

Disease Course of Right- and Left-sided Diverticulitis in a Western Population

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Abstract

Aim: To evaluate the similarities and differences in disease courses between right- and left-sided diverticulitis in a Western population.

Methods: All consecutive patients admitted in a Dutch regional hospital between 2004 and 2008 for conservative or operative management of clinically and radiologically confirmed acute right- and left-sided diverticulitis were analyzed retrospectively. Diverticulitis was clinically suspect if the patient presented with lower abdominal pain combined with at least one elevated inflammatory parameter (temperature, WBC, CRP or ESR). Diverticulitis was radiologically confirmed if at least US or CT demonstrated signs of acute right- or left-sided diverticulitis. Differences in incidence, patient characteristics, clinical presentation and disease course between the two diagnoses were analyzed.

Results: The hospital system yielded 425 patients with a diverticulosis/diverticulitis discharge coding. 57% was excluded because these patients had another diagnosis demonstrated by imaging, besides diverticulosis (19%), had no imaging at all (16%), were elective or referred (7%), were not admitted (4%) or had other reasons (11%). A total of 183 admitted patients with both clinical and radiological confirmed acute colonic diverticulitis were included. The incidence of right-sided diverticulitis was 8%. Patients with right-sided diverticulitis were predominantly female (86% compared to 47% in left-sided diverticulitis, $P = 0.05$). Median CRP at presentation was lower in right sided diverticulitis, 30 compared to 71 mg/L ($P = 0.001$). No other differences in clinical presentation, like the severity of diverticulitis, and disease course, like the need for acute surgery, were found between right and left-sided diverticulitis.

Conclusions: Disease course of acute right-sided diverticulitis in Caucasians is comparable to left-sided diverticulitis. Left-sided diverticulitis treatment guidelines may also apply for the right-sided diverticulitis in Caucasians.

Keywords: Acute diverticulitis; Colonic diverticulitis; Cecal disease; Ascending colon; Caucasian

Introduction

It is unusual to diagnose a patient with acute right-sided colonic diverticulitis (RCD) in the Western world. Although RCD is more often diagnosed due to the routine use of radiological imaging, incidence of RCD remains low in the Western world [1-3]. In countries like Korea, China or Japan, the incidence of RCD is about a tenfold higher [4-6]. Therefore, RCD can be described as an Asian disease.

RCD is considered to have another etiology than left-sided colonic diverticulitis (LCD) because the type and location of the diverticula differ between Asians and Caucasians [7,8]. In the Asian population, colonic diverticulitis is merely a disease of middle aged patients, mostly right-sided, and originating from solitary true congenital diverticula in the cecum. The typical muscular wall hypertrophy seen in LCD, is never present in RCD [9-14]. On the contrary, diverticulitis in Caucasians is mainly a disease of the elderly population, commonly

left-sided, and originating from multiple acquired pseudo-diverticula [15-18].

Because LCD and RCD are two distinct phenotypes of diverticular disease, they might also have different disease courses. Because RCD in Caucasians might also develop from acquired pseudo-diverticula in the sigmoid with a left to right sequence, a difference in disease course of RCD between Caucasians and Asians may be expected [19-21].

Treatment of a RCD patient is empirical because all guidelines for diverticular disease regard only left-sided diverticulitis [15-17,22]. These guidelines state that the natural disease course of LCD is usually mild and treatment is mostly conservative. It is unclear whether right-sided diverticulitis has the same natural disease course in Caucasians and can be treated likewise.

In daily practice this means that diagnostic and therapeutic approach of RCD follows the same principles as for LCD. However, results of this approach in Caucasian RCD patients is hardly supported by evidence. The data consist mainly of case series, evaluating patients in whom RCD was diagnosed postoperatively, and point into a more

aggressive therapy in RCD [3,5,19-21,23-25]. However, a high operative rate of RCD precludes knowledge on the natural disease course of RCD. Studies describing Caucasian RCD patients that were diagnosed after radiological imaging are even more scarce and compromise only a total of 81 patients [2,24,26-28] (Table 1).

author	year	country	number of RCD patients	uncomplicated RCD	recurrence	Follow Up (months)
Issa	2012	Israel	15	100%	7%	32
Reisman	1999	Israel	11	64%	18%	40
Fluckiger	1998	Switzerland	6	100%	17%	--
Oudenhoven	1998	Netherlands	44	100%	11%	60
Eggimann	1997	Switzerland	5	100%	--	--

Table 1: Radiological confirmed acute right-sided diverticulitis in Caucasians.

