

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2023 December 15; 15(12): 2049-2241



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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 Science and Technology Journal Database, and Superstar Journals Database. The 2023 edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJGO as 3.0; IF without journal self cites: 2.9; 5-year IF: 3.0; Journal Citation Indicator: 0.49; Ranking: 157 among 241 journals in oncology; Quartile category: Q3; Ranking: 58 among 93 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO's CiteScore for 2022 is 4.1 and Scopus CiteScore rank 2022: Gastroenterology is 71/149; Oncology is 197/366.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Xiang-Di Zhang; Production Department Director: Xu Guo; 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

<https://www.wjgnet.com/1948-5204/editorialboard.htm>

PUBLICATION DATE

December 15, 2023

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<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Dual primary gastric and colorectal cancer: A complex challenge in surgical oncology

Luigi Marano

Specialty type: Oncology

Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): A

Grade B (Very good): 0

Grade C (Good): C

Grade D (Fair): 0

Grade E (Poor): 0

P-Reviewer: Liu Z, China; Wan XH, China

Received: October 17, 2023

Peer-review started: October 17, 2023

First decision: November 1, 2023

Revised: November 1, 2023

Accepted: November 17, 2023

Article in press: November 17, 2023

Published online: December 15, 2023



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Abstract

The intricate interplay of colorectal cancer (CRC) and gastric cancer (GC) as dual primary malignancies presents a significant challenge in surgical oncology. CRC is the most common secondary malignancy in GC patients, and vice versa, evidence highlighted by advances in diagnostic procedures and therapy modalities that impact patient survival. A recent study titled "Features of synchronous and metachronous dual primary gastric and colorectal cancer" explores this enigmatic dual malignancy, uncovering crucial insights into the clinical characteristics and prognostic distinctions between synchronous and metachronous presentations. Notably, metachronous cases with a second primary cancer discovered more than six months after the first diagnosis have a better outcome, emphasizing the importance of early detection and treatment. This study underscores the prognostic role of GC stage in patient outcomes. It also sheds light on the complexities faced by synchronous cases, often presenting with unresectable CRC. Surgery-related procedures, like gastrectomy and colon resection, stand out as important predictors of increased survival, necessitating a reevaluation of current therapeutic approaches. A tailored and patient-centered strategy, considering the health of each patient individually and the feasibility of radical treatments, is essential. Continuous follow-up and monitoring are crucial as most second primary cancers arise within five years. In conclusion, early diagnosis, surgical intervention, and watchful surveillance are pivotal in managing dual primary gastric and colorectal cancer patients. Since the incidence of gastric and colorectal cancers continues to rise, the imperative need for further research, ideally with larger sample sizes, becomes evident in our pursuit of comprehensive insights that will refine clinical approaches for this intricate dual malignancy.

Key Words: Multiple primary cancers; Colorectal cancer; Gastric cancer; Dual primary cancers; Synchronous cancers; Metachronous cancers

Core Tip: This editorial explores the complex landscape of dual primary gastric and colorectal cancer (DPGCC), investigating synchronous and metachronous cases. It uncovers a clear prognostic gap, emphasizing the need of early detection. The research underlines the pivotal role of surgical interventions, with gastric cancer stage significantly impacting patient outcomes. It also highlights the need for regular follow-up due to the majority of second primary cancers occurring within five years. The current literature provides guidance for individualized therapeutic approaches, enhancing patient prognoses, and underscores the intricate and multifaceted character of managing DPGCC.

