Szisztémás sclerosis és rokon kórképek

Dr. Szűcs Gabriella

DE ÁOK Reumatológiai Tanszék

KK Reumatológiai és Immunológiai Klinika

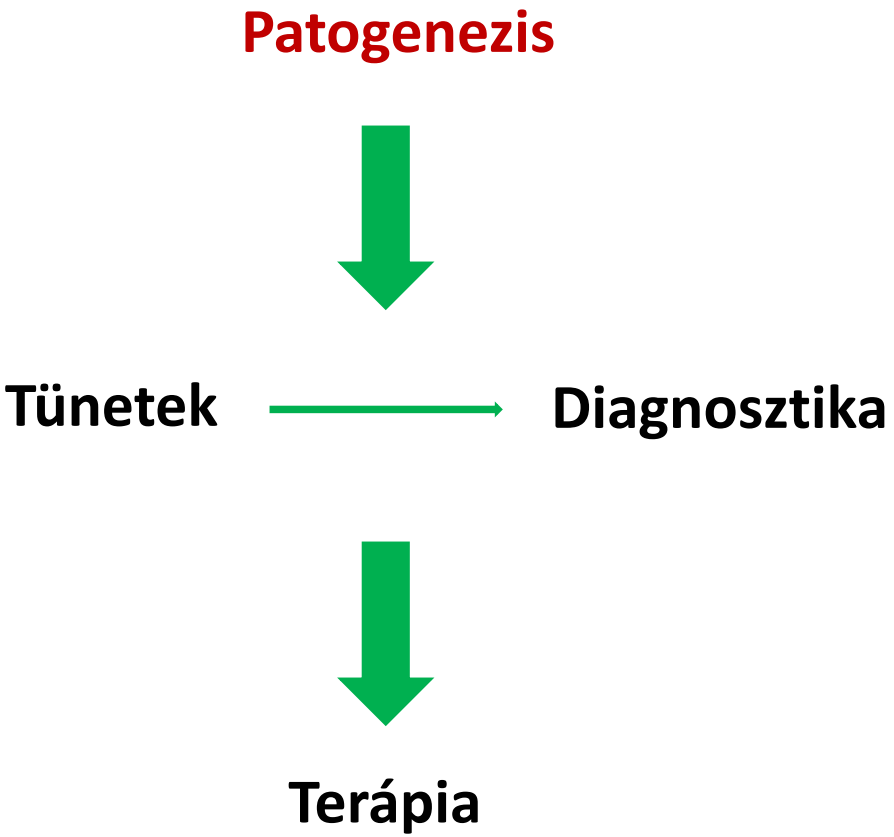
Klinikai immunológia és allergológia II. Klinikum

Semmelweis Egyetem

Reumatológiai és Immunológiai Klinika

2025. Szeptember 30.

Szisztémás sclerosis



- Endothelial cell injury
- Endothelial cell dysfunction
- Defective vascular remodeling
- EndoMT, EMT, AMT

Vasculopathy

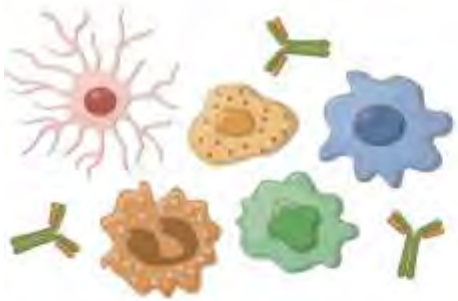
- Microbial infection
- Toxic exposure : Silica, solvents..
- Oxidative stress
- Immune response

Triggers

SSc Pathogenesis

Genetic susceptibility

Environmental factors

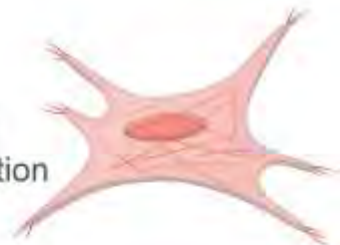


Immune cell activation

- Innate immunity
- Adaptive immunity
- Autoimmunity

Fibrosis

- Excessive ECM deposition
- Persistent fibroblasts activation



Chronic inflammation / Organ damage

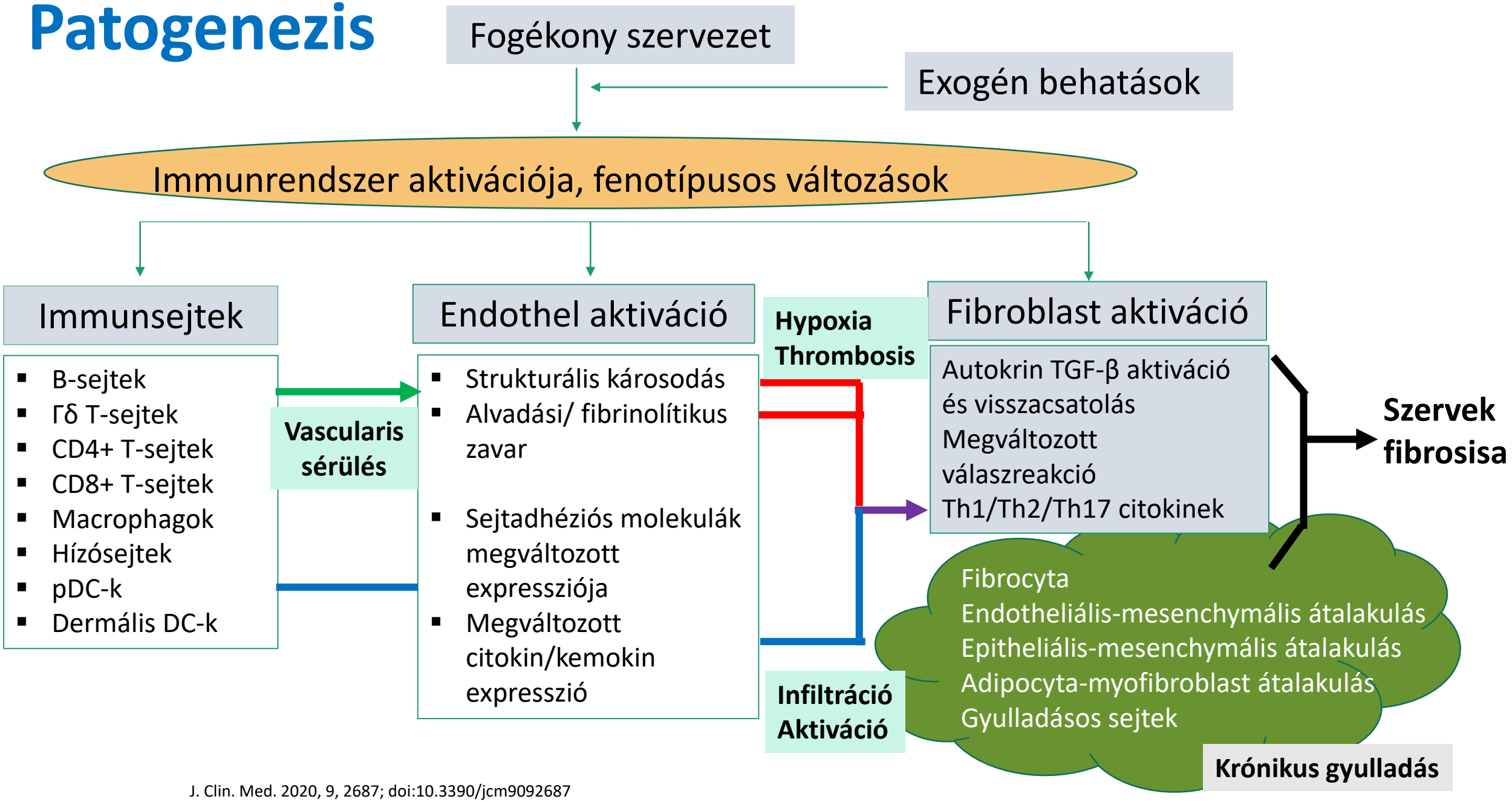
Rheum Dis 2025;32(2):89-104

Table 1. The summary data of the annotated loci associated with SSc trait including all associations with p values below 8×10^{-8} according to the GWAS catalog (http://www.ebi.au.uk/gwas/)

Chromosome	Mapped gene	Reported trait	Ancestry	Chromosome	Mapped gene	Reported trait	Ancestry
1p34.3	KIAA0319L	SSc, SLE	EUR	7p15.2	JAZF1	SSc, SLE	EUR
1p31.3	IL12RB2	SSc, RA, IIM, SLE, CD	EUR	7q11.23	EIF4H, LIMK1	SSc, RA, IIM, SLE	EUR
1p13.2	PTPN22, AP4B1-AS1	SSc, RA, IIM, SLE	EUR	7q32.1	TNPO3	SSc, RA, IIM, SLE	EUR, AA, AC
1q21.3	FLG-AS1, FLG2	SSc	EAS		IRF5, KCP	SSc, RA, IIM, SLE	EUR, AA, AC
1q23.3	FCGR2B, FCGR3B	SSc	EUR, AA, AC		TPI1P2, CYCSP20	SSc, SLE	EUR, AA, AC, EAS
	Y_RNA, RPL31P11	SSc	EAS		RNU6-177P, LINC03072	SSc	EAS
1q24.2	CD247	SSc	EUR	8p23.1	FAM167A, BLK	SSc, RA, IIM, SLE	EUR, AA, AC, EAS
1q25.1	TNFSF4, PRDX6-AS1	SSc, RA, IIM, SLE	EUR, EAS	8q12.1	LINC01301	SSc	EUR, EAS
1q25.3	SMG7, NCF2	SSc, RA, IIM, SLE	EUR	8q12.2	CHD7, RAB2A	SSc	EUR
2q32.2	NAB1, GLS	SSc, RA, IIM, SLE	EUR	11p15.5	SCT, DRD4	SSc, RA, IIM, SLE	EUR
2q32.3	STAT4	SSc, RA, IIM, SLE	EUR, AA, EAS		RNU6-878P, CD81-AS1, CDHR5	SSc	EUR
3p24.1	LINC01967	SSc	EUR, EAS	11q23.3	CXCR5, Y_RNA	SSc	EUR
3p14.3	DNASE1L3	SSc, RA, IIM, SLE	EUR		DDX6	SSc	EUR, EAS
	PXK	SSc, SLE	EUR, EAS	12q13.2	ESYT1, ZC3H10	SSc	EUR
	FLNB	SSc	EUR, EAS	12q15	IFNG-AS1	SSc (ACA-positive)	EAS
3q13.33	ARHGAP31	SSc	EUR, EAS	12q24.13	PTPN11	SSc	EUR
3q25.33	IL12A-AS1	SSc	EUR, EAS	13q13.3	NBEA	SSc-ILD	EAS
	ARL14, RPL6P8	SSc, RA, IIM, SLE	EUR	14q32.33	AHNAK2, IGHM	SSc	EUR, EAS
4p16.3	DGKQ	SSc, RA, IIM, SLE	EUR, EAS	15q24.1	CSK	SSc	EUR, EAS
4q24	NFKB1	SSc	EUR, EAS	15q24.2	Metazoa_SRP, RPL36AP45	SSc, SLE	EUR
4q28.3	STMN1P2, RPS23P2	SSc (ACA-positive)	EAS	16p11.2	ITGAM	SSc, SLE	EUR
4q34.3	RNA5SP173, NDUFB5P1	SSc	EUR, EAS	16q24.1	IRF8-LINC01082, LINC02132	SSc, RA, IIM, SLE	EUR, AA, AC, EAS
4q35.1	UFSP2, ANKRD37	SSc	EAS	17q21.1	GSDMA, GSDMB	SSc	EUR, EAS
5q31.1	IRF1	SSc, CD	EUR		STAT3	SSc, CD	EUR
5q33.1	TNIP1	SSc, RA, IIM, SLE	EUR, EAS	17q25.1	NUP85	SSc	EUR, EAS
5q33.3	MIR3142HG	SSc, RA, IIM, SLE	EUR	19p13.2	TYK2	SSc, RA, IIM, SLE	EUR
6p21.32	HLA-region	SSc	EUR, EAS	19p13.11	IL12RB1	SSc	EUR, EAS
	MTCO3P1, NOTCH4, TSBP1-AS1	SSc	EUR	19q13.33	PRR12	SSc, RA, IIM, SLE	EUR
6p21.31	ZBTB9, GGNBP1	SSc, CD	EUR	20q13.12	SLC12A5	SSc	EUR, EAS
6q21	ATG5	SSc, RA, IIM, SLE	EUR, EAS	20q13.33	RTEL1-TNFRSF6B, RTEL1	SSc (ACA-positive)	EAS
6q23.3	TNFAIP3, SIMALR	SSc, RA, IIM, SLE	EUR, EAS	22q11.21	YDJC, CCDC116	SSc, RA, IIM, SLE	EUR
	LINC02539, WAKMAR2	SSc, SLE	EUR				

