PNEUMOLOGIA 2018 – Milano, 14-16 Giugno 2018

MINICORSO “INTERSTIZIOPATIE E MALATTIE RARE”

MALATTIE FIBROSANTI NON IPF

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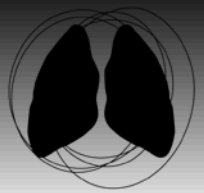
UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA



OUTLINE

- Un caso clinico
- Le polmoniti interstiziali idiopatiche
  - Focus sulla NSIP
- L'interessamento polmonare in corso di malattia collageno-vascolare
- Ritorno al caso clinico
- Il valore aggiunto dell'approccio multidisciplinare

UN CASO CLINICO

- **P.L. uomo di 73 anni**
- **Non patologie di rilievo all'anamnesi familiare**
- **Non fumatore**
- **Pensionato; ex addetto alla manutenzione di frigoriferi industriali, poi autista**

ANAMNESI PATOLOGICA REMOTA

- Difetto interatriale congenito
- Pregressa frattura vertebrale per osteoporosi trattato con vertebroplastica
- Ernioplastica inguinale bilaterale
- Mixedema dell'adulto di recente riscontro.
- In terapia con Acetilsalicilato di Lisina, Simvastatina, Levotiroxina, Calcio Carbonato, Alendronato e Vitamina D.

GIUGNO 2014

- Dispnea da sforzo, progressivamente ingravescente negli ultimi tre mesi, associata a tosse stizzosa cronica.
- Nega fenomeno di Raynaud; riferisce xeroftalmia.
- Riferisce occasionali episodi di reflusso gastro-esofageo.

ESAME OBIETTIVO

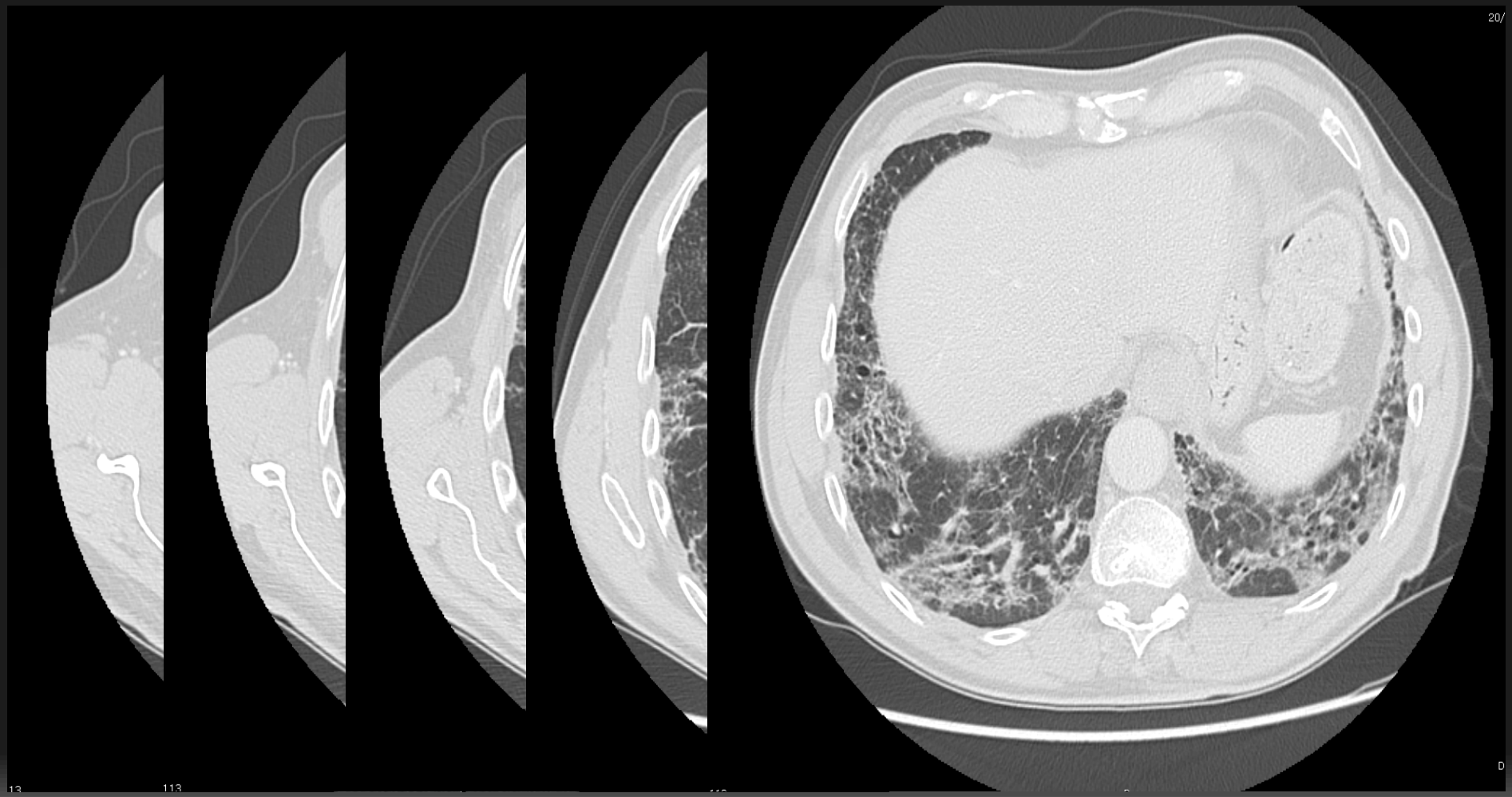
- Rantoli crepitanti “a velcro” ai campi medio-inferiori bilateralmente
- SaO2 96% in AA a riposo
- Prove di funzionalità ventilatoria

  FVC: 80% pred.

  TLC: 79% pred.

  DLCO-SB: 33% pred. - DLCO/Va: 55% pred.
- 6MWD: percorsi 560 m (Nadir SpO2 90% dal 4° minuto).

TC DEL TORACE



ESAMI DI LABORATORIO

- Lieve anemia normocromica normocitica (Hb: 12 g/dl)
- Funzionalità epatica e renale: nella norma
- Esame chimico fisico delle urine: nella norma.
- Sedimento urinario non significativo
- LDH: 727 U/L (v.n. 208-378 U/L)
- CPK: 696 U/L (v.n. 10-171 U/L)

} Mixedema dell'adulto

- VES 51 mm (v.n. 1-15), PCR nella norma
- Elettroforesi siero-proteica: aumento delle catene k sieriche e consensuale aumento delle catene lambda con rapporto non modificato
- Proteina di Bence Jones: assente
- Immunofissazione sierica e urinaria: negativa

ESAMI DI LABORATORIO

- **IgG 1886 mg/dL (v.n. 700-1600) con aumento IgG sottoclasse 1-2-4 (nella norma IgA e IgM)**
- **Fattore Reumatoide 20 IU/ml (v.n. 1-14)**
- **Anti-CCP nella norma**
- **C3-C4 nella norma**
- **ANA ed ENA negativi**
- **positività p-ANCA**
  - **MPO Ab. Anti-mieloperossidasi: 69 UI/ml (v.n. <3.5)**
- **HBsAg e anti-HCV: negativo.**

VALUTAZIONE REUMATOLOGICA

- Test di Schirmer: negativo bilateralmente
- Capillaroscopia: numero di capillari conservato, non alterazioni morfologiche maggiori. Quadro nella norma.
- Non artromialgie, non storia di aftosi, lesioni cutanee o fotosensibilità.
- Il quadro clinico non orienta al momento per una patologia del connettivo o per una vasculite.

Interstitial Lung Disease

Exposure-related:
- Occupational
- Environmental
- Avocational
- Medication

Idiopathic interstitial pneumonia (IIP)

Connective tissue disease:
- Scleroderma
- Rheum. arthritis
- Sjogren
-PM/DM
-LES

Sarcoidosis

Other:
- Vasculitis/Diffuse alveolar hemorrhage (DAH)
- Langherhans cell histiocytosis (LCH)
- Eosinophilic pneumonias
- Neurofibromatosis
- LAM

Rare idiopathic interstitial pneumonia:
- Idiopathic lymphoid interstitial pneumonia
- Idiopathic pleuroparenchymal fibroelastosis

Unclassifiable idiopathic interstitial pneumonias

Major idiopathic interstitial pneumonias

Idiopathic pulmonary fibrosis (IPF)	Respiratory bronchiolitis interstitial lung dis. (RBILD)
Acute interstitial pneumonia (AIP)	Cryptogenic organizing pneumonia (COP)
Nonspecific interstitial pneumonia (NSIP)	Desquamative interstitial pneumonia (DIP)

Interstitial Lung Disease

Exposure-related:
- Occupational
- Environmental
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Idiopathic interstitial pneumonia (IIP)

CONNECTIVE TISSUE DISEASE
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Nonspecific interstitial pneumonia (NSIP)

Desquamative interstitial pneumonia (DIP)

