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The primary aim of World Journal of Gastrointestinal Oncology (WJGO, World J Gastrointest Oncol) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, etc.

INDEXING/ABSTRACTING
The WJGO is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 edition of Journal Citation Reports® cites the 2021 impact factor (IF) for WJGO as 3.404; IF without journal self cites: 3.250; Journal Citation Indicator: 0.53; Ranking: 162 among 245 journals in oncology; Quartile category: Q3; Ranking: 59 among 93 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO’s CiteScore for 2021 is 3.6 and Scopus CiteScore rank 2021: Gastroenterology is 72/149; Oncology is 203/360.

RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Xiang-Di Zhang; Production Department Director: Xiang Li; Editorial Office Director: Jia-Ru Fan.

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS

PUBLICATION DATE
February 15, 2023

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ONLINE SUBMISSION
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Comment on “Crosstalk between gut microbiota and COVID-19 impacts pancreatic cancer progression”

Jian Yang, Ying Liu, Shi Liu

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report’s scientific quality classification
Grade A (Excellent): A
Grade B (Very good): B
Grade C (Good): 0
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Mahmoud MZ, Saudi Arabia; Masyeni S, Indonesia

Received: November 19, 2022
Peer-review started: November 19, 2022
First decision: December 25, 2022
Revised: January 3, 2023
Accepted: February 2, 2023
Article in press: February 2, 2023
Published online: February 15, 2023

Abstract
The coronavirus disease 2019 (COVID-19) pandemic has become a global burden, further exacerbating the occurrence of risk events in cancer patients. The high risk of death from pancreatic cancer makes it one of the most lethal malignancies. Recently, it was reported in the World Journal of Gastrointestinal Oncology that COVID-19 influences pancreatic cancer progression via the lung–gut–pancreatic axis, and the authors provided insights into the intrinsic crosstalk mechanisms in which the gut microbiota is involved, the characteristics and effects of inflammatory factors, and immunotherapeutic strategies for treating both diseases. Here, we review the latest cutting-edge researches in the field of the lung-gut-pancreatic axis and discuss future perspectives to address the severe survival challenges posed by the COVID-19 pandemic in patients with pancreatic cancer.

Key Words: COVID-19; Pancreatic cancer; Lung–gut–pancreatic axis; Gut microbiota; Inflammatory factors; Immunotherapeutic

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Core Tip: The coronavirus disease 2019 (COVID-19) pandemic has become a global burden, further exacerbating the occurrence of mortality risk events in patients with pancreatic cancer. The aim of this new article is to highlight the need for lung-gut-pancreatic axis-based studies with a focus on intra-axis microbiota crosstalk and potential mechanisms of association to address the severe survival challenges posed by the COVID-19 pandemic in patients with pancreatic cancer.
The coronavirus disease 2019 (COVID-19) pandemic has become a global burden, further exacerbating the occurrence of risk events in patients with cancer[1,2]. Contracting COVID-19 significantly increases the risk of morbidity, mortality, and ICU admission in patients with cancer[3]. Additionally, cancer patients have a 60% increased risk of contracting COVID-19 compared with patients without cancer[4]. Owing to the worsening disease and poorer prognosis resulting from COVID-19 in patients with cancer, this patient group is considered a high-risk vulnerable population[5]. The high risk of death from pancreatic cancer makes it one of the most lethal malignancies[6], and the COVID-19 pandemic not only poses a survival challenge for patients with pancreatic cancer but also seriously threatens the execution of pancreatic cancer research[7]. We are very interested in the review by Zhang et al[8] published in the August 2022 issue of the *World Journal of Gastrointestinal Oncology*. We consider it to be a good quality review because the authors included in their article many articles from international high-quality journals, such as *Lancet, JAMA, Nature,* and *Cell,* and the article conclusions accurately and clearly summarize the findings of the included literature. From the 98 literature reviews included by the authors, they identified a key connector between COVID-19 and pancreatic cancer; that is, the gut microbiota regulates the host systemic immune response. The question highlighted by Zhang et al[8] is how COVID-19 affects pancreatic cancer progression, *i.e.*, via the lung–gut–pancreatic axis, and the authors explained the physiological basis, relevance, and potential biological mechanisms of targeting this axis. The novelty of the article is that, the authors highlight therapeutic perspectives in response to COVID-19 and pancreatic cancer based on the intrinsically linked mechanisms of the lung-gut-pancreatic axis, including dietary interventions to stabilize the endostasis of the intestinal flora, the therapeutic efficacy of pharmacological interventions, and strategies to manage inflammatory storms. We thank Zhang et al[8] for their review, which has been instrumental in exploring pancreatic cancer treatment options and the development of risk event prevention programs in the context of the severe challenges of the COVID-19 pandemic.

