



SYSTEMATIC REVIEW

Caecal diverticulitis can be misdiagnosed as acute appendicitis: a systematic review of the literature

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Abstract

Aim: Caecal diverticulitis (CD) is an uncommon condition which can be misdiagnosed as acute appendicitis due to similar clinical presentations. Further, its management varies among medical centres. The aim of this study was to review cases of patients with CD, to identify the factors differentiating CD from acute appendicitis and to provide a summary of existing diagnostic methods and therapeutic alternatives regarding its management.

Methods: This systematic review was conducted in accordance with the PRISMA guidelines and the AMSTAR2 checklist. We searched MEDLINE and Embase from inception until 1 October 2018 for original publications reporting cases of CD.

Results: Out of the 560 identified studies, 146 publications (988 patients) were included in the qualitative synthesis. Most frequent symptoms of CD were right iliac fossa pain (93.2%), nausea and/or vomiting (35.4%) and fever (26.9%). A total of 443 patients (44.8%) underwent radiological imaging, which reported CD in 225 patients (22.8%). For the other patients, the diagnosis was obtained by surgical exploration (73.9%). Among patients diagnosed with CD by imaging, 67 (29.8%) underwent surgery and 158 (70.2%) were treated conservatively. Among patients who underwent surgical exploration, treatment consisted most frequently of right hemi-colectomy (33%), appendectomy (18.8%) and diverticulectomy with appendectomy (16.3%).

Conclusion: CD can be misdiagnosed as acute appendicitis, therefore resulting in unnecessary surgical exploration. The review of the literature starting from 1930 highlights the critical role of medical imaging in supporting the clinician to diagnose this condition and administer adequate treatment.

KEYWORDS

appendicitis, caecal diverticula, caecal diverticulitis, colorectal surgery, diagnosis, treatment

INTRODUCTION

Caecal diverticulitis (CD) was first described by Potier in 1912 [1]. It is a rare condition, representing 3.6% manifestations of diverticular

diseases [2–4]. CD is especially found among the Asian population, in whom diverticular disease predominates in 70% of the cases on the right side of the colon and is solitary in 80% of cases [5]. The exact aetiology of CD remains unknown, but it has been suggested that

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it originates from a congenital defect that appears during the sixth week of gestation as an out-pouching involving the three layers of the colonic wall, frequently termed 'true' diverticulum [6,7]. It can also be acquired (known as 'false' diverticulum) from a protrusion of the mucosa and submucosa through a weakness of the muscular layer, as seen in left sided diverticular disease, predominantly found in Western and industrialized countries [8]. Fifty per cent to 60% of caecal diverticula are found on the anterior wall of the caecum, and the remaining cases are on the posterior wall [4]. They usually remain asymptomatic but can become inflamed in up to 13% of patients, causing a variety of symptoms like pain, bleeding and peritonitis (if perforated) [4,9,10]. Most of the time, CD manifests itself with right iliac fossa pain, and often gets misdiagnosed as acute appendicitis. The diagnosis and management can therefore become very complex, especially if imaging is not easily accessible.

The aim of this study was to conduct a review of reported cases of patients suffering from CD, to identify the factors differentiating CD from acute appendicitis and to provide a summary of existing diagnostic methods and therapeutic alternatives regarding its management.

MATERIALS AND METHODS

The present methodology is in accordance with the PRISMA recommendations and the AMSTAR2 checklist (Tables 1 and Appendix S5).

Literature search and study selection

A literature search was conducted in MEDLINE and Embase from inception to 1 October 2018, searching for studies on cases of CD using the keywords 'cecal diverticulitis', 'caecal diverticulitis' and 'cecal diverticula'. Additional records were identified by probing the reference lists of included publications. To be included, studies had to be written in English or French, report cases of CD, indicate the number of patients and their characteristics (age, gender) and specify the symptomatology, the diagnostic tools used and the types of treatment. Publications that did not meet these criteria were excluded. Conference abstracts, letters to the editor, as well as secondary analyses of previously published papers were also excluded.

Data extraction

Two independent authors (IU, MV) independently selected articles for inclusion and extracted the data according to a pre-established data collection form. Discrepancies were resolved by reaching a consensus with a third author (SN). The following data were extracted: country of the first author, date of publication, number of patients, gender, pain location, other gastrointestinal symptoms (nausea, vomiting, bowel movement alteration such as diarrhoea or

constipation), fever, white blood cell count, type of radiological imaging performed, type of treatment.

