Complete and incomplete intestinal metaplasia at the oesophagogastric junction: prevalences and associations with endoscopic erosive oesophagitis and gastritis

M Voutilainen, M Färkkilä, M Juhola, J-P Mecklin, P Sipponen, and The Central Finland Endoscopy Study Group

Abstract

Background/Aims—Intestinal metaplasia (IM) is a common finding at the oesophagogastric junction, but the aetopathogenesis of the different IM subtypes—that is, incomplete IM (specialised columnar epithelium, SCE) and complete IM—and their associations with gastro-oesophageal reflux disease and Helicobacter pylori gastritis are unclear.

Methods—1058 consecutive dyspeptic patients undergoing gastroscopy were enrolled. The gastric, oesophagogastric junctional, and oesophageal biopsy specimens obtained were stained with haematoxylin and eosin, alcian blue (pH 2.5), periodic acid Schiff, and modified Giemsa.

Results—Complete junctional IM was detected in 196 (19%) of the 1058 subjects, and in 134 (13%) was the sole IM subtype. Incomplete junctional IM (SCE) was detected in 101 (10%) subjects, of whom 62 (61%) also had the complete IM subtype. Of patients with normal gastric histology (n = 426), 6% had complete IM and 7% junctional SCE. The prevalence of both types of IM increased with age in patients with either normal gastric histology or chronic gastritis (n = 611). Epithelial dysplasia was not detected in any patients with junctional IM. In multivariate analysis, independent risk factors for incomplete junctional IM were age (odds ratio [OR] 1.3 per decade, 95% confidence interval [CI] 1.2 to 1.6), endoscopic erosive oesophagitis (OR 1.9, 95% CI 1.1 to 3.2), and chronic cardia inflammation (OR 2.9, 95% CI 1.3 to 6.2), but not gastric H pylori infection (OR 1.0, 95% CI 0.6 to 1.7). In univariate analysis, junctional incomplete IM was not associated with cardia H pylori infection. Independent risk factors for “pure” complete junctional IM (n = 134) were age (OR 1.2 per decade, 95% CI 1.0 to 1.4), antral predominant non-atrophic gastritis (OR 2.6, 95% CI 1.3 to 5.2), antral predominant atrophic gastritis (OR 2.1, 95% CI 1.1 to 5.2), and multifocal atrophic gastritis (OR 7.1, 95% CI 2.5 to 19.8). In univariate analysis, junctional complete IM was strongly associated with chronic cardia inflammation and cardia H pylori infection (p < 0.001).

Conclusions—Both complete and incomplete junctional IM are independent acquired lesions that increase in prevalence with age. Although IM subtypes often occur simultaneously, they show remarkable differences in their associations with gastritis and erosive oesophagitis: junctional complete IM is a manifestation of multifocal atrophic gastritis, while the incomplete form (SCE) may result from carditis and gastro-oesophageal reflux disease. The frequency of dysplasia in intestinal metaplasia at the oesophagogastric junction appears to be low.

(Gut 1999;45:644–648)

Keywords: intestinal metaplasia; oesophagogastric junction; oesophagitis; gastritis; gastro-oesophageal reflux disease; Helicobacter pylori

Intestinal metaplasia (IM) is commonly detected in random biopsy specimens taken immediately distal to the normally located squamocolumnar junction. 1–6 IM at the oesophagogastric junction is a topic of great interest, because it may aetiopathogenetically be linked to the adenocarcinoma at this location. 7 The incidence of this carcinoma has increased at a rate exceeding that of any other cancer. 8 Whether IM at the oesophagogastric junction is a consequence of gastro-oesophageal reflux disease or a manifestation of multifocal gastritis caused by Helicobacter pylori is unclear.

IM is histopathologically divided into three subgroups based on the mucin content of the columnar-type and goblet cells. 9 10 In the complete form of IM (type I), the columnar cells

Abbreviations used in this paper: IM, intestinal metaplasia; SCE, specialised columnar epithelium.
are absorptive and contain neutral mucins, whereas in the incomplete forms of IM, they are at least partly secretory and contain acidic sialomucins (type II) or sulphomucins (type III). IM types II and III are commonly referred to as incomplete IM or specialised columnar epithelium (SCE) and are easily recognised with simple histochemical stains such as alcian blue (pH 2.5)-periodic acid Schiff. SCE is the histological hallmark of Barrett's oesophagus.

