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Opinion

Impact of Duodenal Bulb Biopsies in Coeliac Disease Diagnosis

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Abbreviation

CD: Coeliac Disease

The role of intestinal biopsies for the coeliac disease (CD) diagnosis has changed over time, switching from three biopsies needed in the late 1960s (the first on a gluten containing diet presenting typical histological damage, the second on a gluten free diet showing the healing of the mucosa and the third demonstrating the recurrence of the histological changes after the gluten reintroduction) to the 1990 guidelines requiring only the first intestinal biopsy, but associated with clinical and laboratoristic criteria, arriving to the most recent European paediatric guidelines, that encompass the biopsies sparing in well selected cases [1]. However, the benefit of sampling duodenal mucosa in non-suspected CD patient during an upper gastro-intestinal endoscopy is still debated.

Pitman., *et al.* [2] recently published their study performed on a hospital based endoscopy settings. Among more than 8,000 patients who underwent an upper gastrointestinal endoscopy due to abdominal pain/dyspepsia, gatro-oesophageal reflux, anaemia/iron deficiency, diarrhoea and weight loss, only the 57% underwent the duodenal biopsies and the CD diagnosis was made in 0.49% of cases. The factors associated with intestinal biopsy performance were younger age, female sex and symptoms such as weight loss, diarrhoea and anaemia. It is remarkable that all already diagnosed CD patients or suspected CD patients were not included in the study, so that in this cases the duodenal biopsies avoidance would have resulted in a missed diagnosis.

A recent paper published by Stoven., *et al*. [3] investigated the diagnostic yield from sampling the duodenal bulb in addition to distal duodenum in adults in which an upper gastrointestinal endoscopy was performed without a specific suspicion of CD. In this study, duodenal bulb biopsies did not increased significantly the rate of CD diagnosis (only 0.1% in their cohort) and the authors concluded that routinely mucosal sampling should not be encompassed in low-risk pretest patients. However, it is well known that first degree relatives of CD patients have a ten time higher risk of CD when compared to general population [4] and subjects suffering from iron deficiency anaemia [5] and/or gastrointestinal symptoms (such as diarrhoea, nausea, chronic dyspepsia or bloating) [6] are at higher risk of CD, when compared to general population.

When considering patients with known CD, Stoven., *et al*. reported two cases (7%) with histological lesions localized only in the duodenal bulb and this strengthen the importance of performing biopsies in this site also during the follow-up of CD. In a previous paper we reported our experience of a child on a gluten challenge in which the bulb was the only duodenal area involved [7] and a woman with autoimmune thyroiditis with histological changes consisting with CD localized only in the duodenal bulb [8].

In a not-so-distant past, the only target considered suitable for CD biopsies was the distal duodenum, insofar as the bulb has Brunner's glands and more lymphoid tissue together with the appearance of shorter, broader or blunted villi, that may led to difficulties in histologi-

cal interpretation. Nowadays, an expert pathologist can easily identify histological changes consistent with CD also in the duodenal bulb, and besides, the presence of Brunner's gland make the bulb easily distinguishable from the distal duodenum, so that all specimens collected during upper endoscopy could be fixed in the same formalin bottle, without increasing processing charges.

Analyzing the diagnostic value of bulb biopsies, several studies supported its crucial role for CD, since the rate of histological changes localized only in the duodenal bulb ranges from 1.8% to 7% at diagnosis [8-12].

Another point widely discussed in literature is the benefit of biopsies orientation. Sometimes it is considered a mission impossible, since it is time consuming and requires expert assistants [13]. However in our experience [8] biopsy orientation on filter paper resulted in 90% of well oriented specimen that is important to establish a correct evaluation of the villous/crypt ratio, a crucial point of the CD histological features and avoid the occurrence of inconclusive biopsies.

Some authors tried to increase the diagnosis yield of intestinal biopsies through the use of additional tools. Koskinen., *et al*. [14] demonstrated that anti-transglutaminase2 IgA deposits can be found in all celiac disease patients at diagnosis, even in absence of serum CD specific autoantibodies, and can last for long period even after dietary treatment. This technique could be used in specialized centers as additional diagnostic tool in case of doubts, however it requires a frozen specimen and a skilled pathologist.

The detection of autoantibodies (both anti-endomysium IgA and anti-transglutaminase antibodies) from organ culture has been proposed as complementary diagnostic tool at diagnosis [15], but it has been demonstrated also useful to avoid gluten challenge in selected cases [16]. The technique requires two mucosal samples that are cultured in a specific medium for 48 hours, one in the presence and one in the absence of peptic tryptic digest of gliadin, and the autoantibodies are identified from the supernatant (by indirect immunofluorescence for anti-endomysium and enzyme-linked immunosorbent assay for anti-transglutaminase). In selected cases in which the intestinal biopsies are not conclusive for CD diagnosis or in serum negative histological changes of difficult interpretation, the organ culture system seems to be a promising tool [15], even if some doubts aroused about their specificity [17].

