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# Clinical validation of Endofaster® for a rapid diagnosis of *Helicobacter pylori* infection

Eugenia Sánchez Rodríguez[1], Rubén Sánchez Aldehuelo[1], Raquel Ríos León[1], Rosa María Martín Mateos[1], Ana García García de Paredes[1], Carlos Martín de Argila[1], Alejandra Caminoa[2], Agustín Albillos[1] and Enrique Vázquez-Sequeiros[1]

Departments of [1]Gastroenterology and Hepatology, and [2]Pathology. Hospital Universitario Ramón y Cajal. Madrid, Spain

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**Correspondence:** Enrique Vázquez-Sequeiros. Servicio de Gastroenterología y Hepatología. Hospital Universitario Ramón y Cajal. Ctra. Colmenar Viejo, km. 9,100. 28034 Madrid

e-mail: evazquezse@gmail.com

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## ABSTRACT

**Background:** this study aimed to evaluate the diagnostic accuracy of the Endofaster® for the detection of *Helicobacter pylori.*

**Methods:** during upper gastrointestinal endoscopy, gastric juice was aspirated to perform an analysis using the Endofaster®. This test was considered as positive when the ammonium concentration was > 67 ppm, negative when < 57 ppm and weakly positive between 57 and 67. Biopsy specimens were also taken as the gold standard.

**Results:** among the 86 patients enrolled in the study, the Endofaster® result was positive in 23.7%, negative in 54.7% and weakly positive in 11.6%, whereas infection

was detected via histology in 38.4% of patients. The accuracy was 81.4%, with a Kappa value of 0.57.

**Conclusions:** the Endofaster® could be useful to perform a rapid diagnosis o*f Helicobacter pylori* infection (area under the curve = 0.81).

**Key words:** *Helicobacter pylori.* Gastroscopy. Biopsy. Endofaster®.

## INTRODUCTION

*Helicobacter pylori* (HP) infection plays a main role in the pathogenesis of many digestive diseases (1,4). Therefore, it is crucial to obtain a proper diagnosis of HP infection. Invasive and non-invasive methods are among the different available diagnostic techniques for HP detection. The former requires an esophagogastroduodenoscopy (EGD) to obtain a tissue sample for an anatomopathological examination or a rapid urease test, whereas the latter does not require an endoscopic study (e.g., urea breath test). The choice of strategy depends on its availability, cost and the clinical situation (5,6).

HP infection is estimated to affect 50% of the population worldwide (5), although its prevalence is decreasing in developed countries (15-30%) (6). Thus, most of the patients that have undergone an EGD with tissue sampling are not infected. Therefore, using a device that diagnoses HP infection during EGD would reduce the risk and cost, as tissue sampling could be avoided in non-infected patients with no suspected preneoplastic or neoplastic lesions.

Endofaster® is a recently developed device that allows the diagnosis of HP infection via the analysis of gastric juice aspirated during EGD (7,8). Ammonium that is produced from urea after bacterial metabolism penetrates into the sensor membrane of the device. The concentration correlates with the presence of HP (7,8), enabling the device to provide a positive or a negative result accordingly.

The aim of this study was to evaluate the diagnostic yield of the Endofaster® in our environment and to establish the optimum ammonium concentration cut-off point (COP) in order to consider a result as positive.

## PATIENTS AND METHODS

A prospective study was performed at the Hospital Universitario Ramón y Cajal (Madrid) of patients that underwent EGD between July 1st and August 31st, 2017. The study protocol followed the Declaration of Helsinki and was approved by the Clinical Research Ethics Committee.

### Patients

Inclusion criteria: patients ≥ 18 years old that underwent an EGD, after having signed informed consent.

Exclusion criteria: a) refusal to participate in the study; b) personal history of eradicated HP; and c) insufficient gastric juice (< 2 cc).

