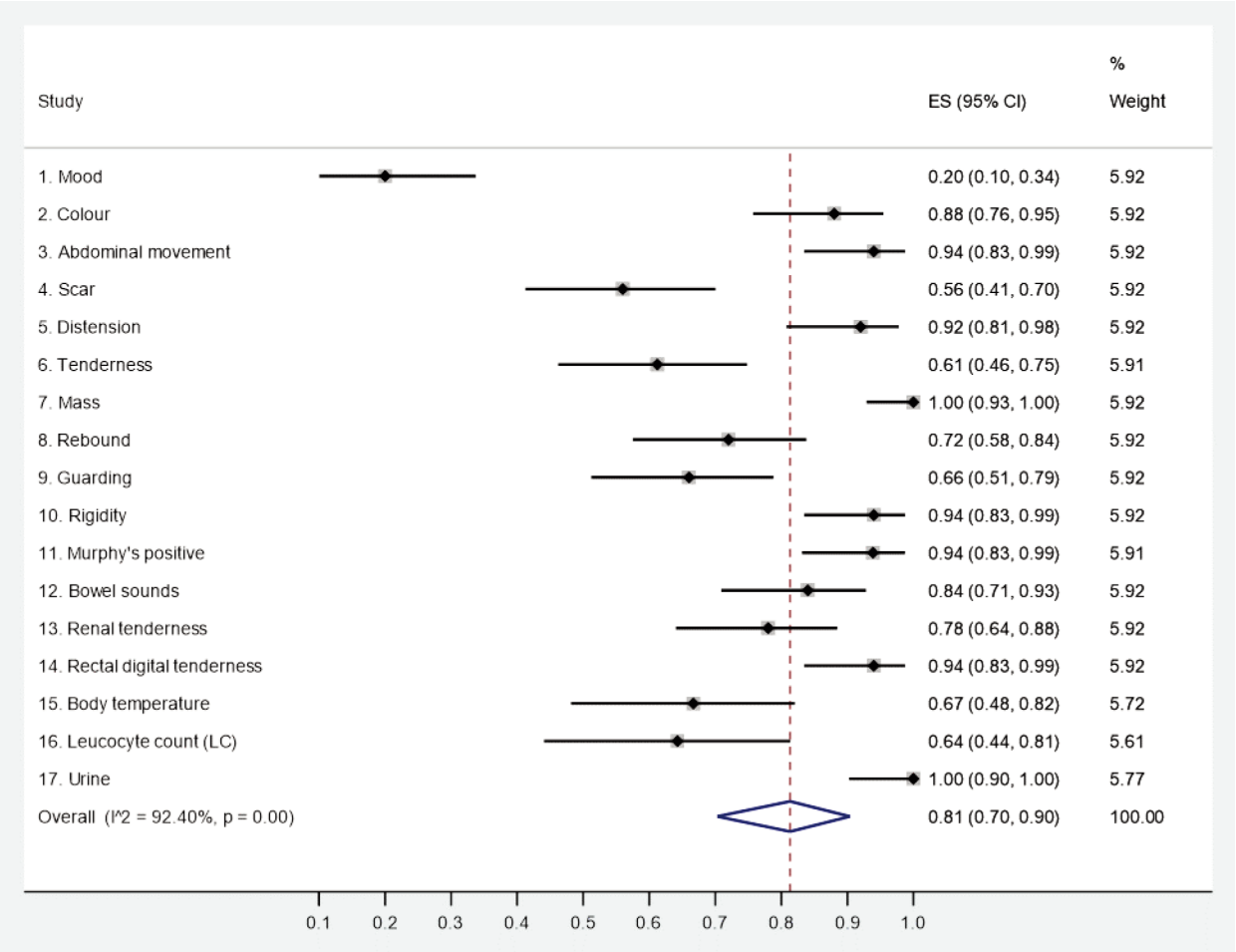

Figure 3. *Sensitivity of the signs and tests in non-organic dyspepsia (NOD) (random-effects model). ES: Estimated sensitivity; CI: confidence interval.*

(n=347) and developed a 42-item quality life score for NOD. Although, this Nepean Dyspepsia Index (NDI) may be a valid tool for NOD symptoms, there is still no HSROC and AUC analysis for the diagnostic accuracy for NOD patients.