MALATTIE FIBROSANTI NON IPF

- Classification of Idiopathic Interstitial Pneumonias

- Lung involvement in CVD

American Thoracic Society

American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias

THIS JOINT STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS), AND THE EUROPEAN RESPIRATORY SOCIETY (ERS) WAS ADOPTED BY THE ATS BOARD OF DIRECTORS, JUNE 2001 AND BY THE ERS EXECUTIVE COMMITTEE, JUNE 2001

TABLE 2. HISTOLOGIC AND CLINICAL CLASSIFICATION OF IDIOPATHIC INTERSTITIAL PNEUMONIAS*

Histologic Patterns	Clinical–Radiologic–Pathologic Diagnosis
Usual interstitial pneumonia	Idiopathic pulmonary fibrosis/cryptogenic fibrosing alveolitis
Nonspecific interstitial pneumonia	Nonspecific interstitial pneumonia (provisional)†
Organizing pneumonia	Cryptogenic organizing pneumonia‡
Diffuse alveolar damage	Acute interstitial pneumonia
Respiratory bronchiolitis	Respiratory bronchiolitis interstitial lung disease
Desquamative interstitial pneumonia	Desquamative interstitial pneumonia
Lymphoid interstitial pneumonia	Lymphoid interstitial pneumonia

* **Unclassifiable interstitial pneumonia**: Some cases are unclassifiable for a variety of reasons (*see* text).
† This group represents a heterogeneous group with poorly characterized clinical and radiologic features that needs further study.
‡ COP is the preferred term, but it is synonymous with idiopathic bronchiolitis obliterans organizing pneumonia.

Am J Respir Crit Care Med. 2002; 165: 277-304

An Official American Thoracic Society/European Respiratory Society Statement: Update of the International Multidisciplinary Classification of the Idiopathic Interstitial Pneumonias

William D. Travis, Ulrich Costabel, David M. Hansell, Talmadge E. King, Jr., David A. Lynch, Andrew G. Nicholson, Christopher J. Ryerson, Jay H. Ryu, Moisés Selman, Athol U. Wells, Jurgen Behr, Demosthenes Bouros, Kevin K. Brown, Thomas V. Colby, Harold R. Collard, Carlos Robalo Cordeiro, Vincent Cottin, Bruno Crestani, Marjolein Drent, Rosalind F. Dudden, Jim Egan, Kevin Flaherty, Cory Hogaboam, Yoshikazu Inoue, Takeshi Johkoh, Dong Soon Kim, Masanori Kitaichi, James Loyd, Fernando J. Martinez, Jeffrey Myers, Shandra Protzko, Ganesh Raghu, Luca Richeldi, Nicola Sverzellati, Jeffrey Swigris, and Dominique Valeyre; on behalf of the ATS/ERS Committee on Idiopathic Interstitial Pneumonias

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) AND THE EUROPEAN RESPIRATORY SOCIETY (ERS) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, JUNE 2013, AND BY THE ERS STEERING COMMITTEE, MARCH 2013

International multidisciplinary panel of 34 experts in ILDs:

- 19 pulmonologists
- 4 radiologists
- 5 pathologists
- 2 experts in evidence-based medicine
- 4 molecular biologists

Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

MULTIDISCIPLINARY APPROACH

- The process of achieving a multidisciplinary diagnosis is **dynamic**, requiring **close communication** **between clinician, radiologist and**, when appropriate, **pathologist**.

- Clinical data and radiologic findings are essential for multidisciplinary diagnosis.

- The multidisciplinary approach **does not lessen** **the importance of lung biopsy** in the diagnosis of IIPs; rather, it **defines the settings where biopsy is more informative** than HRCT.

Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

CATEGORIZATION OF MAJOR IIPs

	CLINICAL-RADIOLOGIC-PATHOLOGIC DIAGNOSES	ASSOCIATED MORPHOLOGIC PATTERNS
Chronic Fibrosing IP	Idiopathic Pulmonary Fibrosis	Usual Interstitial Pneumonia
	Idiopathic Nonspecific Interstitial Pneumonia	Nonspecific Interstitial Pneumonia
Smoking related IIP	Respiratory Bronchiolitis Interstitial Lung Disease	Respiratory Bronchiolitis
	Desquamative Interstitial Pneumonia (occasionally in non-smokers)	Desquamative Interstitial Pneumonia
Acute/Subacute IP	Cryptogenic Organizing Pneumonia	Organizing Pneumonia
	Acute Interstitial Pneumonia/(acute exacerbation of IPF)	Diffuse Alveolar Damage

Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

IDIOPATHIC INTERSTITIAL PNEUMONIAS: CLASSIFICATION ACCORDING TO DISEASE BEHAVIOR

CLINICAL BEHAVIOR	TREATMENT GOAL	MONITORING STRATEGY
Reversible and self-limited (many RB-ILD)	Remove possible cause	Short term observation
Reversible disease with risk of progression (NSIP, DIP, COP)	Achieve response then rationalize longer therapy	Short term/Long term observation
Stable with residual disease (some f-NSIP)	Maintain status	Long term observation to assess disease course
Progressive, irreversible with potential for stabilization (f-NSIP)	Stabilize	Long term observation to assess disease course
Progressive, irreversible despite therapy (IPF, some f-NSIP)	Slow progression	Long term observation/Lung Tx/palliation

Travis WD et al. Am J Respir Crit Care Med. 2013; 188(6):733-748

REVISED ATS/ERS CLASSIFICATION OF IDIOPATHIC INTERSTITIAL PNEUMONIAS: MULTIDISCIPLINARY DIAGNOSES

- **Major idiopathic interstitial pneumonias**
  - Idiopathic Pulmonary Fibrosis
  - Idiopathic Nonspecific Interstitial Pneumonia
  - Respiratory Bronchiolitis–Interstitial Lung Disease
  - Desquamative Interstitial Pneumonia
  - Cryptogenic Organizing Pneumonia
  - Acute Interstitial Pneumonia
- **Rare idiopathic interstitial pneumonias**
  - Idiopathic Lymphoid Interstitial Pneumonia
  - Idiopathic Pleuroparenchymal Fibroelastosis
- **Unclassifiable idiopathic interstitial pneumonias**

Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

REVISED ATS/ERS CLASSIFICATION OF IDIOPATHIC INTERSTITIAL PNEUMONIAS: MULTIDISCIPLINARY DIAGNOSES

- **Major idiopathic interstitial pneumonias**
  - Idiopathic Pulmonary Fibrosis
  - **Idiopathic Nonspecific Interstitial Pneumonia (not anymore provisional!)**
  - Respiratory Bronchiolitis–Interstitial Lung Disease
  - Desquamative Interstitial Pneumonia
  - Cryptogenic Organizing Pneumonia
  - Acute Interstitial Pneumonia
- **Rare idiopathic interstitial pneumonias**
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Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

Idiopathic Nonspecific Interstitial Pneumonia

Report of an American Thoracic Society Project

- 305 cases of idiopathic NSIP, 193 with acceptable clinical, radiologic, and pathologic materials.
- 67 were identified as NSIP
  - definite (n =17)
  - probable (n = 50)
- The final diagnosis was established when:

  (**1**) the SLBx showed NSIP pattern (cellular or fibrosing)

  (**2**) the HRCT showed a pattern consistent with NSIP and not diagnostic of other entities (UIP, HP)

  (**3**) no clinical features of another chronic ILD, such as CVD, drug, or inhaled antigen exposure.

