SCANDINAVIAN JOURNAL OF GASTROENTEROLOGY
2018, VOL. 53, NO. 10-11, 1291–1297
https://doi.org/10.1080/00365521.2018.1517188

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Development and validation of a diagnostic prediction model distinguishing complicated from uncomplicated diverticulitis

Hendrike E. Bolkenstein[a], Bryan Jm van de Wall[b], Esther Cj Consten[b,c], Job van der Palen[d], Ivo Amj Broeders[b,e] and Werner A. Draaisma[b,f]

[a]Department of Surgery, Meander Medical Centre, Amersfoort, The Netherlands; [b]Department of Surgery, Diakonessenhuis, Utrecht, The Netherlands; [c]Department of Surgery, Meander Medical Centre, Amersfoort, The Netherlands; [d]Department of Research Methodology, Measurement & Data Analysis, University of Twente, Enschede, The Netherlands; [e]Department of Surgery, Meander Medical Centre, Amersfoort, The Netherlands; [f]Department of Surgery, Jeroen Bosch Hospital, 's-Hertogenbosch, The Netherlands

ABSTRACT

Objectives: Most diverticulitis patients (80%) who are referred to secondary care have uncomplicated diverticulitis (UD) which is a self-limiting disease and can be treated at home. The aim of this study is to develop a diagnostic model that can safely rule out complicated diverticulitis (CD) based on clinical and laboratory parameters to reduce unnecessary referrals.

Methods: A retrospective cross-sectional study was performed including all patients who presented at the emergency department with CT-proven diverticulitis. Patient characteristics, clinical signs and laboratory parameters were collected. CD was defined as > Hinchey 1A. Multivariable logistic regression analyses were used to quantify which (combination of) variables were independently related to the presence or absence of CD. A diagnostic prediction model was developed and validated to rule out CD.

Results: A total of 943 patients were included of whom 172 (18%) had CD. The dataset was randomly split into a derivation and validation set. The derivation dataset contained 475 patients of whom 82 (18%) patients had CD. Age, vomiting, generalized abdominal pain, change in bowel habit, abdominal guarding, C-reactive protein and leucocytosis were univariably related to CD. The final validated diagnostic model included abdominal guarding, C-reactive protein and leucocytosis (AUC 0.79 (95% CI 0.73–0.84)). At a CD risk threshold of ≤7.5% this model had a negative predictive value of 96%.

Conclusion: This proposed prediction model can safely rule out complicated diverticulitis. Clinical practitioners could cautiously use this model to aid them in the decision whether or not to subject patients to further secondary care diagnostics or treatment.

ARTICLE HISTORY
Received 4 June 2018
Revised 6 August 2018
Accepted 23 August 2018

KEYWORDS
Diverticulitis; complicated; risk score; diagnostic prediction model; primary care; referral

Introduction

Diverticulitis is a very common disease, which poses a great financial burden on health care. It is one of the most costly gastrointestinal diseases worldwide. In the United States, the costs are estimated at $2.1 billion per year [1]. Most patients (80%) have uncomplicated diverticulitis (UD) which is a self-limiting disease [2,3].

In the past years, evidence which justifies a more conservative approach towards this costly disease has been arising. Two recent randomized clinical trials showed that the use of antibiotics in patients with UD does not provide a beneficial effect and this is now considered obsolete [4,5]. Moreover, recent studies have indicated that UD patients can be safely treated in an outpatient setting [6–9]. The Dutch primary care guideline 'Diverticulitis' recommends to only refer patients who are at risk of complicated diverticulitis (CD) to secondary care (emergency department) for evaluation by surgeon or gastroenterologist [10]. However, a considerable number of patients who present with UD in primary care (general/family practice) are still referred to secondary care, with the consequence of unnecessary diagnostics (ultrasound, CT-scan), treatment and hospital admission. To reduce the health care costs of diverticulitis, these unnecessary referrals should be reduced [11]. Such a strategy would demand a proper diagnostic tool to help distinguish UD from CD at presentation.

The aim of this study is to identify clinical and laboratory parameters that can predict the presence or absence of CD to develop and validate a diagnostic model that can be used for adequate and safe selection of patients at risk for CD.

Materials and methods

Study design

A retrospective cross-sectional study was performed in the Meander Medical Centre, a large regional teaching hospital in the Netherlands. Data were collected between January 2005 and January 2017. The study was approved by the local Institutional Review Board.

