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● *Clinical Note*

COLOR DOPPLER TWINKLING ARTIFACT IN DIAGNOSIS OF TUBERCULOUS PLEURITIS: A COMPARISON WITH GRAY-SCALE ULTRASONOGRAPHY AND COMPUTED TOMOGRAPHY

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Abstract—The aim of this study was to determine whether twinkling artifact (TA) detected on color Doppler ultrasonography can effectively determine the presence of pleural calcification compared with computed tomography (CT) and differentiate tuberculous pleuritis (TP) and cancerous pleuritis (CP). One hundred six cases of TP and 26 cases of CP were scanned using gray-scale ultrasonography (GSU) and TA to determine the presence of pleural calcification. With CT as the reference standard, 63.3% and 79.6% of patients with pleural calcification were identified with GSU and TA, respectively. The detection rate of TA was higher than that of GSU ($p = 0.039$). For the whole study population, 37.1% were identified as having pleural calcification with CT, significantly higher than the proportion detected with GSU (25.8%, $p = 0.001$), but not different from that detected with TA (41.7%, $p = 0.327$). The sensitivity, specificity, accuracy, positive predictive value and negative predictive value of TA were 79.6%, 80.7%, 80.3%, 70.9% and 87.0%, respectively. The detection rate of TA was significantly higher than that of GSU ($p < 0.001$). When GSU was combined with TA (GSUTA), the positive rate in the TP group was significantly higher than that in the CP group ($\chi^2 < 0.001$). In conclusion, TA is comparable to CT and more sensitive than GSU in the detection of pleural calcification. Evaluation for GSUTA on pleura may help to differentiate TP from CP.
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Key Words: **Color Doppler ultrasonography, Twinkling artifact, Gray-scale ultrasonography, Tuberculous pleuritis, Cancerous pleuritis, Calcification.**

INTRODUCTION

Twinkling artifact (TA) is a dynamic color mosaic behind a strongly reflective medium in color Doppler imaging (Rahmouni et al. 1996), and it is widely used in clinical practice for diagnosing urinary tract and gallbladder stones. Tuberculous pleuritis (TP) has a high prevalence and is sometimes difficult to distinguish sonographically from cancerous pleuritis (CP), which can also present as a pleural effusion and pleural nodule. Tuberculosis is characterized by calcification and tuberculous granuloma with rich fibrous tissue, with or without caseating necrosis (Xu et al. 2011). Pleural thickening can be seen in a variety of diseases involving the pleura, including both benign and malignant entities, but there are differences in the extent and morphology of pleural involvement between malignant and benign diseases, and pleural calcification is highly suggestive of a benign disease (Hierholzer et al. 2000). Therefore, we supposed that TA might be useful in the detection of pleural calcification and, thus, helpful in the diagnosis of TP. This study focused on the clinical use of TA in the diagnosis of TP as compared with computed tomography (CT) and gray-scale ultrasonography (GSU), with the aim of exploring its capacity in detection of pleural calcification and extending its use in the clinical setting. To our knowledge, there are no previous reports regarding the clinical use of TA in pleural diseases.

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METHODS

Patient population

One hundred six cases of TP and 26 cases of CP admitted to Shandong Provincial Chest Hospital from April 2014 to December 2014 were randomly included in this study. The total patient population included 81 male patients and 51 female patients in the age range 16–84 y,

with the average age 47.2 ± 17.2 y. The TP group included 64 male patients and 42 female patients in the age range 16–84 y, with the average age 44.4 ± 17.5 y. The CP group included 17 male patients and 9 female patients in the age range 38–73 y, with the average age 58.7 ± 9.7 y. In the TP group, 61 cases were confirmed as TP on bacterial cultivation from the pleural effusion, 35 cases were confirmed by needle biopsy histology of the primary lung disease and 10 cases were confirmed by biochemical analysis of the pleural effusion. In the CP group, 14 cases were confirmed by needle aspiration and cytologic analysis of the pleural effusion, 8 cases were confirmed by needle biopsy histology of the primary lung disease and 4 cases were confirmed by needle aspiration cytology of the primary lung disease. This study was approved by the institutional review board of Shandong Provincial Chest Hospital, and informed consent was obtained from all patients.