GWAS: genome-wide association study, SSc: systemic sclerosis, SLE: systemic lupus erythematosus, RA: rheumatoid arthritis, IIM: idiopathic inflammatory myopathies, CD: Crohn's disease, EUR: European, AA: African American, AC: Afro-Caribbean, EAS: East Asian.

Patogenezis



J. Clin. Med. 2020, 9, 2687; doi:10.3390/jcm9092687

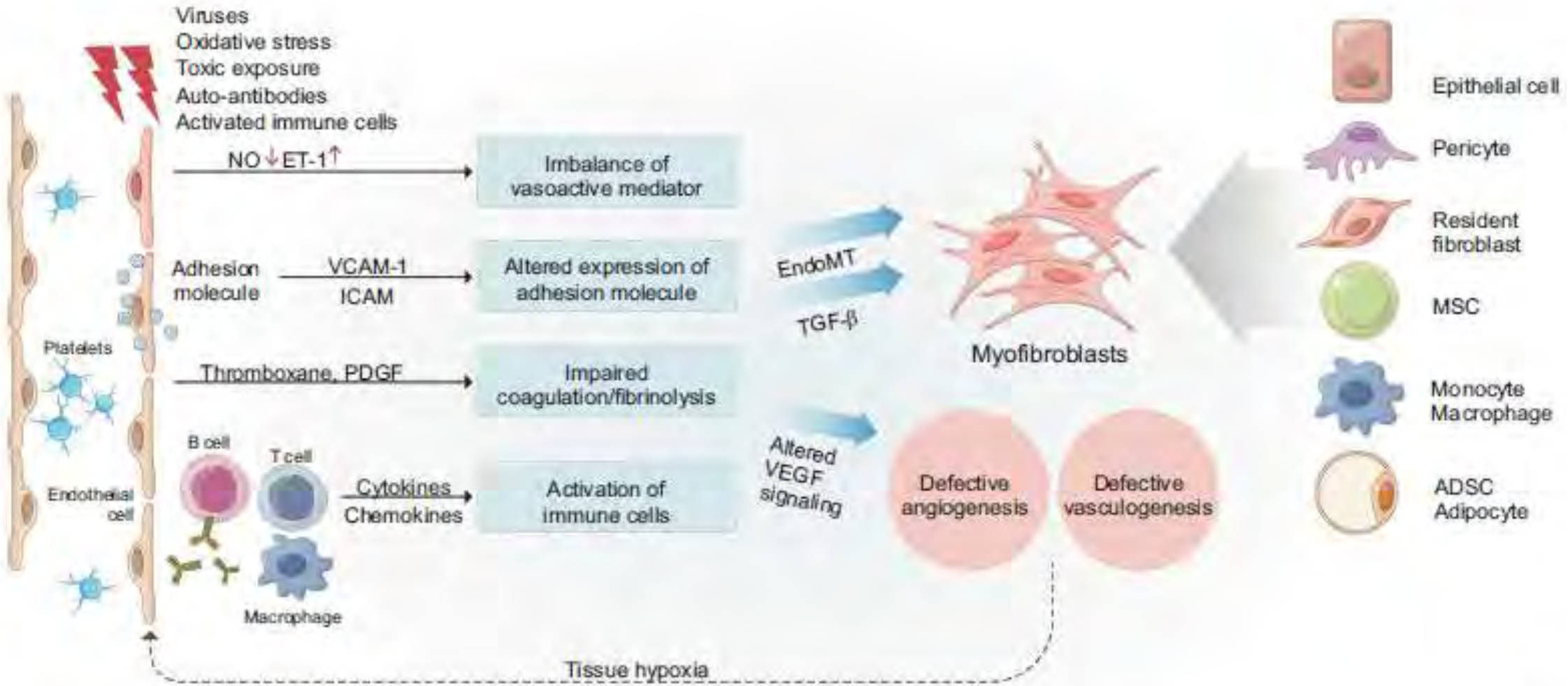


Figure 2. A pathologic association between vasculopathy and fibrosis in SSc. ECs are subjected to damage and dysfunction due to

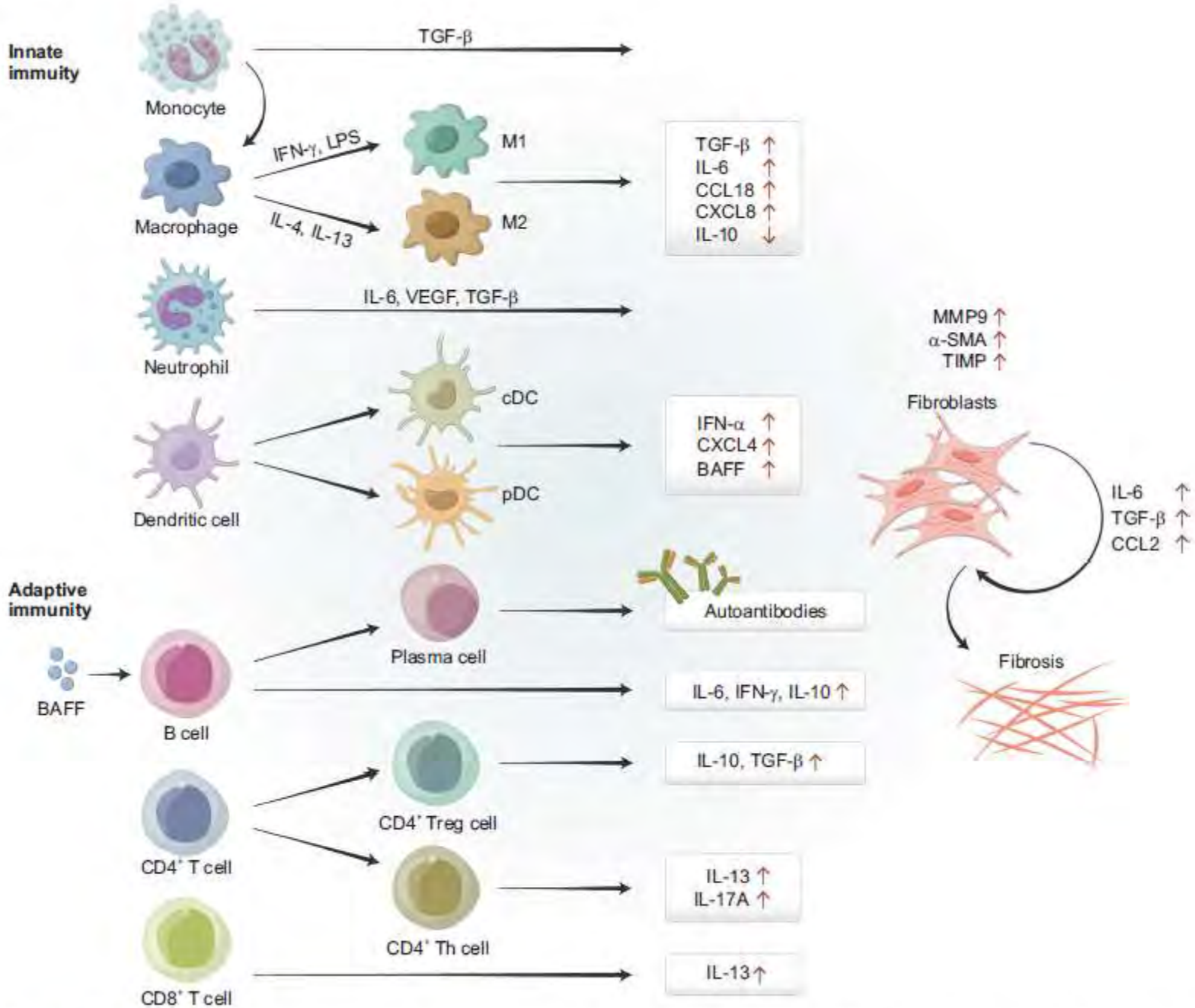


Figure 3. The pro-inflammatory and profibrotic network involved in the pathogenesis of SSc. This figure highlights the intricate

Raynaud tünet

Vazokonstrikció ↑

A simaizomsejtek α-2 adrenoreceptorok reaktivitása ↑

A digitalis artériák hideghatásra, vagy emocionális stresszre bekövetkező kóros válaszreakciója, fokozott vasokonstrikciója

Endothel sérülés

Sejtek közötti adhézió, tight junction fellazulása

Idegrostok (szimpatikus és szenzoros)