CONTACT Hendrike E. Bolkenstein he.bolkenstein@meandermc.nl Meander Medisch Centrum, 3800 BM Amersfoort, The Netherlands

Study population

All adult (>18 y) patients presenting with a first episode of diverticulitis in the emergency department were eligible for inclusion. The diagnosis had to be proven by a Computed Tomography (CT) scan or surgical report. Potentially eligible patients were searched for by using a diagnostic specific code (DBC or DRG), ICD-9 (International Classification of Disease) or ICD-10 codes in the hospital database. In the Meander hospital, all (suspected) diverticulitis patients who present at the ED are primarily evaluated by surgical trainees supervised by a surgeon.

Definition of complicated diverticulitis and secondary care diagnostics/treatment

The primary endpoint was complicated diverticulitis (CD), which was defined as Hinchey >1A based on the radiological reports or surgical reports [12–14]. Secondary care diagnostics are considered as additional imaging in the form of ultrasound or CT-scan. Secondary care treatment might comprise careful observation, analgesics, laxatives, antibiotic treatment, percutaneous abscess drainage and possibly operative intervention, depending on the severity of diverticulitis.

Baseline characteristics

Patient characteristics, clinical signs and symptoms, American Society of Anesthesiologists (ASA) Physical Status classification scores, physical examination, laboratory parameters, CT-findings and initial treatment strategy (e.g., surgery, abscess drainage, antibiotic treatment and careful observation), were collected from hospital records. The review of all medical records was done by H.Bolkenstein and B. van de Wall. If the ASA score was not reported explicitly in the patient record, it was assessed retrospectively from the patient notes (based on comorbidity).

Selection of candidate diagnostic predictors

The most promising diagnostic predictors for CD were preselected based on previous literature [15,16]: three from patient history (gender, age and ASA classification), six from signs and symptoms (duration of symptoms, nausea, vomiting, location of abdominal pain (left lower quadrant or generalized), change in bowel habit and rectal blood loss), three from physical examination (rebound tenderness, abdominal guarding and temperature) and two standard blood tests (C-reactive protein (CRP) and leucocytes). Abdominal guarding was defined as diffuse muscular rigidity on palpation.

Data analysis

All analyses were performed using the statistical software package SPSS 24.0 (IBM Corporation, New York, USA). Results are reported according to the TRIPOD statement [17]. The dataset was randomly split into a derivation and validation set. Multiple imputation techniques were used to impute missing data points to avoid selection bias (multivariable imputation by chained equations, 10 datasets, 25 iterations and healthy convergence). Data were assumed to be missing at random. All reported results are based on the imputed data, where the estimates of interests at the final computational step were combined across the imputed datasets using Rubin's rules [18]. Descriptive statistics are provided for all variables. Continuous variables are presented as means (with standard deviation (SD)) or medians (with inter quartile range (IQR)) according to their distribution. For the categorical variables, the counts and percentages are presented. In the initial analysis, the differences in patient characteristics, signs, symptoms and additional blood tests between patients with and without CD were assessed. Univariable logistic regression analyses were used to calculate the crude odds ratios (OR) with 95% confidence interval (CI) of the independent predictors. Multivariable logistic regression analyses were used in combination with receiver operator curves (ROC) to quantify which (combination of) variables from patient history, physical examination and laboratory measurements are independently related to the presence or absence of CD. Inclusion of relevant diagnostic items in the multivariable model was based on clinical knowledge and *p*-values ($p < .05$). In the first step, all relevant diagnostic predictors from history taking (patient demographics and signs and symptoms) were included. Next, physical examination predictors were added to this selected set of predictors, while keeping the patient history variables selected. Then, the history and physical model was extended by adding (separately and in combination) the blood test results to determine their incremental diagnostic value, both in terms of increase in area under the curve (AUC) and in terms of fewer false-positive and notably false-negative diagnoses. The adjusted OR with 95% CI of the final model were calculated. Nagelkerke's R^2 is presented to illustrate the explained variance of the model. Nagelkerke's R^2 represents the overall performance of the modell by illustrating the distance between the predicted outcome and the actual outcome. Nagelkerke's R^2 can range from 0 to 1, where 1 represents perfect performance. Thus, if Nagelkerke's R^2 increases, the overall performance of the model improves. This final diagnostic model was then validated in the validation dataset, using the same setting, inclusion criteria, outcome and predictors. Diagnostic probability thresholds were introduced based on clinically acceptable percentages of notably false-negative diagnoses to define which combination and order of diagnostic tests yielded the highest diagnostic accuracy (in terms of false-negative (and positive) diagnoses) [19]. Ultimately, a model was developed to predict which patients have an acceptable low probability of CD and can safely be withheld secondary care diagnostic tests or treatment. Thresholds for C-reactive protein (CRP) and leucocytes were introduced to assign points to each variable, based on its regression coefficient. By assigning points to each variable, a scoring system was developed using the method demonstrated by the Framingham Risk Score. This method develops a points system from a multiple logistic regression model,

