Rational Use of BIOHIT tests in Diagnosis of Abdominal Symptoms — The GI-Panel

BIOHIT HealthCare

Innovating for Health

Gastrointestinal disorders are among the most common complaints encountered by the primary care physicians and currently comprise an increasing healthcare and health economic burden.

Despite their increasing significance in the global healthcare, the causes of these gastrointestinal tract diseases are still incompletely understood, and their treatment options are far from optimal. This leaves many patients dissatisfied with their current treatment which far too often is based on outdated guidelines and/or tests that give false positive or false negative results (1-6,14,19,20).

Specific diagnosis cannot be reached on the basis of clinical symptoms

Dyspeptic symptoms include constant or intermittent upper abdominal pain, bloating, hearth burn, belching and nausea, and dyspepsia (20-40% lifetime frequency) belongs among the most frequent clinical symptoms complained by the patients within the primary healthcare.

On the basis of the non-specific symptoms alone, functional dyspepsia cannot be distinguished from often asymptomatic *Helicobacter pylori* (HP)-infection and atrophic gastritis (AG) with related risks, such as gastric cancer (GC)(4,19). In addition, similar symptoms can be caused by a number of clinically important diseases of extra-gastric origin, such as lactose intolerance (LI) (the average at 65% of the global population), celiac disease (CD)(1-2%), inflammatory bowel disease (IBD)(<1%), irritable bowel syndrome (IBS)(10-15%), and colorectal neoplasia (CRC) suggested by fecal occult blood (FOB)(11,12). Far too often in the current clinical practice, the patients are offered invasive endoscopy as the first-line examination.

GastroPanel® - The first-line diagnostic examination

Replacing gastroscopy by the unique plasma biomarker panel (GastroPanel®) as the first-line diagnostic examination for dyspepsia and HP, it is possible to stratify the patients into three categories at different risk for GC, in addition to reaching the specific diagnosis of gastric functional disorders (**Figure 1**)(4,14).

In patients with **normal GastroPanel® biomarker profile**, symptoms determine the direction of the additional testing. Asymptomatic subjects with normal profile do not need further actions, whereas those with symptoms should be examined for Celiac Disease, IBD/IBS and fecal occult blood (FOB), using Biohit CDQT, Calprotectin and ColonView-FIT Quick tests, respectively (**Table 1**).

GastroPanel profile implicating **a dysfunction in the acid output** (high or low), can be affirmed by a simple clinical procedure. In case of high acid output (G-17b low), a 2-week test treatment with PPI-medication should normalize the profile. When low acid output (G-17b high) is ascribed to PPI-medication itself (with no implications of AG), interrupting the PPI-treatment for two weeks should restore acid output to normal level (8,9).

GastroPanel is a sensitive and comprehensive test for ***Helicobacter pylori* (HP) infection** with related risks (3). When HP-infection is detected (with no accompanying AG), the logical next step is eradication of the bacteria by any of the standard therapies (1). Following the international recommendations, eradication should always be controlled. Biohit offers several optional tests for that: GastroPanel, HPQT and UFT300 tests. If the symptoms continue after HP-eradication, a feasible option is to make gastroscopy that enables i) direct visualization of HP as well as ii) testing the biopsy with HP Quick tests. Whenever gastroscopy is performed, testing for LI can be conveniently done using LIQT.

The patients at high risk for subsequent GC include all those with GastroPanel® implicating **AG (atrophic gastritis)**. In this high-risk category, one cannot avoid performing gastroscopy to confirm the AG diagnosis, its severity and topography in the stomach, i.e. antrum, corpus or both (2,6,9,10). Additional information can be obtained by complementing the targeted biopsies with the laboratory tests for HP, LI, CD and vitamin B12 deficiency (15), not infrequently accompanying atrophic corpus gastritis, particularly of the autoimmune type (22).

