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Systematic Review

Accuracy of diagnostic tests for acute diverticulitis that are feasible in primary care: a systematic review and meta-analysis

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Background: Recognition of acute diverticulitis is important to determine an adequate management strategy. Differentiating it from other gastrointestinal disorders is challenging as symptoms overlap. Clinical tests might assist the clinician with this diagnostic challenge. Previous reviews have focussed on prognostic questions and imaging examinations in secondary care.

Objective: To evaluate the diagnostic accuracy of clinical tests feasible in primary care for acute diverticulitis in suspected patients.

Method: We have systematically searched multiple databases for diagnostic accuracy studies of tests feasible in primary care compared to a reference standard in suspected patients. Two reviewers independently selected studies, extracted data, and assessed study quality with the QUADAS-2 tool. We have meta-analysed the results in the case of more than four studies per index test.

Results: Seventeen studies were included, all studies were performed in secondary care (median prevalence 48%). Individual signs and symptoms showed a wide range in sensitivity (range 0.00–0.98) and specificity (range 0.08–1.00). Of the four laboratory tests evaluated, CRP >10 mg/l had the highest sensitivity (range 0.89–0.96) with specificity ranging from 0.28 to 0.61. Ultrasound had the highest pooled sensitivity and specificity of 0.92 (95% CI 0.86–0.96) and 0.94 (95% CI 0.88–0.97), respectively.

Conclusion: None of the studies were performed in primary care. Individual signs and symptoms alone are insufficiently informative for acute diverticulitis diagnosis. CRP showed potential for ruling out and ultrasound had a high diagnostic accuracy. More research is needed about the diagnostic accuracy of these tests in primary care.

PROSPERO registration numberCRD42021230622

Key words: diverticulitis; signs and symptoms; C-reactive protein; ultrasonography; sensitivity and specificity; general practice

Introduction

Acute diverticulitis, which is characterized by inflammation of colonic diverticula, is an increasingly common condition in elderly people, particularly among women and white ethnic groups.[1–3] Around 20% of those with diverticula will eventually develop it.[1,2] Most patients with acute diverticulitis have a favourable prognosis and can be managed in primary care. Diagnosing acute diverticulitis clinically can be challenging due to its similar symptoms to a wide range of conditions ranging from irritable bowel syndrome to colorectal cancer.[4]

In the hospital, computed tomography (CT) is recommended alongside patients history, physical examination, and laboratory results to assist in diagnosing acute diverticulitis.[5,6] CT scans can help reduce the chance of misdiagnosis and discrepancies between the clinical presentation and severity of the condition, by visualizing the location of an inflamed diverticula.[4] However, in primary care, general practitioners (GP) usually rely on simple tests such as signs and symptoms evaluated by patient history and physical examination, laboratory tests, or ultrasound. Diagnostic tests in primary care for acute diverticulitis should have a high sensitivity to ensure that patients with the condition are not missed. This will enable accurate selection of patients for conservative treatment or referral for surgery in patients with high risk of complications while avoiding missing other serious diseases that may mimic diverticulitis.

Although previous studies have evaluated the diagnostic accuracy of tests for acute diverticulitis,[7–10] no meta-analysis has yet been performed to evaluate the diagnostic accuracy specifically of tests that are feasible in a primary care setting. Therefore, the aim of this systematic review and meta-analysis is to evaluate the diagnostic accuracy of individual signs, symptoms, blood tests, ultrasound, and test combinations for diagnosing acute diverticulitis in patients suspected of acute diverticulitis.

Methods

This systematic review and meta-analysis was reported in accordance with the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies (PRISMA-DTA) Checklist and was prospectively registered in PROSPERO (CRD42021230622).

Key messages

- No review was performed on tests for acute diverticulitis feasible in primary care.
- Signs and symptoms alone are not sufficient in triaging acute diverticulitis.
- C-reactive protein showed potential for ruling out acute diverticulitis in secondary care.
- Ultrasound had a high diagnostic accuracy in secondary care.
- Primary care studies were lacking, more research is needed in this setting.

