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Suggestions for automatic quantitation of endoscopic image analysis to improve detection of small intestinal pathology in celiac disease patients

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ABSTRACT

Although many groups have attempted to develop an automated computerized method to detect pathology of the small intestinal mucosa caused by celiac disease, the efforts have thus far failed. This is due in part to the occult presence of the disease. When pathological evidence of celiac disease exists in the small bowel it is visually often patchy and subtle. Due to presence of extraneous substances such as air bubbles and opaque fluids, the use of computerized automation methods have only been partially successful in detecting the hallmarks of the disease in the small intestine—villous atrophy, fissuring, and a mottled appearance. By using a variety of computerized techniques and assigning a weight or vote to each technique, it is possible to improve the detection of abnormal regions which are indicative of celiac disease, and of treatment progress in diagnosed patients. Herein a paradigm is suggested for improving the efficacy of automated methods for measuring celiac disease manifestation in the small intestinal mucosa. The suggestions are applicable to both standard and videocapsule endoscopic imaging, since both methods could potentially benefit from computerized quantitation to improve celiac disease diagnosis.

1. Clinical and quantitative background

The diagnosis and treatment of celiac disease is a ubiquitous problem throughout the world. In part this arises from the fact that the disease varies widely in its presentation [1,2]. The protein gluten, found in wheat, rye, and barley grains, is toxic to celiac disease patients and causes damage to the small intestinal mucosa [2]. Since abnormality may not be evident in small intestinal endoscopic images, however, the diagnosis of the disease can be difficult. For definitive diagnosis, there should be histologic confirmation of the intestinal damage in serologically positive individuals [3]. Improvement on a gluten-free diet is added evidence that the patient has this disorder [4]. Furthermore, celiac disease is associated with the HLA genotypes DQ2 or DQ8 [5]; however, testing for these alleles has limited sensitivity and specificity [6]. When a celiac patient has been diagnosed, treatment with a gluten-free diet is typically the first and only therapy [7].

Another difficulty in the diagnosis of celiac disease is that currently-used pathological scoring techniques are only semi-quantitative. The modified Marsh criteria were developed to gauge the degree of abnormality found when observing pathology slides of small intestinal villi under light microscopy [8]. Marsh type 0 patients are normal. Marsh type I patients have an increase in intraepithelial lymphocytes in the jejunum and duodenum. In Marsh type II, there is hyperplasia of intestinal crypts but normal villi. For Marsh type III, there is increased crypt hyperplasia and presence of villous atrophy ranging from mild (type IIIa), to marked (type IIIb), to complete (type IIIc). Clinical scoring is therefore to some extent qualitative and subjective, with limited efficacy. Since the presence and even the degree of villous atrophy is spatially patchy [9], different biopsies from the same patient may be assigned different Marsh scores.

When celiac disease is undiagnosed and untreated, it can result in maladies. Insufficient absorption of nutrients, minerals, and fat-soluble vitamins is common in these patients [10,11]. There is also an increased risk of malignancy including adenocarcinoma, lymphoma of the small bowel, and other non-Hodgkin's lymphomas [12]. Ulcers may form, particularly at the level of the jejunum, and there can be narrowing of the small bowel with the possibility of complete obstruction as a result of scarring [13]. Calcium and vitamin D malabsorption can occur and result in osteopenia or osteoporosis. There may also be bacterial overgrowth of the small

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intestine due to the lack of normal absorption, which can cause or worsen the malabsorption [14].

1.1. Evaluation of clinical status with videocapsule endoscopic imaging

The use of videocapsule endoscopy rather than standard endoscopy for detection of pathology is advantageous for its limited invasiveness and coverage of the entire small intestine, although biopsies cannot yet be obtained with this method. However, in studies in which videocapsule endoscopy was compared with conventional upper gastrointestinal endoscopy with duodenal biopsy as a gold standard, the videocapsule method has been shown to have good sensitivity (85.0–87.5%) and specificity (100–90.9%) for the diagnosis of celiac disease [15,16]. Videocapsule endoscopy was also shown useful to detect small intestinal villous atrophy in patients with biopsy-proven celiac disease with 92% sensitivity and 100% specificity [17]. Detection of other mucosal abnormalities, exclusion of adenocarcinoma, and identification of signs of ulcerative jejunoileitis or intestinal T-cell lymphoma has also recently been done using the videocapsule method [18,19]. Thus videocapsule endoscopy has a similar capability as compared with standard endoscopy to characterize patient clinical status, and can be useful for automated analysis.