Adam *et al*. (16) enrolled 95 patients with 56 healthy subjects for the assessment of NOD symptoms. They focused on 10 symptoms including UAP, vomiting, poor appetite, nausea, feeling sick, bloating, cramps, early satiety, heartburn and retrosternal discomfort, and developed the gastrointestinal symptom score (GSS). The GSS seems to be a reliable tool to investigate symptom intensities in patients with NOD. Also, this study is limited by the highly selected patient cohort and lack of HSROC analysis.

Taylor *et al*. (17) designed a score to address the lack of symptom-focused measures in NOD patients. They interviewed 45 study participants to identify NOD symptoms and selected seven possible symptoms to construct the Functional Dyspepsia Symptom Diary (FDSD) score. Although, their FDSD score is valid patient-reported outcome measure for NOD patients, there is no HSROC analysis with AUC values for diagnosis of NOD available.

Lacy *et al*. (18) investigated 254 NOD patients and mailed a questionnaire to assess NOD symptoms and Gastroparesis Cardinal Symptom Index (GCSI). The results of the patients who responded (n=123) showed that the GCSI score could not accurately distinguish NOD patients from other diagnoses. They concluded that a more specific DS is needed for NOD diagnosis.

Acute cholecystitis (AC) is a reason of organic dyspepsia and one important differential diagnostic disease in confirming NOD. When comparing the symptoms, signs and tests between NOD patients and those with AC patients reported in the Eskelinen *et al*. study (12), the overall sensitivity of the symptoms in NOD of 67% (95% CI=56-77%) was higher than that detecting AC

