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Crohn's Disease Management: Conclusions of a Comparative Study between UK and Romania

F E Buruiana[1], N Angelescu[2], D Skipper[3]

[1]Core Surgical Trainee Year 2, East of England Deanery, Bedford Hospital, Bedford, UK
[2]Consultant General Surgeon, "Coltea" Hospital, Bucharest, Romania
[3]Consultant General Surgeon, Bedford Hospital, Bedford, UK

Rezumat

Managementul bolii Crohn: concluziile unui studiu comparativ între Marea Britanie și România

Boala Crohn este o afecțiune cronică ce poate implica orice porțiune a tractului digestiv, de la gura până la anus, unde zonele sănătoase alternează cu cele patologice. Este o afecțiune medicală cronică ce necesită intervenția chirurgicală atunci când apar complicații precum strictura, stenoza, fistula etc (1, 2,3). Au fost studiate retrospectiv un număr de 19 cazuri de Boala Crohn de la spitalul "Colțea", București, România, și alte 16 cazuri de Boală Crohn de la Bedford Hospital, Marea Britanie, toți pacienții fiind supuși chirurgiei; au fost comparate tratamentele preoperatorii și postoperatorii, inclusiv urmărirea în ambulator. S-a concluzionat faptul că este necesară o implementare a unui ghid clinic și protocol pentru tratamentul pacienților cu Boala Crohn în România.

Cuvinte cheie: boala Crohn, afecțiune medicală cronică, tratament medicamentos, tratament chirurgical, complicații intestinale, complicații extraintestinale, recurență, urmărire în ambulator

Abstract

Crohn's disease is a chronic inflammatory condition, which may affect any portion of the digestive tract from the mouth to the anus. It is a chronic medical condition which requires surgery when medical treatment fails or complications such as strictures, sepsis or fistulation develop (1,2,3). We retrospectively studied a group of 19 patients with Crohn's disease from "Coltea" Hospital, Bucharest, Romania, and another group of 16 patients with Crohn's disease from Bedford Hospital UK, all of them having undergone surgery; we compared their preoperative and postoperative treatments, including follow up. It was concluded that the implementation of clinical guidelines and protocols for the management of patients with Crohn's disease is needed in Romania.

Key words: Crohn's disease, chronic medical condition, medical treatment, surgical treatment, intestinal complications, extraintestinal complications, recurrence, follow up

Corresponding author: Dr Felicia Elena Buruiana, PhD
Lister Hospital
Coreys Mill Lane
Stevenage
Hertfordshire
SG1 4AB, United Kingdom
E-mail: felicia.buruiana@nhs.net

Aim

To demonstrate the importance of diagnosing Crohn's disease at an early stage and treating it as a chronic medical illness, with surgery reserved for failure of medical treatment or for treating complications such as stricture, sepsis or fistulation.

Material and Methods

This is a retrospective comparative study, in which we collected a total of 19 clinical cases in the Department of Surgery, "Coltea" University Hospital, Bucharest, and a total of

16 clinical cases in the Department of Surgery, Bedford Hospital NHS Trust, UK.

The main criterion for inclusion was that patients had been diagnosed with Crohn's disease and required surgery.

The Romanian patients were all consecutive cases seen and treated during 2010 and 2011.

The UK patients were all consecutive cases followed up at Surgical Outpatient Clinics.

The results were collected on a spreadsheet created in Excel by the authors, and their analysis was done using IBM SPSS Statistics 20 for the calculation of the variables. Nonparametric data were compared using Nonparametric Tests for Independent Samples and Mann-Whitney U and T-Test were used for normally distributed data. We used Significance Level of 5% and a Confidence Interval Level of 95%.

The variables measured both in Romania and the United Kingdom (UK) were:

- sex,
- age at first presentation,
- the period between the appearance of the first symptoms and presentation to the doctor,
- early symptoms (abdominal pain, anorexia, tenesmus, diarrhoea, vomiting, elimination of mucus and blood in defaecation, fatigue, weight loss, mouth ulcers, irritate bilateral slowing bowel, fever, pitiriasis rosea, erythema nodosum, iron deficiency anaemia),
- the first doctor to whom the patient presented (emergency, general practitioner (GP) or family doctor, gastroenterologist, surgeon),
- laboratory tests (blood count, C reactive protein (CRP) erythrocyte sedimentation rate (ESR)),
- initial investigations (plain abdominal radiography, contrast radiography of the abdomen, barium studies, abdominal ultrasound, sigmoidoscopy, colonoscopy, gastroscopy, abdominal CT),
- preoperative, intraoperative, and postoperative management,
- postoperative complications,
- survival rate,
- long term follow up, both surgical and medical.

