Review

Chest high-resolution computed tomography in primary Sjögren's syndrome: an up-to-date primer for rheumatologists

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ABSTRACT

Pulmonary manifestations, including airway involvement and interstitial lung disease, are the most frequent extra-glandular complications of primary Sjögren's syndrome (pSS). Chest high-resolution computed tomography (HRCT) is a cornerstone of pulmonary diagnostic imaging, aiming to detect, characterise, and quantify such conditions. In patients with pSS-related lung abnormalities, HRCT proved helpful in various clinical scenarios, including baseline and follow-up evaluation, assessment of superimposed infections, suspected progressive interstitial lung diseases, and acute exacerbation. This review aims to provide a primer for rheumatologists on chest HRCT, illustrating the up-to-date technique, imaging findings, and clinical indications in pSS and highlighting the importance of rheumatologist-radiologist constructive collaboration in the clinical management of such patients.

Introduction

Pulmonary involvement is one of the most frequent extra-glandular complications of primary Sjögren's syndrome (pSS), with a broad spectrum of conditions due to airway involvement and interstitial lung diseases (1-3). The prevalence of pulmonary involvement in pSS varies across studies, according to the detection methods (imaging, pulmonary function testing, or both) and patient selection criteria (asymptomatic for lung involvement, symptomatic, or mixed patients) (3, 4), ranging from 9-24% when considering only clinically relevant respiratory disease (4-6), and reaching up to 75% when including subclinical disease (3, 7).

Chest high-resolution computed tomography (HRCT) is the imaging modality of choice to detect, characterise, and determine the extent of airway and lung disease. HRCT is also helpful in identifying sites for bronchoalveolar lavage and lung biopsy, guiding treatment strategies, and predicting treatment outcomes (8, 9). HRCT proved to be an accurate imaging modality for evaluating pulmonary abnormalities in patients with connective tissue disorders (CTD), including pSS (10-12).

The broad clinical spectrum of lung complications in pSS has been extensively reviewed (13-15). Nevertheless, due to the potential impact of chest HRCT on pSS patients' management, we believe there is a need to make the rheumatologists conscious of the full potential of this imaging modality, also in the light of recent clinical guidelines update (16) and upcoming therapies that could impact in pSS management (17, 18). This paper aims to provide a primer for rheumatologists, illustrating the state-of-art chest HRCT examination, imaging findings, and updated clinical role in patients with pSS. We briefly describe all these aspects with synoptic tables, graphics, and example illustrations, underlying the importance of rheumatologist–radiologist cooperation in the clinical management of patients with pSS.

Chest HRCT examination

State-of-art technique

Radiologists should perform chest HRCT according to updated recommendations to make the most of its potential, as highlighted in Table I (8, 19-23).

Anatomo-radiologic correlation

Chest HRCT interpretation should rely on a basic understanding of pulmonary anatomy (19). In this regard, the sec-

Table I. Recommended features and parameters to perform a high-quality, state-of-art chest high-resolution computed tomography.

Feature / parameter	Recommended choice	Rationale
Scan-related		
Slice thickness	≤1.5-mm	To approximate the size of lung secondary lobule structures
Reconstruction algorithm	Moderately high spatial frequency (*e.g.*, bone algorithm)	To show fine anatomic structures while avoiding excessive image noise
Gantry rotation time	<1-sec	To reduce breath-hold time and motion artifacts
Tube current	Modulation technique	To image patients in a reduced radiation dose setting
Reconstruction technique	Iterative	To offset the image noise due to tube current modulation
Image windowing	Levels and widths ranging from –600 to –700 and from 1000 to 1500 Hounsfield Units, respectively	To appropriately display pulmonary structures. An optimal protocol should always include complimentary images for evaluation of mediastinal structures, *e.g.*, lymph nodes, and pulmonary artery diameter
Patient-related		
Patient position	Supine position	This standard position is usually sufficient to describe the distribution of lung abnormalities
Patient's breathing	Suspended full inspiration	To maximise the natural contrast between air and pulmonary structures
Additional scan (mandatory at first examination)	Expiratory scan	To characterise conditions in which a lung mosaic attenuation pattern at inspiratory scan may be present, *e.g.* hypersensitivity pneumonitis, and obliterative bronchiolitis
Additional scan (optional)	Prone position	To differentiate gravity-dependent abnormalities from early interstitial lung disease
Other observations		
Post-processing techniques	Multiplanar reformats, three-dimensional reconstructions	To better evaluate the spatial distribution and the extent of the lung abnormalities
Intravenous contrast agent administration	Usually not indicated	The intrapulmonary contrast can obscure subtle pulmonary findings, while adding little value to the interpretation of diffuse lung diseases

ondary pulmonary lobule represents the smallest lung unit (10 to 25 mm in diameter) of the lung architecture, being of paramount importance for proper HRCT interpretation of lung abnormalities. It is composed of three primary components: (i) the interlobular septa and septal structures, (ii) the centrilobular region and centrilobular structures, and (iii) the lobular parenchyma (24-25) (Fig. 1).

i. *Interlobular septa and septal structures*

Interlobular septa are sheetlike structures 10–20-mm long that form the borders of lobules, containing connective tissue, lymphatic vessels, and pulmonary venules (25-26). A few septa are often visible at the lung periphery in healthy patients. Septa become conspicuous in various pathological conditions, *e.g.* pulmonary oedema, interstitial pneumonia, lymphoproliferative disorders, and amyloidosis (27).

ii. *Centrilobular region and centrilobular structure*

The central portion of the secondary pulmonary lobule contains the pulmonary artery and bronchiolar branches supplying the lobule, as well as lymphatics and supporting connective tissue (25). Centrilobular abnormalities include (a) nodules, (b) linear branching opacities, *i.e.* "tree-in-bud pattern", indicating small-airways disease, (c) interstitial thickening or infiltration, and (d) abnormal low attenuation areas due to centrilobular emphysema (26).

iii. *Lobular parenchyma*

The functioning lung parenchyma includes alveoli, small airways, and branches of the pulmonary arteries, veins, and lymphatics, supported by a fine network of thin fibres within the alveolar septa. Only a few intralobular vascular branches are detectable in healthy subjects, while the lung acini are not visible (25). Structures become conspicuous in the case of lung pathologies, with alveolar spaces filling with fluid or cells: in this condition, the portions of the affected parenchyma show greater attenuation than healthy lung areas (28).

Structured reporting

All the stakeholders across the healthcare system should behove a transition from volume-based to value-based healthcare, aiming to improve the health outcomes achieved for the patient while reducing their costs (29, 30). In this light, disease-based structured reporting in clinical practice has been regarded as a new process metric to ensure high-quality radiological activity (31, 32). Indeed, the structured report clarifies terminology and provides a checklist to avoid missing relevant information, thus preventing ambiguity and facilitating comparison with prior studies (33, 34). A recent study involving patients with pSS and other CTD-

ILD demonstrated that when radiologists provided structured reports of chest HRCT, the referring rheumatologists perceived better completeness, clarity, and clinical relevance than free text reports (35). Moreover, structured reporting improved radiology residents' performance in reporting chest HRCT in patients with connective tissue diseases, including pSS (36).

HRCT findings of pSS chest involvement

Figure 2 and Supplementary Tables S1 and S2 report an updated, synoptical resume of the chest HRCT findings in patients with pSS, including airway and lung parenchyma abnormalities.

Airways. Airway involvement in pSS can occur in isolation or combination with other pulmonary manifestations, usually in the form of lymphocytic cell infiltration and exocrine glands atrophy (12). All the airway levels may be potentially involved, *i.e.* trachea, bronchi, or bronchioles, causing non-productive cough, xerotrachea, and xerobronchitis (52). While severe forms are rarely observed (37), airway manifestations may affect the quality of life, sometimes preceding CTD diagnosis by several years (14).

Airway abnormalities are frequent findings on chest HRCT, ranging from 48–68% (12). HRCT can detect the involvement of central and peripheral airways, with inflammatory infiltration and fibrosis mainly resulting in bronchiectasis and bronchiolitis (5, 11, 14, 37-39, 41, 53-56).

Bronchiectasis. Bronchiectasis is an irreversible, abnormal dilation of the bronchi due to a vicious cycle of infection and inflammation (26, 57), correlating with an augmented risk of developing respiratory infections and pneumonia (57). Patients present variable and non-specific symptoms, including dry cough, wheezing, dyspnoea, and rarely haemoptysis.

HRCT shows bronchial dilatation compared to the accompanying pulmonary artery (*i.e.* the signet ring sign), lack of bronchial tapering, and visibility of the bronchial branches within 1 cm from the pleural surface (26). In pSS, bronchiectasis predominantly presents a cylindrical shape, with lower lobes location (13, 57) (Fig. 3).

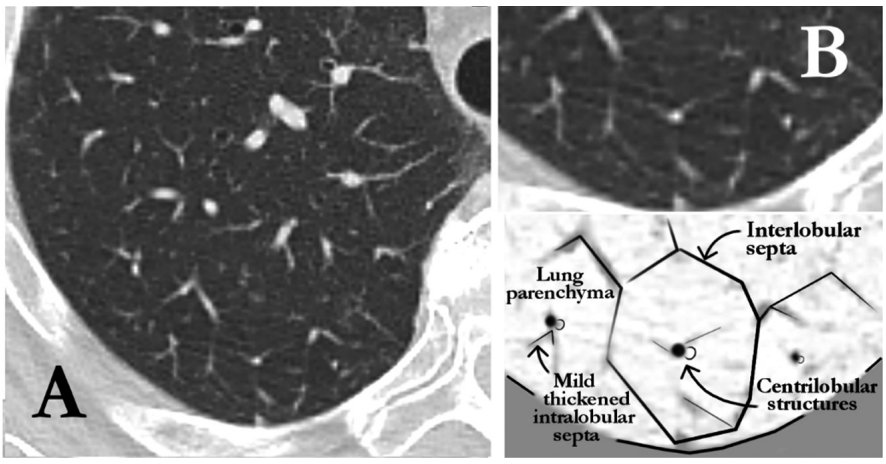

Fig. 1. The secondary pulmonary lobule. **A.** Axial HRCT magnification of the right upper lung lobe shows normal secondary pulmonary lobules. **B.** The detail of the HRCT image and the corresponding drawing scheme illustrate the normal anatomy of the smallest lung unit.