Only one study compared LCD with RCD in Caucasian patients and concluded that RCD is associated with more complications than LCD [24]. In contrast, several Asian studies demonstrate good results of a conservative management of RCD patients. Moreover, these studies demonstrate that acute RCD patients present with less complications and have a milder disease course than LCD patients [4,9,10,12-14,29-31].

The different etiology and possible different disease courses between LCD and RCD, the lack of adequate data for RCD in a Caucasian population and the good results of conservative therapy of RCD in Asian patients were reasons to question whether it is justified to follow the same diagnostic and treatment approach for Caucasian RCD patients as for LCD patients [32]. We hypothesized that the disease course of RCD is similar to LCD in Caucasians patients, and resembles that of RCD in Asians, provided that the diagnosis of RCD is established adequately by imaging. To this purpose we retrospectively analyzed a consecutive series of Caucasian patients who were admitted to the hospital with acute right or left-sided diverticulitis and had imaging.

Materials and Methods

Patients

This retrospective study was performed in a non-teaching hospital in the Netherlands with an adherence of 175.000 inhabitants and encompasses a 5-year period, from January 2004 to December 2008. We searched the electronic hospital information system for the Diagnosis Treatment Combination Code for diverticular disease/diverticulitis to identify all consecutive emergency patients admitted with left or right-sided diverticulitis, who were potentially eligible for inclusion in the study.

Inclusion criteria

All consecutive patients admitted for conservative or operative management of clinically and radiologically confirmed acute LCD or RCD were included. Diverticulitis was considered to be clinically

suspect if the patient presented a history of pain at the left and/or right lower abdomen combined with at least one of the following elevated inflammatory parameters: T > 37.5° Celsius, ESR > 10 mm/hr, or WBC > 10.000/m³ or CRP > 5 mg/L. Radiological diagnosis of diverticulitis was established if at least one imaging modality, US or CT, performed within one week after admission, demonstrated signs of acute LCD or RCD: colonic wall thickness greater than 4 mm, pericolic fat displaying straining and/or signs of complicated diverticulitis like pericolic abscess, pelvic abscess, extraluminal fluid, air or contrast [33]. Acute diverticulitis located in the cecum, ascending colon or proximal transverse colon was classified as RCD. Diverticulitis in the rest of the colon was defined as LCD.

The modified Hinchey-Wasvary classification (stage 0-IV) was used to stage acute diverticulitis (Table 2). Stages 0 and I were considered mild and stages II-IV severe diverticulitis [33,34].

0	Direct visualization of the diverticulum with symptoms
Ia	Confined pericolic inflammation (phlegmon)
Ib	Confined pericolic abscess
II	Distant intra-abdominal or retroperitoneal abscess
III	Generalized purulent peritonitis
IV	Fecal peritonitis

Table 2: Modified Hinchey-Wasvary classification for acute diverticulitis.

Exclusion criteria

If a patient had more than one episode of diverticulitis in the study period (2004-2008) only the first episode is included. Recurrent episodes were not included.

Patients with symptomatic diverticular disease, i.e. confirmed presence of diverticula in the colon, without elevated inflammatory parameters and/or without radiological diagnosis of acute diverticulitis are excluded.

Data extraction

The following data were extracted from the electronic and hardcopy medical records: Patient characteristics: age, gender, previous appendectomy, previous episode(s) of diverticulitis; Clinical presentation: location of abdominal pain, presence of vomiting, body temperature in degrees Celsius; Laboratory findings: ESR in mm/h, WBC in 10³/l and CRP in mg/L; Radiology: type of imaging modality (US and/or CT) for the final diagnosis. Clinical course: conservative or operative management, early operative management (within 30 days after initial hospital admission) and length of hospital stay (days). In case of RCD, follow-up investigations, i.e. colonoscopy and colonic enema were documented and patients were interviewed by telephone regarding the number of recurrences and surgery for RCD. The duration of follow up was defined by the number of years between the first admission for RCD and last month of data accrual (September 2013).

