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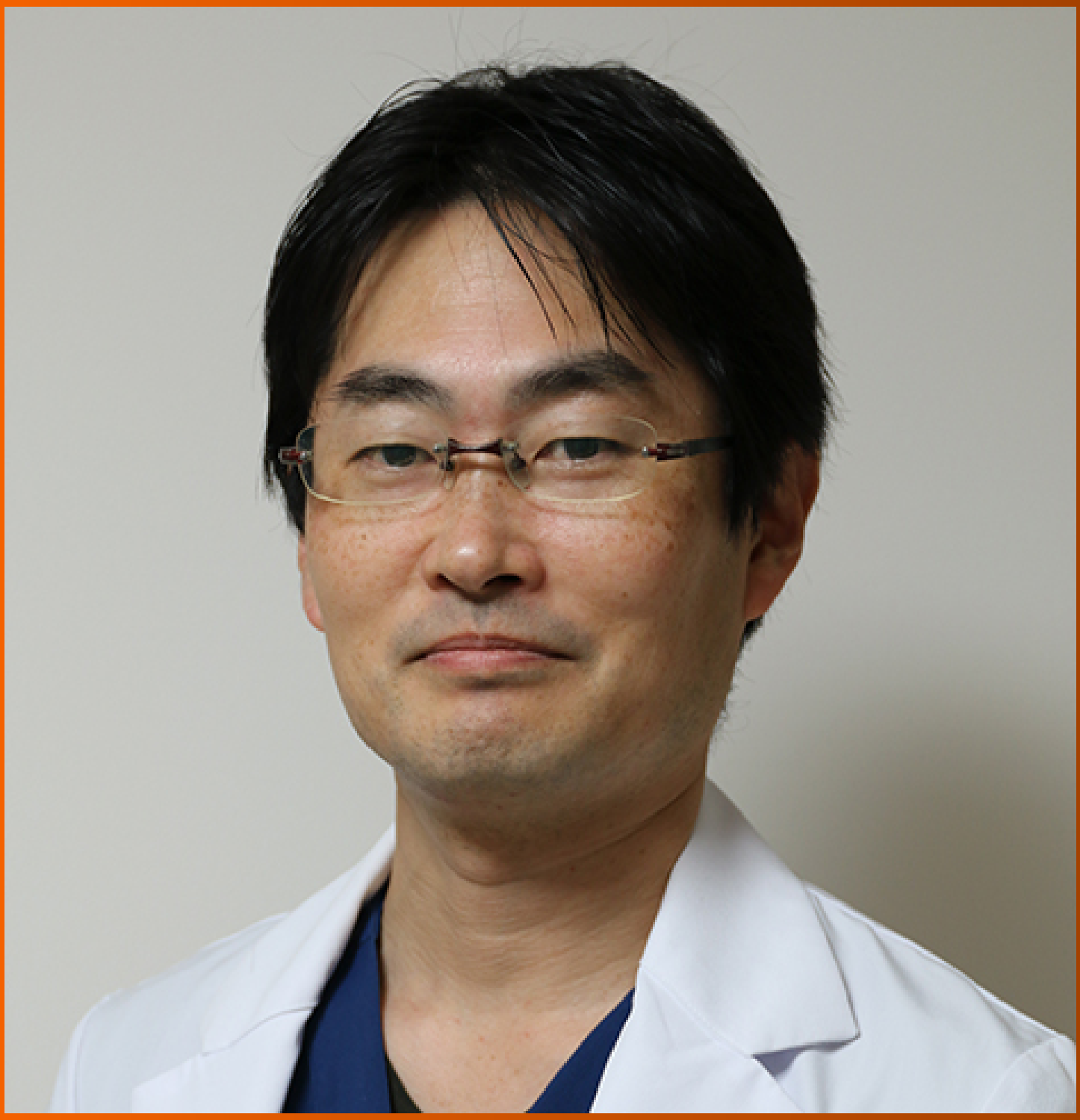

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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms,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

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EDITORIAL

Cardiotoxicity induced by fluoropyrimidine drugs in the treatment of gastrointestinal tumors

Mo-Wei Kong, Feng-Di Sun, Zhen-Ying Pei, Li Xu, Ze-Bi Wang, Yan Chen, Shu-Qing Tang, Ting-Fang Yang, Guo-Xiang He

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Abstract

In this editorial, we review the article published in *World J Gastrointest Oncol* 2019, 11: 1031-1042. We specifically focus on the occurrence, clinical characteristics, and risk factors of fluoropyrimidine drug-related cardiotoxicity in patients with gastrointestinal tumors. Despite significant advancements in diagnostic and therapeutic techniques that have reduced mortality rates associated with digestive system tumors, the incidence and mortality rates of treatment-related cardiotoxicity have been increasing, severely impacting the survival and prognosis of cancer patients. Fluoropyrimidine drugs are widely used as antimetabolites in the treatment of malignant tumors, including gastrointestinal tumors, and they represent the second largest class of drugs associated with cardiotoxicity. However, there is often a lack of awareness or understanding regarding their cardiotoxic effects and associated risks.