Regional citrate anticoagulation (RCA) is an artificial intelligence technology-based open multidisciplinary citation analysis database. We searched the RCA database for articles in cutting-edge fields in the last 2 years using the search terms “COVID-19”, “pancreatic cancer”, and “gut microbiota”. In addition to highlighting that the gut microbiota regulates immune and inflammatory responses to influence disease severity in COVID-19 and pancreatic cancer[9,10], recent studies have revealed a complex intrinsic association between the three. Current studies indicate that the microbiota alters the malignant phenotype and prognosis of pancreatic cancer in ways that include stimulating persistent inflammation, altering the tumor microenvironment, modulating the anti-tumor immune system, and affecting cellular metabolism[11]. The emerging link between the gut microbiota and pancreatic cancer has recently highlighted the concept of local (direct pancreatic effects) and remote (non-pancreatic) effects of bacteria on organ physiology, which offers potential therapeutic options for pancreatic cancer[12]. However, research on the microbiota influencing pancreatic cancer progression has focused mainly on bacteria, and studies involving intestinal fungi and viruses are just starting to be published[12]. Future work on how these gut microbes are intrinsically linked and on the exact mechanisms by which they influence pancreatic cancer progression is needed. The latest cutting-edge research has bridged the gap between COVID-19 and the gut microbiota, discovering mechanisms that link the gut microbiota to the expression of the viral entry receptor angiotensin-converting enzyme 2 (ACE2)[13], the inflammatory response[14], the immune homeostasis[15], the microbiota metabolism[16], and the “gut–lung axis”[17]. In COVID-19, the main factor associated with disease severity is the involvement of a cytokine storm in the immune response, *i.e.*, tissue damage and systemic inflammation[13]. The gut microbiota may influence the severity of COVID-19 by regulating the host immune response[18]. However, it is unclear whether the reported gut microbial changes are directly responsible for the inflammatory storm in patients with COVID-19 or if they represent the result of severe disease[19], and future studies investigating these possibilities are pending. Zhang et al[8] reported that the inflammation-induced immune response is an intrinsic mechanism through which the lung–gut–pancreatic axis produces crosstalk between COVID-19 and pancreatic cancer. On the basis of this mechanism, the authors proposed some strategies on how to manage COVID-19 and pancreatic cancer, including the regulation of microbiota homeostasis to improve patient immunity and the application of anti-inflammatory drugs to reduce the amount of inflammatory damage[8]. However, the survival outcomes of applying these strategies for treating COVID-19 and pancreatic cancer co-morbidity and the effectiveness of such strategies during radiotherapy are not yet known. Future studies could focus on these issues. In conclusion, COVID-19 impacts pancreatic cancer progression based on lung–gut–pancreatic axis, nevertheless, more studies
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investigating the potential mechanisms of the crosstalk between COVID-19, pancreatic cancer and gut microbiota are needed in patients with COVID-19 and pancreatic cancer co-morbidity to achieve a better management. Focusing on the lung-gut-pancreatic axis is expected to move us into a new paradigm of treatment for COVID-19 in patients with pancreatic cancer.

FOOTNOTES

Author contributions: Yang J designed and wrote this report; Liu S gave guidance on article revision; Liu Y reviewed the literature and contributed to drafting the manuscript; all authors issued final approval for the version to be submitted.

Conflict-of-interest statement: All the authors report no relevant conflicts of interest for this article.

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