

# Diagnostic Value of 64-Slice Spiral CT Combined with Serum Tumor Markers in Lymph Node and Distant Metastasis of Gastric Cancer

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**Background:** Preoperative staging is of great significance in determining treatment strategies and outcome evaluation. This study aims to investigate the diagnostic value of 64-slice spiral computed tomography (CT) in combination with serum tumor markers for lymph nodes and distant metastasis in gastric cancer.

**Methods:** We retrospectively analyzed the clinical data of 124 gastric cancer patients who underwent surgical treatment between April 2015 and April 2020. Based on the occurrence of lymph nodes and distant metastasis, the differences in CT examination results and tumor markers such as carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), and CA125 were compared.

**Results:** The serum CEA and CA199 levels and the rate of positive lymph node identified through CT were significantly lower in the N0 group compared to the N1-3 group ( $p < 0.05$ ). Similarly, the serum CEA, CA125 levels, and the rate of the positive lymph node were significantly lower in the M0 group than those in the M1 group ( $p < 0.05$ ). Additionally, in diagnosing preoperative lymph node metastasis in gastric cancer, the areas under the curve of serum CEA, CA199 levels, and their combined detection were 0.602, 0.694, and 0.708, respectively. The areas under the curve of serum CEA and CA125 levels and their combined detection in the diagnosis of preoperative distant metastasis of gastric cancer were 0.657, 0.838, and 0.888, respectively. The sensitivity, specificity, and accuracy of 64-slice spiral CT in the diagnosis of preoperative lymph node metastasis in gastric cancer were 87.32%, 90.56%, and 88.71%, respectively. The combined diagnosis with serum CEA and CA199 levels exhibited a sensitivity of 91.55%, a specificity of 86.79%, and an accuracy of 89.52%. The sensitivity, specificity, and accuracy of 64-slice spiral CT in the diagnosis of preoperative distant metastasis in gastric cancer were 71.43%, 90.63%, and 86.29%, respectively. The combined diagnosis with serum CEA and CA125 levels demonstrated a sensitivity of 92.86%, a specificity of 88.54%, and an accuracy of 89.52%.

**Conclusion:** 64-slice spiral CT combined with serum tumor markers can improve the diagnostic value of lymph node and distant metastasis of gastric cancer.

**Keywords:** gastric cancer; preoperative diagnosis; 64-slice spiral CT; tumor marker

## Introduction

Gastric cancer, a common malignant tumor of the digestive system, ranks as the third in incidence and mortality in China after lung cancer and colorectal cancer [1]. Presently, the primary treatment approach for gastric cancer involves comprehensive therapy based on radical resection. Preoperative staging holds immense significance in determining treatment plans and evaluating outcomes. According to the Eighth Edition of the Cancer Staging Manual by the American Joint Committee on Cancer (AJCC) [2], staging of gastric cancer includes clinical staging (cTNM), pathological staging (pTNM), and staging after neoadjuvant chemotherapy (ypTNM).

The preoperative staging and postoperative outcomes in gastric cancer are primarily influenced by lymph node

and distant metastasis [3–5]. While the prognosis of early gastric cancer is generally favorable, it becomes significantly poor for patients with lymph node metastasis. Previous studies involving large sample sizes have demonstrated lymph node metastasis rates ranging from 9.8% to 16.7% in early gastric cancer cases [6,7]. Multi-slice spiral computed tomography (CT) is the predominant preoperative evaluation technique, offering substantial reference value in assessing the depth of tumor invasion and metastasis. It can directly reflect gastric cancer staging and accurately evaluate the lesions, making it valuable for clinical diagnosis and treatment [8]. At low radiation doses, antiretroviral therapy can produce better high-quality images, so it aims to establish antiretroviral therapy to segment and reconstruct original CT images to improve the accuracy of imaging examinations [9]. The dynamic changes within the gastric wall in

a specific lesion area can be observed using a 64-slice spiral CT-enhanced scan, facilitating the identification of the nature of gastric wall thickening.

