International Journal of General Medicine

Dovepress

Open Access Full Text Article

ORIGINAL RESEARCH

Comparative Evaluation of CEUS and CECT in the Detection of Liver Metastases of Middle and Low Rectal Cancer

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Objective: To explore the imaging manifestations and clinical application value of contrast-enhanced ultrasound (CEUS) in liver metastases of middle and low rectal cancer by performing CEUS in patients. Additionally, we compared the results of CEUS with those of abdominal contrast-enhanced computed tomography (CECT) to assess the reliability of diagnosing liver metastases in patients with middle and low rectal cancer.

Methods: Hepatic CEUS was performed in 1095 patients with middle and low rectal cancer, and all patients underwent abdominal CECT examinations to determine the presence or absence of liver metastases. The results of both examinations were compared to evaluate the value of hepatic CEUS for detecting liver metastases in patients with middle and low rectal cancer.

Results: Among 1095 patients with middle and low rectal cancer, 132 were diagnosed with liver metastases of middle and low rectal cancer. 130 cases of liver metastases of rectal cancer were identified using hepatic CEUS, whereas 126 cases were identified using abdominal CECT. The detection rates of hepatic CEUS and abdominal CECT for liver metastases of middle and low rectal cancer showed no statistically significant differences ($P > 0.05$). The Kappa value for the diagnosis of liver metastases of middle and low rectal cancer between hepatic CEUS and abdominal CECT was 0.974 ($P < 0.001$), indicating good consistency between the two imaging modalities in detecting liver metastases of middle and low rectal cancer.

Conclusion: Hepatic CEUS can be used to diagnose liver metastases in middle and low rectal cancer, providing crucial imaging evidence for clinical treatment planning. It exhibited higher sensitivity than that of abdominal CECT in diagnosing liver metastases of middle and low rectal cancer, enabling the identification of higher number of liver metastases of middle and low rectal cancer cases.

Keywords: middle and low rectal cancer, hepatic CEUS, abdominal CECT, liver metastases

Introduction

Rectal cancer is a common malignant tumor of the digestive system that occurs more frequently in middle-aged and older adults, with the highest incidence occurring between the ages of 40–70 years. Changes in dietary structure and lifestyle habits have led to an increasing trend in the incidence and mortality of rectal cancer in recent years, significantly affecting the quality of life and survival.

During its growth, rectal cancer can metastasize and spread to other adjacent tissues and distant organs through the lymphatic, blood circulation, and direct extension pathways. Liver metastases is the most common type of hematogenous metastasis in rectal cancer. When liver metastases occur in patients with rectal cancer, the treatment plan depends on the condition of the metastatic lesions to improve the patient's quality of life and survival. Complete removal of liver metastatic lesions can greatly improve the 5-year survival rate of patients, reaching 30–57%.[1–4]

Abdominal CT and MRI are commonly used in clinical practice to assess liver metastases in patients with rectal cancer.[5] With the continuous improvement in ultrasound contrast agents, CEUS is increasingly used in clinical settings

Received: 12 September 2024
Accepted: 1 December 2024
Published: 5 December 2024

and has shown good efficacy in diagnosing liver metastases in rectal cancer. It is suitable for determining the presence of liver metastases in patients with rectal cancer. Hepatic CEUS not only evaluates the presence of liver metastases in patients with rectal cancer but also provides quantitative analysis of contrast enhancement, offering relatively accurate imaging information on hepatic tissue microperfusion for assessing the effectiveness of chemotherapy in metastatic tumors.[6]

This study explored the diagnostic efficacy of hepatic CEUS in liver metastases of middle and low rectal cancer through a comparison of hepatic CEUS and abdominal CECT in the detection of liver metastatic lesions in patients with middle and low rectal cancer. We hope this study offers insights into novel imaging data for the diagnosis of liver metastatic lesions in middle and low rectal cancers and the formulation of treatment plans for rectal cancer.