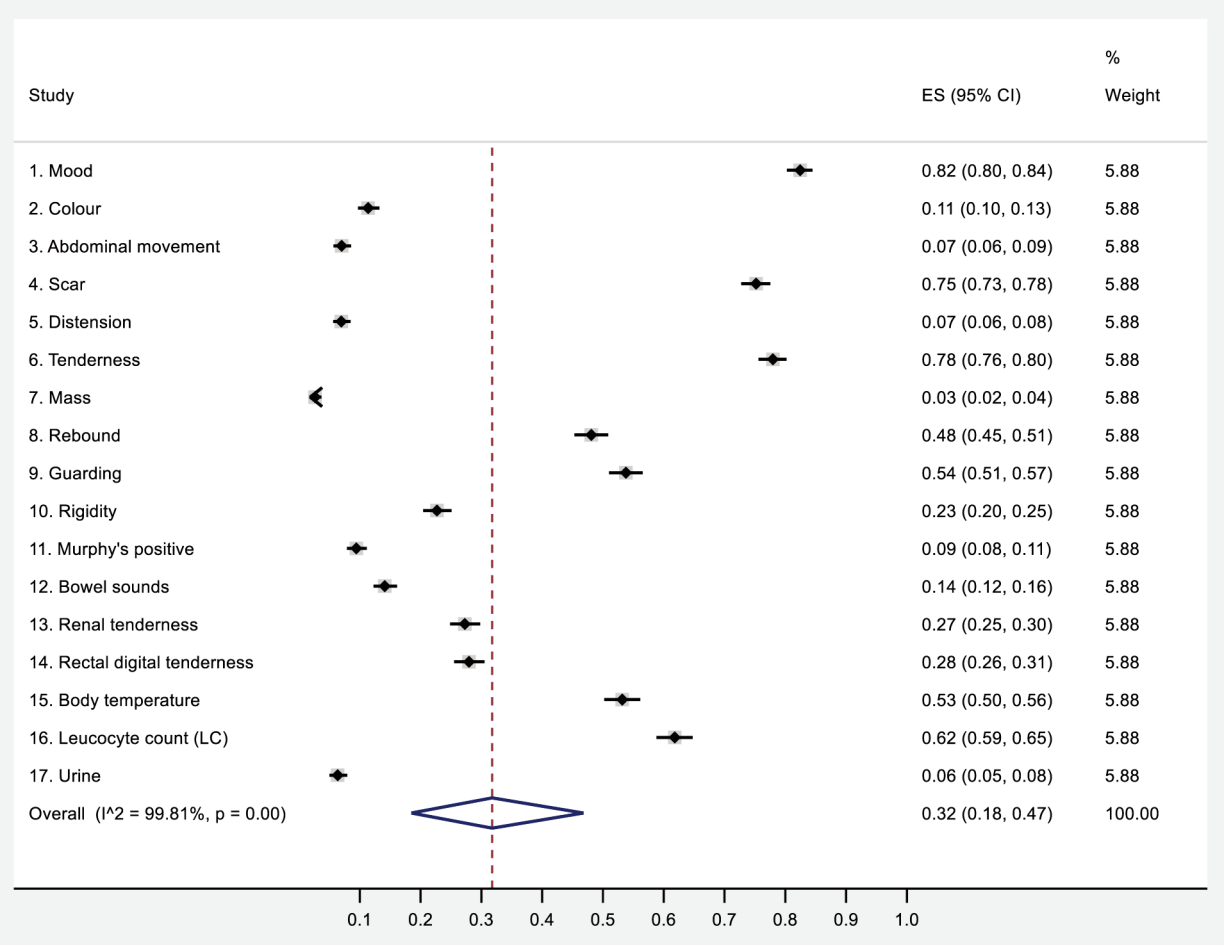

Figure 4. *Specificity of the clinical signs and tests in non-organic dyspepsia (NOD) (random-effects model). ES: Estimated specificity; CI: confidence interval.*

among AAP patients, which was 59% (95% CI=45-73%). However, the overall specificity of the symptoms in NOD patients was similar to that in AC patients; 46% (95% CI=32-61%) *vs*. 44% (95% CI=28-61%). The overall Se of the signs and tests in detecting NOD was 81% (95% CI=70-90%), which was significantly higher than that among AC patients (68%; 95% CI=53-81%). However, the pooled Sp of the signs and tests in detecting NOD was 32% (95% CI=18-47%) and was inferior to that of the AC patients, which was 41% (95% CI=23-60%).

When NOD and AC patients are compared in the scoring models, the trend is similar. The overall Se of the DS models in NOD is 74% (95% CI=69-79%), significantly lower than that in AC patients (86%; 95% CI=83-88%). Although Se and Sp usually behave reciprocally, this was not the case with the overall Sp of the DS in NOD patients (86%; 95% CI=84-87%), which is significantly lower than for the AC patients (94%; 95% CI=93-95%). In addition, the diagnostic accuracy of the DS (AUC=0.877; 95% CI=0.835-0.919) is significantly lower for NOD patients than that (AUC=0.953; 95% CI=0.923-0.969) in the AC patients.

Conclusion

We could not perform direct comparisons to previous DS studies in NOD, because the present study is the first to provide evidence that DS could be used to facilitate the diagnosis of NOD among patients with AAP. The major advantages of our DS is that this model does not need imaging, endoscopy or laboratory analyses to reach a relatively high diagnostic accuracy for NOD, compared to clinical findings alone.

Conflicts of Interest

The Authors report no conflicts of interest or financial ties.

