DYSPEPSIA MANAGEMENT

Role of endoscopy and biopsy in the work up of dyspepsia

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Endoscopy is recommended as the first investigation in the work up of a patient with dyspeptic symptoms and is essential in the classification of the patient's condition as organic or functional dyspepsia. Although the correlation between mucosal alterations and symptom pattern is difficult, endoscopy will remain the initial investigation of choice for clinically relevant abnormalities that need proper detection and biopsy.

SUMMARY

Endoscopy is recommended as the first investigation in the work up of a patient with dyspeptic symptoms. The most commonly reported major endoscopic abnormalities are: gastric ulcer (1.6–8.2%), duodenal ulcer (2.3–12.7%), oesophagitis (0–23.0%), and gastric malignancy (0–3.4%). The relationship between the organic causes of dyspepsia and dyspepsia symptomatology can often be uncertain, with healing of the organic cause not always resulting in complete symptom resolution. The relationship between mild or equivocal endoscopic inflammatory gastroduodenal abnormalities and dyspeptic symptoms is also confusing, as shown in the poor or non-existent correlation between erythematous/exudative duodenitis or gastritis and symptoms. When endoscopic findings in patients with dyspepsia are compared with those in age and sex matched controls, they show no clinically relevant association with dyspeptic symptoms, with the possible exceptions of peptic ulcer disease and duodenitis seen by endoscopy. The dividing line between organic and functional dyspepsia, which largely depends on endoscopic findings, remains highly arbitrary. It is therefore proposed that the line is drawn between the presence or absence of endoscopically visible tissue destruction or gross mucosal alteration. The scoring of drug induced mucosal damage remains an unresolved problem. The requirement for routine biopsies in the absence of unequivocal endoscopic abnormalities is highly controversial but it is the author's "belief" that biopsies are justified and appropriate whenever the indication for endoscopic examination is deemed appropriate. Biopsies should be taken from the antrum, the angulus, and the corpus, according to the Sydney-Houston system for grading gastritis.

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INTRODUCTION

Endoscopy is recommended as the first investigation in the work up of a patient with dyspeptic symptoms.[1] Endoscopic examination is essential in the classification of the patient's condition as organic or functional dyspepsia. Ideally, endoscopy should be carried out during a symptomatic phase of the disease and in the absence of any drug therapy, particularly acid suppressants, that may obscure relevant features or interfere with the interpretation of endoscopic abnormalities.

ENDOSCOPIC FINDINGS

Before discussing the usual endoscopic findings, it should be made clear that most of the studies of dyspepsia were carried out when patients with predominant gastro-oesophageal reflux symptoms were included within the definition of dyspepsia. As a result, the proportions of patients with reflux oesophagitis may appear to be excessive and variable. It should also be realised that there were major differences in how patients were selected and in the inclusion and exclusion criteria used.[2]

The distribution of the main endoscopic findings varies substantially across study populations, as shown in table 1, reflecting in part the methodological differences. Table 2 gives the median values and ranges. The major endoscopic abnormalities found were as follows: gastric ulcer (1.6–8.2%), duodenal ulcer (2.3–12.7%), reflux oesophagitis (0–23.0%), and gastric malignancy (0–3.4%). Not shown in the tables are the variable proportions of patients with gastric or duodenal erosions. Clearly, a substantial number of patients (at least half?) had no detectable abnormalities, incidental findings, or changes of uncertain significance with regard to their symptoms.

Patients with oesophagitis form a rather heterogeneous group because the severity of their abnormalities is quite variable—mild abnormalities are the most common. The distribution of grades of abnormalities was recently determined in a large scale French study that evaluated the prevalence of endoscopic lesions in patients with gastro-oesophageal reflux disease: 85.5% of 961 patients had mild to moderate oesophagitis (grade I (solitary break), 54.2%; grade II (confluent breaks), 31.3%) and 14.5% had severe oesophagitis.[26] The distribution of abnormalities seen in patients with "genuine" dyspepsia, without predominant reflux symptoms, is unknown. Presumably, severe grades of reflux oesophagitis would be rare.

Abbreviations: ASA, acetylsalicylic acid; CMV, cytomegalovirus.