Table 1. Distribution and association of individual predictors with complicated diverticulitis[1,2].

	Distribution in RISICO study				
	Total $N = 475$	UD $N = 393$ (82%)	CD $N = 82$ (18%)	Association with complicated diverticulitis (>Hinchey 1A)	
Diagnostic Variable[3]				*p*-value	OR (95%CI)
Patient history: demographics					
Female gender; *N* (%)	283 (60)	229 (58)	54 (66)	.22[5]	1.38 (0.84–2.27)
Age in years; mean (SD)	61 (14)	60 (13)	65 (15)	<.01[8]	1.03 (1.01–1.05)
ASA score >2[4]; *N* (%)	56 (12)	44 (11)	12 (15)	.38[6]	1.36 (0.68–2.71)
Patients history: Signs and symptoms					
Duration of symptoms in days; median (IQR)	3 (1–7)	3 (1–5)	4 (2–7)	.07[8]	1.01 (0.98–1.03)
Nausea; *N* (%)	219 (46)	177 (45)	42 (51)	.41[5]	1.25 (0.77–2.03)
Vomiting; *N* (%)	65 (14)	43 (11)	22 (27)	<.01[5]	2.90 (1.58–5.31)
Abdominal pain in lower left quadrant; *N* (%)	256 (54)	218 (55)	38 (46)	.15[5]	0.98 (0.41–2.37)
Generalized abdominal pain; *N* (%)	34 (3)	20 (5)	14 (18)	<.01[5]	3.96 (1.91–8.22)
Change in bowel habit; *N* (%)				<.01[6]	
Diarrhea	84 (18)	60 (15)	24 (29)		2.75 (1.51–5.01)
Obstipation	79 (17)	64 (16)	15 (18)		1.61 (0.82–3.19)
Alternating	28 (6)	20 (5)	8 (10)		2.67 (1.09–6.55)
Rectal blood loss (%)	36 (8)	33 (8)	3 (4)	.19[5]	0.47 (0.14–1.54)
Physical examination					
Rebound tenderness (%)	164 (34)	140 (36)	24 (29)	.23[5]	0.73 (0.42–1.27)
Abdominal guarding (%)	11 (2)	4 (1)	7 (9)	<.01[5]	10.81 (2.53–46.15)
Temperature in Celsius, mean (SD)	37.5 (0.8)	37.5 (0.8)	37.5 (0.8)	.94[7]	1.01 (0.75–1.37)
Blood tests					
CRP (mg/L), median (IQR)	103 (54–166)	96 (51–145)	198 (102–269)	<.01[8]	1.01 (1.01–1.01)
Leucocytes(10^9/L), mean (SD)	12.3 (4.3)	11.9 (3.7)	14.6 (5.7)	<.01[7]	1.14 (1.08–1.21)

[1]All results in this table are results of multiple imputation and are based on univariable evaluation.
[2]Complicated diverticulitis is defined as > Hinchey IA.
[3]Variables are coded such that the reported category indicates a higher risk of complication diverticulitis.
[4]Cut-off value based on previous literature.
[5]Chi^2 test.
[6]Fisher exact Test.
[7]independent *T*-test.
[8]Mann-Whitney *U* test.
UD: uncomplicated diverticulitis; CD: complicated diverticulitis; ASA: American Society of Anesthesiologists; OR: odds ratio; SD: standard deviation; IQR: interquartile range; CI: confidence interval; CRP: C-reactive protein.

using the regression coefficient of each significant predictor [20].