Search strategy

A systematic literature search was conducted for eligible diagnostic studies in Pubmed, Embase, and Clarivate Web of Science (from inception to 2022 November 2) using Medical Subject Headings, Emtree terms, and free text words related to acute diverticulitis and diagnostic accuracy (Supplementary material 1). The strategy was developed based on a previously published search strategy and in consultation with a medical information expert (central medical library, University Medical Center Groningen).[11] To assure completeness, the references of all included full-text articles were hand-searched by two authors (N.V., M.B.) independently. No language restrictions were applied.

Eligibility criteria

We used five inclusion criteria to select studies for our analysis: (1) the study population consisted of patients over sixteen years of age with symptoms and signs suggestive of acute diverticulitis (e.g. abdominal pain and fever); (2) the study evaluated one or more index tests feasible for primary care, such as individual or combinations of signs, symptoms, routine laboratory tests (e.g. white blood cell count (WBCC) and C-reactive protein (CRP)), or ultrasound; (3) the reference standard for the final diagnosis of acute diverticulitis was CT, colonoscopy, surgery findings (histopathology), and/or findings at follow-up; (4) the target condition was explicitly stated as acute diverticulitis; and (5) the study report, or the subsequent data requested, enabled the construction of a 2 × 2 table. Authors were contacted if data for the 2 × 2 table were insufficient or missing.

We excluded studies that included a population with known acute diverticulitis, healthy controls, studies with fewer than 20 patients, and studies where all reported patients underwent surgery, since this could point to a population consisting mostly of severe diverticulitis cases and their inclusion could introduce spectrum bias.

Study selection, data extraction, and quality assessment

Two reviewers (N.V., G.H.) independently screened titles and abstracts using Rayyan, and screened full-text articles for eligibility.[12] One reviewer (N.V.) extracted data from the full-text papers using a pre-designed data extraction form, and another reviewer (M.B.) verified the data extraction. The following data were extracted: first author, year, country, setting, sample size, prevalence of acute diverticulitis (and if provided complicated diverticulitis), selection criteria and patient characteristics, type of index test(s), test cut offs, reference standard(s), and data for 2 × 2 table(s). Two reviewers (N.V., M.B.) independently assessed the risk of bias and applicability concerns using the QUADAS-2 tool.[13] This is an evidence-based quality assessment tool for diagnostic test accuracy studies. The QUADAS-2 signalling questions were adjusted for the purpose of our review and, when necessary, specified per type of index test (Supplementary material 2). When multiple tests were evaluated in one study, we scored the risk of bias and applicability concerns for each test separately. Any disagreements between reviewers during the process of study selection, data extraction, and quality assessment were resolved through discussion until consensus was reached.

Data synthesis and analysis

Review Manager Web 5.0 (RevMan Web, Cochrane Collaboration Diagnostic) was used to import data from 2 × 2 tables and to construct forest plots for each index test (e.g. symptom, sign, blood test, ultrasound, and test combinations) to present the sensitivity and specificity.[14] Dumbbell plots were drawn for physical examination signs and patients' history symptoms. The dumbbell plots depict pre-test probability, post-negative test probability, and post-positive test probability for a given test. We estimated summary parameters using bivariate random effects model with the metadta program in Stata/SE version 18.0 (Stata Corp, College Station, TX) to calculate the pooled estimates of sensitivity, specificity, and likelihood ratios.[15–17] Summary receiver operating characteristics (SROC) plots with corresponding prediction regions were produced in the case of ten or more studies per index test.[17]

Exploring heterogeneity

We examined heterogeneity by visually assessing the forest plots, and we provided insight to the variation of prevalence of diverticulitis and different study characteristics (e.g. prospective vs retrospective design). We performed subgroup analyses a posteriori for ultrasound on publication year (before or after 2000), and sensitivity analyses a posteriori on the use of point-of-care (POC) ultrasound, because differences between modern and outdated ultrasound devices or between techniques could have impacted results.