Table 1 Endoscopic findings in dyspepsia

Study	n	Peptic ulcer disease (%)		Oesophagitis (%)	Cancer (%)	No organic finding (%)
		Gastric ulcer	Duodenal ulcer			
Beavis *et al*[3]	187	6	5	18	1.1	
Gear and Barnes[4]	346	6	12		1.2	
Edenholm *et al*[5]	165	4	10		1.2	
Fjosne *et al*[6]	676				1.3	
Williams *et al*[7]	686	8	12	14	1.6	
Kagevi *et al*[8]	172	4	9	11	1.2	
Bernersen *et al*[9]	309	2	2		0.0	
Hallissey *et al*[10]	2585	7	10		2.2	
Johannessen *et al*[11]	930	5	13	9	1.0	71
Kerrigan *et al*[12]	1091	19		23	2.0	40
Johnsen *et al*[13]	273	8		12	<1.0	53
Sobala *et al*[14]	293	20		15	2.0	63
Talley *et al*[15]	820	8	4	14	3.4	20
Klauser et al [16]	220	5	10	17	1.8	
Mansi *et al*[17]	2253	2	5	5	2.0	
Halter *et al*[18]	376	1		3	<1.0	
Crean *et al*[19]	1540	7			3.2	
Bytzer *et al*[20]	207	22		10	1.0	67
Heikkinen *et al*[21]	400	15		15	2.0	34
Hu *et al*[22]	1006	40		?	2.0	50
Adang *et al*[23]	317	6	7		<1.0	75
Bianchi Porro *et al*[24]	2229	18		9	1.0	56
Gonvers *et al*[25]	450	17		14	<1.0	51

Table 2 Range of endoscopic findings in dyspepsia (median (range) values from 22 studies)[3–24]

Gastroduodenal ulcer combined	17% (1–44)
Gastric ulcer	5.5% (1.6–8.2)
Duodenal ulcer	10% (2.3–12.7)
Reflux oesophagitis	12% (0–23.0)
Gastric malignancy	1.2% (0–3.4)
Normal findings/miscellaneous irrelevant findings	51% (2–71)

Table 3 Endoscopic findings in patients with dyspepsia compared with those of age and sex matched controls[13]

	Dyspepsia (%)	Controls (%)
Oesophagitis, grades I–II	12	8
Hiatal hernia	3	3
Gastritis (superficial)	20	16
Atrophic gastritis	4	4
Duodenogastric reflux	18	13
Peptic ulcer disease	8* (p=0.02)	4
Duodenitis	20* (p=0.0005)	9
Normal	54 (p=0.003)	66

*Number of discordant pairs in the 2×2 table (there are two more columns in the table—that is, discordant pairs and significance (p value)).

Which findings are incidental or of uncertain significance?

Few would dispute that peptic ulcer disease, oesophagitis, or malignancy relate to dyspeptic symptomatology. The nature of the latter relationship however is sometimes uncertain or debatable. For example, the disappearance of dyspeptic symptoms after peptic ulcer healing through *Helicobacter pylori* eradication is often incomplete or even absent. According to McColl *et al*, complete freedom from symptoms three years after *H pylori* eradication was seen in only 55% of peptic ulcer patients.[27]

Even more difficult to determine is the relationship between gastroduodenal erosions (erosive gastroduodenitis) and dyspeptic symptoms. Some would consider erosive duodenitis to be part of the spectrum of duodenal ulcer disease. Others consider a few erosions in the stomach to be clinically irrelevant.

Finally, the relationship between mild or equivocal endoscopic gastritic abnormalities and dyspeptic symptoms is utterly confusing. The correlation of erythematous/exudative duodenitis or gastritis (so-called non-erosive duodenitis and gastritis) with symptoms is often poor or non-existent. As a result, many consider such abnormalities as clinically irrelevant, yet this may not always be so.

Comparison of endoscopic findings in patients with dyspepsia versus controls

The situation becomes even more perplexing when we compare endoscopic findings in patients with dyspepsia with those in non-patient controls. For example, Johnsen *et al* compared endoscopic findings in patients with dyspepsia with those in age and sex matched controls (table 3).[13] The diagnostic findings, with the possible exceptions of peptic ulcer disease and duodenitis seen on endoscopy, showed no clinically relevant association with dyspeptic symptoms.

UNRESOLVED PROBLEMS

The dividing line between organic and functional dyspepsia, which largely depends on endoscopic findings, remains arbitrary. Some would consider any evidence of tissue necrosis/destruction, seen as flat or raised erosions, as evidence of organic disease. Others are willing to accept a limited number of erosions (up to five?) as still compatible with functional disease.[28] Equally, if not more confusing, is the acceptance by some of minor or equivocal changes in the distal oesophagus and cardia as evidence of reflux induced inflammation whereas others require evidence of mucosal breaks as a minimum. All this is obviously highly arbitrary and most unsatisfactory because it confuses the clinician.

I would therefore propose that, for the time being, the dividing line between organic and functional dyspepsia is drawn between the presence or absence of endoscopically visible tissue destruction or gross mucosal alteration (table 4).