Serum tumor markers are widely used in early diagnosis, efficacy evaluation, and recurrence monitoring [10]. Previous studies have indicated strong associations between the expression levels of carcinoembryonic antigen (CEA), carbohydrate antigen 199 (CA199), and CA125 with the clinical staging of gastric cancer [11,12], helping predict the tumor stage [13]. This study primarily investigated the significance of combining 64-slice spiral CT with tumor markers for identifying preoperative gastric cancer staging, providing valuable information to enhance the continuous improvement of gastric cancer treatment.

## Material and Method

### General Information

This retrospective study analyzed the clinical data of 124 gastric cancer patients who underwent surgical treatment in Yongkang First People's Hospital between April 2015 and April 2020. There were 55 males and 69 females, with ages ranging from 31–79 years and an average age of  $56.19 \pm 8.24$  years. Postoperative pathological outcomes showed 58 cases of poorly differentiated adenocarcinoma, 12 cases of moderately differentiated adenocarcinoma, 46 cases of highly differentiated adenocarcinoma, and 8 others. This study was approved by the Medical Ethics Committee of Yongkang First People's Hospital (2020ZY013). Furthermore, all study participants provided signed informed consent, and the entire experimental process was performed with informed consent from the patients or their families. The study design adhered to the Declaration of Helsinki.

The inclusion criteria for study participants were set as follows: (1) Patients who underwent radical resection and lymph node dissection with confirmed gastric cancer based on pathological findings. (2) Those aged between 18 to 80 years. (3) Those who underwent 64-slice CT and serum CEA, CA199, and CA125 examinations within 1 week before surgery. (4) Patients with complete and intact clinical data. However, the exclusion criteria were as follows: (1) Patients with other types of malignant tumors. (2) Those who were diagnosed with secondary or metastatic gastric cancer. (3) Those who had received other anti-tumor therapies such as neoadjuvant chemotherapy before hospital admission. (4) Those with a history of organic gastrointestinal lesions or surgical trauma. (5) Patients presented with factors affecting CT examination, such as high fever.

### Methods

All patients underwent preoperative examinations such as CT scans and serum tumor markers assessment within 1 week of hospital admission. Before the CT examination, patients were instructed to fast for 8–12 hours and orally consume 800–1000 mL of warm boiled water. Fur-

thermore, they received a 10 mg intramuscular injection of anisodamine (H33021707, Minsheng Pharmaceutical Co., Ltd., Hangzhou, China) for 10 minutes before the examination. Plain and enhanced scans were conducted using a 64-slice CT scanner (Somatom Definition, Siemens, Forchheim, Germany), ranging from the diaphragmatic dome to the umbilicus. The nonionic iohexol contrast agent (30 g/100 mL) (M07237, Biolab, Beijing, China) was injected at the rate of 2.8–3.0 mL/s, with a dose of 1.5 mL/kg. Staged real-time tracking scans were performed at 25 seconds, 60–70 seconds, and 3–4 minutes after injection. The imaging parameters included a tube voltage of 120 kV, a current of 250 mA, a slice thickness of 5 mm, and a slice pitch of 1. Afterwards, the data were imported into Syngo.via workstation (VA20A, Siemens, Erlangen, Germany) for 3D reconstruction, they used parameters of a slice thickness of 1.25 mm and a slice spacing of 0.5 mm.

### Diagnosis of Lymph Node Metastasis and Distant Metastasis

Two experienced radiologists independently evaluated the images in a double-blind manner to assess lymph node and distant metastasis. The criteria for identifying lymph node metastasis included a short diameter of perigastric lymph node >6 mm, a short diameter of peripheral lymph node >8 mm, or a CT value in the portal venous phase on enhanced scan >100 hounsfield unit (HU).

### Tumor Marker Detection

For the tumor marker examination, 3 mL of fasting peripheral venous blood was collected from each patient and allowed to coagulate naturally at room temperature. The supernatant was collected to detect serum CEA (16842403, Roche Diagnostics, Rotkreuz, Switzerland), CA199 (16483403, Roche Diagnostics, Rotkreuz, Switzerland), and CA125 (18748901, Roche Diagnostics, Rotkreuz, Switzerland) levels using electrochemiluminescence immunoassay, following the instructions provided with the kits. All patients underwent surgery by the same team, ensuring negative surgical margins, and underwent lymph node dissection (D1+, D2, and D2+). After surgery, pathological specimens were fixed in formaldehyde (252549, Sigma-Aldrich, Saint Louis, MO, USA) for 24 hours, dehydrated in ethanol (E7023, Sigma-Aldrich, Saint Louis, MO, USA), embedded in paraffin, and serially sliced into sections. These sections were stained with hematoxylin (H3136, Sigma-Aldrich, Saint Louis, MO, USA) and eosin (199540, Sigma-Aldrich, Saint Louis, MO, USA), followed by pathological diagnosis. The diagnostic values of serum CEA, CA199, and CA125 levels, and the 64-slice CT scan in diagnosing lymph node and distant metastasis of gastric cancer were evaluated based on the diagnostic results. The combined diagnostic value was analyzed based on the positive reaction for either serum tumor marker or CT outcomes.

