Contrast enhanced ultrasonography (CEUS) in peripheral lung lesions: A study of 60 cases

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KEYWORDS

Bronchopneumonia;
Pulmonary neoplasia;
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Abstract *Introduction:* The authors report their experience in 60 patients with infectious and neoplastic peripheral pulmonary lesions studied by conventional radiology, B-Mode ultrasound (US) and computed tomography (CT). In view of the particular pulmonary vascularization (consisting of both pulmonary and bronchial arteries) the patients underwent also contrast enhanced ultrasound (CEUS) using a II-generation contrast agent, SonoVue (sulphur hexafluoride microbubbles surrounded by a phospholipid shell).

Methods and results: In this study, the sensitivity of CEUS reached 95% in the characterization of peripheral pulmonary lesions, which is similar to the sensitivity of CT (97%). The method used in this case-study was free of significant side effects.

Discussion: This preliminary clinical experience seems to confirm the possibility of using SonoVue enhanced US to make a differential diagnosis between infectious and neoplastic lesions based on a qualitative and quantitative assessment, by evaluating the enhancement pattern (homogeneous or inhomogeneous), arrival time of the contrast agent in the lesion, the possibility to identify the pulmonary arteries and time of contrast agent elimination.

Sommario *Introduzione:* Gli autori riportano la loro esperienza in 60 pazienti con patologia polmonare periferica, infettiva e neoplastica, studiati con la radiologia convenzionale, ecografia B-Mode, TC e data la peculiare vascularizzazione con l'ecografia con mezzo di contrasto di II generazione (SonoVue).

Metodi e risultati: La sensibilità di questa metodica in questo lavoro raggiunge nella caratterizzazione delle lesioni polmonari periferiche il 95%, percentuale molto simile a quella della TC polmonare. La metodica non è stata complicata da effetti collaterali.

Discussione: Questa preliminare esperienza sembra mostrare la possibilità di poter usare SonoVue nella diagnosi differenziale tra lesioni periferiche polmonari sia infettive che neoplastiche, mediante valutazioni qualitative e quantitative, come la presenza di un enhancement omogeneo o disomogeneo, il tempo di arrivo del mezzo di contrasto nella

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lesione, la possibilità di evidenziare le arterie polmonari ed il tempo di eliminazione del mezzo di contrasto.

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Introduction

Ultrasound (US) examination of the thorax is considered difficult because of obstacles caused by air and ribcage. However, the use of convex 3.5–5 MHz and linear 7.5–10 MHz probes provides subcostal, intercostal, suprasternal and parasternal access routes, thus making it possible to study diaphragm, pleura, lungs and the anterior and middle mediastinum.

In fact, US is increasingly being used for detecting and following the clinical evolution of infectious pathologies, such as pleuritis, empyema, pneumonia, bronchopneumonia, parasitic cysts, mediastinal lymphadenitis and abscesses of the thoracic wall, as well as primary or secondary neoplastic pathologies of the pleura with or without pleural effusion, peripheral pulmonary neoplasia, embolism, atelectasis, thymoma, mediastinal lymphoma and neoplasia of the thoracic wall [1–3]. US has furthermore recently been used in pulmonary edema, interstitial pathologies and pneumothorax [4–7].

Among the peripheral pulmonary pathologies, pneumonia and bronchopneumonia may present some suggestive, although non-diagnostic, aspects characterized by triangular and roundish lesions with images of air bronchogram, sometimes with a liver-like appearance and increased vascularization with a high-impedance flow and reversed diastolic flow in the branches of the pneumonic arteries. In some studies US has reached high indices of sensitivity and specificity in pneumonia and bronchopneumonia [8,9].

Most cases of pulmonary neoplasia appear as hypoechoic lesions with irregular and blurred contours, absence of air bronchogram, and reduced vascular flow, sometimes no vascular flow in the central part and characterized by a low-impedance monophasic arterial flow profile because most of the pulmonary arteries are invaded by the neoplasia while neoangiogenesis originates from the bronchial arteries [10–14].