Simaizomsejtek

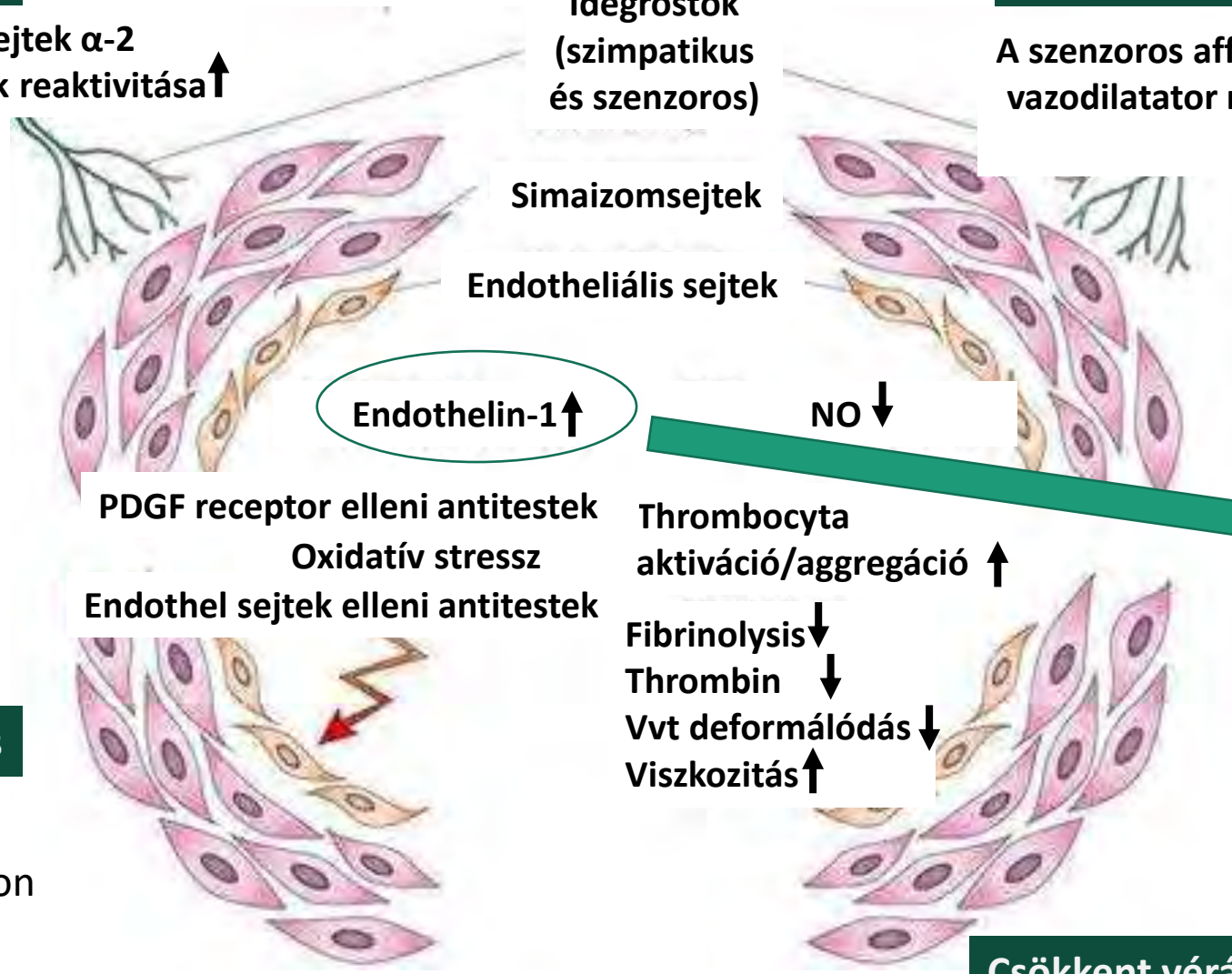
Endotheliális sejtek

Endothelin-1 ↑

PDGF receptor elleni antitestek

Oxidatív stressz

Endothel sejtek elleni antitestek



NO ↓

Thrombocyta aktiváció/aggregáció ↑

Fibrinolysis ↓

Thrombin ↓

Vvt deformálódás ↓

Viszkozitás ↑

Vazodilatáció ↓

A szenzoros afferens rostokból származó vazodilatator neuropeptidek (pl. CGRP) szintje ↓

Fibrosis

Csökkent véráramlás/ prokoaguláns állapot

Vasculopathia

Autoimmunitás (endothel sejt elleni at és egyéb környezeti tényezők

Vascularis sejtek aberráns aktivációja

Endothel károsodás, apoptosis

NO elérhetősége csökken

Sejtadhéziós molekulák fokozott expressziója: ICAM-1, GlyCAM-1, E-szelektin, P-szelektin, vWF

ROS produkció

EndoMT

Kóros angiogenezis és vasculogenezis

Arteriola stenosis

Capillaris dilatatio

Capillaris pusztulás

vSMC prolferáció

Th2, Th17 és B-sejt, M2 macrophag, hízósejt, plasmocytoid dendritikus sejt infiltráció, koaguláció>> fibrinolysis

Fibrin depozíció

IL-4, IL-6, IL-10, IL-13, IL-17A, TGF-β, CTGF, PDGF

Szöveti hypoxia

Szöveti hypoxia

Vascularis tünetek

PAH

Scleroderma renális krízis

Digitális fekélyek

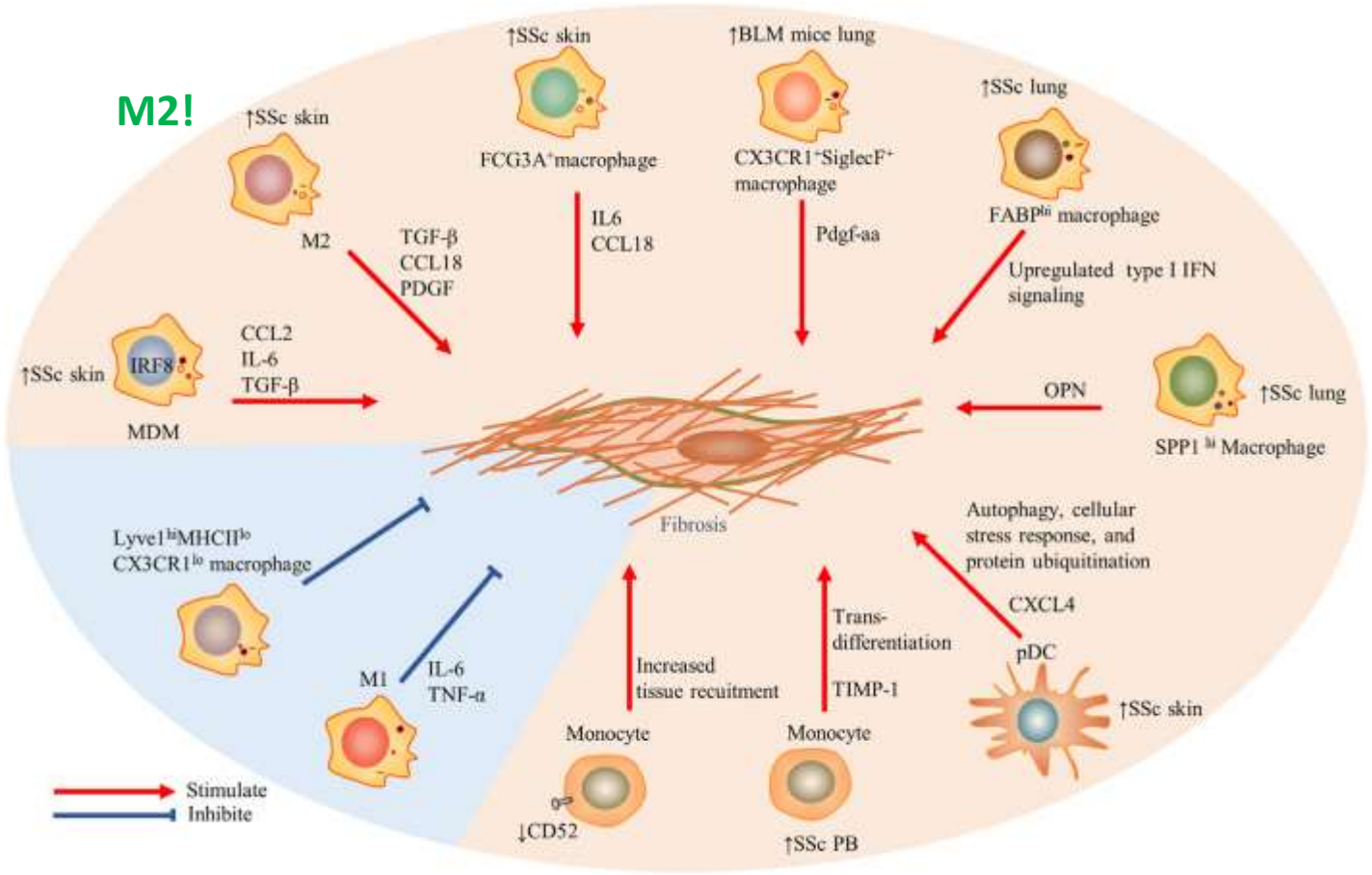
Szöveti fibrosis

J. Clin. Med. 2020, 9, 2687; doi:10.3390/jcm9092687

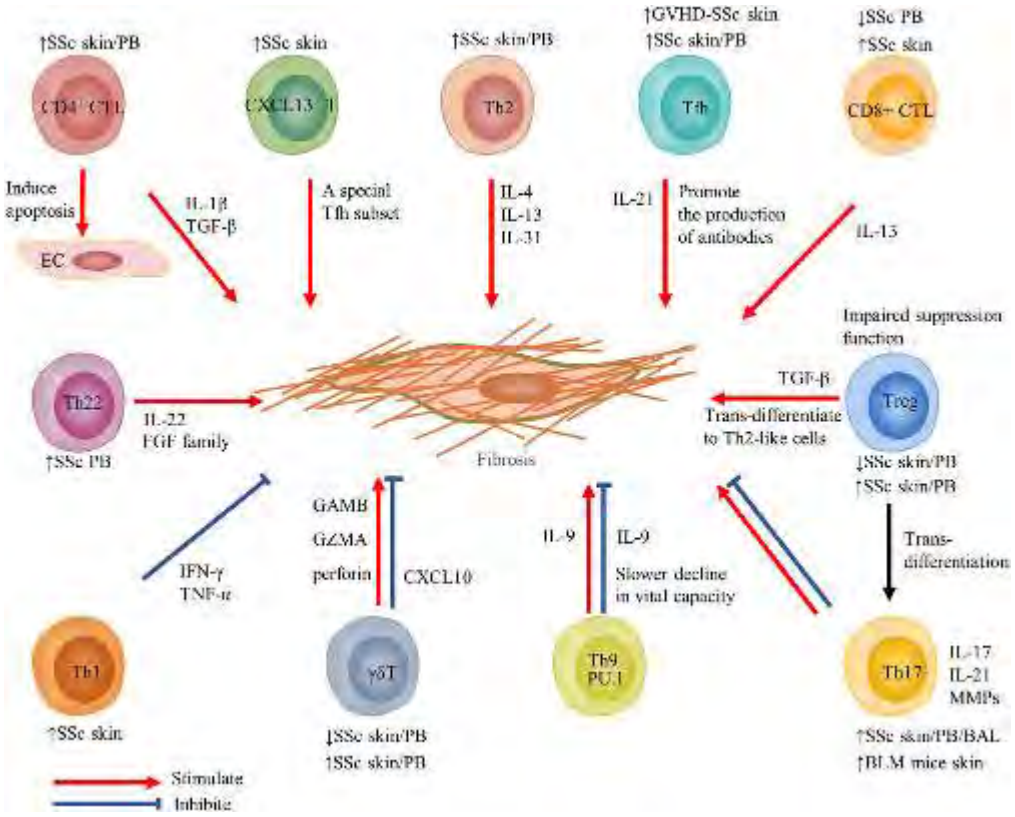
Contributions of Immune Cells and Stromal Cells to the Pathogenesis of Systemic Sclerosis: Recent Insights

Bingying Dai et al. 2022. Front. Pharmacol. 13:826839.