Results

Study population

A total of 1514 consecutive patients presented to the emergency department between January 2005 and January 2017 with a clinically suspected episode of diverticulitis. Of these, 572 patients were excluded as they underwent sonography only ($n = 476$), or they had no radiological examination at all ($n = 96$). A total of 942 patients were included of whom 171 (18%) had CD and 771 (82%) had UD. The dataset was randomly split into a derivation and validation set. The validation dataset contained 467 patients of whom 90 (19%) had CD. The derivation dataset contained 475 patients of whom 82 (18%) patients had CD. The Hinchey classification of the complicated cases in the derivation dataset was as follows: 37 (8%) Hinchey IB, 17 (4%) Hinchey II, 23 (5%) Hinchey III and 5 (1%) Hinchey IV. Of the uncomplicated cases, 250 (64%) patients were treated as in inpatients and 99 (26%) patients received antibiotics. Of the complicated cases, 76 (93%) patients were treated as in-inpatients and 65 (79%) patients received antibiotics. Complicated cases that did not receive antibiotics were all Hinchey IB patients. Patient characteristics are shown in Table 1.

Missing data

All candidate predictors had missing data except for age, gender, and ASA classification. The percentage of missing data per predictor was between 1% (CRP) and 7% (nausea and vomiting). In total 221 (4%) data items were imputed and 375 (79%) patients had a complete dataset for all candidate predictors.

Initial evaluation of candidate predictors

Table 1 shows the diagnostic accuracy of the individual candidate predictors. In the initial evaluation, none of the candidate predictors could safely rule out CD individually. Based on the univariable analysis, the following predictors were selected for inclusion in the multivariable regression analysis: age, vomiting, generalized abdominal pain, change in bowel habit, abdominal guarding, CRP and leucocytes.

Initial model

Table 2 shows the development of the model. In the initial model, four predictors from patient history were retained: age, vomiting, change in bowel habit and generalized abdominal pain. The AUC of this model was 0.70 (95%CI 0.64–0.76). In the next step, abdominal guarding was added to the model. When added to the initial model, this predictor

Table 2. Adjusted Odds Ratios with 95% CI for the probability of complicated diverticulitis[1,2].

Variable	β coefficient[3]	OR	95% CI	*p*-value	AUC (95%CI)	R^2
Model (I) Patient history					0.70 (0.64–0.76)	0.11
Age	0.02	1.02	1.00–1.04	.07		
Vomiting	0.67	1.96	1.00–3.85	.05		
Change in bowel habit						
Diarrhea	0.75	2.12	1.12–4.00	.02		
Obstipation	0.30	1.35	0.66–2.77	.41		
Alternating	0.72	2.06	0.81–5.25	.13		
Generalized abdominal pain	1.03	2.81	1.29–6.13	.01		
Model (II) Patient history and physical examination					0.71 (0.65–0.76)	0.14
Age	0.02	1.02	1.00–1.04	.09		
Vomiting	0.51	1.66	0.81–3.41	.17		
Change in bowel habit						
Diarrhea	0.79	2.21	1.16–4.22	.02		
Obstipation	0.25	1.29	0.61–2.69	.51		
Alternating	0.75	2.12	0.81–5.57	.13		
Generalized abdominal pain	0.97	2.63	1.18–5.88	.02		
Abdominal guarding	1.99	7.34	1.53–35.15	.01		
Model (III) Patient history, physical examination and inflammatory parameters					0.79 (0.74–0.85)	0.27
Age	0.02	1.02	1.00–1.04	.13		
Change in bowel habit						
Diarrhea	0.52	1.69	0.84–3.39	.14		
Obstipation	0.13	1.13	0.52–2.46	.75		
Alternating	1.07	2.93	1.05–8.11	.04		
Generalized abdominal pain	0.89	2.43	1.00–5.91	.05		
Abdominal guarding	2.04	7.70	1.51–39.35	.02		
CRP mg/L	0.01	1.01	1.00–1.01	<.01		
Leucocytes 1×10^9/L	0.09	1.10	1.03–1.17	.01		

[1]All results in this table are results of multiple imputation and analyses are based on multivariate logistic regression analysis with ENTER stepwise selection procedures.
[2]Complicated diverticulitis is defined as > Hinchey IA.
[3]β coefficients are expressed per 1 unit increase for the continuous variables and for the condition present in dichotomous variables.
OR: Odds ratio, CI: confidence interval, AUC: Area under the receiver operating characteristic curve, R^2: Nagelkerke's R^2; CRP: C-reactive protein.

Table 3. Validated final Model[1].