Travis WD et al. Am J Respir Crit care Med. 2008; 177: 1338-1347

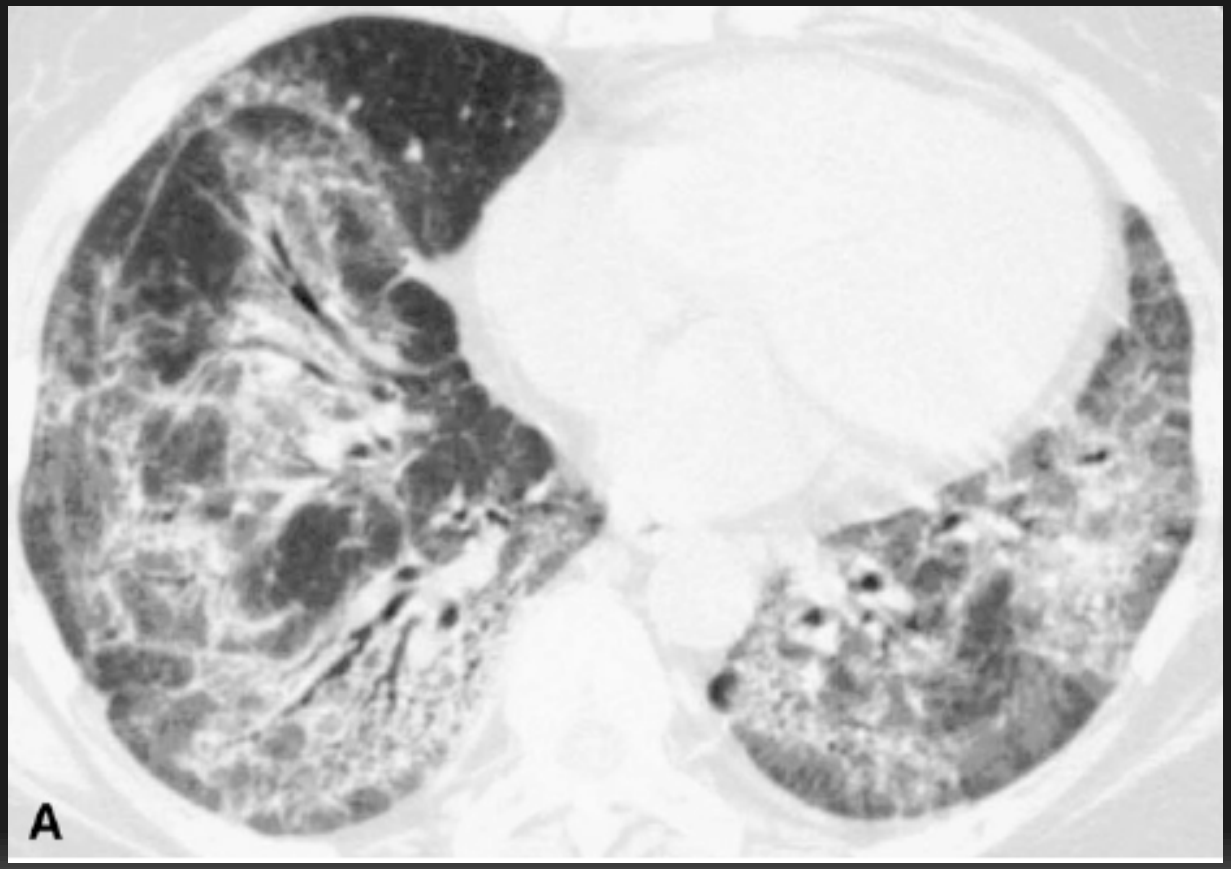
NSIP: CLINICAL FEATURES

- AGE: Mean 52 years
- SEX: F: 67%; M: 33%
- SYMPTOMS:
  - Cough: 87%
  - Dyspnea: 96%
  - Fever: 21%
  - Skin rush: 5%
  - Arthritis: 3%
  - Clubbing: 8%

5 year mortality rate < 18%

Travis WD et al. Am J Respir Crit care Med. 2008; 177: 1338-1347

Confluent fine GGO/reticular abnormality with traction bronchiectasis



Travis WD et al. Am J Respir Crit care Med. 2008; 177: 1338-1347

Idiopathic Nonspecific Interstitial Pneumonia

Report of an American Thoracic Society Project

William D. Travis[1*], Gary Hunninghake[2*], Talmadge E. King, Jr.[3*], David A. Lynch[4*], Thomas V. Colby[5*], Jeffrey R. Galvin[6*], Kevin K. Brown[7], Man Pyo Chung[8], Jean-François Cordier[9], Roland M. du Bois[10], Kevin R. Flaherty[11], Teri J. Franks[12], David M. Hansell[13], Thomas E. Hartman[14], Ella A. Kazerooni[15], Dong Soon Kim[16], Masanori Kitaichi[17], Takashi Koyama[18], Fernando J. Martinez[11], Sonoko Nagai[19], David E. Midthun[20], Nestor L. Müller[21], Andrew G. Nicholson[22], Ganesh Raghu[23], Moisés Selman[24], and Athol Wells[10]

Idiopathic NSIP (iNSIP) represents a distinct clinical entity, notably most frequently occuring in middle-aged and never smoking women, showing a good long-term prognosis.

Am J Respir Crit Care Med. 2008; 177: 1338-1347

NSIP – HRCT Features

- The most common HRCT abnormality is **bilateral ground-glass opacity**.
- **Reticular opacities** with **traction bronchiectasis**/bronchiolectasis occur in approx. **75% of cases**.
- **Subpleural sparing** may be helpful in distinguishing NSIP from UIP.
- *Consolidation, if present, reflects an OP component and may suggest CVD.*
- *Honeycombing is absent at presentation but may increase in prevalence and extent during follow-up.*

Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

Differential diagnosis of NSIP pattern

- The NSIP pattern occurs not only as an idiopathic condition, but it can be found also in
  - **Collagen Vascular Disease**
  - Hypersensitivity Pneumonitis
  - drug toxicity
  - in some patients with familial pulmonary fibrosis.
- MDD is especially important to establish the diagnosis of idiopathic NSIP.

Travis WD et al Am J Respir Crit Care Med. 2013; 188: 733-748

MALATTIE FIBROSANTI NON IPF

- Classification of Idiopathic Interstitial Pneumonias

- Lung involvement in CVD

Assessment and management of connective tissue disease-associated interstitial lung disease

Sandra Chartrand[1,2], *Aryeh Fischer*[1]
[1]National Jewish Health, Department of Medicine, Denver, Colorado, USA;[2]Hôpital Maisonneuve-Rosemont affiliated to Université de Montréal, Department of Medicine, Montréal, Québec, Canada

Although often considered as a single entity, "CTD-ILD" actually reflects a heterogeneous spectrum of diverse CTDs and a variety of patterns of interstitial pneumonia. The evaluation of patients with CTD that develop ILD, or the assessment for underlying CTD in those presenting with presumed "idiopathic" ILD can be challenging and these evaluations can be optimized by effective multidisciplinary collaboration.

Sarcoidosis Vasc Diffuse Lung Dis. 2015 Jun 22; 32: 2-21

Pulmonary manifestations of connective tissue diseases (CTDs)

Pleural disease
Pleuritis
Effusion
Thickening
Airways
Upper
Cricoarythenoid disease
Tracheal disease
Lower
Bronchiectasis
Bronchiolitis
Parenchyma
Interstitial lung disease
Diffuse alveolar hemorrhage
Acute pneumonitis
Nodules
Granulomatous diseases
Vascular
Pulmonary hypertension
Vasculitis
Thrombo-embolic disease

Sarcoidosis Vasc Diffuse Lung Dis. 2015 Jun 22; 32: 2-21

CTDs and common pulmonary manifestations

	ILD	Airways	Pleural	Vascular	DAH
Systemic sclerosis	+++	–	–	+++	–
Rheumatoid arthritis	++	++	++	+	–
Primary Sjögren's syndrome	++	++	+	+	–
Mixed CTD	++	+	+	++	–
Polymyositis/ dermatomyositis	+++	–	–	+	–
Systemic lupus erythematosus	+	+	+++	+	++

The signs show prevalence of each manifestation (–=no prevalence; +=low prevalence; ++=medium prevalence; +++=high prevalence). ILD=interstitial lung disease. DAH=diffuse alveolar haemorrhage. CTD=connective tissue disease.

Fischer A and du Bois R. Lancet 2012; 380: 689-698

Relative frequency of patterns of pulmonary involvement in CVD-ILD

Pattern	LES	AR	SSP	PM/DM	SS	Connettivite mista
UIP	+	++	++	++	+	++
NSIP	+	+	++++	++++	+	+++
DAD	++	+	+	+		
OP	+		+	++	+	
LIP					+++	+

Kim EA, *et al*. Radiographics 2002; 22:S151-S165

Prevalence of ILD in CVD

Diseases	ILDs	Comment
Classical connective tissue diseases		
Systemic sclerosis (SSc)	55–65% [34,48]	Clinically overt ILD; mainly in diffuse cutaneous SSc subset [49]; NSIP pattern more frequently reported [50]
Systemic lupus erythematosus (SLE)	1–15% [51]	Mainly in long-lasting disease duration and older patients; possible evolution from SLE pneumonitis [52]
Sjögren's syndrome (SS)	2–45% [53-55]	ILD prevalence directly correlated with SS duration [55]
Inflammatory myopathies (DM/PM)	up to 75% [56]	Anti-synthetase antibodies mark the presence/development of ILD [56]
Mixed connective tissue disease	35–66% [57,58]	
Undifferentiated connective tissue disease (UCTD)	n.a.	ILD is not reported in UCTD cohort studies [16-24]
Other systemic autoimmune diseases		
Rheumatoid arthritis	4–68% [59]	Smoking, male gender, and long-standing disease are frequently reported as risk factors for ILD [59]; UIP pattern present in 2/3 cases [60]
Ankylosing spondylitis	35–65% [61]	data from small case series
Behçet's disease	n.a.	nodular or reticular opacities have been occasionally described and considered residuals of lung hemorrhage/infarcts [62]
Cryoglobulinemic vasculitis	Anecdotal [63]	Subclinical lymphocytic alveolitis (BAL) [64,65]
ANCA-associated vasculitides[a]	~3 [66]	Association with MPO-ANCA antibodies [66]

Ferri C et al. Autoimmun Rev. 2015

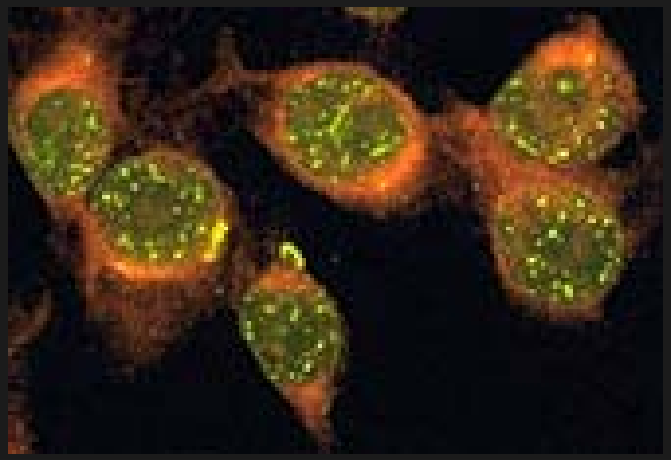
Lung involvement in CVD

- **Systemic sclerosis (Scleroderma)**
- **Rheumatoid arthritis-associated lung disease**
- **…**