**Table 1. Comparison of baseline characteristics.**

Items	Metastasis group	Non-metastasis group	$\chi^2/t$ value	$p$ value
Gender (Male/Female)	32/39	23/30	0.034	0.853
Age (years)	53.19 $\pm$ 7.54	55.76 $\pm$ 8.73	1.755	0.082
Body Mass Index (kg/m <sup>2</sup> )	23.16 $\pm$ 2.34	23.78 $\pm$ 2.83	1.344	0.185

**Table 2. Preoperative lymph node metastasis and comparison of CT and tumor marker test results in patients with gastric cancer.**

Lymph node metastasis	n	CEA (ng/mL)	CA125 (U/mL)	CA199 (U/mL)	CT positive [n (%)]
N0 group	53	19.26 $\pm$ 4.39	29.53 $\pm$ 5.82	36.47 $\pm$ 6.54	5 (9.43)
N1-3 group	71	21.47 $\pm$ 5.08	31.46 $\pm$ 6.25	40.23 $\pm$ 7.19	62 (87.32)
$t/\chi^2$		2.537	1.751	2.993	74.126
$p$		0.012	0.082	0.003	<0.001

CEA, carcinoembryonic antigen; CT, computed tomography; CA199, carbohydrate antigen 199.

**Table 3. Preoperative distant metastases and comparison of CT and tumor marker test results in patients with gastric cancer.**

Distant metastases	n	CEA (ng/mL)	CA125 (U/mL)	CA199 (U/mL)	CT positive [n (%)]
M0 group	96	19.96 $\pm$ 4.33	29.21 $\pm$ 6.02	38.83 $\pm$ 6.65	7 (7.29)
M1 group	28	23.17 $\pm$ 5.48	36.76 $\pm$ 5.23	40.14 $\pm$ 7.63	21 (75.00)
$t/\chi^2$		3.242	6.004	0.887	56.847
$p$		0.002	<0.001	0.377	<0.001

## Statistical Methods

Counting data were expressed as rate (%), and the  $\chi^2$  test was used to compare between groups. The normally distributed measurement data were presented as ( $\bar{x} \pm s$ ), and the independent samples  $t$ -test was employed to compare the two groups. The diagnostic value of serum CEA, CA199, and CA125 levels in identifying lymph node and distant metastasis in gastric cancer patients was assessed by constructing receiver operating characteristic curves (ROC), and the area under the curve (AUC) was calculated. The consistency Kappa test was applied to analyze the combined diagnostic value of 64-slice spiral CT and tumor markers. Statistical analyses were conducted employing SPSS 19.0 software (IBM, Armonk, NY, USA). A  $p$ -value < 0.05 was considered statistically significant.

## Results

### Comparison of Baseline Characteristics

There were no significant differences in age, sex, and body mass index between the two groups ( $p > 0.05$ , Table 1).

### Preoperative Lymph Node Metastasis and Comparison of CT and Tumor Marker Test Results in Patients with Gastric Cancer

Serum CEA and CA199 levels and CT positive rate of lymph nodes were significantly lower in the N0 group compared to the N1-3 group ( $p < 0.05$ , Table 2).

### Preoperative Distant Metastasis and Comparison of CT and Tumor Marker Test Results in Patients with Gastric Cancer

The serum CEA and CA125 levels and CT positive rate of lymph nodes were significantly lower in the M0 group compared to the M1 group ( $p < 0.05$ , Table 3).