M2!



CXCL13+ T-sejt!



Contribution of T-cell subsets and their cytokines to fibrosis in SSc

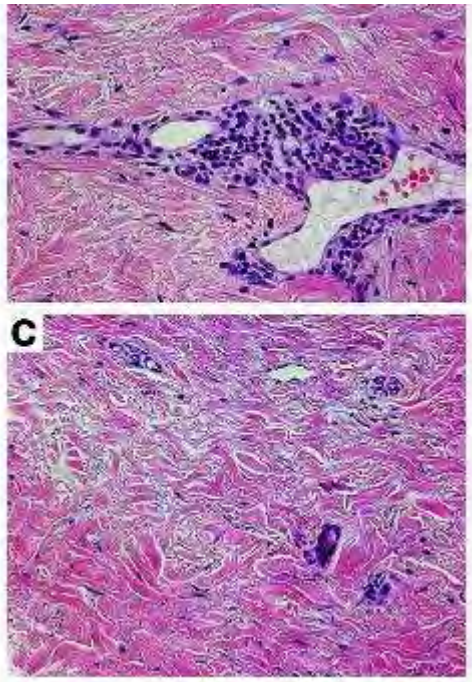
The role of innate immune cells including monocytes, macrophages, and dendritic cells in the fibrosis in SSc.