Variable	β coefficient[2]	OR	95% CI	*p*-value	AUC (95% CI)	R^2
Abdominal guarding	2.17	8.79	2.28–33.84	<.01		
CRP mg/L	0.01	1.01	1.01–1.01	<.01		
Leucocytes 1×10^9/L	0.08	1.09	1.02–1.16	.01		
					0.79 (0.73–0.84)	0.29

[1]Analyses based on multivariate logistic regression analysis with ENTER stepwise selection procedures.
[2]β coefficients are expressed per 1 unit increase for the continuous variables and for the condition present in dichotomous variables.
OR: Odds ratio; CI: confidence interval; AUC: Area under the receiver operating characteristic curve; R^2=Nagelkerke's R^2; CRP: C-reactive protein.

was significantly related to CD. Adding the variable only slightly increased the AUC compared with the initial model to 0.71 (95%CI 0.65–0.76). Vomiting did not remain significantly related in this model and was, therefore, removed in the next step.

Added value of inflammatory parameters

When added to the model, CRP and leucocytes were both positively and significantly related to CD risk, both in isolation and when added in combination. The addition of these inflammatory parameters significantly increased the AUC compared with the second model (with predictors from patient history and physical examination) from 0.71 (95% CI 0.65–0.76) to 0.79 (95% CI 0.74–0.85) and led to the development of the final diagnostic model (model III) as depicted in Table 2. This final model (model III) was then validated in the validation dataset by entering all significant predictors that remained in the final model (change in bowel habit, abdominal guarding, CRP and leucocytes) in a multivariable logistic regression analysis. Upon this validation, only three predictors remained significantly related to CD: abdominal guarding, CRP and leucocytes. Table 3 shows the final validated model. The AUC of this model was 0.79 (95% CI 0.73–0.84).

Ruling out CD and risk score

Table 4 shows the diagnostic accuracy of the model at different probability thresholds for CD. A CD risk of ≤7.5% was considered as a clinically acceptable percentage of notably false-negative diagnoses. At this threshold, the final diagnostic model would prevent secondary care diagnostics/treatment in 25% of all patients, with a NPV of 96%. Five CD patients would have been missed, of whom four patients had Hinchey 1B. All these Hinchey 1B

Table 4. Diagnostic accuracy when basing secondary care diagnostics/treatment on varying complicated diverticulitis probability thresholds.

			CD missed (n)					Diagnostic accuracy for CD			
CD risk threshold	% secondary care diagnostics/ treatment (95%CI)	CD detected (n)	Hinchey IB	Hinchey II	Hinchey III	Hinchey IV	Total	Sensitivity % (95%CI)	Specificity % (95%CI)	PPV % (95%CI)	NPV % (95%CI)
≤5%	93 (90–95)	88	2	0	0	0	2	98 (92–100)	8 (6–12)	20 (17–24)	94 (80–99)
≤7.5%	75 (70–78)	85	4	0	1	0	5	94 (88–98)	30 (26–35)	24 (20–29)	96 (90–99)
≤10%	60 (55–64)	78	4	3	5	0	12	87 (78–93)	47 (42–52)	28 (23–34)	94 (89–97)

CD: complicated diverticulitis defined as > Hinchey 1A; PPV: positive predictive value; NPV: negative predictive value; CI: confidence interval.

Table 5. Scoring system to identify complicated diverticulitis.

Diagnostic variable	Points
Abdominal guarding present	4
CRP mg/L	
0–100	0
101–150	3
151–200	4
201–250	5
>250	7
Leucocytes $\times 10^9$/L	
0–15.0	0
15.1–20.0	1
>20.0	2
Point total	Estimate of CD risk (%)
0	4.2
1	6.8
2	10.7
3	16.6
4	24.7
5	35.0
6	47.1
7	59.5
8	70.7
9	79.9
10	86.8
11	91.6
12	94.7
13	96.7

CD: complicated diverticulitis defined as Hinchey > 1A.
CRP: C-reactive protein.

