Author's response to reviews

Title: Endoscopic findings in uninvestigated dyspepsia

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Author's response to reviews: see over
Dear Editor

According your suggestions we request a statistical review of the work. Thus we suppress the old tables V and VI and add new tables V and VI, which contains data from simple and multiple logistic regressions of variables, with their respective confidence intervals.

In tables:

Table V: Organic dyspepsia in simple binary logistic regression with variables.
Table VI: Organic dyspepsia in multiple binary logistic regression

With the findings of relevance to organic dyspepsia and age, smoking and *H. pylori* infection we present a value to consider age as an alarm signal, and a score to indicate endoscopy (Figures 1 and 2).

In figures:

Figure 1 – Age indication for alarm feature
Figure 2 – Upper digestive endoscopy score.

We are also attaching the approval of the work by the ethics committee.

In attached files:

Ethic approval
Ethic approval English version

Replies to the comments of the referee 1

The manuscript was reviewed by an expert in medical English language.

In attached files:

English language review.

The new tables V and VI were presented with their confidence intervals.

In tables:

Table V: Organic dyspepsia in simple binary logistic regression with variables.
Table VI: Organic dyspepsia in multiple binary logistic regression
Specified in the text were the findings of reflux disease and non-erosive esophagitis. At footnotes of Table IV were presented the findings of non-erosive esophagitis.

**In Results (second paragraph):**

Reflux disease included cases of erosive esophagitis, Barrett’s esophagus and esophageal ulcer.

**In Tables: Table IV: Footnotes**

Non erosive esophagitis: enanthematous esophagitis: 6 cases, esophageal candidiasis: 2 cases.

Also in the footnotes of Table IV are the other endoscopic findings of the esophagus.

**In Tables: Table IV: Footnotes**

Others esophagus findings: Hiatal hernia: 6 cases, Papillomatosis esophagitis: 2 cases, Esophageal varix: 1 case, Retention cyst: 1 case.

The text has been specified that the gastritis diagnosis is an endoscopic diagnosis.

**In Discussion: Paragraph 9:**

In Denmark, gastric inflammation was recently found in 11% of the patients with upper gastrointestinal symptoms [27]; our study did not include histological examination of the gastric mucosa, and thus, gastritis was an endoscopic diagnosis, which after the exclusion of other concurrent diagnoses showing a prevalence of 46%.

In the analysis of the endoscopic findings was not specifically given the findings of antrum-gastritis, corpus-gastritis and pangastritis.

In the text defined the concept of typical epigastric pain: pain relieved by food or antacids and / or presence of clocking.

**In Methods: Study patients and setting:**

Symptom intensity was determinate by the Leeds Dyspepsia Questionnaire [23] and epigastralgia was considered typical when pain was relieved by food or acid suppression or clocking was present.

Discussion and Conclusion were revised and re-written according to your suggestions.

The “test and treat” strategy for the city of São Paulo was better discussed in the text.
In Discussion: paragraph 11:

This high prevalence of infection associated with the low availability of non-invasive tests for its detection prevent the use of the proposed approach of test and treat strategy for undiagnosed dyspepsia. H. pylori eradication treatment is always high cost and complex, with limited efficiency of 88% [33]. The number of cases of functional dyspepsia responsive to treatment is low [34], as only 50% of ulcer patients attain symptom resolution [35, 36], whereas the symptoms of patients with reflux disease do not improve with treatment [37]. Therefore, the test and treat strategy may not be adequate for developing countries, which usually have very high prevalence of H. pylori infection and low level of resources for health care. Empirical treatment for young patients without alarm signs may be the possible approach for undiagnosed dyspepsia in our country.

Statistical analysis was redone by a statistician, new tables were presented and a score for the indication for endoscopy and an age value as an alarm signal were proposed.

In tables:

Table V: Organic dyspepsia in simple binary logistic regression with variables.

Table VI: Organic dyspepsia in multiple binary logistic regression

In figures:

Figure 1 – Age indication for alarm feature

Figure 2 – Upper digestive endoscopy score.

Replies to the comments of the referee 2

The “test and treat” strategy for the city of São Paulo was better discussed in the text.

In Discussion: paragraph 11:

This high prevalence of infection associated with the low availability of non-invasive tests for its detection prevent the use of the proposed approach of test and treat strategy for undiagnosed dyspepsia. H. pylori eradication treatment is always high cost and complex, with limited efficiency of 88% [33]. The number of cases of functional dyspepsia responsive to treatment is low [34], as only 50% of ulcer patients attain symptom resolution [35, 36], whereas the symptoms of patients with reflux disease do not improve with treatment [37]. Therefore, the test and treat strategy may not be adequate for developing countries, which usually have very high prevalence of H. pylori infection and low level of resources for health care. Empirical treatment for young patients without alarm signs may be the possible approach for undiagnosed dyspepsia in our country.
A discussion of the alarm signs designated for this work was presented in the text.

**In Discussion: paragraph 3:**

In this study, older age, mass or lymphadenopathy and family history of upper gastrointestinal cancer were not included as alarm features. In Brazil there is no consensus on this matter and the AGA guidelines are usually followed [16]. In our sample, all patients with malignancy were older than 55 years, but considering the finding of organic dyspepsia (reflux disease, peptic ulcer and malignancy) our study suggests the age of 48 as indicative of alarm symptom.

Frequent vomiting was not considered an alarm symptom, as it was disregarded when reported as a chief complaint in dyspeptic syndrome and thus, it is unlikely that this symptom, when present for at least three months, will not result in weight loss.

The presence of adenopathy or abdominal tumor changes the diagnosis of undiagnosed dyspepsia into undiagnosed adenopathy or tumor and in these cases, the best approach requires imaging assessment and not an esophagogastroduodenoscopy.

Family history of upper gastrointestinal cancer is a type of information that is difficult to obtain, when patients know the cause of the disease, they cannot provide information on its type and precise location.

The validation of the Leeds Dyspepsia Questionnaire was held in our service, when a study of *H. pylori* prevalence in our service was held in 2001. However the results of the work were not published. We are organizing to conduct a new survey on the *H. pylori* prevalence in our service and compare it with the previous study, during which we also intend to publish a validating that questionnaire. To tell the truth, we are attaching the approval of the Ethics committee for the work, his record in the Research Register and the list of patients included in the study.

**In attaching files:**

- Ethic approval Leeds Questionnaire
- Ethic approval Leeds Questionnaire English version
- Research register Leeds Questionnaire
- Research register Leeds Questionnaire English version.
- List of the patients included in Leeds questionnaire

According to your suggestion, we reviewed the statistical analysis, considering only patients who underwent endoscopy and pointed out the cause of the exclusion of other patients.

**In tables (I – VI).**
The redundant text: “that did not require referral to specialists first.” was deleted, according your suggestion.

In Methods: First paragraph:

This prospective observational study was carried out in a tertiary hospital, which provides open-access service to endoscopy.

The authors.