

Audit of the histopathological diagnosis of non-neoplastic colorectal biopsies: achievable standards for the diagnosis of inflammatory bowel disease

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Abstract

Aim—To assess the performance of a histopathology department in diagnosing inflammatory bowel diseases with comparison of reports from other centres.

Study population—1067 sets of endoscopic biopsies received in the department of histopathology, Royal Hallamshire Hospital, 1990–1995.

Methods—The histopathological diagnosis of non-neoplastic endoscopic colorectal biopsies was audited using data from histopathology reports. The biopsy diagnosis by the initial reporting pathologist and final diagnosis after additional investigations (endoscopy, radiology, microbiology) or surgery were used to derive sensitivity, specificity, and positive predictive values for categories of disease.

Results—Diagnosis was validated for 1067 biopsy sets (43% of those initially assessed). For all biopsies (with or without active inflammation) reports highly suggestive or suggestive of Crohn's disease had a sensitivity of 50%; for ulcerative colitis the comparable figure was 62%. Sensitivity was the same for both diagnoses (74%) in those biopsies with active inflammation. Positive predictive values for highly suggestive diagnoses of ulcerative colitis or Crohn's disease were 100%. In all biopsies the specificity of a histopathological diagnosis of normality was 96%.

Conclusions—These results compare favourably with the other published audits and present an achievable level of performance for non-specialist hospitals with non-specialist histopathology services.

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Keywords: audit; colorectal biopsies; endoscopic biopsies; inflammatory bowel disease

Many conditions mimic the clinical symptoms of chronic idiopathic inflammatory bowel disease,^{1–6} and thus histopathological examination of colorectal biopsies is important, both in confirming the diagnosis and in excluding other conditions, such as infective colitis^{6–8} which may be made worse by steroid treatment. In addition, a distinction may be drawn between ulcerative colitis and Crohn's disease, allowing appropriate treatment to be planned.^{9–11} The recent evidence based review of reports on the histopathological diagnosis of idiopathic inflammatory bowel disease¹² pro-

vides valuable information that can be used by practising histopathologists but it does not suggest what the attainable levels of performance in this area might be.

Many factors lead to variation in biopsy interpretation between reporting histopathologists.¹³ These include the experience the individual has in reporting such biopsies, biopsy adequacy, and the amount of other information known at the time of reporting. In a large teaching hospital this problem might be compounded by the presence of trainee histopathologists, with less experience, and a comparatively high staff turnover.

The aim of the study was to assess the sensitivity, specificity, and positive predictive value of the histopathological diagnosis of chronic idiopathic inflammatory bowel disease in our hospital, comparing our performance with the two previously published audits.^{14 15}

Methods

The study was carried out at the Royal Hallamshire Hospital, Sheffield. This is a large teaching hospital with 730 beds and an active endoscopy service. We used data from primary histopathological reports of large bowel endoscopic biopsies generated between 1990 and 1995 inclusive. Biopsies originating in diverted bowel, rectal stumps, or pouches were excluded, as were those with a diagnosis of neoplasm. The original reports were reviewed by two pathologists (AKD and SSC) and the report diagnosis was assigned to one of the defined set of diagnostic categories given in table 1 using a previously agreed set of synonyms (for example, “the appearances are more in keeping with ulcerative colitis than Crohn's disease” was assigned to the “suggestive of ulcerative colitis” category, whereas “the

Table 1 The histopathological diagnostic categories to which the original reports were assigned (categories taken from Jenkins et al¹²)

CIIBD highly suggestive of Crohn's disease
CIIBD suggestive of Crohn's disease
CIIBD highly suggestive of ulcerative colitis
CIIBD suggestive of ulcerative colitis
CIIBD of indeterminate type
Infective colitis
Ischaemic colitis
Radiation colitis
Mucosal prolapse
Melanosis coli
Inflammation unclassified, acute
Inflammation unclassified, chronic
Normal
Other specific diagnoses, eg pneumatosis coli

CIIBD, chronic idiopathic inflammatory bowel disease.