Materials and Methods

Study Participants

A total of 1095 patients with middle and low rectal cancer were recruited from the First Affiliated Hospital of Guangxi Medical University. Middle and low rectal cancer refer to rectal cancer within 5–10 cm of the anal margin. All patients underwent hepatic CEUS. Among them, 709 were male and 386 were female, with an age range of 20 to 89 years and an average age of 57.80±11.68 years. The inclusion criteria were as follows: (1) complete clinical data; (2) hepatic CEUS and abdominal CECT examination performed before treatment, with CEUS conducted before CECT; (3) underwent rectal tumor resection surgery with postoperative pathological confirmation of rectal cancer; and (4) no prior chemotherapy or radiotherapy before surgery. The exclusion criteria were as follows: (1) concurrent malignant tumors with possible liver metastases, (2) potential allergy to contrast agents used in ultrasonography, (3) severe cardiovascular or cerebrovascular diseases or significant liver or kidney dysfunction that might hinder examination and surgery, and (4) unconfirmed liver metastases of rectal cancer. The study was approved by The Medical Ethics Committee of First Affiliated Hospital of Guangxi Medical University, and there were no ethical issues. Patients and their families were informed of the risks and potential accidents related to hepatic CEUS, and relevant documents were signed and archived.

Instruments and Methods

Hepatic CEUS Examination Equipment, Materials, and Methods

A TOSHIBA Aplio 500 multifunctional color Doppler ultrasound diagnostic instrument (TOSHIBA Group, Japan) with a convex array probe operating at a frequency of 6–8 MHz was used. SonoVue (Bracco Suisse SA, Switzerland) was used as the contrast agent for ultrasonography.

Hepatic CEUS was performed in all patients with middle and low rectal cancer. For focal lesions identified during two-dimensional ultrasound examination, CEUS was used to observe the enhancement characteristics, time, level, and morphology; changes in the discovered focal lesions; and the infiltration of adjacent tissues to determine the nature of the lesions. For patients in whom focal lesions were not detected in the two-dimensional ultrasound examination, we performed a comprehensive evaluation of the entire liver in both the arterial and portal venous phases using CEUS. If lesions with abnormal enhancement or regression were identified, a second CEUS examination targeting the lesions was performed after a 15-min rest.

Upper Abdominal CECT Examination Equipment, Materials, and Methods

CECT was performed using a Siemens SOMATOM Definition Flash CT scanner (Siemens, Germany) with 128 rows. Iopromide was the contrast agent used for CT. The scanning range for abdominal CECT was the upper abdomen, from the diaphragmatic apex to the lower margin of the liver, with plain scans, followed by enhanced scans.

Image Analysis

Hepatic CEUS Image Analysis

Hepatic CEUS images were jointly reviewed by two ultrasound physicians with more than 5 years of experience in CEUS imaging. The CEUS process was divided into three phases: 5–30 s for the arterial phase, 31–120 s for the portal venous phase, and 121–360 s for the delayed phase.

Table 1 Distribution of Nodules in 132 Cases of Liver Metastases of Middle and Low Rectal Cancer (Cases)

Examination Method	1 Metastatic Lesion	2 Metastatic Lesions	≥3 Metastatic Lesions	No Nodule(s)	Total
CEUS	52	9	71	0	132
CECT	47	10	72	3	132

Abdominal CECT Image Analysis

Abdominal CECT images were jointly interpreted by two radiologists with more than 5 years of experience in CECT images. The enhancement patterns and degrees during the arterial and portal venous phases on CECT were judged based on the contrast with the surrounding liver parenchyma density of the corresponding lesion.

Statistical Analysis

Statistical analysis of the study data was performed using the SPSS software (version 23.0; IBM, Armonk, NY, USA). Count data are expressed as rates or composition ratios, and the chi-square test was used with $P<0.05$ indicating statistical significance. A consistency analysis between CEUS and CECT diagnoses of liver metastases of rectal cancer was conducted using the Kappa index. A higher Kappa value indicated better consistency, with Kappa≥0.75 considered good consistency, 0.40<Kappa<0.75 indicating relatively good consistency, and Kappa≤0.40 indicating poor consistency.

Results

Hepatic CEUS Examination Results

Among the 1095 patients with middle and low rectal cancer, 132 were diagnosed with liver metastases of rectal cancer. In total, 130 cases of liver metastases of rectal cancer were identified using hepatic CEUS, with four misdiagnoses (two cases of liver metastases of rectal cancer misdiagnosed as benign nodules and two cases of benign nodules misdiagnosed as liver metastases of rectal cancer). Among these, 50 patients had a single metastatic lesion, nine patients had two metastatic lesions, and 71 patients had three or more metastatic lesions (Table 1). Notably, in two cases, focal lesions were not detected via conventional ultrasound but were identified after hepatic CEUS. Conventional ultrasound identified 130 cases, of which two cases showed no nodules; the largest lesion measured approximately 14.2 cm × 13.7 cm, while the smallest measured about 0.7 cm × 0.6 cm (Figures 1–3).