RESULTS

Literature search

In all, 314 publications were identified in MEDLINE and 246 in Embase, and five records were added after reference screening of the included articles. There were 136 duplicate studies which were excluded. Of the 424 publications that were identified as eligible, 81 were excluded because they were not written in French or English and 30 because they were not original publications. In total, 138 publications were excluded after title/abstract screening for not reporting cases of CD. Fourteen publications were excluded because the full text was not available. During full-text screening, 20 publications were further excluded. Ultimately, 146 publications were included in the qualitative synthesis (Figure 1).

Characteristics of included publications

Eighty-six articles were case reports and 59 were retrospective case series. One paper was a prospective case series [11]. All articles but one [12] were monocentric studies. Fifty-four papers came from the USA (37.5%), 44 from Europe (30.6%), 16 from the Middle East (11.1%), 14 from Asia (9.7%), seven from Oceania (4.9%), six from Canada (4.2%) and three from South Africa (2.1%). The information about the origin could not be identified for two articles [13,14]. Eighty articles (80/146, 54.8%) were published before 1980 [12-91] and 66 (66/146, 45.2%) after 1980 [2-4,7,9,11,92-151] (Figure 2, Appendix S1).

Clinical and biological presentation of caecal diverticulitis

Included publications aggregated 988 patients, 301 in papers published before 1980 and 687 after 1980. The included patients were 513 men and 456 women, with ages ranging from 20 to 73 years. The details of gender were not available for 19 patients. Of the total, 662 patients complained of abdominal pain (662/988, 67%). Among them, 617 patients (617/662, 93.2%) had abdominal pain located in the right iliac fossa. The pain was diffuse in 13 (13/662, 1.9%), periumbilical in 11 patients (11/662, 1.7%), located in the superior hemi-abdomen (epigastrium, right or left hypochondrium) in 10 (10/662, 1.5%) and in the inferior hemi-abdomen in 11 (11/662, 1.7%). In all, 210 patients (210/590, 35.6%) had nausea and/or vomiting. Information about the presence or absence of bowel movement alteration was present in 495 patients (495/988 patients, 50.1%); nine had haematochezia (9/495, 1.8%), 77 (77/495, 15.6%) had bowel movement alteration (diarrhoea or constipation) and the rest had no

TABLE 1 PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
Title			
Title	1	Identify the report as a systematic review, meta-analysis or both	1
Abstract			
Structured summary	2	Provide a structured summary including, as applicable, background; objectives; data sources; study eligibility criteria, participants and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	4
Introduction			
Rationale	3	Describe the rationale for the review in the context of what is already known	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes and study design (PICOS)	5
Methods			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., web address) and, if available, provide registration information including registration number	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale	5–6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated	N/A
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis)	5–6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made	N/A
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means)	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis	N/A
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies)	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified	N/A
Results			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram	6

(Continues)

TABLE 1 (Continued)

Section/topic	#	Checklist item	Reported on page #
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations	6
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12)	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms) present for each study: (a) simple summary data for each intervention group; (b) effect estimates and confidence intervals, ideally with a forest plot	6–8
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15)	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see item 16])	N/A
Discussion			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users and policy makers)	8–10
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias) and at review level (e.g., incomplete retrieval of identified research, reporting bias)	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research	10
Funding			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review	8–10

From Moher et al. [166]. For more information see www.prisma-statement.org.

gastrointestinal symptoms. In total, 119 patients (119/443, 26.9%) had fever $\geq 38^{\circ}\text{C}$. An elevated white blood cell count >11 G/l was described in 256 patients (256/411, 62.3%) (Table 2).

Radiological presentation and diagnosis of caecal diverticulitis

In all, 443 patients (443/988, 44.8%) underwent radiological imaging (Figure 3). Based on the radiological results, a diagnosis of CD could be successfully established in 225 cases (225/988, 22.8%). Acute appendicitis was incorrectly diagnosed in 85 cases (85/988, 8.6%).

Before 1980, 44 of the 301 patients had a radiological workup (44/301, 14.6%), 15 with an abdominal X-ray and 29 with a barium enema. Fifteen were diagnosed with CD (15/988, 0.01%).

After 1980, 399 of the 687 patients had radiological imaging (399/687, 57.1%), of whom 202 got a CT scan (202/443, 45.6%), 80 an abdominal ultrasound (US) (80/443, 18.1%), 27 a barium enema and 29 an abdominal X-ray (29/443, 0.07%). The remaining details are described in Figure 3. CD was diagnosed in 210 patients (210/988, 21.3%). Most of these patients had a CT scan (154/225 patients, 68.4%).