\+ Effektor B sejtek

Regulatorikus B sejtek

\+ Hízósejtek, Neu

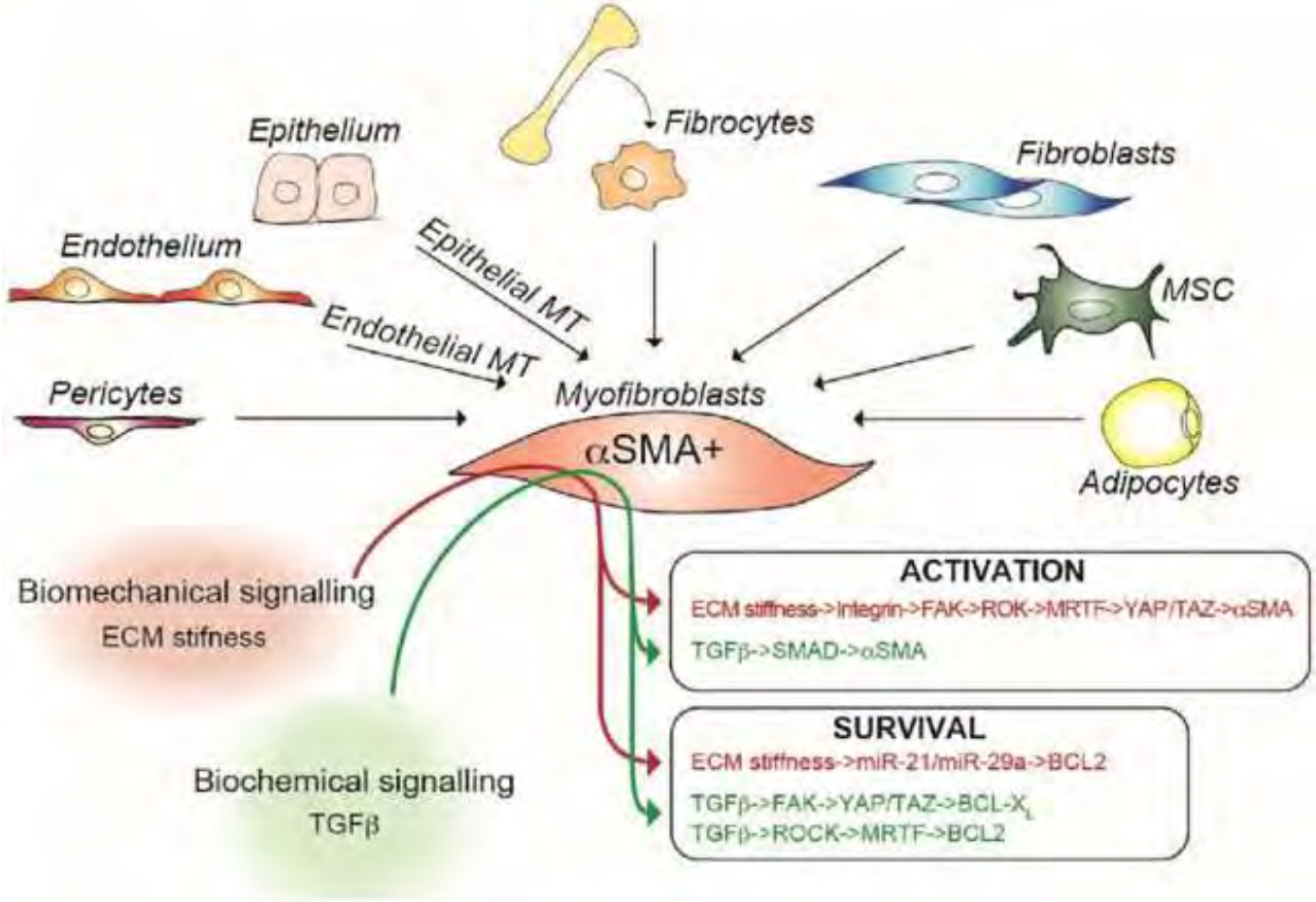
Fibrosis



Gyulladásos mikrokörnyezet

+

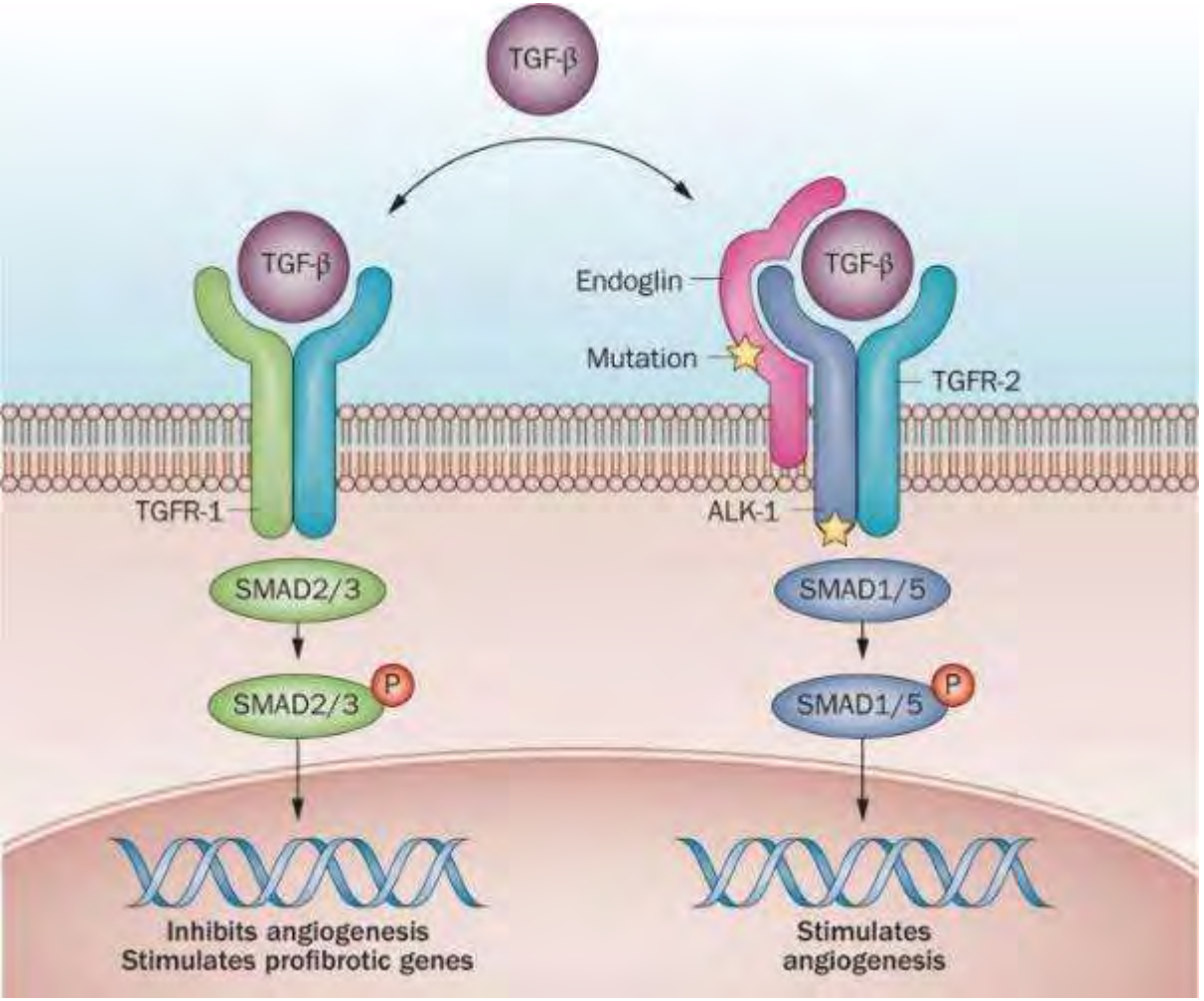
Szöveti sérülés, hypoxia, stressz



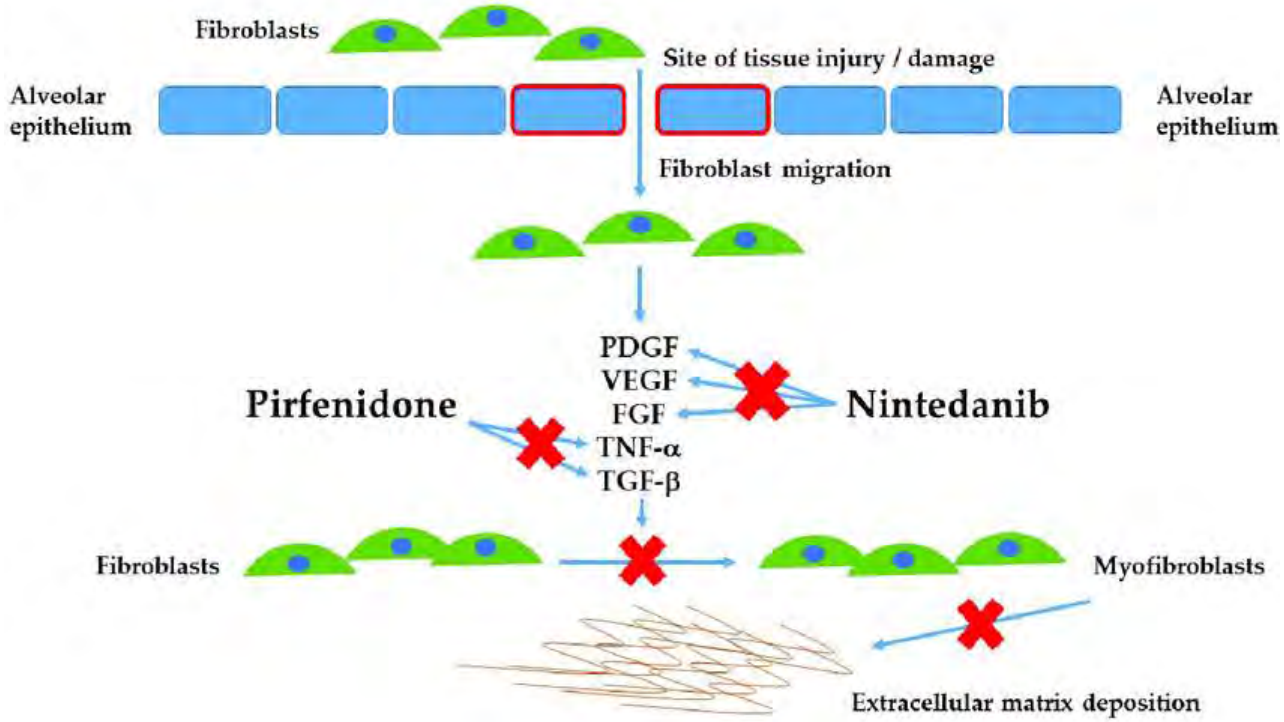
Kóros fibrosis: fibroblast-myofibroblast (α-simaizom aktint expresszáló) átalakulás, fibroblast apoptosis csökkenés,autokrin aktiváció miatt túlzott kollagén és ECM termelés

Megvastagodott kollagén rostok: I, III, VII-es típusú kollagén, subcutan zsírszövet csökken, kollagén keresztkötések

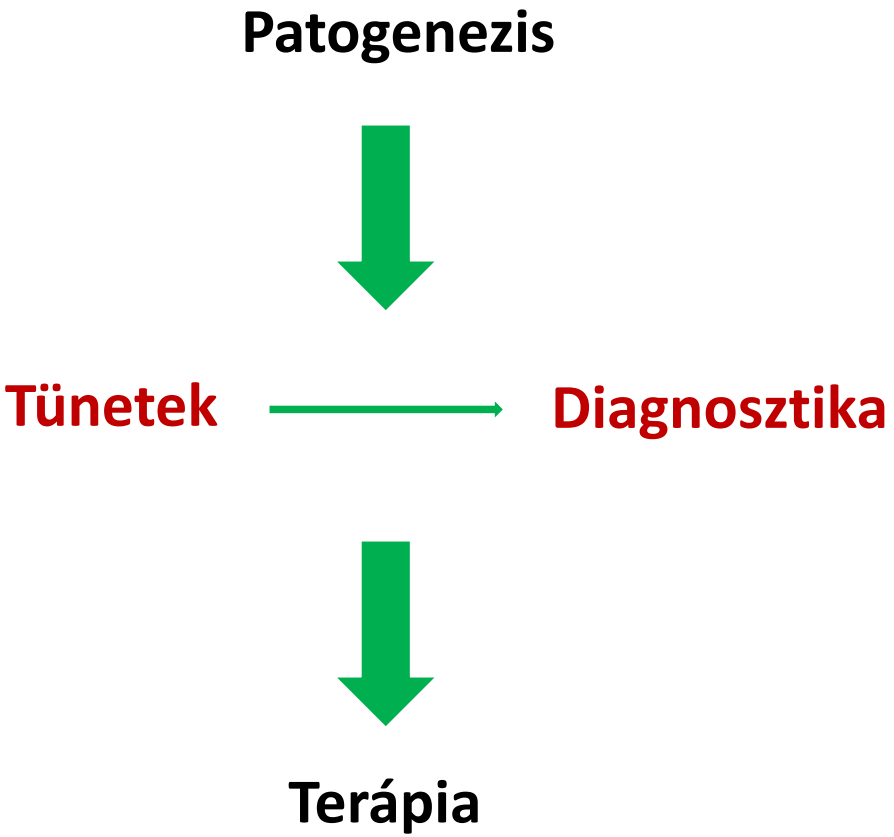
TGF-β

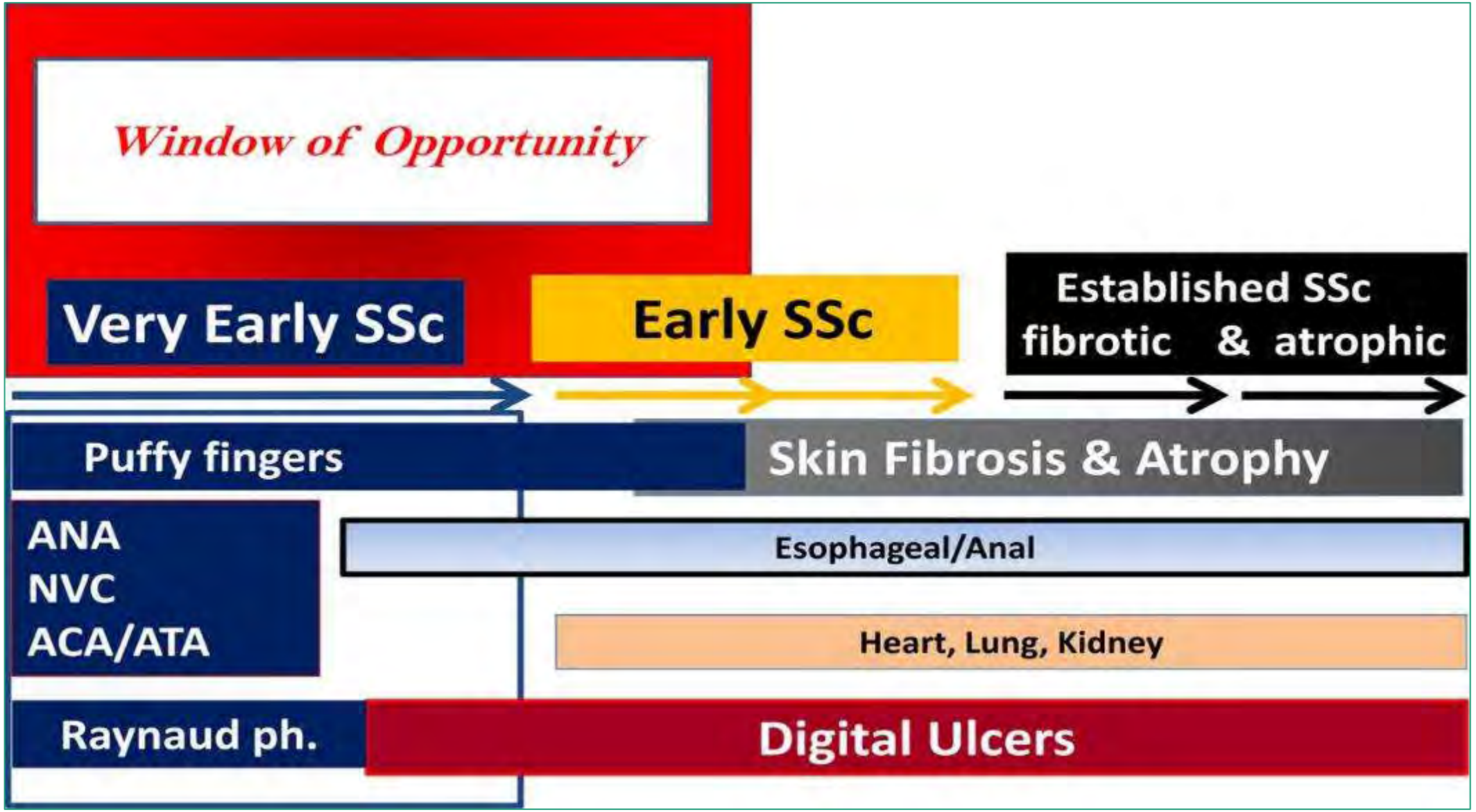


- **Fibrosis: központi szerep, ECM termelés fokozása, lebontás gátlása**
- **Forrása: fibroblasztok, miofibroblasztok, T-sejtek, monociták, makrofágok és vérlemezkék**
- **I-es típusú kollagén, I-es típusú plazminogén aktivátor inhibitor, CTGF és α-SMA gén expresszió fokozása**