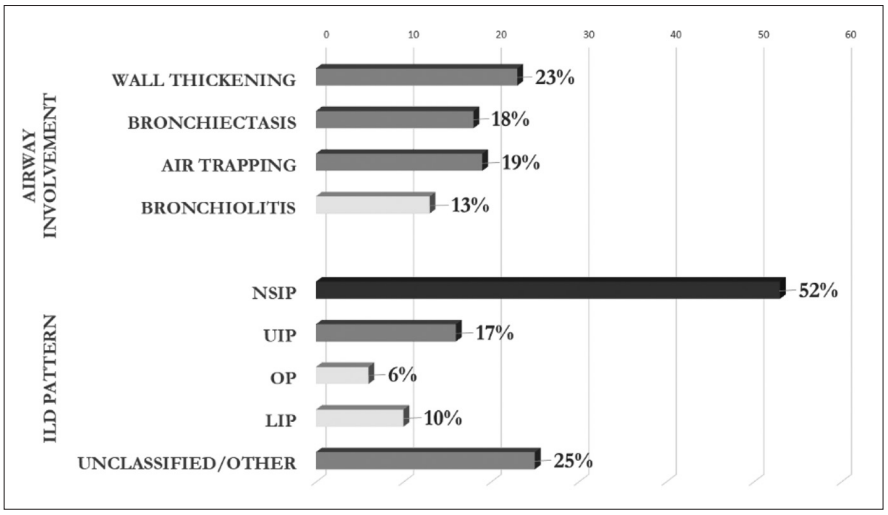

Fig. 2. Bar charts illustrating the prevalence of airway involvement and interstitial lung disease patterns in patients with pSS-related lung disease. For each sign and pattern, the percentage value represents the weighted arithmetic mean of the prevalences reported in literature.
- Airway involvement: references 3, 5, 6, 11, 37-46;
- ILD pattern: references 41, 43-45, 47-51.

Bronchiolitis. Bronchiolitis in pSS has a prevalence comprised between 12% in biopsy-proven cases and up to 29% with HRCT evaluation (3, 5, 11, 38, 41). It can be classified into two main types: follicular bronchiolitis (FB) and constrictive or obliterative bronchiolitis (OB), with the former more frequent than the latter (58).

FB derives from an antigenic stimulation and subsequent polyclonal hyperplasia of the bronchus-associated lymphoid tissue, showing reactive germinal centres along the bronchovascular bundles (59, 60). HRCT may reveal signs of bronchiolar inflammation, *i.e.* nodular, centrilobular, or ground-glass opacities, mild thickening of interlobular septa and bronchovascular bundles, and tree-in-bud pattern (26). Occasionally, air cysts occur, making a true continuum with lymphocytic interstitial pneumonia (LIP) (Fig. 4) (61).

OB is a rare form of bronchiolitis, poorly understood, and typically associated with progressive airflow obstruction (58). Submucosal fibrous tissue narrows the terminal and respiratory bronchioles' lumen while sparing

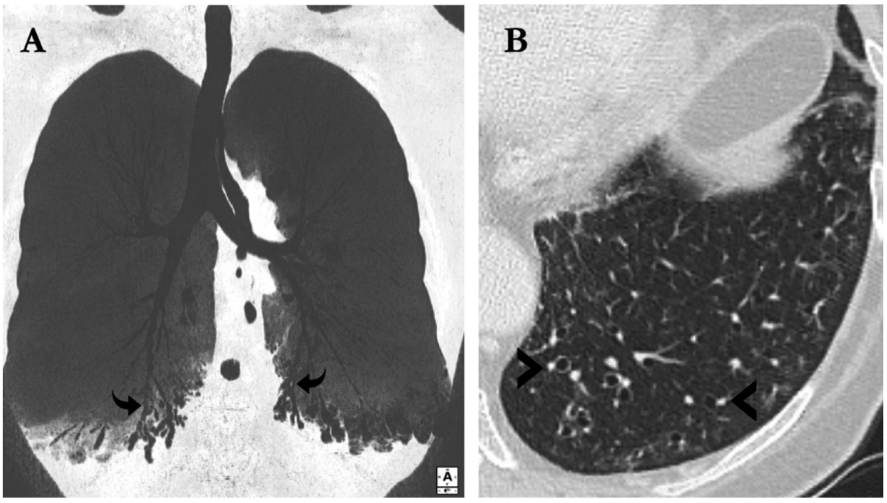

Fig. 3. Bronchiectasis. **A.** Minimum Intensity Projection (minIP) 5-cm-thick coronal oblique HRCT image shows dilated peripheral bronchi in both lower lobes, with a lack of distal tapering (curved arrows). **B.** The axial HRCT magnification of the left lower lung lobe shows bronchi larger than the corresponding arteries (signet ring sign, arrowheads).

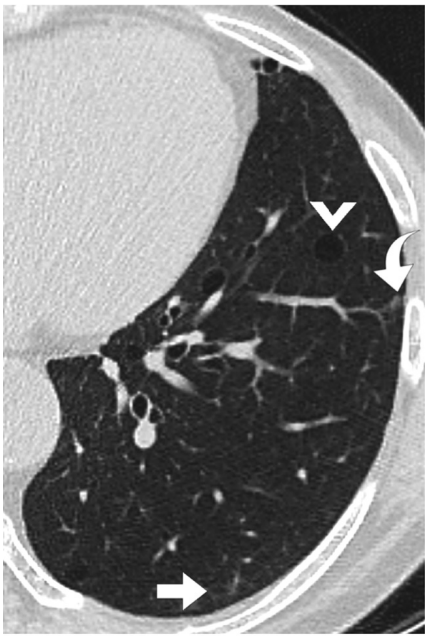

Fig. 4. Follicular bronchiolitis. HRCT image of the left lung shows small subsolid nodules with peripheral, peribronchial distribution (curved arrow). Scarce cysts with regular shape and thin wall (arrowhead) and subtle subpleural interstitial thickening (straight arrow) are also visible.

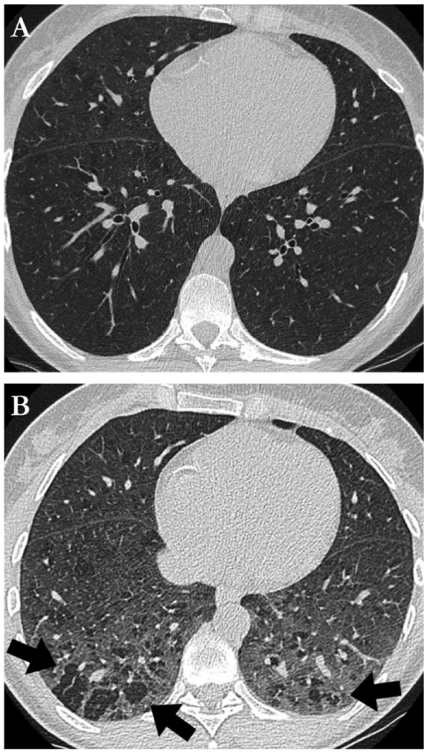

Fig. 5. Obliterative bronchiolitis. **A.** Inspiratory HRCT image shows a faint mosaic attenuation pattern due to subtle differences in density between adjacent secondary lobules. **B.** The corresponding end-expiratory HRCT image enhances differences in lobular attenuation, with darker areas representing air trapping distal to obliterative bronchiolitis (arrows).

the distal lung parenchyma (59, 62). Chest HRCT usually reveals a mosaic attenuation pattern with air trapping on expiratory images (Fig. 5) (58).

Interstitial lung disease

Interstitial lung disease (ILD) is a frequent pulmonary manifestation of pSS, with prevalence widely ranging from 6–79% (5, 6, 11, 38, 39, 42-44, 47, 53, 56, 63). Older age, smoking, increased antinuclear antibodies, rheumatoid factor titre, and C-reactive protein levels have been described as potential risk factors for ILD development (44, 48, 64-66). Symptoms are non-specific, including dyspnoea and dry cough.

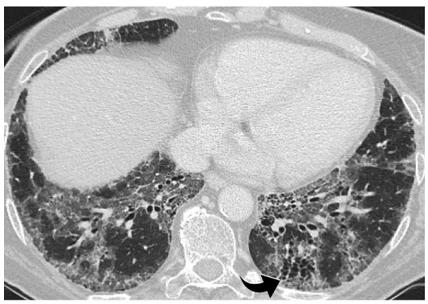

Fig. 6. Interstitial lung disease with nonspecific interstitial pneumonia (NSIP) pattern. HRCT image depicts bilateral, symmetrical areas of ground-glass attenuation with diffuse distribution and associated with signs of fibrosis, *i.e.* reticulation and traction bronchiectasis (curved arrow).

On clinical examination, inspiratory "crackles" may be heard at the lung bases. Pulmonary function tests reveal constrictive changes (52).

The pathological and HRCT classification of idiopathic interstitial pneumonia (IIP) patterns can be translated into the setting of CTD-ILD (67, 68). Similar to IIP, the correlation between pathological and HRCT findings in CTD-ILD is good (43, 69), allowing a confident HRCT-based ILD diagnosis, while avoiding lung biopsy (70).

Non-specific interstitial pneumonia (NSIP) (Fig. 6) is the most common pSS-ILD pattern. Less frequent HRCT patterns include usual interstitial pneumonia (UIP), organising pneumonia (OP), and LIP (2, 52). Of note, patients frequently present with a combination of different pathological and HRCT patterns (43, 69), often with the coexistence of airway abnormalities (12). When chest HRCT shows an NSIP and/or OP pattern, causes other than pSS should be excluded, *i.e.* drug toxicity and infection (12).

Features associated with a worse prognosis in pSS-ILD are heterogeneous. Various studies assessed the demographic, serological, and clinical features associated with a worse outcome, with mixed results. Some authors reported that pSS-ILD was more commonly detected in males, older patients, and smokers, suggesting that aging, cigarette smoking, and ANA positivity may be potential risk factors in developing ILD in pSS patients (44). Other authors detected higher levels

of erythrocyte sedimentation rate, C-reactive protein, fibrinogen, IgG, and C3 and lower levels of albumin in ILD-pSS patients compared with pSS patients without ILD (71). Clinical and serological features associated with the progression of ILD included male sex, non-sicca disease onset, and higher levels of baseline lactic dehydrogenase (LDH), as well as low baseline forced vital capacity (FVC) (72). Novel blood biomarkers are under study as predictors of the prognosis for pSS-ILD patients, including Krebs von den Lungen-6 (KL-6). High blood KL-6 level has been recently reported as an independent prognostic factor for survival in patients with pSS-ILD (73). Further risk factors associated with death are decreased FVC and forced expiratory volume (FEV1), as well as severe lung involvement (74). A higher CO2 arterial pressure, and lymphoblastic foci in biopsy samples have also been reported as associated with death in ILD-pSS patients (75). Of note, patients with pre-existing ILD seem at risk of acute exacerbation, which is associated with poor prognosis and high mortality (76). Furthermore, He SH *et al*. showed that pSS patients with progressive ILD were characterized by low baseline FVC, high baseline LDH, and more reticular pattern on chest HRCT, compared with stable ILD-pSS subjects. The antinuclear antibodies (ANA) spectrum was not different between these two groups (72). In contrast, the absence of honeycombing and higher levels of oxygen partial pressure (PaO2) were associated with increased survival (41), and sicca complaints at initial referral and preserved baseline FVC resulted in being protective from ILD progression (72).