However, these US findings may not always be present in bronchioloalveolar carcinomas, whose intense vascularization could originate not only from neoangiogenesis, but also from the pulmonary arteries [15].

The pulmonary vascularization is particular since the parenchyma is reached by the pulmonary arteries bringing venous blood useful for gaseous exchange, and by the bronchial arteries bringing arterial blood necessary for parenchymal nutrition. The pulmonary arteries give way to the pulmonary veins carrying arterial blood to the left side of the heart, while the bronchial arteries give way to the bronchial veins. This means that intravenously injected contrast agent reaches the lung in the early phase via the pulmonary arteries and immediately thereafter via the bronchial arteries and is eliminated in the late phase via both the pulmonary and bronchial veins.

In this study, we assume that infectious pathologies present intense pulmonary and bronchial vascularization,

while neoplastic lesions present neoangiogenesis originating mainly from the bronchial arteries, often with chaotic vascularization and arteriovenous anastomosis.

We therefore used contrast enhanced ultrasound (CEUS) to evaluate 60 patients with peripheral pulmonary lesions, using the II-generation contrast agent SonoVue (sulphur hexafluoride microbubbles surrounded by a phospholipid shell) to identify US signs characterizing neoplastic lesions and infectious pulmonary pathology.

Materials and methods

From January 2003 to December 2005, 60 patients with peripheral pulmonary lesions visible at US were evaluated in our Division of Infectious Diseases: 34 patients were males and 26 females, mean age 56 years (range 18–84 years). Of these patients 33 had a lesion located on the right side, 27 on the left side, and three on both sides of the thorax, with dimensions between 3 and 6 cm; 6 were HIV positive and 4 were affected by non-pulmonary neoplasia. Written informed consent was obtained from all patients, and the procedures followed were in accordance with the ethical standards of the Committee on Human Experimentation of this institution.

At conventional radiography and B-mode US all patients presented a peripheral pulmonary lesion. All patients underwent multidetector helical computed tomography (CT) of the lung using contrast agent, Mantoux test, urinary antigen test for *Legionella* and *Pneumococcus*, sputum culture (to assess the presence of common germs, mycobacteria and atypical cells), and serology for *Legionella*, *Chlamydia pneumoniae*, *Coxiella burnetii* and mycoplasma.

In 24 patients with suspected pulmonary neoplasia, a US-guided biopsy of the lesion was performed after a negative bronchoscopy, using a 19 Gauge automatic needle.

Before therapy, all patients were evaluated with CEUS using the II-generation contrast agent, SonoVue (Bracco Imaging Srl, Milano, Italy). SonoVue consists of microbubbles filled with sulphur hexafluoride and covered by a stabilizing phospholipidic membrane. The patients were in supine position, and contrast agent was administered intravenously: 2.4 ml bolus injection followed by a flush of saline solution. The examination was carried out using a 3.5 MHz convex probe with a low mechanical index.

The contrast distribution in the lesions was observed in real-time for the first 60 s and then at 120, 180, 240 and 300 s. In view of the particular pulmonary vascularization, the examination was divided into two phases: early (0–120 s) and late (over 120 s).

In the early phase, we recorded the time required by the contrast agent to reach the lesion, the type of enhancement (homogeneous, inhomogeneous, spots, points, rings), and the presence of areas that did not take up contrast agent or showed reverberation artifacts inside the lesion. In the early phase, we observed the distribution of the contrast agent through the pulmonary arteries, while in the late phase we observed the elimination of the contrast agent and measured the duration of the washout phase.

According to the different hemodynamic behaviors described in infectious and neoplastic diseases, the following CEUS patterns were defined in order to differentiate infectious from neoplastic conditions.