Results

The literature search yielded 3,230 studies from we included seventeen studies, involving a total of 5,227 adults with suspected acute diverticulitis, of whom 1,470 (28%) had diverticulitis (Supplementary materials 3 and 4). We contacted five authors for additional data and received data from one.[18]

Fifteen studies included patients prospectively and two studies retrospectively.[19,20] The majority of studies were performed in Europe (twelve studies, N = 4,372, 510 cases),[18,21–31] the rest was performed in Asia (two studies, N = 283, 86 cases)[19,32] and North America (three studies, N = 672, 282 cases)[20,33,34] (Supplementary material 4). The prevalence of

acute diverticulitis in the populations ranged from 11% to 65% (median 48%, IQR 37–58). All studies were performed in secondary care and the majority were performed at the emergency department (eight studies, *N* = 3,511, 881 cases).[21,23,27,28,31–34] Four studies were performed at the radiology department (*N* = 433, 233 cases),[20,24,26,29] two studies at the surgery department (*N* = 976, 166 cases),[18,25] and in three studies the department was not mentioned (*N* = 407, 190 cases).[19,22,30] Fifteen studies used multiple reference standards, usually a combination of clinical outcomes, surgery, CT, follow-up, and clinical experts.[18–32] Two studies used CT alone.[33,34]

Risk of bias

Table 1 presents the risk of bias in the included studies. Ten studies were assessed as demonstrating a high risk of bias in ≥1 domains,[19–21,23,24,27,28,31,33,34] and fourteen studies scored unclear risk of bias in ≥1 domains[19,20,22–33] (Table 1). High risk of bias in the domain patient selection was related to inappropriate exclusions in two studies.[19,21] The domain index test was scored high risk of bias in two studies, because the index test results were interpreted with knowledge of the reference standard,[30] or the threshold was not pre-specified.[23] Six studies scored high risk of bias for the domain reference standard since the studies had only used CT as a reference standard,[33,34] and/or the reference standard was interpreted with knowledge of the index test.[20,23,27,31,33,34] Four studies scored a high risk of bias for domain flow and timing because not all patients were included in the analysis,[26,34] or the time interval between the index test and the reference standard was either too long[20] or too short.[28] Applicability concerns were low in all domains for four studies.[27,29,31,33]

Signs and symptoms

The sensitivity and specificity outcomes were heterogeneous across all signs and symptoms (Table 2, Supplementary materials 5.1 and 5.2). None of the clinical features had a consistently high sensitivity or specificity in more than one study. Notably, one study evaluating pain in right lower quadrant (RLQ) and diffuse pain reported a lower post-positive test probability than post-negative test probability. This study had more false positives than true positives, which could be explained by a very low sample size in combination with the fact that this symptom is not a common predictor for left-sided diverticulitis that was the target condition in this study.

Laboratory tests

Anaemia and sedimentation rate were evaluated in only one study and showed low diagnostic accuracy (Supplementary material 5.3). CRP >10 mg/l (three studies, *N* = 1,203, 271 cases) showed homogenous sensitivities (range 0.89–0.96) and heterogeneous specificities (range 0.28–0.61) (Supplementary material 5.3). In comparison, WBCC (four studies, *N* = 1,297, 284 cases) at cut-offs ranging from >1 to >10 × 10^9 l showed a pooled sensitivity of 0.68 (95% CI 0.54–0.80) and a pooled

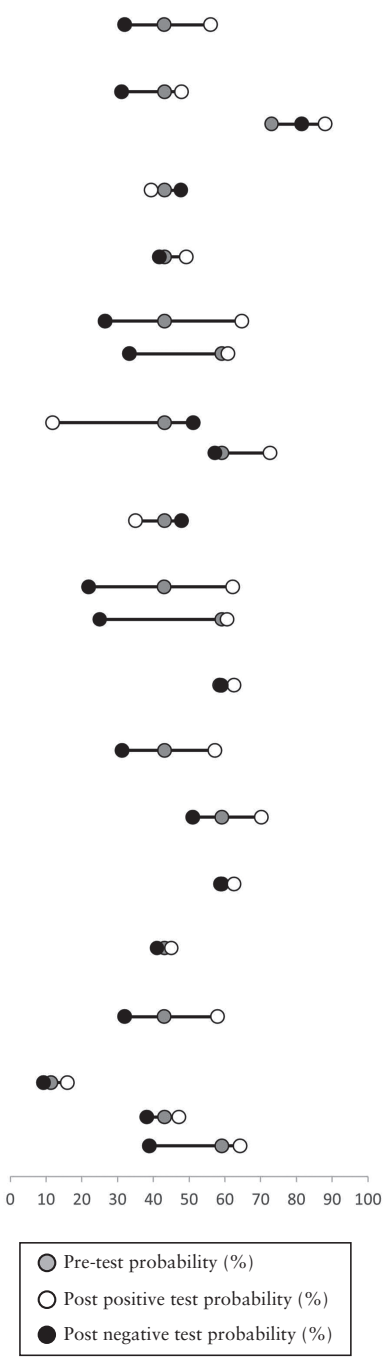
Table 1. Risk of bias assessment for all included studies.

