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Overcoming Barriers to Timely Diagnosis and Classification of Interstitial Lung Disease: Considerations for Radiologists

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Dr. Lynch:
Thank you for joining us for this Continuing Medical Education webinar, which is entitled, Overcoming Barriers to Timely Diagnosis and Classifications of Interstitial Lung Disease: Considerations for Radiologists. My name is Dr. David Lynch from National Jewish Health in Denver, where I've worked for over 30 years. And what I hope to do tonight is to share some of what we've learned over that really amazing span of time in improving our understanding of interstitial lung disease. This webinar is provided by Clinical Care Options LLC, and it's supported by an educational grant from Boehringer Ingelheim Pharmaceuticals. During our presentation here we will have several pretest questions. We will present the educational content and then we will have the posttest content.

Okay, so now we're going to talk about the CT features of interstitial lung disease. And I'm not going to spend too much time on them, but the primary thing that when we were interpreting chest CTs, the one of the big distinctions in the bifurcations really in our decision-making, is this a fibrotic interstitial lung disease or non-fibrotic? The signs of fibrotic abnormality are reticular pattern, traction bronchiectasis, honeycombing, architectural distortion, and lobar volume loss. However, you should note that reticular abnormality on its own is not a sufficient sign of fibrosis. The non-fibrotic signs you're familiar with, nodules, ground glass consolidation, crazy paving, cysts, and calcifications. This is going to focus on fibrotic lung disease.

So here are the signs on an image. So in this patient, you know, we refer to the reticular abnormality when we see this fine network of abnormality scattered throughout the lung reticulum, it’s the Latin for a net. But importantly, in addition to that, we also have traction bronchiectasis, dilation and irregularity of the bronchi and sometimes the bronchioles. We can see honeycombing which you don't see in this particular case. It has some irregularity we're going to talk about a little bit because I think, increasingly, we're recognizing this as a very early feature of lung fibrosis, particularly in the context of interstitial lung abnormalities. Architectural distortion, we'll talk about, and lobar volume loss.

So then to define a particular pattern, these are the Fleischner Society definitions, is a collection of innumerable small linear opacities that, by summation, produce an appearance resembling a net. And you can have a coarse reticular abnormality which this is. And notice incidentally that this abnormality is reticular, there is clearcut traction bronchiectasis, but there is subpleural sparing, and we'll talk about why that’s important.

And then this is in contrast to that. This is a much finer reticular abnormality. And when you look at this, first of all, you might just say, oh, this is ground-glass abnormality. But when you look very closely, you can see that within the ground glass, there is a fine network reticular pattern, also visible here. And there's also evidence of traction bronchiectasis. So even though this at first glance looks like ground glass, this really counts as a fine reticular pattern. And that's what we go with.

This is just to compare fibrotic and non-fibrotic reticular abnormality. Again, this patient was fibrotic and hypersensitivity pneumonitis with a clearcut reticular abnormality with traction bronchiectasis, whereas this patient with a crazy paving pattern, look at it first glance, look

quite similar, ground-glass abnormality and reticular abnormality, but no traction bronchiectasis, and therefore no evidence of fibrosis. This was pulmonary alveolar proteinosis.

So that brings us to traction bronchiectasis and bronchiolectasis which remains our most important sign of fibrosis. It is defined as this irregular bronchial and bronchiolar dilatation caused by surrounding retractile pulmonary fibrosis. So it's really telling you that the lung in this area is so – there's so much fibrosis that it's pulling the bronchi open. Also in this case, you'll see a little bit of honeycombing, which we'll talk about further on a couple of next slides.

So traction bronchiectasis is important in pulmonary fibrosis, it correlates with the extent of fibroblastic foci on histology and with a diagnosis of usual interstitial pneumonia and with prognosis, so it is an important prognostic clue. And location is important too. If you have predominantly peripheral traction bronchiectasis, as in this case, that's more common in UIP. Whereas, if you have more central traction bronchiectasis, as in this case, you should think much more commonly about NSIP or chronic hypersensitivity pneumonitis. And notice again, this subpleural sparing in this patient with nonspecific interstitial pneumonia.