Focus on LIP. LIP is a rare disease that classically develops in patients with pSS (14), with a reported prevalence of about 1% (77) and rarely preceding the pSS clinical manifestations (78). LIP is characterized by severe and diffuse hyperplasia of bronchus-associated lymphoid tissue. The diffuse polyclonal lymphoid cell infiltrate surrounds the airways and expands the lung interstitium (26), particularly the alveolar septa (12). Severity and distribution of the lymphoid infiltrate are variable, thus determining a continuum of various conditions (14, 60), including (i) FB, where the lymphoid infiltrate is limited to the peribronchiolar lymphoid follicle (60); (ii) cellular NSIP, with a lower density of infiltrates compared to LIP (14); (iii) diffuse lymphoid hyperplasia, where lymphocytes are distributed along the lymphatics (interlobular septa, bronchovascular bundles, and pleura); and (iv) LIP, which may be considered both a lymphoproliferative disorder and an interstitial pneumonia. While diffuse lymphoid hyperplasia and LIP differ in the anatomical distribution of the lesions (that is, respectively, predominantly perilymphatic and alveolar), from a clinical point of view, the two conditions exhibit no differences (12).

Bilateral ground-glass opacities and well-defined, thin-walled, peri-bronchovascular cysts are the main HRCT findings (Fig. 7) (79). Ground-glass opacities mirror infiltration by inflammatory cells, which causes airway compression, expansion of terminal bronchioles, and cysts development (77). Other findings include interlobular and peribronchovascular interstitial thickening and blurred centrilobular or subpleural nodules (12).

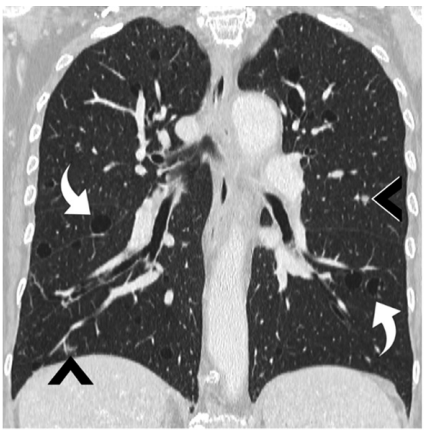

Fig. 7. Lymphoid interstitial pneumonia (LIP). The coronal HRCT image shows a few bilateral, thin-walled, regular-shaped air-containing cysts with peri-vascular locations (curved arrows). Rare, small centrilobular nodules are also visible (arrowheads).

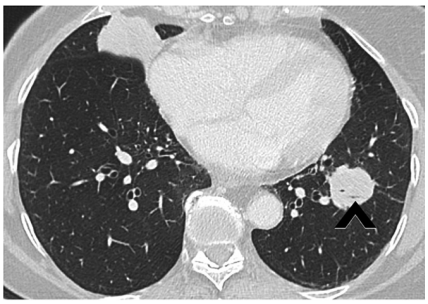

Fig. 8. Pulmonary mucosa-associated lymphoid tissue (MALT) lymphoma. HRCT image shows a 3-cm large mass-like consolidation area in the left lower lobe, with regular margins and internal air-bronchogram (arrowhead).

Lymphoma and other malignancies

Non-Hodgkin's B-cell Lymphoma (NHL) is one of the major complications of pSS, representing the leading cause of patient decreased survival (80-82). It occurs in 5–7% of primary and secondary SS patients, who carry a 7-fold increased risk of developing lymphoma than the normal population (83). In most cases, lymphomas arise from salivary glands, particularly the parotid glands, but they can also involve nodes or extranodal organs, including the lung (83-85). The chronic polyclonal lymphocytic infiltration of airways and lung parenchyma can progress to a monoclonal B-cell proliferation, with a high risk for NHL development (12). Mucosa-associated lymphoid tissue (MALT) lymphoma is the most common subtype of NHL in pSS (86-88), with slow growth and a favourable prognosis (12). Indeed, only a small percentage of MALT lymphomas progress to diffuse large B-cell lymphomas (DLBCL) (37,89). Symptoms are generally absent or mild, including slowly progressive cough, dyspnoea, and classic B symptoms (52).

Chest HRCT findings of pulmonary MALT lymphoma include solitary or multiple consolidation areas located along the bronchovascular bundle, with frequent air bronchogram, as an effect of marked interstitial expansion (Figure 8). Traction bronchiectasis, interlobular septal thickening within or around the lesion, bilateral nodules, and masses are also possible (12, 90, 91). Mediastinal lymphadenopathy and pleural effusions may also be present. Of note, HRCT can help differentiate LIP and MALT lymphoma in case of coexistence: indeed, cysts are often

found in LIP, while large nodules, consolidation, and pleural effusions suggest lymphoma (92).

Previous studies demonstrated that pSS carries an increased risk of lung cancer (93), with standardised incidence ratio, *i.e.* the ratio of the observed number of cases of cancer in pSS patients to the expected number of cases in the general population, of 1.55 (95% C.I. 1.29–1.85) (94). Since an association between lung adenocarcinoma and LIP in patients with pSS has been reported, the appearance of new nodular lesions at chest CT should include lung cancer in the differential diagnosis (Fig. 9) (84, 95).

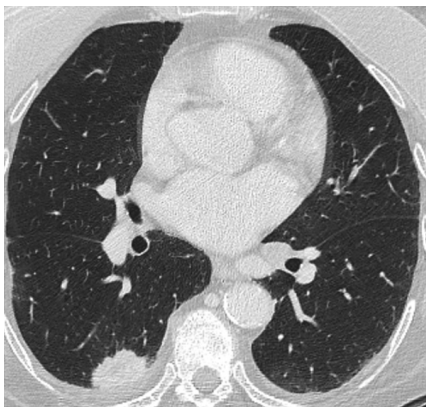

Fig. 9. Pulmonary adenocarcinoma. HRCT image shows a 3-cm large mass-like area of consolidation in the right lower lobe, with subpleural location, micro-spiculated margins, and abutting pleural effusion.

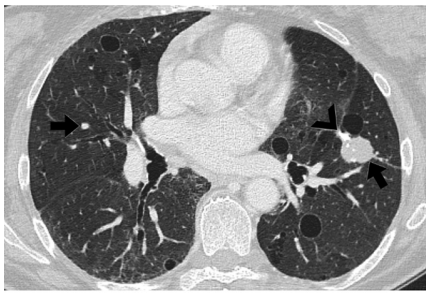

Fig. 10. Lung amyloidosis. HRCT image shows rare, bilateral thin-walled regular-shaped cysts and solid nodules that are heterogeneous in size (arrows) and partially calcified (arrowhead).

Amyloidosis

Amyloidosis is a heterogeneous group of localized or systemic disorders caused by extracellular deposition as fibrils of misfolding autologous protein, whose type is determinant for clinical classification (96). Pulmonary amyloidosis is a rare complication of pSS, presenting in up to 10% of patients with pSS and ILD (2, 97).

While histopathology provides a definite diagnosis and amyloid typing (light-chain amyloidosis in most cases) (97, 98), chest HRCT can raise the suspicion of lung parenchymal amyloid involvement (99). The typical presentation consists of multiple cystic lesions, with random distribution and without zonal predominance, associated with small, randomly distributed, multiple nodules (100, 101). Nodules can be solid or mixed attenuation, with occasional cavitation or calcification (89, 99, 102). Parenchymal opacities, bronchiectasis, or areas of septal thickening may also be present (100, 101) (Figure 10). LIP is the main radiological differential diagnosis, presenting with cysts that are bigger (up to 3-cm in diameter) and fewer, with bilateral, peri-lymphatic distribution, along with more frequent ground-glass opacities, consolidation areas, small nodules, and interstitial thickening (102).

Pulmonary hypertension

Pulmonary hypertension (PH) is an altered haemodynamic state defined by an increase in mean pulmonary arterial pressure (mPAP) >20 mmHg at rest at right heart catheterisation (103). PH has been classified into five clinical groups, namely (I) pulmonary arterial hypertension (PAH); (II) PH due to left-sided heart disease; (III) PH due to chronic lung disease; (IV) chronic thromboembolic PH; and (V) patients with unclear and/or multifactorial mechanisms (104).

In patients with pSS, PH mainly belongs to group I (105, 106). Limited data support the association between pSS and both group III and group IV PH due to fibrotic ILD with hypoxia (107, 108) and inherently increased risk of thromboembolic disease (particularly when associated with the antiphospholipid syndrome) (109, 111), respectively.

Chest CT may raise the suspicion of PH by showing an increased pulmonary artery diameter (≥29 mm), a pulmonary-to-ascending aorta diameter ratio ≥1, and a segmental artery-to-bronchus ratio ≥1 in three or four lobes

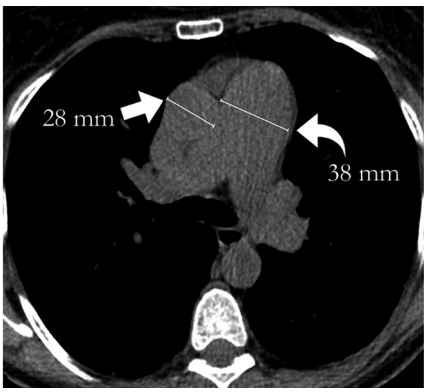

Fig. 11. Pulmonary hypertension. Measurement of the pulmonary artery (PA, curved arrow) and ascending aorta (AA, straight arrow) diameters were obtained in an axial HRCT image with mediastinal windowing. PA diameter is larger than the normal values (>29-mm) and the AA diameter at the same level, suggesting pulmonary hypertension. No relevant pulmonary abnormalities were present (not shown).

(Figure 11) (112). Other relevant chest CT features in patients with established or suspected PH may help differentiate group I pSS-PH from the other groups. These features include lung fibrosis or emphysema extension (if <20% is unlikely to cause PH); signs that should raise the suspicion of pulmonary veno-occlusive disease, *i.e.* centrilobular nodules and smooth interlobular septal thickening; ancillary sign of chronic thromboembolic pulmonary hypertension, *i.e.* peripheral calcification and eccentric filling defects in pulmonary arteries (113).