Statistical analysis

Differences in patient characteristics between the group with LCD and RCD were analyzed using the Mann-Whitney U test for

continuous data because of the large discrepancy in numbers between the groups, and with Fisher's exact test for categorical data. SPSS software (PASW statistics 20.0) was used to analyze data. The statistical methods of this study were reviewed by HJ van der Zaag-Loonen, MD, epidemiologist from the Department of Epidemiology, Gelre Hospitals in Apeldoorn, The Netherlands.

Results

The hospital information system revealed 425 patients with the diverticular disease/diverticulitis code during the 5 year study period of whom 183 (43%) unique patients were eligible for analysis. Patients were excluded because US or CT was negative for acute diverticulitis but demonstrated another diagnosis, besides presence of diverticulosis (19%) or was not performed at all (16%) (Figure 1). The remaining 22% of the patients was excluded for duplicity, elective surgery for complications of diverticulitis, referred from other hospitals or were not admitted at all. The clinical diagnosis of diverticulitis proved false in 79/279 (28%) of the patients.

A total of fourteen patients (8%) was diagnosed with RCD. Table 3 summarizes the annual incidence of RCD compared to LCD.

	2004	2005	2006	2007	2008	Total
RCD patients	2	6	1	2	3	14
LCD patients	37	31	35	39	27	169
Total	39	37	36	41	30	183
incidence of RCD	5%	16%	3%	5%	10%	8%

Table 3: Annual incidence of admitted patients with right- and left-sided diverticulitis.

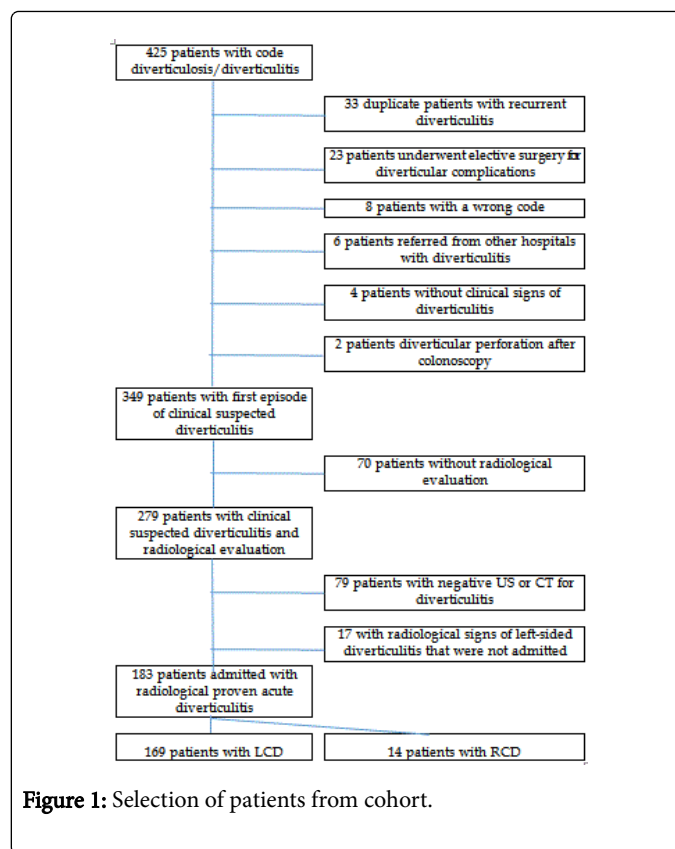


Figure 1: Selection of patients from cohort.

Table 4 summarizes the patient characteristics and clinical outcome of patients with acute LCD lower (P = 0.001). No other differences were found in patient characteristics, clinical presentation or disease course data between patients with RCD and with LCD. More specifically the percentage of severe diverticulitis cases and of operative treatment was comparable.