Honeycombing, again, you're probably all familiar with this. But just to define it, it is defined as clustered cystic airspace, it's usually 3 to 10 mm, it's usually quite small. And usually in a row, in a subpleural row, either a single layer, or as in this case, several layers of subpleural honeycomb cysts. Mostly, we used to think of this as just end-stage pulmonary fibrosis, but most recent work seems to suggest that these honeycomb cysts are actually the result of end-stage bronchiolar dilation. So this is really advanced traction bronchiolectasis, where the rest of the lobule is completely obliterated. And that's why we see it as honeycombing. But it remains a useful sign of advanced fibrosis and has some specificity for diagnosis if UIP. So important to look for it. And then this is, you know, smaller honeycombings, and just in a single layer. Both of these patients had UIP.

Architectural distortion is when you have distortion of either central or peripheral bronchial bronchovascular anatomy, just irregularity and deviation of the normal architecture. It's helpful particularly in the non-UIP cases and particularly in upper lobe disease, where you can see the volume loss as well.

So plural irregularity, we often see that in, particularly in upper lobe disease, and we're learning actually that this is actually one of the helpful early signs sometimes of UIP. So, you know, I think we're increasingly going to be paying attention to that sign, particularly when it's present in the upper lobes like this.

Lobar volume loss, important to pay attention to that. Very easy to see on multiplanar imaging. Here in the lower lobes, you can see the marked downward displacement of the fissures, indicating marked bilateral lower lobe volume loss in this patient with NSIP. And then upper lobe volume loss with a lot of bronchial distortion in this patient with pleuroparenchymal fibroelastosis.

Again, I talked earlier about ground-glass opacity in lung fibrosis. This is actually a case we showed at the start of the thing – of this talk. So the point about ground-glass abnormality, a lot has been written and it's a bit confusing about ground-glass abnormality in lung fibrosis. If you have pure ground-glass abnormality without reticular abnormality or traction bronchiectasis, that's usually non-fibrotic. Conversely, and this patient had respiratory bronchiolitis related to cigarette smoking, smoking-related interstitial lung disease, conversely, this patient at first glance, has ground-glass abnormality, as I showed in that earlier slide. But, you know, when you look really closely, you see a fine reticular pattern and some traction bronchiectasis, reticular pattern that are shown here. So when you see ground-glass with reticular traction bronchiectasis, that's just fibrosis, and you don't have to pay – you just treat it as a fibrotic lung disease.

So this is the classification that you've probably seen before of idiopathic interstitial pneumonias. And the good news here is we're just going to be talking about the chronic fibrosing interstitial pneumonias, which will be UIP, NSIP, and hypersensitivity pneumonitis, which is not on this slide, because it's not regarded as idiopathic.

It is important to remember the frequency of these conditions. So UIP, as the name suggests, is the most common diagnosis in most practices. NSIP is less common. These smoking-related institutional pneumonias, less common. Organizing pneumonia and diffuse alveolar damage are less common. And LIP are rare. And this is why it's important, one of the reasons why it's really important to make this distinction, before we had treatments for UIP, if you, or I as a radiologist, made a diagnosis of UIP or IPF, we were telling the patients that they had about a 40% 5- year survival. Pretty bad, right? Worse than breast cancer, worse than lung cancer – worse than breast cancer and not much different from lung cancer. So it's a really significant diagnosis. And radiologists, by and large, are responsible for making this diagnosis. Fibrotic NSIP has an intermediate prognosis, and most of the other interstitial pneumonias have a much better prognosis.

So, right, so the rest of this talk is going to be about the types of fibrosing interstitial pneumonias. We're going to talk about UIP. And UIP is a morphologic diagnosis. And it may be idiopathic, in which case it's called idiopathic pulmonary fibrosis, or it may be secondary to underlying connective tissue diseases. And we'll talk about those. NSIP, likewise, may be idiopathic or secondary, but the difference is

that NSIP in about 80 to 90% of cases is secondary, and not idiopathic, whereas UIP, in about 70 or 80% of cases, it's idiopathic. So that's the difference. And we'll talk about the other etiologies.

Chronic hypersensitivity pneumonitis, we will also discuss, because this is the triad, every week when we go to interstitial lung disease conference, these are the entities we're trying to tease out. Idiopathic pleuropulmonary fibroelastosis, pretty uncommon, and we don't worry too much about that.

