Real-time determination of gastric juice pH with EndoFaster® for atrophic gastritis assessment

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A B S T R A C T

Background: In patients with atrophic gastritis involving gastric body mucosa the pH value of gastric juice is distinctly increased, so that pH assessment would allow predict this precancerous lesion. We tested whether EndoFaster® – a device allowing real-time pH measure and *H. pylori* diagnosis – may optimize the need of taking gastric biopsies.
Methods: In this prospective, multicentre study, the accuracy of EndoFaster® for ruling out gastric atrophy involving corporal mucosa was assessed. Real-time pH and ammonium determination was performed by aspirating 3–6 ml gastric juice during endoscopy. Histology performed on 5 standard gastric biopsies was used as gold standard.
Results: A total of 1008 consecutive patients were observed in 12 centres. At histology, gastric body mucosa atrophy/metaplasia was detected in 65 (6.4%) cases, and a pH value >4.5 in the gastric juice was observed in 150 patients. The values of EndoFaster® performance in predicting the presence of atrophic gastritis were as follow: 51% sensitivity, 84% specificity, 18% PPV, 96% NPV, and 82% accuracy. The NPV value was not distinctly affected by neither ongoing proton pump inhibitor therapy nor *H. pylori* infection. By considering also data of ammonium concentrations, the values of EndoFaster® in detecting extensive atrophy on gastric mucosa were 74% sensitivity, 84% specificity, 24% PPV, 98% NPV, and 83% accuracy.
Conclusion: The very high NPV of EndoFaster® might allow to safely rule out presence of atrophic gastritis, reducing the need of taking gastric biopsies in unselected patients managed in clinical practice

1. Introduction

Upper endoscopy is largely performed in developed countries to diagnose or rule out different diseases [1–3]. According to current European guidelines and some expert recommendations

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[4–7], five standard biopsies should be performed on normal appearing gastric mucosa, beyond those directed on macroscopic lesions. This method of mucosal sampling is mainly advised for detection of both *H. pylori* infection and gastric precancerous lesions (atrophy and intestinal metaplasia) requiring management and follow-up options to reduce the risk of gastric cancer development [4–7]. In detail, scheduled endoscopic controls are recommended when extensive atrophy/metaplasia – i.e., involving the gastric body mucosa – is detected [4]. Similarly, atrophy/metaplasia confined in the gastric body, as occurs in autoimmune gastritis, deserves a follow-up due to the documented increased risk of gastric cancer development [8,9]. Some studies found that these conditions are encountered in less than 10% of adult patients [10–12]. Therefore, the diagnostic yield of gastric biopsies on normal appearing mucosa is distinctly low.

Oxyntic mucosa constantly produces a lot of acid by specific cells, and normal gastric juice approximately pH 2 [13]. When atrophy (with or without intestinal metaplasia) involving gastric body mucosa develops – due to either *H. pylori* infection or autoimmune process – gastric acid output is impaired and pH values distinctly increased [14]. Therefore, determining gastric juice pH would allow to suspect or rule out extensive mucosal atrophy. EndoFaster® is an innovative device which accurately measures H^+ concentrations on gastric juice during upper endoscopy [15].

To date, only few data are available on the accuracy of this tool in predicting atrophic gastritis [15–17]. We therefore designed this large, multicentre study to assess whether EndoFaster® might be useful for excluding presence of extensive atrophy on gastric mucosa.

2. Methods

2.1. Upper endoscopy

This prospective study involved a total of 12 Italian Endoscopic Units. Consecutive patients referred by General Practitioners to undergo diagnostic upper GI endoscopy for any indications were invited to participate. All consenting patients underwent upper GI endoscopy with a standard biopsy sampling (2 antrum, 1 *angulus*, and 2 gastric body). Gastric biopsies were handled as routine practice in each participating centre, to searching for both gastric mucosal changes and *H. pylori* infection. All pathological reports were anonymously centralized and reviewed by a single investigator (AZ). Demographic data and information on therapy with proton pump inhibitor (PPI) were collected. In detail, PPI therapy was considered ongoing until one day prior to the endoscopic examination. Data of patients with the presence of atrophy/metaplasia on gastric body mucosa (with or without antral involvement) were considered. Each patient was informed before endoscopy and signed the consent for both procedure and anonymous use of their data for scientific purposes. Since 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, a formal approval by Investigational Review Boards was waived.

2.2. Gastric juice analysis

In each centre, EndoFaster® device was provided for a duration of 2 months to 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. No adjunctive costs were required by neither hospitals or patients. The device was interposed between the endoscope and the suction system, without causing any discomfort to the patient. During endoscopy, lumen washing was avoided until the stomach was reached and 3–6 ml of gastric juice aspirated. Atrophy involving gastric body mucosa was suspected when pH values of gastric juice were >4.5, as reported elsewhere [16,17]. The device allows to simultaneously measure ammonium concentration on the juice disclosing *H. pylori* infection when values are >62 ppm [18,19].

Table 1
Accuracy of EndoFaster® in suspecting extensive atrophic gastritis according to proton pump inhibitor (PPI) therapy or *H. pylori* infection.

Parameter	PPI No		*H. pylori*	
	(N = 638)	Yes (N = 370)	No (N = 826)	Yes (N = 182)
Sensitivity	44%	63%	57%	25%
Specificity	93%	69%	86%	78%
PPV	31%	12%	21%	7%
NPV	96%	97%	97%	94%
Accuracy	90%	69%	84%	74%

PPV: Positive predictive value; NPV: Negative predictive value.