In conclusion intestinal biopsies for CD diagnosis seems to be a controversial topic that requires further investigations. In our opinion routinely biopsies should not be recommended in individuals with low pre-test risk of CD. However, a correct definition of these patients is crucial, since CD presentation is not limited to malabsorptive symptoms anymore and a delayed or a missed diagnosis could lead to not negligible complications, such as osteoporosis [18] infertility [19] and intestinal lymphoma [20].

Conflict of Interest

None.

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Bibliography

1. Husby S., *et al*. "European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease". *Journal of Pediatric Gastroenterology and Nutrition* 54.1 (2012): 136-160.

2. Pitman M., *et al*. "Rates of Duodenal Biopsy During Upper Endoscopy Differ Widely Between Providers: Implications for Diagnosis of Celiac Disease". *Journal of Clinical Gastroenterology* (2017).

3. Stoven SA., *et al*. "Analysis of Biopsies From Duodenal Bulbs of All Endoscopy Patients Increases Detection of Abnormalities but has a Minimal Effect on Diagnosis of Celiac Disease". *Clinical Gastroenterology and Hepatology* 14.11 (2016): 1582-1588.

4. Bonamico M., *et al*. "Serologic and genetic markers of celiac disease: a sequential study in the screening of first degree relatives". *Journal of Pediatric Gastroenterology and Nutrition* 42.2 (2006): 150-154.

5. Broide E., *et al*. "Cost effectiveness of routine duodenal biopsies in iron deficiency anemia". *World Journal of Gastroenterology* 22.34 (2016): 7813-7823.

6. Bardella MT., *et al*. "Increased prevalence of celiac disease in patients with dyspepsia". *Archives of Internal Medicine* 160.10 (2000): 1489-1491.

7. Bonamico M., *et al*. "Patchy villous atrophy of the duodenum in childhood celiac disease". *Journal of Pediatric Gastroenterology and Nutrition* 38.2 (2004): 204-207.

8. Nenna R., *et al*. "Duodenal bulb in celiac adults: the "whether biopsying" dilemma". *Journal of Clinical Gastroenterology* 46.4 (2012): 302-307.

9. Pace LA and Crowe SE. "Duodenal Bulb Biopsies Remain Relevant in the Diagnosis of Adult Celiac Disease". *Clinical Gastroenterology and Hepatology* 14.11 (2016): 1589-1592.

10. Hopper AD., *et al*. "Patchy villous atrophy in adult patients with suspected gluten-sensitive enteropathy: is a multiple duodenal biopsy strategy appropriate?" *Endoscopy* 40.3 (2008): 219-224.

11. Cammarota G., *et al*. "Role of the "immersion technique" in diagnosing celiac disease with villous atrophy limited to the duodenal bulb". *Journal of Clinical Gastroenterology* 41.6 (2007): 571-575.

12. Gonzalez S., *et al*. "Prospective study of the role of duodenal bulb biopsies in the diagnosis of celiac disease". *Gastrointestinal Endoscopy* 72.4 (2010): 758-765.

13. Green PH. "Celiac disease: how many biopsies for diagnosis?" *Gastrointestinal Endoscopy* 67.7 (2008): 1088-1090.

14. Koskinen O., *et al*. "Usefulness of small-bowel mucosal transglutaminase-2 specific autoantibody deposits in the diagnosis and follow-up of celiac disease". *Journal of Clinical Gastroenterology* 44.7 (2010): 483-488.

15. Bonamico M., *et al*. "Antiendomysial antibody detection in biopsy culture allows avoidance of gluten challenge in celiac children". *Journal of Pediatric Gastroenterology and Nutrition* 40.2 (2005): 165-169.

16. Picarelli A., *et al*. "Usefulness of the organ culture system when villous height/crypt depth ratio, intraepithelial lymphocyte count, or serum antibody tests are not diagnostic for celiac disease". *Translational Research* 161.3 (2013): 172-180.

17. Maglio M., *et al*. "Intestinal Production of Anti-Tissue Transglutaminase 2 Antibodies in Patients with Diagnosis Other Than Celiac Disease". *Nutrients* 9.10 (2017): E1050.

18. Stazi AV., *et al*. "Osteoporosis in celiac disease and in endocrine and reproductive disorders". *World Journal of Gastroenterology* 14.4 (2008): 498-505.

19. Nenna R., *et al*. "Immediate effect on fertility of a gluten-free diet in women with untreated coeliac disease". *Gut* 60.7 (2011): 1023-1024.

20. Cellier C., *et al*. "Refractory sprue, coeliac disease, and enteropathy-associated T-cell lymphoma. French Coeliac Disease Study Group". *Lancet* 356.9225 (2000): 203-208.

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