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Spleen Size in Patients with Inflammatory Bowel Disease Does It Have Any Clinical Significance?

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The finding that splenic atrophy is associated with a high complication rate in colitis has led to a long-term, prospective study of spleen size in inflammatory bowel disease. The spleen has been measured in 116 patients undergoing laparotomy for inflammatory bowel disease—80 Crohn's disease and 36 ulcerative colitis—from 1975 to 1985. Small spleen size, of lesser degree than that of classic splenic atrophy, is associated with presurgery disease complications as well as infective problems after surgery. Spleen size was not related to site or extent of disease, or to recurrence, but the wide range of spleen size seen in inflammatory bowel disease, comparable to that seen in malignancy suggests that more sophisticated tests of splenic function might show a closer correlation with disease patterns. [Key words: Spleen size; Crohn's disease; Colitis; Complications]

RECENT INTEREST IN the significance of the spleen has led to increasing knowledge of its involvement in a wide range of diseases. This has come from research and the development of new techniques which can be used to investigate the anatomic and functional aspects of the spleen.

Splenic abnormalities have been reported in association with a number of disorders treated by surgery, including malignant tumors and inflammatory bowel disease.¹⁻⁹ This has led to speculation that such diseases

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involving immunologic phenomena could interrelate with the spleen because it contains the largest single accumulation of lymphoid tissue in the body¹⁰ and has important immunologic functions. Enlarged spleens have been reported infrequently in patients with Crohn's disease.^{11,12} On the other hand, splenic atrophy, with defective splenic function, was suggested by a group of workers to be a common finding in severe colitis. In their study hyposplenic patients complications were more likely to develop after colectomy.² Apart from these case reports of splenomegaly or splenic atrophy, there has been no large, long-term study of spleen size in inflammatory bowel disease.

Before the advent of imaging techniques such as ultrasound, x-ray computerized tomography, and radioisotope scintigraphy, estimation of the spleen size in clinical work was based on external physical examination and conventional radiography. Studies showed both methods to be unreliable because of the uncertainty and inaccuracy with which the spleen could be demonstrated.^{13,14} For the past 12 years spleen size has been routinely measured and recorded at all laparotomies performed by the authors.

From this experience it was clear that a wider variation in spleen size is seen in patients with inflammatory bowel disease than in patients undergoing laparotomy for other common abdominal diseases. This has led to a study of

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spleen size in inflammatory bowel disease, in order to determine whether spleen size taken as an isolated parameter during laparotomy has any clinical significance in these patients, and to compare the findings between patients with Crohn's disease and ulcerative colitis. To clarify these points, the operation sheets and clinical notes of patients with spleen size recorded at laparotomy for inflammatory bowel disease at the authors' institution from 1975 to 1985 were reviewed.

Patients and Methods

A total of 116 patients submitted to laparotomy for inflammatory bowel disease from January 1975 to July 1985 had their spleen size measured at surgery and recorded on a special proforma, together with full details of operative findings. Eighty had Crohn's disease and 36 had ulcerative colitis. All these patients had their operation sheets and general data reviewed, but fully detailed clinical notes with follow-up to the present time were available in only 83 patients (60 with Crohn's disease and 23 with ulcerative colitis). The initial diagnosis was based on clinical, radiologic, and endoscopic findings. The final diagnosis was based on histologic examination of the surgical specimen.

Care was taken not to include any patients with diseases other than inflammatory bowel disease which could affect spleen size. For this reason one patient with ulcerative colitis who had splenomegaly and a large cirrhotic liver was excluded from the study. All other patients had macroscopically normal livers on laparotomy. Age, sex, weight, and height were recorded for each patient, as well as the presence of anemia and low protein levels. Previous administration of steroids, including dosage and duration of treatment, was also considered. All patients received antibiotics preoperatively or postoperatively.

Method of Measuring Spleen Size: The spleen was measured by a single observer standing on the right side of the abdomen, placing the fingers of both hands contiguously over the convex surface of the spleen along its long axis, starting with the left fifth finger at the upper pole. This method was chosen after a preliminary study showed it to be more accurate and reproducible, and much easier than using a tape measure.