Citation: Marano L. Dual primary gastric and colorectal cancer: A complex challenge in surgical oncology. *World J Gastrointest Oncol* 2023; 15(12): 2049-2052

URL: <https://www.wjgnet.com/1948-5204/full/v15/i12/2049.htm>

DOI: <https://dx.doi.org/10.4251/wjgo.v15.i12.2049>

INTRODUCTION

The intersection of colorectal cancer (CRC) and gastric cancer (GC) as dual primary cancers presents a significant challenge in surgical oncology[1]. CRC, with an incidence of 11.4%, ranks among the most frequent tumors associated with multiple primary cancers[2], while GC can evolve into a second primary cancer, with an incidence ranging from 1% to 4.2% in GC patients[3-5]. The intricate relationship between these malignancies is bidirectional, with CRC being the most common second primary cancer in GC patients, and GC the most common second primary cancer in CRC patients [6-8]. Advances in diagnostic techniques and treatment modalities leading to extended patient survival will likely increase the detection and incidence of multiple primary cancers. This necessitates a comprehensive approach to the evaluation and management of dual primary gastric and CC (DPGCC). A recent study by Lin *et al*[9], titled "Features of synchronous and metachronous dual primary gastric and colorectal cancer", addresses this complex aspect of surgical oncology, providing valuable insights into the clinical characteristics and prognosis of DPGCC patients. Notably, the study reveals a distinct difference in prognosis between synchronous and metachronous DPGCCs. Patients with metachronous DPGCC exhibited a more favorable prognosis, underlining the significance of early diagnosis and intervention. The study also highlights the high rate of unresectable CC in synchronous DPGCC patients, emphasizing the complexity of managing this dual malignancy. Additionally, it underscores the critical influence of GC stage on patient outcomes, with stage III-IV patients experiencing a considerably worse prognosis. Surgical interventions, such as gastrectomy and colorectal resection, significantly improved survival rates. Regular follow-up and surveillance emerged as crucial components, with the majority of second primary cancers in DPGCC cases occurring within five years. The study's findings have important implications for tailoring treatment strategies and improving patient outcomes in DPGCC.

SYNCHRONOUS VS METACHRONOUS DPGCC: A PROGNOSTIC GAP

The theory of the etiologic field effect, frequently invoked in the field of multiple primary cancers, offers valuable insights into the pathogenesis and evolution of DPGCC[10]. This theoretical framework postulates that the epithelium of the gastrointestinal tract is subjected to a dynamic interplay of genetic and environmental variables, which increases the tendency for carcinogenesis. Both the stomach and the colorectum are equally sensitive to these factors' effect because they are both essential parts of the continuous mucosal epithelium lining the digestive tract, exposing patients to synchronous or metachronous carcinogenesis. Empirical research confirms a detectable relationship between the initial primary cancer and the second primary cancer in patients with multiple primary neoplasms, highlighting the intricate multifactorial etiology of DPGCC[11-13]. This enriches our understanding of the intricate dynamics at play in the DPGCC landscape, shedding light on the relationships governing its occurrence. Importantly, the study's primary finding, that patients with metachronous DPGCC exhibit a more favorable prognosis compared to synchronous cases, is consistent with previous studies on multiple primary cancers' prognosis[14-16]. This observation underscores the need for tailored treatment strategies and watchful surveillance for patients with synchronous DPGCC, further illuminating the factors influencing this gap in prognosis and refining our approach to managing these challenging cases.

RESECTION AS A PROGNOSTIC KEY FACTOR

The study emphasizes the central role of clinicopathologic characteristics of DPGCC and the inclusion of therapeutic factors in the prognostic analysis[16]. Gastrectomy and colorectal resection were associated with better prognosis, highlighting the importance of early diagnosis and surgical intervention. The identification of GC resection as an

independent predictor of overall survival aligns with the benefits of surgical intervention in GC[17]. This underscores the value of radical surgery in synchronous DPGCC cases, encouraging a reconsideration of treatment strategies and the need for improved diagnostic and therapeutic approaches for this specific dual malignancy.

On the other hand, the research also highlights the high rate of unresectable CC in synchronous DPGCC patients as well as the significant impact of GC stage on patient prognosis, underscoring the importance of early detection and further investigation to identify contributing factors. It is essential to emphasize that the treatment approach for DPGCC remains challenging and multifaceted, requiring individualized evaluation and consideration of patient health and the feasibility of perioperative multidisciplinary treatments associated with radical surgeries.