This study set out to examine the prevalences and demographics of complete IM and SCE at the oesophago gastric junction in a large consecutive series of dyspeptic patients sent for open access gastroscopy. We wanted to evaluate the associations between these IM subtypes and gastritis, *H pylori* infection, and endoscopic and histological signs of gastro-oesophageal reflux disease, as well as the extent to which junctional complete IM and SCE are similar or dissimilar in these associations.

**Methods**

**PATIENTS**

The study population totalled 1698 consecutive dyspeptic patients sent for gastroscopy over a four month period. The patients with classical Barrett's oesophagus—that is, SCE detected above the oesophago gastric junction (n = 28)—were excluded. Patients for whom no adequate gastric antral, corpus, and oesophagogastric junctional biopsy specimens were available were also excluded, leaving a final study population of 1058 patients.

**ENDOSCOPY**

Two biopsy specimens were obtained from the gastric antrum 2 cm or more from the pylorus, and two others from the large curve of the gastric body, the oesophagogastric junction, and the distal oesophagus 2 cm or more above the junction (eight samples in all).

The oesophagogastric junctional biopsy specimens were obtained by first identifying the junction between the oesophagus and stomach at the level of the proximal end of the gastric folds. The normal squamocolumnar mucosal junction, or Z line, is coincident with the aforementioned junction. In this report, junctional IM denotes the IM detected in biopsy specimens obtained immediately distal to normal appearing Z line. Junctional biopsy specimens were obtained under direct vision with the gastroscope in antegrade position. If gastric type mucosa extended circumferentially or as tongues above the oesophagogastric junction, biopsy specimens were taken separately from this mucosa to detect Barrett's oesophagus. Subjects with Barrett's oesophagus or incomplete IM detected in the oesophagus were excluded from the present analysis.

Subjects with endoscopic oesophagitis grades II-IV by Savary-Miller classification were classified as having erosive oesophagitis.

**HISTOLOGY**

Formalin fixed biopsy samples were embedded in paraffin wax, and tissue sections stained with haematoxylin-eosin, alcian blue (pH 2.5)-periodic acid Schiff, and modified Giemsa. The presence of gastritis, activity of gastritis, gastric gland atrophy, IM, and *H pylori* infection were classified according to the Sydney System. Chronic gastritis subtypes were classified as follows: 1, normal gastric histology; 2, antral predominant gastritis (inflammation or inflammatory activity more severe in the gastric antrum than in the corpus, but no gastric gland atrophy); 3, antral predominant atrophic gastritis (gastric gland atrophy detected in the antrum but not the corpus); 4, corpus predominant gastritis (gastric gland atrophy detected only in the corpus or non-atrophic gastritis with more severe inflammation or inflammatory activity in the corpus); 5, multifocal atrophic gastritis (gastritis with atrophy detected in both the antrum and corpus).

The presence of complete and/or incomplete IM, chronic inflammation, and *H pylori* infection in the cardia was evaluated in junctional biopsy specimens. Only cases showing typical mucus secreting glandular gastric cardia epithelium were included in this study. Chronic cardia inflammation was defined as infiltration of the lamina propria by lymphocytes and plasma cells. Complete IM was defined as the presence of goblet cells without acidic alcian blue (pH 2.5)-periodic acid Schiff positive material in columnar-type cells.

Incomplete IM or SCE was defined as the presence of goblet cells, with acidic mucins in goblet and adjacent columnar-appearing cells. Figure 1 shows examples of complete IM and SCE.
and incomplete forms of metaplasia. Dysplasia, when present and definite, was graded as low grade or high grade.22 The study population was divided into three groups according to the histological findings at the oesophagogastric junction: group 1, patients with only complete type junctional IM; group 2, patients with SCE or incomplete junctional IM (61% of them also had complete IM); group 3, control subjects without either type of IM.

Microscopic oesophagitis was defined as papillae extending into the upper third of the oesophageal mucosa with or without the infiltration of inflammatory cells.8

Table 1 Demographic, endoscopic, and histological characteristics of patients with junctional complete or incomplete intestinal metaplasia (IM) compared with those of the control group without these lesions.