The clinical role of chest HRCT

Chest HRCT is crucial in assessing lung involvement in patients with pSS (16). Other diagnostic tools include complete pulmonary function tests (PFTs) and chest radiograph (CXR). Moreover, when pSS patients present with respiratory symptoms, bronchoscopy with bronchoalveolar lavage (BAL) may be of help in ruling out infections and other endobronchial abnormalities (*e.g.* amyloidosis), as well as in determining other causes of sicca symptoms (*e.g.* sarcoidosis) (16). Various studies reported increased lymphocytosis on BAL specimens (41, 114), which may predict a higher risk for mortality and an increased need for immunologic treatment (52, 115). Dissimilarly, Salaffi *et al.* reported that the presence

of alveolar neutrophils (neutrophilic BAL) was associated with a significantly greater reduction of carbon monoxide diffusing capacity (DLCO) compared with lymphocytosis on BAL (116). In recent years, the possibility of quantifying cytokine levels on BAL is gaining interest, and some authors are aiming to explore the expression and significance of various chemokine (*i.e.* CCL18) and miRNA (*i.e.* miR-200c) in patients with CTD-ILD (117,118). Further studies are needed to provide a complete picture of BAL's role in pSS-related lung involvement.

When dealing with chest HRCT and pSS, two different clinical scenarios can be described, which are "when pSS is known" and "when pSS is (still) unknown", respectively.

When pSS is known

Chest HRCT indications. Due to the high prevalence of subclinical pulmonary disease and the risk of overlooking/misinterpreting non-specific respiratory symptoms, clinical practice guidelines recommend ruling out lung involvement in patients with known CTD (16). Indeed, newly-diagnosed pSS patients that are without respiratory symptoms may undergo pulmonary function tests (PFTs) and chest radiograph (CXR). The main aims of CXR include (i) identification of pulmonary involvement despite the absence of symptoms; (ii) detection of alternative diagnosis or other pathologies associated with pSS, *e.g.* sarcoidosis, vasculitis, and lymphoma; (iii) providing a time-zero snapshot for future comparisons.

Chest HRCT should serve as a second-level imaging modality to characterise CXR-detected findings or when encountering abnormalities at baseline PFTs (restrictive pattern or DLCO reduction) and should be regarded as the preferred imaging modality whenever there is a concern for lung involvement or ILD is suspected (16). Points of strength of HRCT include the capability of identifying ILD, estimating the extent of lung involvement, and detecting concurrent or alternative abnormalities (*e.g.* emphysema or pulmonary hypertension) that may impact pulmonary function tests (119).

While there is a strong recommendation to perform serial PFTs every 6 months in asymptomatic patients with pSS-related ILD, the timing for follow-up HRCTs should be scheduled on a per-patient basis, according to clinical, functional, and radiological findings. HRCT is of help in assessing disease progression or lung complications, including lymphoproliferative abnormalities, acute exacerbations, and alternative diagnoses such as infection or drug-induced pneumonitis (119).

Progressive fibrosing interstitial lung diseases. The clinical course of pSS-related ILD is usually milder than other CTD-ILD or idiopathic pulmonary fibrosis (IPF) (72). However, when ILD progression occurs, it leads to clinical deterioration, impaired quality of life, and a higher rate of morbidity and mortality (14, 120-123). The progressive decline of lung function can derive from progressive pulmonary fibrosis. Indeed, patients with fibrotic ILD may show a disease course similar to IPF (*i.e.* the archetypal ILD with progressive phenotype), the proportion of patients developing a progressive fibrosing phenotype depending on the ILD type (123). Fibrosing ILDs may benefit from anti-fibrotic drugs such as nintedanib, which demonstrated to reduce the progression of lung fibrosis in patients with ILD other than IPF, including CTD-ILD (17). Although the study cohort of the INBUILD trial included no patients with pSS, the results suggested that all the progressive fibrosing ILDs share a similar pathobiological mechanism, regardless of the clinical diagnosis (124). Therefore, it has been proposed that anti-fibrotic therapies may also benefit pSS-related progressive fibrosing ILD (PF-ILD) (14, 125).

No standard definition of PF-ILD exists, all relying on different combinations of clinical, functional, and imaging findings modifications within 24 months (Fig. 12) (17, 72, 123, 126, 127). While all the proposed definitions include the evaluation of lung fibrosis extent through HRCT, no specific criteria concerning the term "progressive" at imaging have been provided yet (123, 128, 129).

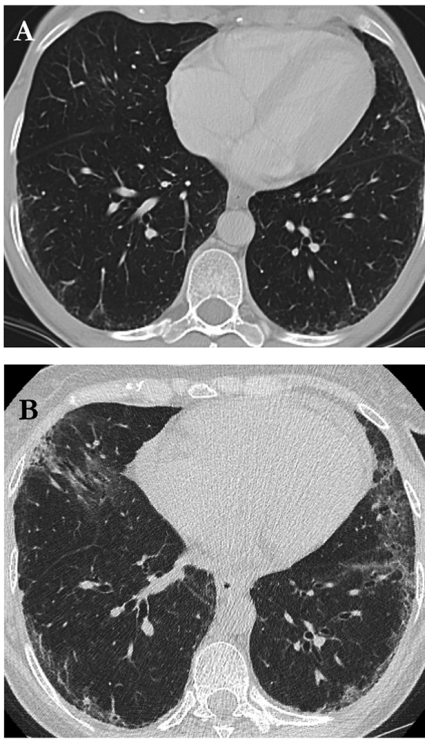

Fig. 12. Progressive fibrosing interstitial lung disease. **A.** Initial chest HRCT shows bilateral, subpleural, subtle interstitial reticulation. **B.** Chest HRCT performed nearly two years later showed progression of interstitial abnormalities, with peripheral ground-glass areas superimposed to intralobular septal thickening and mild bronchiectasis.

In patients with pSS-related ILD, the risk of ILD progression should not be underestimated, the prevalence ranging from 20–50% of cases (17, 50, 72, 128, 130, 131). A few papers only investigated the potential association between specific signs at baseline HRCT and the subsequent development of PF-ILD, with conflicting results. Indeed, while Zhang *et al*. reported that the UIP pattern was a predictor of ILD progression (50), Enomoto *et al*. and He *et al*. did not find different survival rates when comparing patients with NSIP and UIP patterns (72, 75). He *et al*. also showed that an extensive reticular pattern was more frequent in progressive than stable ILD (72). Further studies are needed to identify baseline HRCT features predicting PF-ILD, thus helping identify patients who may benefit from more frequent follow-up and aggressive therapies.

CTD-ILD acute exacerbation. Borrowing the acute exacerbation (AE)-

IPF criteria, AE occurring in pSS-related ILD has been defined as an acute, clinically significant respiratory deterioration with new, widespread alveolar abnormalities (132-134). Two types of AE exist, namely "idiopathic" AE if no inciting cause is identified, and "triggered" AE when a known external event, *e.g.* interventional procedure, drug toxicity, infection, or aspiration, leads to the acute lung injury (132). Only a few studies reported the incidence of AE in pSS-related ILD, ranging from 6–11% (75, 131-135). Chest HRCT plays a central role in the CTD-ILD AE diagnosis due to inherent transbronchial and surgical lung biopsy limitations, *i.e.* the problematic identification of acute lung injury in small lung tissue and the high risk of complications, respectively (132). The recognition at HRCT of new bilateral ground-glass abnormalities and/or consolidations, superimposed on a background consistent with UIP pattern, is a cornerstone of CTD-ILD AE diagnosis once cardiac failure and fluid overload are excluded (134, 136) (Fig. 13).

Pulmonary drug toxicity. Patients with uncontrolled systemic disease, particularly with severe organ impairment, may benefit from glucocorticoids associated with immunosuppressive agents as glucocorticoid-sparing agents (137). Since some immunosuppressors, including biologic drugs, have been associated with interstitial pneumonia, they should be used carefully in ILD patients due to the risk of lung toxicity. HRCT findings include those typically encountered in hypersensitivity pneumonitis, OP, AIP, or pulmonary fibrosis pattern, and pleural effusion (14, 138). As a second-line treatment option, B-cell targeted therapies (*e.g.*, rituximab) may be considered in pSS patients with refractory, severe systemic disease, particularly when associated with cryoglobulinaemic vasculitis (137) and ILD (139). Although rituximab carries a higher risk of infection and acute lung toxicity in patients with CTD-ILD (140, 131), no cases of rituximab-induced lung toxicity in patients with pSS have been reported.

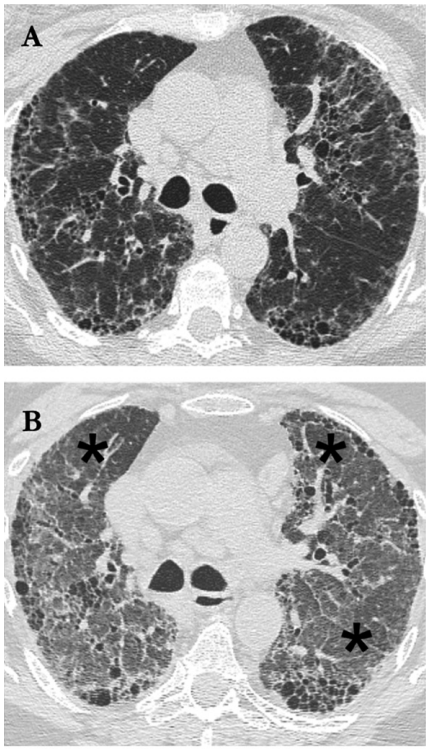

Fig. 13. Acute exacerbation of interstitial lung disease. **A.** Initial chest HRCT shows extensive fibrosing lung disease, with usual interstitial pneumonia (UIP) pattern.
B. Chest HRCT performed at the time of clinical worsening revealed the appearance of diffuse, bilateral ground-glass areas involving the non-fibrotic lung regions (asterisks), suggesting diffuse alveolar damage. The lung fibrosis global extent did not change.

When pSS is (still) unknown

Interstitial lung abnormalities. The term "interstitial lung abnormalities" (ILA) refers to chest HRCT-detected, incidental, diffuse, non-dependent pulmonary abnormalities with a threshold of 5% to exclude minimal findings (142). HRCT studies involving large cohorts of asymptomatic patients showed an ILA prevalence of 4–9% in cigarette smokers and 2–7% in never-smokers (143).

While HRCT-detected pulmonary abnormalities in patients with known pSS should be regarded as subclinical/preclinical ILD and not ILA (143), the presence of ILA in "naïve" patients should prompt excluding an occult CTD among the possible secondary causes (*e.g.* cigarette smoking, inhalation exposures, drug toxicity, and recurrent aspirations) (142). Indeed, 10–51% of patients may develop lung manifestations years before pSS clinical onset, thus making an early diagnosis difficult (97). In this light, previous studies suggested performing minor salivary gland biopsy when evaluating patients with lung abnormalities of undetermined aetiology to identify the salivary component of pSS (144-146).

From an imaging point of view, in the case of ILA, a follow-up HRCT examination (within 12 months or sooner in case of newly onset symptoms or impaired pulmonary function) has been advised, mainly when ILA presents with subpleural location and fibrotic appearance (142).