### Endofaster®

The Endofaster® 21-42 (NISO Biomed S.r.l.) was used to analyze the aspirated gastric juice during the procedure. This device is interposed between the endoscope and the suction system.

### Endoscopic procedure and Endofaster test®

An EGD with a conventional endoscope and white-light was performed in all patients; 2 cc of gastric juice was obtained when intubating the stomach through the aspiration channel of the endoscope, which was connected to the Endofaster® device. The pH and ammonium concentration were analyzed, determining the presence or absence of HP infection within 30 seconds and providing a written and oral (through a speaker) report. The test was considered as positive when the ammonium concentration was > 67 ppm and negative when < 57 ppm; values between 57 and 67 were considered as weakly positive (7,8). Subsequently, gastric biopsies were taken for histological examination according to the modified Sydney Protocol (9), using hematoxylin-eosin and/or Giemsa, at the discretion of the pathologist.

### Statistical analysis

Continuous variables are shown as the arithmetic mean ± standard deviation (SD) if they were normally distributed and as the median and interquartile range if not. Categorical variables were expressed using absolute values and relative frequencies. Validity indexes (sensitivity [S] and specificity [E]), positive and negative predictive values (PPV and NPV), diagnostic accuracy, Kappa correlation coefficient for different COPs (COP1 ≥ 57 ppm; COP2 ≥ 67 ppm) and the area under ROC curve (AUROC) were calculated. Stata software version 13 (StataCorp) was used for the analysis. Histological examination was considered as the gold standard.

**RESULTS**

Eighty-eight consecutive patients were included in the study; two were excluded as they had insufficient gastric juice (2.2%, 2/88). Basal features, endoscopic findings, Endofaster® and histological examination results are summarized in table 1. When COP1 was used, S was 73.6%, E = 75.8%, diagnostic accuracy = 74.4%, NPV = 64.1%, PPV = 82.9% and the Kappa correlation coefficient = 0.47 ± 0.1. For COP2, S was 88.7%, E = 69.7%, diagnostic accuracy = 81.4%, NPV = 79.3%, PPV = 82.5% and the Kappa correlation coefficient = 0.57 ± 0.1. The AUROC obtained was 0.84 ± 0.05 (confidence interval 95%, 0.75-0.93) (Fig. 2). Table 2 shows the results in relation to proton pump inhibitors (PPIs) treatment.

**DISCUSSION**

HP infection is the main risk factor for the development of upper gastrointestinal preneoplastic and neoplastic lesions (1,10). Worldwide, its prevalence is still high, even though it is decreasing in developed countries (15-30%) (5,6). Therefore, the probability of obtaining a positive result in a tissue sample obtained during EGD is lower than 30%, which decreases even more if only patients without macroscopic lesions are considered (6). Therefore, routine biopsy tissue sampling for HP infection diagnosis may not be so useful, increasing costs, procedure length and the risk of complications. Rapid urease test emerged as an alternative to histological diagnosis despite that fact that it also requires tissue sampling and it takes some minutes to obtain the result. Endofaster® provides a result in 30 seconds and does not require

gastric biopsies.

An accuracy of 80% with a NPV of 87% was obtained in the present study. These figures are similar to that already reported by similar studies (7), suggesting that Endofaster® allows gastric sampling to be avoided in a high proportion of patients. The main drawback would be missing a diagnosis of a preneoplastic or neoplastic lesion, as histological examination is not performed. However, the probability of finding these lesions in the absence of HP infection is low (10,11). Moreover, routine histological studies have not been established in patients with HP infection that do not show any macroscopic lesions suggestive of preneoplastic lesions or alarm clinical features (12). Consequently, Endofaster® would allow the selection of non-infected patients in whom tissue sampling could be avoided in the absence of macroscopic lesions (10,11). At the same time, malignant lesions appear more frequently if hypochlorhydria is present (13). The Endofaster® also analyzes gastric pH, which could be a useful piece of additional information, although this aspect was not assessed in our study. Gastric juice analysis is a potential indicator of gastric mucosa status via ammonium concentration (15) (as it is a surrogate marker of HP infection) and gastric pH.