- (A) Neoplastic lesions (presence of at least two US signs):
1. inhomogeneous enhancement in the first 10–15 s (spots, points, rings);
 2. absence of linear hyperechogenic image due to pulmonary arterial enhancement;
 3. rapid washout occurs in the early phase (Figs. 1a–d and 2a, b).
- (B) Infectious lesions (presence of at least two sonographic signs):
1. homogeneous enhancement within the first 10 s;
 2. evidence of pulmonary arteries, observed as linear hyperechogenic images with greater enhancement compared to the parenchyma;
 3. rapid washout occurs in the late phase (Figs. 3a–c and 4a–c).
- (C) The presence of areas without contrast agent inside homogeneous or inhomogeneous lesions, in either the early or late phase, was interpreted as necrotic–abscessual alterations (abscesses, tuberculous caverns, tumoral necrosis).
- (D) The presence of reverberation artifacts inside homogeneous or inhomogeneous lesions, in either the early or late phase, was interpreted as air or gas inside the lesions, i.e. the expression of abscesses originating from anaerobic or tuberculous caverns.

Possible pleural and/or pericardial effusions were also evaluated.

Results

Of the 60 patients, 40 had an infectious disease, 18 had neoplasia, 1 had pulmonary inflammatory pseudotumor, and 1 had infarction. The cases of neoplasia and

pseudotumor were diagnosed by biopsy, while infectious pathologies were diagnosed by sputum culture and serology, except in 5 cases (4 cases of abscess and 1 of bronchopneumonia) which were diagnosed by biopsy.

CEUS pattern in the 60 lesions

Enhancement of the lesion

In the early phase, CEUS enhancement was described as homogeneous in the first 10 s in 35 patients: 33 cases of bronchopneumonia, 1 of pulmonary adenocarcinoma and 1 of pulmonary inflammatory pseudotumor. CEUS enhancement was inhomogeneous in 20 patients: 3 cases of pneumonia, 15 of primary pulmonary neoplasia, 2 of metastasis. In 4 lesions with homogeneous enhancement there were areas lacking contrast agent in 2 cases and intralesional reverberation artifacts in the other two: 2 cases of pulmonary abscess and 2 of tubercular cavern.

Visibility of pulmonary arteries

The pulmonary arteries were visible in 30 patients: 29 cases of bronchopneumonia and 1 of adenocarcinoma (Fig. 5).

CEUS washout

CEUS early washout, i.e. within the first 120 s occurred in 15 cases of primary neoplasia, 2 of metastasis and in the patient with pulmonary inflammatory pseudotumor, while prolonged CEUS washout after 120 s occurred in 31 cases of bronchopneumonia, in 4 lesions with areas lacking contrast agent or with artifacts, and in 1 case of primary

Fig. 1 (a) Left anterior intercostal scan: left anterior peripheral pulmonary lesion with a roundish shape and hypoechogenic echostructure, 58 mm (calipers), absence of air bronchogram, irregular and blurred contours. (b) Left anterior intercostal scan: the left anterior peripheral pulmonary lesion does not show vascular signals at Power–Doppler. (c) Left anterior intercostal scan with contrast ultrasound: 20 s after injection of SonoVue, there is inhomogeneous enhancement at the periphery (arrows) of the left anterior pulmonary lesion with a ring appearance. (d) Left anterior intercostal scan with contrast ultrasound: 2 min after injection of SonoVue, the left anterior peripheral pulmonary lesion appears hypoechogenic due to almost complete loss of contrast agent. US-guided biopsy confirmed the CEUS suspicion of peripheral pulmonary neoplasia.

Fig. 2 (a) Right subclavicular intercostal scan: right peripheral pulmonary lesion with irregular triangular shape and inhomogeneous hypoechogenic echotexture with irregular and blurred contours (arrows). (b) Right subclavicular intercostal scan with contrast ultrasound: 30 s after injection of SonoVue, the left anterior peripheral pulmonary lesion shows an inhomogeneous punctiform enhancement (arrows). US-guided biopsy confirmed the CEUS suspicion of peripheral pulmonary neoplasia.