The spleen was considered small, normal, or large if it measured less than 6, between 6 and 8, and more than 8 fingerbreadths in length, respectively, corresponding to < 11 cm, 11.5 to 15.5 cm, and > 16 cm. On this basis, both Crohn's disease and ulcerative colitis patients were placed into three groups. The choice of figures for the normal range was based on measurement of spleen size at many hundreds of laparotomies for conditions which would not be expected to alter the spleen size. It was notable that the other two dimensions, *i.e.*, width and thickness,

almost always followed length changes in the same proportion as classically recognized clinically and anatomically, *i.e.*, a ratio of $5 \times 3 \times 1$. In a few cases, the spleen was notably narrower than usual. This has the effect of reducing volume by about half and was taken into account when considering the organ small, normal, or enlarged. A narrow spleen was placed in a group one smaller than for the corresponding "normal" length. It is interesting that spleens tend to fall into two groups—"normal" and "narrow"—rather than form a continuous spectrum in relation to the ratio between length and breadth.

When analyzing the notes, the main points looked at were: 1) correlation between spleen size and severity of disease, including site and extent of bowel affected; 2) correlation between spleen size and complications of the primary disease, namely abscesses, fistulas, bleeding, perforation, and toxic megacolon; 3) correlation between spleen size and postoperative complications, mainly infective; 4) correlation between spleen size and recurrence of disease in Crohn's disease patients; and 5) variation of spleen size on repeated laparotomy over a long period of time. Statistical analysis was made using the student's *t*-test and the chi-square test.

Some results could be based on the operation sheets and initial records data alone (115 patients) while others required detailed study of clinical notes over the full period of follow-up (82 patients). This explains the lack of uniformity observed in the totals of different tables. It also accounts for the fact that, among patients with ulcerative colitis, only females had their mean ages, heights, and weights compared; the number of males who had this information available was insufficient for statistical analysis.

Results

The groups of patients according to spleen size and sex are shown in Table 1. Both sexes are considered together as a percentage of the overall group in Fig. 1. Patients with Crohn's disease had a higher proportion of large spleens (38.7 percent) when compared to patients with ulcerative colitis (28.5 percent). The reverse situation was found in normal spleens, 38.7 and 51.4 percent, respectively. The results of breaking down the groups more precisely according to splenic length in centimeters are shown in Table 2.

A graphic representation of all patients with inflammatory bowel disease, combining the mean length of the spleen and sex distribution in each group of spleen size, is seen in Fig. 2. The mean spleen length is very similar in both diseases, showing no trend within each group to a larger or smaller spleen for Crohn's disease or ulcerative colitis.

TABLE 1. Spleen Size and Sex Distribution of Patients With Crohn's Disease and Ulcerative Colitis

Size of the spleen	Crohn's N = 80		Ulcerative Colitis N = 35	
	Males N = 34	Females N = 46	Males N = 14	Females N = 21
	Small	4	14	2
Normal	15	16	10	8
Large	15	16	2	8

Patient Characteristics

Sex: The sex distribution in patients with Crohn's disease can be seen in Table 1. In the group with small spleens, females outnumbered males by more than three to one. The only significant age difference lay between the mean ages of males with normal (44.1 ± 9.92 years, mean \pm SD) and large spleens (26 ± 11 years, $P < 0.05$ *t*-test). In patients with ulcerative colitis, there is again a predominance of females in patients with small spleens, but this is seen also in the group with large spleens, which was not seen in patients with Crohn's disease (Table 1). No correlation was found between age and spleen size in ulcerative colitis patients.