Interstitial pneumonia with autoimmune features. The European Respiratory Society and American Thoracic Society (ERS/ATS) research statement proposed the term "interstitial pneumonia with autoimmune features" (IPAF) to describe a heterogeneous group of patients that present radiological or histopathological ILD with autoimmune features (147). Chest HRCT plays a major role in defining IPAF providing suggestive ILD patterns (NSIP, OP, NSIP/OP, and LIP), and showing multi-compartment involvement, including unexplained pleural/pericardial effusion or thickening, airways disease, and indirect signs of pulmonary vasculopathy (147).

Previous authors highlighted the risk of underdiagnosing pSS in patients defined as having IPAF due to lack of the dry eye test (DET) and histopathological major salivary glands biopsy (MSGB) among the IPAF clinical and morphologic domain-defining features (146, 148). Indeed, both DET and MSGB are within the pSS classification criteria set proposed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) (149). On these bases, although neither HRCT nor histopathological pattern of lung involvement could differentiate between patients with and without pSS, Autieri *et al.* demonstrated that 27/67 (41%) patients with IPAF fulfilled the criteria for being reclassified as having pSS, thus allowing their categorization despite an undefined ILD (146). Further studies with prospective designs

and long-term follow-up are needed to refine IPAF features, outcomes, and management, including the timing of HRCT follow-up (148, 150).

Conclusion

Chest HRCT is a cornerstone imaging modality for detection, characterisation, and extent determination of pSS pulmonary manifestations, including airways and interstitial lung diseases. Basic knowledge of chest HRCT technical aspects, imaging findings, and current role in patients with pSS is something the rheumatologist should know in the light of constructive collaboration with chest-devoted radiologists to improve patient management.

References

1. MANFRÈ V, CAFARO G, RICCUCCI I *et al*.: One year in review 2020: comorbidities, diagnosis and treatment of primary Sjögren's syndrome. *Clin Exp Rheumatol* 2020; 38 (Suppl. 126): S10-22.
2. DEPASCALE R, DEL FRATE G, GASPAROTTO M *et al*.: Diagnosis and management of lung involvement in systemic lupus erythematosus and Sjögren's syndrome: a literature review. *Ther Adv Musculoskelet Dis* 2021; 13: 1-24. https://doi.org/10.1177/1759720X211040696
3. KAMPOLIS CF, FRAGKIOUDAKI S, MAVRAGANI CP, ZORMPALA A, SAMAKOVLI A, MOUTSOPOULOS HM: Prevalence and spectrum of symptomatic pulmonary involvement in primary Sjögren's syndrome. *Clin Exp Rheumatol* 2018; 36 (Suppl. 112): S94-101.
4. RAMOS-CASALS M, SOLANS R, ROSAS J *et al*.: Primary Sjögren syndrome in Spain. *Medicine* (Baltimore) 2008; 87: 210-9. https://doi.org/10.1097/MD.0b013e318181e6af
5. PALM O, GAREN T, BERGE ENGER T *et al*.: Clinical pulmonary involvement in primary Sjögren's syndrome: prevalence, quality of life and mortality - a retrospective study based on registry data. *Rheumatology* (Oxford) 2013; 52:173-9. https://doi.org/10.1093/rheumatology/kes311
6. YAZISIZ V, ARSLAN G, OZBUDAK İH *et al*.: Lung involvement in patients with primary Sjögren's syndrome: what are the predictors? *Rheumatol Int* 2010; 30: 1317-24. https://doi.org/10.1007/s00296-009-1152
7. JIN Y, ZHANG T, YE W, ZHU X, WANG L, WANG X: Clinical profile and associated factors of pulmonary involvement in primary Sjögren's syndrome. *Med Clin* (Engl Ed) 2019; 153: 305-11. https://doi.org/10.1016/j.medcli.2019.01.016
8. AMERICAN COLLEGE OF RADIOLOGY: ACR-STR practice parameter for the performance of High-Resolution Computed Tomography (HRCT) of the lungs in adults - Revised 2020 (Resolution 33). *Website (cited 2022 Sep 28);* Available from: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/HRCT-Lungs.pdf
9. WALSH SLF, DEVARAJ A, ENGHELMAYER JI *et al*.: Role of imaging in progressive-fibrosing interstitial lung diseases. *Eur Respir Rev* 2018; 27: 180073. https://doi.org/10.1183/16000617.0073-2018
10. AHUJA J, ARORA D, KANNE JP, HENRY TS, GODWIN JD: Imaging of pulmonary manifestations of connective tissue diseases. *Radiol Clin North Am* 2016; 54: 1015-31. https://doi.org/10.1016/j.rcl.2016.05.005
11. LOHRMANN C, UHL M, WARNATZ K *et al*.: High-resolution CT imaging of the lung for patients with primary Sjögren's syndrome. *Eur J Radiol Open* 2004; 52: 137-43. https://doi.org/10.1016/j.ejrad.2004.01.006
12. EGASHIRA R, KONDO T, HIRAI T *et al*.: CT findings of thoracic manifestations of primary Sjögren syndrome: radiologic-pathologic correlation. *Radiographics* 2013; 33: 1933-49. https://doi.org/10.1148/rg.337125107
13. FLAMENT T, BIGOT A, CHAIGNE B, HENIQUE H, DIOT E, MARCHAND-ADAM S: Pulmonary manifestations of Sjögren's syndrome. *Eur Respir Rev* 2016; 25: 110-23. https://doi.org/10.1183/16000617.0011-2016
14. LUPPI F, SEBASTIANI M, SVERZELLATI N, CAVAZZA A, SALVARANI C, MANFREDI A: Lung complications of Sjögren syndrome. *Eur Respir Rev* 2020; 29: 200021. https://doi.org/10.1183/16000617.0021-2020
15. LUPPI F, SEBASTIANI M, SILVA M *et al*.: Interstitial lung disease in Sjögren's syndrome: a clinical review. *Clin Exp Rheumatol* 2020; 38 Suppl 126: 291-300.
16. LEE AS, SCOFIELD RH, HAMMITT KM *et al*.: Consensus Guidelines for evaluation and management of pulmonary disease in Sjögren's. *Chest* 2021; 159: 683-98. https://doi.org/10.1016/j.chest.2020.10.011
17. WELLS AU, FLAHERTY KR, BROWN KK *et al*.: Nintedanib in patients with progressive fibrosing interstitial lung diseases – subgroup analyses by interstitial lung disease diagnosis in the INBUILD trial: a randomised, double-blind, placebo-controlled, parallel-group trial. *Lancet Respir Med* 2020; 8: 453-60. https://doi.org/10.1016/S2213-2600(20)30036-9
18. LEE J, LEE J, KWOK SK *et al*.: JAK-1 inhibition suppresses interferon-induced BAFF production in human salivary gland: potential therapeutic strategy for primary Sjögren's syndrome. *Arthritis Rheumatol* 2018; 70: 2057-66. https://doi.org/10.1002/art.40589
19. GOTWAY MB, REDDY GP, WEBB WR, ELICKER BM, LEUNG JWT: High-Resolution CT of the lung: patterns of disease and differential diagnoses. *Radiol Clin North Am* 2005; 43: 513-42. https://doi.org/10.1016/j.rcl.2005.01.010
20. KAZEROONI EA: High-Resolution CT of the Lungs. *AJR Am J Roentgenol* 2001; 177: 501-19. https://doi.org/10.2214/ajr.177.3.1770501
21. KASHIWABARA K, KOHSHI S: Additional computed tomography scans in the prone position to distinguish early interstitial lung disease from dependent density on helical computed tomography screening patient characteristics. *Respirology* 2006; 11: 482-7. https://doi.org/10.1111/j.1440-1843.2006.00869.x
22. BEERES M, WICHMANN JL, PAUL J *et al*.: CT chest and gantry rotation time: does the rotation time influence image quality? *Acta Radiol* 2015; 56: 950-4. https://doi.org/10.1177/0284185114544242
23. BANKIER AA, O'DONNELL CR, BOISELLE PM: Quality initiatives. respiratory instructions for CT examinations of the lungs: a hands-on guide. *Radiographics* 2008; 28: 919-31. https://doi.org/10.1148/rg.284085035
24. GRIFFIN CB, PRIMACK SL: High-resolution CT: normal anatomy, techniques, and pitfalls. *Radiol Clin North Am* 2001; 39: 1073-90. https://doi.org/10.1016/s0033-8389(05)70332-8
25. WEBB WR: Thin-Section CT of the secondary pulmonary lobule: anatomy and the image - The 2004 Fleischner Lecture. *Radiology* 2006; 239: 322-38. https://doi.org/10.1148/radiol.2392041968
26. HANSELL DM, BANKIER AA, MACMAHON H, MCLOUD TC, MÜLLER NL, REMY J: Fleischner Society: Glossary of terms for thoracic imaging. *Radiology* 2008; 246: 697-722. https://doi.org/10.1148/radiol.2462070712
27. OIKONOMOU A, PRASSOPOULOS P: Mimics in chest disease: interstitial opacities. *Insights Imaging* 2013; 4: 9-27. https://doi.org/10.1007/s13244-012-0207-7
28. CHIARENZA A, ESPOSTO ULTIMO L, FALSAPERLA D *et al*.: Chest imaging using signs, symbols, and naturalistic images: a practical guide for radiologists and non-radiologists. *Insights Imaging* 2019; 10: 114. https://doi.org/10.1186/s13244-019-0789-4
29. TEISBERG E, WALLACE S, O'HARA S: Defining and implementing value-based health care: a strategic framework. *Acad Med* 2020; 95: 682-5. https://doi.org/10.1097/ACM.0000000000003122
30. LIEW DFL, DAU J, ROBINSON PC: Value-based healthcare in rheumatology: axial spondyloarthritis and beyond. *Curr Rheumatol Rep* 2021; 23: 36. https://doi.org/10.1007/s11926-021-01003-z
31. EUROPEAN SOCIETY OF RADIOLOGY (ESR): ESR concept paper on value-based radiology. *Insights Imaging* 2017; 8: 447-54. https://doi.org/10.1007/s13244-017-0566-1
32. SARWAR A, BOLAND G, MONKS A, KRUSKAL JB: Metrics for radiologists in the era of value-based health care delivery. *Radiographics* 2015; 35: 866-76. https://doi.org/10.1148/rg.2015140221
33. EUROPEAN SOCIETY OF RADIOLOGY (ESR): ESR paper on structured reporting in radiology. *Insights Imaging* 2018; 9: 1-7. https://doi.org/10.1007/s13244-017-0588-8
34. SVERZELLATI N, ODONE A, SILVA M *et al*.: Structured reporting for fibrosing lung disease: a model shared by radiologist and pulmonologist. *Radiol Med* 2018; 123: 245-53. https://doi.org/ 10.1007/s11547-017-0835-6
35. CERESER L, MARCHESINI F, DI POI E *et al*.: Structured report for chest high-resolution computed tomography in patients with connective tissue disease: Impact on the report