Results

Both groups of patients were similar in size, 19 in Romania and 16 in the UK, respectively. The age distribution was comparable without a statistically significant difference (*Table 1*). The sex distribution was also similar, with a slight predominance in females (*Table 2*).

Table 2. *Demographics*

	Romania n=19	UK n = 16
Males	8	5
Females	11	11

Table 3. *Presenting symptoms*

Symptoms at first presentation	Romania = n 19	UK = n 16
Abdominal pain	12	13
Diarrhoea	13	12
Weight loss	12	9
Mucus and blood in stools	6	6
Pyrexia	6	0
Tenesmus	5	0
Fatigue	5	2
Anorexia	4	6
Vomiting	3	3
Decreased peristalsis	2	1
Mouth ulcers	1	1
Iron deficiency anaemia	1	1
Pitiriasis	0	1
Erythema nodosum	0	1
Arthritis	0	1

The mean age at first presentation to the doctor was higher in Romania, 42 years as compared to 35 years in the UK; nevertheless this did not reach a statistical significance. The minimum (16 and 14 years) and maximum ages (76 and 73 years) in both Romania and the UK were comparable.

The clinical symptoms at presentation were similar in both groups, as they do not change much regardless of the severity and progression of Crohn's disease (*Table 3*). In the majority of the patients the main complaints were: abdominal pain, 12 of 19 in Romania, 13 of 16 in UK; diarrhoea 13 of 19 in Romania, 12 of 16 in UK; weight loss 12 of 19 in Romania and 9 of 16 in UK.

Other less common symptoms were: anorexia 4 of 19 in Romania, 6 of 16 in UK and stools with mucus and blood 6 of 19 in Romania and 6 of 16 in the UK (*Table 3*).

The initial investigations were imaging, endoscopy, biopsy and blood tests. (*Table 4*)

Abdominal radiography (11 of 19 patients) and abdominal ultrasound (11 of 19 patients) were the investigations used most frequently in Romania, followed by abdominal CT (7 of 19 patients). In the UK group, abdominal radiography (8 of 16

Table 1. *Demographics*

	Romania n=19 Mean (SD)	UK n=16 Mean (SD)	NPTESTS/INDEPENDENT TEST
Age in years	42 (18)	35 (18)	No Sig difference (s. 0.781)
Statistic used: T-Test			

Table 4. *Initial investigations*

Initial investigations	Romania n=19	UK n=16
Imaging:		
Abdominal ultrasound	11	0
Abdominal X-rays	11	8
CT abdomen	7	3
Barium X-rays	4	5
Contrast X-rays	1	0
Endoscopic:		
Colonoscopy & Biopsy	6	5
Gastroscopy	0	1
Sigmoidoscopy	0	2

Table 5. *Laboratory results*

Laboratory results	Romania n = 19	UK n = 16
Anaemia	15	4
Elevated CRP-ESR	17	12

Table 6. *Type of doctor to whom initial presentation was made*

	Romania n = 19	UK n = 16
General Practitioner	1 (5%)	10 (63%)
Emergency Department	5 (26.5%)	6 (37%)
Gastroenterologist	8 (42%)	0
Surgeon	5 (26.5%)	0

patients) followed by barium studies (5 of 16 patients) and CT abdomen (3 of 16 patients) were the commonest imaging techniques used.

Colonoscopy and biopsy was the commonest endoscopic test in both groups, 6 of 19 Romanian patients, and 5 of 16 UK patients, respectively.

The above investigations reflect the tendency for more frequent biopsies in the UK, and as a consequence a faster diagnosis sometimes without the need of radiological tests.

Preoperative full blood count, CRP and ESR tests were performed in all patients. (*Table 5*) Anaemia was very common in the Romanian group at 78% and less in the UK group at 25%. Raised inflammatory markers were predominant in both Romania (89%) and the UK (75%). These differences in the instance of anaemia may reflect differences in presentation. In Romania patients presented with more advanced disease.