Systemic sclerosis (SSc)

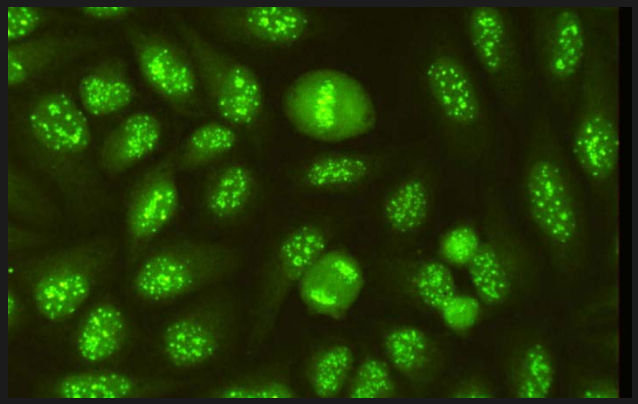
- SSc is a systemic disorder characterized by excessive fibroblast proliferation, autoimmunity, and endothelial dysfunction leading to organ dysfunction involving the skin, lung, heart, GI and kidneys.
- Early features include sclerodactyly, Raynaud syndrome with cutaneous ulcers, telangiectasia, a limited oral aperture, and nail fold capillary changes.
- SSc may be diffuse or limited in nature based on the extent of skin disease.

speckled



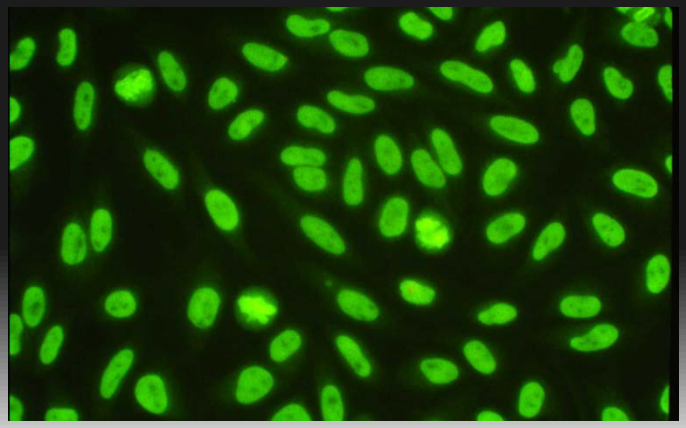
PAH risk

centromere



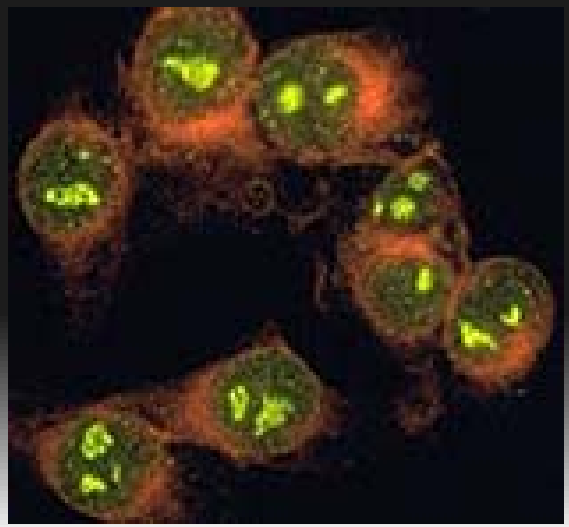
ANA patterns

homogenous (diffuse)



ILD risk

nucleolar/ATA



The lung is the major cause of death in systemic sclerosis

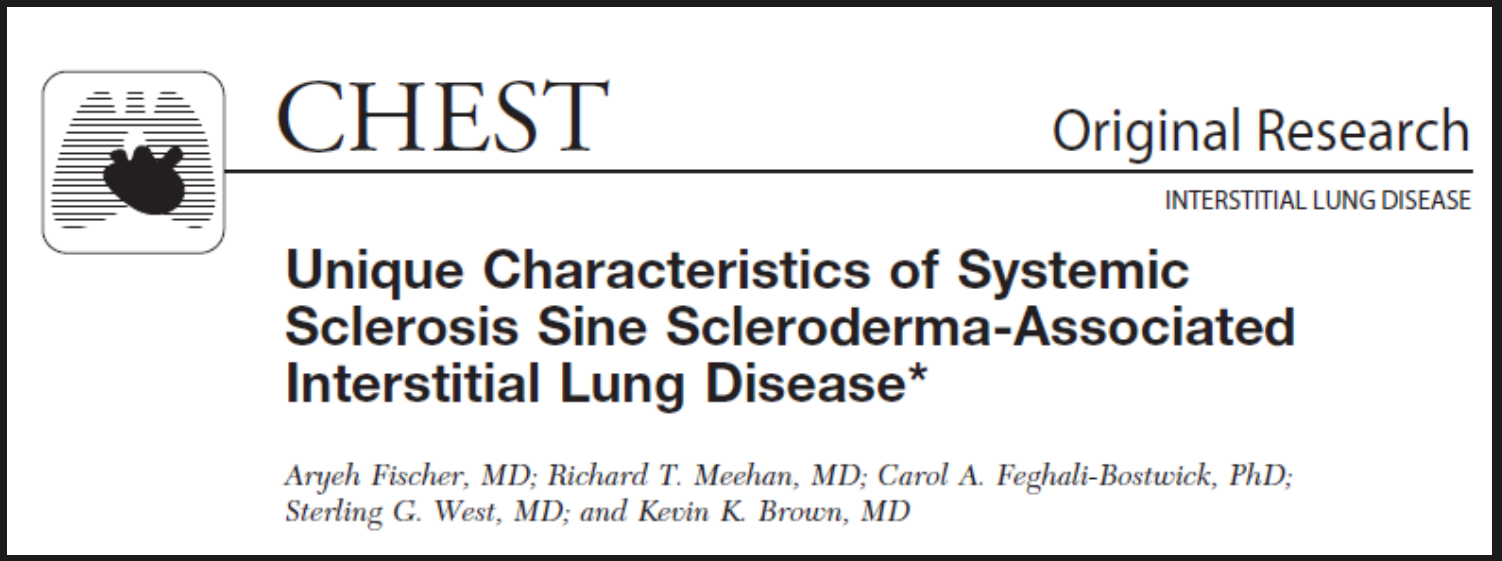
"The change in the pattern of scleroderma-related mortality over the past 30 years demonstrates that the lung (both pulmonary hypertension and pulmonary fibrosis) is the primary cause of scleroderma related deaths today.

It is important that aggressive searches continue to develop better therapies for these severe pulmonary complications of systemic sclerosis."

Steen et al. Ann Rheum Dis 28 Feb 2007.

Systemic sclerosis (SSc) & ILD

- Clinically significant **ILD** tends to develop **earlier**.
- More frequent in diffuse SSc but reported even in patients without skin involvement (sine scleroderma).



CHEST

Original Research

INTERSTITIAL LUNG DISEASE

Unique Characteristics of Systemic Sclerosis Sine Scleroderma-Associated Interstitial Lung Disease*

Aryeh Fischer, MD; Richard T. Meehan, MD; Carol A. Feghali-Bostwick, PhD; Sterling G. West, MD; and Kevin K. Brown, MD

- Six patients for evaluation of IIP
- Sclerodactyly, skin thickening, and digital edema absent

- All had nucleolar-staining anti-nuclear antibodies
  - one anti-Scl-70 +; anti-Th/To negative
  - all five anti-Scl-70 –anti-Th/To positive