	RCD (14)	LCD (169)	P value
patient characteristics			
mean age (years)	53 ± 15	56 ± 13	
gender (M/F)	2/12 (14%)	90/79 (53%)	0.05
history of acute appendicitis	4 (29%)	23 (14%)	
history of diverticulitis	2 (14%)	41 (24%)	
clinical presentation			
pain left lower abdomen	0	159 (94%)	
pain right lower abdomen	14 (100%)	51 (30%)	
pain left and right lower abdomen	0	41 (24%)	
vomitus present	2 (14%)	24 (14%)	
mean body temperature	37.0 ± 0.6	37.4 ± 0.8	
median CRP(mg/L)	30 (5-228)	71 (1-413)	b<0.01
median WBC (X103/l)	13.2 (6.5-27.7)	13.2 (1.5-27.4)	

median ESR (mm/h)	32 (2-78)	33 (0-149)	
US performed	14 (100%)	162 (96%)	
CT performed	6 (43%)	46 (27%)	
mild diverticulitis	14 (100%)	154 (91%)	
clinical course			
median days of hospital stay	5.5 (3-8)	6.0 (1-49)	
operative treatment < 30 days	2 (14%)	18 (11%)	

Table 4: Disease course in confirmed acute right- and left-sided diverticulitis.

Table 5 describes patient characteristics and clinical outcome of all patients with acute RCD in detail. Two out of 14 RCD patients underwent immediate surgery after initial radiological imaging. Both patients had inconclusive radiological findings of an atypical

appendicitis or cecal diverticulitis. A gridiron incision was performed in both patients and an inflamed cecum with a normal appendix was seen.

Case, age/sex	Clinical diagnosis	DoS (day)	T	ESR	WBC	CRP	US/CT	radiology diagnosis	HW	Treatment	HS (day)	FU (year)	FU exam
1, 65/F	APP	3	37.2	34	11.9	10	US	RCD/APP	Ia	AB	6	10	CE
2, 61/M	RCD	1	36.9	2	17.6	21	US	RCD	Ia	AB	5	8	CE+CS
3, 62/F	CHOL	1	35.4	5	27.7	10	US	RCD/MAL	Ia	AB	5	8	CE
4, 73/F	RCD	21	37.2	59	8.6	5	US	RCD/MAL	Ia	AB	8	6	CE+CS
5, 67/F	RCD/APP	2		72	12.6	43	US	RCD	Ia	AB	6	6	CS
6, 31/F	APP	5	37.5	36	15.2	40	US	RCD	Ia	AB	5	6	CS
7, 39/F	APP	1	37.2	78	13.8	161	US	RCD	Ia	SUP	3	5	CE+CS
8, 54/F	PN	14	37.1	42	8.3	60	US+CT	RCD/MAL	Ia	AB	8	6	CS
9, 61/F	APP	2	36.3	26	9.1	8	US+CT	RCD/MAL	Ia	AB	5	8	CS
10, 41/F	APP/RCD	3	36.7	2	16.2	11	US+CT	APP /RCD	Ia	ICR	3	9	none
11, 51/F	APP	2	37.4	41	16.5	43	US+CT	RCD/APP	Ia	AB	7	8	none
12, 44/F	GE	1	37.7	6	20	50	US+CT	RCD	Ia	AB	7	8	CE
13, 78/M	APP	2	37.5		6.5	39	US+CT	RCD	Ia	AB	6	7	none
14, 44/F	APP	2	-	8	9.9	16	US	APP/RCD	Ia	ICR	4	9	none

DoS: Duration of Symptoms; T (°Celsius); HW: Modified Hinchey-Wasvary classification; HS:hospital stay; FU: Follow-up; FU exam; M: male; F: female; RCD: Right-sided colonic diverticulitis; APP: Appendicitis; CE: Colon Enema; CE: Colonic enema; CS: Colonoscopy; CHOL: Cholecystitis; MAL: Malignancy; SUP: Supportive therapy PN: PyeloNefritis; ICR: IleoCecal Resection; GE: GastroEnteritis

Table 5: Patient characteristics and outcome of patients with acute right-sided diverticulitis.

Uncertainty concerning the diagnosis led to ileocecal resection in both patients. Both recovered uneventful. Histopathological examination demonstrated a non-inflamed appendix and a solitary inflamed diverticulum in the cecum in both cases. The 12 remaining RCD patients were successfully managed by conservative means with a median hospital stay of 6 days. One patient had a prolonged hospital stay for non-RCD related reasons. All RCD patients had a follow up with a median time of 7 (range 5-10) years. Follow up colonoscopy was not performed in one patient due to significant co-morbidities and refused by another patient. Only one patient, a 31-year old female, experienced a second episode of RCD (recurrence rate 7%), which was again successfully treated without operation. None of the RCD patients had late elective or acute surgery for RCD during the follow-up period. Combining the radiological findings with the postoperative pathology reports or follow-up colonoscopy reports, it was concluded that ten patients had a solitary diverticulum and four patients had multiple diverticula present in the cecum and ascending colon.