In the Romanian group 8 patients went directly to the specialist gastroenterologist, 5 went to the Emergency Department and the other 5 to the Surgical Outpatient Clinic. Only one patient went to the family doctor. The reverse is true in the UK, where 10 patients went to the GP, and 6 to the Emergency Department while none presented to the gastroenterologist or surgeon directly (*Table 6*).

The above demonstrates the different access to medical care and different care pathways in each country. It is common in Romania for patients to go direct to a specialist and very rarely to see a GP. A similar number attend Accident and Emergency due to abdominal pain. Although direct access to the specialist may improve the outcome, we did not see this in our Romanian study group, most likely due to the fact that patients presented late.

The interval between the onset of symptoms and the first presentation to the doctor is much longer in Romania with a median of six months compared to the UK at one month. In Romania patients had symptoms for up to twenty-four months before presentation whereas in the UK all patients had presented by three months (*Table 7*). We found this difference to be statistically significant with an s = 0.018.

The time between the initial clinical assessment and surgery was one of the biggest differences between the groups. While all the Romanian patients were hospitalised and underwent surgery during the same hospital admission, the UK patients were treated medically for a variable period of time. In the UK group the medical management lasted from months to years, surgery being reserved for those patients who did not respond to medication and other non-operative measures.

Surgical Treatment

The surgical procedures themselves do not differ between Romania and the UK, the principles of surgical treatment being the same in relation to the location and stage of the lesion, single or multiple sites, the type of lesion (stricture, stenosis, fissure, entero-cutaneous fistula, entero-vaginal fistula) and any immediate postoperative complications requiring prompt surgical intervention.

Although most of the surgical procedures in the UK consisted of bowel resection, (13 out of 16) there were 3 patients who required less extensive surgery (diagnostic laparoscopy; drainage of an abscess; appendicectomy). We believe these

Table 7. *Timing of Presentation*

	Romania n=19 Median (range) in months	UK n=16 Median (range) in months	NPTESTS/ INDEPENDENT TEST
Time from first symptom to first presentation to a doctor	6 (2-24)	1 (1-3)	Significant difference (S. 0.018)
Time from first presentation to a doctor to surgery	0 (0-0)	16 (7-113)	Significant difference (S. 0.000)

Statistic used: Mann-Whitney U

Table 8. *Surgical Treatment*

Surgical Procedure	Romania N (%)	UK N (%)
Bowel resection	19 (100%)	9 (57%)
Laparoscopic bowel resection		4 (25%)
Diagnostic laparoscopy		1 (6%)
Examination under anaesthesia & drainage of abscess		1 (6%)
Appendicectomy		1 (6%)

differences reflect the fact that the patients in Romania were treated as emergency cases after long standing illness (*Table 8*).

Some patients in the UK had several operations over the years with close follow up.

The postoperative complications were very different between the two groups. The Romanian group had more immediate postoperative complications while the UK group has later postoperative complications probably related to progression of the disease (*Table 9*).

There were two deaths in the Romanian group and none in the UK group. The two Romanian patients who died had a delayed first presentation, with no prior medical treatment. One death occurred two months after the operation due to an internal haemorrhage and the other death was two weeks post-operatively due to intraperitoneal abscess, which led to sepsis and death.

Post-operative follow up and treatment

There was no record of medical follow up, and only one case of postoperative surgical follow-up for the 19 Romanian patients.

There was no record of medical treatment in the Romanian patients.

In the UK group, 15 patients had a medical follow up with treatment. 16 patients had surgical follow up at an interval of three to six months, with adjustment of medication depending on the evolution of the disease.

Discussion

The management of Crohn's disease (CD) should be a key component of the clinical practice of the gastroenterologist. CD is primarily a medical condition, which becomes inter-disciplinary when complications arise.

The present retrospective study revealed a significant difference between the management of CD in Romania and the UK, not so much in the surgery itself but in terms of managing these patients in general, especially the preoperative and postoperative management (4).

The analysis of the results will be made from three perspectives:

- the Patient;
- the Doctor;
- the Medical System.