Key Words: Cardiotoxicity; Gastrointestinal tumors; Risk factors; Fluoropyrimidine; Chest pain

Core Tip: This editorial focuses on the occurrence, clinical characteristics, and risk factors of fluoropyrimidine drug-related cardiotoxicity in patients with gastrointestinal tumors. Despite advancements in diagnostic and therapeutic techniques for digestive system tumors, treatment-related cardiotoxicity rates have been increasing, impacting the survival and prognosis of cancer patients. Fluoropyrimidine drugs, widely used in treating malignant tumors, including gastrointestinal tumors, are the second largest class of drugs associated with cardiotoxicity. However, there is often a lack of awareness or understanding regarding their cardiotoxic effects and associated risks.

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INTRODUCTION

Chemotherapy based on fluoropyrimidine drugs can improve the quality of life (QOL) and survival time of patients with gastrointestinal tumors[1]. Regrettably, a substantial number of patients endure various levels of cardiac damage during or following fluoropyrimidine chemotherapy, occasionally resulting in permanent harm. This not only drastically impairs patients' QOL, but also places their lives at risk[2]. Hence, it is imperative to precisely gauge the prevalence of fluoropyrimidine-induced cardiac toxicity (FIC) and pinpoint predisposing factors. This will help identify the population at high risk of developing FIC and guide the safe administration of medication. However, due to the absence of a universally accepted definition and diagnostic criteria for FIC, coupled with imprecise data on its incidence and correlation with risk factors, the estimation of FIC is often either over or under-calculated. In this editorial, we review the article by Lam *et al*[3] published in *World J Gastrointest Oncol* 2019, 11: 1031-1042[3].

SYMPTOMS, INCIDENCE, AND ELECTROCARDIOGRAM MANIFESTATIONS

Recent studies have found that the clinical manifestations of cardiac toxicity associated with 5-fluorouracil (5-FU) and Capecitabine are similar[4]. The most common symptoms are chest pain or angina, with an incidence rate of about 2.27%, often accompanied by ischemic electrocardiogram (ECG) changes[5]. Other relatively common symptoms include dyspnea (0.89%), palpitations (0.64%), and hypertension (0.04%)[6]. A small number of patients have experienced severe cardiac adverse events such as heart failure (0.39%), myocardial infarction, cardiogenic shock, cardiac arrest, and sudden death[7]. Fortunately, these severe cardiac events are not common, and deaths due to cardiac toxicity are rare.

Fluorouracil can also affect the conduction of cardiac signals, leading to significant prolongation of the PR interval, P wave duration, and QT interval, resulting in various arrhythmias[8]. Common arrhythmias include atrial fibrillation, ventricular fibrillation, premature ventricular contractions, and atrioventricular block[9]. Although these ECG manifestations are often detected when symptoms occur during fluorouracil treatment, other causes need to be ruled out, such as pre-existing or current atherosclerotic heart disease, hypertensive heart disease, and rheumatic heart disease, various myocarditis, endocarditis, myocardial or pericardial tumor infiltration, past or current radiation therapy, and other drugs and biological agents with cardiac toxicity[10]. Therefore, only ECG abnormalities that occur during fluorouracil treatment and are new, and other causes have been ruled out, can be considered as ECG abnormalities induced by fluorouracil.

INCIDENCE AND MONITORING

It must be noted that during chemotherapy based on fluorouracil, some patients only show transient ECG abnormalities and may be asymptomatic. In the study by Südhoff *et al*[11], these asymptomatic ECG abnormalities occurred in 6.45% of single ECG collections. Dynamic ECG monitoring by Rezkalla *et al*[12] found that asymptomatic ST-segment elevation could reach 64%. FIC or ECG abnormalities usually occur within the first 72 h of initial treatment with fluoropyrimidine drugs, but a few patients may experience FIC at any time thereafter. In addition, research by Kosmas *et al*[13] showed that most patients with newly occurring symptomatic FIC will have ischemic ECG changes, which disappear with the disappearance of symptoms. Talapatra *et al*[14] reported transient asymptomatic bradycardia during continuous infusion of 5-FU. This suggests that we should closely monitor patients' ECG changes, especially dynamic ECG monitoring can detect more FIC, even subclinical FIC, otherwise the incidence of FIC may be underestimated, because some patients will have transient cardiac toxicity (including symptoms and/or ECG abnormalities).

For patients with gastrointestinal tumors, the incidence of cardiac toxicity related to fluoropyrimidine drugs is about 4.28%, the incidence of severe cardiac adverse events is about 0.45%, and the mortality rate related to cardiac toxicity is about 0.39%[15,16]. The most common symptom of cardiac toxicity is chest pain/angina, followed by dyspnea, palpitations, hypertension, *etc*. The incidence of new ECG abnormalities is about 3.12%, and the incidence of ECG abnormalities

in symptomatic patients is about 2.49%[15]. Some patients may experience transient FIC and/or asymptomatic FIC. Arrhythmias and ischemic changes are the most common ECG changes.

CONCLUSION

We hope that this editorial can raise awareness of the cardiac toxicity associated with fluoropyrimidine drugs and its harm, identify high-risk groups prone to FIC, and ensure the safe use of drugs in patients with gastrointestinal tumors.

FOOTNOTES

Author contributions: He GX and Yang TF provided crucial suggestions and guidance for the writing; Kong MW wrote the manuscript; Chen Y, Sun FD, Pei ZY, Wang ZB and Tang SQ reviewed and revised the manuscript; all authors read and approved the final manuscript.

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