Height and Weight: In Crohn's disease, female patients with large spleens were significantly taller (1.63 ± 0.04 m, mean \pm SD) than those with normal (1.54 ± 0.09 m) and small (1.55 ± 0.04 m) spleens, ($P < 0.05$ *t*-test). Males showed no such difference. Females with large spleens were significantly heavier (54.05 ± 7.29 kg, mean \pm SD) than those with normal spleens (45.52 ± 8.25 kg, $P < 0.05$

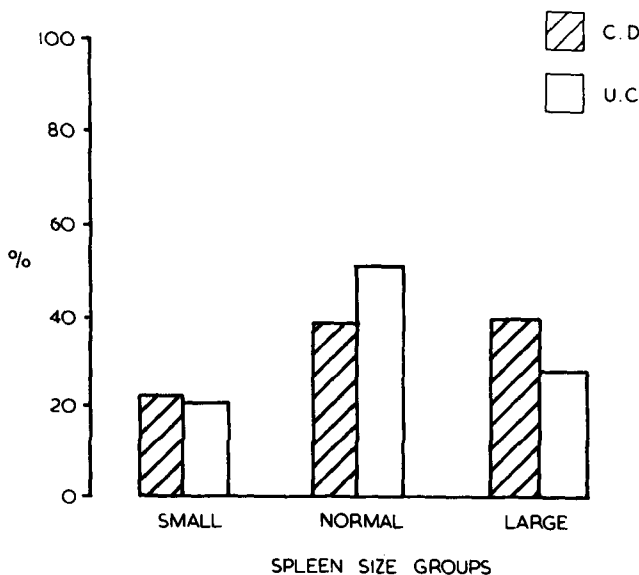


FIG. 1. Percentage of the total number of patients that corresponded to each group of spleen size, for Crohn's disease and ulcerative colitis.

TABLE 2. Spleen Size of Patients With Crohn's and Ulcerative Colitis According to Its Length in Centimeters

Size of the spleen/ spleen length (cms)	Crohn's	Ulcerative Colitis
	Number of patients	Number of patients
Small	N = 18	N = 7
7.5 cm	2	1
9.5 cm	5	2
10.5 cm	11	4
Normal	N = 31	N = 18
12.5 cm	14	6
13.5 cm	10	6
14.5 cm	7	6
Large	N = 31	N = 10
16.5 cm	13	5
18 cm	9	4
19.5 cm	9	1

t-test), but there was no significant difference between other groups. Males showed no significant difference regarding their weights.

No significant relationship could be demonstrated in the smaller groups with ulcerative colitis.

Blood Parameters and Steroid Administration: There was no difference between hemoglobin and protein levels of patients with large, normal, and small spleens suffering from either Crohn's disease or ulcerative colitis. No relationship was detected with administration of steroids.

Anatomic Location of Disease: The site of diseased bowel in patients with Crohn's disease is shown in Table 3. Thirty six patients had small-bowel (usually terminal ileum) involvement alone, 32 had ileocolic disease (with or without rectal involvement), and only 12 had isolated colonic disease. The site and extent of bowel involvement

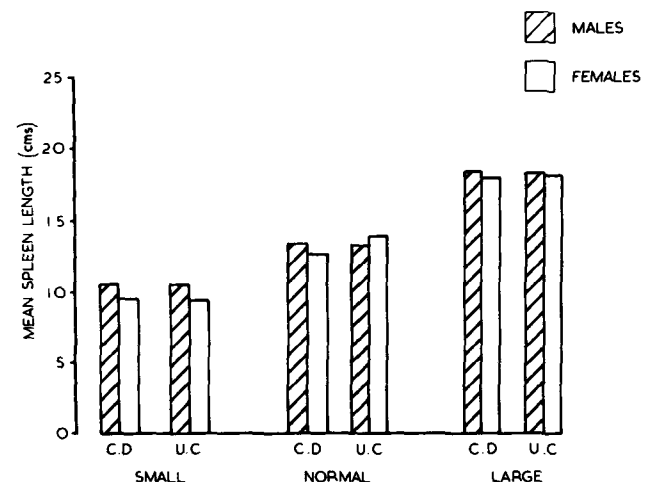


FIG. 2. Mean spleen length in the groups of spleen size, comparing males and females, and ulcerative colitis and Crohn's disease.

