Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 F 206.625.7245

March 17, 2023

Dear Dr. Schemmer and *World Journal of Gastrointestinal Surgery* Editorial Board,

Attached please find our revised manuscript for consideration to *World Journal of Gastrointestinal Surgery* as an invited opinion review entitled "Diverticulitis is a Population Health Problem: Lessons and Gaps in Strategies to Implement and Improve Contemporary Care" (83506). The manuscript has been improved according to the suggestions of reviewers, with all changes highlighted in the text:

Reviewer 1:

1. *"It is regrettable that the authors did not complete their analysis with a few methodological proposals to be implemented in order to progress in the analysis of the severity of acute and chronic complications. This would have laid the foundations for new updated consensus conferences to re-specify the medical and surgical therapeutic indications, why not going so far as to define reference decision-makers like other indications ranging from bariatric surgery to metastatic colorectal cancer. Indeed, an inappropriate or complicated gesture is particularly harmful for a usually benign pathology."*

   Response: We agree that the manuscript could benefit from providing specific, actionable recommendations. To address this concern, we have added the following:

   a. Our recommendations for first steps to evaluate the value of regionalization have been modified to include (page 11-12): "Given the lack of supporting data and potential challenges of regionalization, more studies should evaluate the distribution of diverticulitis care focusing beyond single

Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 F 206.625.7245

institutions and perhaps at the health system or state level. Characterizing distribution of care allows researchers to explore the association of volume and clinical outcomes in diverticulitis. If diverticulitis care is broadly distributed across institutions, this decentralized model of care has profound implications for how diverticular disease is studied and for implementation of quality improvement initiatives. This work should consider also regional practice patterns to better characterize how diverticular disease is actually treated in the general population."

b. We have added proposals for specific and actionable ways to address the challenges associated with patient-reported outcomes/QOL (page 13): "There is no consensus regarding when or how QOL should be assessed, and the timing of evaluation could change a surgeons' propensity to offer surgery. These global and disease specific QOL metrics need to be validated across a spectrum of diverticular disease patients with consideration paid to clinically meaningful changes for each metric. Consolidating these data, and providing an actionable tool for clinicians would likely require consensus and multidisciplinary agreement. As an example, the Pelvic Floor Consortium, a multidisciplinary organization that aims to enhance care of patients with pelvic floor disorders, recently modeled how to establish a combined, validated patient reported outcomes tool to standardize QOL assessments across subspecialties.[96] A consortium of colorectal surgeons, general surgeons, gastroenterologists, and primary care providers could offer similar guidance and allow for longitudinal evaluations of QOL in diverticular disease."

Reviewer 2:

Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 F 206.625.7245

In my opinion some concepts should be better explained:

1. *"The proportion of patients developing acute diverticulitis has been revised, being less than 5% over an 11-year follow-up period (see Shahedi K et al, Clin Gastroenterol Hepatol. 2013 Dec;11(12):1609-13)."*

   Response: This comment brings up an excellent point about the exact incidence of diverticulitis and we appreciate the opportunity to review additional literature. The study cited showed that the incidence of diverticulitis was low (4.3%) among a cohort of VA patients with endoscopy-confirmed diverticulosis. This study highlighted challenges of studying the natural history of diverticular disease, which is typically an asymptomatic disease. As the authors correctly point out, it is unknown whether some patients were diagnosed with diverticulitis at non-VA facilities. This citation suggests that the 10-25% risk of symptomatic disease which is commonly quoted is likely an overestimation, particularly when the baseline incidence of diverticulosis is not entirely known. To reflect this complexity, we included the above reference and revised our statement on page 3 to read: "The rate of symptomatic diverticulitis is estimated to range from <5 to 25%, though its precise incidence is controversial. Of patients with symptomatic disease, 15% will develop acute or chronic complications such as abscess, fistula, obstruction, bleeding, or perforation.[2–4]"

2. *"I'm not sure that Segmental colitis associated to diverticulosis (SCAD) could be considered a complication of diverticulitis. SCAD can be considered a separate entity, with a various clinical presentation. To my knowledge no data regarding the incidence of post diverticulitis SCAD is available."*

Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 F 206.625.7245

Response: Thank you for bringing up this point of clarification. We agree that the pathophysiology of SCAD and its relationship to diverticulitis is not well elucidated Our understanding of the literature is similar regarding SCAD's relationship to diverticulitis, and the language of the manuscript as presented does not reflect this nuance. We have updated our language surrounding this discussion (page 3): "These chronic symptoms ~~[complications]~~ can range from ongoing abdominal pain in the absence of inflammation (symptomatic uncomplicated diverticular disease, incidence: 20%) to refractory symptoms with inflammation/early recurrence (smoldering diverticulitis, incidence: 10%), and cryptogenic segmental colitis associated with diverticulosis (incidence: 1-11%).[34,35]

3. *"Regarding quality of life, it is important to underline that not only patients with previous diverticulitis presented reduction of quality of life. Some data showed that symptomatic uncomplicated diverticular disease and patients with previous diverticulitis have similar scores both concerning physical and mental components (see Carabotti M et al,. United European Gastroenterol J. 2018 Jul;6(6):926-934)."*

Response: This is an excellent point and enriches the discussion surrounding the importance and challenges of assessing QOL in diverticular disease. To the manuscript, we add this commentary to page 12: "It is important to note, however, that patients with diverticulosis and no history of diverticulitis may exhibit higher physical and mental QOL scores than patients with SUDD and a history of diverticulitis. However, differences in QOL scores were small (1-3 points) and whether these findings are clinically meaningful is not established.[94] Comparisons between studies is challenging due to a lack of standardization in assessing QOL in diverticular disease. Some studies rely on more global assessments, such as the

Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 F 206.625.7245

highly-validated and global SF-12, whereas others rely on more specific, but less broadly validated, and potentially convoluted measures, such as the diverticulitis quality of life scale (DV-QOL) .[46,68,87,88,91–95] To date, there is no consensus regarding when or how QOL impact of diverticulitis should be assessed, and whether the timing of evaluation could change a surgeons' propensity to offer surgery."

Reviewer 3:

1. *"The authors should explain more about performing Hartmann's procedure or primary anastomosis."*

Response: Thank you for the opportunity to expand upon this important element of diverticulitis care. Indeed, many CPGs recommend primary anastomosis with or without proximal diversion in stable patients, but this is not necessarily practiced in the real world. We added the following to pages 6-7 of the text: "The management of acute complicated diverticulitis has undergone a similar evolution. While emergency colectomy remains non-controversial in feculent or purulent peritonitis, the routine use of Hartmann's procedure has been increasingly challenged in the past decade. Multiple clinical trials and meta-analyses have demonstrated the safety and efficacy of sigmoid colectomy with primary anastomosis (with or without diverting ostomy) in the short- and long-term.[59–66] In the short-term, morbidity and mortality were equivalent or decreased after resection with primary anastomosis compared to Hartmann's procedure. Despite similar recurrence rates, notable differences between the procedures were seen at follow-up.[59–62,64–66] Specifically, stoma non-reversal and complication rates were

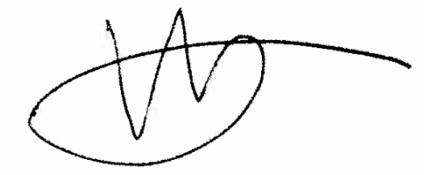
Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 F 206.625.7245

higher after reversal in patients who underwent Hartmann procedures, compared to primarily anastomosed patients.[30,59,61,63] The practical implication of these data is that anastomosis should be considered in most emergent cases, rather than defaulting to the traditional Hartmann's. This is particularly important, as Hartmann procedures are associated with a decrease in general quality of life (QOL) compared to primary anastomosis for perforated diverticulitis, and the presence of a stoma was shown to be an independent predictor of lower QOL in one study.[63,67] In the modern era, most CPGs advise against routine use of the Hartmann procedure in stable patients, favoring primary anastomosis with or without proximal diversion. However, data showing whether the practice of routine anastomosis in emergent diverticulitis has been meaningfully implemented is lacking ."

We are thankful for the opportunity to submit this revised manuscript and are appreciative of our reviewers' time and energy directed at evaluating this work.



Vlad V. Simianu, MD MPH

Section of Colon and Rectal Surgery, Virginia Mason Franciscan Health

Medical Director, Colorectal Service Line, Floyd and Delores Jones Cancer Institute

Virginia Mason Franciscan Health™

DEPARTMENT OF SURGERY
1100 Ninth Avenue, Buck Pavilion, Sixth Floor
Seattle, Washington 98101
Colon and Rectal Surgery Clinical Office

T 206.341-0060 **F** 206.625.7245

Associate Medical Director, Colorectal Surgery, Surgical Care Outcome Assessment Program

Email: vlad.simianu@commonspirit.org

Twitter: @ValSimianu