In all, 413 patients (413/988, 41.8%; essentially those reported in the oldest publications) did not benefit from a preoperative imaging

workup. Preoperative diagnosis included notably acute appendicitis (281/988, 28.4%), appendicular abscess (9/988, 0.9%) and colorectal cancer (4/988, 0.4%) (Appendix S4). Except for one patient with suspicion of appendicular abscess treated conservatively, these patients were all taken to the operating room.

In 132 patients (132/988, 13.4%), the information about an imaging workup was not available or unclear in the paper. Among them, 104 (104/988, 10.5%) had a diagnosis of acute appendicitis. Consequently, a total of 470 patients had a preoperative diagnosis of acute appendicitis (470/988, 47.6%).

Treatment of caecal diverticulitis

In total, 191 patients (191/988, 19.3%) underwent conservative management consisting of antibiotics, hydration and bowel rest. This group included 33 patients with an alternative diagnosis and 158 of the 225 cases originally diagnosed radiologically with CD (158/225, 70.2%) (Figure 4). Furthermore, it should be noted that among these 158 patients, 6.3% (10/158) had recurrent symptoms of CD and five patients originated from the 15 patients diagnosed before 1980.

In total, 797 patients (797/988, 80.7%) were taken to the operating theatre (Figure 4), of whom 293 of 301 patients were in the group before 1980 (293/301, 97.3%).