<table>
<thead>
<tr>
<th></th>
<th>Junctional complete IM (%) (n=134)</th>
<th>Junctional incomplete IM (%) (n=101)</th>
<th>Non-IM group (%) (n=828)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (95% CI) age (y)</td>
<td>65.0 (62.5 to 67.4)</td>
<td>65.3 (62.8 to 67.7)</td>
<td>54.9 (53.8 to 56.1)</td>
</tr>
<tr>
<td>Male:female</td>
<td>1:1.5</td>
<td>1:1.2</td>
<td>1:1.5</td>
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<tr>
<td>NSAID use</td>
<td>17 (11–24)</td>
<td>14 (7–21)</td>
<td>14 (13–17)</td>
</tr>
<tr>
<td>Reflux symptoms</td>
<td>21 (14–28)</td>
<td>28 (19–37)</td>
<td>22 (19–25)</td>
</tr>
<tr>
<td>Hiatal hernia</td>
<td>21 (7–42)</td>
<td>26 (17–36)</td>
<td>19 (13–29)</td>
</tr>
<tr>
<td>Smoking</td>
<td>10 (2–27)</td>
<td>25 (14–40)</td>
<td>18 (14–22)</td>
</tr>
<tr>
<td>Male:female</td>
<td>87 (82–93)</td>
<td>92 (85–97)</td>
<td>73 (70–76)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentage with 95 confidence interval of the total amount of the IM subtype.

https://doi.org/10.1136/gut.2017.282975

Figure 2 Prevalence of junctional complete and incomplete (specialised columnar epithelium, SCE) intestinal metaplasia (IM) in different age groups. NH, normal gastric histology (n = 426); CG, chronic gastritis (n = 632). The correlation of age with both IM types was significant in the CG (p<0.001) for complete IM and incomplete IM (SCE) as the sole type of IM at the oesophagogastric junction. The mean age of the “pure” complete IM group was 65.0 (95% CI 62.5 to 67.4) years and that of the “pure” incomplete IM group 62.9 (95% CI 58.5 to 67.3) years. A total of 62 patients harboured both types of IM simultaneously, giving overall prevalence for complete IM of 19% (n = 196), and for incomplete IM or SCE of 10% (n = 101). Henceforth patients with complete IM denotes the patients with this type of IM only (n = 134), whereas the incomplete IM or SCE group refers to patients with SCE only plus those with complete IM as well as SCE (n = 101).

Table 2 The prevalences of oesophagogastric junctional complete and incomplete intestinal metaplasia (IM) in different types of gastritis.

<table>
<thead>
<tr>
<th></th>
<th>Junctional complete IM (%) (n=134)</th>
<th>Junctional incomplete IM (%) (n=101)</th>
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<tbody>
<tr>
<td>Normal gastric histology (n=417)†</td>
<td>24 (18; 11 to 24)</td>
<td>29 (29; 20 to 38)*</td>
</tr>
<tr>
<td>Antral predominant atrophic gastritis (n=421, 78% H pylori positive)</td>
<td>60 (45; 36 to 53)</td>
<td>40 (40; 30 to 49)</td>
</tr>
<tr>
<td>Antral predominant atrophic gastritis (n=86, 81% H pylori positive)</td>
<td>18 (13; 8 to 19)</td>
<td>20 (20; 12 to 28)</td>
</tr>
<tr>
<td>Corpus predominant atrophic gastritis (n=75, 26% H pylori positive)</td>
<td>17 (13; 7 to 18)</td>
<td>10 (10; 5 to 17)</td>
</tr>
<tr>
<td>Multifocal atrophic gastritis (n=360, 57% H pylori positive)</td>
<td>15 (11; 6 to 17)**</td>
<td>2 (2; 0 to 7)</td>
</tr>
<tr>
<td>Chronic gastritis, all types (n=618, 71% H pylori positive)</td>
<td>110 (82; 76 to 89)*</td>
<td>72 (71; 63 to 80)</td>
</tr>
</tbody>
</table>

Values in parentheses are percentage with 95 confidence interval of the total amount of the IM subtype.

Within each type of gastritis, the prevalences of IM subtypes were compared with each other using the rest of the study population with junctional IM as reference group (χ² test).