TABLE 3. Site of Disease Related to Spleen Size in Crohn's Patients

Site of disease	Small N = 18		Normal N = 31		Large N = 31	
	Number of patients	Percent	Number of patients	Percent	Number of patients	Percent
Small bowel alone	7	39	14	46	15	48
Small and large bowel (ileocolic)	8	44	11	35	13	42
Large bowel alone	3	17	6	19	3	10

was not related to spleen size. Although isolated small-bowel disease was less common in patients with small spleens, and isolated colitis less common in patients with large spleens, this did not reach significance. Almost all patients with ulcerative colitis had involvement of the entire colon and rectum.

Presurgery Complications of Disease: In Crohn's disease, patients with small spleens had the highest incidence of complications of the disease process itself and patients with large spleens the lowest (Table 4). In ulcerative colitis, the highest incidence of complications also was found in the group with small spleens (Table 5).

Postoperative Complications: Patients with Crohn's disease presenting with small spleens had more postoperative infective problems (wound infection and/or abdominal abscesses) than patients having large and normal spleens (Table 6). Without exception, patients in the three groups with postoperative problems also had presurgery complications such as abscesses and fistulas. More than half of the patients with infective complications had small spleens, although there were fewer patients with small spleens than with normal or large ones. In ulcerative colitis patients, no trend could be detected regarding infective complications in the three groups, but numbers were small. No relationship between spleen size and other types of complications was found in patients with Crohn's disease or ulcerative colitis. There were four postoperative deaths in patients with Crohn's disease; all but one had isolated large-bowel disease. Two of them had normal spleens, one a small spleen, and the fourth a large spleen. All these patients were elderly (64 to 78 years). One (with a large spleen) died of an unexpected perforated duodenal ulcer, and a second (small spleen)

from postoperative respiratory failure. The two with normal spleen size died of septic complications, one early in the postoperative period and one some years later. No postoperative death occurred in the ulcerative colitis patients analyzed.

Recurrence of Disease in Crohn's Disease: The incidence of recurrent disease over a mean follow-up of 66 months (range, two months to ten years) is shown in Table 7. All clinical episodes of recurrent disease, including both true recurrence and relapse, where macroscopic disease was left behind at the first operation, were included.¹⁵ Most recurrences were proven histologically, but a few were based on accepted radiologic and clinical findings. No relationship between recurrence and spleen size was found.

Variation of Spleen Size: In 18 patients enough data was recorded to compare spleen size measured at two or even three successive laparotomies over a mean period of time of 44 months (range, six months to seven years). Fourteen had Crohn's disease and four ulcerative colitis. Of the 14 Crohn's disease patients, the spleen had enlarged in six, remained unchanged in five, and diminished in three. In all but two patients the changes were relatively minor—3 cm or less change in length, respectively. In two patients there was a greater degree of increase—9 and 14 cm in length. Enlargement was associated with recurrent disease in both patients, although the disease course in these two patients was unremarkable otherwise. In four patients with ulcerative colitis, the spleen had enlarged (one patient), remained constant (one patient), and diminished in two. There was no trend in alteration of spleen size in ulcerative colitis patients following colectomy.

TABLE 4. Presurgery Complications of Crohn's Disease Related to Spleen Size

	Small N = 18		Normal N = 31		Large N = 31	
	Number of patients	Percent	Number of patients	Percent	Number of patients	Percent
Presence of complications*	14	78	21	68	16	52

*Perforation, fistulas, abscess.

TABLE 5. *Presurgery Complications of Ulcerative Colitis Related to Spleen Size*

	Small N = 7		Normal N = 18		Large N = 10	
	Number of patients	Percent	Number of patients	Percent	Number of patients	Percent
Presence of complications*	4	57	3	17	4	40

*Perforation, fistulas, abscesses, bleeding, toxic megacolon.

Discussion

A number of factors must be taken into account when assessing the significance of splenic size in relation to other disease: the reliability of the method of measurement, the influence of other factors which may affect spleen size, such as age, sex, body height, etc., and other coexisting disease processes.

Method of Measurement: Many different techniques have been used to assess the size and weight of the spleen, apart from measurement following splenectomy or at autopsy.