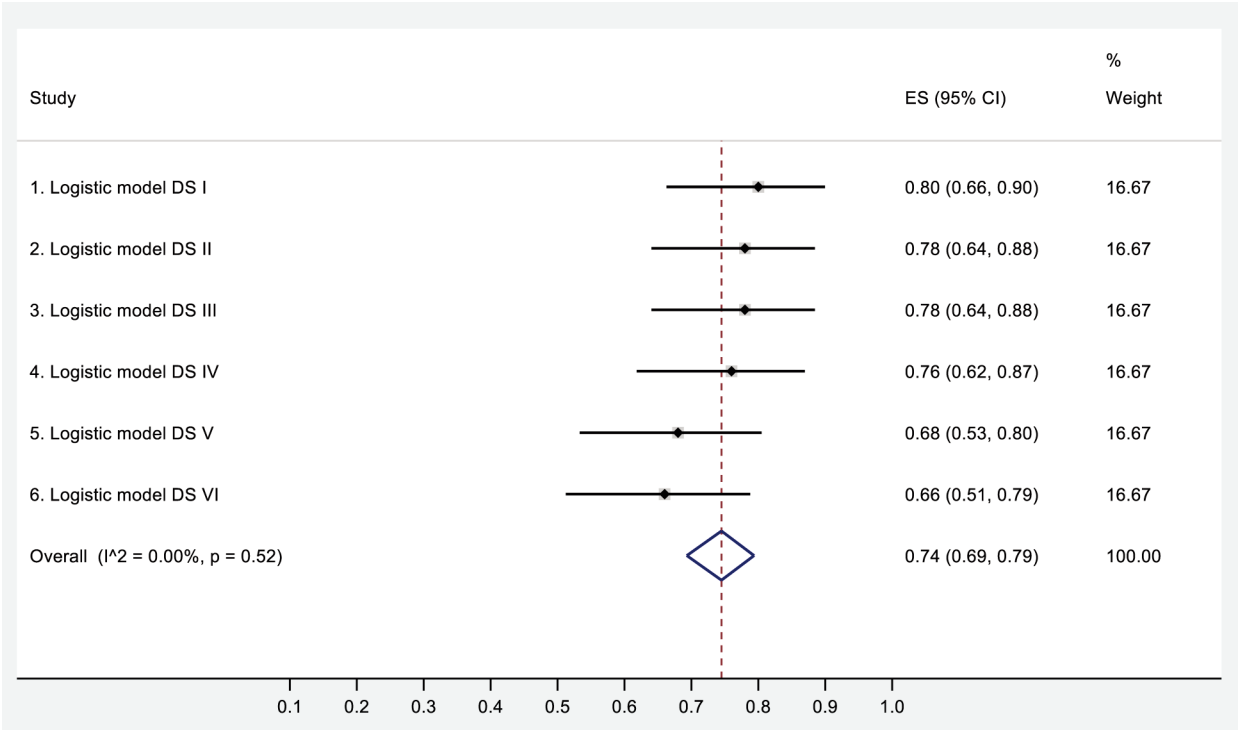

Figure 5. *Sensitivity of diagnostic scores at six different cut-off levels (DS I-VI). ES: Estimated sensitivity; CI: confidence interval.*