### Diagnostic Value of Serum Tumor Markers in Preoperative Lymph Node and Distant Metastasis of Gastric Cancer

In the diagnosis of preoperative lymph node metastasis in gastric cancer, the AUCs of serum CEA, CA199, and their combination were 0.602, 0.694, and 0.708, with sensitivities of 36.62%, 43.66%, and 40.85%, and specificities of 92.45%, 92.45%, and 96.23%, respectively. Similarly, in the diagnosis of preoperative distant metastasis in gastric cancer, the AUCs of CEA, CA125, and their combination were 0.657, 0.838, and 0.888, with sensitivities of 46.43%, 78.57%, and 82.14%, and specificities of 82.29%, 96.04%, and 93.33%, respectively. These findings are shown in Table 4.

### Diagnostic Value of Serum Tumor Markers Combined with CT in Preoperative Lymph Node Metastasis of Gastric Cancer

The sensitivity, specificity, and accuracy of 64-slice spiral CT in diagnosing lymph node metastasis were 87.32%, 90.56%, and 88.71%, respectively. The consistency Kappa value associated with this analysis was 0.772. However, when CT was combined with serum CEA and

**Table 4. Diagnostic value of serum tumor markers combined with CT in preoperative lymph node metastasis in gastric cancer.**

Laboratory indicators	AUC	95% CI	SE	Cutoff value	Sensitivity (%)	Specificity (%)
Lymph node metastasis						
CEA	0.602	0.510~0.689	0.051	>23.43	36.62	92.45
CA199	0.694	0.605~0.733	0.047	>42.78	43.66	92.45
Combined detection	0.708	0.620~0.786	0.046	>0.71	40.85	96.23
Distant metastasis						
CEA	0.657	0.566~0.740	0.063	>23.43	46.43	82.29
CA125	0.838	0.761~0.898	0.040	>32.89	78.57	76.04
Combined detection	0.888	0.819~0.938	0.035	>0.25	82.14	83.33

AUC, area under the curve; CI, confidence interval; SE, standard error.

**Table 5. Diagnostic value of serum tumor markers combined with CT in preoperative lymph node metastasis of gastric cancer.**

Inspection method	Lymph node metastasis			Total
		N0	N1-3	
CT	+	62	5	67
	–	9	48	57
	Total	71	53	124
CT + tumor marker	+	65	7	72
	–	6	46	52
	Total	71	53	124

**Table 6. Diagnostic value of serum tumor markers combined with CT in preoperative distant metastasis of gastric cancer.**

Inspection method		Distant metastasis		Total
		M0	M1	
CT	+	20	9	29
	−	8	87	95
	Total	28	96	124
CT + tumor marker	+	26	11	37
	−	2	85	87
	Total	28	96	124

CA199 levels, the sensitivity, specificity, and accuracy of CT were 91.55%, 86.79%, and 89.52%, respectively, with a consistency Kappa value of 0.785 (Table 5).