Szisztémás sclerosis



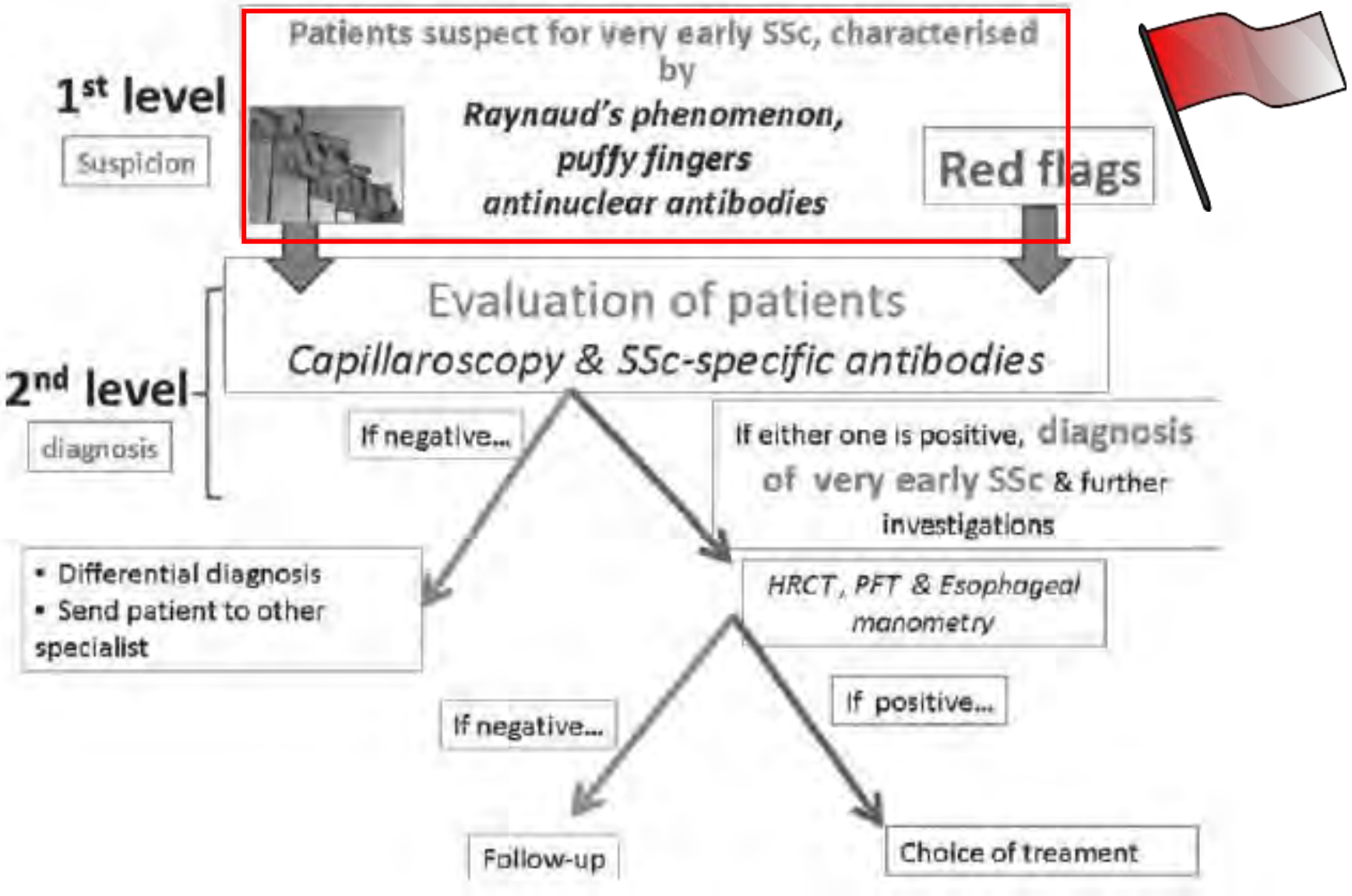


Matucci-Cerinic M et al. Ann Rheum Dis doi:10.1136/annrheumdis-2012-202295

Preliminary criteria for the very early diagnosis of systemic sclerosis: results of a Delphi Consensus Study from EULAR Scleroderma Trials and Research Group

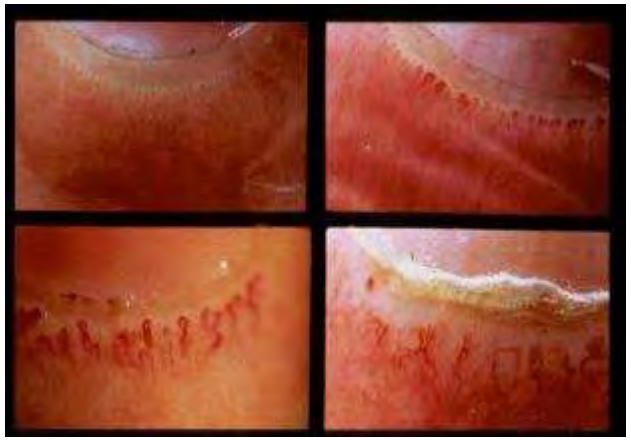
J Avouac,[1] J Fransen,[2] UA Walker,[3] V Riccieri,[4] V Smith,[5] C Muller,[5] I Miniati,[7] IH Tamer,[8] S Bellando Randone,[6] M Cutolo,[9] Y Allanore,[1] O Distler,[10] G Valentini,[11] L Czirjak,[12] U Müller-Ladner,[8] DE Furst,[13] A Tyndall,[3] M Matucci-Cerinic,[7] EUSTAR Group

Ann Rheum Dis 2011;**70**:476–481. doi:10.1136/ard.2010.136929



Very early systemic sclerosis - diagnózis

- Raynaud phenomen
- Puffy fingers (sclerodactylia-ba forduló)
- Antinuclearis antitest +
- Specifikus SSc antitest + (anticentromer és antitopoisomerase-I - antiScl70)
- Kóros capillaroscopos kép - scleroderma pattern



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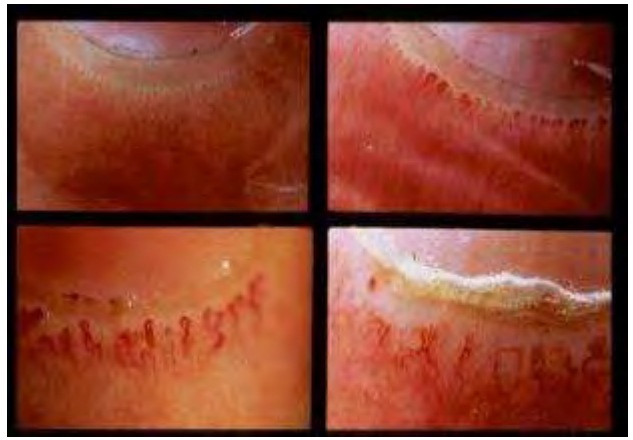
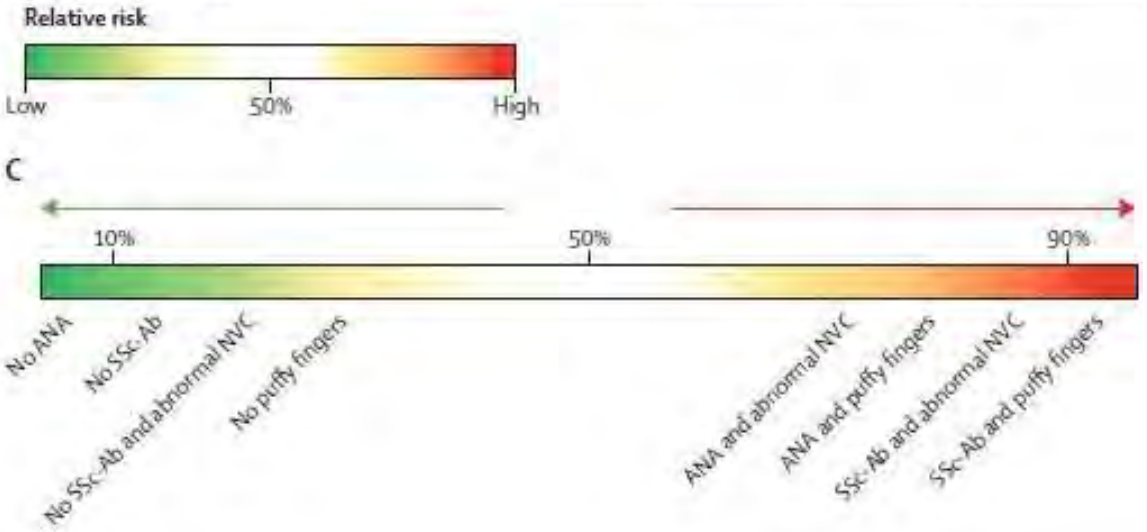
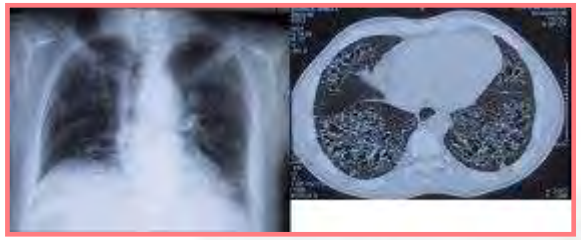


Progression of patients with Raynaud's phenomenon to systemic sclerosis: a five-year analysis of the European Scleroderma Trial and Research group multicentre, longitudinal registry study for Very Early Diagnosis of Systemic Sclerosis (VEDOSS)
***Lancet Rheumatol* 2021; 3: e834–43)**

Proportion fulfilling 2013 ACR-EULAR criteria		ANA	Ssc-Ab	SSc pattern on NVC	Puffy fingers
In the presence of	ANA	58·9%	70·2%	75·0%	79·0%
	SSc-Ab	70·2%	**70·2%**	82·2%	94·1%
	SSc-Ab pattern on NVC	75·0%	82·2%	**70·1%**	69·2%
	Puffy fingers	79·0%	94·1%	69·2%	**70·8%**
In the absence of	ANA	**10·8%**	31·0%	40·4%	47·5%
	SSc-Ab	31·0%	**31·0%**	41·9%	49·6%
	SSc-Ab pattern on NVC	40·4%	41·9%	**41·5%**	50·9%
	Puffy fingers	47·5%	49·6%	50·9%	**47·9%**