Summary

Replacing gastroscopy by GastroPanel® as the first-line diagnostic test in patients with dyspeptic complaints allows a rational diagnostic algorithm whereby carefully selected BIOHIT non-invasive tests are applied to screen for specific clinical conditions that all share in common the non-specific abdominal symptoms.

Substantial savings in healthcare costs can be achieved while avoiding up to 80% of unnecessary gastroscopies by screening the dyspeptic patients at first by GastroPanel®, and targeting the other tests using a rational diagnostic algorithm (Figure 1; Table 1).

However, if GastroPanel® detects i) symptomatic *H.pylori* (HP)-infection after eradication, ii) atrophic gastritis (AG) or iii) symptomatic high acid output, these are indications for gastroscopy and biopsy examination (4).

Figure 1. Diagnostic algorithm for symptomatic (dyspeptic) patients

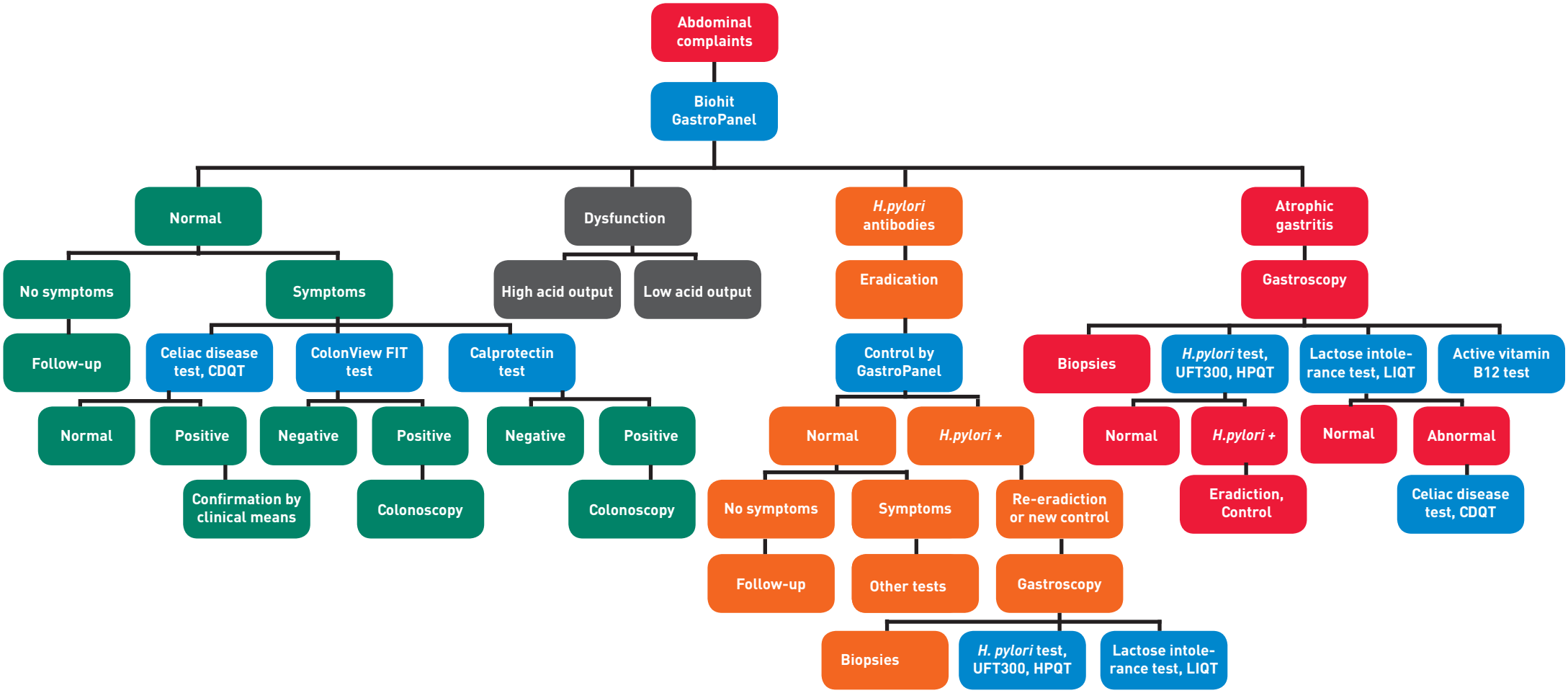

Table 1. Rational use of BIOHIT tests at each optional step of the algorithm ("The GI-Panel")

