rax was observed which required the placement of a chest tube, as the patient had developed dyspnea. He subsequently presented with moderate right pleural effusion, treated by ultrasound-guided pleural drainage on February 28th, 2017. During the procedure, pulmonary CEUS was performed to assess a potential infection in the lesion treated with RFA. The lesion showed no contrast uptake throughout the examination; this finding was suggestive of necrosis, indicating a complete response to RFA (Fig. 1C). Subsequent CT and PET-CT monitoring confirmed complete response to date (January 10th, 2019) (Fig. 1D).

CEUS has been shown to be a comparable alternative to CT and MRI in the evaluation of the response of neoplastic lesions treated with RFA, particularly in liver and kidney disease.[6,7] In pulmonary CEUS, entities such as pulmonary infarctions or necrosis tend not to show contrast uptake during the entire examination,[8] so in the post-RFA CEUS follow-up contrast enhancement would not be expected in lesions with complete response. Given the increasing use of RFA as alternative treatment to surgical resection in patients with oligometastatic or primary early-stage lung disease and the difficulty of detecting early recurrences by CT and PET-CT,[5] pulmonary CEUS may be a complementary tool in the post-treatment monitoring of subpleural lesions accessible to ultrasound evaluation, especially when CT and PET-CT assessment are unclear. In addition, pulmonary CEUS may be useful to guide the biopsy of subpleural lesions in which recurrence is suspected.[9]

A factor limiting the evaluation of lung lesions by CEUS may be the lack of scientific literature available for the characterization of the different histological types of lung tumors, since only retrospective studies are available.[10] As such, since the expected pretreatment appearance of lung lesions has not been established, it is difficult to compare them with the post-treatment image.

This is the first reported case of response assessment of percutaneous pulmonary treatment with CEUS. Additional studies are required to prove the usefulness of this technique in this context.

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Bronchial Infection due to *Pseudomonas Aeruginosa* in Patients with Cystic Fibrosis Diagnosed in Neonatal Screening☆

Infección bronquial por Pseudomonas aeruginosa *en los pacientes con fibrosis quística diagnosticados por cribado neonatal*

Dear Editor,

Chronic *Pseudomonas aeruginosa* lung infection is the most important risk factor for a poor respiratory outcome in patients with cystic fibrosis, and is associated with higher morbidity and mortality, which is worse the earlier it occurs.[1–4]

Eradication of the pathogen is essential to avoid chronic colonization, but this can only be achieved in the early stages, so it is essential that the infection is diagnosed early and treated intensively in order to prevent progression to chronicity.[5–7]

In Spain, newborn screening (NBS) began in 1999 in Catalonia, Castilla-León and the Balearic Islands, and in 2015 it was extended to all communities.[8] The diagnosis of cystic fibrosis in the neonatal period allows the early detection of the primary bronchial infection with *P. aeruginosa*. If intensive and persistent treatment is established as soon as this pathogen is isolated, eradication can be achieved in most cases and chronic colonization can be delayed, improving survival.[9–11]

The main objective of this study was to describe the prevalence of primary infection, intermittent infection, and chronic infection with *P. aeruginosa* (according to Leeds criteria[12]) in patients with cystic fibrosis diagnosed by newborn screening (D-NBS) compared with patients not diagnosed by neonatal screening (ND-NBS) who are being or who have been followed up in our Pediatric Cystic Fibrosis Unit. The secondary objective was to describe the prevalence in both groups in terms of mutations.

This was a retrospective descriptive study that included all patients diagnosed with cystic fibrosis before the age of 18 years from 1985 to 2018. We compared D-NBS with ND-NBS patients (including false negatives on NBS). Patients were sub-classified as no function (NF): patients with 2 mutations with no or minimal CFTR function (group I, II or III mutations), and residual function (RF): patients with a mutation with no or minimal CFTR function

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Table 1
Characteristics of Patients Diagnosed With Cystic Fibrosis by Newborn Screening and Those Not Diagnosed by Newborn Screening.

	D-NBS	ND-NBS
Patients (*n*)	56	26 (2 false negatives per NBS)
Mean age at diagnosis	1.5 months	4.38 (0.13–15)
Current mean age in years	10.38 (0.8–18)	21.5 (5–36)[a]
Sex n (%)	Male: 33 (58.9) Female: 23 (41.1)	Male: 13 (50) Female: 13 (50)
Lung transplantation	0	5
Deceased	0	8
NF group *n* (%)	36 (64.28)	19 (73)
RF group *n* (%)	20 (35.71)	7 (26.92)

D-NBS: diagnosed by newborn screening; NBS: newborn screening; ND-NBS: not diagnosed by newborn screening; NF: no function, patients with 2 mutations with no or minimal CFTR function (group I, II or III mutations); RF: residual function, patients with a mutation with no or minimal CFTR function and a mutation with residual CFTR function (group IV, V, VI or VII mutation) or patients with 2 mutations with residual CFTR function.

