Real-time gastric juice analysis with EndoFaster for *H. pylori* diagnosis: a large, multicentre study

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Background *Helicobacter pylori* infection is the main cause of the most frequent gastroduodenal diseases. Because its prevalence is decreasing in developed countries, gastric biopsies are negative in several patients. By measuring ammonium in the gastric juice, EndoFaster allows to exclude *H. pylori* infection during endoscopy. This study aimed to assess the accuracy of device versions working with either 6 ml or 3 ml of gastric juice.
Study design This prospective study involved 12 endoscopic units. During endoscopy, EndoFaster testing was performed and standard five gastric biopsies were taken. The accuracy was calculated by considering histological assessment as the gold standard for *H. pylori* diagnosis.
Results Gastric juice analysis was attempted in 1279 patients, but it failed in 131 (15.5%) and in 10 (2.3%), with the 6 ml and the 3 ml device, respectively ($P<0.001$). Overall, EndoFaster detected *H. pylori* infection with an 86.3% sensitivity, 83.3% specificity, 52.7% positive predictive value, 96.6% negative predictive value and 83.8% accuracy. The performance was not affected either by ongoing proton pump inhibitor therapy or a previous *H. pylori* eradication. No significant difference in accuracy emerged between the two versions of the device.
Conclusion The novel version of the EndoFaster device operating with 3 ml gastric juice may be performed in virtually all patients, and it allows excluding *H. pylori* infection with a very high accuracy. Gastric biopsies can be avoided in a definite portion of cases without endoscopic lesions or other clinical indications.

Introduction

Helicobacter pylori infection causes nonulcer dyspepsia and peptic ulcers, interacts with NSAIDs in determining lesions on the gastroduodenal mucosa, and it is a major factor for both carcinoma and MALT-lymphoma of the stomach [1–3]. Moreover, it plays a role in the pathogenesis of both idiopathic thrombocytopenic purpura and idiopathic iron deficiency anaemia [4]. Indeed, the risk of developing these conditions definitely falls when the infection is ruled out. Fortunately, the incidence of *H. pylori* is decreasing in developed countries [5]. Indeed, two multicentre, endoscopic studies found an *H. pylori* prevalence of 34% in 2012 and 22.3% in 2020, respectively, in Italy [6,7], and a value as low as 10% was computed in a large histological database in the USA [8]. Therefore, when gastric biopsies are performed during endoscopy, *H. pylori* is absent in several patients, particularly in those aged less than 50 years [9]. EndoFaster is an innovative device which performs real-time *H. pylori* detection by measuring ammonium concentration on gastric juice analysis during upper endoscopy [10]. Some studies found a high accuracy of this tool for *H. pylori* detection, including patients with an ongoing proton pump inhibitor (PPI) therapy which significantly decreases the accuracy of all available diagnostic tests for *H. pylori* [7,10,11]. Moreover, in a preliminary study, EndoFaster was found to be useful in detecting *H. pylori* infection in some patients with chronic active gastritis without a clear presence of bacteria at standard histological evaluation, avoiding the need for further diagnostic tests [12]. The initial version of the device required aspiration until 6 ml of gastric juice to perform analysis, an amount not detectable in all patients [7,10]. The technical performance of device was improved so that with the new machine until to 3 ml of gastric juice are needed. We designed this study to enlarge the experience on EndoFaster in testing for *H. pylori* infection, and

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to compare the performance between devices operating with either 6 ml or 3 ml of gastric juice. The usefulness of the tool in diagnosing *H. pylori* in chronic active gastritis without evident bacteria at histology was also assessed.

Methods

Upper endoscopy

This prospective study involved a total of 12 Italian Endoscopic Units. Consecutive patients referred by general practitioners to undergo diagnostic upper endoscopy were invited to participate in the study. All consenting patients underwent upper endoscopy with standard biopsy sampling (2 antrum, 1 *angulus* and 2 gastric body) according to the updated Sydney System [13]. *H. pylori* infection was considered present when bacteria were detected at the histological assessment on haematoxylin-eosin or modified Giemsa staining in doubtful cases, as for routine practice. Informed consent was obtained for all procedures. In detail, following the explanation of the clinical research, patients were informed and asked to sign the consent for both procedure and anonymous use of their data for scientific purposes. Because no experimental drugs were administered, no additional costs or procedures for the patients were required, no identification of patients was allowed, and no funds were received, formal approval by investigational review boards could be waived.