FIGURE 1 PRISMA flowchart of the inclusion process and article selection

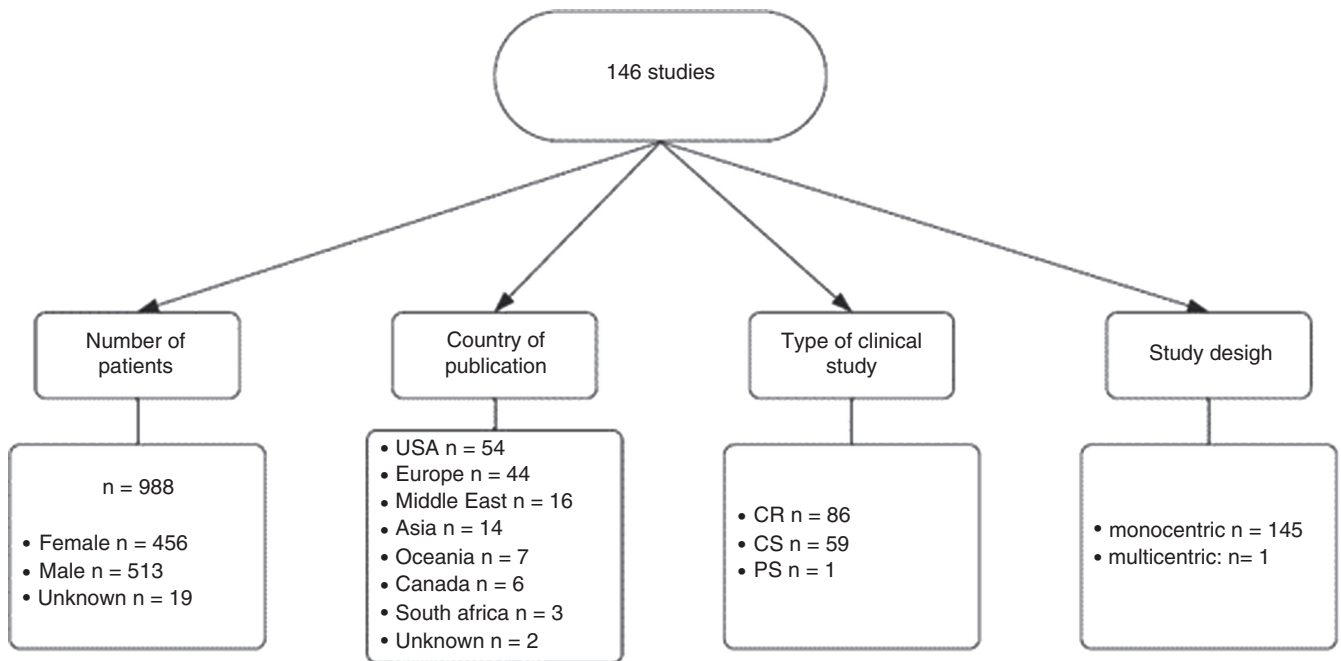
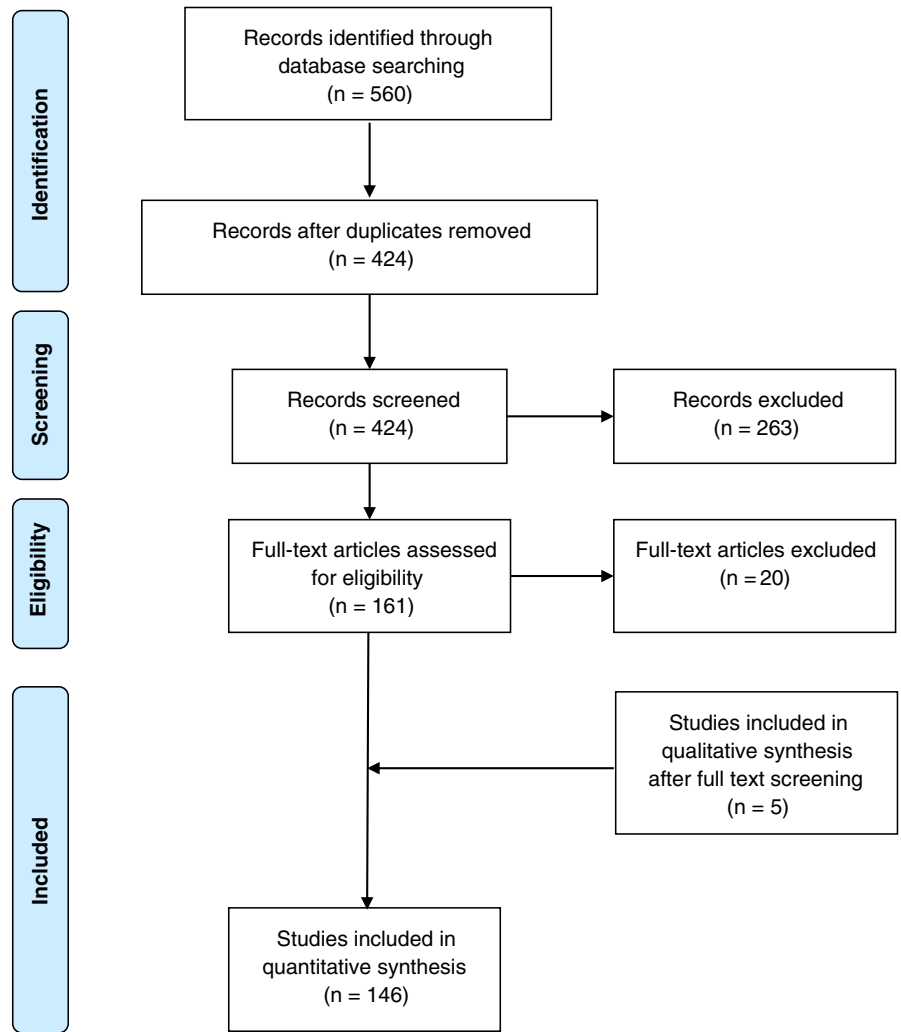


FIGURE 2 Characteristics of included papers

	Information available (n =)	Information not available (n =)	Condition present (n = mean)
Abdominal pain	662/988	319/988	662
RIF			617
Diffuse			13
PU			11
IHA			11
SHA			10
No abdominal pain	7/988		7
Bowel movement	495/988	493/988	495
Haematochezia			9
Diarrhoea/constipation			77
Normal			409
Nausea/vomiting	590/988	398/988	210
Fever $\geq 38^\circ\text{C}$	443/988	545/988	119
WBC ≥ 11 G/l	411/988	577/988	256

TABLE 2 Clinical and biological characteristics of patients

Abbreviations: IHA, inferior hemi-abdomen; PU, peri-umbilical; RIF, right iliac fossa; SHA, superior hemi-abdomen; WBC, white blood cells.