Study	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Andeweg et al. (2011)[21] [a]	High	Unclear	Unclear	Low	High	Unclear	High
	High	Unclear	Unclear	Low	High	Unclear	High
Cohen et al. (2020)[33]	Low	Low	High	Low	Low	Low	Low
Farag Soliman et al. (2004)[22]	Low	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear
Hollerweger et al. (2001)[26]	Low	Low	Unclear	High	Low	High	Low
Jamal Talabani et al. (2017)[18]	Low	Unclear	Unclear	Low	Low	Low	Unclear
Laméris et al. (2010)[27]	Low	Unclear	High	Low	Low	Low	Low
Lee et al. (2008)[32]	Unclear	Unclear	Unclear	Unclear	High	Low	Low
Min et al. (2017)[19]	High	Low	Unclear	Unclear	High	Low	Low
Nazerian et al. (2021)[28] [b]	Unclear	Low	Unclear	High	Low	Low	Unclear
	Unclear	Low	Unclear	High	High	Low	Unclear
Pradel et al. (1997)[29]	Low	Low	Low	Unclear	Low	Low	Low
Schwerk et al. (1993)[30]	Low	Low	Low	Unclear	Low	High	Unclear
Shokoohi et al. (2022)[34]	Low	Low	High	High	Unclear	Unclear	Low
Stefánsson et al. (1997)[31]	Unclear	Unclear	High	Low	Low	Low	Low
Van Randen et al. (2011)[23]	Low	High	High	Low	Low	High	Low
Verbanck et al. (1989)[24]	Low	Low	Unclear	Unclear	High	Low	Unclear
Wilson et al. (1990)[20]	Unclear	Low	High	High	Low	High	Unclear
Zielke et al. (1997)[25]	Low	Low	Unclear	Unclear	Low	High	Low

The table is presented without the incorporation of differential verification bias, because almost all studies scored a high risk of differential verification bias, except the studies of Cohen et al.[33] and Shokoohi et al.[34].
[a]First row of Andeweg et al.[21] is the risk of bias for signs and symptoms, second row for blood tests.
[b]First row Nazerian[28] is the risk of bias for ultrasound, second row is for signs and symptoms.

Table 2 The diagnostic accuracy of patient history's symptoms and clinical examination signs for acute diverticulitis testing