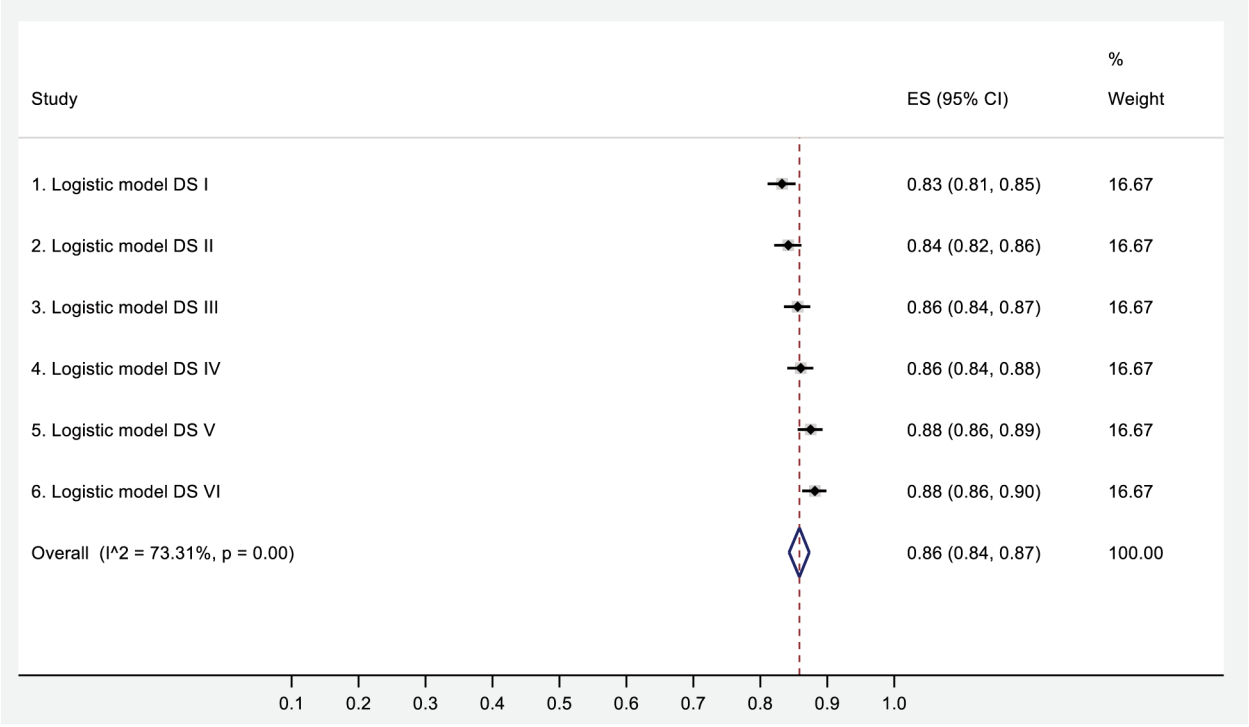

Figure 6. *Specificity of diagnostic scores at six different cut-off levels (DS I-VI). ES: Estimated specificity; CI: confidence interval.*

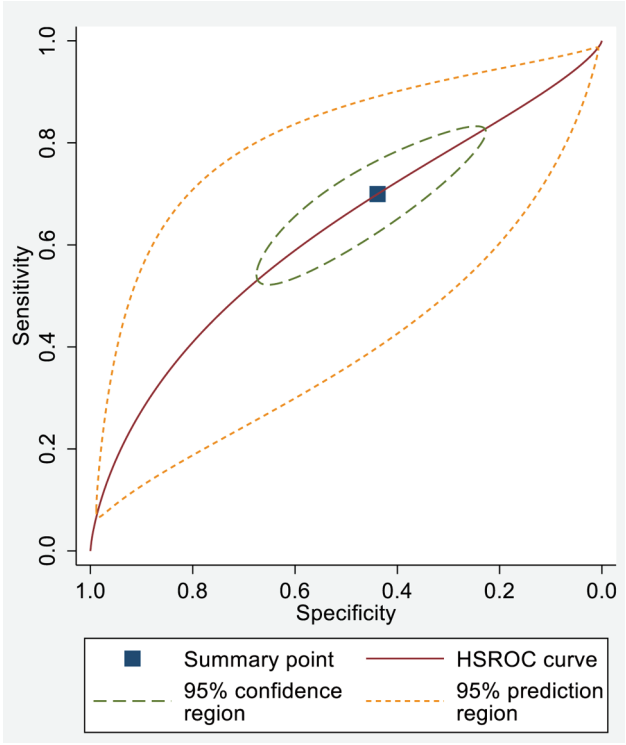

Figure 7. *Hierarchical summary receiver operating characteristic (HSROC) curve of the history-taking in non-organic dyspepsia (NOD).*