There can be marked differences in standard or videocapsule images obtained from celiac patients with pathology as compared with normal patients, and the goal of any quantitative automated system is to detect both marked and subtle pathology. In Fig. 1, examples of videocapsule images are shown at the level of the duodenum. Panels A and B are from control patients without celiac disease or villous atrophy. Panels C and D are from celiac patients prior to following a gluten free diet. The control patients have mucosal folds with smooth edges (panels A and B). The mucosal surface itself is approximately consistent in texture and appearance in all image areas in panel A, and also for all image areas in panel B. There are evident fine surface projections at the limit of resolution which represent either villi or clusters of villi. In panel C, the surface is greatly mottled. In panel D, the edges of the mucosal folds are highly scalloped. The appearance of the small intestinal mucosa in panel C and D are typical of areas with substantial pathology in untreated celiac patients. Although measures have yet to be devised to numerically gauge the severity of abnormality throughout the small intestine, the extent of villous atrophy can be approximated by measuring the time in which abnormality is observed as a percentage of total small bowel transit time [20]. This can be done by simply counting the number of images with evident pathology, versus the total number of images in the series taken at the level of the small intestine.

1.2. Automated quantitative systems

Based on the difficulty in diagnosis and characterization of celiac disease, the large proportion of undiagnosed patients with the disease [21], and the potential for severe complications when untreated, there is a significant need for improved quantitative and automated diagnostic methods. Most helpful would be the possibility to provide an actual Marsh score based upon a computerized endoscopic imaging and quantitative analysis paradigm. The ultimate goal of such a system should be to provide a continuous score, that is, a score using numbers with decimal

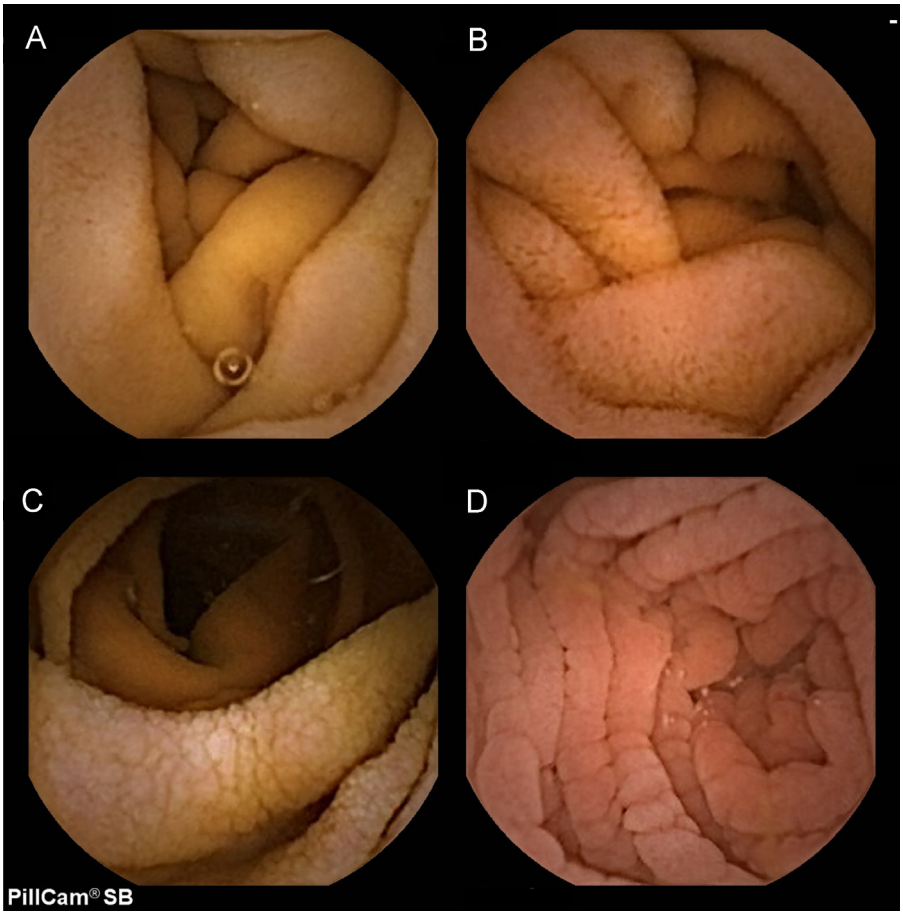

Fig. 1. Color videocapsule images obtained from the level of the duodenum. (A and B) Images from two control patients. (C and D) Images from two celiac patients. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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