Table 9. *Types of postoperative complications*

	Romania n = 19	UK n=16
Early Complications		
Anastomotic fissure	3	0
Incisional abscess	3	0
Haemoperitoneum	1	0
Late Complications		
Haemorrhage and death	1	0
Sepsis due to intraperitoneal abscess and death	1	0
Recto-vaginal fistula	1	0
Vitamin B malabsorption	0	2
Reactive hepatitis to azathioprine	0	1

The Patient

The period between onset of symptoms and the first presentation to the doctor was on average 13.8 months in Romania and 3.5 months in the UK, with a maximum of 60 months in Romania and 24 months in the UK. Romanian patients who were shown to have the same presenting symptoms as UK patients went to the GP at a rate of 5% compared with 63% in the UK and to the emergency service at the rate of 27% compared to 37% in the UK. However, in Romania, 42% went directly to the specialist gastroenterologist and 26% directly to the surgical outpatient clinic.

The late presentation seen in Romanian patients may be a function of the patients' level of education or the structure of the healthcare system. The fact that the patient presents so late to see a doctor is cause for concern, as most often they are seen by specialists when they already have complications.

With a few exceptions that require surgical intervention from the earliest stages, the disease can often be controlled by adequate medical treatment for a number of years, as it can be observed in our UK series, for 10 or even 20 years after the onset of the disease. There is a need for public education in Romania and the need for a system allowing early presentation to the doctor. There were two post-operative deaths in Romania, and this may have been due to late presentation (*Table 9*).

The Doctor

The family doctor (GP in the UK) should be the first contact with these patients, followed by the emergency medicine physician. GPs and emergency physicians need to be alert to the symptoms and signs of Crohn's disease. In Romania, as patients go directly to specialists, inflammatory bowel disease services should be a priority.

Initial non-operative management in the UK differs from Romania, as in the UK the disease may be treated by conservative measures for a number of years whilst in Romania surgical intervention occurs much earlier for the reasons out-lined above. The lack of non-operative medical treatment

means that patients with CD in Romania are diagnosed late and mostly when they have complications. The perioperative treatment in the two systems however is similar in terms of fluid and electrolyte administration and antibiotics. The incidence of anaemia is much greater in Romania (15/19 - 79%) as compared to the UK (4/16 - 25%).

In Romania abdominal ultrasound was performed in 11 out of 19 cases, whilst none of the 16 UK patients had ultrasound. Plain abdominal radiography, barium studies and colonoscopy with biopsy were performed in both groups.

Only one case received surgical follow up in the postoperative period in Romania, and no medical follow-up, while in the UK almost all patients were followed both by the gastroenterologist and the surgeon in the postoperative period.

The Medical System

In the UK there is a highly structured medical system in which the patient first presents to the GP, or if the patient believes that symptoms are severe, goes directly to Accident and Emergency. The system allows the patient to present early to the GP, which may make a substantial difference in the evolution of the disease. In the UK patients are encouraged to present to their GP with symptoms. It should be noted that in the UK it is difficult for a patient to gain direct access to a specialist in the public health system.

Also in the UK the treatment of diseases in general, including Crohn's disease, is based on clinical guidelines and protocols, to ensure a high and consistent standard of treatment is given to all patients, that patients are involved in clinical decision-making and options and that benefits and risks are discussed in detail.

We believe that clinicians treating CD in Romania should refer to the Clinical Guidelines for the Management of Inflammatory Bowel Disease (IBD) introduced in Britain in 2004 by the British Society of Gastroenterology (BSG) and revised and republished in 2011. The analysis and review were based on advances in management strategies in all aspects of clinical care.

This document is addressed primarily to clinicians in the UK and serves to replace the Clinical Guidelines of the BSG on IBD, but also complements the consensus recently published by the European Crohn's and Colitis (European Crohn's and colitis Organisation, ECCO) (5,6).

The authors of the above mentioned guidelines (5) considered that there were strong reasons to formulate a set of clinical guidelines for practice in UK to date and they are as follows:

1. CD is complex and recent national audits have shown a wide variation in clinical practice.
2. There are important differences between clinical guidelines and consensus. Clinical practice guidelines are systematised documents to assist clinicians and patients in making decisions for treatment and care appropriate in the context of specific clinical circumstances. Their objective is to make explicit recommendations with intent to influence a clinician's practice (5). Recommendations for practice with specific reference to certain countries may not always be identical to that which appears in the consensus (e.g., use of anti-tumor necrosis factor during the remission of CD).
3. The recent publication of a set of standards for UK Healthcare Services treating CD is relevant to clinical practice guidelines in the UK. http://www.ibdstandards.org.uk (5).
4. The practice in the UK is influenced by guidance from NICE (National Institute of Clinical Excellence) (7).
5. The UK approach differs from the European consensus (8) on certain issues, and certainly differs from North American practice (9). These clinical guidelines are needed, especially today, when new treatments for CD and management paradigms accepted in previous years are being revised (10).