Abdominal CECT Examination Results

Among 1095 cases of patients with middle and low rectal cancer, 132 were diagnosed with liver metastases of rectal cancer, of which 126 were identified through abdominal CECT, including 44 cases with a single metastatic lesion, 10 cases with two metastatic lesions, and 72 cases with three or more metastatic lesions. Notably, one case of liver metastases of rectal cancer with a solitary lesion was not visible on CT scans, both in the plain and enhanced phases,

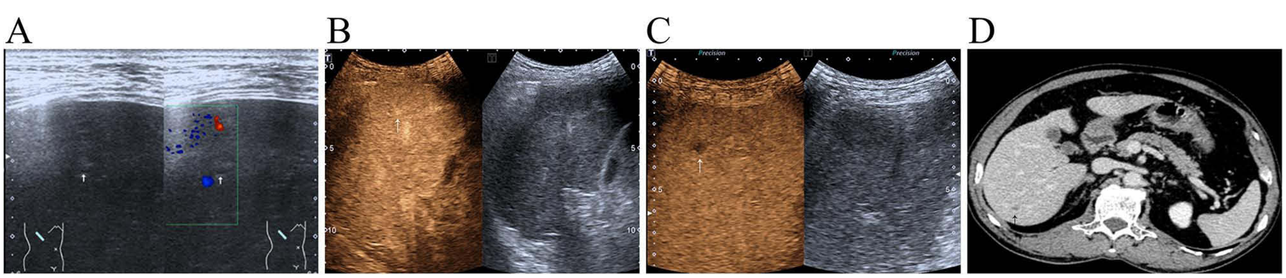

Figure 1 Liver Metastasis of Middle and Low Rectal Cancer. (**A**) Conventional hepatic ultrasound showing a nodule, approximately 0.7 cm × 0.6 cm, with clear boundaries and regular morphology; Color Doppler Flow Imaging (CDFI) did not show blood flow signals. (**B**) Hepatic CEUS demonstrating uniformly high enhancement during the arterial phase of the liver metastasis of rectal cancer. (**C**) Hepatic CEUS showing no enhancement during the delayed phase of the liver metastasis of rectal cancer. (**D**) Abdominal CECT showing circular enhancement around the liver metastasis of rectal cancer. (white and black arrows showed the liver metastasis).

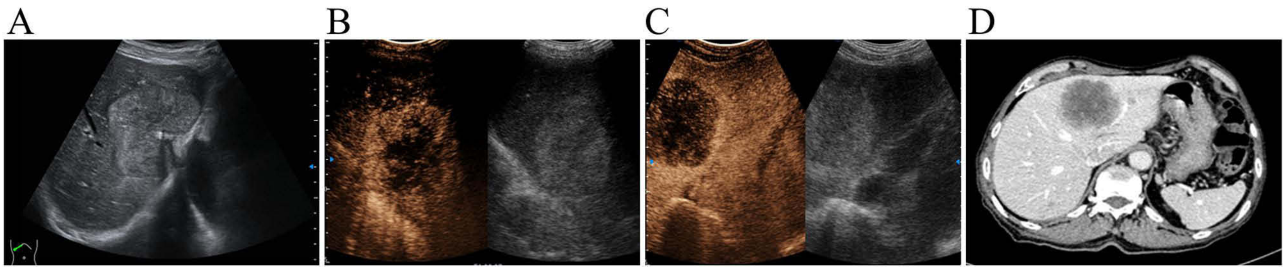

Figure 2 Liver Metastasis of Middle and Low Rectal Cancer. (**A**) Conventional ultrasound showing liver occupancy in a rectal cancer patient. (**B**) Hepatic CEUS revealing thick circular enhancement during the arterial phase (25s), with low enhancement inside the lesion. (**C**) Hepatic CEUS showing no enhancement during the delayed phase. (**D**) Abdominal CECT showing circular echo enhancement inside the liver metastasis.