Contrary to that reported so far, a COP of ≥ 67 ppm was found in this study as the threshold with the highest accuracy for HP detection. We decided not to exclude those patients that were taking or had been treated with PPIs, as previous studies have shown that the diagnostic yield of the Endofaster® was not affected in this clinical scenario. This may occur with other diagnostic strategies due to the heterogeneous distribution of the bacteria in the stomach as a result of PPI chronic treatment. A statistical analysis that separated patients that received PPI from those that did not receive them was performed and similar results were obtained to those previously reported. Nevertheless, the small sample size of both groups and the fact that this was not the aim of our study prevented us from drawing conclusions.

This study does have important methodological limitations, most deriving from the small number of patients included and from the use of histology as the gold standard, instead of the urea breath test or rapid urease test. However, among its main strengths is the lack of any previous analyses in the clinical practice in our area.

In conclusion, this study establishes an appropriate accuracy for HP infection diagnosis using the Endofaster®. This device may be useful to select those patients in which gastric tissue sampling could be avoided.

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**Table 1. Classification of patients according to age, gender, PPI and antibiotics consumption, endoscopic findings, histological evaluation and the Endofaster® test result**

| | n = 86 |
|---|---|
| Age, mean (SD) | 52.33 (14.79) |
| Female gender | 46 (53%) |
| PPI consumption during the month prior to EGD | 33 (38.3%) |
| Antibiotics consumption during the month prior to EGD | 2 (2.5%) |
| Upper digestive history | 31 (26.6%) |
| Endoscopic findings | |
| Nile | 24 (28%) |
| Suggestive of gastritis | 54 (62.4%) |
| Gastric peptic ulcer | 4 (4.66%) |
| Duodentis | 7 (8.13%) |
| Duodenal ulcer | 1 (1.16%) |
| Others | 7 (8.12%) |
| Histological findings* | |
| Inflammation | |
| Absent | 7 (8.14%) |
| Mild | 46 (53.49%) |
| Moderate | 22 (25.58%) |
| Severe | 10 (11.63%) |
| Activity | 29 (33.72%) |
| Metaplasia | 10 (11.63%) |
| Atrophy | 11 (12.79%) |
| Dysplasia | 0 (0%) |
| Presence of HP on gastric biopsies | |
| Present | 33 (38.4%) |
| Absent | 53 (61.6%) |
| Endofaster® test result | |
| < 57 ppm | 47 (54.7%) |
| 57-67 ppm | 10 (11.6%) |
| > 67 ppm | 29 (33.7%) |

SD: standard deviation; PPI: proton pump inhibitors; EGD: esophagogastroduodenoscopy; HP: *Helicobacter pylori.* *Following the scale proposed by the Sidney system.

**Table 2. Sensitivity, specificity, positive predictive value, negative predictive value, diagnostic accuracy and Kappa correlation coefficient for the two different cut-off points regarding PPI consumption**

