The appropriate management of symptomatic gastro-oesophageal reflux disease (GORD) in primary care : a systematic analysis of expert opinion

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Abstract

Objective : **To explore the appropriate indications for endoscopy and short-term anti-secretory treatment in patients with symptoms of gastro-oesophageal reflux disease (GORD).**

Methods : **The RAND Appropriateness Method (RAM) was used to systematically investigate the opinions of an expert panel (6 gastroenterologists and 6 general practitioners) on the appropriateness of either endoscopy or short-term medication for 768 different patient scenarios (cases). Each case was defined by the unique combination of diagnostic characteristics considered to be relevant in treatment choice. Panel members firstly individually rated the appropriateness of all indications using a 9-point scale (9 = extremely appropriate, 1 = extremely inappropriate). Subsequently, the panel discussed the results and re-rated some of the indications. Based on the median score and agreement figures, the individual ratings were converted to panel statements (appropriate, inappropriate, and uncertain) for each of the indications. Logistic regression was used to study the relationship between diagnostic characteristics and panel outcomes.**

Results : **Disagreement was seen in only 18% of cases. Statistical analysis revealed consistent patterns that determined the panel judgements. The most pronounced patterns and regression results were used to indicate situations in which either medication or referral was considered appropriate by the panel.**

Conclusion : **The RAND panel method proved to be useful in the systematic analysis of expert opinion on the appropriate management of symptomatic GORD.**

Nevertheless, as the recommendations still reflect the subjective opinion of the panel members, their validity and usefulness for daily practice should be the subject of further investigations.
(Acta gastroenterol. belg., **2003**, 66, **265-270**).

Key words : gastroesophageal reflux, gastrointestinal endoscopy, anti-secretory medication, expert opinion, RAND method.

Introduction

Gastro-oesophageal reflux disease (GORD) is one of the most common digestive disorders. It has been estimated that heartburn, which is the most typical symptom of GORD, is experienced by 40% of the general population at least once a month (1,2). Symptoms may occur with or without histopathological changes (3). A significant proportion of patients presenting with GORD-like symptoms show no macroscopic mucosal abnormalities indicative of oesophagitis (3). Those endoscopically negative patients often show the same extent of symptom severity and similar chronicity as those with proven oesophagitis (3). Since the introduction of effective medication, the majority of patients with uncomplicated GORD can be managed in a primary care setting, beginning with anti-secretory medication without the necessity of further diagnostic evaluation. However, in a small percentage of patients, GORD-like symptoms may indicate the presence of more severe disease or concomitant complications such as strictures, Barrett's oesophagus, and adenocarcinoma. For these patients, the initial medical approach may result in an undesirable delay in arriving at the actual diagnosis and starting appropriate treatment. For doctors practising in primary care, there is often substantial doubt as to whether patients presenting with GORD-like symptoms should be referred for endoscopy immediately, or whether anti-secretory treatment is justified as an initial option. Although a number of guidelines have paid attention to this issue (4-6), their applicability to the wide range of patients seen in everyday practice remains a subject of debate. In order to explore the possibilities of refining the indications for either endoscopy or short-term anti-secretory medical treatment in patients with symptoms of GORD, we performed a modified Delphi study in which a panel of experts assessed the appropriateness of these options for a large number of hypothetical patients.

Methods

RAND Appropriateness Method

In order to systematically investigate the opinions of experts on the appropriateness of treatment choice in patients with GORD-like symptoms, we made use of the RAND Appropriateness Method (RAM) (7,8). This method is particularly helpful when scientific evidence is lacking or is not detailed enough to establish clear indications for a particular procedure or treatment choice. Since its development in the mid-eighties by the American RAND Institute and the University of California, it has been applied to a number of medical