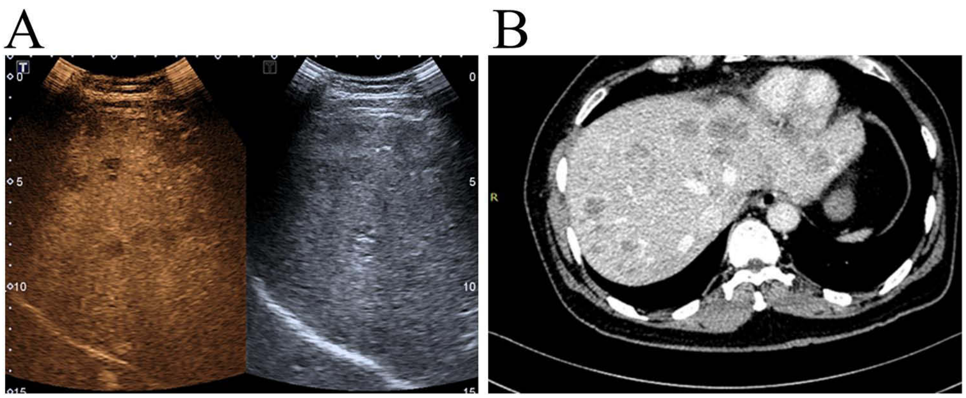

Figure 3 Multiple Liver Metastases of Middle and Low Rectal Cancer. (**A**) Hepatic CEUS showing no enhancement during the delayed phase of multiple liver metastases of rectal cancer. (**B**) Abdominal CECT showing multiple low-echo lesions of liver metastases of rectal cancer.

but was later detected in the venous phase. Abdominal CT identified 128 cases, of which four showed no nodules. The largest lesion measured approximately 15.0 cm × 13.5 cm, and the smallest measured approximately 0.9 cm × 0.7 cm.

Comparison of Two Imaging Diagnoses

The diagnosis of liver metastases of middle and low rectal cancer was based on clinical history, typical imaging data, relevant laboratory indicators, and postoperative follow-up data. Despite the considerable number of confirmed cases lacking a pathological diagnosis, the basis for diagnosing liver metastases of middle and low rectal cancer in this study was reliable. A total of 132 confirmed cases of liver metastases of middle and low rectal cancer were identified. There was no statistically significant difference between the results of hepatic CEUS and abdominal CECT (Table 2). The consistency between the two imaging methods for detecting liver metastases of middle and low rectal cancer was good.

Table 2 Comparison of Hepatic CEUS and Abdominal CECT in Diagnosing Liver Metastases in Patients with Middle and Low Rectal Cancer (Cases)

CECT	CEUS		Total
	+	–	
+	126	2	128
–	4	963	967
Total	130	965	1095

Notes: "+" indicates detection of liver metastases of rectal cancer, and "-" indicates no detection of liver metastases of rectal cancer (*P*=0.69).

Table 3 Comparison of Accuracy, Sensitivity, and Specificity Between Hepatic CEUS and Abdominal CECT in Diagnosing Liver Metastases of Middle and Low Rectal Cancer (%)

Examination Method	Diagnostic Results		Accuracy	Sensitivity	Specificity
	Correct	Error			
CEUS	1091	4	99.63	98.48	99.79
CECT	1087	8	99.27	95.45	99.79

The Kappa value for the diagnosis of liver metastases of rectal cancer using hepatic CEUS and abdominal CECT was 0.974, with $P < 0.001$. The accuracy, sensitivity, and specificity of the two imaging methods for diagnosing liver metastases of middle and low rectal cancer are shown in Table 3.

Discussion

The main site of hematogenous metastasis in rectal cancer is the liver. The presence of liver metastases of rectal cancer directly determines different treatment plans for patients in clinical practice. Patients diagnosed with rectal cancer without liver metastases require active treatment of the primary tumor, while actively preventing the occurrence of liver metastases. For patients diagnosed with rectal cancer concurrent with liver metastases, treatment plans are divided into two categories based on whether metastatic lesions can be excised and whether clinical remission without tumors can be achieved. Liver metastases is a major cause of death in patients with rectal cancer, making the diagnosis of liver metastases one of the key and challenging aspects of rectal cancer treatment.[7,8]