| | Cut-off point ≥ 57 ppm | Cut-off point ≥ 67 ppm |
|---|---|---|
| Total population (n = 86) | | |
| Sensitivity | 73.6% (60.5-83.62) | 88.7% (77.4-94.7) |
| Specificity | 75.8% (58.9-87.2) | 69.7% (52.6-82.6) |
| PPN | 82.9% (69.9-91.2) | 82.5% (70.6-90.2) |
| NPV | 64.1% (48.4-77.3) | 79.3% (61.6-90.2) |
| Diagnostic accuracy | 74.4% (64.3-82.5) | 81.4% (71.9-88.2) |
| Kappa correlation coefficient | 0.57 ± 0.107 | 0.47 ± 0.106 |
| Patients with PPI consumption (n = 33) | | |
| Sensitivity | 68.2% (41.3-83.6) | 90.9% (72.2-97.5) |
| Specificity | 72.7% (43.35-90.3) | 63.6% (35.4-84.8) |
| PPN | 83.3% (60.8-94.2) | 83.3% (64.1-93.3) |
| NPV | 53.3% (30.1-75.1) | 77.8% (45.3-93.7) |
| Diagnostic accuracy | 69.7% (52.6-82-6) | 81.8% (65.6-91.4) |
| Kappa correlation coefficient | 0.45 ± 0.16 | 0.59 ± 0.15 |
| Patients without PPI consumption (n = 53) | | |
| Sensitivity | 77.4% (60.2-88.6) | 87.1% (71.1-94.9) |
| Specificity | 77.3% (56.6-89.8) | 72.7% (51.8-86.8) |
| PPN | 82.8% (65.5-92.4) | 81.8% (65.6-91.4) |
| NPV | 70.8% (50.8-85.1) | 80% (58.3-91.9) |
| Diagnostic accuracy | 77.4% (64.4-86.5) | 81.8% (68.6-89.4) |
| Kappa correlation coefficient | 0.49 ± 0.12 | 0.56 ± 0.12 |

PPV: positive predictive value; NPV: negative predictive value; COP: cut-off point; PPI: proton pump inhibitors.

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Fig. 1. The Endofaster® device. Displayed with the permission of NISO Biomed S.r.l.

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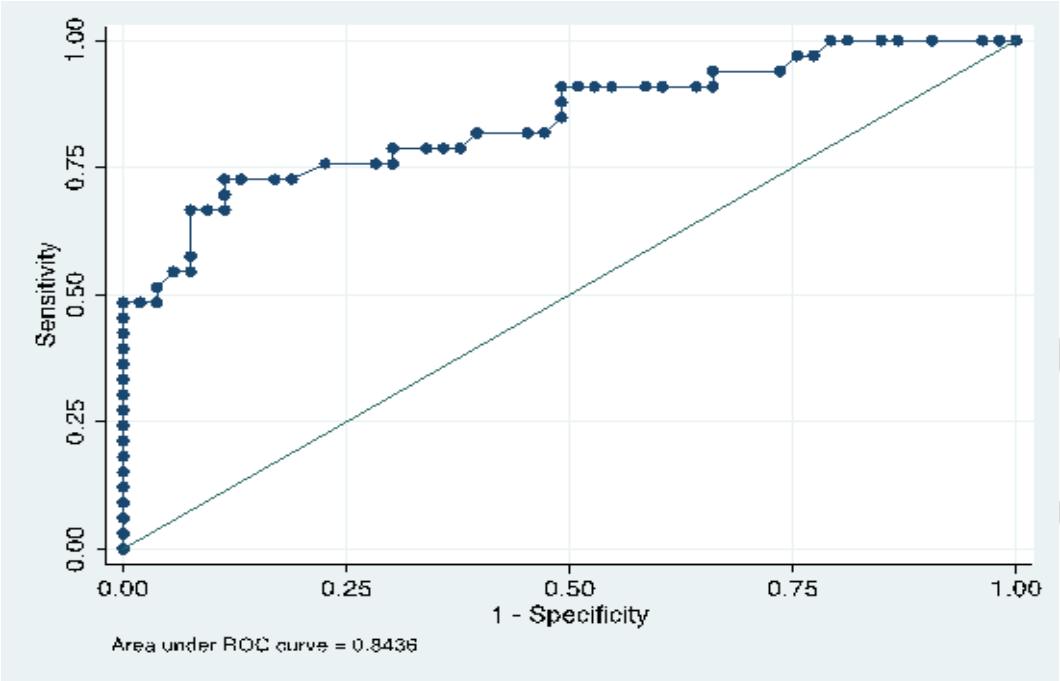


1-specificity

Fig. 2. ROC curve. 1-specificity. Area under the curve = 0.84 ± 0.05 (CI 95%: 0.75-0.93).