Okay, so we're going to start then our next part of the talk with what are the criteria for diagnosing idiopathic pulmonary fibrosis. This was a white paper we published now about 5 years ago. And that's the basis. That, and there's also an ATS paper that has similar criteria. So we'll go through the criteria in that paper. And these are the typical – the categories. This is the language that we as radiologists use when we're reporting a case of fibrosing interstitial pneumonia. We can choose to call it typical UIP, probable UIP, indeterminate or consistent with an alternative diagnosis. And those things are based on distribution and features. And we're going to go through each of those in turn.

Here is the typical UIP pattern, and it has to have all of these features. You see, lower – and I think the distribution is by far the most important, subpleural predominant; this disease almost invariably just hugs the pleura. It's exquisitely so pleural, and it is as you can see, lower lung predominant. And then the CT features are reticular abnormality and traction bronchiectasis which you see here, and subpleural honeycomb. So again, these are the classic features of UIP. And if you make this diagnosis based on these features, as I'll show you, you'll be correct about 90% of the time. Again, to summarize, basal and subpleural predominant, occasionally diffuse distribution is often somewhat heterogeneous. And the CT features are honeycombing, reticular pattern, traction bronchiectasis, or bronchiolectasis, and absence of features to suggest an alternative diagnosis.

Here's the next pattern. And this one we diagnose almost always just on the coronal images. So this patient has, again, subpleural predominant abnormality lower lung predominant. And you can see that there is a fine reticular pattern here. There is evidence of traction bronchiectasis, as seen, I think, in that left lower lobe here, and but there is no honeycombing. So this looks exactly like UIP but with no honeycombing. We call it probable UIP. And I'll get into the reasons why it's important to make that distinction. Again, and then these are the axial images showing the lower lung predominant reticular abnormality and traction bronchiectasis. So basal and subpleural predominant, again, the distribution may be heterogeneous, as opposed to NSIP. Reticular pattern, traction bronchiectasis, bronchiolectasis, no honeycombing, and no features to suggest an alternative diagnosis.

Now, what's interesting is this happens several times, well at least once a week to me, I look at a case of fibrosing interstitial pneumonia and I say, I don't know what this is. It clearly has traction bronchiectasis, there is some reticular abnormality, there wasn't any honeycombing, but there's a moderate amount of ground-glass abnormality here, maybe a little bit of mosaic attenuation. It's lower lung predominant, it's somewhat subpleural predominant, but there's some peribronchovascular predominance. And so these are the cases that we put it in this indeterminate box. This is the CT pattern indeterminate for UIP. So you can have a variable distribution. And you just have some inconspicuous features that are suggestive of a non-UIP pattern. Like as I said, the patchy ground glass, the peribronchovascular distribution, etc. And it's helpful, although the trouble with that is, you know, depending on your level of diagnostic confidence, you can put a lot of cases into this indeterminate box or very few, so it's pretty subjective, is the problem. But I think I find it a useful category.

And then finally, we have this kind of case, upper lobe predominant reticular abnormality. Really nothing much in the mid or lower lungs, clearcut traction bronchiectasis. And we would regard this as most consistent with a non-IPF diagnosis. If you have upper midline fibrosis, peribronchovascular predominance with subpleural sparing, if you have a lot of ground-glass abnormality without an acute exacerbation, if you have extensive mosaic attenuation with lobular air trapping, nodules or cysts, if you have consolidation. So all of these things make us say, this is not likely to be IPF.

So here's the interesting thing. If you look at, there are two papers from Dr. Chung, one from National Jewish when he was working with us and the other from University of Chicago. And they both show that if a radiologist, thoracic radiologist, makes the diagnosis of typical UIP, they are going to predict a histologic UIP diagnosis in about 90% of cases, not 100%, but 90% is actually really remarkably good for a non-invasive test. And this is why patients with typical UIP and probable UIP usually don't get biopsies. You will notice that the predictive probability of probable UIP is a little less at about 80%. So a little less certainty. And that's why we have elected to keep that distinction. Also of interest is that even in this indeterminate and alternative diagnostic group, the probability of histologic UIP is about 50%. So even though we can't make the diagnosis of UIP, about half of these cases are going to end up having histologic UIP, even in this alternative diagnosis. It just keeps us humbled to say that, you know, we don't always have the answer. The most important thing we do for the patient and the clinician is to put people in these two boxes because that means they can be eligible for treatment without further diagnostic evaluation.