Signs & Symptoms (%prevalence)	Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio + (95% CI)	Likelihood ratio – (95% CI)
Duration of pain >1 day				
Andeweg (43%)	0.61 (0.52–0.70)	0.63 (0.55–0.71)	1,67 (1.30–2.12)	0,61 (0.48–0.79)
Absence of vomiting*				
Andeweg (43%)	0.80 (0.72–0.87)	0.34 (0.27–0.42)	1.20 (1.05–1.39)	0.60 (0.40–0.90)
Nazerian (56%)	0.60 (0.54 – 0.65)	0.64 (0.52–0.75)	1.68 (1.22–2.32)	0.62 (0.50 – 0.77)
Anorexia				
Andeweg (43%)	0.50 (0.41–0.59)	0.42 (0.34–0.50)	0.86 (0.69–1.07)	1.19 (0.93–1.54)
Diarrhea*				
Andeweg (43%)	0.23 (0.16–0.32)	0.82 (0.75–0.87)	1.27 (0.81–2.00)	0.94 (0.83–1.06)
Left lower quadrant pain				
Andeweg (43%)	0.65 (0.56–0.74)	0.73 (0.66–0.80)	2.42 (1.82–3.21)	0.47 (0.37–0.62)
Stefánsson (59%)	0.96 (0.87–1.00)	0.11(0.03–0.26)	1.08 (0.95–1.22)	0.35 (0.07–1.79)
Right lower quadrant pain				
Andeweg (43%)	0.06 (0.02–0.11)	0.68 (0.60–0.75)	0.17 (0.08–0.38)	1.39 (1.24–1.55)
Stefánsson (59%)	0.15 (0.07–0.28)	0.92 (0.78–0.98)	1.85 (0.53–6.49)	0.92 (0.79–1.07)
Diffuse pain				
Andeweg (43%)	0.29 (0.21–0.38)	0.59 (0.51–0.67)	0.71 (0.51–0.98)	1.20 (1.02–1.43)
Left lower quadrant tenderness				
Andeweg (43%)	0.76 (0.67–0.83)	0.65 (0.57–0.72)	2.17 (1.72–2.73)	0.37 (0.27–0.52)
Stefánsson (59%)	0.98 (0.90–1.00)	0.08 (0.02–0.22)	1.07 (0.96–1.19)	0.23 (0.02–2.13)
Right lower quadrant tenderness				
Stefánsson (59%)	0.10 (0.03–0.21)	0.92 (0.78–0.98)	1.15 (0.29–4.53)	0.99 (0.86–1.13)
Rebound tenderness				
Andeweg (43%)	0.60 (0.51–0.69)	0.66 (0.58–0.73)	1.76 (1.36–2.27)	0.60 (0.47–0.77)
Rectal tenderness				
Stefánsson (59%)	0.50 (0.36–0.64)	0.69 (0.52–0.84)	1.64 (0.93–2.87)	0.72 (0.51–1.02)
Left lower quadrant mass				
Stefánsson (59%)	0.10 (0.03–0.21)	0.92 (0.48–0.98)	1.15 (0.29–4.53)	0.99 (0.86–1.13)
Signs of illness				
Andeweg (43%)	0.56 (0.46–0.65)	0.48 (0.41–0.56)	1.08 (0.87–1.34)	0.92 (0.71–1.18)
Aggravation of pain on movement				
Andeweg (43%)	0.59 (0.50–0.68)	0.67 (0.60–0.75)	1.81 (1.39–2.36)	0.61 (0.48–0.77)
Body temperature				
Jamal Talabani (11%)	0.44 (0.34–0.55)	0.71 (0.68–0.74)	1.53 (1.18–1.96)	0.79 (0.65–0.95)
Andeweg (43%)	0.60 (0.51–0.69)	0.48 (0.41–0.56)	1.17 (0.96–1.44)	0.82 (0.62–1.07)
Stefánsson (59%)	0.84 (0.74–0.94)	0.31 (0.16–0.48)	1.25 (0.98–1.59)	0.44 (0.19–1.03)



The dumbbell plots show the probability (%) of having the disease after a positive or negative test result in relation to the probability (%) of having the disease before testing (pre-test probability).
*The study of Lee (2008) used appendicitis as control condition and is therefore not visible in the dumbbell plots.

specificity of 0.56 (95% CI 0.41–0.70) (Table 3). Values for both sensitivity (range 0.54–0.85) and specificity (range 0.47–0.79) were heterogeneous across studies (Supplementary material 5.3).

Combination of tests

Three studies reported the diagnostic accuracy of combinations of tests and/or symptoms (clinical decision tools), where the study of Laméris et al.[27] focussed on tenderness only in the left lower quadrant, absence of vomiting, and CRP >50 mg/l, and showed a high specificity of 1.00 (95% CI 0.99–1.00) and a lower sensitivity of 0.27 (95% CI 0.19–0.36) (Supplementary material 5.4). The study of Lee et al.[35] evaluated a multiple diagnostic criteria score with minor criteria (history of similar pain, no nausea/vomiting, history of diarrhoea/

Table 3. Pooled diagnostic accuracy of white blood cells count and ultrasound for acute diverticulitis testing.