patients were treated conservatively, without further complications. One patient was classified as Hinchey 3, who presented late in the evening with complaints present since 1 h. It is likely that due to the short presence of disease the inflammatory parameters were not yet elevated. The inflammatory parameters were in fact elevated the next morning, and if we introduce these values, the model would classify this patient as CD. The patient received a CT-scan the next morning and went for surgery after confirmation of perforated diverticulitis. When lowering the CD risk threshold to ≤5%, the sensitivity would increase to 98% but the NPV would decrease to 94% and in only 7% of all patients secondary care diagnostics/treatment would be prevented. Increasing the threshold to ≤10% would prevent secondary care diagnostics/treatment in 40% of the patients, but would result in 12 missed CD cases. Table 5 shows a risk score which can be used to calculate the predicted CD risk when combining the individual parameters. The risk score illustrates that when a diverticulitis patient presents with a CRP <100 mg/L, leucocytes $<15.0 \times 10^9$/L and no signs of abdominal guarding (diffuse muscular rigidity on palpation), the risk for CD is very low (4%). Patients presenting with abdominal guarding and/or a CRP >100 mg/L have a much higher risk for CD (16–25%).

Discussion

This study showed that abdominal guarding at physical examination and inflammatory parameters (CRP and leucocytes) are predictors of CD in patients presenting at the ER with a first episode of diverticulitis. Use of a diagnostic model combining these parameters could safely rule out CD with a NPV of 96% at a 7.5% probability for CD. A scoring system was provided to illustrate the predicted CD risk when combining the individual parameters, which can be easily used in clinical practice. The risk score illustrates that when a diverticulitis patient presents with a CRP <100 mg/L, leucocytes $<15.0 \times 10^9$/L and no signs of abdominal guarding (diffuse muscular rigidity on palpation), the risk for a CD is very low (4%). These patients can be safely withheld secondary care diagnostics or treatment. It should, however, be noted that the predicted CD risk derived from the scoring system is less accurate than the predicted CD risk derived from the actual prediction model, as the model uses more accurate continuous values of the individual variables.

There is strong evidence for the safety and cost-effectiveness of outpatient treatment for uncomplicated diverticulitis. Multiple studies have compared outpatient treatment with in-hospital treatment and all conclude that there is no difference between the two groups in morbidity, mortality or patient outcome [6–8]. The next step in increasing the cost-effectiveness of diverticulitis care is to decrease the number of referrals to secondary care. A major concern of not referring patients to secondary care and withholding additional imaging is that the diagnosis 'diverticulitis' cannot be assumed with 100% certainty. Lameris et al. [21]. studied all patients who presented in the ER with abdominal pain and developed a clinical prediction model for diagnosing acute diverticulitis. They concluded that, in a patient who presents with abdominal pain in the lower left quadrant, CRP of >50 mg/L and absence of vomiting, additional imaging can safely be withheld as the combination of these symptoms can accurately diagnose 'acute diverticulitis' with a specificity of 98% and a PPV of 88%. However, only a quarter of patients with suspected diverticulitis presented with these three symptoms [21]. Moreover, the model does not distinguish between UD and CD. Toorenvliet et al. [22]. also analysed the accuracy of clinical diagnosis for diverticulitis and conclude that this is low (PPV 65%, NPV 98%). Ultrasound and CT have superior diagnostic accuracy (PPV 95%, NPV

99%), but rarely change the initial management proposal based on clinical examination [22]. Moreover, as only patients who are at risk of CD should be referred to secondary care for additional imaging or treatment [10], it is pertinent that we identify clinical and laboratory parameters (which are at the disposal of primary care doctors) that can help primary care doctors to diagnose (complicated) diverticulitis.

In a recent systematic review, CRP, leucocytes and clinical signs (constipation, generalized abdominal pain and vomiting) were found to be risk factors for CD [16]. The evidence in the current literature for these findings is, however, weak. The primary aim of the present study was to develop a clinical prediction model, which can safely rule out CD. The ultimate goal is to decrease the number of unnecessary diverticulitis referrals to secondary care, thus improving cost-effectiveness of diverticulitis care. When we started our quest to develop such a model, we aimed to conduct a prospective nationwide study including all patients with a *suspicion of* diverticulitis in primary care who are referred to secondary care, as this is the population of interest. However in the initiation of this study, we encountered several practical issues which made the execution of such a study design not feasible. Considering the large sample size that would be required for this study (at least 600 patients), we would need to include 300 general practitioner (GP) practices as an average GP practice sees only two diverticulitis patients per year. Moreover the definition 'suspicion of diverticulitis' is subjective and this would result in a heterogeneous study population. We, therefore, chose to develop the model in our own population, and accepted subsequent limitations of this study. As this study was conducted in secondary care, it cannot directly be translated to primary care. Moreover, only patients with CT-proven diverticulitis were included, and therefore, we missed all patients suspected having diverticulitis who had gotten other diagnosis after CT. The model is, therefore not applicable to all patients presenting with abdominal pain in the emergency department and when applying the risk score, clinical practitioners should be wary of other (serious) diagnoses. The model can, however, safely select patients that can be withheld further secondary care diagnostics or treatment. If we would combine our results and the results of Lameris et al. [21], we might conclude that patients who have localized left lower quadrant pain, in absence of vomiting and abdominal guarding should be screened by primary care doctors for CRP and leucocyte level. If CRP is less than 100 mg/L and leucocyte count is less than 15×10^9/L these patients may be refrained from additional imaging and referral to a secondary care center. Emergency physicians could also use these findings to select patients that can be discharged home from the emergency department with follow-up with their primary care doctors.