Ultrasonic imaging is relatively simple to perform, atraumatic, noninvasive, and free of radiation effects. It has the potential to give important information about the anatomy, and possibly the pathology, of the spleen, yet this potential does not seem to have been exploited by pathologic correlation.

X-ray computerized tomography is also noninvasive and atraumatic, but time-consuming and involves radiation dosage. The equipment is not available routinely and is expensive to buy and operate.

Radioisotopic methods, easy to perform and atraumatic, and used most widely for imaging the spleen. They record the anatomy and some of the functions of the spleen which can be related to pathology. The images are relatively crude, and with labeled colloids the liver image can interfere with study of the spleen. Labeled, damaged, red cells image the spleen only¹³ and this technique is probably the most suitable. The volume of the spleen can be calculated from scintigraphy using computer methods. A high correlation coefficient between the assessment of spleen size from splenic scintigraphs and exsanguinated spleen weight has been recorded.¹⁴ This is surprising to

some extent, since it is noted that surgical interference, such as tying the splenic artery, can have a profound effect on spleen size, and the extent of change varies markedly with different patients and different disease processes. Likewise, the exsanguinated spleen after surgery is much smaller than that in the living patient and this factor must affect interpretation of spleen size measurement. Repeat examination during prolonged surgery has shown no variation in size during the operative period.

Nuclear magnetic resonance has not been used widely as yet for spleen imaging.

Normal Spleen Size: The spleen has been recorded in anatomic textbooks as being 12 cm in length, 7 cm in width, and 3 cm in thickness. On scintigraphy, the normal spleen length lies between 8.5 and 13.5 cm.² Splenic weight has been divided into broad categories from normal to markedly enlarged.¹⁴ This study records a normal spleen as less than 250 gm, slightly enlarged as 250 to 500 gm, moderately enlarged as 500 to 1000 gm, and markedly enlarged as more than 1000 gm; no figure is given for a small spleen. The authors' experience in laparotomy over many years has shown that a normal spleen is rarely less than 11 cm long except in the very elderly.

It is difficult to compare this directly with the findings on scintigraphy, where a normal spleen is taken as 8.5 cm in length. Scintigraphy is likely to give a slightly smaller length than direct measurement, since direct measurement includes the convexity of the spleen. This study also is related to people of middle age or younger, since the majority of patients coming to surgery with inflammatory bowel disease are from this age group.

The method of measurement used in this study was simple and direct thus avoiding the need for invasive or

TABLE 6. *Postoperative Infective Complications and Mortality Related to Spleen Size in Crohn's Disease Patients*

	Small N = 16		Normal N = 22		Large N = 22	
	Number of patients	Percent	Number of patients	Percent	Number of patients	Percent
Wound infection and/or abdominal abscesses	6	38	2	9	3	14
Mortality	1	6	2	9	1	4.5

TABLE 7. *Recurrence Related to Spleen Size in Crohn's Disease*

	Small N = 16		Normal N = 22		Large N = 22	
	Number of patients	Percent	Number of patients	Percent	Number of patients	Percent
Recurrence rate*	10	62.5	11	50	13	59

*Mean follow-up: five years and six months.

expensive techniques. The fact that all spleens were measured by a single surgeon using an identical technique adds reproducibility to the procedure, and allows an accuracy which is at least as great as that of any of the commonly used imaging techniques. Certainly it allows spleens to be classed into broad groups of small, normal, and large. To support this attitude interesting study exists in which the size of the spleen was visually evaluated on scintigrams by an experienced examiner who was able to place the spleens in broad groups as accurately as could be done by mathematical calculation.¹⁴

Other Factors which Affect Splenic Size: Normal variables which affect spleen size include sex and age. DeLand¹⁵ found spleen weight to decrease between the ages of 20 and 29 years and above 60 years of age. It is relatively constant between 30 and 59 years of age. Spleen weight is less in females than in males for all ages.¹⁵ Splenic weight also increased with increasing body weight, height, and surface area, although the changes are not great in relation to the changes occurring among the three groups described in this paper. Spleen weight may be controlled for height according to a formula,¹⁶ but again the changes are minimal.