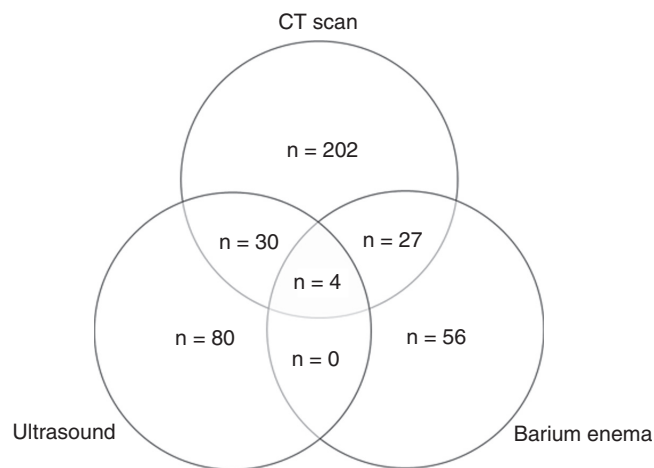


FIGURE 3 Radiological imaging workup

Of the 225 patients diagnosed preoperatively with CD, 67 (67/225, 29.8%) had surgical treatment because of signs of peritonitis, persistent symptomatology despite conservative medical treatment or important abdominal symptomatology. Surgical procedures performed were right hemi-colectomy (22/67, 32.8%), appendectomy (13/67, 19.4%), diverticulectomy associated with appendectomy (10/67, 14.9%) and cecectomy (8/67, 11.9%). Details about other procedures can be found in Appendix S4.

The remaining 730 patients (730/988, 73.9%) treated surgically had right hemi-colectomy (241/730, 33%), appendectomy (137/730, 18.8%), diverticulectomy associated with appendectomy (119/730, 16.3%), diverticulectomy (68/730, 9.3%), ileo-caecal resection (48/730, 6.6%), cecectomy (14/730, 1.9%) and inversion with or without appendectomy (8/730 and 7/730 patients, 1.1% and 0.9% respectively). Other procedures were also performed (51/730, 7%),

such as radiological abscess drainage in one case or a right salpingo-oophorectomy in another case, given that the ovary and the Fallopian tube were involved in the inflammatory mass formed by the CD. Thirty-seven patients (37/730, 5.1%) had a surgical procedure sparing the inflamed diverticula; one had a cecostomy, seven an ileo-transverse colostomy, 17 a surgical drainage, one a wedge biopsy and one a suture. Despite being taken to the operating theatre for an exploratory surgery, no further procedures were performed in 10 cases. All these patients received postoperative antibiotics or a second operation a few days or weeks later.

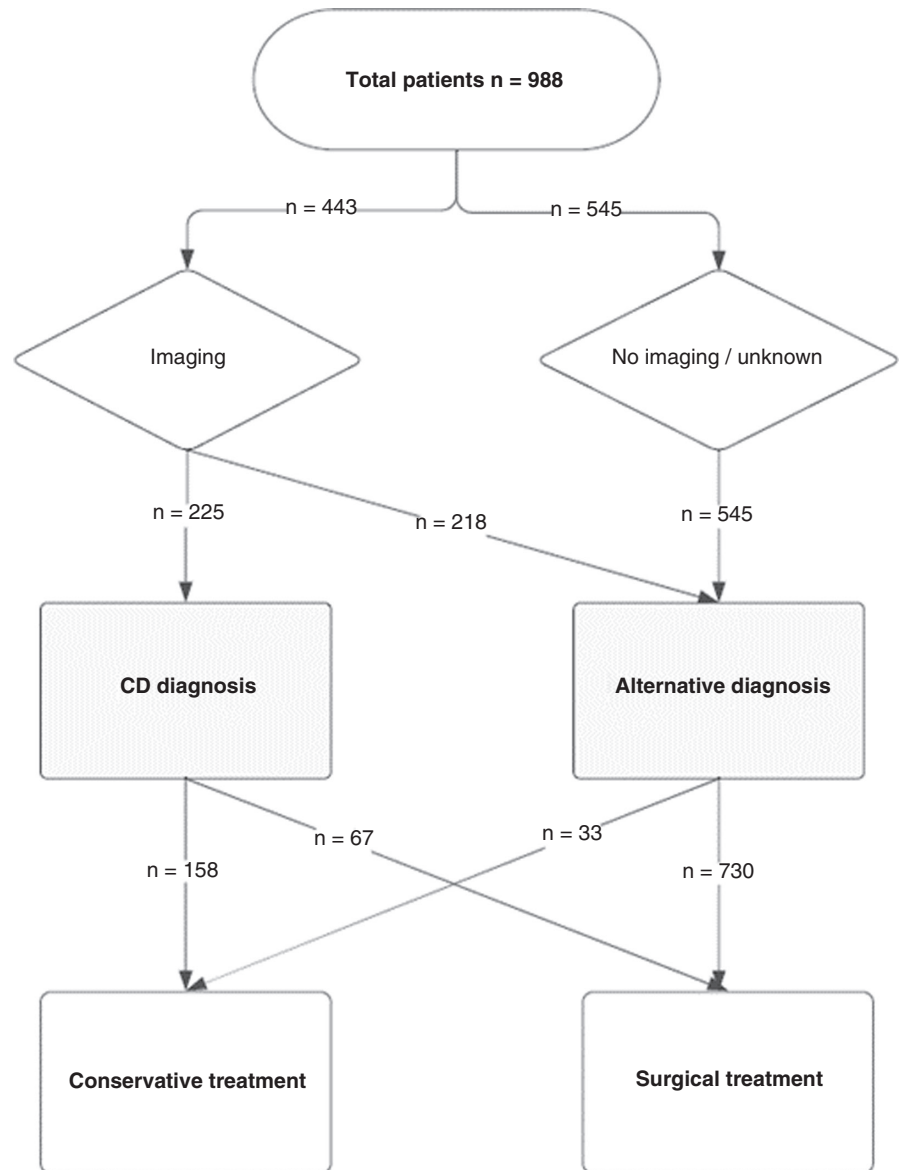
Among the 797 patients treated surgically, details about the surgical approach were not available for 241 patients (241/797, 30.2%). Of the 556 patients with information available, 481 (481/556, 86.5%) had open surgery, 63 (63/556, 11.3%) a laparoscopic approach and in 12 cases (12/556, 2.2%) the procedure was converted from laparoscopy to laparotomy.

