# JNM



## Are There Any Association Between Colonic Diverticula and Bowel Symptoms?

(Neurogastroenterol Motil 2015;27:333-338)

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#### Summary

The association of constipation and colonic diverticula was a wide-spread hypothesis. But there are no previous reports showing a relationship of diverticula and their location with bowel habits. Recently, Yamada et al<sup>1</sup> suggested constipation was not associated with colonic diverticula, but on the other hand it was more prevalent in patients without diverticula than with diverticula. They evaluated the association between diverticula and bowel habits in Japanese individuals. Bowel habits and stool form were evaluated using the Gastrointestinal Symptom Rating Scale (GSRS)<sup>2</sup> and a part of the Bristol Scale with Rome III criteria, respectively. The presence of constipation was associated with a significantly reduced likelihood of diverticula (odds ratio [OR], 0.70; 95% confidence interval [CI], 0.52-0.93), especially left-sided diverticula (OR, 0.39; 95% CI, 0.16-0.93). Stool form was unrelated with the presence or absence of diverticula.

The authors concluded that the absence of diverticula was associated with constipation, suggesting the need to reassess the etiology of colonic diverticula.

#### Comments

Diverticular disease (DD) is a common entity in world-wide and its incidence is increasing. Although the pathophysiology is poorly understood, multifactorial factors such as increasing age, dietary changes, increased colonic pressure, alteration in colonic motility, and structural changes within the colon wall are considered.<sup>3,4</sup> Also, altered ENS may lead to DD in recent studies.<sup>5,6</sup> Constipation has been considered as a risk factor for the development of DD by increased intraluminal pressure. In this study, Yamada et al<sup>1</sup> revealed that constipation was less prevalent in left-sided DD. In recently, they documented a similar study that the left-sided DD was associated with diarrhea-predominant irritable bowel syndrome (D-IBS).<sup>7</sup> Both studies were cross-sectional studies, so it was impossible to know whether IBS-D was results of DD or causes of DD. In other population-based cohort study, the patients with DD and no IBS symptom were enrolled from 1988 and 1993, and then their symptoms were followed up at 2003.8 In this cohort, DD was related with IBS-D, but not with constipation/diarrhea. Based on this study, IBS-D symptoms might be developed after DD development.

Intestinal peristalsis is mediated by serotonin receptors and serotonin receptor 4 (5-HT<sub>4</sub>R) of them play an important role in

Received: March 22, 2015 Revised: March 24, 2015 Accepted: March 25, 2015

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Conflicts of interest: None.

 $\odot$  2015 The Korean Society of Neurogastroenterology and Motility

J Neurogastroenterol Motil, Vol. 21 No. 2 April, 2015 www.inmiournal.org

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Financial support: None.

gut motility. Böttner M et al<sup>9</sup> studied about 5-HT<sub>4</sub>R distribution in patients with DD. In patients with DD, 5-HT<sub>4</sub>R distribution was significantly decreased within the circular muscle and myenteric ganglia and upregulated in the mucosal region. The activation of 5-HT<sub>4</sub>R on smooth muscle cells led to muscular relaxation by inhibitory response.<sup>10</sup> On the contrary, mucosal 5-HT<sub>4</sub>R activation accelerated propulsive motility.11 Moreover, mucosal 5-HT<sub>4</sub>R regulated independently intestinal motility from directly exerted effects at the level of the enteric nervous system and smooth muscle cells. Consequentially, The alteration of 5-HT<sub>4</sub>R in both the mucosal and muscular layers resulted in complex response in patients with DD. The decreased 5-HT<sub>4</sub>R distribution in circular muscle may contribute to a loss of relaxation of smooth muscle cells and the upregulation of 5-HT4R in the mucosa may lead to increased intestinal propulsive motility in patients with DD.<sup>10,11</sup> In the previous studies, serotonin-producing cells increased in the mucosa and mucosal serotonin re-uptake transporter levels significantly decreased in patients with DD.<sup>12,13</sup> Therefore, bowel symptoms associated with increased propulsive motility may be more frequently in patients with DD than decreased motility related bowel symptoms. This finding is a possible explanation for association between constipation and the absence of diverticula, especially the left sided ones in this study. The location of DD is important because the predominant location is mainly right-sided in Asian and sigmoid colon involvement in Western population.<sup>14</sup> And the occurrence risk of DD depends on the location.<sup>15,16</sup> Therefore, it is necessary to research according to location of DD.

There are some limitations in present study. The authors used the GSRS<sup>2</sup> for evaluation of bowel habits. The GSRS included only 3 questions about constipated symptoms such as reduced frequency of evacuation, hard stools, and feeling of incomplete evacuation. For ascertaining association between DD and constipation, it may be necessary to reconsider using Rome III criteria for diagnosis of constipation. And as the authors described, the analysis should consider the number of diverticula.

Left-sided DD was more prevalent in IBS-D and less prevalent in constipation from both Yamada's cross-sectional studies.<sup>1,7</sup> And there is some explanation for these results, but bowel symptoms might be the results of having DD. We need further prospective cohort study for the causality.

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