Fig. 3 (a) Right subclavicular intercostal scan: right subscapular peripheral pulmonary lesion, roundish with hypoechogenic echotexture (arrows) with reverberation artifacts due to air bronchogram. (b) Right subclavicular intercostal scan with contrast ultrasound: 15 s after injection of SonoVue, the right subclavicular peripheral pulmonary lesion shows homogeneous enhancement (white arrows) with an intensely echogenic tubular internal structure (black arrow) caused by enhancement of the bronchial artery. (c) and (d) Right subclavicular intercostal scan without and with contrast agent: 4 min after injection of SonoVue, the right subclavicular peripheral pulmonary lesion (arrows) still shows the presence of contrast agent (d). Pulmonary CT, positive urinary *Pneumococcus* antigen test and complete resolution after antibiotic therapy confirmed the CEUS suspicion of bronchopneumonia.

Fig. 4 (a) Left anterior intercostal scan: left anteroinferior peripheral pulmonary lesion with triangular shape and hypoechogenic echostructure with reverberation artifacts (due to the presence of air bronchogram) and well-defined irregular contours but delimited by a hyperechogenic margin (arrows). (b) Left anterior intercostal scan with contrast ultrasound: 16 s after injection of SonoVue, the left anteroinferior peripheral pulmonary lesion shows homogeneous enhancement (white arrows) with two hyperechogenic tubular internal structures depicting the pulmonary arteries (black arrows). (c) Left anterior intercostal CEUS scan: 5 min after injection of SonoVue, the left anteroinferior peripheral pulmonary lesion (arrows) still shows the presence of contrast agent. CT, seroconversion for *Chlamydia pneumoniae* and complete resolution after antibiotic therapy confirmed the CEUS suspicion of bronchopneumonia.

Fig. 5 Right anterior intercostal scan with contrast ultrasound: patient with pneumonia from *Pneumococcus* evaluated 8 s after injection of SonoVue. There is intense enhancement of the pulmonary arteries (arrows) which in this case are well visible before enhancement of the pulmonary parenchyma.

neoplasia. One lesion failed to take up contrast agent in either CEUS phase.

The 3 CEUS signs indicating an infectious pathology (homogeneous enhancement within 10 s, presence of pulmonary arteries, elimination of contrast agent after 120 s) were recorded in 29/40 patients with infectious disease (72.5%).

The 3 signs indicating a neoplastic pathology (inhomogeneous enhancement, absence of pulmonary arteries, elimination of contrast agent within the first 120 s) were recorded in 16/18 patients with neoplastic lesions (88.8%) (Table 1).

Therefore, a total of 45 lesions were correctly characterized as benign or malignant using the 3 diagnostic criteria patterns in question.

The finding of at least two CEUS criteria patterns allowed us to diagnose 57 of the 60 lesions correctly (95.0%): 35/36 cases of bronchopneumonia (97.22%), 17/18 of neoplastic lesion (94.44%), 4/4 of necrotic infectious lesion (2 of abscess and 2 of tuberculous cavern) and 1 infarction.

A pulmonary inflammatory pseudotumor was interpreted as a neoplastic lesion; there was homogeneous enhancement but absence of pulmonary arteries, and washout occurred within the first 120 s.

Table 1 Correlation between pulmonary pathology and CEUS: hemodynamic distribution in the lesions

CEUS	Pneumonia	Neoplasm	Abscess/cavern	Infarction	Pseudotumor
Homogeneous enhancement <10 s	33	1	4 (Around the lesions)	0	1
Inhomogeneous enhancement >10 s	3	17	0	0	0
Visibility of the pulmonary artery	29	1	0	0	0
CEUS early washout <120 s	0	17	0	0	1
CEUS prolonged washout >120 s	31	1	4	0	0
Complete lack of enhancement	0	0	0	1	0
Area with absence of enhancement	0	0	2	0	0
Reverberation artifacts inside the lesion	0	0	2	0	0

A bacterial bronchopneumonia which presented inhomogeneous enhancement and absence of pulmonary arteries was diagnosed as a neoplastic lesion. Moreover, an infectious pathology was suspected in a patient with bronchioloalveolar carcinoma due to homogeneous enhancement and prolonged washout but absence of pulmonary vessels.