This study was financially supported by an unconditional educational grant from AstraZeneca, Brussels (Belgium).
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and surgical procedures in various fields of medicine (9). The RAM consists of a modified Delphi approach in which a panel of experts judges the appropriateness of particular clinical decisions in an iterative way. Firstly, a literature study is done to critically appraise and summarise the evidence from clinical studies. Using the results of this overview and the additional comments of experts, particular patient characteristics are selected that may be relevant for the clinical decision under investigation. By combining these characteristics, a set of hypothetical patients (different cases) is generated, and a panel of experts is then asked to rate the appropriateness of certain clinical decisions for each of these cases. A decision is called "appropriate" when the expected benefits (e.g. symptom reduction) exceed the expected risks (e.g. adverse events). The extent of appropriateness is expressed using a 9-point scale in which 9 = extremely appropriate, 1 = extremely inappropriate, and 5 = equivocal or uncertain. After the panellists have individually rated all indications, a plenary meeting is organised to discuss the results. The aim of this discussion is not primarily to reach consensus, but to investigate whether disagreement is due to differences in the interpretation of the definitions or cases that are used. After this discussion, a second round takes place, in which all or part of the indications are rated a second time. By combining the data on agreement and appropriateness, for each of the clinical scenarios a panel statement (appropriate, uncertain, and inappropriate) is calculated. The results of RAM studies may be used retrospectively (e.g. as reference values to assess the appropriateness of clinical decisions in daily practice), or prospectively (e.g. in the construction or refinement of practice guidelines).

Selection of panel members

As input from gastroenterologists and general practitioners was considered important, these disciplines were equally represented in the 12-member Belgian panel. Selection of experts was based on their particular expertise in the field of GORD.

Selection of study population and clinical variables

After a thorough review of the currently available scientific literature and practice guidelines, the panel convened to define the patient population to be considered, and to select the clinical variables relevant to the choice between referral and short-term anti-secretory medication. It was decided that all patients presenting with heartburn and/or regurgitation to a general practitioner should be taken into consideration. Patients with previously documented mucosal damage ≥ grade 2 (Savary-Miller classification) (10) fell beyond the scope of the study. Patients with particular alarm symptoms (obstructive dysphagia, odynophagia, signs of upper gastrointestinal bleeding or unexplained weight loss), as well as those who had failed on previous treatment with a proton pump inhibitor (PPI), were excluded from further analysis because the panel found that these conditions always necessitate further (specialised) diagnostic evaluation. For reasons of efficiency of the rating procedure, all other patients were divided into 4 subgroups ("chapters") according to their specific medical history (Fig. 1). For each of these patient groups, particular clinical variables relevant to treatment choice were defined (Table I).

