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Special Article

Guidelines for the management of *Helicobacter pylori* infection in Italy: The III Working Group Consensus Report 2015

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ABSTRACT

Knowledge on the role of *Helicobacter pylori* (HP) infection is continually evolving, and treatment is becoming more challenging due to increasing bacterial resistance. Since the management of HP infection is changing, an update of the national Italian guidelines delivered in 2007 was needed. In the III Working Group Consensus Report 2015, a panel of 17 experts from several Italian regions reviewed current evidence on different topics relating to HP infection. Four working groups examined the following topics: (1) "open questions" on HP diagnosis and treatment (focusing on dyspepsia, gastro-oesophageal reflux disease, non-steroidal anti-inflammatory drugs or aspirin use and extra-gastric diseases); (2) non-invasive and invasive diagnostic tests; (3) treatment of HP infection; (4) role of HP in the prevention of gastric cancer. Statements and recommendations were discussed and a consensus reached in a final plenary session held in February 2015 in Bologna. Recommendations are based on the best current evidence to help physicians manage HP infection in Italy. The guidelines have been endorsed by the Italian Society of Gastroenterology and the Italian Society of Digestive Endoscopy.

1. Introduction

Our knowledge on the role of *Helicobacter pylori* (HP) in different clinical conditions has improved over the last decade, whereas the treatment of infection has become more challenging. According to the European guidelines the management of HP may differ among European countries (i.e. indications for a test- and- treat strategy, the regimen to choose for first-line treatment) in parallel with different prevalence rates of infection and levels of antimicrobial resistance, in particular to clarithromycin [1]. Attempts to standardize HP management within countries have led to the publication of several national guidelines, and Gastroenterologists and referring physicians have been shown to comply with these guidelines [2]. This is the third time a group of Italian experts convenes to review and discuss the relevant evidence concerning the clinical management of HP infection in Italy [3,4]. As HP testing and

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treatment should be managed in close cooperation between specialists and general practitioners, it is particularly important that data on diagnostic tools and therapeutic approaches be applied appropriately in clinical practice in specific national settings.

This consensus project aimed to summarize current evidence on the management of HP infection and update the Italian guidelines produced in the II Working Group Report 2006 [4]. At the III Working Group Consensus Report 2015, 17 experts from different Italian regions, chosen for their expertise and research contribution on HP and/or guideline methodology, convened at an official meeting by the coordinator (MC) of the two previous working group meetings [3,4]. Italian experts focused on updating indications, diagnosis and treatment of HP and its relationship with gastric cancer.

2. Methodology and consensus meeting structure

The guidelines are endorsed by the Italian Society of Gastroenterology (SIGE) and the Italian Society of Digestive Endoscopy (SIED), which were not however promoters of the Consensus. Representatives from both SIGE (MR and FDM) and SIED (RMZ and CC) participated to the Consensus process. A panel of Italian gastroenterologists and pathologists met in April 2014 in Ferrara, where current European guidelines – Maastricht IV/Florence – [1] were reviewed at the introductory plenary session. The panel further agreed on the "Maastricht methodology" to be applied [1], on a set of key questions to be addressed and on preliminary statements to guide literature research. The panel worked in subgroups (working groups) to perform a systematic literature search, review statements on the basis of best available evidence and report graded statements and recommendations. Four working groups examined the following topics:

(1) "Open questions" for HP diagnosis and treatment, focusing on dyspepsia, gastro-oesophageal reflux disease (GORD), use of non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin (acetylsalicylic acid – ASA) and extra-gastric diseases
(2) Non-invasive and invasive diagnostic tests
(3) Treatment of HP
(4) Role of HP treatment in the prevention of gastric cancer

For each topic, individual key questions were addressed. The quality level of evidence and the strength of recommendation were graded according to the same system used in the Maastricht IV/Florence report (Table 1) [1]. After discussion, the working group produced statements with the level of available evidence and the strength of the recommendation. Researchers prioritized data from systematic reviews and meta-analyses of randomized controlled trials (RCTs) when available, or individual RCTs with narrow 95% confidence intervals (CI). The clinical applicability of statements and recommendations and their implementations in primary care were also taken into account.

Statements and recommendations with supporting evidence were edited and discussed at a one-day final plenary session in February 2015 in Bologna. After a thorough discussion, all participants were asked to vote on their agreement with evidence-based statements, and consensus was defined when at least 70% of participants agreed with the statement. Recommendations are based on the best current evidence to aid physicians manage HP infection in Italy. Previous strong indications for HP eradication, such as peptic ulcer and gastric mucosa associated lymphoid tissue (MALT) [4], have been reconfirmed.

Table 1
Grades of recommendation and levels of evidence [1].

Grade of recommendation	Level of evidence		Type of study
A	1	1a	Systematic review of RCTs of good methodological quality and with homogeneity
		1b	Individual RCT with narrow 95% confidence interval
		1c	Individual RCT with risk of bias
B	2	2a	Systematic review of cohort studies
		2b	Individual cohort studies (including low quality RCT, <80% follow-up)
		2c	Non-controlled cohort studies or ecological studies
	3	3a	Systematic review of case-control studies
		3b	Individual case-control study
C	4		Case series or poor quality cohort or case-control studies
D	5		Expert opinion without explicit critical appraisal or based on physiology, bench research or "first principles"

RCT, randomized controlled trial.

3. Statements

3.1. Open questions for diagnosis and treatment

3.1.1. HP and dyspepsia

Several well-designed studies support the use of the HP test-and-treat for the initial management of uninvestigated dyspepsia in young patients without alarm signs or symptoms (i.e. unintentional weight loss, iron-deficiency anaemia, gastrointestinal bleeding, dysphagia) [5]. European guidelines recommend this strategy in countries where HP prevalence is higher than 20% [1]. In Italy, as well as in other Southern European countries, such as Greece and Spain, HP prevalence in adults is around 50% [6,7]. Thus, a test-and-treat strategy is still recommended in Italy. The specific cut-off age for referring patients with uninvestigated dyspepsia without alarm symptoms to endoscopy is controversial; it depends on the local age-specific incidence of gastric cancer [1]. The Italian cancer registry shows that the incidence of gastric cancer increases in subjects over 50 years of age [8]. In addition, a recent Italian survey reported a very low prevalence of gastric cancer (0.3%) in approximately one thousand patients referred for upper endoscopy [9]. Based on these data, a cut-off age of 50 years in Italy should be appropriate. Therefore, all dyspeptic patients older than 50 years or with alarm signs or symptoms should be referred for upper endoscopy [10]. When the test-and-treat strategy is applied, an accurate diagnosis is mandatory using a non-invasive test, either the ^{13}C-urea breath test (UBT) or the monoclonal stool antigen test (SAT) [1].

Many dyspeptic patients have no major lesions at endoscopy [6] and some of these are HP-infected (functional dyspepsia). A recent meta-analysis demonstrated that 1 out of 13 HP-infected patients with functional dyspepsia benefit from eradication [11]. Therefore, HP eradication is recommended in this setting.