quality as perceived by referring clinicians. *Eur J Radiol* 2020; 131: 109269. https://doi.org/10.1016/j.ejrad.2020.109269
36. CERESER L, MARCHESINI F, DI POI E *et al*.: Structured report improves radiology residents' performance in reporting chest high-resolution computed tomography: a study in patients with connective tissue disease. *Diagn Interv Radiol* 2022 *(in press)*. Available online at https://www.dirjournal.org/EN. https://doi.org/10.5152/dir.2022.21488
37. PAPIRIS SA, MANIATI M, CONSTANTOPOULOS SH, ROUSSOS C, MOUTSOPOULOS HM, SKOPOULI FN: Lung involvement in primary Sjögren's syndrome is mainly related to the small airway disease. *Ann Rheum Dis* 1999; 58: 61-4. http://doi.org/10.1136/ard.58.1.61
38. TAOULI B, BRAUNER MW, MOUREY I, LEMOUCHI D, GRENIER PA: Thin-section chest CT findings of primary Sjögren's syndrome: correlation with pulmonary function. *Eur Radiol* 2002; 12: 1504-11. https://doi.org/10.1007/s00330
39. MATSUYAMA N, ASHIZAWA K, OKIMOTO T, KADOTA J, AMANO H, HAYASHI K: Pulmonary lesions associated with Sjögren's syndrome: radiographic and CT findings. *Br J Radiol* 2003; 76: 880-4. https://doi.org/10.1259/bjr/18937619
40. PERTOVAARA M, KORPELA M, SAARELAINEN S *et al*.: Long-term follow-up study of pulmonary findings in patients with primary Sjögren's syndrome. *Scand J Rheumatol* 2004; 33: 343-8. https://doi.org/10.1080/03009740410006196
41. ITO I, NAGAI S, KITAICHI M *et al*.: Pulmonary manifestations of primary Sjögren's syndrome: a clinical, radiologic, and pathologic study. *Am J Respir Crit Care Med* 2005; 171: 632-8. https://doi.org/10.1164/rccm.200403-417OC
42. WATANABE M, NANIWA T, HARA M, ARAKAWA T, MAEDA T: Pulmonary manifestations in Sjögren's syndrome: correlation analysis between chest computed tomographic findings and clinical subsets with poor prognosis in 80 patients. *J Rheumatol* 2010; 37: 365-73. https://doi.org/10.3899/jrheum.090507
43. DONG X, ZHOU J, GUO X *et al*.: A retrospective analysis of distinguishing features of chest HRCT and clinical manifestation in primary Sjögren's syndrome-related interstitial lung disease in a Chinese population. *Clin Rheumatol* 2018; 37: 2981-8. https://doi.org/10.1007/s10067-018-4289-6
44. WANG Y, HOU Z, QIU M, YE Q: Risk factors for primary Sjögren syndrome-associated interstitial lung disease. *J Thorac Dis* 2018; 10: 2108-17. https//doi.org/10.21037/jtd.2018.03.120
45. KAMIYA Y, FUJISAWA T, KONO M *et al*.: Prognostic factors for primary Sjögren's syndrome-associated interstitial lung diseases. *Respir Med* 2019; 159: 105811. https://doi.org/10.1016/j.rmed.2019.105811
46. SAHIN OZDEMIREL T, OZDEMIREL AE, AKINCI OZYUREK B, YENIBERTIZ D, ERDOGAN Y: The evaluation of lung involvement and functional capacities in patients diagnosed with primary Sjögren's syndrome. *Int J Clin Pract* 2021; 75. https://doi.org/10.1111/ijcp.14635
47. ROCA F, DOMINIQUE S, SCHMIDT J *et al*.: Interstitial lung disease in primary Sjögren's syndrome. *Autoimmun Rev* 2017; 16: 48-54. https://doi.org/10.1016/j.autrev.2016.09.017
48. GAO H, ZHANG X-W, HE J *et al*.: Prevalence, risk factors, and prognosis of interstitial lung disease in a large cohort of Chinese primary Sjögren syndrome patients: A case-control study. *Medicine* (Baltimore) 2018; 97: e11003. https://doi.org/ 10.1097/MD.0000000000011003
49. SOGKAS G, HIRSCH S, OLSSON KM *et al*.: Lung involvement in primary Sjögren's syndrome. an under-diagnosed entity. *Front Med* (Lausanne) 2020; 7: 332. https://doi.org/10.3389/fmed.2020.00332
50. ZHANG T, YUAN F, XU L, SUN W, LIU L, XUE J: Characteristics of patients with primary Sjögren's syndrome associated interstitial lung disease and relevant features of disease progression. *Clin Rheumatol* 2020; 39: 1561-8. ttps://doi.org/10.1007/s10067-019-04906-6
51. LIN W, XIN Z, ZHANG J *et al*.: Interstitial lung disease in Primary Sjögren's syndrome. *BMC Pulm Med* 2022; 22: 73. https://doi.org/10.1186/s12890-022-01868-5
52. NATALINI JG, JOHR C, KREIDER M: Pulmonary Involvement in Sjögren Syndrome. *Clin Chest Med* 2019; 40: 531-44. https://doi.org/10.1016/j.ccm.2019.05.002
53. UFFMANN M, KIENER HP, BANKIER AA: Lung manifestation in asymptomatic patients with primary Sjögren syndrome: assessment with high resolution CT and pulmonary function tests. *J Thorac Imaging* 2001; 16: 282-9. https://doi.org/10.1097/00005382-200110000-00009
54. KOYAMA M, JOHKOH T, HONDA O *et al*.: Pulmonary involvement in primary Sjögren's syndrome: spectrum of pulmonary abnormalities and computed tomography findings in 60 patients. *J Thorac Imaging* 2001; 16: 290-6. https://doi.org/10.1097/00005382-200110000-00010
55. FRANQUET T, DÍAZ C, DOMINGO P, GIMÉNEZ A, GELI C: Air trapping in primary Sjögren syndrome: correlation of expiratory CT with pulmonary function tests. *J Comput Assist Tomogr* 1999; 23: 169-73. https://doi.org/10.1097/00004728-199903000-00002.
56. FRANQUET T, GIMÉNEZ A, MONILL JM, DÍAZ C, GELI C: Primary Sjögren's syndrome and associated lung disease: CT findings in 50 patients. *AJR Am J Roentgenol* 1997; 169:655-8. https://doi.org/10.2214/ajr.169.3.9275871
57. SOTO-CARDENAS M-J, PEREZ-DE-LIS M, BOVE A *et al*.: Bronchiectasis in primary Sjögren's syndrome: prevalence and clinical significance. *Clin Exp Rheumatol* 2010; 28: 647-53.
58. WIGHT EC, BAQIR M, RYU JH: Constrictive Bronchiolitis in Patients With Primary Sjögren Syndrome. *J Clin Rheumatol* 2019; 25: 74-7. https.// doi.org/10.1097/RHU.0000000000000771.
59. NAKANISHI M, FUKUOKA J, TANAKA T *et al*.: Small airway disease associated with Sjögren's syndrome: clinico-pathological correlations. *Respir Med* 2011; 105: 1931-8. https://doi.org/10.1016/j.rmed.2011.08.009
60. CHUNG A, WILGUS ML, FISHBEIN G, LYNCH JP: Pulmonary and bronchiolar involvement in Sjögren's syndrome. *Semin Respir Crit Care Med* 2019; 40: 235-54. https://doi.org/10.1055/s-0039-1688448
61. HOWLING SJ, HANSELL DM, WELLS AU, NICHOLSON AG, FLINT JD, MÜLLER NL: Follicular bronchiolitis: thin-section CT and histologic findings. *Radiology* 1999; 212: 637-42. https:// doi.org/10.1148/radiology.212.3.r99se04637
62. LYNCH J, WEIGT S, DERHOVANESSIAN A, FISHBEIN M, GUTIERREZ A, BELPERIO J: Obliterative (Constrictive) bronchiolitis. *Semin Respir Crit Care Med* 2012; 33: 509-32. https://doi.org/10.1055/s-0032-1325161
63. MANDL T, DIAZ S, EKBERG O *et al*.: Frequent development of chronic obstructive pulmonary disease in primary SS--results of a longitudinal follow-up. *Rheumatology* (Oxford) 2012; 51: 941–6. https://doi.org/10.1093/rheumatology/ker409
64. TER BORG E-J, KELDER JC: Is extra-glandular organ damage in primary Sjögren's syndrome related to the presence of systemic auto-antibodies and/or hypergammaglobulinemia? A long-term cohort study with 110 patients from the Netherlands. *Int J Rheum Dis* 2017; 20: 875-81. https://doi.org/10.1111/1756-185X.13070
65. DAVIDSON BK, KELLY CA, GRIFFITHS ID: Ten year follow up of pulmonary function in patients with primary Sjögren's syndrome. *Ann Rheum Dis* 2000; 59: 709-12. https://doi.org/10.1136/ard.59.9.709
66. AERNI MR, VASSALLO R, MYERS JL, LINDELL RM, RYU JH: Follicular bronchiolitis in surgical lung biopsies: Clinical implications in 12 patients. *Respir Med* 2008; 102: 307-12. https://doi.org/10.1016/j.rmed.2007.07.032
67. TRAVIS WD, COSTABEL U, HANSELL DM *et al*.: An Official American Thoracic Society/European Respiratory Society Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med* 2013; 188: 733-48. https:// doi.org/10.1164/rccm.201308-1483ST
68. TABAJ GC, FERNANDEZ CF, SABBAGH E, LESLIE KO: Histopathology of the idiopathic interstitial pneumonias (IIP): A review. *Respirology* 2015; 20: 873-83. https://doi.org/10.1111/resp.12551
69. DE LAURETIS A, VEERARAGHAVAN S, RENZONI E: Review Series: Aspects of Interstitial lung disease: Connective tissue disease-associated interstitial lung disease: How does it differ from IPF? How should the clinical approach differ? *Chron Respir Dis* 2011; 8: 53-82. https://doi.org/10.1177/1479972310393758
70. VERSCHAKELEN JA: The role of high-resolution computed tomography in the work-up of interstitial lung disease. *Curr Opin Pulm Med* 2010; 16: 503-10. https.// doi.org/10.1097/MCP.0b013e32833cc997
71. ZHANG R, SUN T, SONG L, ZUO D, XIAO W: Increased levels of serumgalectin-3 in patients with primary Sjögren's syndrome:

associated with interstitial lung disease. *Cytokine* 2014; 69: 289-9. https://doi.org/10.1016/j.cyto.2014.06.008
72. HE SH, HE YJ, GUO, KJ, LIANG X, LI S-S, LI T-F: Risk factors for progression of interstitial lung disease in Sjögren's syndrome: a single-centered, retrospective study. *Clin Rheumatol* 2022; 41: 1153-1161. https://doi.org/10.1007/s10067-021-05984-1
73. KIM YJ, CHOE J, MOON SJ, SONG JW: Blood KL-6 predicts prognosis in primary Sjögren's syndrome-associated interstitial lung disease. *Sci Rep* 2022; 12: 5343. https://doi.org/10.1038/s41598-022-09283-w
74. CHEN MH, CHOU HP, LAI CC *et al.*: Lung involvement in primary Sjögren's syndrome: correlation between high-resolution computed tomography score and mortality. *J Chin Med Assoc* 2014; 77: 75-82. https://doi.org/10.1016/j.jcma.2013.11.001
75. ENOMOTO Y, TAKEMURA T, HAGIWARA E *et al*.: Prognostic factors in interstitial lung disease associated with primary Sjögren's syndrome: a retrospective analysis of 33 pathologically–proven cases. *PLoS One* 2013; 8: e73774. https://doi.org/10.1371/journal.pone.0073774
76. KOLB M, BONDUE B, PESCI A *et al*.: Acute exacerbations of progressive-fibrosing interstitial lung diseases. *Eur Respir Rev* 2018; 27: 180071. https://doi.org/10.1183/16000617.0071-2018
77. DONG X, GAO Y, LU Y, ZHENG Y: Characteristics of primary Sjögren's syndrome related lymphocytic interstitial pneumonia. *Clin Rheumatol* 2021; 40: 601-12. https://doi.org/10.1007/s10067-020-05236-8
78. BAHARUDDIN H, HANAFIAH M, AFLAH SSS, ZIM MAM, CH'NG SS: Asymptomatic lymphocytic interstitial pneumonia with extensive HRCT changes preceding Sjögren's syndrome. *Case Rep Pulmonol* 2021; 2021: 6693031. https://doi.org/10.1155/2021/6693031
79. FERGUSON EC, BERKOWITZ EA: Lung CT: Part 2, The interstitial pneumonias - clinical, histologic, and CT manifestations. *AJR Am J Roentgenol* 2012; 199: W464-76. https://doi.org/10.2214/AJR.10.7309
80. DE VITA S, GANDOLFO S: Predicting lymphoma development in patients with Sjögren's syndrome. *Expert Rev Clin Immunol* 2019; 15: 929-38. https://doi.org/10.1080/1744666X.2019.1649596
81. ALUNNO A, LEONE MC, GIACOMELLI R, GERLI R, CARUBBI F: Lymphoma and Lymphomagenesis in Primary Sjögren's Syndrome. *Front Med* (Lausanne) 2018; 5: 102. https://doi.org/10.3389/fmed.2018.00102
82. ALUNNO A, LEONE MC, BARTOLONI E, GERLI R, CARUBBI F: Novel insights on lymphoma and lymphomagenesis in primary Sjögren's Syndrome. *Panminerva Med* 2021; 63: 491-8. https://doi.org/10.23736/S0031-0808.20.04079-3
83. VIVINO FB: Sjögren's syndrome: Clinical aspects. *Clin Immunol* 2017; 182: 48-54. https://doi.org/10.1016/j.clim.2017.04.005
84. IGOE A, MERJANAH S, SCOFIELD RH: Sjögren Syndrome and Cancer. *Rheum Dis Clin North Am* 2020; 46: 513-32. https://doi.org/10.1016/j.rdc.2020.05.004
85. BELFEKI N, BELLEFQUIH S, BOURGARIT A: Breast MALT lymphoma and AL amyloidosis complicating Sjögren's syndrome. *BMJ Case Rep* 2019; 12: e227581. https://doi.org/10.1136/bcr-2018-227581
86. THEANDER E: Lymphoma and other malignancies in primary Sjögren's syndrome: a cohort study on cancer incidence and lymphoma predictors. *Ann Rheum Dis* 2006; 65: 796-803. https://doi.org/10.1136/ard.2005.041186
87. TONAMI H, MATOBA M, KUGINUKI Y *et al*.: Clinical and imaging findings of lymphoma in patients with Sjögren syndrome. *J Comput Assist Tomogr* 2003; 27: 517-24. https://doi.org/10.1097/00004728-200307000-00011
88. PAPIRIS SA, KALOMENIDIS I, MALAGARI K *et al*.: Extranodal marginal zone B-cell lymphoma of the lung in Sjögren's syndrome patients: Reappraisal of clinical, radiological, and pathology findings. *Respir Med* 2007; 101: 84-92. https://doi.org/10.1016/j.rmed.2006.04.005
89. BAQIR M, KLUKA EM, AUBRY M-C *et al*.: Amyloid-associated cystic lung disease in primary Sjögren's syndrome. *Respir Med* 2013; 107: 616-21. https://doi.org/10.18632/oncotarget.16010
90. CERESER L, PASSAROTTI E, DE PELLEGRIN A *et al*.: Chest high-resolution computed tomography in patients with connective tissue disease: pulmonary conditions beyond "the usual suspects". *Curr Probl Diagn Radiol* 2022; 51(5): 759-67. https://doi.org/10.1067/j.cpradiol.2021.07.007
91. YACHOUI R, LEON C, SITWALA K, KREIDY M: Pulmonary MALT lymphoma in patients with Sjögren's syndrome. *Clin Med Res* 2017; 15: 6-12. https://doi.org/10.3121/cmr.2017.1341
92. HARE SS, SOUZA CA, BAIN G *et al*.: The radiological spectrum of pulmonary lymphoproliferative disease. *Br J Radiol* 2012; 85: 848-64. https://doi.org/10.1259/bjr/16420165
93. XU Y, FEI Y, ZHONG W *et al*.: The Prevalence and clinical characteristics of primary Sjögren's syndrome patients with lung cancer: An analysis of ten cases in China and literature review. *Thorac Cancer* 2015; 6: 475-9. https://doi.org/10.1111/1759-7714.12216
94. ZHONG H, LIU S, WANG Y *et al*.: Primary Sjögren's syndrome is associated with increased risk of malignancies besides lymphoma: A systematic review and meta-analysis. *Autoimmun Rev* 2022; 21: 103084. https://doi.org/10.1016/j.autrev.2022.103084
95. BANDOH S, FUJITA J, HABA R *et al*.: Lung Cancer with Focal Lymphocytic Interstitial Pneumonia. *Intern Med* 2002; 41: 997-1001. https://doi.org/10.2169/internalmedicine.41.997
96. MILANI P, BASSET M, RUSSO F, FOLI A, PALLADINI G, MERLINI G: The lung in amyloidosis. *Eur Resp Rev* 2017; 26: 170046. https://doi.org/10.1183/16000617.0046-2017
97. SAMBATARO G, FERRO F, ORLANDI M *et al*.: Clinical, morphological features and prognostic factors associated with interstitial lung disease in primary Sjögren's syndrome: A systematic review from the Italian Society of Rheumatology. *Autoimmun Rev* 2020; 19: 102447. https://doi.org/10.1016/j.autrev.2019.102447
98. LI H, LU Y: Pulmonary amyloidosis and cystic lung disease in primary Sjögren's syndrome: a case report and literature review. *Clin Rheumatol* 2021; 40: 3345-50. https://doi.org/10.1007/s10067-021-05596-9
99. ZAMORA AC, WHITE DB, SYKES A-MG *et al*.: Amyloid-associated cystic lung disease. *Chest* 2016; 149: 1223-33. https://doi.org/10.1378/chest.15-1539
100. BRANDELIK SC, HEUSSEL CP, KAUCZOR H-U *et al*.: CT features in amyloidosis of the respiratory system – Comprehensive analysis in a tertiary referral center cohort. *Eur J Radiol* 2020; 129: 109123. https://doi.org/10.1016/j.ejrad.2020.109123
101. JEONG YJ, LEE KS, CHUNG MP *et al*.: Amyloidosis and lymphoproliferative disease in Sjögren syndrome: thin-section computed tomography findings and histopathologic comparisons. *J Comput Assist Tomogr* 2004; 28: 776-81. https://doi.org/10.1097/00004728-200411000-00008
102. GRUDEN JF, NAIDICH DP, MACHNICKI SC, COHEN SL, GIRVIN F, RAOOF S: An algorithmic approach to the interpretation of diffuse lung disease on chest CT imaging: a theory of almost everything. *Chest* 2020; 157: 612-35. https://doi.org/10.1016/j.chest.2019.10.017
103. HUMBERT M, KOVACS G, HOEPER MM *et al*.: ESC/ERS Scientific Document Group. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022 Aug 26. https://doi.org/10.1093/eurheartj/ehac237
104. SIMONNEAU G, MONTANI D, CELERMAJER DS *et al*.: Haemodynamic definitions and updated clinical classification of pulmonary hypertension. *Eur Respir J* 2019; 53: 1801913. https://doi.org/10.1183/13993003.01913-2018
105. LAUNAY D, HACHULLA E, HATRON P-Y, JAIS X, SIMONNEAU G, HUMBERT M: Pulmonary arterial hypertension: a rare complication of primary Sjögren syndrome: report of 9 new cases and review of the literature. *Medicine* (Baltimore) 2007; 86: 299-315. https://doi.org/10.1097/MD.0b013e3181579781
106. FAYED H, COGHLAN JG: Pulmonary hypertension associated with connective tissue disease. *Semin Respir Crit Care Med* 2019; 40: 173-83. https://doi.org/10.1055/s-0039-1685214
107. ARCA BARCA B, PAREDES VILA S, MAZAIRA RIOCABO A: Primary pulmonary hypertension in Sjögren's syndrome: a rare association. *Reumatol Clin* (Engl Ed) 2011; 7: 212-4. https://doi.org/10.1016/j.reuma.2010.06.006
108. ALHAMAD EH, CAL JG, ALRAJHI NN *et al*.: Clinical characteristics and outcomes in patients with primary Sjögren's syndrome-associated interstitial lung disease. *Ann Thorac Med* 2021; 16: 156-64. https://doi.org/10.4103/atm.atm_632_20
109. QUARTUCCIO L: Risk of thrombosis in

Sjögren syndrome: the open question of endothelial function immune-mediated dysregulation. *J Rheumatol* 2017; 44: 1106-8. https://doi.org/10.3899/jrheum.170462