Table 4 Dyspepsia—endoscopic evaluation. Tissue destruction or gross alteration as the dividing line between organic dyspepsia and functional dyspepsia

Organic dyspepsia	Functional dyspepsia
• Gastric ulcer • Duodenal ulcer • Oesophagitis with or without hiatal hernia • Neoplasm • Erosive gastritis • Erosive duodenitis	• Erythematous/exudative gastritis • Atrophic gastritis • Incidental miscellaneous abnormalities (vascular ectasia, polyp, mucosal tag, etc)

Table 5 Scoring system for drug induced mucosal damage[29]

Grade 0	No visible injury
Grade 1	<10 (petechial) haemorrhages with no erosions
Grade 2	10–25 haemorrhages and/or 1–5 erosions
Grade 3	>25 haemorrhages and/or 6–10 erosions
Grade 4	>10 erosions and/or ulcer

Grades 0–2, clinically insignificant; grades 3–4, clinically significant.

A further unresolved problem is that of gastric mucosal inflammation arising from infectious causes, such as *H pylori*, the cytomegalovirus (CMV), syphilis, etc. Is this sufficient evidence for organic disease causing the symptoms? The endoscopic spectrum of abnormalities linked with *H pylori* infection is highly variable. In the majority of infected individuals, the mucosal changes, if present at all, are so minor that distinguishing them from the "normal" pattern becomes impossible. Only in a minority does the infection cause undeniable patchy erythematous changes, often with punctate exudate and occasionally mixed with patchy areas of atrophy. Conspicuous nodular deformity, particularly of the antrum, is rare in adults. Also rare is raised erosive, rugal hyperplastic, or markedly atrophic endoscopic change. It therefore seems sensible to refrain from adding *H pylori* infection to the list of organic diseases causing dyspepsia until we better understand when, why, and how symptoms are generated in *H pylori* associated gastritis and when and why symptoms may regress after cure. This conservative view is based mainly on the lack of regression in dyspeptic symptomatology that is commonly observed following *H pylori* eradication. Again, this may change once the relationship between inflammation and symptom generation, if any, is better understood. It should also be realised that the distinction between "organic" and "functional" dyspepsia is based on a dynamic process, with patients constantly crossing the dividing line in both directions. An example of this is the common experience that some patients with "functional" dyspeptic complaints will develop a peptic ulcer during follow up.

Equally problematic and arbitrary is the scoring of drug induced mucosal damage. Table 5 summarises one of the most commonly used grading schemes.[29] Grades 0–2 are considered clinically insignificant but this dividing line is again arbitrary and not based on validated findings. Long term low dose oral acetylsalicylic acid (ASA) is widely used to prevent cardiovascular and cerebrovascular thrombotic events but ASA doses as low as 10 mg can be associated with gastric mucosal damage.[30 31] The endoscopist should meticulously question patients for possible ASA or non-steroidal anti-inflammatory drug use whenever confronted with erosive or haemorrhagic lesions in the upper intestinal tract, as patients often do not spontaneously admit to such drug consumption.

APPROPRIATE USE OF ENDOSCOPY

The appropriate use of endoscopy has attracted particular interest. Gonvers *et al* audited an open access endoscopy service in Switzerland[25] using the guidelines of the American Society for Gastrointestinal Endoscopy.[32] The authors found that 46% of 442 consecutive referrals for endoscopy were "inappropriate" although a clinically significant lesion was almost as likely to be present in the "non-appropriate" as in the "appropriate" group. Of those judged "inappropriate", 13% had peptic ulcer disease compared with 16% in the "appropriate" group. Similar findings were published from the UK.[33]

NEED FOR BIOPSIES

The requirement for routine biopsies in the absence of unequivocal endoscopic abnormalities is highly controversial. Many feel that the results gained from routine biopsies, which are costly and time consuming, are minimal and do not justify the expense. Others feel that routine biopsies are mandatory for detecting and grading gastric inflammation, atrophy, intestinal metaplasia, and even dysplasia; for detecting various infections, such as *Giardia*, coccidiosis, CMV, etc.; and for detecting Crohn's disease, sarcoidosis, amyloidosis, eosinophilic gastritis, lymphocytic gastritis, etc.[34–36] There are no solid scientific data to guide us in this dilemma. It is my "belief" that biopsies are justified and appropriate whenever the indication for endoscopic examination is deemed to be appropriate. Biopsies should be taken from the antrum, the angulus, and the corpus according to the Sydney-Houston system for grading gastritis.[37]

CONCLUSION

Endoscopy is, and will remain, the initial investigation of choice for clinically relevant abnormalities that need proper detection and biopsy. Whether small calibre transnasal endoscopy, which can also be carried out by primary care physicians, will become the standard procedure is uncertain at present.[38] The correlation between mucosal alterations and symptom pattern will remain difficult to determine and confusing as long as the genesis of the various symptoms of dyspepsia remains obscure.

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