2.3. Statistical analysis

Frequencies, percentages and means values with their 95% confidence intervals were calculated for all observations. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and overall accuracy were calculated.

3. Results

Overall, complete data were available for 1008 patients (M/F = 444/564; Mean age: 55 ± 16 years), with 370 (37.6%) in ongoing PPI therapy. At histology, *H. pylori* infection was present in 182 (18%) patients. A feature of atrophy/metaplasia on gastric body mucosa was detected in 65 (6.4%) cases (M/F = 23/42; Mean age: 62 ± 14 years), including 28 patients with atrophy restricted to the gastric body mucosa and 37 with also antral mucosa involvement. Extensive atrophy was present in 12 (6.6%; 95% CI = 3–10.2) out of 182 and in 53 (6.4%; 95% CI = 4.7–8) out of 826 patients with or without *H. pylori* infection, respectively.

At EndoFaster®, a pH value >4.5 in gastric juice was present in 183 patients, and *H. pylori* infection in 300 cases. The overall values of EndoFaster® in detecting gastric body mucosa atrophy were as follows: 51% sensitivity, 84% specificity, 18% PPV, 96% NPV, and 82% accuracy. The estimates of accuracy in patients with or without PPI therapy as well as *H. pylori* infection are provided in Table 1. *H. pylori* infection was disclosed at EndoFaster® in 15 (46.9%; 95% CI = 29–65.3) out of 32 patients with extensive atrophy on gastric mucosa at histology, but with pH values ≤4.5 at EndoFaster®.

When taking into account pH levels (≤4.5) and ammonium concentrations (>62 ppm) of gastric juice, the overall values of EndoFaster® in detecting extensive atrophy on gastric mucosa were 74% sensitivity, 84% specificity, 24% PPV, 98% NPV, and 83% accuracy.

4. Discussion

Upper endoscopy is largely performed worldwide in patients with gastrointestinal symptoms (dyspepsia, reflux disease, dysphagia, vomiting) and/or signs, such as anaemia or bleeding [1–3]. Different guidelines suggest taking five standard biopsies even on normal appearing gastric mucosa at standard endoscopic examination to search for gastric precancerous lesions and scheduling an appropriate follow-up [4–7]. In detail, patients with atrophy/intestinal metaplasia in both antrum and corpus or only in the corpus deserve endoscopic surveillance [4]. However, these lesions are absent in the large majority of histological examinations, undermining the diagnostic yield of routine gastric biopsies, and uselessly increase resources expend. This is even more evident in inappropriate upper endoscopies, which still account for more than 20% of

upper endoscopies [20,21]. Therefore, a device able to accurately exclude during endoscopy the presence of extensive or corpus-restricted atrophy on gastric mucosa could be advantageous, thus allowing to avoid standard gastric biopsies in patients without endoscopic lesions or other indications. A tool with a very high NPV is needed to achieve this target. By real-time measuring of pH values on gastric juice, EndoFaster® could be a reliable candidate for this purpose [15–17]. Data of our large study found that prevalence of atrophy on gastric mucosa deserving follow-up – that is extensive or corpus-restricted – is 6.4%. This is in agreement with data of previous Italian studies showing a prevalence ranging from 2.3 to 7.8% in routine endoscopic examinations [10–12]. Noteworthy, we found a valuable discriminant role of EndoFaster® in excluding presence of these premalignant lesions on gastric mucosa with a very high (96%) NPV, which is not affected by an ongoing PPI therapy or *H. pylori* infection. This is an acceptable error when considering the number of gastric biopsies safely avoided. Indeed, it should be considered that the probability of detecting intestinal metaplasia on gastric mucosa at histology by performing 5 standard biopsies is 90%, which increases to 97% only when 9 biopsy specimens are taken [22]. Therefore, we currently accept to overlook 10% of precancerous lesions in the stomach following the standard mucosa sampling at endoscopy.

Beyond gastric premalignant lesions, gastric biopsies are useful to look for *H. pylori* infection, that is the main factor of different gastroduodenal diseases [23]. EndoFaster® allows to real-time assess ammonium concentrations on gastric juice, a product of *H. pylori* urease activity [15]. A recent, large study found that EndoFaster® may rule out the presence of *H. pylori* during endoscopy with a NPV as high as 97% by considering a cut-off of $\leq$62 ppm [19]. By simultaneously disclosing presence of *H. pylori* infection, EndoFaster® allows to recollect some cases with extensive atrophy overlooked because of normal ($\leq$4.5) pH values, and this occurs in until to half patients with extensive atrophy according to data of present study. Noteworthy, we observed a very high (98%) NPV when combining results of both pH values and ammonium concentrations at EndoFaster®. Such an approach would allow identifying a definite portion of patients in whom gastric biopsies might be safely avoided, reducing the considerable workload on pathologists and costs. Since a Health Technology Assessment has been conducted by the Italian Ministry of Health showing a positive benefit/cost ratio of device use [24], further studies specifically designed for cost-effective analysis assessment are urged in this field.

In conclusion, data of present study showed a very high accuracy of EndoFaster® in ruling out presence of extensive atrophic gastritis, so that its use might allow reducing the need of taking standard gastric biopsies on normal appearing mucosa.

Declaration of Competing Interest

None declared.

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