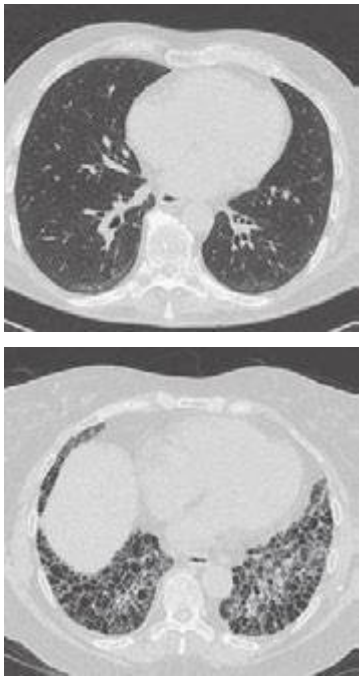

FIGURE 382-8 HRCT images of the chest from patients with systemic sclerosis. ***Top panel:*** Early interstitial lung disease. Mild changes with sub pleural reticulations and ground glass opacities in the lower lobes of the lung. Patient in supine position. ***Bottom panel:*** Extensive lung fibrosis with ground glass opacities, coarse reticular honeycombing, and traction bronchiectasis. *(Courtesy of Rishi Agrawal, MD.)*

the course of the disease (within the first 3 years), when the FVC can decline by 30% per year.

Pulmonary involvement can remain asymptomatic until it is advanced. The most common presenting respiratory symptoms—exertional dyspnea, fatigue, and reduced exercise tolerance—are subtle and slowly progressive. A chronic dry cough may be present. Physical examination may reveal "Velcro" crackles at the lung bases. Pulmonary function testing (PFT) is a sensitive method for detecting early pulmonary involvement. The most common abnormalities are reductions in FVC, total lung capacity (TLC), and DLCO. A reduction in DLCO that is significantly out of proportion to the reduction in lung volumes should raise suspicion for pulmonary vascular disease, but may also be due to anemia. Oxygen desaturation with exercise is common.

Chest radiography can rule out infection and other causes of pulmonary involvement, but compared to HRCT, it is relatively insensitive for detection of early ILD. HRCT shows subpleural reticular linear opacities and ground-glass opacifications, predominantly in the lower lobes, even in asymptomatic patients (Fig. 382-8). Additional HRCT findings include mediastinal lymphadenopathy, pulmonary nodules, traction bronchiectasis, and uncommonly, honeycomb changes. The extent of pulmonary interstitial changes on HRCT is a predictor of mortality in SSc. Bronchoalveolar lavage (BAL) can demonstrate inflammation in the lower respiratory tract and may be useful for ruling out infection. Although an elevated proportion of neutrophils (>2%) and/or eosinophils (>3%) in the BAL fluid is correlated with more extensive lung disease on HRCT and is associated with more rapid decline in FVC and reduced survival, BAL is not useful for identifying reversible alveolitis. Lung biopsy is indicated only in patients with atypical findings on chest radiographs and should be thoracoscopically guided. The histologic pattern on lung biopsy may predict the risk of progression of ILD. The most common pattern in SSc, NSIP, carries a better prognosis than UIP.

Pulmonary Arterial Hypertension (PAH) PAH, defined as a mean pulmonary arterial pressure ≥25 mmHg with a pulmonary capillary wedge pressure ≤15 mmHg, develops in approximately 15% of patients with SSc and can occur in association with ILD or as an isolated abnormality. The natural history of SSc-associated PAH is variable, but in many patients, it follows a downhill course with development of right heart failure. The median survival of SSc patients with untreated PAH is 1 year following diagnosis. Risk factors for PAH include limited cutaneous disease, older age at disease onset, severe Raynaud's phenomenon, and the presence of antibodies to centromere, U1-RNP, U3-RNP (fibrillarin), and B23.

The initial symptom of PAH is typically exertional dyspnea and reduced exercise capacity. With disease progression, angina, exertional near-syncope, and symptoms and signs of right-sided heart failure appear. Physical examination may show tachypnea, a prominent split S_2 heart sound, palpable right ventricular heave, elevated jugular venous pressure, and dependent edema. Doppler echocardiography provides a noninvasive method for estimating the pulmonary arterial pressure. In light of the poor prognosis of untreated PAH, all SSc patients should be screened for its presence at initial evaluation. Echocardiographic estimates of pulmonary arterial systolic pressures >40 mmHg at rest suggest PAH. Pulmonary function testing may show a reduced DLCO in isolation or out of proportion with the severity of restriction. Right heart catheterization is the gold standard for diagnosing PAH. Because echocardiography can result in over- or underestimation of pulmonary arterial pressures in SSc, cardiac catheterization is always required to confirm the presence of PAH; accurately assess its severity, including the degree of right heart dysfunction; and rule out venoocclusive disease and other cardiac causes of pulmonary hypertension. Yearly echocardiographic screening for PAH is recommended in most patients with SSc; an isolated decline in DLCO may also be indicative of developing PAH. Serum levels of brain natriuretic peptide (BNP) and N-terminal pro-BNP correlate with the presence and severity of PAH in SSc, as well as survival. While BNP measurements can be useful in screening for PAH and in monitoring the response to treatment, elevated BNP levels are not specific for PAH and also occur in other forms of right and left heart disease. The prognosis of SSc-associated PAH is worse, and treatment response poorer, than in idiopathic PAH

GASTROINTESTINAL INVOLVEMENT

The gastrointestinal tract is affected in up to 90% of SSc patients with both limited and diffuse cutaneous forms of the disease. The pathologic features of atrophy of smooth muscle, intact mucosa, and obliterative small-vessel vasculopathy are similar throughout the length of the gastrointestinal tract.

Upper Gastrointestinal Tract Involvement Oropharyngeal manifestations due to a combination of xerostomia, reduced oral aperture, periodontal disease, and resorption of the mandibular condyles are frequent and cause much distress. The frenulum of the tongue may be shortened. Most patients have symptoms of gastroesophageal reflux disease (GERD): heartburn, regurgitation, and dysphagia. A combination of reduced lower esophageal sphincter pressure resulting in gastroesophageal reflux, impaired esophageal clearance of refluxed gastric contents due to diminished motility in the distal two-thirds of the esophagus, and delayed gastric emptying accounts for GERD. Manometry shows abnormal upper intestinal motility in most patients with SSc. Extraesophageal manifestations of GERD include hoarseness, chronic cough, and aspiration pneumonitis, which may aggravate underlying ILD. Chest computed tomography (CT) scan characteristically shows a dilated esophagus with intraluminal air. Endoscopy may be necessary to rule out opportunistic infections with *Candida*, herpes virus, and cytomegalovirus. Severe erosive esophagitis may be found on endoscopy in patients with minimal symptoms. Esophageal strictures and Barrett's esophagus may complicate chronic GERD. Because Barrett's esophagus is associated with an increased risk of adenocarcinoma, SSc patients with Barrett's esophagus need periodic endoscopy and esophageal biopsy.

Gastroparesis with early satiety, abdominal distention, and aggravated reflux symptoms is common. The presence and severity of gastroparesis can be assessed by radionuclide gastric emptying studies. Gastric antral vascular ectasia (GAVE) in the antrum may occur. These subepithelial lesions, reflecting the diffuse small-vessel vasculopathy of SSc, are described as "watermelon stomach" due to their endoscopic appearance. Patients with GAVE can have recurrent episodes of gastrointestinal bleeding, resulting in chronic unexplained anemia.