INTENSIVE FOLLOW-UP: A KEY ISSUE

Early diagnosis and timely intervention are essential in the clinical management of DPGCC[14]. The research demonstrates that most second primary cancers in DPGCC cases occur within five years, highlighting the importance of intensive surveillance and follow-up for patients with gastric or CC. Postoperative monitoring of the entire digestive tract is essential, and patients who have extensive resections might need protracted monitoring, underlining the importance of thorough, long-term follow-up to achieve the best outcomes.

CONCLUSION

In conclusion, early diagnosis, surgical resection, and watchful follow-up are essential for managing DPGCC patients. The current literature conclusions call for a reevaluation of therapeutic approaches, particularly in synchronous cases when radical surgery may hold the key to improved outcomes. Furthermore, economic considerations should also be explored to determine the cost-benefit ratio of surveillance strategies. As the incidence of gastric and colorectal cancers continues to rise, the insights derived from this research, as well as the current body of literature, will steer us toward more effective treatment and follow-up strategies for DPGCC. Further research, ideally with larger sample sizes, is imperative to corroborate and expand upon these findings, thereby offering a more comprehensive understanding of DPGCC and guiding more effective clinical approaches in the future.

FOOTNOTES

Author contributions: Marano L designed the overall concept and outline of the manuscript, wrote and edited the manuscript and review of literature.

Conflict-of-interest statement: The author reports no relevant conflicts of interest for this article.

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S-Editor: Wang JJ

L-Editor: A

P-Editor: Zhang XD

REFERENCES

1. Vogt A, Schmid S, Heinimann K, Frick H, Herrmann C, Cerny T, Omlin A. Multiple primary tumours: challenges and approaches, a review. *ESMO Open* 2017; **2**: e000172 [PMID: 28761745 DOI: 10.1136/esmoopen-2017-000172]
2. Tanjak P, Sukitipat B, Vorasan N, Juengwiwattanakit P, Thientrong B, Songjang C, Therasakvichya S, Laiteerapong S, Chinswangwatanakul V. Risks and cancer associations of metachronous and synchronous multiple primary cancers: a 25-year retrospective study. *BMC Cancer* 2021; **21**: 1045 [PMID: 34556087 DOI: 10.1186/s12885-021-08766-9]
3. Ikeda Y, Saku M, Kawanaka H, Nonaka M, Yoshida K. Features of second primary cancer in patients with gastric cancer. *Oncology* 2003; **65**: 113-117 [PMID: 12931016 DOI: 10.1159/000072335]
4. Eom BW, Lee HJ, Yoo MW, Cho JJ, Kim WH, Yang HK, Lee KU. Synchronous and metachronous cancers in patients with gastric cancer. *J Surg Oncol* 2008; **98**: 106-110 [PMID: 18452218 DOI: 10.1002/jso.21027]
5. Ha TK, An JY, Youn HG, Noh JH, Sohn TS, Kim S. Surgical outcome of synchronous second primary cancer in patients with gastric cancer.