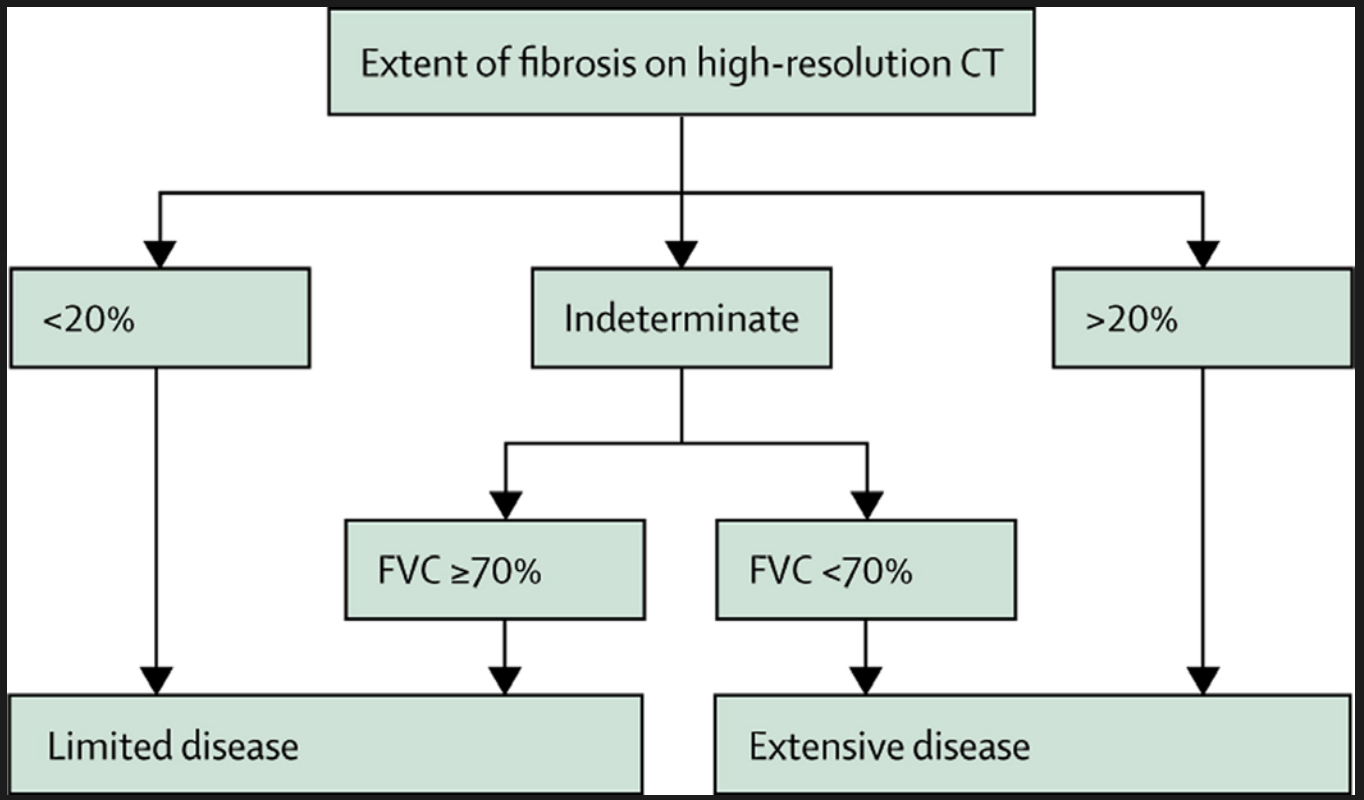
- Other systemic features present in all (i.e. GERD, telangiectasia)

Chest. 2006. 130: 976-981

Systemic sclerosis (SSc) & ILD

- Clinically significant **ILD** tends to develop **earlier**.
- More frequent in diffuse SSc but reported even in patients without skin involvement (sine scleroderma).
- **Risk factors** for the development of **progressive ILD**:
  - Anti **SCL-70** positive
  - African Americans
  - older patients
  - **male** patients, with **early decline in FVC and DLCO** and a **greater extent of disease** seen on HRCT

A simple staging system for SSc-ILD



Goh NS et al. Am J Respir Crit Care Med. 2008; 177:1248-54

Lung involvement in CVD

- **Systemic sclerosis (Scleroderma)**
- **Rheumatoid arthritis-associated lung disease**
- **…**

Pulmonary manifestations of rheumatoid arthritis

Parenchymal
- Interstitial lung disease (*i.e.* usual interstitial pneumonia, nonspecific interstitial pneumonia, acute interstitial pneumonia/diffuse alveolar damage and organising pneumonia)

Pleural disease
- Pleural effusion
- Pneumothorax
- Bronchopleural fistula
- Trapped lung syndrome

Airway obstruction
- Cricoarytenoid arthritis
- Bronchiectasis
- Follicular bronchiolitis
- Obliterative (constrictive) bronchiolitis

Nodules
- Rheumatoid nodules
- Caplan syndrome

Vascular disease
- Rheumatoid vasculitis
- Pulmonary hypertension

Other
- Drug toxicity
- Infection
- Malignancy
- Thoracic cage restriction
- Thromboembolic disease

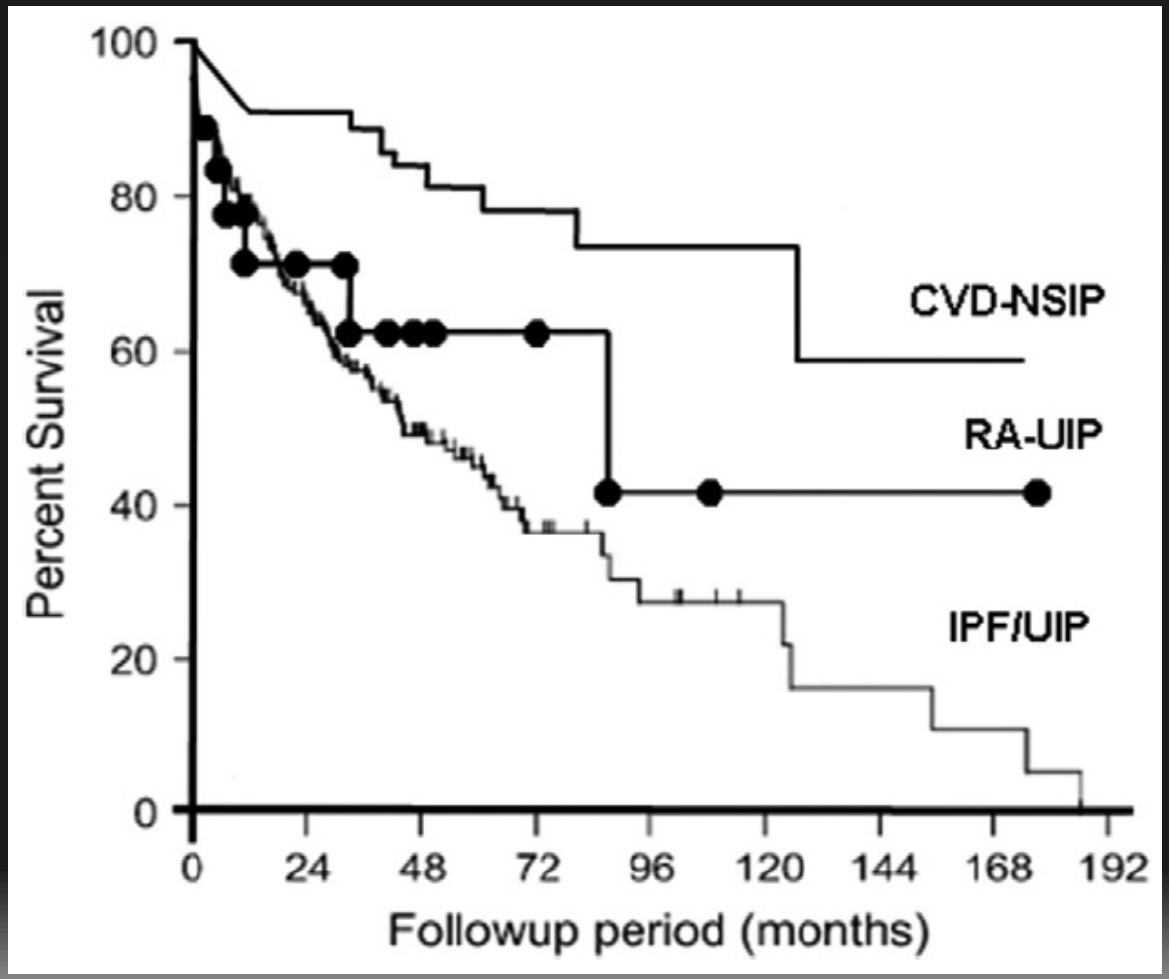
Shaw M et al. Eur Respir Rev. 2015; 24: 1-16

Conditions associated with a UIP pattern

- Idiopathic (IPF)
- Collagen vascular disease (including RA)
- Drug toxity
- Hypersensitivity pneumonitis (chronic)
- Asbestosis
- Familial idiopathic pulmonary fibrosis
- Hermansky-Pudlak syndrome