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Table 2 Histological diagnoses and outcomes in the 1067 biopsy sets with known diagnoses

Outcome	Histopathological diagnosis								Totals
	Highly suggestive of Crohn's disease	Suggestive of Crohn's disease	Highly suggestive of ulcerative colitis	Suggestive of ulcerative colitis	CIIBD indeterminate	Inflammation unclassified	Normal	Other diagnoses	
Crohn's disease	84	21	0	1	47	29	26	4	212
Ulcerative colitis	0	5	292	46	147	25	19	10	544
Other diagnoses*	0	0	0	0	1	2	4	52	59
Normal	0	0	0	0	1	4	243	4	252
Totals	84	26	292	47	196	60	292	70	1067

*31 mucosal prolapse, 19 radiation colitis, 5 infective colitis, 2 melanosis coli, 1 ischaemic colitis, 1 pneumatosis coli. CIIBD, chronic idiopathic inflammatory bowel disease.

Table 3 Histological diagnoses and outcomes in the 522 biopsy sets with known diagnoses and active inflammation

Outcome	Histopathological diagnosis								Totals
	Highly suggestive of Crohn's disease	Suggestive of Crohn's disease	Highly suggestive of ulcerative colitis	Suggestive of ulcerative colitis	CIIBD indeterminate	Inflammation unclassified	Normal	Other diagnoses	
Crohn's disease	75	18	0	1	26	4	0	1	125
Ulcerative colitis	0	4	250	37	91	5	0	2	389
Other diagnoses*	0	0	0	0	0	0	0	8	8
Normal	0	0	0	0	0	0	0	0	0
Totals	75	22	250	38	117	9	0	11	522

*3 radiation colitis, 3 infective colitis, 2 mucosal prolapse. CIIBD, chronic idiopathic inflammatory bowel disease.

appearances are those of active ulcerative colitis" was assigned to the "highly suggestive of ulcerative colitis" category).¹²

Only the original biopsy diagnosis was used in the audit, even if this opinion had later been altered by a second biopsy or after discussion at clinicopathological meetings. All reports were assigned to one of the categories of Jenkins *et al*¹²; if there was difficulty in interpreting whether the report indicated the definite presence of chronic idiopathic inflammatory bowel disease then it was assigned to the "inflammation unclassified" category.

Also recorded were the age of the patient, the number of biopsies taken per case, and the presence of active inflammation (as judged by the documented presence of polymorphonuclear neutrophils). Diagnosis was confirmed by the finding of typical endoscopy appearances seen on video photographs in the clinical notes, subsequent bowel resection, and pattern of disease on radiological investigation or microbiological culture results. In cases without confirmation by subsequent resection specimens, this final diagnostic outcome was made jointly by a histopathologist (SSC) and gastroenterologist (AJL) with review of the case notes. Cases where data were incomplete were excluded from the final analysis.

From these data the false negative and false positive rates were calculated. Sensitivity, specificity, and positive predictive values were derived for the diagnostic categories pertaining

to idiopathic inflammatory bowel disease. These values were then compared with those of published studies of a similar nature.

Results

Overall, 2507 endoscopic biopsy sets were reported during the time of the study by 11 consultant histopathologists and 30 supervised trainees. Diagnosis was confirmed, by the methods discussed above, in 1067 of these sets and these were used for the final analyses. The age was known for 1064 of these cases. Mean patient age was 46 years (range 14 to 88 years). Diagnosis was confirmed by endoscopy in 988 cases, by histological examination of a resection specimen in 84, by evidence of small bowel disease on barium follow through studies in five, and on positive microbiological culture in three (some cases were confirmed by more than one method). The number of biopsies taken per case ranged from one to 12 (mean 2, mode 1), giving a total of 2111 individual biopsy events for these 1067 cases.

Two similar published audit studies^{14 15} were identified by extensive searching on computerised bibliographic databases. Four other studies which used non-routine methods of diagnosis on selected biopsies were identified, from which similar outcome measures could be calculated for comparison,^{6 16-18} although these included few, if any, normal biopsies so the specificity could not be calculated.^{6 16 17 19}

The results are summarised in tables 2-5. The specificity of histopathological diagnosis

Table 4 Studies used for comparison

Authors	Year of publication	Ref No	Number of biopsies	Type of study
Frei and Morson	1982	14	209	Audit of routine histopathological diagnoses in a specialist colorectal centre
Thompson <i>et al</i>	1985	16	75	Multivariate discriminant analysis applied to measurements made on rectal biopsies using an image analysis system
Jenkins and Vicery	1988	17	50	Multivariate discriminant analysis applied to measurements made on rectal biopsies using an image analysis system
Seldenrijk <i>et al</i>	1991	19	61	Multivariate discriminant analysis applied to defined human observations in selected sets of biopsies
Surawicz <i>et al</i>	1994	6	133	Multivariate discriminant analysis applied to defined human observations in selected sets of biopsies
Dundas <i>et al</i>	1997	15	118	Prospective audit of routine histopathological diagnoses in a district general hospital