- Yonsei Med J* 2007; **48**: 981-987 [PMID: [18159590](#) DOI: [10.3349/ymj.2007.48.6.981](#)]
- 6 **Lee JH**, Bae JS, Ryu KW, Lee JS, Park SR, Kim CG, Kook MC, Choi IJ, Kim YW, Park JG, Bae JM. Gastric cancer patients at high-risk of having synchronous cancer. *World J Gastroenterol* 2006; **12**: 2588-2592 [PMID: [16688807](#) DOI: [10.3748/wjg.v12.i16.2588](#)]
- 7 **Lim SB**, Jeong SY, Choi HS, Sohn DK, Hong CW, Jung KH, Chang HJ, Park JG, Choi IJ, Kim CG. Synchronous gastric cancer in primary sporadic colorectal cancer patients in Korea. *Int J Colorectal Dis* 2008; **23**: 61-65 [PMID: [17724601](#) DOI: [10.1007/s00384-007-0366-z](#)]
- 8 **Yoon SN**, Oh ST, Lim SB, Kim TW, Kim JH, Yu CS, Kim JC. Clinicopathologic characteristics of colorectal cancer patients with synchronous and metachronous gastric cancer. *World J Surg* 2010; **34**: 2168-2176 [PMID: [20532772](#) DOI: [10.1007/s00268-010-0623-0](#)]
- 9 **Lin YJ**, Chen HX, Zhang FX, Hu XS, Cheng YZ, Peng JS, Lian L. Features of synchronous and metachronous dual primary gastric and colorectal cancer. *World J Gastrointest Oncol* 2023; **15**: 1864-1873 [DOI: [10.4251/wjgo.v15.i11.1864](#)]
- 10 **Lochhead P**, Chan AT, Nishihara R, Fuchs CS, Beck AH, Giovannucci E, Ogino S. Etiologic field effect: reappraisal of the field effect concept in cancer predisposition and progression. *Mod Pathol* 2015; **28**: 14-29 [PMID: [24925058](#) DOI: [10.1038/modpathol.2014.81](#)]
- 11 **Samowitz WS**, Albertsen H, Sweeney C, Herrick J, Caan BJ, Anderson KE, Wolff RK, Slattery ML. Association of smoking, CpG island methylator phenotype, and V600E BRAF mutations in colon cancer. *J Natl Cancer Inst* 2006; **98**: 1731-1738 [PMID: [17148775](#) DOI: [10.1093/jnci/djj468](#)]
- 12 **Toyomura K**, Yamaguchi K, Kawamoto H, Tabata S, Shimizu E, Mineshita M, Ogawa S, Lee KY, Kono S. Relation of cigarette smoking and alcohol use to colorectal adenomas by subsite: the self-defense forces health study. *Cancer Sci* 2004; **95**: 72-76 [PMID: [14720330](#) DOI: [10.1111/j.1349-7006.2004.tb03173.x](#)]
- 13 **Leggett BA**, Worthley DL. Synchronous colorectal cancer: not just bad luck? *Gastroenterology* 2009; **137**: 1559-1562 [PMID: [19789087](#) DOI: [10.1053/j.gastro.2009.09.025](#)]
- 14 **Park JH**, Baek JH, Yang JY, Lee WS, Lee WK. Clinicopathologic characteristics and survival rate in patients with synchronous or metachronous double primary colorectal and gastric cancer. *Korean J Clin Oncol* 2018; **14**: 83-88 [DOI: [10.14216/kjco.18015](#)]
- 15 **Ueno M**, Muto T, Oya M, Ota H, Azekura K, Yamaguchi T. Multiple primary cancer: an experience at the Cancer Institute Hospital with special reference to colorectal cancer. *Int J Clin Oncol* 2003; **8**: 162-167 [PMID: [12851840](#) DOI: [10.1007/s10147-003-0322-z](#)]
- 16 **Watanabe M**, Kochi M, Fujii M, Kaiga T, Mihara Y, Funada T, Tamegai H, Shimizu H, Takayama T. Dual primary gastric and colorectal cancer: is the prognosis better for synchronous or metachronous? *Am J Clin Oncol* 2012; **35**: 407-410 [PMID: [21659834](#) DOI: [10.1097/COC.0b013e318218585a](#)]
- 17 **Wu J**, Yu J, Chen Z, Zhu H, Zhong C, Liang Y, Mai Z, Lin Z, Wan Y, Li G. Survival benefit of primary tumor resection for gastric cancer with liver metastasis: A propensity score-matched, population-based study. *Front Oncol* 2022; **12**: 1039086 [PMID: [36465378](#) DOI: [10.3389/fonc.2022.1039086](#)]



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