It is important for us to remember the clinical context of idiopathic pulmonary fibrosis. This is not something you should diagnose in a 50-

year-old woman. Nearly always, these patients are over 60 in age, they have to have no evidence of an exposure, an environmental exposure or medications that could cause fibrosis, and no evidence of connective tissue disease. Again, it's important to remember, and typically in my dictation of a UIP pattern, I will put in a differential, connective tissue disease, particularly rheumatoid arthritis, which is what this patient had. About 70% of ILD from rheumatoid arthritis is going to be a UIP pattern. And hypersensitivity pneumonitis is a funny thing, can cause a typical UIP pattern.

One interesting thing, again from Dr. Chung, is that if you have UIP in a patient with connective tissue disease, these three signs can be useful. The fibrosis for some unclear reason tends to be quite sharply demarcated in the lower lungs. So you have this straight horizontal demarcation in the lower lungs. You tend to have this exuberant honeycombing, where the honeycombing actually occupies most of the volume of the fibrotic lung. And then you can also have involvement of the anterior rows. Those are clues that you can use to suggest that maybe this patient has UIP that is related to a connective tissue disease.

Okay, so now we're going to move on to NSIP. NSIP, it's different, and it's importantly different because I showed you that there was a substantial difference in fibrosis. And you can see that the primary difference for the pattern of NSIP is that it is much more lower lung predominant, even than UIP, it tends to extend along bronchovascular bundles and tends to spare the subpleural lung; we already talked about this subpleural sparing. The other feature that's very common is we see lower lobe volume loss, really marked decrease in volume of the lower lobes, which we tend not to see in UIP and IPF. Okay? And the features tend to be a mixture of reticular abnormality and ground-glass abnormality, we see both of those here. Prominent traction bronchiectasis, lobar volume loss, which I showed you, and often consolidation.

Now, as I mentioned, the important point about NSIP is that when you see this pattern, you should strongly suggest that this patient either has a connective tissue disease such as scleroderma, myositis, or anti-synthetase syndrome, or some sort of indeterminate autoimmune features without a defined connective tissue disease. So that's something that you can point the clinician towards when you see an NSIP pattern that looks like this. This patient I think had scleroderma with an abnormal appearing esophagus. You should also in your differential include toxicity and include hypersensitivity pneumonitis.

What's important for us as radiologists is that NSIP, the CT features often are not as distinct as UIP. They can overlap with UIP, LIP, DIP, or HP, so I tend not to give a confident diagnosis of NSIP in most cases. What saves me, however, is if I know the patient has a connective tissue disease, and the pattern looks like NSIP, then I usually dictate that this is probably NSIP.

The third member of the diagnostic triad that we have to look at is hypersensitivity pneumonitis. This is a paper from a couple of years ago that published diagnostic criteria for hypersensitivity pneumonitis. And these are the CT language categories that we use in patients with suspected fibrotic HP. And I'll show you examples of each of these. So typical fibrotic HP compatible with fibrotic HP and indeterminate. As the name suggests, this is a sliding scale of probabilities. Typical is the most likely to have fibrotic HP. And you should use that term if you have CT signs of fibrosis with either poorly defined centrilobular nodules or ground-glass abnormality affecting all lungs zones, or inspiratory mosaic attenuation with the three-density sign. Now, you may not have heard of the three-density sign, we're going to talk about it on the next couple of slides. And of course, lack of features to suggest an alternative diagnosis.

This is compatible with fibrotic HP, you can see that the CT features are less typical, patchy or diffuse ground glass, patchy centrilobular nodules, mosaic attenuation, lobular air trapping but without that three-density sign. And then there's a group of patients with fibrotic lung disease with fibrotic HP, who have basically imaging features that are not suggestive of HP.

So this is what we're talking about with the three-density sign. And it refers to the three densities, of course, are areas of preserved lung density, increased lung density or ground-glass abnormality, and lobular areas of decreased attenuation. Now most of you who were trained in California, particularly if you're trained at UCSF, will have known this as the headcheese sign from Dr. Webb. But I think this is a much better term because it actually describes what you're seeing, instead of having to explain what the headcheese is. And the useful point though is that this is highly specific for hypersensitivity pneumonitis, with a 93% specificity. So if you see this sign, you should be highly confident in suggesting a diagnosis of fibrotic HP.

