

imaging) will switch the attention from the traditional cornerstone of clinical medicine, projecting us towards the precision medicine.

However, the problem may be unexpectedly even more complex than the one described so far, as the prediction of cardiometabolic risk, hepatic disease progression and the effects of treatment on such outcomes may occasionally diverge (notably, this seems particularly evident for some genetic determinants of NAFLD) [13]. For instance, targeting liver fibrosis with obeticholic acid may result in an adverse cardiometabolic profile, while treating liver fibrosis through the changes of glucose and lipid metabolism may provide only a small result [13]. These findings have led to an intense debate (in the literature) whether the optimal strategy for NAFLD patients must be focused on anti-fibrotic or cardiometabolic approaches [13]. Reasonably, waiting for future studies to answer this important question, the choice of one strategy or the other or both may be based on the main characteristics of the NAFLD patient (such as age, sex, ethnicity, disease duration, patient attitude and expected treatment efforts, comorbidities, social context and life expectancy), as well as the resources and support system.

In conclusion, I strongly believe that additional and new studies investigating this issue (i.e., personalized hepatic and cardiometabolic goals for different types of NAFLD patients) should be timely planned in order to offer each NAFLD patient the best therapeutic approach and to update our guidelines in the forthcoming era of personalized medicine. Therefore, the desirable future studies may work as follows: (a) assess the stated issue with clinical trials (e.g., a trial in which NAFLD patients are randomly assigned to one of the following interventions: routine care or personalized hepatic and cardiometabolic targets); (b) determine the optimal personalized hepatic and cardiometabolic targets for NAFLD patients according to the presence of important clinical and social factors; and (c) if advantageous, integrate the personalized hepatic and cardiometabolic targets in clinical decision support systems.

#### Conflict of interest

None declared.

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#### Long-term treatment with linaclotide of intestinal pseudo-obstruction secondary to Ehlers-Danlos syndrome<sup>☆</sup>



Dear Editor,

Ehlers-Danlos patients frequently display abdominal symptoms [1], and retrospective studies have shown the possible presence of gastrointestinal dysmotility in a number of these patients [2]. However, to the best of our knowledge intestinal pseudo-obstruction has never been previously reported in adults, and only one such pediatric case has been described, associated to intestinal  $\alpha$ -actin deficiency [3]. This pediatric case was very difficult to manage and required multiple surgical procedures.

We report the case of an adult woman affected by Ehlers-Danlos syndrome, with abdominal symptoms related to intestinal pseudo-obstruction and refractory to treatment, symptoms resolved after a new therapeutic agent, linaclotide, was used.

A 62 yr-old woman, with a diagnosis of classical Ehlers-Danlos syndrome made in 1997 in the rheumatologic clinic of our University, came to our attention in January 2011 for repeated subocclusive episodes. The patient had previously undergone abdominal surgery elsewhere for persistent constipation associated to megacolon. In December 2009 total colectomy with ileo-rectal anastomosis was carried out. After surgery, her dysmotility problems persisted, with several pseudo-occlusive episodes per year in the time course, and decreased spontaneous bowel movements (average two per week) associated with abdominal pain. These symptoms were often unresponsive to medical treatment and severely impaired the patient's quality of life. After excluding mechanical obstruction by entero-CT scan examination, that showed only mild dilatation of the small bowel, a 6-h gastro-jejunal manometry was carried out (4 h fasting, 2 h after a meal) according to a standard procedure [4]. This examination revealed normal gastric motor activity and neurogenic abnormalities, during both fasting and after the meal, involving the duodenum and the proximal jejunum. These abnormalities consisted of uncoordinated contractile activity during phase II and III of the migrating motor complex, and inability to convert the fasting into a fed pattern. Although we would have expected myogenic-type abnormalities, it is worth noting that Zarate et al. [2] described similar neuropathic

<sup>☆</sup> Written informed consent was obtained by the patient to publish her case.

small bowel abnormalities in three out of seven patients with joint hypermobility syndrome without pseudo-obstructive episodes.

An intensive therapeutic approach was started with high-dose daily macrogol and bi-weekly magnesium sulfate, but the clinical response was quite scarce. Prucalopride, 2 mg/day was therefore started, but the results were only partial, still requiring association with other laxatives, and did not improve abdominal pain. When in 2014 linaclotide, a potent peptide agonist of the guanylate cyclase C receptor effective on both constipation and abdominal pain in patients with constipation and irritable bowel syndrome [5] became available in our country, we proposed this approach to the patient. After careful explanation of the possible side effects, a dose of 290 µg/day was started in July 2014, and the patient referred improvement of her symptoms within a week, with progressive decrease up to disappearance of abdominal pain within two weeks, and resolution of subocclusive episodes and normalization of bowel movements (average, three per week) within the first month, leading to withdrawal of the other laxatives. Since then, the patient continues linaclotide without experiencing further pseudo-obstructive symptoms or abdominal pain.

Linaclotide is a potent guanylate cyclase agonist, recently available in clinical practice for the treatment of chronic constipation and constipation-predominant irritable bowel syndrome [5]. The interest of this drug in our case was due to the fact that linaclotide has been shown to be effective to relieve symptoms related to constipation, with the further advantage of being effective on abdominal pain [5]; these considerations induced us to try this treatment after failure of conventional treatments.

Therefore, we feel that this report on the long-term benefit of linaclotide treatment might be interesting and to give suggestion to add another potentially useful treatment for patients with pseudo-obstruction, in whom the drug might help to improve their quality of life, and perhaps to spare further surgical interventions.

#### Conflict of interest

None declared.

#### Ethics committee approval

N/A.

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#### Patient age determines adherence to preventive care measures among patients with ulcerative colitis



Dear Editor,

Ulcerative colitis (UC), a type of inflammatory bowel disease (IBD), affects approximately 900,000 people in the United States. In light of the impact IBD has on quality of life, costs, and disease burden, IBD-specific quality measures were adopted by the Center for Medicaid and Medicare Services Physician Quality Reporting System (PQRS) [1]. Despite these metrics, adherence has remained low in both academic and community based practices, particularly among IBD patients <50 years of age [2,3]. The aim of this study was to assess the influence of patient age and gender on adherence to quality metrics among patients with UC.

We performed a retrospective, cross-sectional study of outpatients with UC seen between January 1, 2014 and December 31, 2015. Patients with UC were identified using the International Classification of Diseases, Ninth Revision (ICD-9) codes (556.X). UC diagnosis was validated based on chart review for standard clinical, endoscopic, and histopathologic criteria. Patients were excluded if <18 years of age or underwent colectomy prior to 2014.

Our study focused on assessing adherence and predictors of adherence to eight outpatient IBD-specific PQRS quality metrics [1]:

1. Assess IBD type, anatomic location, and status of disease activity (PQRS #269)
2. Assess use of corticosteroid-sparing therapy (PQRS #270)
3. Assess bone-loss assessment for those on corticosteroids  $\geq 10$  mg/d for  $\geq 60$  days or more (PQRS #271)
4. Recommendation, administration, or documentation of receipt of influenza immunization in 2013 and 2014 (PQRS #272)
5. Recommendation, administration, or documentation of receipt of pneumococcal vaccination within past 5 years (PQRS #273)
6. Testing for latent tuberculosis before initiating anti-TNF therapy (PQRS #274)
7. Testing for hepatitis B virus before initiating anti-TNF $\alpha$  therapy (PQRS #275)
8. Assess for tobacco use within preceding year (PQRS #226)