[a] Although the current age is 21.5 years, respiratory secretion cultures were only reviewed up to the age of 18.

and a mutation with residual CFTR function (group IV, V, VI, or VII mutation) or 2 mutations with residual CFTR function. Table 1 summarizes the characteristics of both patient groups.

Patients' medical records and all cultures of respiratory secretions (from birth to age 18 or January 2018 if they were younger) were reviewed. Cultures were performed monthly and, when positive, weekly until negativization. The treatment used for *P. aeruginosa* primary bronchial infection was inhaled colistin, tobramycin, or aztreonam (3–6 months) along with oral ciprofloxacin (3 weeks). In chronic infections, continuous inhaled treatment with colistin or 28-day on-off cycles with tobramycin or aztreonam were prescribed. During mild-moderate exacerbations, treatment was oral ciprofloxacin (2–3 weeks) and in severe exacerbations, intravenous (β-lactam combined with an aminoglycoside according to sensitivity testing) therapy was administered.

From a statistical perspective, quantitative variables were described by mean and range, and qualitative variables by relative and absolute frequencies. The χ^2 test was used to compare prevalences between groups.

Table 2 shows the prevalences of *P. aeruginosa* infection in both D-NBS and ND-NBS patients, and in the NF and RF patient subgroups.

A comparison of the prevalences of *P. aeruginosa* infection between D-NBS and ND-NBS patients revealed statistically significant differences in primary infection (*P*=.0014), intermittent infection (*P*<.001), and chronic infection (*P*<.001). This may be due in part to age differences between the 2 groups, since the mean age of the D-NBS patients was 10.38 years and the ND-NBS patients were followed up to the age of 18 years.

Patients with more severe mutations (NF group) diagnosed by neonatal screening had a higher prevalence of primary *P. aeruginosa* infection than the RF group (*P*=.018). It should be noted that none of the patients in the RF group (neither D-NBS nor ND-NBS) had chronic *P. aeruginosa* infection.

Of the D-NBS patients, 53.57% (30/56) had *P. aeruginosa* infection at some time. Mean age at the time of primary infection was 6 years and the eradication rate was 100%. The median time between first and second infection was 29 months (range: 1.4–96.8). Only 1.78% (1/56) of this group had chronic infection.

Of the ND-NBS patients, 92.30% (24/26) had *P. aeruginosa* infection at some time. Overall, 19.23% (5/26) already had chronic infection at diagnosis, without eradication. The mean age at diagnosis of these 5 patients was 5.66 years, whereas the mean age at diagnosis for the whole group was 4.38 years. Another 19.23% (5/26) had intermittent infection at diagnosis, but this eventually became chronic. In total, 38.46% (10/26) of this group had chronic infection.

Our results are consistent with other publications, which also show a decrease in the prevalence of chronic *P. aeruginosa* infection after the introduction of neonatal screening.[13–15] In Canada,[13] the prevalence of chronic *P. aeruginosa* infection was 28.4% in D-NBS and 61.8% in ND-NBS patients (*P*<.001). In the United Kingdom,[14] prevalence in children under 15 was 16% in the D-NBS and 20% in the ND-NBS group. The 2018 American Cystic Fibrosis Foundation registry shows that 46.2% of cystic fibrosis patients under the age of 18 had *P. aeruginosa* infection (17% intermittent and 28.3% chronic) with a median age at primary infection of 5.2 years.[15] If we compare the results of these publications with ours, we can see that, although all of them show a decrease in the prevalence of chronic

Table 2
Prevalence of *Pseudomonas aeruginosa* infection in patients diagnosed with cystic fibrosis by newborn screening and those not diagnosed by newborn screening.