Here's another example, normal lung density, decreased lung attenuation, ground-glass last abnormality on the same image. It's very helpful, of course, to have the expiration scans confirming the areas of multifocal lobular air trapping. Again, highly suggestive of fibrotic HP.

And then this is the category of compatible with fibrotic HP. You can see there is some fibrosis, there are some areas of lobular decreased attenuation, mosaic attenuation, which do show air trapping on expiratory imaging, but you don't have the three-density sign, so we would call this compatible with fibrotic HP. Because some cases of UIP or IPF can look like this. And then, as I said, some patients like this patient, this patient has a UIP pattern. It's very similar to what I showed you, subpleural reticular, traction bronchiectasis, honeycombing, lower lung predominant, you would read this as UIP. But he turned out to have a hypersensitivity

pneumonitis on biopsy with an exposure. So that's why, when I'm dictating my cases of UIP, I always add in, you know, this still could be hypersensitivity pneumonitis. And that's, you know, a confusing thing, but I think it's important for the patient. And of course, we call those – we would call this typical UIP. And, you know, but we have to remember that it also could be hypersensitivity pneumonitis.

Okay, this I think is an old paper, but it summarizes the radiologic findings in chronic HP, as distinct from UIP and NSIP. And as I mentioned, this is something we go through every day in people with fibrotic lung disease. If you see honeycombing, here it does, it's present in many cases of chronic HP or UIP, uncommon and NSABP. If you see centrilobular nodules, as we've already said, that's suggestive of chronic HP or fibrotic HP. If you see subpleural sparing, that's our big sign that suggests NSIP, present in about 50 or 60% of cases. If you see lower lung predominance, it's likely to be UIP or NSIP, but about 1/3 of cases of chronic HP are lower lung predominant. So, you know, HP as you will gather from this, is the most difficult diagnosis, unless you have your classic three-density sign, because you can have a real variety of imaging signs.

Now we're going to just talk for a couple of minutes about complications of UIP, of IPF. This patient came in, had UIP at baseline, this is the mid lungs, subpleural reticular abnormality, I think it was basal honeycombing. And then came in 5 months later short of breath for a CT angiogram. And the CT, there was no pulmonary embolism, but the patient had diffuse ground-glass abnormality. How would you dictate this? It's really important to dictate this as possibly an acute exacerbation of IPF, because that's an important condition and it actually is a significant morbidity and mortality for the patient. The patient would usually get a bronchoscopy to exclude infection such as a PJP or a viral infection. But assuming it's not an infection, it's usually an acute exacerbation of IPF. So that's an important thing that, again, radiologists are the people who make this diagnosis. It presents with acute respiratory stress. Histologically, you get this acute interstitial pneumonia superimposed on background like fibrosis. And then it's most common in IPF, but you can also see it in the other fibrosing interstitial pneumonias, you rule out PE, infection, lung edema.

Okay, here's the other important complication of IPF. Here's a patient with UIP, and she presented with a lung nodule. Most important thing you know, of course, with lung nodules, get the old films, it wasn't there 12 months before, and then you follow it, in 18 months it had grown. The difficult thing about lung cancer in fibrotic lung disease is it tends to develop in areas of pre-existing fibrosis. So it can be quite difficult to see, particularly in the early examples like in this case. So you have to be very sensitive to nodules that are arising in areas of fibrosis, in or adjacent to areas of fibrosis. Yeah, so we do a PET/CT, very helpful. And this was, of course, a lung cancer. And lung cancer happens in 10% of people with UIP. So, you know, it's a very common complication, usually within or close to areas of lung fibrosis, and PET/CT is often helpful, particularly because some of these areas may just be focal fibrosis.

We're going to talk about two more topics. First of all, multidisciplinary discussion in ILD. MDD can change the clinical diagnosis, certainly often changes the imaging diagnosis, and even changes the pathology diagnosis. So this is why we do I commonly, and it provides better patient care. It improves observer agreement, improves diagnostic confidence, should include clinician, radiologists, and if there is tissue, a pathologist, may also include a rheumatologist or occupational lung person. You can do it virtually. We did it virtually during COVID. It's always better in person, but you know, if you're remote, if you're somewhere else, it's still helpful to do it virtually.