A major strength of this study is the large study population. Following existing guidance for required number of patients in studies aiming to develop prediction models, we needed to include 80–90 subjects with complicated diverticulitis to have sufficient power to identify predictors for complicated diverticulitis. With 82 complicated cases in the derivation dataset and 90 complicated cases in the validation dataset our study population was therefore sufficient to develop a prediction model. Although the study was of a retrospective design, the number of missing values was relatively low (with the highest percentage of missing data per predictor being 7% and a total of 4% missing data). Moreover, we used multiple imputation techniques to prevent selection bias. A prediction model was developed and validated in a cohort of non-overlapping patients, increasing the robustness of the model.

A limitation of the study is that, we did not re-analyse all CT scans to confirm the presence of (un)complicated diverticulitis, but collected this from the initial CT report. Previous studies have shown that reevaluation can give more accurate answers regarding occurrence of complications in diverticulitis. It could, therefore, be that a few complications were missed [23,24]. Another limitation subsequent to the retrospective design is the that physical examination was performed by many doctors with different level of competence and intersect (and different ways to express the assessment in the records). Especially, abdominal guarding can be interpreted differently by different doctors. The primary outcome of this study was CD defined as > Hinchey 1A. We chose this classification as it is the most commonly used in clinical practice. It is, however, questionable whether Hinchey 1B patients should be considered as 'complicated'. Most patients with small abscesses are treated without percutaneous drainage or surgery and recover quickly without further complications [25]. However, to develop a safe prediction model, we felt it was pertinent to retain a strict definition of CD, which is why we chose to define Hinchey 1B patients as complicated.

Previous studies investigating antibiotic and outpatient treatment for uncomplicated diverticulitis excluded patients with high fever (which was not further specified), signs of sepsis, immunosuppression, dehydration, pain needing intravenous treatment, ASA classification > III, pregnant patients and patients who were unable to take care of themselves at home [4,5,7–9]. In the present study, fever was not a predictor of complicated diverticulitis, nor was ASA classification. Dehydration, extensive pain or inability to take care of oneself were not considered in the present study as these are naturally reasons to refer and admit patients to secondary care. Immunosuppression and signs of sepsis were also not considered in the present study. As sepsis is associated with high morbidity and mortality and immunosuppression can increase the complication rate, it stands to reason that these patients should receive secondary care diagnostics and treatment [26]. The present study focused on the clinical diagnosis of complicated diverticulitis, and not the optimal treatment strategy. As stated above, secondary care treatment might comprise careful observation, analgesics, laxatives, antibiotic treatment and possibly operative intervention, depending on the severity of diverticulitis. Previous studies have shown that uncomplicated diverticulitis can be treated at home without antibiotics.

Adequate follow-up is, however, advisable to detect any complications that might arise [4–9].

Conclusion

This study has proven that the proposed prediction model can distinguish uncomplicated from complicated diverticulitis. We suggest that clinical practitioners could use this model in clinical practice to assess the risk of complicated diverticulitis at presentation and aid them in the decision whether or not to subject patients to further secondary care diagnostics or treatment.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] Peery A, Dellon ES, Lund J, et al. The burden of gastrointestinal disease in the united states. Gastroenterology. 2012;143:1179–1187.

[2] Tursi A, Papa A, Danese S. Review article: the pathogenesis and medical management of diverticulosis and diverticular disease of the colon. Aliment Pharmacol Ther. 2015;42:664–684.

[3] Chabok A, Andreasson K, Nikberg M. Low risk of complications in patients with first-time acute uncomplicated diverticulitis. Int J Colorectal Dis. 2017;32:1699–1702.