	Definition According to Leeds[12]	D-NBS	ND-NBS	*P*
Primary infection	First positive culture of *P. aeruginosa*	53.57% (30/56) By group: NF: 66.6% (24/36) RF: 30% (6/20)	92.30% (24/26) By group: NF: 89.4% (17/19) RF: 100% (7/7)	.0014
Intermittent infection	Consecutive cultures intermittently positive and negative after initial infection. Microbiological criteria: ≤50% of cultures positive for *P. aeruginosa* in the previous 12 months	33.92% (19/56) By group: NF: 44.4% (16/36) RF: 15% (3/20)	76.92% (20/26) By group: NF: 84.2% (16/19) RF: 57.1% (4/7)	<.001
Chronic infection	Cultures persistently positive for *P. aeruginosa* with no new clinical signs of infection and with inflammatory response. Microbiological criteria: >50% of cultures positive for *P. aeruginosa* in the previous 12 months	1.78% (1/56) By group: NF: 1.4% (1/36) RF: 0%	38.46% (10/26) By group: NF: 52.6% (10/19) RF: 0%	<.001

They are also analyzed by patient subgroups: NF group: 2 mutations with no or minimal CFTR function (group I, II or III mutations), RF group: a mutation with no or minimal CFTR function and a mutation with residual CFTR function (group IV, V, VI, or VII mutation) or 2 mutations with residual CFTR function.
D-NBS: diagnosed by newborn screening; NBS: newborn screening; ND-NBS: not diagnosed by newborn screening; NF: no function; RF: residual function.

P. aeruginosa infection in D-NBS patients, prevalence in our series is lower. This may be due to very close follow-up, with monthly visits and respiratory secretion cultures, and early and intensive treatment of primary *P. aeruginosa* infection, and also because there are more patients in the RF group.

In conclusion, we observed a change in the natural history of *P. aeruginosa* bronchial infection in cystic fibrosis following the implementation of NBS, with a significant decrease ($P<.001$) in the prevalence of chronic infection with this pathogen in these patients.

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Conflict of interests

The authors state that they have no conflict of interests.

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Acute Respiratory Failure Caused by Pulmonary Lymphangitic Carcinomatosis in a Patient With Lung Adenocarcinoma at Initial Diagnosis

Insuficiencia respiratoria aguda causada por linfangitis carcinomatosa pulmonar en un paciente con adenocarcinoma de pulmón desde el diagnóstico inicial

Dear Editor:

Pulmonary lymphangitic carcinomatosis is associated with poor prognosis and tissue collection is difficult depending on the respiratory condition in such patients.[1] Liquid biopsy could be highly effective and help in addressing the problem of poor prognosis in lymphangitic carcinomatosis patients. Here, we report a case of lung adenocarcinoma with acute severe respiratory failure caused by pulmonary lymphangitic carcinomatosis at initial diagnosis, who could receive appropriate therapy by using liquid biopsy.

A 70-year-old man with a 30 pack-year history of smoking was referred to our hospital with a 1-month history of slight fever and dyspnea on exertion. Initial diagnosis at a previous hospital had indicated bacterial pneumonia accompanied by interstitial pneumonia, which had been treated with an antibacterial drug. Sputum cytology had revealed adenocarcinoma and the patient was referred to our hospital.

On admission, the patient had bilateral inspiratory crackles on chest auscultation. Laboratory findings showed severe hypoxemia and elevated levels of Krebs von den Lungen-6 (KL-6, 2638 U/mL) and carcinoembryonic antigen (CEA, 6.9 ng/mL). Chest X-ray showed a mass shadow in the left hilar region and bilateral diffuse interstitial opacities (Fig. 1A). Computed tomography (CT) imaging revealed a mass in the left upper pulmonary lobe, bilateral diffuse beaded thickening of the intralobular septum, and minor bilateral pleural effusions (Fig. 1 B and C). Performing bronchoscopy was considered difficult because high flow of oxygen (reservoir mask: 6 L/min) was required for severe respiratory failure.

Adenocarcinoma was confirmed by cytological examination of the pleural effusions obtained by left pleural puncture, and epidermal growth factor receptor (EGFR) exon 19 deletion was found in the plasma EGFR gene mutation test at the time of hospitalization. The patient was confirmed for EGFR mutation-positive lung adenocarcinoma accompanied by carcinomatosis lymphangitis and pleurisy, and treatment with osimertinib (80 mg/day) was initiated on the fourth day of admission.

Although respiratory failure exacerbated and noninvasive positive pressure ventilation (NPPV) was required temporarily, respiratory failure resolved and NPPV treatment was withdrawn after two weeks. After four weeks of treatment, the patient experienced symptomatic relief as evidenced by marked improvement in the patient's X-ray (Fig. 1D). EGFR exon 19 deletion was also detected in the pleural effusion samples. The patient was returned to the previous hospital. Currently, the patient is in partial remission following 12 months of treatment with osimertinib.

Pulmonary lymphangitic carcinomatosis is mainly detected in patients with adenocarcinoma, especially those with lung, breast, and gastric cancers, and associated with poor prognosis.[1] In advanced non-small cell lung cancer (NSCLC), identifying driver gene mutations is recommended, but tissue collection is difficult