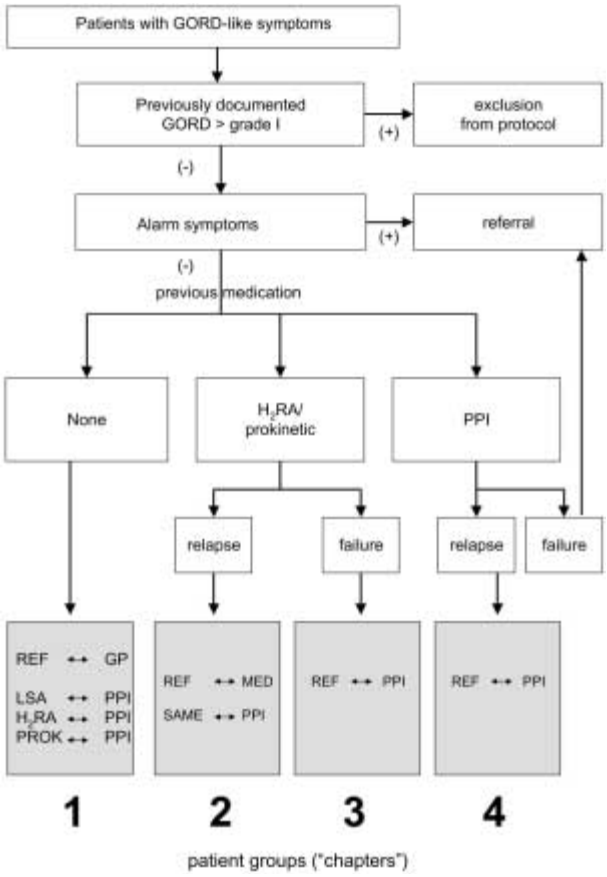

Fig. 1. — Conceptual framework of the study and rating structure.
Grey boxes indicate the patient groups and treatment comparisons that were considered by the panel.
REF = referral for endoscopy ; GP = treatment in general practice ; LSA = Life style advice with or without the use of antacids ; PROK = prokinetics ; MED = medication ; SAME = same medication.

Rating process

Based on the number of diagnostic variables and categories included, the total number of cases (all possible combinations of the values of the variables) to be considered varied between 128 (chapters 1 and 3) and 256 (chapters 2 and 4). For each of the chapters, different treatment options had to be considered (Fig. 1). The first decision level concerned the choice between referral for endoscopy versus short-term medication. Thereafter, panellists had to rate the various medical options. In

Table I. — **Overview of clinical variables and categories used for the construction of cases**

Variables	Categories
1. Relapse (chapters 2 and 4)	a. Early (< 6 months) b. Late (≥ 6 months)
2. Dyspeptic symptoms (all chapters)	a. No b. Yes
3. Extra-intestinal symptoms (all chapters)	a. No b. Yes
4. Duration of symptoms (chapter 1)	a. < 2 months b. ≥ 2 months
5. Impact on quality of life (all chapters)	a. Slight or tolerable interference with daily living activities b. Strong impact on daily living activities
6. Age (all chapters)	a. < 45 years b. ≥ 45 years
7. NSAID use (all chapters)	a. No b. Yes
8. Substantial alcohol/tobacco use (all chapters)	a. No b. Yes
9. Recent (< 2 years) endoscopy (chapters 2, 3, and 4)	a. No recent endoscopy b. Yes, but normal results

Table II. — **Criteria for agreement (A) and appropriateness (B)**

	Category	Description
A	Agreement	≤ 3 individual scores outside the section in which the median score fell
	Disagreement	≥ 4 individual scores in each of the sections 1-3 and 7-9
	Indeterminate	All other outcomes
B	Appropriate	The median score lies in section 7-9 without disagreement
	Inappropriate	The median score lies in section 1-3 without disagreement
	Uncertain	All other outcomes

order to allow uniform assessments, PPI was chosen as the reference therapy (Fig. 1). The number of ratings was 512 for chapters 1 and 2, 128 for chapter 2, and 256 for chapter 4, a total of 1408 ratings. Most previously conducted RAM studies have used printed rating forms. To improve the ease and efficiency of the rating process, and to increase the accuracy of data processing, we developed a user-friendly electronic rating program that allowed quick data entry with checks on completeness and validity. Panellists received the program together with concise instructions and definitions of terms used. A help desk was provided in case users had problems with the program.

Statistical analysis

Individual ratings were aggregated to panel outcomes using the typical RAM calculations. Based on the median score and the extent of agreement among the panellists, for each of the indications an appropriateness statement (appropriate, uncertain, and inappropriate) was calculated (Table II). Logistic regression was used to assess the robustness of the ratings, and to study the relationship between the diagnostic variables and the panel outcomes.