It is important to realise the impact of CD on patients and therefore on society. The BSG reports a prevalence of IBD of 400 per 100,000 in the UK (5). Thus approximately 240,000 patients in the UK have IBD, 87,000 of whom have CD, the prevalence being 145 per 100,000. CD in the UK has increased dramatically between the 1950s and 1980s. Since the 1980s it has continued to increase but at a lower rate.

Most patients are referred to the outpatient clinic for evaluation and about 30% of them have regular hospital follow-up (5). About 2000 people each year are subjected to surgical interventions. In CD the incidence of surgery is 70-80% over a lifetime, depending on the severity of the disease and its location (5).

The care costs of patients with CD in the UK have recently been reviewed (5). Costs over a lifetime are comparable with those of a number of major diseases, including heart disease and cancer. This implies a substantial burden of disease and disability that is reflected in the large number of academic and commercial activities increasingly expanding to develop more efficient treatments (11). CD patients describe symptoms as shameful and humiliating. CD can interfere with education and cause difficulties in finding a job or obtaining insurance. It may cause psychological problems and lack of growth and development, including delayed sexual development in young people. Medical treatments such as steroids and immunosuppressive medications may cause secondary health problems and the surgery in turn may cause complications such as impotence and bowel dysfunction. The impact of CD on society is disproportionately high because presentation is often at a young age and can cause poor health over a long period of time (5).

In light of the above, education of patients and support for patients are very important. CD patients should receive written information in outpatient clinics, on the ward and in endoscopy units. Patients considered for surgery should receive clear information about their operation and, where possible, the option to meet patients who already have a stoma. Advice on accessing additional information should

be offered and help in interpreting information should be given where this is needed (5,7).

Conclusions

We acknowledge the methodological issues concerning the selection, sample sizes and comparison between the two groups. Nevertheless we feel that each group is representative of UK and Romanian patients respectively and although extrapolation of our results to the national practice of both countries needs to be guarded, we believe that the differences in practices between the two systems are so clear that our analysis is reasonable and acceptable.

1. Crohn's disease is a chronic disease that can affect any part of the digestive tract. Unfortunately it is an incurable disease despite advances in diagnosis and treatment.
2. GPs, the A&E Doctors, as well as gastroenterologists and surgeons should consider this condition as part of their differential diagnosis.
3. The symptomatology is not specific or pathognomonic; the definitive diagnosis is made by imaging and endoscopy and biopsy. Therefore the patient should receive appropriate clinical and laboratory investigations in a timely manner. The fact that the first symptoms of the disease may be extraintestinal manifestations (arthritis, uveitis, erythema nodosum, pyoderma gangrenosum, primary sclerosing cholangitis) should be considered.
4. Each CD patient must be treated individually. Early diagnosis of the disease may delay or avoid surgery.
5. Surgery should be reserved for intestinal complications such as strictures, obstruction, perforation, sepsis or fistulation.
6. The patients should be followed both by gastroenterologists and surgeons. Patients must understand that this is a chronic disease and even long periods of remission do not mean the disease is cured. They must attend follow up clinics. Patients may be followed up at longer intervals if they are in remission.
7. We would recommend that Romania adopt a system of care for Crohn's disease based on guidelines and protocols utilised in the UK. This would develop a system whereby patients may present early and therefore be managed conservatively. Surgery where necessary may be utilised in a more timely and planned fashion rather than in the emergency and urgent situation that it is now. We would recommend that CD patients are followed up by gastroenterologists and where appropriate with surgeons also.

Authors contributions

Dr. Felicia Elena Buruiana - first author. This is part of my PhD Thesis. I established patients' inclusion and exclusion criteria, the material and methods, and I analysed the data. I wrote the discussions and I interpreted the results in the context of the literature. I also wrote the conclusions.
Prof Dr N Angelescu coordinated and supervised the PhD thesis, including this study.
Mr D Skipper directly supervised this study, made valuable suggestions which were taken into account.

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