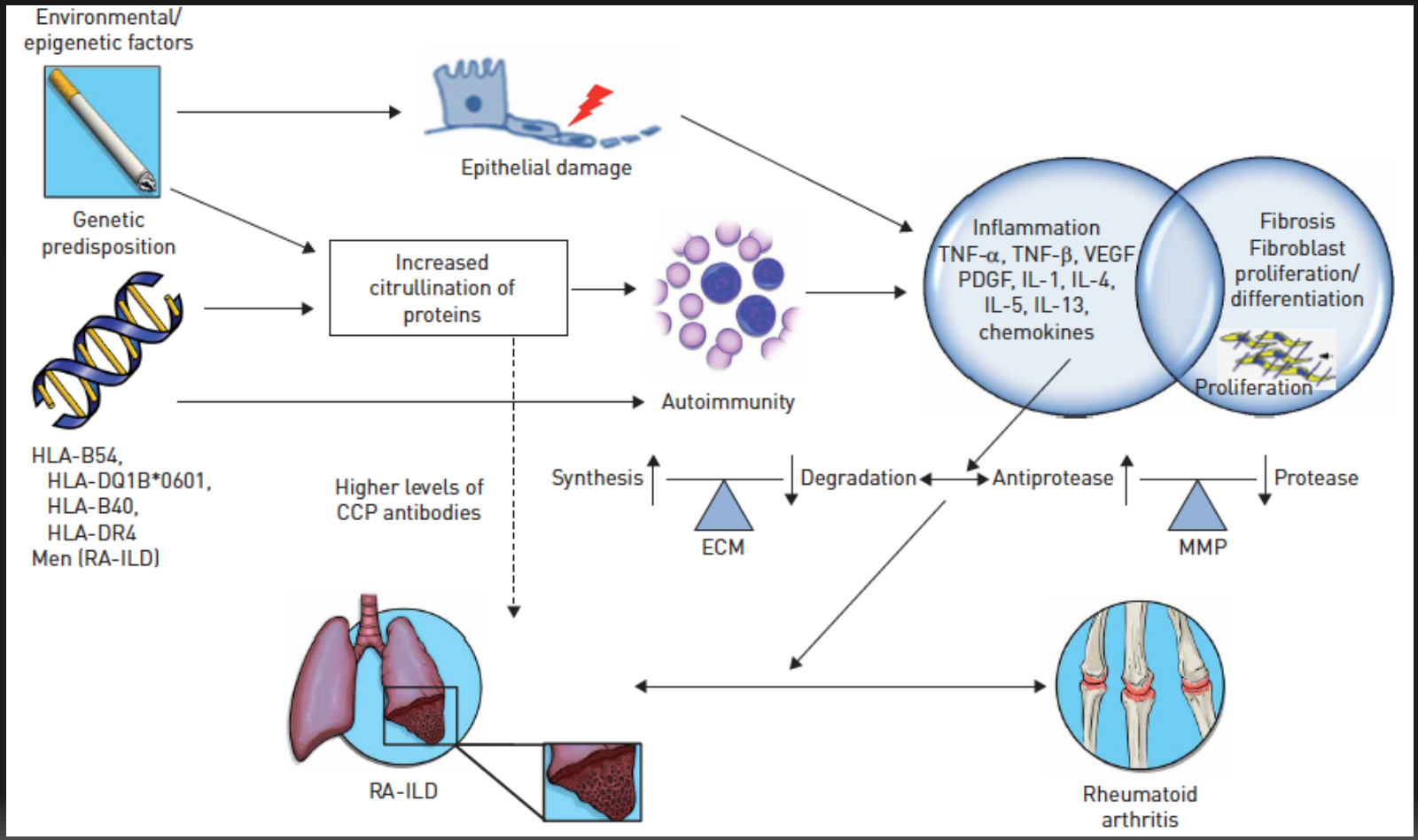
Travis WD et al. Am J Surg Pathol. 2000; 24: 19-33

Survival of RA-ILD w/ UIP pattern on SLBx can be as poor as in IPF



Park JH et al *AJRCCM* 2007; 175:705-711

Pathogenesis of RA-ILD

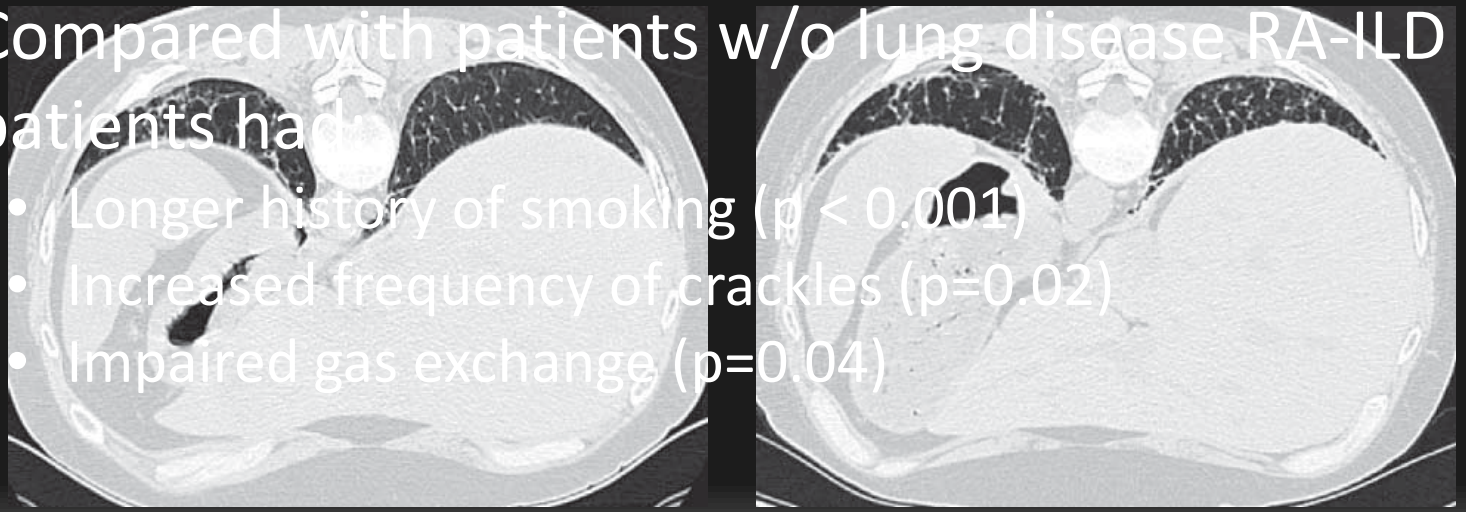


Shaw M et al. Eur Respir Rev. 2015; 24: 1-16

Compelling evidence to initiate HRCT screening?

- 21/64 (33%) RA patients without dyspnea or cough had “pre-clinical” ILD by HRCT
- HRCT progression was noted in 12/21 (57%)

- Compared with patients w/o lung disease RA-ILD patients had:
  - Longer history of smoking ($p < 0.001$)
  - Increased frequency of crackles ($p=0.02$)
  - Impaired gas exchange ($p=0.04$)



Gochuico et al *Arch Intern Med* 2008

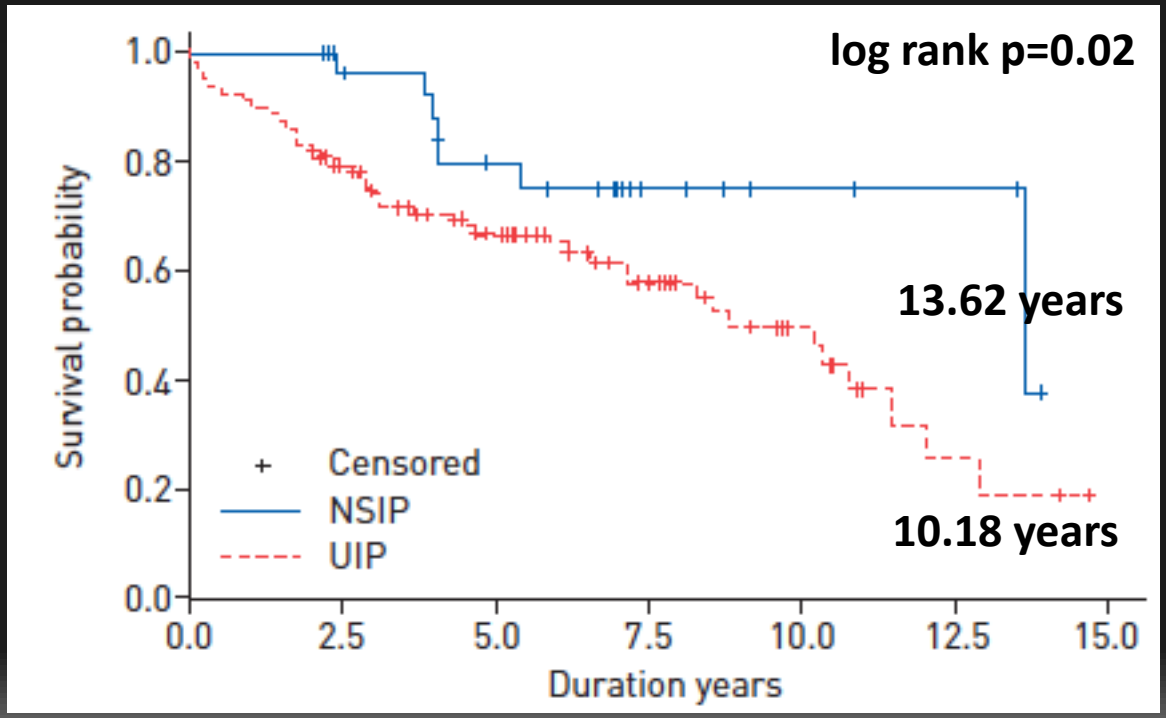
Screening for lung disease in rheumatoid arthritis

- 150 unselected consecutive patients with RA
- Twenty eight (19%) had diffuse lung disease on HRCT
  - 54 % bilateral basal chest crackles
  - 82% reduced DLco
  - 14% restrictive pulmonary function tests
  - 14% bilateral chest radiographic signs
  - 11% chest signs

Dawson JK et al. *Thorax* 2001;56:622–627

Predictors of mortality in RA-ILD

- 137 patients with RA-ILD at a single center
  - 108 with UIP pattern / 29 with NSIP pattern



Solomon JJ et al *Eur Respir J* 2016; 47:588-596

Predictors of mortality in RA-ILD

- 137 patients with RA-ILD at a single center
- Independent predictors of mortality (after controlling for age, sex, smoking and HRCT pattern)
  - **Lower baseline FVC** % pred (HR 1.46; p<0.0001)
  - **10% decline in FVC** % pred from baseline to any time during follow up (HR 2.57; p<0.0001)

Conclusions: survival differs between HRCT subgroups. However, in multivariate models, pulmonary physiology, but not HRCT pattern, independently predicts mortality.