DISCUSSION

CD is an uncommon disease, and there is still some challenge regarding the appropriate diagnostic and therapeutic management of this condition. Our objective was to provide an overview of the existing diagnostic methods and therapeutic alternatives through a systematic review of the field.

We noted that 662 patients (662/988, 67%) experienced abdominal pain, which was localized in the right iliac fossa in 93.2% of them. In early reports, imaging techniques were not well developed, leading surgeons to perform explorative surgery, more than 70% of the time upon a preoperative assumption of acute appendicitis, as suggested by Issa et al. [138]. Our own review confirms this difficulty in differentiating the two conditions; 47.6% of the total patient

FIGURE 4 Detailed number of patients with radiological workup and treatment administered



group had a preoperative diagnosis of acute appendicitis. Therefore, preoperative medical imaging constitutes an essential step in the diagnostic approach, resulting in a reduction in the rate of explorative surgery for CD.

Until the 1980s, imaging performed for the diagnosis of colonic diverticulitis was based on barium enemas, as confirmed in our review; except for one, all cases of CD until 1975 pre-diagnosed with an imaging test were based on this method. Nowadays, state-of-the-art imaging of CD is performed with US and/or CT.

US has the advantage of being a technology available in basically any emergency and radiology department. Moreover, it is used in most of these centres as an early-stage workup procedure for patients with acute abdominal pain, especially if located in the right iliac fossa. Chou et al. found that US has a sensitivity and specificity of, respectively, 91.3% and 99.8% for the diagnosis of right sided diverticulitis [152]. The features that can be found suggesting CD are round or oval hypoechoic shaped structures that protrude out of the colonic wall, as opposed to appendicitis

which is usually tubular. They can notably be surrounded by hyperechoic heterogeneous soft tissue, representing the inflamed pericolic fat [152].

However, even if US is more accessible and less expensive, CT has the advantage of being less operator dependent. Furthermore, CT can detect a complicated form of CD (perforation, abscess) as well as other pathologies among patients with right iliac fossa pain, such as appendicitis, typhlitis or carcinoma [153]. Kircher et al. [154] found that CT has a sensitivity and specificity of 99% in the diagnosis of acute diverticulitis, either left or right sided. Detected features include an inflamed diverticulum or a contrast-filled mass surrounded by a colonic wall thickening and pericolic fat inflammation (these two are the most frequent signs), localized oedema, free fluid or extra-luminal air [154,155]. Furthermore, low-dose CT has become more popular and is used in some hospitals as first intention imaging. It notably provides similar performance to contrast-enhanced CT with lower radiation doses, equivalent to those delivered in standard radiography [156,157]. Unlike the Hansen

and Stock or modified Hinchey classification for left sided diverticulitis, a specific radiological score for CD has not been established yet. But when diagnosed intra-operatively, a grading system has been described by the American Society of Colon and Rectal Surgeons and the American College of Surgeons depending on the extension of the inflammation: Grade I is an inflamed diverticulum, Grade II is an inflamed mass, Grade III a localized abscess or fistula and Grade IV a ruptured abscess or a perforation with generalized peritonitis [10,158].