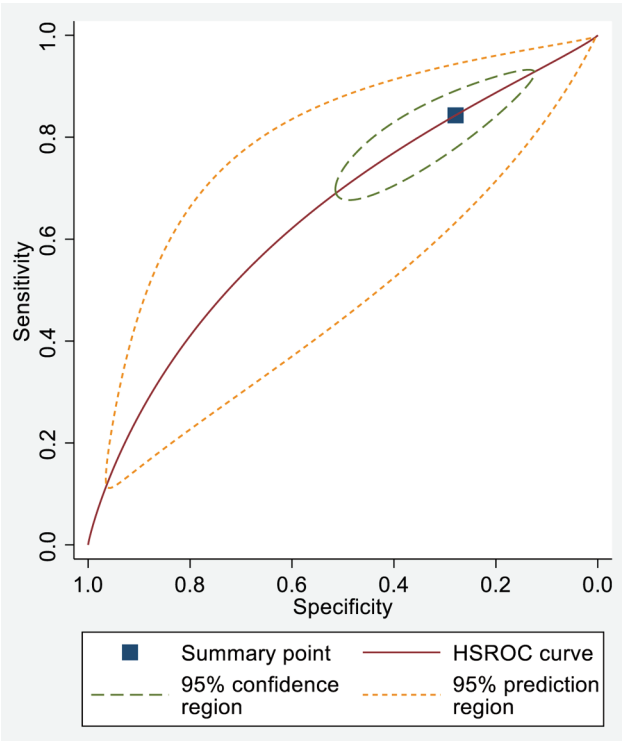

Figure 8. *Hierarchical summary receiver operating characteristic (HSROC) curve of the clinical signs and tests in non-organic dyspepsia (NOD).*

Authors' Contributions

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

Acknowledgements

The study was funded by the Päivikki and Sakari Sohlberg Foundation.

References

1 Talley NJ, Vakil NB and Moayyedi P: American gastroenterological association technical review on the evaluation of dyspepsia. Gastroenterology *129(5)*: 1756-1780, 2005. PMID: 16285971. DOI: 10.1053/j.gastro.2005.09.020

2 Talley NJ and Ford AC: Functional dyspepsia. N Engl J Med *373(19)*: 1853-1863, 2015. PMID: 26535514. DOI: 10.1056/NEJMra1501505

3 Saad RJ and Chey WD: Review article: current and emerging therapies for functional dyspepsia. Aliment Pharmacol Ther *24(3)*: 475-492, 2006. PMID: 16886913. DOI: 10.1111/j.1365-2036.2006.03005.x

4 Barberio B, Mahadeva S, Black CJ, Savarino EV and Ford AC: Systematic review with meta-analysis: global prevalence of uninvestigated dyspepsia according to the Rome criteria. Aliment Pharmacol Ther *52(5)*: 762-773, 2020. PMID: 32852839. DOI: 10.1111/apt.16006

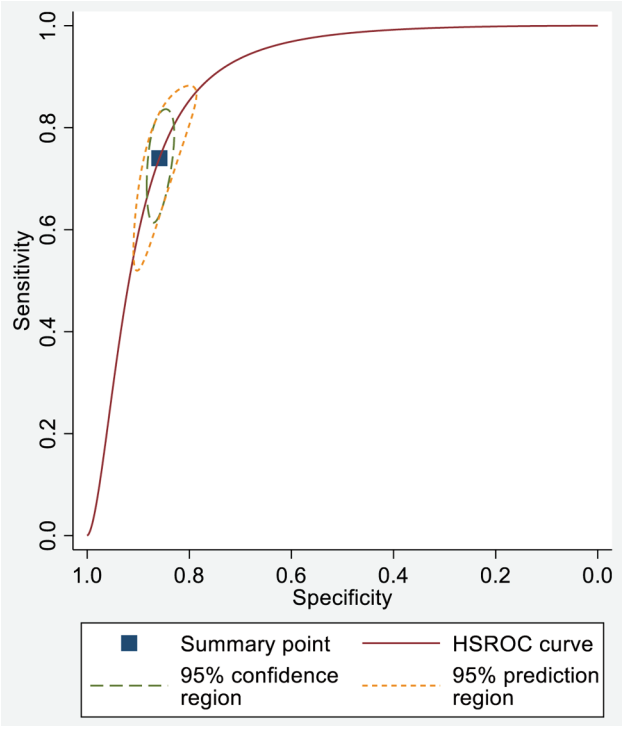

Figure 9. *Hierarchical summary receiver operating characteristic (HSROC) curve of the six diagnostic score models.*