Gastric juice analysis

In each centre, the EndoFaster device was provided for 2 months use by the manufacturer (NISO Biomed S.r.l, Turin; Italy) and by the Italian distributor (Waldner Tecnologie Medicali, Trento; Italy) to the participating centres without any adjunctive cost for both hospitals and patients. The device was interposed between the endoscope and the suction system, that is, without any discomfort for the patient (Fig. 1). During endoscopy, lumen washing was avoided until the stomach was reached and until 6 ml or 3 ml of gastric juice was aspirated, according to the device version. *H. pylori* diagnosis was based on the determination of ammonium concentration, as a consequence of the urease activity of the bacterium within 30–90 s, that is, during endoscopy. *H. pylori* infection was diagnosed when the ammonium concentration was >62 ppm/ml and negative when ≤62 ppm/ml, as reported elsewhere [7,10].

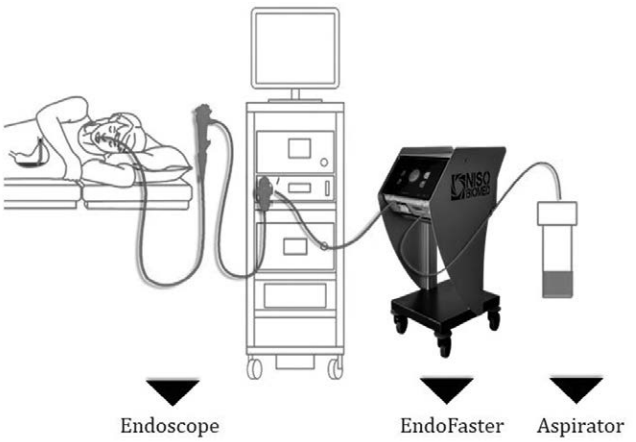

Fig. 1. Real-time of gastric juice analysis with EndoFaster.

Statistical analysis

Frequencies, percentages and means values with SD were calculated for all observations. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and overall accuracy were calculated. The chi-square test was used for comparisons.

Results

Descriptive analysis

A total of 1279 patients were evaluated, with a median enrolment of 95 cases (range: 35–237). In 141 (11.0%) cases there was not sufficient gastric juice to accomplish the EndoFaster testing, whereas an adequate biopsy sampling of gastric mucosa was lacking in further 69 (5.4%) patients. Thus, full data of 1069 (male/female = 471/598; mean age ± SD: 55 ± 16 years) patients were eventually available. There were 181 (16.9%) patients with previous treatment for *H. pylori* infection, and 388 (36.3%) patients in ongoing PPI therapy at moment of the endoscopy. The 6 ml device was tested in five centres and the 3 ml devices in five centres, whereas in the remaining two centres both versions were utilised. Among the *H. pylori* infection was detected at histology in 190 patients corresponding to an overall prevalence of 17.8% and a value of 21.4% when only the 888 naïve patients were considered.

Endofaster accuracy

The values of EndoFaster performance in detecting *H. pylori* infection were as follows: 86.3% sensitivity, 83.3% specificity, 52.7% PPV, 96.6% NPV and 83.8% accuracy. The estimates did not significantly differ when considering patients undergoing PPI therapy or those with previous eradication therapy (Table 1). When comparing the devices, an insufficient amount of gastric juice to accomplish the test occurred in 131 (15.5%) cases with the 6 ml and in 10 (2.3%) with the 3 ml tool ($P < 0.001$). The accuracy values of the two device versions were reported in Table 2.

A histological feature of chronic active gastritis without evidence of bacteria was detected in a total of 66 (6.2%) patients. The EndoFaster disclosed the presence of *H. pylori* infection in 33 (50%) cases (Table 3).

Discussion

H. pylori plays a major role in different benign and malignant gastroduodenal diseases, and its eradication

Table 1. Accuracy of EndoFaster in detecting *H. pylori* infection in different settings

	Ongoing PPI therapy (%)	Previous eradication therapy (%)
Sensitivity	79.1	95.5
Specificity	81.4	85.5
Positive predictive value (PPV)	34.7	47.7
Negative predictive value (NPV)	96.9	99.3
Accuracy	81.2	86.7

PPI, proton pump inhibitor.

