



## A Response to: Letter to the Editor Regarding [Esophageal Dysfunction and Systemic Sclerosis: Drugs Should be Kept in Mind]

Bo Li · Junqing Yan · Jincheng Pu · Jianping Tang · Shuchang Xu ·  
Xuan Wang

Received: March 25, 2022 / Accepted: April 26, 2022 / Published online: June 18, 2022  
© The Author(s) 2022

In our previously published systematic review of esophageal dysfunction in patients with SSc, we summarized the treatment options for esophageal dysfunction in patients with SSc [1]. Our analysis suggests a general strategy for this group of patients similar to patients with gastroesophageal reflux disease (GERD), and by avoiding the consumption of tobacco, alcohol, and non-steroidal anti-inflammatory drugs. It is also suggested that choices regarding hypertensive medications such as the CCB class may affect esophageal sphincter function, thus these medications should be avoided in the course of treatment.

---

B. Li · S. Xu (✉)  
Department of Gastroenterology, Tongji Institute of Digestive Disease, Tongji Hospital, School of Medicine, Tongji University, Shanghai 200065, China  
e-mail: xschang@163.com B. Li  
e-mail: 1553040libo@alumni.tongji.edu.cn

J. Yan  
Department of Surgery Medicine, Tongji Hospital, School of Medicine, Tongji University, Shanghai 200065, China  
e-mail: yanjunqing@tongji.edu.cn

J. Pu · J. Tang · X. Wang (✉)  
Department of Rheumatology and Immunology, Tongji Hospital, School of Medicine, Tongji University, Shanghai 200065, China  
e-mail: xuan2018@tongji.edu.cn J. Pu  
e-mail: 1910829@tongji.edu.cn J. Tang  
e-mail: tangjp6512@126.com

The recent letter by DB-B et al. summarizes the potential effects of drugs that are commonly used in patients with SSc on esophageal function, and provides a reference on the further selection of drug regimens. It further complements the general treatment section of our article. The investigators consider that acid reflux due to esophageal complications in patients with systemic sclerosis may cause the development of Barrett's esophagus or even esophageal adenocarcinoma. Therefore, careful selection of SSc therapeutic agents to reduce their impact on esophageal function needs to be a matter of caution for clinicians.

However, regardless of the proportion of patients with SSc esophageal dysfunction in the GERD population, only 10–15% of GERD patients develop Barrett's esophagus in the future, and there is a clear correlation between the duration of symptoms and the development of BE [2, 3]. The survival time for SSc patients is unfortunately short, with a cumulative survival rate of 74.9% at 5 years and 62.5% at 10 years after diagnosis [4]. Also, the survival time of SSc patients does not yet support the progression of patients with reflux symptoms to Barrett's esophagus or even esophageal adenocarcinoma. Even though Barrett's esophagus is a known precursor to the development of esophageal adenocarcinoma, only a minority of patients with Barrett's esophagus have an estimated risk of developing esophageal adenocarcinoma of

only 0.1–0.5% [5]. Eventually, SSc patients die from esophageal dysfunction due to malnutrition, aspiration, or acute gastrointestinal complications (e.g., mechanical or pseudo-obstruction), and rarely from esophageal adenocarcinoma [6]. Therefore, it is even more important to intensify the motivational and acid suppression therapy in these patients.

Injury from PDE-5 inhibitors, bisphosphonates, nitrates, benzodiazepines, and antidepressants affects esophageal function [7–9]. The functional severity of esophageal damage caused by the above drugs in patients with systemic sclerosis has not waited for definitive data. However, the severity of mycophenolate ester-related gastrointestinal adverse events are insufficient to exclude their use, which is supported by relevant studies [10]. Therefore, further studies are needed to clarify the degree of functional impairment of the esophagus caused by the drugs mentioned above. In addition to the drugs that may affect esophageal function, anti-inflammatory drugs (steroids) are also thought to increase the risk of tumor development in patients. However, Fortuny J. et al. showed that these steroids do not influence the incidence of esophageal cancer or gastric cancer [11]. Meanwhile, prednisone has shown the potential to improve esophageal dysfunction in other diseases [12, 13]. This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

## ACKNOWLEDGEMENTS

**Funding.** No funding was received for the publication of this article.

**Authorship.** All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

**Author Contribution.** All authors have made substantial contributions to this work. Please see the specific contribution of each author as following. Authors' contributions: Bo Li and Xuan Wang conducted the research and wrote this manuscript. Shuchang Xu designed the idea of the article. Junqing Yan and Jincheng Pu collected relevant data. Jianping Tang has embellished and revised the article. This article has been reviewed and revised by all members.

**Disclosures.** Bo Li, Xuan Wang, Shuchang Xu, Junqing Yan, Jincheng Pu, Jianping Tang declare that they have nothing to disclose.

**Compliance with Ethics Guidelines.** This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

**Open Access.** This article is licensed under a Creative Commons Attribution-Non-Commercial 4.0 International License, which permits any non-commercial use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by-nc/4.0/>.

## REFERENCES

1. Li B, et al. Esophageal dysfunction in systemic sclerosis: an update. *Rheumatol Ther*. 2021;8(4): 1535–49.

2. Schlottmann F, Patti MG, Shaheen NJ. From heartburn to Barrett's esophagus, and beyond. *World J Surg.* 2017;41(7):1698–704.
3. Schlottmann F, Molena D, Patti MG. Gastroesophageal reflux and Barrett's esophagus: a pathway to esophageal adenocarcinoma. *Updates Surg.* 2018;70(3):339–42.
4. Rubio-Rivas M, et al. Mortality and survival in systemic sclerosis: systematic review and meta-analysis. *Semin Arthritis Rheum.* 2014;44(2):208–19.
5. Runge TM, Abrams JA, Shaheen NJ. Epidemiology of Barrett's esophagus and esophageal adenocarcinoma. *Gastroenterol Clin North Am.* 2015;44(2):203–31.
6. Shreiner AB, et al. Gastrointestinal manifestations of systemic sclerosis. *J Scleroderma Relat Disord.* 2016;1(3):247–56.
7. Wong MW, et al. Influence of sildenafil on esophageal motor function in humans: studies using high-resolution manometry. *Neurogastroenterol Motil.* 2020;32(7): e13840.
8. Tutuian R. Adverse effects of drugs on the esophagus. *Best Pract Res Clin Gastroenterol.* 2010;24(2):91–7.
9. Mungan Z, Pınarbaşı Şimşek B. Which drugs are risk factors for the development of gastroesophageal reflux disease? *Turk J Gastroenterol.* 2017;28: S38–43.
10. Omair MA, Alahmadi A, Johnson SR. Safety and effectiveness of mycophenolate in systemic sclerosis. A systematic review. *PLoS One.* 2015;10(5): e0124205.
11. Fortuny J, et al. Use of anti-inflammatory drugs and lower esophageal sphincter-relaxing drugs and risk of esophageal and gastric cancers. *Clin Gastroenterol Hepatol.* 2007;5(10):1154–1159.e3.
12. Chu Y, et al. Long-term efficacy and safety of intralesional steroid injection plus oral steroid administration in preventing stricture after endoscopic submucosal dissection for esophageal epithelial neoplasms. *Surg Endosc.* 2019;33(4): 1244–51.
13. Nennstiel S, et al. High-resolution manometry in patients with eosinophilic esophagitis under topical steroid therapy—a prospective observational study (HIMEOS-study). *Neurogastroenterol Motil.* 2016;28(4):599–607.