CEUS provided the correct diagnosis in 95% of the cases

B-Mode US correctly diagnosed 50/60 lesions: it failed to diagnose the infarction, the pseudotumor and 3 cases of bronchopneumonia, which did not present air bronchograms and ample vascularization at color-Doppler, while 2 cases of metastasis and 3 of bronchioloalveolar carcinoma were diagnosed as infectious lesions because of the presence of air bronchograms in the 3 cases of bronchioloalveolar carcinoma and ample vascularization in all 5 cases.

Conventional radiology provided a correct diagnosis in 52/60 lesions (86.66%): it was not diagnostic in 1 patient with pseudotumor and 1 with infarction, in 2 patients with bronchopneumonia (suspected to be neoplastic lesions), in the 3 patients with bronchioloalveolar carcinoma and in 1 with adenocarcinoma (in whom an infectious pathology was suspected).

CT provided a correct diagnosis in 58/60 lesions (36/36 cases of bronchopneumonia, 17/18 of neoplasia, 2/2 of abscess, 2/2 of tuberculous cavern, 1/1 of infarction), but it suggested bronchopneumonia in the patient with the pulmonary inflammatory pseudotumor and a tuberculous pathology in an HIV positive patient with pulmonary adenocarcinoma.

Sensitivity of the 4 diagnostic methods was the following: CEUS 95.0%, CT 96.66%, B-Mode ultrasound 83.33% and conventional radiology 86.66%.

CEUS using II-generation contrast agent also detected 8 cases of pleural and 3 of pericardial effusion, whereas CT identified 8 cases of pleural and 2 of pericardial effusion, B-mode US identified 7 cases of pleural and 1 of pericardial effusion, and conventional radiology 5 cases of pleural and no case of pericardial effusion.

Mild side effects were observed in less than 5% of the CEUS examinations, including burning during injection of contrast agent in 2 cases and dizziness at the end of the examination in 1 patient.

US-guided biopsy was carried out in 24 patients with pulmonary lesions using an automatic 19 Gauge, 15 cm

needle; biopsy was performed after a non-diagnostic bronchoscopy.

Biopsy was performed in 19 patients whose CT outcome was uncertain; in 18 cases biopsy confirmed a malignant neoplastic lesion (6 cases of adenocarcinoma, 6 of squamous cell carcinoma, 3 of bronchioloalveolar carcinoma, 2 of metastasis and 1 of non-small-cell anaplastic carcinoma), and in one patient a pulmonary pseudotumor was diagnosed.

In 5 patients (3 with bronchopneumonia and 2 with cavity lesions) microbiological culture of biopsy samples yielded 2 cases of coagulase-positive *Staphylococcus*, 1 of *Mycobacterium tuberculosis* complex, 1 of *Pneumococcus* and 1 of *Pseudomonas* spp., being diagnostic in 95.83% of cases (23/24).

US-guided pulmonary biopsy did not cause major complications, only 1 case of non-hypertensive pneumothorax which resolved without treatment. Therefore, the incidence of minor complications was 4.1%.

Sputum culture was positive in 8 patients, pneumococcal antigen in 9 and *Legionella* antigen in 2. Two patients presented seroconversion for *C. pneumoniae*.

The etiological diagnosis of pneumonia/bronchopneumonia was possible in 26/36 patients (72.22%), particularly in all the patients (4) who had abscess and pulmonary cavern.