Results

First rating round and panel discussion

The first rating round was conducted in May, 2001. All panellists completed the electronic program which they perceived to be easy to understand and user-friendly. Mean time for completing the 1408 ratings was approximately 5 hours. The figures on agreement were mixed. For the first decision level (choice between referral and medication), the percentage of agreement ranged from 12 (chapter 1) to 52 (chapter 4), while the percentages for disagreement lay between 17 (chapter 3) and 76 (chapter 1). For the choice between the various medical options (chapters 1 and 2), the agreement was generally much higher (66-94%), with PPI being preferred in the majority of cases (82-94%). The only exception was the choice between PPI and life style advice (chapter 1), for which the ratings were predominantly indeterminate (76%). During the one-day panel meeting (June, 2001), a number of questions about the interpretation of definitions were raised. It is very likely that these led to differences in ratings and disagreement between the panel members. For example, not all panellists had interpreted "referral" as being "referral for endoscopy". Furthermore, in patients using non-steroidal anti-inflammatory drugs (NSAIDs), some panellists would have preferred the option of discontinuation of this type of medication before referral was taken into consideration. There also seemed to be some confusion about the interpretation of the potential relation between previous findings (such as endoscopy results, use of NSAIDs in the past) and current symptoms. For all these items, a number of alterations and refinements were made in the rating scheme for the second round. Furthermore, we adopted the suggestion that only the comparison "referral versus medication" had to be taken into consideration. The results of the first round showed that PPI was preferred in the majority of cases, and the panel discussion revealed no indications that re-rating of these choices was necessary.

Second rating round

The second rating round was also done using the electronic program, and took place some weeks after the panel discussion (July, 2001). Again, all ratings were complete. Given the panel discussion and the subsequent refinement of the definitions, the figures on agreement showed marked differences in comparison with those of the first round (Table III). The results for chapter 1 showed a strong decrease of disagreement, leading to an increase of both agreement and indeterminate ratings. For the other chapters, there was also a substantial increase of agreement and/or decrease of disagreement, albeit less pronounced. Changes in appropriateness of either referral or medication differed in direction (Table III). In chapter 1, a shift from "uncertain" towards referral was seen, whereas the percentage of appropriateness

Table III. — **Agreement and appropriateness after the second rating round ; first round results between parentheses ; percentages (sum of row totals is 100%)**

chapter/agreement	agreement		indeterminate		disagreement	
1. No previous treatment	34	(12)	44	(12)	22	(76)
2. Relapse after H_2RA*/prokinetics	35	(29)	41	(41)	23	(30)
3. Failure of H_2RA/prokinetics	46	(29)	44	(54)	10	(17)
4. Relapse after PPI	51	(52)	33	(23)	16	(25)
Total	42	(43)	40	(33)	18	(34)
chapter/appropriateness	medication appropriate		uncertain		referral appropriate	
1. No previous treatment	12	(9)	33	(76)	55	(15)
2. Relapse after H_2RA/prokinetics	32	(23)	35	(35)	33	(42)
3.Failure of H_2RA/prokinetics	47	(22)	18	(29)	35	(49)
4. Relapse after PPI	32	(14)	21	(29)	48	(57)
Total	31	(18)	27	(38)	42	(44)

* H_2RA = H_2-receptor-antagonists.

for medication did not change much. In the other chapters, a marked shift in favour of medication was seen. Statistical analysis showed strong patterns (combinations of diagnostic variables) which almost exclusively determined the panel statements on appropriateness. Given these strong patterns, further (logistic regression) analysis on the relationship between the diagnostic variables and panel statements was possible only for subgroups. In table IV, the most pronounced patterns and regression results are summarised. Previous endoscopy (chapters 2-4), age and the use of NSAIDs (in all chapters) were the most important factors in the choice between referral and medication. Other variables were also determinants of treatment choice, albeit in combination with others.