110. AVIÑA-ZUBIETA JA, JANSZ M, SAYRE EC, CHOI HK: The Risk of Deep Venous Thrombosis and Pulmonary Embolism in Primary Sjögren Syndrome: A General Population-based Study. *J Rheumatol* 2017; 44: 1184-9. https://doi.org/10.3899/jrheum.160185
111. PUEBLA-ALDAMA D, CUETO-ROBLEDO G, BARRAGAN-MARTINEZ M-P *et al*.: Review of functional status and hemodynamic parameters in patients diagnosed with Chronic Thromboembolic Pulmonary Hypertension (CTEPH) with and without Antiphospholipid Syndrome (APLS). *Curr Probl Cardiol* 2022; 101154. https://doi.org/10.1016/j.cpcardiol.2022.101154
112. ASCHA M, RENAPURKAR R, TONELLI A: A review of imaging modalities in pulmonary hypertension. *Ann Thorac Med* 2017; 12: 61-73. https://doi.org/10.4103/1817-1737.203742
113. ALUJA JARAMILLO F, GUTIERREZ FR, DÍAZ TELLI FG, YEVENES ARAVENA S, JAVIDAN-NEJAD C, BHALLA S: Approach to pulmonary hypertension: from CT to clinical diagnosis. *Radiographics* 2018; 38: 357-73. https://doi.org/10.1148/rg.2018170046
114. GARDINER P, WARD C, ALLISON A *et al*.: Pleuropulmonary abnormalities in primary Sjögren's syndrome. *J Rheumatol* 1993; 20:831-7.
115. DALAVANGA YA, VOULGARI PV, GEORGIADIS AN *et al*.: Lymphocytic alveolitis: A surprising index of poor prognosis in patients with primary Sjögren's syndrome. *Rheumatol Int* 2006; 26(9): 799-804. https://doi.org/10.1007/s00296-005-0092-1
116. SALAFFI F, MANGANELLI P, CAROTTI M *et al*.: A longitudinal study of pulmonary involvement in primary Sjögren's syndrome: relationship between alveolitis and subsequent lung changes on high- resolution computed tomography. *Br J Rheumatol* 1998; 37: 263-9. https://doi.org/10.1093/rheumatology/37.3.263
117. HE XW, LUO QZ, SHANG Y, GAO ZC: Expression and clinical significance of CCL18 in bronchoalveolar lavage fluid of connective tissue disease-associated interstitial lung disease. *Zhonghua Yi Xue Za Zhi* 2019; 99(38): 2976-81. https://doi.org/10.3760/cma.j.issn.0376-2491.2019.38.003
118. JIANG Z, TAO JH, ZUO T *et al*.: The correlation between miR-200c and the severity of interstitial lung disease associated with different connective tissue diseases. *Scand J Rheumatol*. 2017; 46: 122-9. https://doi.org/10.3109/03009742.2016.1167950
119. JEE AS, SHEEHY R, HOPKINS P *et al*.: Diagnosis and management of connective tissue disease-associated interstitial lung disease in Australia and New Zealand: A position statement from the Thoracic Society of Australia and New Zealand. *Respirology* 2021; 26: 23-51. https://doi.org/10.1111/resp.13977
120. REINA D, ROIG VILASECA D, TORRENTE-SEGARRA V *et al*.: Sjögren's syndrome-associated interstitial lung disease: A multicenter study. *Reumatol Clin* (Engl Ed) 2016; 12: 201-5. https://doi.org/10.1016/j.reuma.2015.09.003
121. ZHAO R, WANG Y, ZHOU W *et al*.: Associated factors with interstitial lung disease and health-related quality of life in Chinese patients with primary Sjögren's syndrome. *Clin Rheumatol* 2020; 39: 483-9. https://doi.org/10.1007/s10067-019-04753-5
122. GUPTA S, FERRADA MA, HASNI SA: Pulmonary manifestations of primary Sjögren's syndrome: underlying immunological mechanisms, clinical presentation, and management. *Front Immunol* 2019; 10: 1327. https://doi.org/10.3389/fimmu.2019.01327
123. SPAGNOLO P, DISTLER O, RYERSON CJ *et al*.: Mechanisms of progressive fibrosis in connective tissue disease (CTD)-associated interstitial lung diseases (ILDs). *Ann Rheum Dis* 2021; 80: 143-50. https://doi.org/10.1136/annrheumdis-2020-217230
124. FLAHERTY KR, WELLS AU, COTTIN V *et al*.: Nintedanib in progressive fibrosing interstitial lung diseases. *N Engl J Med* 2019; 381: 1718-27. https://doi.org/10.1056/NEJMoa1908681
125. MANFREDI A, VACCHI C, DELLACASA G *et al*.: Fibrosing interstitial lung disease in primary Sjögren syndrome. *Joint Bone Spine* 2021; 88: 105237. https://doi.org/10.1016/j.jbspin.2021.105237
126. FISCHER A, DISTLER J: Progressive fibrosing interstitial lung disease associated with systemic autoimmune diseases. *Clin Rheumatol* 2019; 38: 2673-81. https://doi.org/10.1007/s10067-019-04720-0
127. COTTIN V, LEGA J-C, COURY F, NASSER M: A call for evidence in connective tissue diseases-associated interstitial lung disease. *Joint Bone Spine* 2022; 89: 105274. https://doi.org/10.1016/j.jbspin.2021.105274
128. CHIU Y-H, SPIERINGS J, DE JONG PA *et al*.: Predictors for progressive fibrosis in patients with connective tissue disease associated interstitial lung diseases. *Respir Med* 2021; 187: 106579. https://doi.org/10.1016/j.rmed.2021.106579
129. SHUMAR JN, CHANDEL A, KING CS: Antifibrotic Therapies and Progressive Fibrosing Interstitial Lung Disease (PF-ILD): Building on INBUILD. *J Clin Med* 2021; 10: 2285. https://doi.org/10.3390/jcm10112285
130. FISCHER A, DU BOIS R: Interstitial lung disease in connective tissue disorders. *Lancet* 2012; 380: 689-98. https://doi.org/10.1016/S0140-6736(12)61079-4
131. KIM YJ, CHOE J, KIM HJ, SONG JW: Long-term clinical course and outcome in patients with primary Sjögren syndrome-associated interstitial lung disease. *Sci Rep* 2021; 11: 12827. https://doi.org/10.1038/s41598-021-92024-2
132. COLLARD HR, RYERSON CJ, CORTE TJ *et al*.: Acute Exacerbation of Idiopathic Pulmonary Fibrosis. An International Working Group Report. *Am J Respir Crit Care Med* 2016; 194: 265-75. https://doi.org/10.1164/rccm.201604-0801CI
133. PARAMBIL JG, MYERS JL, LINDELL RM, MATTESON EL, RYU JH: Interstitial lung disease in primary Sjögren syndrome. *Chest* 2006; 130: 1489-95. https://doi.org/10.1378/chest.130.5.1489
134. SUDA T, KAIDA Y, NAKAMURA Y *et al*.: Acute exacerbation of interstitial pneumonia associated with collagen vascular diseases. *Respir Med* 2009; 103: 846-53. https://doi.org/10.1016/j.rmed.2008.12.019
135. MANFREDI A, SEBASTIANI M, CERRI S *et al*.: Acute exacerbation of interstitial lung diseases secondary to systemic rheumatic diseases: a prospective study and review of the literature. *J Thorac Dis* 2019; 11: 1621-8. https://doi.org/10.21037/jtd.2019.03.28
136. CAO M, SHENG J, QIU X *et al*.: Acute exacerbations of fibrosing interstitial lung disease associated with connective tissue diseases: a population-based study. *BMC Pulm Med* 2019; 19: 215. https://doi.org/10.1186/s12890-019-0960-1
137. RAMOS-CASALS M, BRITO-ZERÓN P, BOMBARDIERI S *et al*.: EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies. *Ann Rheum Dis* 2020; 79: 3-18. https://doi.org/10.1136/annrheumdis-2019-216114
138. DISTEFANO G, FANZONE L, PALERMO M *et al*.: HRCT patterns of drug-induced interstitial lung diseases: a review. *Diagnostics* (Basel) 2020; 10: 244. https://doi.org/10.3390/diagnostics10040244
139. PRICE EJ, RAUZ S, TAPPUNI AR *et al*.: The British Society for Rheumatology guideline for the management of adults with primary Sjögren's Syndrome. *Rheumatology* (Oxford) 2017; 56: 24-48. https://doi.org/10.1093/rheumatology/kex166.
140. VACCHI C, MANFREDI A, CASSONE G, ERRE GL, SALVARANI C, SEBASTIANI M: Efficacy and safety of rituximab in the treatment of connective tissue disease-related interstitial lung disease. *Drugs Context* 2021; 10: 1-12. https://doi.org/10.7573/dic.2020-8-7
141. KAEGI C, WUEST B, SCHREINER J *et al*.: Systematic review of safety and efficacy of rituximab in treating immune-mediated disorders. *Front Immunol* 2019; 10: 1990. https://doi.org/10.3389/fimmu.2019.01990
142. HATABU H, HUNNINGHAKE GM, RICHELDI L *et al*.: Interstitial lung abnormalities detected incidentally on CT: a Position Paper from the Fleischner Society. *Lancet Respir Med* 2020; 8: 726-37. https://doi.org/10.1016/S2213-2600(20)30168-5
143. HATA A, SCHIEBLER ML, LYNCH DA, HATABU H: Interstitial lung abnormalities: state of the art. *Radiology* 2021; 301: 19-34. https://doi.org/10.1148/radiol.2021204367
144. FISCHER A, SWIGRIS JJ, DU BOIS RM *et al*.: Minor salivary gland biopsy to detect primary Sjögren syndrome in patients with interstitial lung disease. *Chest* 2009; 136: 1072-8. https://doi.org/10.1378/chest.08-2839
145. ALHAMAD EH, CAL JG, PARAMASIVAM MP *et al*.: Clinical significance of minor salivary gland biopsy in patients with idiopathic interstitial pneumonia. *Respir Med* 2020; 174: 106189. https://doi.org/10.1016/j.rmed.2020.106189
146. AUTERI S, ALBERTI ML, FERNÁNDEZ ME *et al*.: Occult primary Sjögren Syndrome in

patients with interstitial pneumonia with autoimmune features. *Respir Med* 2021; 182: 106405. https://doi.org/10.1016/j.rmed.2021.106405

147. FISCHER A, ANTONIOU KM, BROWN KK *et al*.: An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J* 2015; 46: 976-87. https://doi.org/10.1183/13993003.00150-2015
148. SAMBATARO G, SAMBATARO D, TORRISI SE *et al*.: State of the art in interstitial pneumonia with autoimmune features: a systematic review on retrospective studies and suggestions for further advances. *Eur Respir Rev* 2018; 27: 170139. https://doi.org/10.1183/16000617.0139-2017
149. SHIBOSKI CH, SHIBOSKI SC, SEROR R *et al*.: 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. *Arthritis Rheumatol* 2017; 69: 35-45. https://doi.org/10.1002/art.39859
150. SEBASTIANI M, CASSONE G, DE PASQUALE L *et al*.: Interstitial pneumonia with autoimmune features: A single center prospective follow-up study. *Autoimmun Rev* 2020; 19: 102451. https://doi.org/10.1016/j.autrev.2019.102451