Solomon JJ et al *Eur Respir J* 2016; 47:588-596

Ritorniamo al nostro caso clinico…

Dicembre 2014

- **Comparsa di marcati edemi improntabili e parestesie agli AAII**
- **ECOCOLORDOPPLER AAII: non segni clinico-strumentali di TVP e/o TVS agli arti inferiori**
- **VISITA NEUROLOGICA: polineuropatia a calza (prescritta terapia con Gabapentina e L-carnitina)**

ULTERIORI APPROFONDIMENTI

- **Persistente positività dei p-ANCA**
- **MORFOLOGIA ERITROCITARIA URINARIA: nella norma**
- **ECG: nella norma**
- **ECOCARDIOGRAFIA: ipertensione polmonare con PAPs di 55 mmHg (Cateterismo cardiaco: mPAPai limiti superiori della norma)**

BIOPSIA POLMONARE CHIRURGICA

Polmonite interstiziale diffusa fibrosante a **pattern UIP**. Si osserva eterogeneità spaziale e temporale della fibrosi accanto a focolai di microhoneycombing. E' presente un moderato infiltrato flogistico cronico linfo-plasmacellulare con aspetti di metaplasia bronchiolare e fibrosi lassa. **Non granulomi nè segni di vasculite**.

GENNAIO 2015

- **Peggioramento dell'astenia e nessun miglioramento della sintomatologia parestesica AAII, nonostante la terapia.**

- **EMG: polineuropatia sensitivo-motoria prevalentemente assonale di grado medio-marcato.**

Biopsia del nervo surale

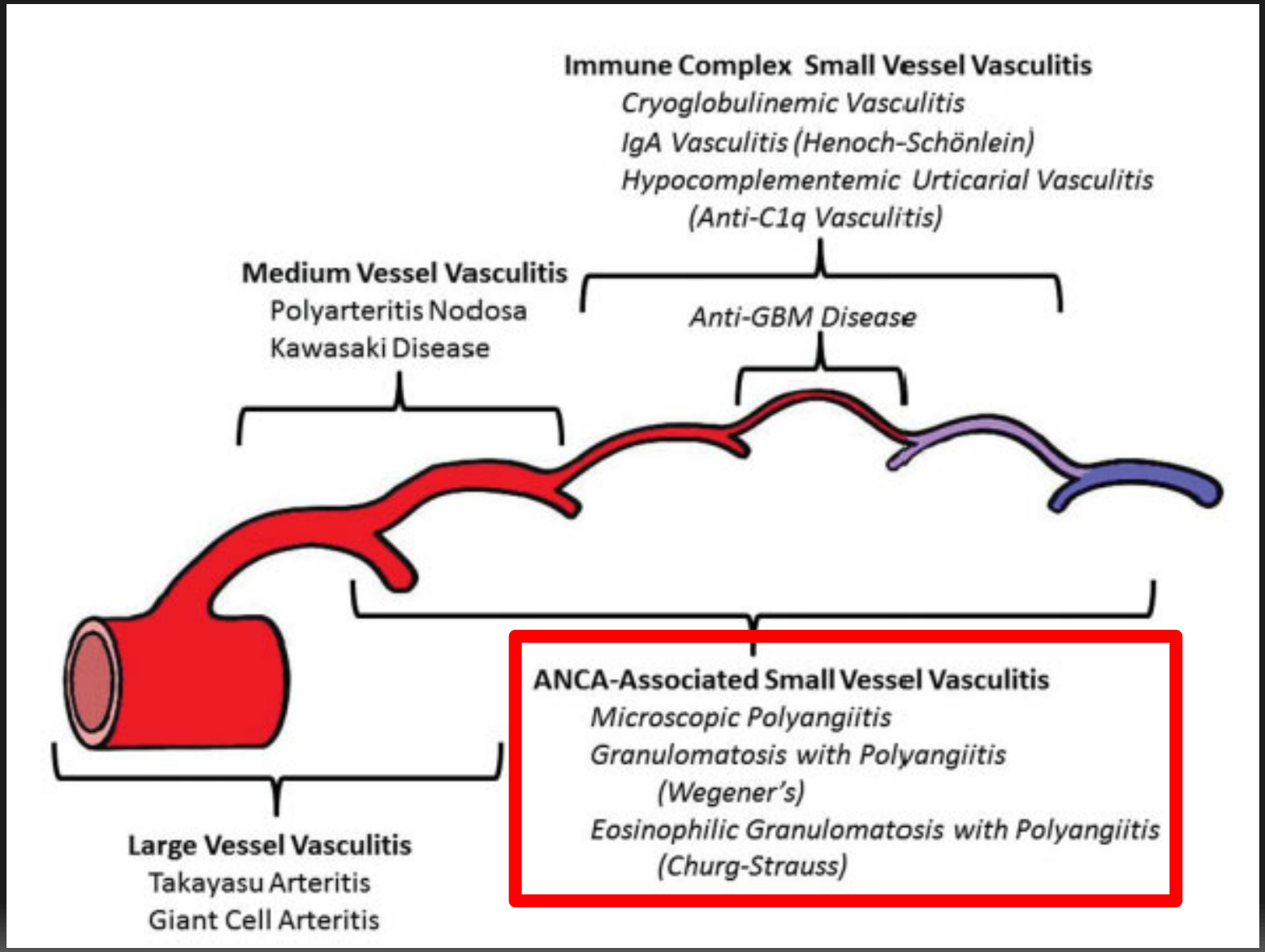
Neuropatia assonale con vasculite dell'arteria epineurale ed infiltrazione tissutale da parte di granulociti eosinofili

CONCLUSIONI

Interstiziopatia polmonare fibrosante con pattern UIP secondaria a vasculite p-ANCA+

Lung involvement in CVD

- **Systemic sclerosis (Scleroderma)**
- **Rheumatoid arthritis-associated lung disease**
- **Rare entities**



Jennette JC et al. Arthritis Rheum. 2013; 65: 1-11

Pulmonary Fibrosis in Antineutrophil Cytoplasmic Antibodies (ANCA)-Associated Vasculitis

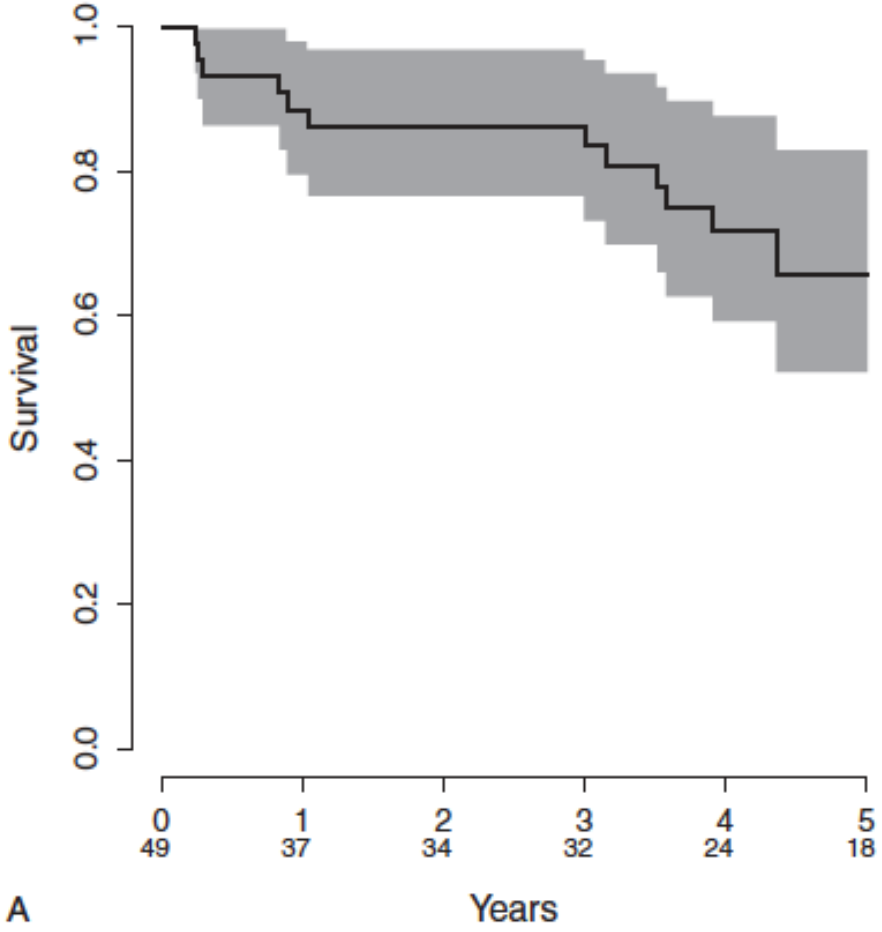
A Series of 49 Patients and Review of the Literature