Discussion

This study questioned whether right-sided diverticulitis has the same natural disease course in Caucasians as left-sided diverticulitis, despite the supposed differences in etiology. This was evaluated retrospectively by assessing differences in clinical presentation and disease course of right- and left-sided diverticulitis in Western patients. This study demonstrated that the disease course of RCD resembles that of LCD in Caucasians, and that the diagnostic and therapeutic approach can be similar.

Major strength of this study is the use of patients with proven diverticulitis. Elevated inflammatory parameters in combination with positive radiological imaging results excludes the erroneous inclusion of patients with an assumed but later unconfirmed diagnosis of diverticulitis. In general, the interpretation of many study results on diverticulitis is hampered by the lack of a classifying diagnosis based on radiological imaging. Comparing RCD with LCD is even more difficult because most studies on RCD in Caucasians lack pre-operative radiological evaluation and are based on intra-operative findings. Hence, imaging is recommended in the diagnostic process of diverticulitis [22,35].

Interpretation of the results is limited by the retrospective nature of this study, the single center design and the relatively small number of RCD patients compared to LCD patients. Also, because standard US or CT was not a routine in the studied episode for every patient presenting with acute indeterminate right or left lower abdominal pain, the true incidence of both left- or right sided diverticulitis might have been underestimated. The mild clinical presentation of RCD may also explain the relative low incidence of RCD in the Western world whereby most patients are not referred to a hospital and remain undiagnosed.

This study demonstrates that RCD is about twelve times less common than LCD in a cohort of Western patients. The 8% prevalence of RCD is in accordance with that reported in literature [24,27,36]. For comparison, this percentage varies between 60-90% in Asians with acute diverticulitis [4,30].

Our study shows a predominant prevalence of RCD in elderly females in contrast to young males in Asian studies [8]. RCD in elderly female patients suggests an acquired origin of diverticula at the right side similar to that at the left side. However, in more than 70% of our patients RCD originated from solitary diverticula, indicative of true

diverticula. Whether a right-sided diverticulum is a true congenital or an acquired pseudo-diverticulum, this study demonstrates that the clinical outcome when the diverticulum is inflamed is not different from LCD in Caucasian patients.

In the past, many studies advocated an aggressive, i.e. operative, treatment of RCD in Caucasians [3,5,19-21,23-25]. The historical concept that RCD in the Western world was a more aggressive disease than LCD was merely a reflection of the unfamiliarity with this disease, an inadequate diagnostic workup and decision making in the operating room.

Arguments exist to believe that RCD even has a milder clinical course than LCD in our patients based on a lower level of CRP and lower rate of severe diverticulitis at presentation, comparable to RCD in the Asian population. In addition, the recurrence rate of RCD of 7% in 7 years follow up in our study, is lower than that reported of LCD (up to 10-20% in 10 years) [4,11,18,33,37-39].

Successful results of non-operative management of uncomplicated RCD in both Western and Asian patients have been published before [6,12,14,24,28-31,37,40]. All but one of our RCD patients received antibiotics as part of their conservative treatment. Oudenhoven [28] and Lee [30] already demonstrated excellent results from non-antibiotic treatment for RCD. No need for antibiotics and successful conservative treatment in the majority of patients supports the theory that RCD in Western patients is in fact a self-limiting disease.

A Caucasian patient with pain in the lower right abdomen suspected of an acute inflammatory process benefits from radiological imaging to avoid unnecessary surgery. Taking into account the mild disease course of RCD demonstrated by this study and the good results of non-operative, and even non-antibiotic, therapy found in recent Asian studies, it seems justified to use the same diagnostic and treatment guideline for both left- and right-sided diverticulitis. Imaging also allows clinicians to determine the optimal management according to the severity of the diverticulitis [40]. This policy will definitively shift RCD from a surgical diagnosis to a radiological diagnosis.

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