All 40 patients with infectious lesions (36 cases of bronchopneumonia, 2 of abscess and 2 of tuberculous cavern) and the patient with pulmonary infarction showed clinical–radiological resolution after appropriate treatment. The 16 patients with primary pulmonary neoplasia underwent surgery, which confirmed the diagnosis; the 2 patients with pulmonary metastases showed subsequent progression of the neoplastic pathology, while the pseudotumor spontaneously resolved.

Discussion

The incidence of pneumonia and bronchopneumonia varies from 30 to 40 cases per 100,000 inhabitants per year. It is 6 times higher in drug addicts and before the introduction of highly active antiretroviral therapy (the pre-HAART era) it affected 4% of AIDS patients [16]. Although the decline in the number of smokers has led to a reduction in lung tumor incidence, this is still the most frequent neoplastic pathology in industrialized countries, with an increase in women due to the growing number of young female smokers in recent years.

Conventional radiology is the first-choice examination in thoracic pathology, but CT is often necessary in small lesions, for a differential diagnosis between alveolar and interstitial pneumonia, and in most cases between infectious and neoplastic pathologies [17].

US is increasingly used in pulmonary infectious diseases, since most alveoli have a subpleural distribution: the bronchoalveolar apparatus branches out peripherally, being distributed mainly near the surface of the thorax, and alveolar inflammatory processes, like pneumonia and bronchopneumonia, are characterized by the production of fibrino-purulent exudate that occupies both the small bronchi and the corresponding alveoli [18].

These two important anatomical–pathological conditions suggest the use of US in these pathologies. Bronchopneumonia and pneumonia, which fill and consolidate the alveoli close to the thoracic wall, can be distinguished by hyperechogenicity of the reverberation caused by air [8,9].

US is also indicated in the search for and characterization of primary and secondary pulmonary peripheral neoplastic lesions. Peripheral pulmonary carcinomas include adenocarcinoma, squamous cell carcinoma, bronchioloalveolar carcinoma and large-cell anaplastic carcinoma, while microcytoma has a mainly hilar location with peribronchial growth. These neoplastic pathologies are situated subpleurally near the thoracic wall and can be revealed by US [19].

The US signs of pneumonia and bacterial bronchopneumonia are hypoechogenic lesions with an air bronchogram, intense vascularization at color-Doppler, and a high impedance flow and reversed diastolic flow in the branches of the pneumonic arteries.

The US pattern is characterized by roundish or triangular subpleural hypoechogenic lesions with or without fine internal echoes, i.e. air bronchogram, and delimited by a clear echogenic line or by triangular hypoechogenic formations containing asonic canalicular formations, due to the presence of vessels, and linear hyperechogenic structures with comet-tail reverberation artifacts indicative of air bronchogram. Also in this case, the lesions are delimited by an echogenic margin representing compressed lung tissue.

From the anatomical–pathological point of view, the massive parenchymal consolidation caused by pneumonia is the cause of hepatization, and it can result in a liver-like picture with or without air bronchogram.

The sensitivity of US in pneumonia and bronchopneumonia is very high, reaching 90–100%. There is also a high sensitivity for pulmonary abscess and pathologies affecting the anterior mediastinum, even though the overall specificity is not very high.

Pulmonary neoplasia does not have a specific sonographic pattern and can appear as hypoechogenic, hypoanechogenic, hypo/hyperechogenic or inhomogeneous lesions of about 5–15 cm with irregular and blurred contours, absence of air bronchogram, and irregular vascularization with high velocity and high resistance.

The sensitivity of US is high in peripheral neoplastic lesions, but the specificity is low because some types of carcinoma, e.g. bronchiolo-alveolar, can show images of air bronchogram, and the acoustic impedance at Doppler analysis can be either high or low.

In these pathologies, CT is the imaging method with highest diagnostic accuracy. In fact, the non-specificity of

the signs in conventional radiology and B-Mode US can make it difficult to differentiate neoplastic lesions from infectious pathologies to the point that US- or CT-guided pulmonary biopsy is often required [20].