<table>
<tr><td colspan="15">SYMPTOMATIC PATIENTS WITH DYSPEPTIC COMPLAINTS</td></tr>
<tr><td colspan="15">GastroPanel test</td></tr>
<tr><td colspan="4">NORMAL</td><td colspan="2">DYSFUNCTION</td><td colspan="4">HP-INFECTION (No AG)</td><td colspan="5">ATROPHIC GASTRITIS (AG)</td></tr>
<tr><td>No Symptoms</td><td colspan="3">Symptoms</td><td>High acid output</td><td>Low acid output</td><td colspan="4">Eradication (Standard regimens)</td><td colspan="5">Gastroscopy</td></tr>
<tr><td>NActs</td><td colspan="2">CDQT</td><td colspan="2">Colon View</td><td>Calprotectin</td><td>PPI+</td><td>PPI-</td><td colspan="4">Eradication control (GastroPanel, HPQT, UFT300)</td><td>Bx</td><td colspan="2">UFT300, HPQT</td><td colspan="2">LIQT</td><td>B12</td></tr>
<tr><td rowspan="4"></td><td>T-</td><td>T+</td><td>T-</td><td>T+</td><td>T-</td><td>T+</td><td colspan="2">GastroPanel re-testing</td><td colspan="2">Normal</td><td colspan="2">HP-Positive</td><td></td><td>T-</td><td>T+</td><td>T-</td><td>T+</td><td rowspan="2"></td></tr>
<tr><td colspan="6" rowspan="3"></td><td colspan="2">Normal profile</td><td>N-Sympt</td><td>Sympt</td><td colspan="2">Re-eradication</td><td colspan="2"></td><td>ERA</td><td></td><td>CDQT</td></tr>
<tr><td colspan="2" rowspan="2"></td><td>NActs</td><td>OTests</td><td colspan="2">Gastroscopy</td><td colspan="5" rowspan="2"></td></tr>
<tr><td></td><td></td><td>Bx</td><td>HPQT</td><td>LIQT</td></tr>
</table>

Explanation of the abbreviations:	
HP; *Helicobacter pylori*	CTs; Clinical tests for Celiac Disease
AG; Atrophic gastritis	CS; Colonoscopy
NActs; No specific actions needed	N-Sympt; No symptoms
CDQT; Celiac Disease Quick Test	Sympt; Symptoms
PPI+; Test PPI-treatment for 2 weeks	OTests; Other diagnostic tests
PPI-; Interrupt PPI-treatment for 2 weeks	Bx; Gastroscopic biopsies
HPQT; *Helicobacter pylori* Quick Test	LIQT; Lactose Intolerance Quick Test
UFT300; *Helicobacter pylori* UFT300 Test	B12; Active B12-vitamin test
T-; Test-negative	ERA; Eradication and controls
T+; Test-positive	

Biohit diagnostic tests used in the algorithm (in blue):
GastroPanel®
Active Vitamin-B12®
Calprotectin®
Lactose Intolerance Quick Test®
Helicobacter Pylori UFT300 Quick Test®
Helicobacter Pylori Quick Test®
ColonView-FIT®
Celiac Disease Quick Test®

Appendix

The GastroPanel® innovation is based on follow-up studies on gastritis patients conducted by research groups in Finland and Estonia and the discovery of the role of *Helicobacter pylori* in pathogenesis of gastritis and peptic ulcer disease, which led to Nobel Prize in 2005. Of crucial importance has been Biohit's R&D and the microplate immunoassay analyzers, based on the invention of the vertical light beam measurement principle, one of the inventions of Biohit's founder, currently the worldwide global standard. Starting from the 1970's, this invention has prompted an extensive research on and fast development of microplate immunoassay techniques, e.g., for analysis and screening of infectious diseases, including *Helicobacter pylori* gastritis, atrophic gastritis and related risks, such as peptic ulcer disease and gastric cancer (1-4, www.biohithealthcare.com/About Us/History: Aggressive innovation and patenting strategy).