†Total number of patients
‡Prevalence rates from histological examination
*p=0.05, **p=0.001.
Junctional intestinal metaplasia subtypes

Incomplete junctional intestinal metaplasia

Complete junctional intestinal metaplasia

Acid Schi, which also enables di

application of alcian blue(pH 2.5)-periodic

erent methods of biopsy sampling or stain-

varied from 5.3 to 36%.2 – 462 12 2The width of

study population had either or both forms of

agogastric junction in a consecutive series of

IM to be common findings at the oesoph-

This study showed complete and incomplete

Discussion

The prevalence of junctional complete IM and SCE was detected at a similar age in subjects with normal gastric histology. Proper and correct analysis of the background factors for junctional IM subtypes is difficult because obviously there are varying degrees of overlap with regard to the pathogenic factors for junctional complete IM and SCE.

The present findings suggest important clinical and practical conclusions on junctional SCE: the presence of SCE at the oesophago-gastric junction in subjects with a normal stomach—that is, histologically normal antral and gastric corpus mucosa—may predict gastro-oesophageal reflux disease with high certainty. This could also apply to junctional SCE patients with chronic gastritis. The presence of complete junctional IM may not indicate reflux, but is a manifestation of multi-focal atrophic gastritis. These conclusions are concordant with an earlier study indicating that junctional SCE is related to gastro-oesophageal reflux disease detected by 24 hour oesophageal pH monitoring.28

In this study, none of the patients with junc-
tional IM showed dysplasia, which accords
with an earlier report.3 Dysplasia is quite a
common finding at Barrett’s epithelium and
precedes the appearance of adenocarcinoma.12
This may also be the case in the adenocarcino-
mas of the oesophago-gastric junction, which
are on the increase in many western coun-
tries.24 25 29 The low rate of dysplasia in junctional IM suggests that neither junctional SCE nor complete IM are as high risk carci
noma precursor lesions as Barrett’s oesophagus is for oesophageal adenocarcinoma. On the other hand, junctional complete IM and SCE are common lesions, and the absence of dysplasia in a limited number of patients does not exclude the possibility that junctional SCE or complete IM could progress to dysplasia and carcinoma in some patients.

In conclusion, this study indicates that com-
plete and incomplete IM at the oesophago-
gastric junction are common acquired lesions.

They may not be directly related to Barrett’s oesophagus or junctional adenocarcinomas because of the differences in their basic demo-

graphics. It seems that incomplete junctional

IM (SCE) and complete IM are dissimilar

<table>
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<th>Table 3</th>
<th>Results of multivariate analyses to determine the independent risk factors for junctional complete and incomplete intestinal metaplasia</th>
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<tr>
<td>Odd ratio (95% confidence interval)</td>
<td>Age 1.3 (1.2 to 1.6) Endoscopic erosive oesophagitis 2.9 (1.3 to 6.2) Antral predominant non-atrophic gastritis 1.4 (0.9 to 2.4) Gastric H pylori 1.0 (0.6 to 1.7)</td>
</tr>
</tbody>
</table>
lesions in terms of their pathogenesis: the former seems to be a consequence of gastro-
oesophageal reflux disease and the latter a manifestation of multifocal atrophic gastritis.

In addition to the authors, the following doctors are members of The Central Finland Endoscopy Study Group: Liisa Ahlbgog-Muraja, Teuvo Antikanen, Sirpa Annila, Jorma Anttinen, Matti Halikais, Kari-Pekka Hamalainen, Heikki Janthonen, Matti Kää-
ralauma, Kerikko Karjalainen, Pekka Kauranen, Matti Kolu, Heikki Koivonen, Jari Korhonen, Riina Koskela, Raimo Kreos, Ilika Kunnamo, Vesa Karja, Päivi Laakso, Matti Laukkanen, Remo Liisanantti, Manja Lohman, Timo Man-
tynen, Kviisti Nuova, Antero Palmu, Ulla Palmu, Matti Pellinen, Pertti Särkkä, Harri Selänne, Tuula Tervo, Marianne Udd, Jukka Vainikka.

21 Hirota WK, Loughney TM, Lazas DJ, et al. The prevalence and demographics of specialized intestinal metaplasia at the esophagogastric junction in a cohort of 889 prospectively studied patients [abstract]. *Gastroenterology* 1997;112:A149.
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Gut 1999 45: 644-648
doi: 10.1136/gut.45.5.644