definitely changes the natural history of peptic ulcer, nonulcer dyspepsia and gastric MALT-lymphoma [1–3]. Therefore, current European guidelines suggest searching for the infection under different clinical conditions [14]. On the other hand, the risk of developing gastroduodenal diseases is distinctly low when *H. pylori* is excluded. There is evidence that the prevalence of *H. pylori* infection is decreasing in developed countries [5–7,15] so the majority of histological assessments of gastric mucosa performed in routine practice are negative. This would limit the clinical impact of routine biopsies and increase resources expend. In such a scenario, the availability of a device able to accurately exclude *H. pylori* infection during upper endoscopy could be advantageous, consenting to avoid biopsies in patients without endoscopic lesions or other indications [7]. A tool with a very high NPV is needed to achieve this target. EndoFaster is a device firstly introduced in 2004, and the technology was constantly improved thereafter. A health technology assessment has been conducted by the Italian Ministry of Health showing a positive benefit/cost ratio of device use [16]. The most investigated is the tool performing with until 6 ml of gastric juice, with recent studies showing very high accuracy in excluding *H. pylori* [7,10]. However, previous studies observed that the 6 ml amount of gastric juice is not encountered in many (17%) patients, making the test more challenging [7]. Thereafter, a 3 ml EndoFaster device was developed and introduced on the market. By considering data of nearly 1300 patients, we found a very high (96.6%) NPV for EndoFaster in excluding *H. pylori* infection during endoscopy. This high value was achieved even in patients undergoing PPI therapy and in those previously treated for infection, namely two conditions where a low bacterial load is generally present, affecting the performance of other diagnostic tests [17]. Notably, the comparison between the 6 ml and 3 ml tools showed an identical high (96.5% and 96.7%) NPV. However, the low volume tool significantly increased the performance of the test reducing at only 2.3% the rate of patients in whom the amount of gastric juice was insufficient. Therefore, the new version further improved the applicability of EndoFaster in routine practice. The real-time exclusion of *H. pylori* during endoscopy would allow us to avoid performing biopsies in several patients unless endoscopic lesions are detected or specific clincal conditios are present. The high (20%) rate of inappropriate upper endoscopy and the absence of relevant alterations in young (<50 years) patients further support the use of EndoFaster for avoiding useless biopsies [9,18].

H. pylori is the most frequent cause of chronic active gastritis, that is, the first step of Correa's sequence of gastric carcinogenesis [19]. Therefore, the infection should be otherwise searched for when bacteria are not seen at standard histology in these patients [13]. Special histological stains, immunohistochemistry or other tests were advised for this purpose [20]. It was suggested that a portion of these cases might be related to infection with a low bacterial load that can only be detected by methods more sensitive than the visualisation of the bacteria [21]. In a recent study, the infection was detected in 61% out of 33 with chronic active gastritis and without clear evidence of bacteria at histology by using EndoFaster [12]. Data of the present larger study confirm that *H. pylori* can be diagnosed in 50% of patients with chronic active gastritis eliminating the need of other diagnostic tests. Likewise, by analysing gastric juice, the EndoFaster allows an indirect sampling of the entire stomach, overcoming the sampling error of biopsies, particularly when the presence of bacteria is confined in only some particular gastric sites [22].

Beyond *H. pylori*, to take biopsies during endoscopy is clinically relevant to rule out the presence of premalignant lesions on gastric mucosa, such as diffuse (or corpus-predominant) atrophy/metaplasia deserving follow-up [23]. However, EndoFaster also allows a real-time measure of pH values on gastric juice, and reduced acidity (pH >4.5) might be a surrogate of atrophy/metaplasia presence. Interestingly, some preliminary data found a very high accuracy of EndoFaster in excluding the presence of extensive atrophy on gastric mucosa [24,25], but further studies are needed to confirm this finding.

The multicentre collection of data and the large sample size considered are sure points of strength of the present study, whereas the lacking of precise calculations on cost saving by applying the device in routine practice as well as data on pH and gastric premalignant lesions are potential limitations.

In conclusion, data of this large, multicentre study found that EndoFaster with 3 ml of gastric juice is highly accurate in ruling out *H. pylori* infection during endoscopy allowing to avoid biopsies in a definite portion of patients.

Table 2. Comparison between the two EndoFaster devices

	6 ml gastric juice (*N* = 675)	3 ml gastric juice (*N* = 394)
Sensitivity	85.3	87.8
Specificity	83.5	82.8
Positive predictive value (PPV)	51.8	55.2
Negative predictive value (NPV)	96.5	96.7
Accuracy	83.9	83.8

Table 3. Endofaster testing in patients with chronic active gastritis without apparent bacteria at histology

Setting	Test positive	% (95% CI)
Ongoing PPI	12/28	43
Previous eradication therapy	3/7	43
PPI plus previous eradication	3/3	100
None	15/28	58
Total	33/66	50 (38–62)

CI, confidence interval; PPI, proton pump inhibitor.

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Conflicts of interest

There are no conflicts of interest.

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