[4] Daniels L, Ünlü Ç, de Korte N, et al. Randomized clinical trial of observational versus antibiotic treatment for a first episode of CT-proven uncomplicated acute diverticulitis. Br J Surg. 2017;104:52–61.

[5] Chabok A, Påhlman L, Hjern F, et al. Randomized clinical trial of antibiotics in acute uncomplicated diverticulitis. Br J Surg. 2012;99:532–539.

[6] Etzioni DA, Chiu VY, Cannom RR, et al. Outpatient treatment of acute diverticulitis; rates and predictors of treatment failure. Dis Colon Rectum. 2010;53:861–865.

[7] Jackson JD, Hammond T. Systematic review; outpatient management of acute uncomplicated diverticulitis. Int J Colorectal Dis. 2014;29:775–781.

[8] Biondo S, Golda T, Kreisler E, et al. Outpatient versus hospitalization management for uncomplicated diverticulitis: a prospective, multicenter randomized clinical trial (DIVER Trial). Ann Surg. 2014;259:38–44.

[9] Isacson D, Thorisson A, Andreasson K, et al. Outpatient, non-antibiotic management in acute uncomplicated diverticulitis: a prospective study. Int J Colorectal Dis. 2015;30:1229–1234.

[10] Berger MY, De Wit NJ, Vogelenzang R, et al. NHG-standaard diverticulitis. Huisarts Wet. 2011;54:490–498.

[11] Isacson D, Andreasson K, Nikberg M, et al. Outpatient management of acute uncomplicated diverticulitis results in health-care cost savings. Scand J Gastroenterol. 2018;53:449–452.

[12] Hinchey EJ, Schaal PG, Richards GK. Treatment of perforated diverticular disease of the colon. Adv Surg. 1978;12:85–109.

[13] Wasvary H, Turfah F, Kadro O, et al. Same hospitalization resection for acute diverticulitis. Am Surg. 1999;65:632–635.

[14] Kaiser AM, Jiang JK, Lake JP, et al. The management of complicated diverticulitis and the role of computed tomography. Am J Gastroenterol. 2005;100:910–917.

[15] Tan JPL, Barazanchi AWH, Singh PP, et al. Predictors of acute diverticulitis severity: A systematic review. Int J Surg. 2016;26:43–52.

[16] Bolkenstein HE, van de Wall BJM, Consenten ECJ, et al. Risk factors for complicated diverticulitis: systematic review and meta-analysis. Int J Colorectal Dis. 2017;32:1375–1383.

[17] Collins GS, Reitsma JB, Altman DG, et al. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the tripod statement. Br J Surg. 2015;102:148–158.

[18] Rubin D. Multiple imputation for non-response in surveys. New York: John Wiley; 1987.

[19] Rothman KJ, Boice JD. Epidemiologic analysis with a programmable calculator. NIH publications. U.S. Dept. 1979.

[20] Sullivan LM, Massaro JM, D'Agostino RB. RBS Tutorial in biostatistics. Presentation of multivariate data for clinical use: the Framingham Study risk score functions. Statist Med. 2004;23:1631–1660.

[21] Lameris W, van Randen A, van Gulik TM, et al. A clinical decision rule to establish the diagnosis of acute diverticulitis at the emergency department. Dis Colon Rectum. 2010;53:896–904.

[22] Toorenvliet BR, Bakker RF, Breslau PJ, et al. Colonic diverticulitis: a prospective analysis of diagnostic accuracy and clinical decision-making. Colorectal Dis. 2010;12:179–186.

[23] Thorisson A, Smedh K, Torkzad MR, et al. CT imaging for prediction of complications and recurrence in acute uncomplicated diverticulitis. Int J Colorectal Dis. 2016;31:451–457.

[24] Dijk van ST, Daniels L, Nio CY, et al. Predictive factors on CT imaging for progression of uncomplicated into complicated acute diverticulitis. Int J Colorectal Dis. 2017;32:1693–1698.

[25] Dharmarajan S, Hunt SR, Birnbaum EH, et al. The efficacy of nonoperative management of acute complicated diverticulitis. Dis Colon Rectum. 2011;54:663–671.

[26] Sartelli M, Catena F, Ansaloni L, et al. WSES guidelines for the management of acute left sided colonic diverticulitis in the emergency setting. World J Emerg Surg. 2016;11:37.