Tests	Studies	Total population (*n* = cases)	Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio + (95% CI)	Likelihood ratio – (95% CI)
White blood cells count (>1–10 × 10^9 l)	4	1,297 (284)	0.68 (0.54–0.80)	0.56 (0.41–0.70)	1.6 (1.1–2.1)	0.56 (0.38–0.83)
Ultrasound	12	2,999 (1,062)	0.92 (0.86–0.96)	0.94 (0.88–0.97)	15.3 (7.7–30.6)	0.08 (0.04–0.15)

constipation, and abdominal pain over 7 days), and major criteria (no pain migration, leukocyte count <10,000/mm³, right-sided abdominal pain and history of right colonic diverticulitis) (Supplementary material 5.4). This showed a sensitivity of 0.85 (95% CI 0.55–0.98) and a specificity of 0.68 (95% CI 0.57–0.77). Stefánsson et al.[31] looked at elevated blood test results (CRP ≥10 mg/l, WBCC >9 × 10^9 l or sedimentation rates with thresholds based on age and sex) and had a sensitivity of 0.90 (95% CI 0.79–0.97) and a specificity of 0.33 (95% CI 0.19–0.51) (Supplementary material 5.4).

Ultrasound

The pooled sensitivity for ultrasound (twelve studies, *N* = 2,999, 1,062 cases) was 0.92 (95% CI 0.86–0.96) and the pooled specificity was 0.94 (95% CI 0.88–0.97) (Table 3). In the SROC plot ultrasound shows an AUC of 0.98 (95% CI 0.96–0.99) (Fig. 1). The ultrasound forest plot show homogeneous outcomes with a sensitivity range of 0.61–1.00 and a specificity range of 0.68–1.00 (Supplementary material 5.5). The subgroup analysis showed that the sensitivity and specificity of studies that were published after 2000 (seven studies) were 0.92 (95% CI 0.84–0.96) and 0.96 (95% CI 0.90–0.99), respectively (Supplementary material 6). A sensitivity analysis without the studies that had used POC ultrasound (ten studies), the sensitivity and specificity were 0.93 (95% CI 0.85–0.97) and 0.94 (95% CI 0.86–0.98), respectively (Supplementary material 6).

Discussion

This systematic review evaluated the diagnostic accuracy of several symptoms, signs, blood tests, ultrasound, and test combinations in adults suspected of acute diverticulitis. The review included seventeen study reports, all of which were conducted in secondary care and reported a high median prevalence of acute diverticulitis (48%, IQR 37–58). Therefore, the results cannot be translated to the primary care where the prevalence, severity, and case-mix is different. The diagnostic performance of individual symptoms was evaluated in a maximum of four studies, and results were heterogeneous and generally reflected limited diagnostic accuracy in secondary care. Among laboratory tests, CRP levels >10 mg/l had the highest sensitivity. The combination of tests from Laméris et al. had a high specificity but a much lower sensitivity as compared to the other clinical decision rules. Results for ultrasound showed a consistently high pooled sensitivity and specificity.

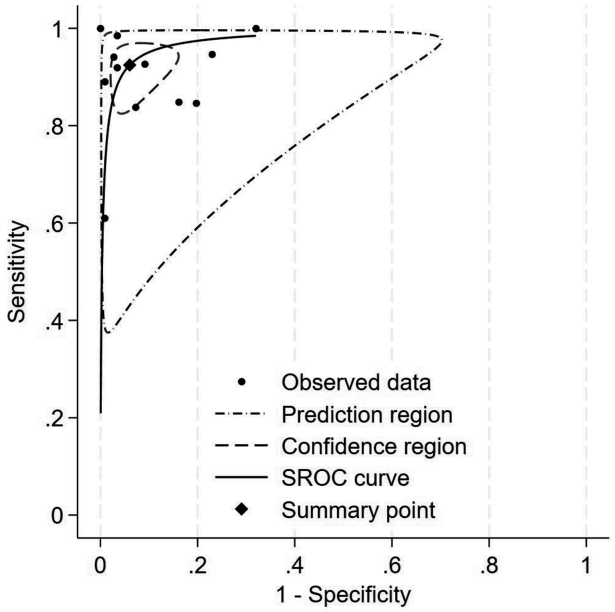


Fig. 1. Summary receiver operating characteristics plot of ultrasound for acute diverticulitis testing.