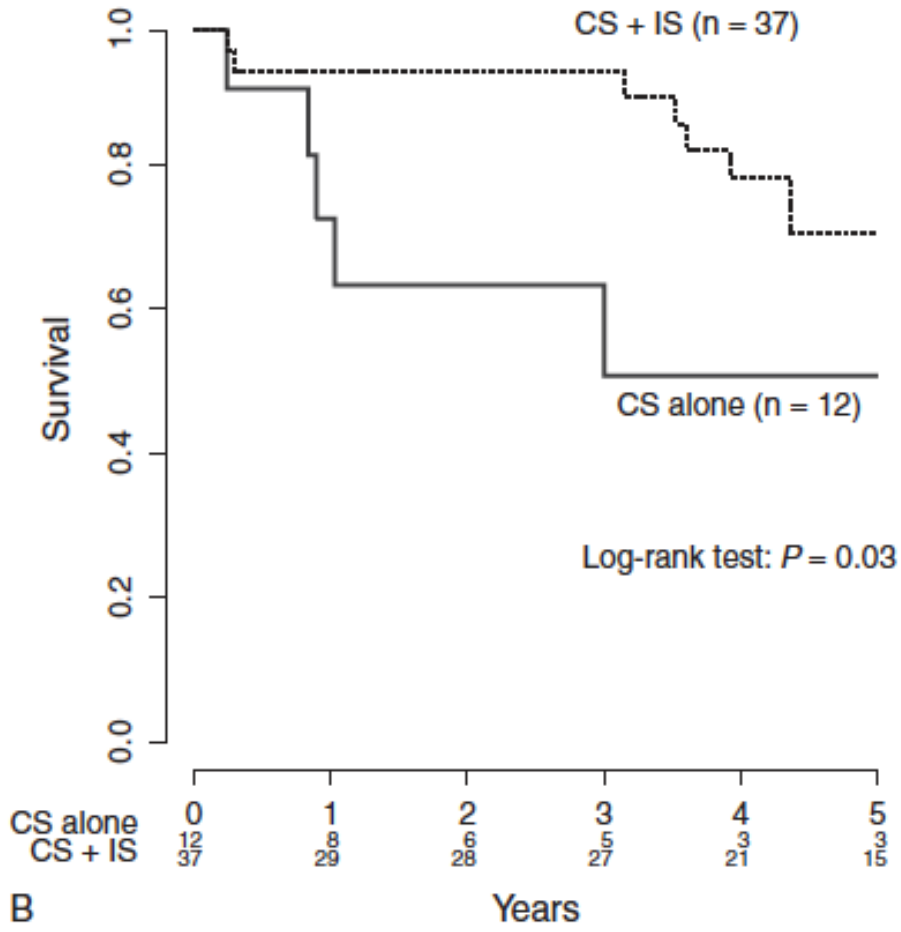
Cloé Comarmond, MD, MSc, Bruno Crestani, MD, PhD, Abdellatif Tazi, MD, PhD, Baptiste Hervier, MD, Sylvain Adam-Marchand, MD, PhD, Hilario Nunes, MD, PhD, Fleur Cohen-Aubart, MD, PhD, Marie Wislez, MD, PhD, Jacques Cadranel, MD, PhD, Bruno Housset, MD, Célia Lloret-Linares, MD, PhD, Pascal Sève, MD, PhD, Christian Pagnoux, MD, MPH, Sébastien Abad, MD, Juliette Camuset, MD, Boris Bienvenu, MD, PhD, Michaël Duruisseaux, MD, PhD, Eric Hachulla, MD, PhD, Jean-Benoît Arlet, MD, PhD, Mohammed Hamidou, MD, PhD, Alfred Mahr, MD, PhD, Matthieu Resche-Rigon, MD, Anne-Laure Brun, MD, Philippe Grenier, MD, Patrice Cacoub, MD, and David Saadoun, MD, PhD

- Retrospective study.
- 49 patients with ANCA-Associated Vasculitis and Pulmonary Fibrosis (16 medical centers, between January 1996 and June 2013).
- 43% with typical UIP pattern on HRCT

Medicine (Baltimore). 2014; 93: 340-349

Survival curve of patients with AAV-PF (A) and survival curves according to remission induction treatment with CS alone or combined with CYC (B)





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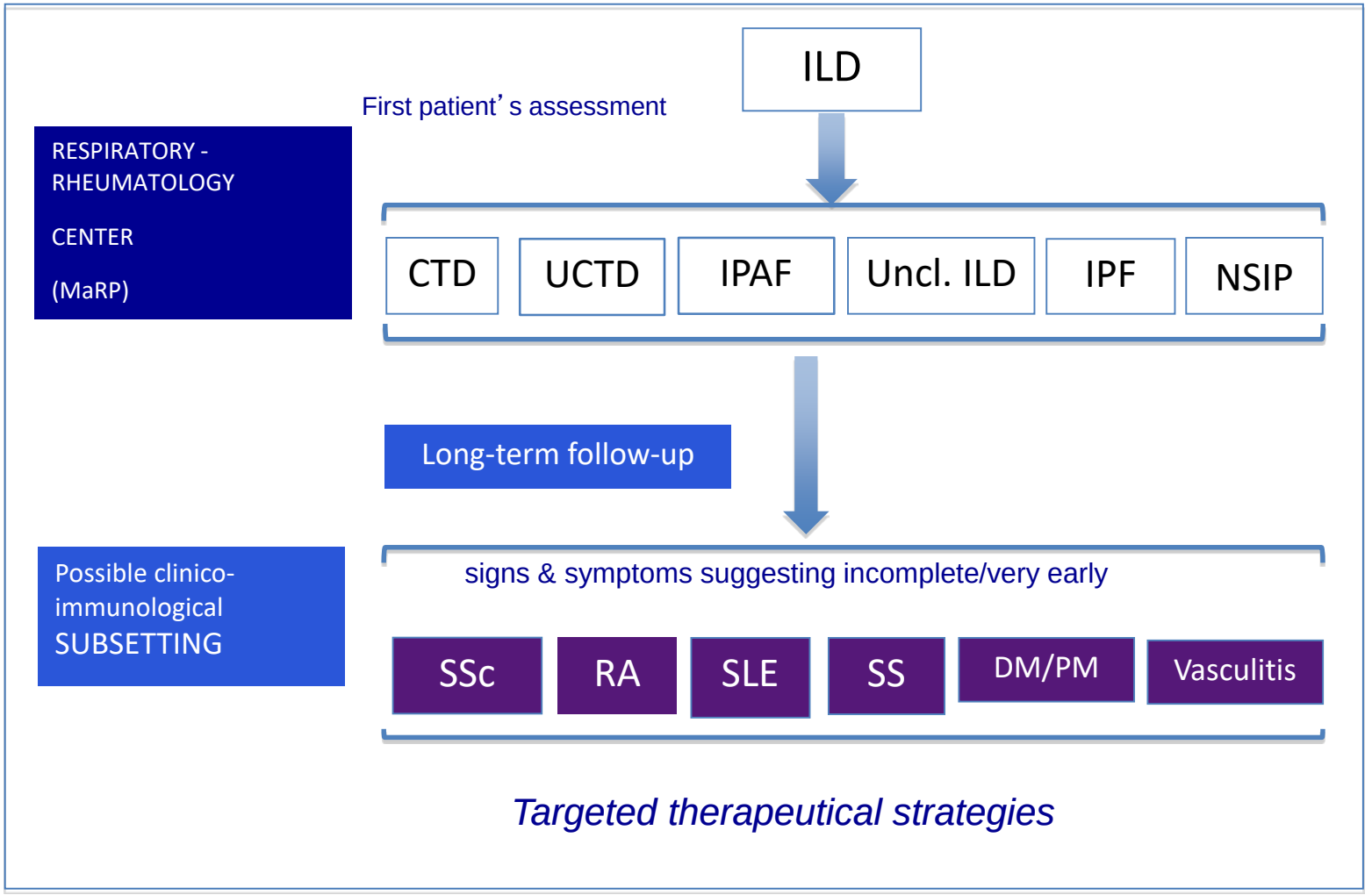
Pulmonary Fibrosis is a **rare** manifestation of ANCA-Associated vasculitis with a **very poor prognosis**. Induction therapy with CYC might improve the outcome.

Medicine (Baltimore). 2014; 93: 340-349

The value of a multidisciplinary approach



rev. from Ferri C. et al. Autoimmunity Reviews 2016;15(1):61-70.

PNEUMOLOGIA 2018 – Milano, 14-16 Giugno 2018

MINICORSO “INTERSTIZIOPATIE E MALATTIE RARE”

MALATTIE FIBROSANTI NON IPF

Stefania Cerri

Centro per le Malattie Rare del Polmone
Clinica di Malattie dell’Apparato Respiratorio
AOU di Modena - UNIMORE

UNIMORE
UNIVERSITÀ DEGLI STUDI DI MODENA E REGGIO EMILIA