#### *Diagnostic Value of Serum Tumor Markers Combined with CT in Preoperative Distant Metastasis of Gastric Cancer*

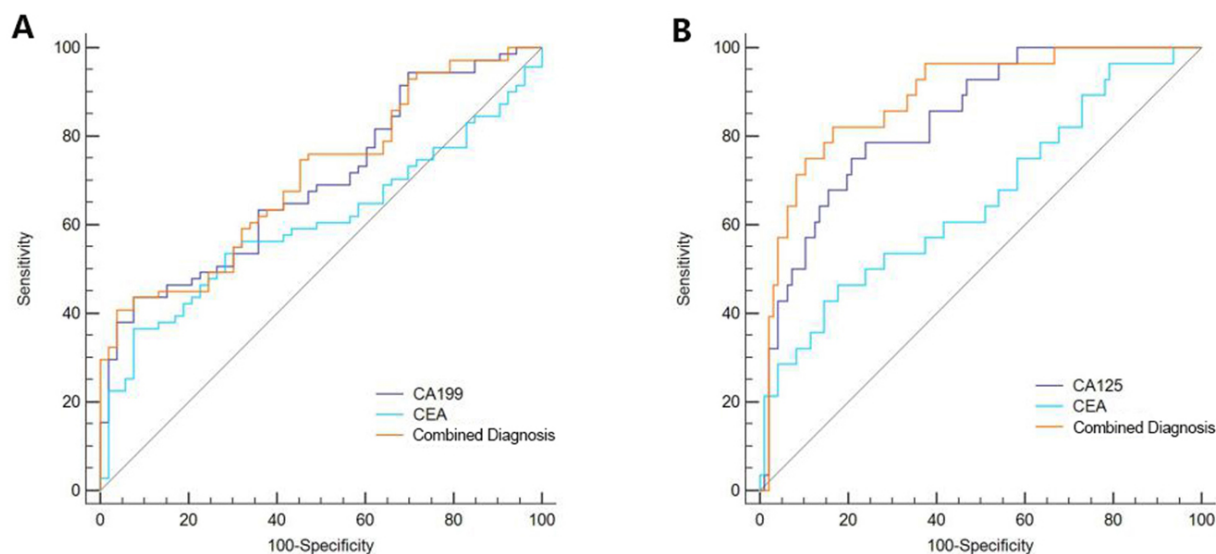
In diagnosing preoperative distant metastasis of gastric cancer, the 64-slice spiral CT indicated sensitivity, specificity, and accuracy of 71.43%, 90.63%, and 86.29%, respectively, with a consistency Kappa value of 0.613. However, when CT was combined with serum CEA and CA125 levels, it yielded sensitivity, specificity, and accuracy of 92.86%, 88.54%, and 89.52%, respectively, with a consistency Kappa value of 0.731 (Table 6, Fig. 1).

## Discussion

Gastric cancer stands as a prevalent malignancy. Despite a decrease in both incidence and mortality rates, it is the fifth most diagnosed cancer and the fourth leading cause of cancer-related death worldwide [14]. It affects men two times higher than women, with East Asia bearing the highest incidence [15]. Due to rapid medical advancements, the surgical management of gastric cancer has advanced the era of precision surgery, demanding continuous requirements in the accuracy of preoperative staging. Imaging examinations and tumor markers play crucial roles in diagnosing, staging, and predicting outcomes of gastric cancer.

Commonly used imaging techniques for gastric cancer include B-ultrasound, CT, MRI, and PET/CT, each with its own advantages and limitations. Among them, CT is the most widely used method. The use of multi-slice spiral CT has been increasing, particularly its application in the preoperative staging of gastric cancer. However, its effectiveness in diagnosing lymph node and intra-abdominal metastasis remains controversial [16,17]. The criteria for identifying lymph node metastasis include the diameter of perigastric lymph node >6 mm, the diameter of peripheral lymph node >8 mm, or the CT value in portal venous phase on enhanced scan >100 HU. Distant metastases may occur in the liver or ascites by enhanced CT scan [18]. The results of our study indicated that the detection rates for lymph nodes and distant metastases in gastric cancer using 64-slice spiral CT were 87.32% and 82.14%, respectively. Misdiagnosis rates were 9.43% and 9.38%, with the diagnostic accuracy rates reaching 88.71% and 86.29%, respectively. These rates were generally higher than those reported in a previous study [19], attributed to many factors affecting the observation of lymph nodes and distant metastases. Firstly, the size of lymph nodes can directly affect the results of CT examinations. Small lymph nodes are often difficult to identify accurately, resulting in missed diagnosis or misdiagnosis. Secondly, inflammation can alter lymph node volume and CT value, adversely impacting lymph node observation. Thirdly, reducing abdominal fat can decrease organ space, affecting the CT display effect [20,21]. The liver and peritoneal cavity are common sites for distant metas-





**Fig. 1.** ROC curves of tumor markers in the diagnosis of lymph node metastasis (A) and distant metastasis (B) of gastric cancer.

tasis in gastric cancer. A previous study demonstrated the difficulty in identifying small or peritoneal metastases using CT imaging [22]. The findings from our present study reveal that 64-slice spiral CT holds significant utility as a reference tool in preoperative diagnoses of lymph nodes and distant metastases in gastric cancer. However, some patients may be difficult to identify due to inherent factors. Therefore, combining other examination methods may further enhance overall diagnostic accuracy.