In this study, the detection rate of liver metastases in patients with middle and low rectal cancer upon admission was 12.05%, which was slightly lower than the results indicating that 15%-25% of patients with colorectal cancer had liver metastases at the time of diagnosis.[9–11] Even after radical surgery for the primary lesion in patients with rectal cancer, 15–25% develop liver metastases. In this group of middle and low rectal cancer cases, patients with multiple liver metastases accounted for 54.55% of total metastatic cases. Considering that single and double lesions of liver metastases of rectal cancer cannot be surgically removed, these patients represent the majority of cases in which liver metastases of rectal cancer cannot be treated by resection,[12–15] theoretically resulting in a 5-year survival rate of less than 5%.[16,17] Throughout the disease course, the occurrence of liver metastases in patients with rectal cancer can reach 50%-70%.[18] Microscopic liver metastases and hidden cancers that cannot be detected using preoperative imaging are essential risk factors for recurrence.[19] After surgery for liver metastases, 65–85% of patients experience recurrence within 2 years.[20] Therefore, it is crucial to determine the presence of liver metastases before initiating treatment for middle and low rectal cancers.

In patients with liver metastases of middle and low rectal cancer, conventional two-dimensional ultrasound examination identified 96.97% (128/132) of liver metastases of rectal cancer cases. Among the 130 cases diagnosed with CEUS, two cases (1.52%, 2/132) of liver metastases of rectal cancer with metastatic nodules were not detected via two-dimensional ultrasound. The presence of metastatic nodules was identified only during the delayed phase of CEUS, showing a nonenhancing "black hole" sign. Subsequently, a second hepatic CEUS scan was performed to confirm the nature of the liver nodules. Two cases were misdiagnosed as benign lesions when using hepatic CEUS, where one case involved a liver metastasis of rectal cancer measuring 1.5 cm × 0.9 cm, located near the diaphragmatic apex in the right posterior lobe, showing high echogenicity. Enhancement during CEUS was essentially triphasic, with minimal regression during the delayed phase, resulting in low enhancement without characteristic non-enhancement. The other case had a high echogenic nodule in liver segment 6 (S6), measuring 1.8 cm × 1.5 cm, displaying global enhancement during the arterial phase, with ultrasonography failing to observe the typical thick circular high enhancement. The delayed phase did not show significant regression, and the enhancement was essentially synchronous with the liver parenchyma, leading to a misjudgment on CEUS; however, circular enhancement was visible on abdominal CECT.

In this study, abdominal CECT missed 8 cases of liver metastases of middle and low rectal cancer, and three cases (2.27%, 3/132) showed no lesions on both plain CT and CECT scans, possibly owing to a lack of density difference between the liver metastases of rectal cancer lesion and the adjacent normal tissue, making it challenging to display the lesion. One case was misdiagnosed as a benign nodule with the enhancement phase of the metastatic lesions missed during scanning, leading to a qualitative error. One patient was misdiagnosed as having an inflammatory nodule owing to the lack of obvious enhancement during the arterial phase and minimal regression during the portal venous and delayed phases, exhibiting overall low enhancement with minimal changes. Another one case of liver metastasis of rectal cancer was misjudged because of atypical low-to-moderate enhancement and insignificant changes. The other two cases were misdiagnosed as benign nodules of liver metastases of rectal cancer.

Regarding the determination of the number of lesions, two cases of liver metastases of rectal cancer on hepatic CEUS showed underestimated evaluations. In one patient with two lesions, only one lesion was detected on ultrasound examination. In another case of multiple metastases, conventional ultrasonography and CEUS revealed only one lesion, with the largest lesion measuring 0.8 cm × 0.7 cm. Liver metastases of rectal cancer with several metastatic lesions was identified through CECT and confirmed by enhanced MRI. However, routine hepatic ultrasonography did not detect smaller lesions, and arterial phase enhancement and portal venous phase regression were not evident in the other lesions. Consequently, CEUS failed to detect other metastatic lesions, possibly owing to their small size and insufficient recognition. When liver metastases of rectal cancer measure less than 0.5 cm, and these lesions was not detected through two-dimensional ultrasound, it becomes crucial to consider specific characteristics during CEUS. If the metastasis does not exhibit significant enhancement in the arterial phase of CEUS, and if the late and delayed portal vein phases show a pattern of low enhancement or even no enhancement after the complete disappearance of the contrast agent, there might be a lack of obvious contrast between the lesion and surrounding tissues. This discrepancy in enhancement patterns during hepatic CEUS could lead to missed diagnosis of liver metastases of middle and low rectal cancer.