However, the lung has a particular vascularization: the organ is supplied by the pulmonary arteries, carrying venous blood for gaseous exchanges, and the bronchial arteries, which arise from the aorta and provide arterial blood for nutrition of the pulmonary tissues. Therefore, contrast agent will appear quickly in the pulmonary lesion via the pulmonary arteries (generally in the first 8–10 s) and a few seconds later via the branches of the bronchial arteries, and it will be eliminated quickly via both the pulmonary veins and bronchial veins.

In bacterial pneumonia and bronchopneumonia, the alveoli fill with fibrinopurulent material, preceded and followed by expansion and permeabilization of the vessels involved in the inflammatory process. For this reason, II-generation contrast agent shows a rapid, intense and homogeneous enhancement in the early phase, beginning as early as 8–10 s after injection. In this phase, the pulmonary artery also appears as a hyperechogenic tubular structure with greater enhancement than the pulmonary parenchyma [21,22]. The washout begins after 2–3 min and is complete within 5–6 min.

In neoplasia, the nutritional input is in most cases due to neoangiogenesis deriving from the bronchial arteries, since the pulmonary arteries have a low angiogenetic capacity. Moreover, the pulmonary tissue involved by the neoplasia shows invasion of the pulmonary arteries in 56–87% of cases, and the vascularization of the central part of the tumor is clearly reduced or absent because of stenosis and obstruction of the pulmonary arteries.

These considerations, and the often anarchic neoangiogenesis and arteriovenous anastomosis of these tumors, explain the later distribution of contrast agent in a neoplastic lesion (10–15 s) compared to an infectious lesion. Distribution is also irregular showing inhomogeneous enhancement (punctiform, spotted, ringed), and contrast agent is eliminated within 120 s. The neoplastic lesion returns to being hypoechogenic in the early phase [23,24].

In a previous retrospective study [25], 137 patients with peripheral pulmonary lesions were evaluated with CEUS considering three parameters: contrast enhancement time (short <6 s, delayed >6 s), extent of enhancement comparing to the splenic parenchyma, and homogeneous or inhomogeneous enhancement. These three dynamic parameters did not vary significantly in malignant and benign lesions, and in this study CEUS did not provide a distinction of benign from malignant pleural-based lesions [25].

In the present study, another dynamic parameter was evaluated: contrast agent washout time. Our results demonstrate the high diagnostic accuracy of the technique, as malignant lesions are characterized by a rapid washout time (<120 s) compared to benign lesions (>120 s). Moreover, another important element allowing distinction between neoplastic and infectious disease is the appearance of a great contrast enhancement from the pulmonary arteries which is a US sign of infectious lesions.

The diagnosis of bronchioloalveolar carcinoma is difficult even using CEUS, while diagnosis of the rare inflammatory pseudotumor of the lung is impossible: only US-guided biopsy can remove the diagnostic doubt.

In this preliminary study of peripheral pulmonary lesions, the diagnostic accuracy of CEUS was comparable to that of CT and very much higher than conventional radiology and B-Mode US. CEUS is not an alternative to CT, however, if these data are confirmed CEUS may become a diagnostic method which is useful in the differential diagnosis between infectious and neoplastic lesions (particularly in patients in whom iodized contrast agent is contraindicated), as well as in the rapid diagnosis of abscessualization of infectious and neoplastic pulmonary pathologies, to reveal necrotic areas and to guide sampling procedures and biopsies.

Conclusions

The use of II-generation contrast agent is useful in peripheral pulmonary lesions, since there is a substantial divergence between neoplastic and non-neoplastic vascularization. Moreover, it can easily reveal avascular lesions (infarction, cysts, necrotic areas). CEUS may be useful in the differential diagnosis between bronchopneumonia and neoplastic lesions, as well as in revealing neoplastic and inflammatory areas of necrosis and avascular lesions, such as in infarction. Finally, it is useful in the guidance of sampling procedures.

Conflict of interest

The authors have no conflict of interest.

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