The application of tumor markers for preoperative diagnosis in gastric cancer has been gradually rising due to their simplicity, safety, and non-invasiveness. Among them, CEA, CA125, and CA199 exhibit high diagnostic values for gastric cancer and are strongly associated with its clinicopathological characteristics [11]. In this study, the evaluation of serum CEA, CA125, and CA199 expression in gastric cancer patients demonstrated that serum CEA and CA199 levels were significantly increased in patients with lymph node metastasis, while serum CEA and CA125 levels were substantially increased in patients with distant metastasis. These observations align with previous findings by Bao *et al.* [23]. CEA is the most crucial tumor marker for gastric cancer and colorectal cancer at this stage, playing a significant role in preoperative diagnosis, postoperative recurrence or metastasis monitoring, and outcome evaluation [24,25]. CA125 is mainly used in diagnosing and treating ovarian cancer patients. However, its application in malignant tumors of the digestive tract has gradually increased. Numerous predictive models established in clinical studies have reported CA125 as an indicator of prognosis and metastasis in gastric cancer [26,27].

Additionally, CA199 has the highest sensitivity in diagnosing pancreatic cancer. A previous study has found that CA199 serves as a good reference value for diagnosing

gastric cancer and is closely related to tumor volume, infiltration depth, and lymph node metastasis [28]. Our study demonstrated that CEA and CA199 could be used for differential diagnosis of preoperative lymph node metastasis in gastric cancer, with AUCs of 0.602 and 0.694, respectively. The combined detection yielded an AUC of 0.708, with sensitivity and specificity of 40.85% and 96.23%, respectively. Therefore, the combination of CEA and CA199 shows poor sensitivity in diagnosing lymph node metastasis in gastric cancer, highlighting the inability to evaluate the lymph node metastasis in gastric cancer independently. The AUCs of serum CEA and CA125 levels in diagnosing preoperative distant metastasis of gastric cancer were 0.657 and 0.838, respectively, both displaying certain reference value. Combining them showed an AUC of 0.888, with a sensitivity of 82.14% and a specificity of 93.33%, which are significantly higher than those in the application alone, but the sensitivity remains insufficient. The study employed a parallel method for the combined diagnosis, using serum tumor markers and 64-slice spiral CT. The results indicated that the combination of CT with serum CEA and CA199 levels yielded a sensitivity of 91.55%, a specificity of 86.79%, and an accuracy of 89.52% in diagnosing lymph node metastasis in gastric cancer. CT in combination with serum CEA and CA125 achieves a sensitivity of 92.86%, a specificity of 88.54%, and an accuracy of 89.52% in diagnosing distant metastasis of gastric cancer. This shows a substantial improvement in the diagnostic significance compared to the individual utilization of these two methods. Particularly, increased sensitivity is of great significance for reducing missed diagnoses and improving patient outcomes. There is a large room for improvement in sensitivity and specificity. Therefore, additional research is needed to investigate more advanced CT examination techniques and more

sensitive tumor markers, thereby promoting the continuous development and progress in the diagnosis and treatment of gastric cancer.

This study performed preoperative staging of different tumor markers in gastric cancer to provide a scientific basis for clinical diagnosis and treatment. However, this study was a retrospective study with limited sample size, which may affect the extrapolation of results. Further multi-center, large sample, and prospective studies are needed for confirmation.

## Conclusion

In conclusion, 64-slice spiral CT and tumor markers are common methods for preoperative diagnosis of gastric cancer. Compared to the two methods alone, the diagnosis of lymph node metastasis of gastric cancer by CT combined with serum CEA and CA199 and the diagnosis of distant metastasis of gastric cancer by CT combined with serum CEA and CA125 are beneficial for improving the diagnostic value of lymph node and distant metastasis of gastric cancer in this study. In particular, improving the sensitivity of detection holds great significance in reducing missed diagnoses and improving prognosis.

## Availability of Data and Materials

All experimental data included in this study can be obtained by contacting the corresponding author if needed.

## Author Contributions

YPS, DYL and KFZ designed the research study. YPS and KFZ performed the research. YPS and DYL provided help and advice on the experiments. YPS analyzed the data. YPS drafted the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

## Ethics Approval and Consent to Participate

This study was approved by the Medical Ethics Committee of Yongkang First People's Hospital (2020ZY013). Furthermore, all study participants provided signed informed consent, and the entire experimental process was performed with informed consent from the patients or their families. The study design adhered to the Declaration of Helsinki.

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## Conflict of Interest

The authors declare no conflict of interest.

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