Table 5 Comparison of sensitivity and positive predictive values (PPV) of the histopathological diagnoses of ulcerative colitis and Crohn's disease from this audit and published studies; 95% confidence intervals are given for the figures in this study where calculable (that is, where more than one misclassification)

Study (ref No)	Sensitivity for Crohn's disease	PPV for Crohn's disease	Sensitivity for ulcerative colitis	PPV for ulcerative colitis
This study; all biopsies, highly suggestive of diagnosis (A)	40% (33–46%)	100%	54% (49–58%)	100%
This study; all biopsies, highly suggestive and suggestive of diagnosis (B)	50% (43–56%)	95% (92–99%)	62% (58–66%)	99%
This study; active inflammation, highly suggestive of diagnosis (C)	60% (51–69%)	100%	64% (60–69%)	100%
This study; active inflammation, highly suggestive and suggestive of diagnosis (D)	74% (67–82%)	96% (92–99%)	74% (69–78%)	99%
Frei and Morson, 1982 (14)	40%	82%	72%	96%
Thompson <i>et al</i> , 1985 (16)	45%	82%	70%	74%
Jenkins and Vicery, 1988 (17)	77%	73%	71%	76%
Seldenrijk <i>et al</i> , 1991 (19)	70%	93%	75%	88%
Surawicz <i>et al</i> , 1994 (6)	67%	77%	82%	98%
Dundas <i>et al</i> , 1997 (15)	100%	N/A	99%	N/A

N/A, not assessed.

(that is, the correct identification of normal cases) was 96% for all biopsies with known outcome in this study.

Discussion

Despite the large study size, only 43% of patient diagnoses were confirmed. This was partly because many hospital departments were involved in validation of the outcome. In particular, confirmation of infective colitis was low for a number of reasons—inaccessible microbiology results, presentation after the acute phase, culture not always being undertaken, and because the causative organism was not isolated in many cases. Another problem encountered was lack of standardisation in the report conclusions, which sometimes made it difficult to assign cases to a diagnostic category.

One criticism of the study that can be made was the acceptance of typical endoscopic appearance as validation of the histopathological diagnosis, the usual flow of information in the diagnostic process being the confirmation of endoscopic appearances by histopathological assessment of biopsies. Whilst this criticism has some validity, discounting the endoscopic appearances from the validation process would have dramatically reduced the number of biopsies that could be audited (only 89 outcomes were validated by the histology of large resection specimens or small bowel radiology). The endoscopic appearances were reviewed carefully, most with pictures taken at the time of endoscopy, and often these appearances were very characteristic of the particular disease (for example, confluent distal inflammation with a sharp proximal demarcation boundary in ulcerative colitis). Despite these possible reservations, the study is large and reflects daily practice.

During the study sensitivity for a diagnosis “highly suggestive of Crohn's disease” at our hospital was 40% and for a diagnosis “highly suggestive of ulcerative colitis” 54% in all cases with or without active inflammation (row A, table 5). The positive predictive value for both was 100%. These results can be compared with the audit of the diagnosis of inflammatory bowel disease was performed by Frei and Morson at St Mark's Hospital in London,¹⁴ a major centre for the study of colorectal disease. This study included biopsies with and without active inflammation. Whilst we categorised disease on the basis of report summaries in accordance with the recommendations of Jenkins *et al*,¹²

they calculated sensitivity and specificity of diagnosis for Crohn's disease, ulcerative colitis, and indeterminate colitis and did not include categories “suggestive of” the diagnosis separately. In Frei and Morson's study the sensitivity of diagnosis was 40% for Crohn's disease and 70% for ulcerative colitis, comparable with our figures of 50% and 62% respectively (amalgamating “highly suggestive” and “suggestive” diagnoses to form comparable diagnostic categories; row B, table 5). Overall we diagnosed a higher proportion of biopsy sets as idiopathic inflammatory bowel disease of indeterminate type (30% *v* 22%). The recent study by Dundas *et al* did not divide the histopathological diagnosis into Crohn's disease and ulcerative colitis but amalgamated these diagnostic groups into chronic inflammatory bowel disease.¹⁵ This means that most of the indices calculated in our study (such as positive predictive value and specificity) cannot be directly compared, but the sensitivity attained by Dundas *et al* is higher than in our study. In the Dundas study all biopsies were reported by one histopathologist specialising in gastrointestinal pathology using a protocol with defined histopathological observations and this may account for the high sensitivity.