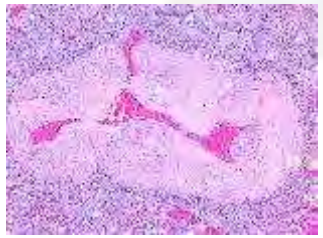
Klinikai manifesztációk

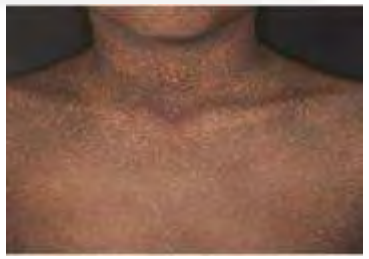


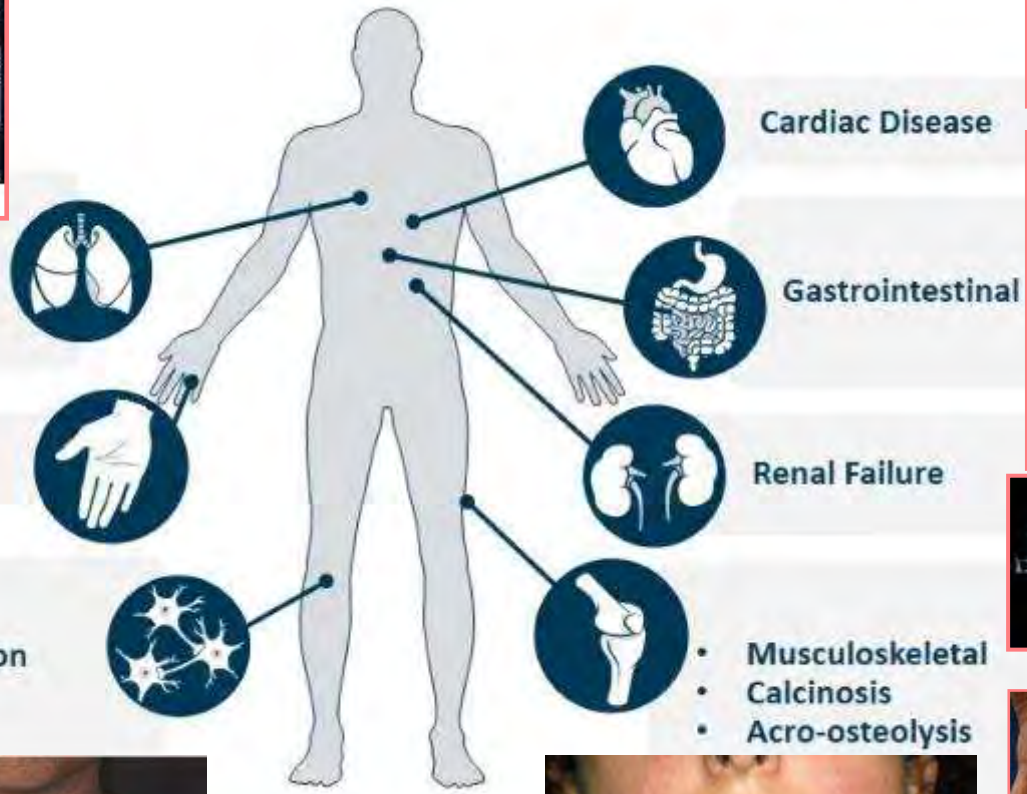
Lung Fibrosis

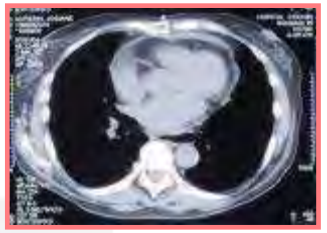
Digital Vasculopathy

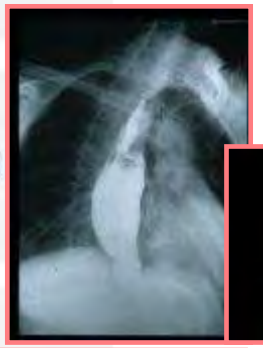
Pulmonary Hypertension

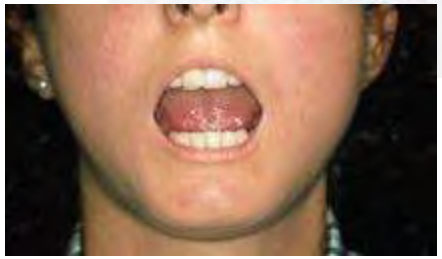












2013 EULAR/ACR klasszifikációs kritériumok - SSc diagnózis – szenzitivitás javulása

Panel 1: Summary items from the 2013 American College of Rheumatology and European League Against Rheumatism criteria for the classification of systemic sclerosis*

Proximal skin involvement
- Skin thickening of the fingers of both hands, extending proximal to the metacarpophalangeal joints (sufficient criterion; score 9)

Skin thickening of the fingers (only count the higher score)
- Puffy fingers (score 2)
- Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints; score 4)

Fingertip lesions (only count the higher score)
- Digital tip ulcers (score 2)
- Fingertip pitting scars (score 3)

Telangiectasia (score 2)

Abnormal nailfold capillaries (score 2)

Pulmonary arterial hypertension or interstitial lung disease (maximum score of 2)
- Pulmonary arterial hypertension (score 2)
- Interstitial lung disease (score 2)

Raynaud's phenomenon (score 3)

Systemic sclerosis-related autoantibodies (maximum score of 3)
- Anti-centromere (score 3)
- Anti-topoisomerase I (score 3)
- Anti-RNA polymerase III (score 3)

*A total score of 9 is needed for a definite classification.

A szubklasszifikáció nem fedi le a SSc-spektrum különböző fenotípusait

Panel 2: Typical features of the major subsets of systemic sclerosis

Limited cutaneous systemic sclerosis
- Distal skin sclerosis
- Long history of Raynaud's phenomenon
- Late-stage complications frequent
- Pulmonary arterial hypertension and severe gut disease frequent and serious

Diffuse cutaneous systemic sclerosis
- Proximal limb or trunk involvement, with skin sclerosis
- Short history of Raynaud's phenomenon
- Increased risk of renal crisis and cardiac involvement
- High frequency of severe lung fibrosis

Sine scleroderma
- Raynaud's phenomenon
- Typical systemic sclerosis serology or capillaroscopic features
- No skin thickening
- Organ-based or other vascular manifestations

Systemic sclerosis overlap syndrome
- One of the three subsets together with clinical and investigational features of another autoimmune rheumatic disease

Denton CP et Kanna D. Systemic sclerosis Lancet. 2017 Oct 7;390(10103):1685-1699

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Fingertip lesions (only count the higher score)
- Digital tip ulcers (score 2)
- Fingertip pitting scars (score 3)

Telangiectasia (score 2)

Abnormal nailfold capillaries (score 2)

Pulmonary arterial hypertension or interstitial lung disease (maximum score of 2)
- Pulmonary arterial hypertension (score 2)
- Interstitial lung disease (score 2)

Raynaud's phenomenon (score 3)

Systemic sclerosis-related autoantibodies (maximum score of 3)
- Anti-centromere (score 3)
- Anti-topoisomerase I (score 3)
- Anti-RNA polymerase III (score 3)

*A total score of 9 is needed for a definite classification.

A szubklasszifikáció nem fedi le a SSc-spektrum különböző fenotípusait

Panel 2: Typical features of the major subsets of systemic sclerosis

- **Bőrtünetek kiterjedtsége**
- **Autoantitest profil**
- **Szervi érintettség**
- **Betegség progresszió és kimenetel**

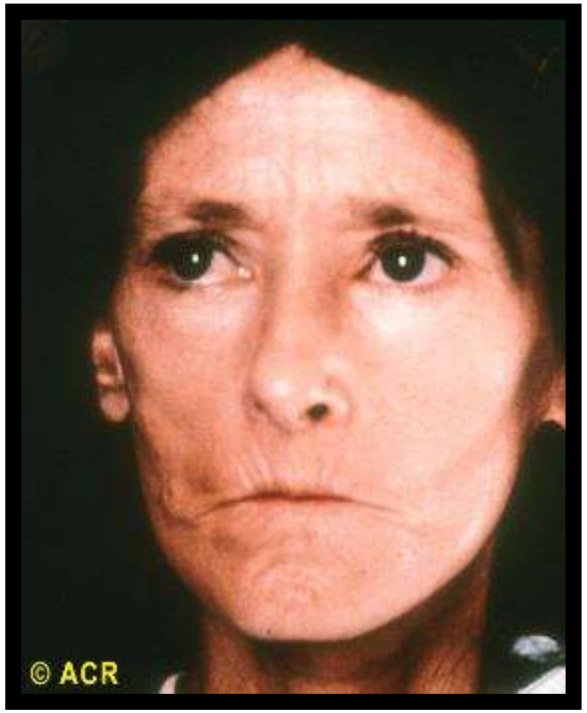
Diffuse cutaneous systemic sclerosis
- Proximal limb or trunk involvement, with skin sclerosis
- Short history of Raynaud's phenomenon
- Increased ment
- High frequ

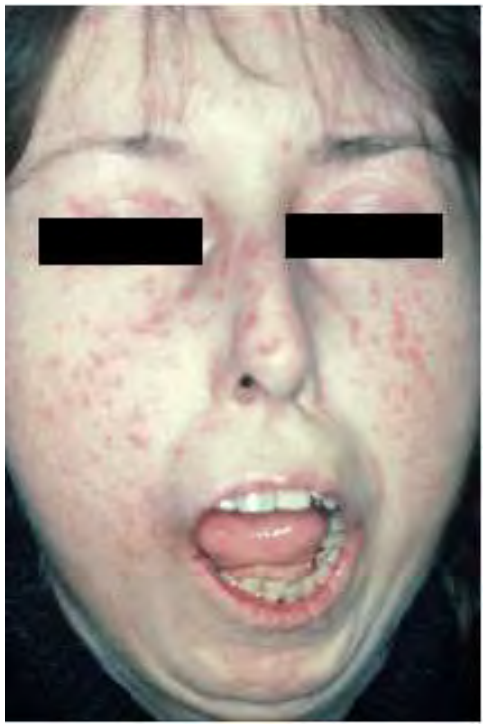
Sine scleroderma
- Raynaud's
- Typical sys pic features
- No skin th
- Organ-bas

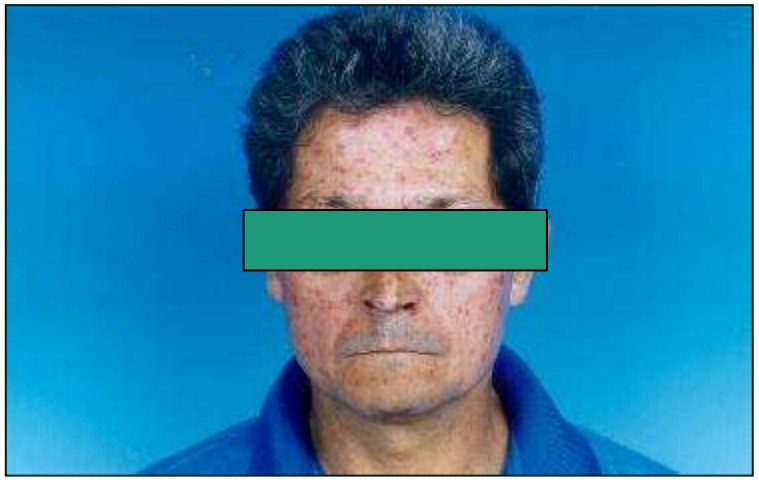
Systemic sclerosis overlap syndrome
- One of the three subsets together with clinical and investigational features of another autoimmune rheumatic disease

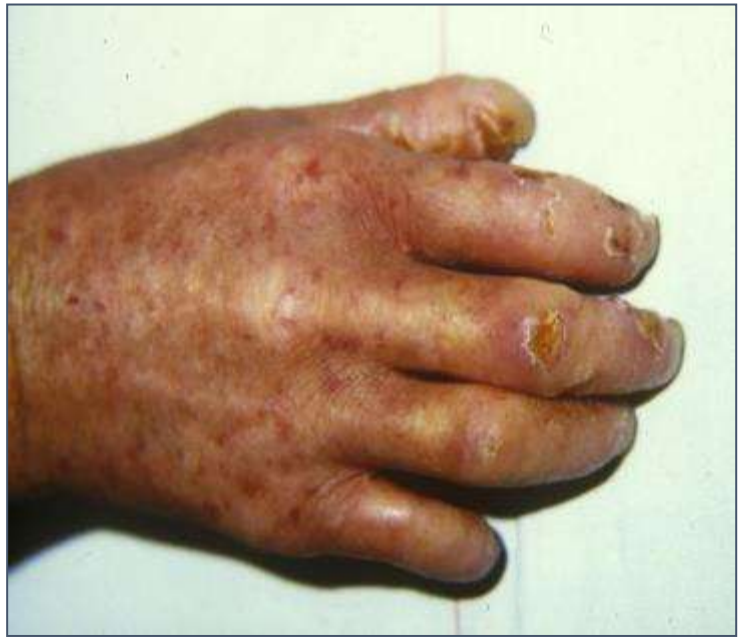
Denton CP et Kanna D. Systemic sclerosis Lancet. 2017 Oct 7;390(10103):1685-1699