The unique GastroPanel® is the primary examination from a blood sample for dyspepsia (the prevalence 20-40%) to reveal *H. pylori* infection (5-80%) and atrophic gastritis (2-12%) with related risks, such as gastric cancer and the deficiency of vitamin B12 (2,4). GastroPanel® increases patient safety and decreases healthcare costs. Biohit has launched the GastroPanel screening model which can be used to calculate levels of savings achievable with the use of the GastroPanel® in the screening program of the risk of gastric cancer. For example in Finland, the total lifetime savings are over € 800 million for 10 age groups (6).

Today, the ageing population has a great benefit of GastroPanel® diagnosis/screening – and needless to reiterate, GastroPanel® could be the test-of-choice for the diagnosis/screening of gastric and esophageal cancer risks. In addition to this increased cancer risk, atrophic gastritis due to *H. pylori* infection or autoimmune disease, may cause malabsorption of vitamin B12, iron, magnesium, zinc, calcium and some drugs.

As to the diagnosis of *H. pylori* infection, 13C-urea breath test (UBT) or stool *H. pylori* antigen test (SAT) frequently give false negative results, and *H. pylori* infection (with all its possible consequences) remains undetected. UBT may also give false positive results in subjects with acid-free stomach colonized by urease-positive bacteria. In addition, the conventional *H. pylori* tests (UBT, SAT) and antibody tests do not detect atrophic gastritis with all the above mentioned risks (2-5,19,20).

Because GastroPanel® does not have the limitations of the conventional *H. pylori* tests (8,20), GastroPanel® is recommended for the primary diagnosis of dyspepsia and *H. pylori* infection. Similarly, all subjects should be tested before prescribing any PPI medication, because PPIs are contraindicated for patients with acid-free stomach due to atrophic gastritis (18).

In addition to the reliable diagnosis of *H. pylori* infection and atrophic gastritis, GastroPanel® also reveals high acid output of the gastric mucosa, which remains undiagnosed with the conventional *H. pylori* tests and which predisposes to esophageal reflux disease (GERD) with potential complications. These are ulcerative esophagitis, Barrett's esophagus or lower esophageal cancer (2,4,14).

We hope that this information will encourage doctors and laboratories to utilize GastroPanel® in checking the stomach health and in diagnosis of symptomatic patients as well as for screening of the risk groups (4,8,21,22).

References

1. Marshall BJ, Warren JR. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. Lancet. 1984;323:1311–15, http://nobelprize.org/medicine/laureates/2005/press.html

2. Suovaniemi O. State of the art GastroPanel and Acetium innovations for the unmet need. www.biohithealthcare.com Scientific/Literature.

3. Sipponen P, Maaroos HI. Chronic gastritis, Scand J Gastroenterol. 2015 Jun 3; 50(6): 657–667.

4. http://www.biohithealthcare.com/additional-information

5. Sipponen P, Graham DY. Importance of atrophic gastritis in diagnostics and prevention of gastric cancer: application of plasma biomarkers. Scand. J. Gastroenterol. 2007;42 (1);2-10.

6. https://www.gastropanel.com/decision-makers/screening-model

7. Storskrubb T, Aro P, Ronkainen J, Sipponen P, Nyhlin H, Talley NJ, Engstrand L, Stolte M, Vieth M, Walker M and Agréus L. Serum biomarkers provide an accurate method for diagnosis of atrophic gastritis in a general population: The Kalixanda study. Scand J Gastroenterol, 2008; 43:1448-1455.