Other studies performed to look at the accuracy of histological diagnosis of inflammatory bowel disease^{6 16 17 19} have been inter-observer studies or have used quantitative image analysis rather than audit of routine practice. These studies have used selected series of biopsies that make direct comparison with our study difficult. Many of them used biopsies from cases with clinically active ulcerative colitis or Crohn's disease and it is likely that the majority of these biopsies would have shown active inflammation. Some studies are even more selective—for example, that of Thompson *et al* only used cases of Crohn's disease that showed granulomas on biopsy.¹⁶ These studies used fewer cases than either our study or those of Morson¹⁴ or Dundas,¹⁵ and found that sensitivities for the diagnosis of acute ulcerative colitis ranged from 70% to 82%, and from 40% to 77% for acute Crohn's disease.^{6 16 17 19} Our sensitivities for Crohn's disease (40–74%, rows A–D, table 5) are very similar to the range in these published studies, as are our sensitivities for ulcerative colitis (54–74%, rows A–D, table 5).

A definite diagnosis of Crohn's disease or ulcerative colitis in our study was proved

correct in 100% of cases; 80.8% of the cases reported as suggestive of Crohn's disease were from patients with Crohn's disease and the remainder had ulcerative colitis. Where the biopsy was reported as suggestive of ulcerative colitis, 97.9% proved to have ulcerative colitis, and the remaining case was of Crohn's disease.

Our figures of lower sensitivity in Crohn's disease concur with those of Frei and Morson, and it seems logical that sampling error owing to the patchy nature of Crohn's disease accounts for much this. In ulcerative colitis, sampling error is reduced by confluence of disease, but biopsy appearances may still be altered by previous treatment. Table 5 shows that our sensitivities for both Crohn's disease and ulcerative colitis were increased when only biopsies with active inflammation were included in the analysis. This increase was proportionately more in Crohn's disease (50% to 74% for amalgamated "suggestive" and "highly suggestive" categories) than ulcerative colitis (62% to 74%), in keeping with the suggestion that sampling error at endoscopy decreases the overall sensitivity for Crohn's disease. We conclude that we are equally good at diagnosing both Crohn's disease and ulcerative colitis if the biopsy is taken from a site of active inflammation, that is, once sampling error is removed.

Our false positive rates were low when compared with other studies: 1% for Crohn's disease and 1% for ulcerative colitis in biopsies reported as highly suggestive or suggestive of those diagnoses, and 0% for the highly suggestive categories. Jenkins *et al* reported 23% and 28%,²⁰ and Seldenrijk *et al*, 10% and 5%.¹⁹

The fact that biopsies had been reported by a large number of people seemed to make little difference. Interobserver agreement has been studied by other investigators^{13 21-23} and has been found to be of the order of 65-76% for a final diagnosis of idiopathic inflammatory bowel disease.¹³ Theodossi *et al* found good agreement in differentiating normal biopsies from those with idiopathic inflammatory bowel disease, but less agreement where non-specific inflammation was reported.¹³ Six per cent of our biopsies were reported as having non-specific inflammation ("inflammation unclassified" category), 14% of biopsies from cases of Crohn's disease, and 9% from patients with ulcerative colitis.

This audit shows that our results are at least as good as previously published audits^{14 15} and also compare favourably with the published studies designed to assess intra- and interobserver variability outside the audit context. Users of the diagnostic histopathology service can be very confident of the positive predictive value of definite histopathological diagnoses of Crohn's disease and ulcerative colitis. We found no cases in which Crohn's disease was initially diagnosed as ulcerative colitis (in the "highly suggestive of" category), an important

finding when pouch surgery may be carried out as a primary procedure. The sensitivity of the diagnoses of ulcerative colitis and Crohn's disease could be increased by specific training, changing thresholds for reporting categories of chronic idiopathic inflammatory bowel disease, or use of standardised reporting methods,¹² but this should not be at the expense of a reduction in the positive predictive value.

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