So now I'm going to go through how multidisciplinary diagnosis happens in this patient, which is kind of a typical person who presents to our clinic. She was 65 years old, she had progressive dyspnea, significant weight loss. And this is an old case, so she was – date's from 2004. She developed progressive dyspnea over 4 months, acutely declined, significant weight loss, never smoker, which is important, because smoking is a risk factor for IPF. Nothing else really in the history of importance. The exposure history, she was a pharmaceutical manager. She used down pillows. So maybe some little clues there that there was some potential exposures. She had crackles on her examination. She had markedly reduced forced vital capacity. She was unable to perform a lung diffusing capacity and she desaturated on 6 liters of oxygen, she desaturated to 91%. So she is significantly impaired.

Here's her imaging, and I want you to look at this and make up your mind what you would – how you would label this patient. So here's the first image. Second image. Third image. Fourth image. Coronal. I think I have an expiration, no that's another coronal. Yeah, and there's the inspiration and expiration. Yeah, so here was the radiologic description, right, so she does have a reticular pattern. But she has too much ground-glass abnormality to call this UIP. There's too much ground glass. And then we have our mosaic attenuation with the three-density sign. So here's your ground glass, here's your normal density, and here's your decreased attenuation. This is another example of the three-density sign which, as we said, it's very highly suggestive of hypersensitivity pneumonitis. There was some expiratory air trapping, which I showed you, just a little bit peribronchovascular predominant, which again, would be against UIP, and lower lung predominant. I know that some of you call it indeterminate, but really when you have the three-density sign, that should push you towards hypersensitivity pneumonitis.

Okay, so this was radiologically diagnosed as typical fibrotic hypersensitivity pneumonitis by confidence. And here's the pathology which shows that this abnormality, this is why we have air trapping because this is a peribronchiolar process, here are the bronchioles and there's a lot of infiltration and fibrosis around the bronchioles. There is also infiltration in the more peripheral lung, but it is

centrilobular. Here's a close-up of the bronchiole with marked cellular inflammation and inflammation within the bronchiole, cellular bronchiolitis. There is a loosely formed granuloma which is one of the other features highly suggestive of hypersensitivity pneumonitis. This is a lymphoid aggregate. And there is a fibroblastic focus.

So, this patient was diagnosed with hypersensitivity pneumonitis with minimal fibrosis. But notice that the CT was actually 10 years after the biopsy, so she had obviously progressed over that time. So this often happens. So we say, the radiologists, and I would have biopsied this patient, we would have said fibrotic HP. And the patients then, the doctor had to go back to the patient and ask in more detail about the exposures, and it turned out that she was using down pillows. And, remember, down contains feathers, and that's actually one of the more common exposures that we see with hypersensitivity pneumonitis.

So we're going to finish with two more topics. This is just about some good news in pulmonary fibrosis. I said that it previously had a – IPF had a terrible prognosis. But there are two drug studies the ASCEND study and the IMPULSIS study that were published about 7 years ago now – 9 years ago now, which showed quite impressive results. So I'm not going to go into the details of the study, but they were both for idiopathic pulmonary fibrosis, randomized, and here's the key slide. Pirfenidone arm compared to placebo arm, change in forced vital capacity. You can see that the pirfenidone arm, pirfenidone slowed the rate of progression of fibrosis in idiopathic pulmonary fibrosis. And just at the same time, this is the IMPULSIS study which is nintedanib. And again, similar results really. The nintedanib slowed – it didn't stop progression, neither of them stopped progression, but it clearly slowed the rate of progression compared to the placebo arm. So those studies were both in IPF. So for about 8 years now we've had approved treatments for IPF, pirfenidone and nintedanib. Both have side effects, but they're approved.

But there was no treatment for non-IPF fibrosis until this study in 2019, which looked at non-IPF progressive fibrosis. Fibrosis that was progressing, and we'll talk about the criteria for progression. And again, it showed similar results. The nintedanib arm, the rate of decrease in FVC was substantially less than in the placebo arm. Even, and this is interesting, so there were some people that had a UIP pattern, others did not. And it was indistinguishable. So even in people without a UIP fibrotic pattern, their rate of progression was reduced.