Depending on the grade, different surgical management strategies have been proposed: for Grades I and II, an appendectomy combined with postoperative antibiotics is the treatment of choice (the appendectomy being applied to avoid misdiagnosis in the case of recurrent symptoms) [4,10,159]. An appendectomy combined with diverticulectomy is also possible, and notably recommended by some authors like Connolly et al. as appendectomy with antibiotics alone could lead to recurrent symptoms [7,10]. For patients with either Grade III or IV large inflammatory masses, or if cancer cannot be ruled out, right colectomy or ileo-caecal resection should be performed [10,146,158]. Fang et al. [119] even recommended an aggressive surgical approach with colonic resection in all cases of CD. Indeed, of the 97 patients included in their study, less than 40% of the patients treated conservatively were recurrence-free. On the other hand, in this analysis, only 6.3% of patients (10/158) with a radiological diagnosis of CD treated conservatively had recurrent symptoms.

In addition, emergency right colectomies have the disadvantage of having a higher risk of stoma, morbidity and mortality, especially in the case of patients with higher American Society of Anesthesiologists scores, as suggested by Tan et al. [160]. In a retrospective analysis, of 207 patients undergoing emergency right colectomy for various indications, 39 patients (18.8%) had severe complications and 20 were deceased (9.7%).

In the case of surgical treatment a laparoscopic approach should be favoured, as it is associated with less blood loss, an earlier return of bowel function and a shorter length of hospital stay [161,162]. However, it is not always feasible, as suggested by Park and Lee [133]; CD originating from the anterior wall is managed more easily than that found in the lateral or posterior wall, and notably when a phlegmon is associated. This can lead to extended dissection or conversion into an open operation.

For non-complicated forms of CD diagnosed preoperatively, a conservative management similar to the one provided for left sided diverticulitis, combining antibiotics and bowel rest, is preferred [2,3,10,158]. If a recurrent episode is present, patients can be treated again safely with antibiotics without the need for surgery and its possible complications [161,163,164]. Finally, there is no clear consensus regarding the inpatient versus outpatient management for CD. Park et al. [165] demonstrated in a prospective study that the oral treatment of right sided diverticulitis was in general as effective as the intravenous treatment, with a recurrence rate of 10% versus 11% respectively. For stable patients presenting with

uncomplicated CD, it therefore seems reasonable to offer outpatient management.

There are some potential limitations in our review. First, the reported findings depend on the underlying quality of the assessed publications, in particular considering that some of them are historical reports (dating back as early as 1930). Second, the treatment depends on the period of publication. So far, specific comparative studies are not available. Third, the follow-up of patients was not systematically carried out, leading to ambiguities in the comparison of outcomes for the different treatments, as well as the risk of recurrence and therefore their efficacy.

Even so, our review offers the first comprehensive review on the subject and goes back to historical findings starting from 1930. The review highlights that the management should remain conservative for uncomplicated forms and surgical in the case of complications (as well as failure of the conservative approach), as is the case for left sided diverticulitis.

CONCLUSION

Caecal diverticulitis is a rare condition, which was historically often misdiagnosed as acute appendicitis, therefore resulting at times in unnecessary exploratory surgery. Analyses of different publications starting from 1930 demonstrate that medical imaging took a critical place in supporting the clinician to diagnose this condition and to administer adequate treatment. Imaging should be part of the standard diagnostic management of right sided lower abdominal pain. Once diagnosed, uncomplicated CD can be safely managed with antibiotics. Surgery should be kept for complicated cases only.

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CONFLICT OF INTERESTS

The authors disclose no conflict of interest.

AUTHOR CONTRIBUTIONS

IU, JM and SN conceived and designed the study. IU, MV and JM acquired the data. IU and JM analysed the data. IU, JM, NC, FR, MV and SN interpreted the data. IU, JM, NC, FR, MV and SN contributed to the writing of the manuscript and to its critical revision. IU, JM, NC, FR, MV and SN approved the final version of the manuscript.

DATA AVAILABILITY STATEMENT

The data are openly available in a public repository that issues datasets with DOIs.

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