Discussion

For patients presenting with GORD-like symptoms to their general practitioner, the choice between endoscopic evaluation and short-term anti-secretory treatment is often surrounded with doubt as to their respective benefits and risks. Whereas a defensive attitude may result in the overuse of upper gastrointestinal endoscopy (thereby increasing discomfort and worry for many patients), the opposite attitude carries the risk of delay of detecting more severe illness, and withholding the patient immediate adequate treatment. The currently available guidelines advocate a short-term anti-secretory treatment in patients with typical symptoms of uncomplicated GORD without further (endoscopic) evaluation (4-6). However, it remains debatable what exactly should be understood by “uncomplicated”. In addition, no specific recommendations are given for treatment indications following relapse or failure of short-term medication. In 1998, a multidisciplinary European expert panel used the RAM methodology to establish the appropriateness criteria for gastroscopy in patients with GORD (11). The principal conclusions were that endoscopy is appropriate in individuals with current symptoms and no endoscopy ever performed (regardless of the use of adequate GORD treatment), as well as in individuals with current symptoms despite adequate treatment (regardless of when previous treatment was performed and/or regardless of the severity of previous oesophagitis) (11). However, because the ratings were done within the framework of a larger study on the appropriateness of upper gastrointestinal endoscopy, the number of indications considered was limited (24 patient scenarios), predominantly referring to the time and diagnosis of previous endoscopy.

The present study showed strong and consistent opinions of a mixed panel regarding the appropriate indications of referral versus short-term anti-secretory medication in patients presenting with typical symptoms of GORD. Although the general conclusions of the panel results are similar to the recommendations of the current guidelines, they offer a more detailed decision framework for patients seen in an everyday primary care setting. For each of the four patient groups, particular combinations of diagnostic characteristics were identified that support the decision in favour or against immediate referral for endoscopy as opposed to medical therapy (Table IV).

The applicability of these results in daily practice depends primarily on the reliability and validity of the panel method. Important methodological aspects, such as internal consistency and agreement between different panels, have been investigated in a number of other RAM studies, showing good to excellent results (12-23). However, as the panel ratings still reflect subjective opinions, the recommendations should be validated in further clinical studies and in daily practice.

Table IV. — **Summary of indications for short-term anti-secretory medication versus referral for endoscopy in patients with symptoms of GORD**

A – Patients without previous treatment (chapter 1).

Referral	Medication
Always appropriate in patients ≥ 45 years and using NSAIDs Always inappropriate in patients < 45 years and not using NSAIDs In other patients, the presence of one or more of the following characteristics substantially contributes to the appropriateness of referral : – symptom duration ≥ 2 months – dyspeptic symptoms – extra-intestinal symptoms – severe impact on quality of life – substantial alcohol/tobacco use	Generally appropriate in patients with no or few unfavourable characteristics Never appropriate in patients using NSAIDs Inappropriate in patients with at least 2 of the following characteristics : – age ≥ 45 years – extra-intestinal symptoms – severe impact on quality of life – substantial alcohol/tobacco use

B – Patients with relapse after previous treatment with H_2RA/prokinetics (chapter 2)

Referral	Medication
Never appropriate in patients with recent endoscopy showing normal results. Appropriate in patients with at least 2 of the following characteristics : – age ≥ 45 years – use of NSAIDs – extra-intestinal symptoms	Appropriate in patients with normal recent endoscopy, and with no or few unfavourable conditions. The presence of dyspeptic symptoms, extra-intestinal symptoms, substantial alcohol-/tobacco use, age ≥ 45 years, late relapse and (most dominantly) the use of NSAIDs decrease the chance of an appropriate indication.

C – Patients with failure of treatment with H_2RA/prokinetics (chapter 3)

Referral	Medication
The presence of extra-intestinal symptoms, the use of NSAIDs and age ≥ 45 years are positively associated with the chance of an appropriate indication.	Never appropriate in patients with no recent endoscopy. Appropriate in patients < 45 years not using NSAIDs, irrespective of other conditions. Always inappropriate in patients ≥ 45 years using NSAIDs

D – Patients with relapse after treatment with PPI (chapter 4).

Referral	Medication
Never appropriate in patients with normal results of recent endoscopy. In the absence of a recent endoscopy, appropriate in patients : – using NSAIDs and/or – aged ≥ 45 years and/or – with early relapse and/or – with dyspeptic symptoms	Never appropriate in patients with no recent endoscopy. In case of normal endoscopic results : – appropriate in patients < 45 years and not using NSAIDs, irrespective of other conditions. – Inappropriate in patients ≥ 45 years using NSAIDs.

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