Imaging procedure

All patients were imaged with a GE VIVID E9 ultrasound system (GE Medical Systems, Horten, Norway). The transducer frequency was 2.5–5.0 MHz. During the scan, the patient sat with his or her back to the sonographer, the upper body slightly leaning forward and the back adequately exposed. The scan was performed along each intercostal space from the spine to the sternum with a whole range covering the region from the inlet of the thorax to the lower boundary of the thoracic cavity. The sample frame was identical for all the patients. The default settings of the ultrasound machine were as follows: color gain, 70%; 2-D gain, 80%; color write priority, 7; wall filter, 83 Hz; pulse repetition frequency, 700 Hz; focus, 1.4 cm; and color box size, 1 × 1 cm in the fundamental imaging mode (Wang et al. 2011). The unenhanced CT scan was performed on a multidetector row CT scanner (Siemens Somatom Sensation 16, Erlangen, Germany). All patients were trained to hold their breath before the scan. The patients assumed supine and head first position. The scan range covered the region from the inlet of the thorax to the posterior costophrenic angle including the whole thorax. Parameters of the CT scan were as follows: 300-mA tube current, 120-kV tube voltage, 5-mm collimation, 5-mm reconstructed slice thickness, pitch 1.75 and display matrix 512 × 512. The source images were transferred to and interpreted on the integrated workstation. The ultrasonography examination and CT scan were conducted within a 4-d interval.

Image interpretation

On CT scan, pleural calcification was defined to be dot-like, nodule-like, linear, or irregular foci of high density of 80–300 Hounsfield Units (HU) located on the pleura. On GSU, calcification was defined as strong echogenic foci with or without posterior acoustic shadowing. TA on color Doppler imaging was defined as the presence of a rapidly changing mixture of red and blue colors behind a strongly reflective structure. A positive result of gray-scale ultrasonography combined with twinkling artifact (GSUTA) was either the presence of a strong echogenic mass with posterior acoustic shadowing or the presence of a rapidly changing mixture of red and blue colors behind a strongly reflective structure.

Statistical methods

The numbers of patients diagnosed as positive and negative with different imaging methods were documented and compared on a per-case basis. The differences in detection rate between imaging methods were calculated using the McNemar χ^2-test for paired nominal scale data. The difference in positive cases detected by GSUTA in the TP and CP groups was calculated using the Pearson χ^2-test. All statistical procedures and tests were performed using SPSS software Version 21 (IBM, Armonk, NY, USA), and $p < 0.05$ was considered to represent statistical significance.

RESULTS

Of the 49 cases positive on CT, GSU detected 63.3% (31/49), TA detected 79.6% (39/49), and GSUTA detected 83.7% (41/49) of positive cases with pleural calcification. The detection rates of TA and GSUTA were both significantly higher than that of GSU ($p = 0.039$ and $p = 0.002$, respectively). Twenty-nine cases were positive at both GSU and TA (Fig. 1). No difference was found between GSUTA and TA ($p = 0.500$) (Tables 1 and 2). For the total of 132 cases with TP and CP, CT yielded a positive rate of 37.1% (49/132), significantly higher than that of GSU (25.8%, 34/132) ($p = 0.001$), but not different from that of TA (41.7%, 55/132) ($p = 0.327$). With CT as reference standard, the sensitivity, specificity, accuracy, positive predictive value and negative predictive value of TA were 79.6% (39/49), 80.7% (67/83), 80.3% (106/132), 70.9% (39/55) and 87.0% (67/77), respectively. The false-positive rate was 29.1% (16/55) (Table 3). The detection

Table 1. Comparison of GSU and TA in detection of pleural calcification in CT-positive cases

	TA		
GSU	Negative	Positive	Total
Positive	2	29	31
Negative	8	10	18
Total	10	39	49

CT = computed tomography, GSU = gray-scale ultrasonography, TA = twinkling artifact.
Values are numbers of cases.