Strengths and weaknesses of the review

This is the first meta-analysis, to the best of our knowledge, that evaluated the accuracy of tests feasible for the primary care setting for diagnosing acute diverticulitis. We, therefore, explicitly included symptoms and signs. Although we have performed an extensive search in several databases, we found five possible eligible papers via reference checking of which one was included. This might be due to that our search terms were restricted to search for diagnostic accuracy studies in titles and abstracts. We also contacted authors about incorrect or insufficient 2 × 2 tables, and this follow-up enabled the construction of optimal 2 × 2 tables of tests. We presented the data of signs and symptoms with dumbbell plots with pre- and post-test probabilities of acute diverticulitis as this is straightforward to interpret for clinicians.

One limitation is the absence of studies that were performed in primary care, despite evaluating tests that in our view can be feasibly deployed in primary care. Also, patients suspected of diverticulitis first present themselves at the GP's office. Therefore, it is unfortunate that we did not retrieve primary care studies. As a consequence of not finding studies in primary care, we cannot determine the diagnostic accuracy of tests for acute diverticulitis in primary care. The diagnostic

test performance in a secondary care setting may not be directly transportable to a primary care setting as there is a different patient group and prevalence due to a referral filter.[36,37]

There was a huge range in prevalence of diverticulitis among the included cohort studies (range 11–68%). Therefore, there could be a variation in case-mix and severity of the disease between the studies, even though we only have studies from secondary care. However, we did not see a variation of sensitivity or specificity by prevalence in the forest plots.

We have also used data on signs and symptoms derived from the baseline characteristics table from one ultrasound and one laboratory test study.[28,31] This means that in these studies these characteristics were not examined as the primary aim of using them as diagnostics for acute diverticulitis. Another limitation of the study may be that we did not differentiate between right-sided or left-sided diverticulitis as target condition. The localization of the inflamed diverticula can have an impact on the accuracy of signs, symptoms, and ultrasound. Three studies reported on left sided,[21,24,27] two studies on right sided,[19,32] and for the rest no side was specified by the authors.[18,20,22,23,25,26,28–31,33,34]

Interpretation of findings

Diagnostic accuracies varied greatly between studies and were low for signs and symptoms. We saw that studies on individual signs and symptoms are scarce. Of the five studies, only three studies evaluated the diagnostic accuracy of signs and symptoms specifically.[18,21,32] The inclusion criteria of the studies varied, that is, one study included patients with abdominal pain,[18] while one included patients suspected of appendicitis or acute diverticulitis,[32] and three studies included patients specifically suspected of acute diverticulitis.[21,28,31] In addition, two studies excluded patients if they were not referred for imaging.[18,21] Furthermore, predefined criteria or thresholds (e.g. diarrhoea duration, consistency, etc.), and if the signs and symptoms were self-reported or reported by the clinician were unclear in some cases. In our review, patients with a positive test result (e.g. positive abdominal pain localization RLQ) but diagnosed with, for example, appendicitis, were counted as false positives.[38] However, in clinical practice, these patients require medical treatment or further diagnostic investigations and therefore these results are less harmful to the patient. Also, we acknowledge that assessing a patient is a multivariable process and clinicians will not diagnose a patient solely on one sign or symptom.

Regarding laboratory tests, we found high sensitivities for CRP at a cut-off value of >10 mg/l, but lower specificities. This suggests that CRP has potential as a triage test for further diagnostic evaluation, as it can effectively rule out acute diverticulitis in patients with normal CRP values (<10 mg/l). We indicated that the quality of the included studies for CRP was low. This was because two of the studies had patients undergo prior testing since they were selected based on CT request forms.[21,27] Also, it was unclear whether index and reference tests were performed blindly with regard to the outcome of the other.[18,21,31] Another systematic review evaluating predictors of severity of diverticulitis showed that CRP >175 mg/l is predictive of a more severe disease process with a higher likelihood of complications.[10] Although in guidelines CRP and WBCC are recommended to use in combination or together with signs and symptoms, we did not see a potential for WBCC (cut-off value ranges >1–>10 × 10^9/l).[39]