5 Eskelinen M, Selander T, Lipponen P and Juvonen P: History-taking and the Usefulness Index in the diagnosis of functional dyspepsia. Isr Med Assoc J *16(8)*: 497-501, 2014. PMID: 25269341.
6 Heikkinen M, Pikkarainen P, Eskelinen M and Julkunen R: GPs' ability to diagnose dyspepsia based only on physical examination and patient history. Scand J Prim Health Care *18(2)*: 99-104, 2000. PMID: 10944064. DOI: 10.1080/028134300750018981
7 Eskelinen M and Lipponen P: Usefulness of history-taking in non-specific abdominal pain: a prospective study of 1333 patients with acute abdominal pain in Finland. In Vivo *26(2)*: 335-339, 2012. PMID: 22351680.
8 Meklin J, Eskelinen M, Syrjänen K and Eskelinen M: Leucocyte count does not improve the diagnostic performance of a diagnostic score (DS) in distinguishing acute appendicitis (AA) from nonspecific abdominal pain (NSAP). In Vivo *34(6)*: 3327-3339, 2020. PMID: 33144440. DOI: 10.21873/invivo.12171
9 Meklin J, Eskelinen M, Syrjänen K and Eskelinen M: Gender-specific performance of a diagnostic score in acute appendicitis. In Vivo *34(6)*: 3687-3703, 2020. PMID: 33144486. DOI: 10.21873/invivo.12217
10 Eskelinen M, Meklin J, Syrjänen K and Eskelinen M: Pediatric acute appendicitis score in children with acute abdominal pain (AAP). Anticancer Res *41(1)*: 297-306, 2021. PMID: 33419824. DOI: 10.21873/anticanres.14776
11 Eskelinen M, Meklin J, Syrjänen K and Eskelinen M: A diagnostic score (DS) is a powerful tool in diagnosis of acute appendicitis in elderly patients with acute abdominal pain. Anticancer Res *41(3)*: 1459-1469, 2021. PMID: 33788738. DOI: 10.21873/anticanres.14904
12 Eskelinen M, Meklin J, Syrjänen K and Eskelinen M: Performance of a diagnostic score in confirming acute cholecystitis among patients with acute abdominal pain. Anticancer Res *40(12)*: 6947-6956, 2020. PMID: 33288589. DOI: 10.21873/anticanres.14719
13 Eskelinen M, Meklin J, Syrjänen K and Eskelinen M: A diagnostic score for acute small bowel obstruction. Anticancer Res *41(4)*: 1959-1970, 2021. PMID: 33813402. DOI: 10.21873/anticanres.14963
14 Pajala M, Heikkinen M and Hintikka J: A prospective 1-year follow-up study in patients with functional or organic dyspepsia: changes in gastrointestinal symptoms, mental distress and fear of serious illness. Aliment Pharmacol Ther *24(8)*: 1241-1246, 2006. PMID: 17014583. DOI: 10.1111/j.1365-2036.2006.03108.x
15 Talley NJ, Haque M, Wyeth JW, Stace NH, Tytgat GN, Stanghellini V, Holtmann G, Verlinden M and Jones M: Development of a new dyspepsia impact scale: the Nepean Dyspepsia Index. Aliment Pharmacol Ther *13(2)*: 225-235, 1999. PMID: 10102954. DOI: 10.1046/j.1365-2036.1999.00445.x
16 Adam B, Liebregts T, Saadat-Gilani K, Vinson B and Holtmann G: Validation of the gastrointestinal symptom score for the assessment of symptoms in patients with functional dyspepsia. Aliment Pharmacol Ther *22(4)*: 357-363, 2005. PMID: 16098003. DOI: 10.1111/j.1365-2036.2005.02572.x
17 Taylor F, Higgins S, Carson RT, Eremenco S, Foley C, Lacy BE, Parkman HP, Reasner DS, Shields AL, Tack J, Talley NJ and Patient-Reported Outcome Consortium's Functional Dyspepsia Working Group: Development of a symptom-focused patient-reported outcome measure for functional dyspepsia: The functional dyspepsia symptom diary (FDSD). Am J Gastroenterol *113(1)*: 39-48, 2018. PMID: 28925989. DOI: 10.1038/ajg.2017.265
18 Lacy BE, Everhart K and Crowell MD: Functional dyspepsia: Clinical symptoms, psychological findings and GCSI scores. Dig Dis Sci *64(5)*: 1281-1287, 2019. PMID: 30382539. DOI: 10.1007/s10620-018-5347-2

Received May 11, 2021
Revised June 2, 2021
Accepted June 11, 2021