In patients with Crohn's disease in this study, age was not a major factor in affecting spleen size as no difference was found in males between the mean age of patients in the large and small spleen group, although numbers were small. Similarly, among female patients, those with large spleens were significantly heavier than those with small spleens, though the range was greater than would be explained by weight alone. Perhaps this reflects the relationship between small spleen size and complications, with an effect on body weight. Differences of sex and height in females were again consistent with the general relationship between body mass and spleen size, although there was no significant difference between the mean heights of females with normal and small spleens.

In ulcerative colitis patients, the predominance of females in the groups with small and large spleens demonstrates the limited role of sex in explaining the differences of spleen size reported in our patients. Thus, it is apparent that patient characteristics alone cannot explain the changes observed in splenic size.

Variations in Splenic Size with Diseases in General: Splenomegaly accompanies many disorders, infections, hematologic disorders, and malignancies.¹⁶ Crohn's disease and ulcerative colitis usually are not mentioned in lists of inflammatory and granulomatous conditions which can cause splenomegaly. Splenic enlargement has been described in patients with malignant tumors^{4,6} and it has been speculated that this splenomegaly may be consequent on underlying immunologic mechanisms.^{3,4} It would not be unreasonable to consider that this could apply also to this study's patients, although splenomegaly can also be a nonspecific response to inflammatory bowel disease.

Splenic size has been specifically related to inflammatory bowel disease in a number of patients. Reports of splenomegaly in Crohn's disease are few,^{11,12} but splenic atrophy in inflammatory bowel disease has been the subject of a number of studies, because Crohn's disease and ulcerative colitis are the two bowel conditions (apart from celiac disease) in which splenic function has been studied most extensively.⁹

The observation that splenic size varied more widely in patients with inflammatory bowel disease than other conditions, and in fact showed a variation equivalent to that seen in malignancy, stimulated the authors' interest and led to this long prospective study of splenic size. No specific cause for splenomegaly in these cases has been found, and there has been no close correlation between enlarged spleens and disease course or outcome. It was hoped that this would be the case, because other variables in Crohn's disease are notable; for instance, the lymph-node size varies greatly from case to case, as do the presence and numbers of granulomas. Only diminished splenic size showed any correlation with disease course, however, being clearly related to a higher instance of complications of the disease process itself and complications of surgery for the disease. This correlates well with previous findings of increased complications after colectomy in the presence of diminished splenic function.^{1,2,17,18,19} This study concentrates on splenic size rather than function, although the two go together, to some extent. A study of the correlation between splenic size and function concluded that neither could be regarded

as being able to replace the other measurement.^{18,20}

It was found that small spleens are associated with increased complication rate, both prior to and after surgery. Whether the small spleen represents some defect of immunologic competence, allowing the disease to progress more rapidly, or whether the diminished spleen size is consequent upon the effects of the disease, perhaps resulting from absorption of toxins from the bowel, can only be open to speculation. The atrophic spleens described in previous publications^{1,2,17,18,19} were very small—vestigial, or on the order of 2×5 cm. This study shows that small spleens can also have a significant effect on complication rates, but at lesser extent than the frank atrophy previously described. There is now strong evidence from this study that patients with inflammatory bowel disease presenting with small spleens at laparotomy are at a higher risk of postoperative infective complications and extra care should be taken before, during, and after surgery to minimize these. This supports the findings and advice of other authors reporting on grosser degrees of splenic atrophy as shown by splenic function tests.^{1,2}

There is room for further investigation into the relationship between splenic function and size in these cases, particularly to determine whether splenic size can be influenced and disease complications reduced, for example, by approaches such as preoperative nutritional supplementation as an attempt to improve immunologic competence, or antibiotic therapy to counter bacterial absorption. While this study has shown no correlation between splenic size and the site or extent of disease, it is possible that more sophisticated immunologic studies might throw greater light on the relationship between the spleen and inflammatory bowel disease.

Acknowledgments

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