8. Agréus L, Kuipers EJ, Kupcinskas L, Malfertheiner P, Di Mario F, Leja M, Mahachai V, Yaron N,van Oijen M, Perez Perez G, Rugge M, Ronkainen J, Salaspuro M, Sipponen P, Sugano K, Sung J. Rationale in diagnosis and screening of atrophic gastritis with stomach-specific plasma biomarkers, Scandinavian Journal of Gastroenterology 2012; 47: 136-147.

9. Syrjänen K, Eronen K. Serological testing in management of dyspeptic patients and in screening of gastric cancer risks. J Gastrointest Disord Liver Funct 2016;2(3):1-5.

10. Syrjänen K. Subjects with compromised stomach health need special attention: Serological biomarker panel (GastroPanel®) for monitoring and slow-release L-cysteine (Acetium® Capsule) for protection of the stomach. EC Gastroenterol Digest Syst 2017;4(3):75-86.

11. Slavescu KC, Pirvan A, Gheban D, Eklund C, Paloheimo L, Syrjänen K. A point-of-care test for anti-transglutaminase (tTG2A) IgA, IgG, IgM antibodies (CELIAC Quick Test®) validated in diagnosis of incident celiac disease (CD) in pediatric patients. EC Gastroenterol Digest Syst 2017;3(1):4-13.

12. http://www.google.com/patents/US4427769, Immunoassay for fecal human hemoglobin

13. Vasilyev S, Smirnova E, Popov D, Semenov A, Eklund C, Hendolin P, Paloheimo L, Syrjänen K. A New-generation fecal immunochemical test (FIT) is superior to guaiac-based test in detecting colorectal neoplasia among colonoscopy referral patients. Anticancer Res 2015;35:2873-2880.

14. Syrjänen K. Diagnosis of the patients with upper abdominal symptoms (dyspepsia) using non-invasive serological tests. EC Gastroenterol Digest Syst 2017;4(6):XX-XY. In press.

15. Benberin V, Bektayeva R, Karabayeva R, Lebedev A, Akemeyeva K, Paloheimo L, Syrjänen K. Prevalence of H.pylori infection and atrophic gastritis among asymptomatic and dyspeptic adults in Kazakhstan. A Hospital-Based screening with a panel of serum biomarkers. Anticancer Res 2013;33:4595-4602.

16. Aine R, Kahar E, Aitokari K, Salminen J, Eklund C, Paloheimo L, Peetsalu A, Syrjänen K. Atrophic gastritis (AG) and its clinical sequels among elderly people in Finland and Estonia. A comparative study using GastroPanel and B12-vitamin testing of the residents in assisted-housing facilities. J Aging Res Clin Pract 2016;5:194-202.

17. Vohlonen I, Pukkala E, Malila N, Härkönen M, Hakama M, Koistinen V, Sipponen P. Risk of gastric cancer in Helicobacter pylori infection in a 15-year follow-up, Scand J Gastroenterol 2016;51:10,1159-1164.

18. Ahn JS, Eom C-S, Jeon CY, Park MS. Acid suppressive drugs and gastric cancer: A meta-analysis of observational studies. World J Gastroenterol 2013;19:2560-2568

19. http://www.biohithealthcare.com/limitations-of-helicobacter-pylori-diagnostics

20. Syrjänen K. Caveats in diagnosis of Helicobacter pylori infection can be avoided by a panel of serum biomarkers (GastroPanel®). J Carcinog Mutagen 2017;7(6), e123. doi:10.4172/2157-2518.1000e123

21. www.GastroPanel.com /GastroPanel® Sample Collection Instructions

22. www.biohithealthcare.com/resource/files/media/articles/autoimmune-screening-panel-2r.pdf

BIOHIT HealthCare

Innovating for Health

www.biohithealthcare.com

Biohit Oyj, Laippatie 1, 00880 Helsinki, Finland, Tel. +358 9 773 861, info@biohit.fi