Patients often present with a range of gastrointestinal symptoms that can be difficult to distinguish from those of other gastrointestinal disorders as there are no clear criteria defining the symptoms of diverticular disease.[40] Therefore, International and Dutch National guidelines recommend the combination of multiple tests for the diagnosis of acute diverticulitis.[11,39,41,42] We only found three studies that assessed the diagnostic accuracy of combinations of tests.[27,31,32] The clinical decision rules varied greatly from each other with different combinations of tests evaluated, different aims, and limited sample sizes, presenting a low level of evidence. The clinical decision rule of Laméris et al. had a perfect specificity which was in accordance with their aim, because they wanted to identify suspected patients that did not need imaging to establish the diagnosis.[27] This could be suitable for specialized/referred care, but in primary care a triage test is needed with high sensitivity instead of specificity, to be able to safely rule out acute diverticulitis in order to explore other conditions. The clinical decision rule of Lee et al. was constructed with the aim to distinguish between right-sided acute diverticulitis and appendicitis.[32] In Western countries 90% of the diverticulitis is on the left side of the colon (colons descendens), and in African and Asian countries right-sided diverticulitis (colon ascendens) is more prevalent.[42] This clinical decision rule may, therefore, be more applicable to populations from African and Asian countries than others.

Ultrasound showed a high sensitivity and a high specificity based on twelve studies. Four studies did not comply with the diagnostic criteria that we used for the assessment of the applicability of the index test.[20,23,25,30] Except for one study,[23] these studies were published before the year 2000, thus it could be that the diagnostic criteria changed over time or were not widely available. However, our subgroup analysis showed that publication year did not influence the diagnostic accuracy. Our diagnostic accuracies are in accordance with, to our knowledge, the most recent previous meta-analysis on the diagnostic value of ultrasound, which showed a pooled sensitivity of 0.92 (95% CI 0.80–0.97) and a pooled specificity of 0.90 (95% CI 0.82–0.95).[9] The minimal differences in outcome could stem from slightly different inclusion criteria, for example, with respect to study design.

Implication for practice and research

In secondary care, the NICE guideline recommends blood tests in testing for diverticulitis as the costs of these tests are small and a normal test result could indicate that no imaging (ultrasound or CT) is needed.[39] However, our results showed that only CRP has the potential as a triage test and WBCC does not. A further advantage of CRP is that it can be performed by a POC test enhancing its use in primary care. CRP with a higher threshold of >50 ml/l together with signs and symptoms could indicate which patient needs further imaging.[27] More studies are needed to develop and validate clinical prediction rules in the hospital and the diagnostic accuracy of these tests for diverticulitis in primary care.

Although CT has a higher diagnostic accuracy for acute diverticulitis compared to ultrasound, both can be used as an initial diagnostic tool in the assessment of patient suspected of having acute diverticulitis.[9] Ultrasound examinations are non-invasive and do not involve ionizing radiation and

the POC test could be easily used by the GP. It should be noted that ultrasound evaluated in our included studies was performed by an experienced executor in secondary care, because the experience of the executor and interpreter are crucial factors in the accuracy of ultrasound. A recent systematic review found low ultrasound use among GPs around the world.[43] This could result in lower diagnostic accuracy of ultrasound in the primary care as the average GP is less experienced. Therefore, more studies are needed to evaluate the diagnostic accuracy and applicability of ultrasound in primary care.

Conclusion

The studies are all performed in a secondary care setting, hence not directly generalizable to a primary care population. In hospital patients, symptoms alone are insufficient in triaging for acute diverticulitis. CRP with a cut-off value >10 mg/l showed potential for ruling out acute diverticulitis. In addition, ultrasound showed a high diagnostic accuracy. Although both tests could be easily used as POC tests in primary care, studies are needed to provide insight into the diagnostic accuracy of these test for acute diverticulitis in this setting thereby helping in deciding which patients could be treated in primary care or who needs a referral.

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Supplementary material

Supplementary material is available at *Family Practice* online.

Author contributors

N.D.V. conceptualized and designed the study, selected studies, extracted data, assessed study quality, conducted the analyses, and drafted the initial manuscript; G.A.H. conceptualized and designed the study, selected studies, and critically reviewed and revised the manuscript; M.d.B. conceptualized and designed the study, extracted data, assessed study quality, and critically reviewed the manuscript; H.B. conceptualized and designed the study, critically reviewed and revised the manuscript; M.Y.B. conceptualized and designed the study, critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Conflict of interest

None declared.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

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None declared.

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Data availability

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