Sawatzki indicated that hepatic CEUS could detect greater number of colorectal cancer liver metastases than that by CECT. In T3 and T4 stage colorectal cancer, the additional detection of liver metastases can reach 4%. In all stages of colorectal cancer, CEUS could detect an additional 2.7% of liver metastases. In this study, among the confirmed cases of liver metastases of middle and low rectal cancer, without staging comparison, CEUS detected an additional 3.03% (4/132) of metastatic lesions compared to CECT, and the results of the two methods were essentially consistent,[21] whereas in patients with middle and low rectal cancer, 82.9% (466/562) were in stages T3 and T4.

In this study, CEUS utilized a pure blood pool contrast agent, such as SonoVue, which was injected intravenously and did not permeate through the vessel walls into the extravascular space. Throughout the contrast-enhanced examination, it was possible to observe in real-time how the contrast agent entered and exited the lesions, manifesting different enhancement patterns that correspond to various manners of perfusion within the local lesions and normal tissues. This allowed for an accurate reflection of the blood perfusion patterns of both the lesions and the surrounding normal tissues. In contrast, the Iopromide used in abdominal enhanced CT scans was an extracellular contrast medium. After intravenous injection, it was not only distributed within the capillaries but also diffused into the perivascular connective tissue spaces through the permeability of the capillary basement membrane. The uneven distribution of the contrast agent created density differences between the diseased tissue and the surrounding normal tissues, with an increase in density within the diseased tissue.[22]

This study of liver metastases in middle and low rectal cancer showed that, although the accuracy and sensitivity of hepatic CEUS were slightly higher than those of abdominal CECT, higher number of liver metastases of rectal cancer cases were detected using hepatic CEUS; however, there was no significant difference between the two examination methods. It is possible that the sample size of liver metastases of rectal cancer cases in this group was limited to patients with middle and low rectal cancer, excluding high rectal and colon cancers. Moreover, some cases were excluded from the statistical analysis because of the inability to confirm whether they had liver metastases of rectal cancer, resulting in insufficient total samples for liver metastases of rectal cancer and a statistical bias. The Kappa value for the diagnosis of liver metastases of middle and low rectal cancer using hepatic CEUS and abdominal CECT in this group was 0.974, with $P < 0.001$. This indicates good consistency between the two imaging methods in detecting liver metastases of middle and low rectal cancer, making them suitable for evaluating the diagnosis of liver metastases of rectal cancer.

CEUS offers valuable imaging data for the assessment of liver metastases arising from middle and low rectal cancer, and its safety is especially for patients in whom CT is contraindicated due to radiation or intolerance/allergy and nephrotoxicity to contrast material, which is particularly beneficial for patients who require frequent monitoring. Moreover, CEUS addresses the limitations in diagnostic accuracy that may be encountered with CECT. Additionally, CEUS helps to alleviate the challenges posed by the long waiting times and high costs associated with enhanced MR imaging, providing a more accessible and efficient alternative for monitoring liver metastasis in rectal cancer patients.[23,24]

However, CEUS is based on cross-sectional scanning, and its overall quality is inferior to enhanced MR, as some parts of the liver are difficult to detect in ultrasound examination. We have to admit that this may lead to a decrease in diagnostic accuracy.[25]

The limitation of this study was that although most of the cases in this study did not have histopathological confirmation, the diagnosis of liver metastasis in clinical practice was cautious and objective.

Conclusion

In This study, CEUS identified greater number of liver metastases cases than abdominal CECT, guiding the clinical treatment of liver metastases in middle and low rectal cancers. It was a crucial step to identify the presence of liver metastases in patients with middle and low rectal cancer before formulating diagnosis and treatment plans, so we strongly recommend the use of hepatic CEUS for the diagnosis of liver metastases in patients with middle and low rectal cancers.

Data Sharing Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

The authors ensured that the research involving human participants complied with the Declaration of Helsinki. This study was approved by The Medical Ethics Committee of First Affiliated Hospital of Guangxi Medical University (approval number: 2024-S069-01). All participants provided informed consent.

Acknowledgments

The authors extend their sincere gratitude to the volunteers involved in this study. Acknowledgment is also due to the staff of Department of Medical Ultrasound for their vital contribution to the research.

Author Contributions

Each author has made a substantial contribution to all areas of the significant work reported. These areas encompass the inception, study design, execution, acquisition of data, analysis and interpretation. They have also been engaged in drafting, revising, and critically reviewing the article; they have collectively given final approval for the publication version and consented to the chosen submission journal for the article. Moreover, they agreed to be responsible for every aspect of the project.

Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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