So, there are criteria then, clinicians will come to you asking, does this patient have progressive pulmonary fibrosis? And then if they have progression, if they have worsening respiratory symptoms without an alternative explanation, if they have changed progression of their FVC. But importantly, radiology is an important criterion for progression, increased extent or severity of traction bronchiectasis, new ground-glass abnormality with traction bronchiectasis, you find reticulation, increased extent or increased coarseness of reticulation, new or increased honeycombing, increased lobar volume loss. So these criteria we use to identify progression. It actually sounds easy, but it's really quite difficult in practice.

Here's a patient with fibrotic hypersensitivity pneumonitis. And you can see that there is substantial decrease in lung volume and progression increase in reticular abnormality, increasing traction bronchiectasis. A patient with scleroderma showing substantial progression with increase in extent of abnormality, but also notice the dramatic increase in traction bronchiectasis.

Okay, this is the final topic. Here's a 65-year-old woman, we were following her for a lung nodule. This is a patient of mine who was actually a friend of mine. And she had bilateral mild linear abnormalities of the bases. And I remember telling her at the time, don't worry about this, these we see these things, and they don't mean anything. And of course, we used to call this, you know, aging lung or something like this.

So this is the issue of interstitial lung abnormalities. So it's defined as incidental identification of nondependent. So you, you weren't looking for it. You weren't doing a high-res CT looking for ILD, but you were doing a PE/CT, you were doing abdominal CT and you found some abnormalities, which are listed here. And they have to be non-trivial involving at least 5% of a lung zone in individuals in whom interstitial lung disease is not suspected. And what's important is this whole group of studies, so almost 30,000 subjects from various studies, either lung cancer screening or cohort screening in like three different continents, and you'll see that the prevalence of ILA, and these are all relatively older individuals, is really about 7 or 8%, average of 8% in this study, maybe a little less in Asia, and we're not sure why that is. And you'll notice that, again, the mean age of people is relatively old, this is not something you're going to see in a 40-year-old. So it's a common finding in our practice, and you should see it about in 1 and every 12 CTs in older individuals.

But here's what's important. This, in itself, is an important risk factor for death in four different studies. And it also tends to progress over time. Notice, though, that it tends to progress slowly, typically about 50% progress at about 5 years. So this is, again, an indolent disease.

Here's what happened to my friend, who we saw first in 2003, you can see that she had a really mild abnormality, by 2007 you can see that she had fibrosis with traction bronchiectasis, 2010 she had more established fibrosis, and 2015 she was oxygen dependent with UIP. And about 3 years later, she unfortunately died. So this is the importance.

And the important point, most important point from this is how indolent this is. If you're reading a CT in this case, and you want to know if it's got worse, you're going to have to dig back 4 or 8 years to really see this progression. And you're going to have to follow it for a long time to make sure, to see whether it's stable. We categorize this ILA as non-subpleural, subpleural non-fibrotic, and subpleural fibrotic, which is the most likely to progress.

And just briefly, I'll show you examples of each of those. non-subpleural ILA, subpleural reticular ILA that is still pleural, but not fibrotic. Here's another example – but not – and this is now fibrotic ILA with traction bronchiectasis. So that's the subtype that's most likely to progress. And here is the management plan. If you see it, and you're going to be the one to see it, first of all, you should consider high-resolution CT, if you found this on a cardiac CT or abdominal CT, or if there's too much dependent lung density, so you should consider high-res CT. Secondly, the patient should receive a clinical evaluation by a pulmonologist, by at least a clinician or a pulmonologist, to see if there are respiratory symptoms, impaired pulmonary function, or extensive disease on CT. If there is clinically significant disease, then they get referred to a pulmonologist and they get a diagnosis, either clinically significant ILD, clinically driven management, or if they don't seem to have significant disease, they can be still diagnosed with ILA. And then the question is monitoring these patients, this gets to we don't know how quickly to repeat CT, I would say, I usually say 24 months. This is an indolent disease, so I don't usually follow at 12 months, but it does depend on the clinician and how they feel. So key signs of fibrosis or traction bronchiectasis and bronchiolectasis, honeycombing, architectural distortion, lobar volume loss. I hope you've learned the CT features of UIP, distinguished from NSIP and fibrotic HP. Multidisciplinary evaluation helps improve diagnostic confidence. And early interstitial abnormality is important and should be followed up if fibrosis is present.

So thank you all again very much for your attention. Thanks again. Have a good evening.

Announcer Close:
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