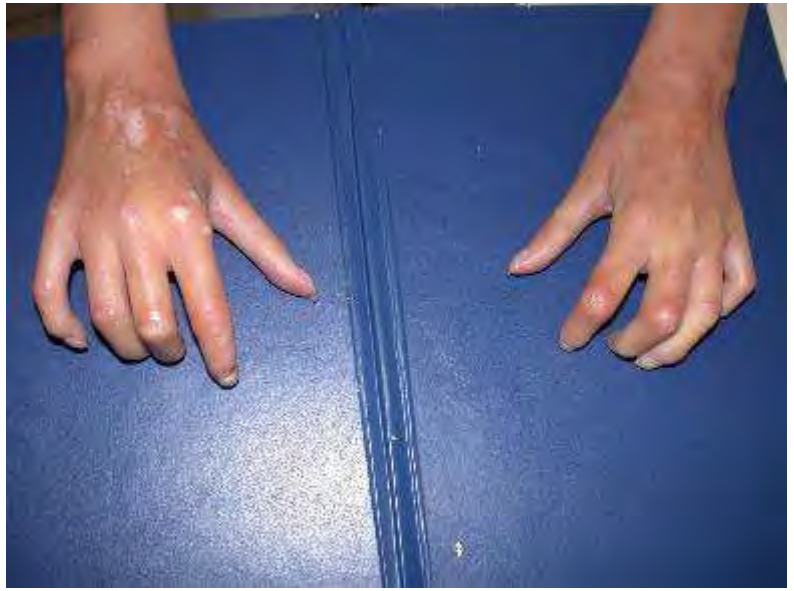
SSc



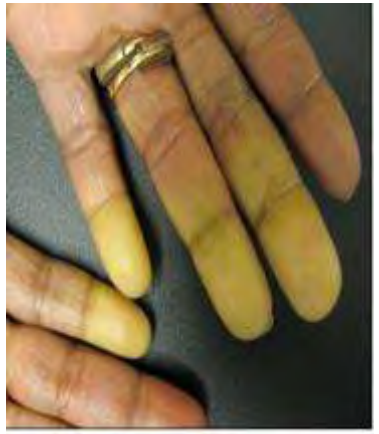
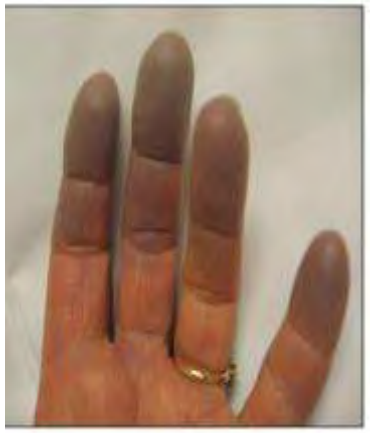
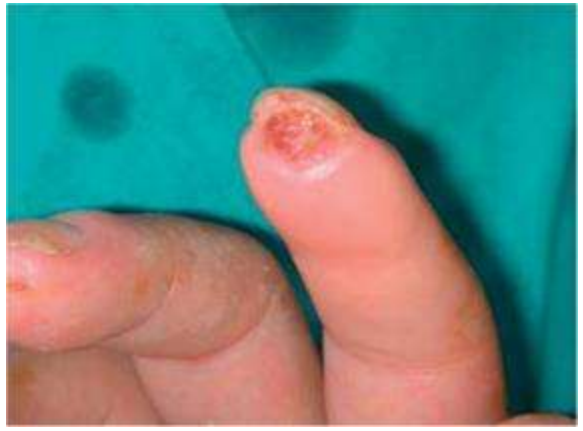
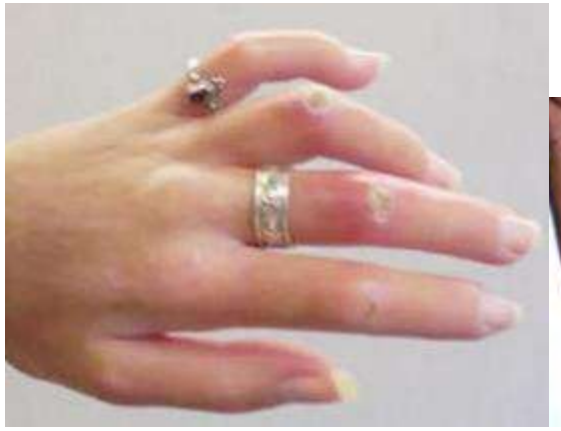
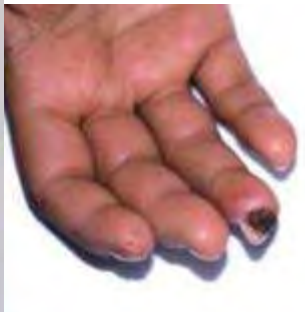






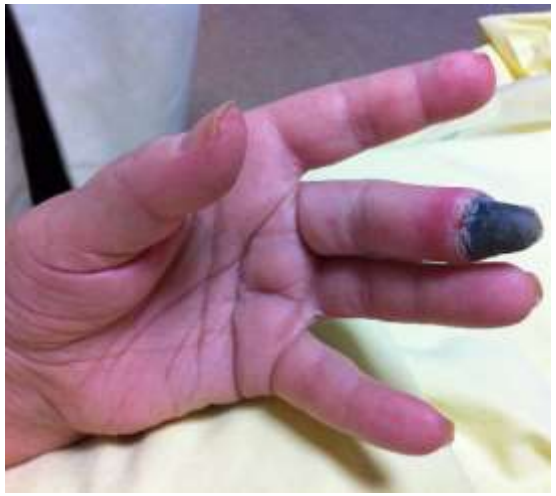


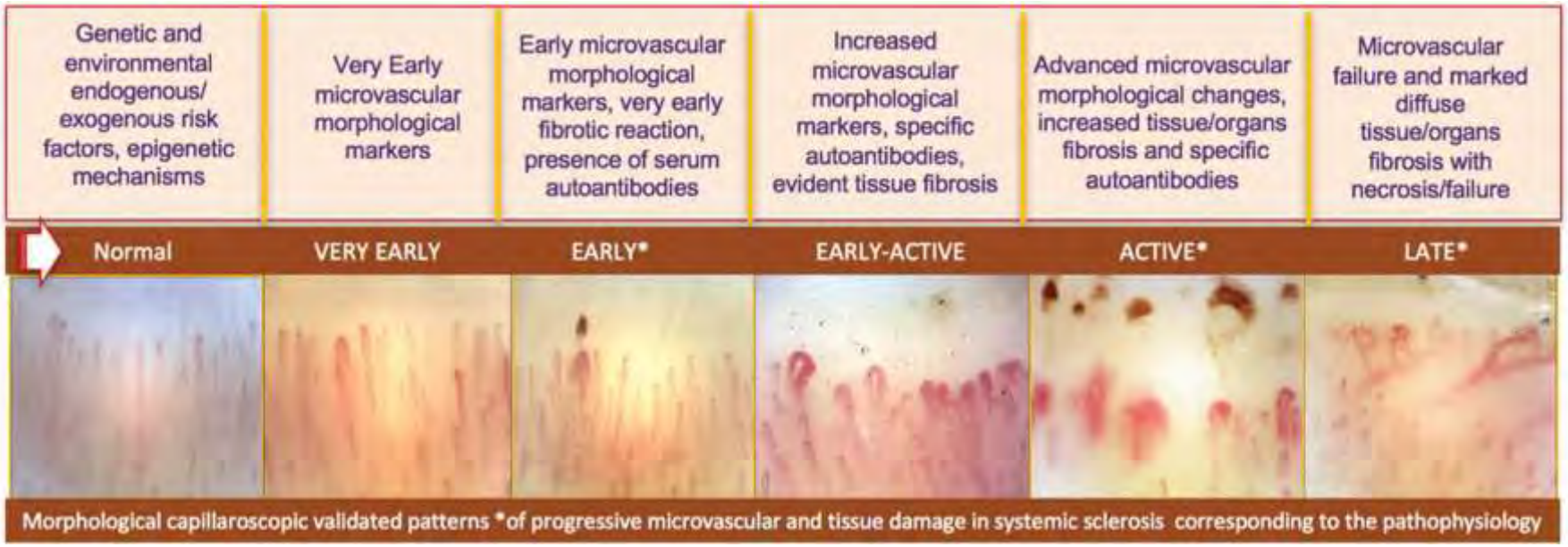
SSc – Raynaud sy - DU


- **DU: SSc-ban *kb. 50%-ban* alakulnak ki**
- **dcSSc-ben korábban jelennek meg, anti-Scl70 pozitívakban gyakoribb, gyakori asszociáció a CV eltérésekkel**

- **Szövődmények: infekció, gangraena, osteomyelitis, autoamputáció!**

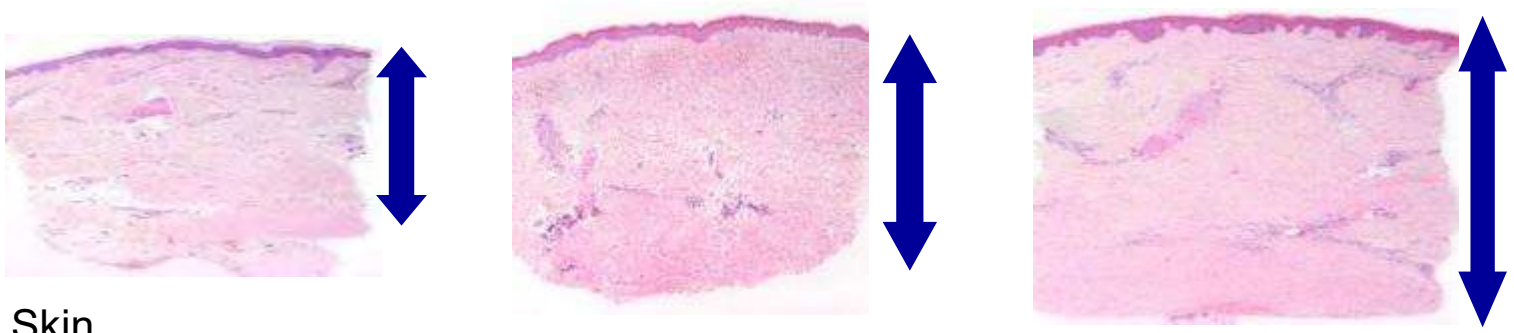




Cutulo M. EXPERT REVIEW OF CLINICAL IMMUNOLOGY https://doi.org/10.1080/1744666X.2019.1614915

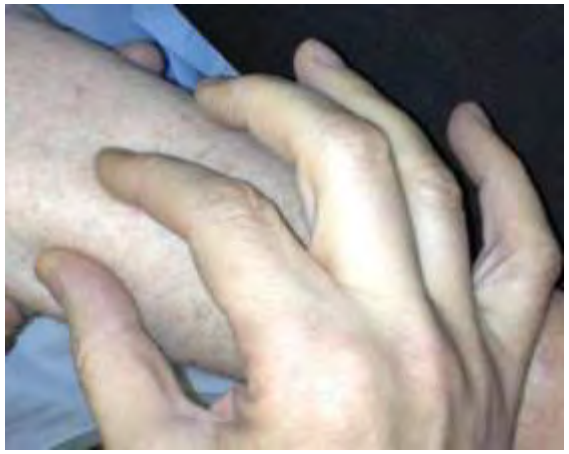
Bőrtünetek vizsgálata

Modified Rodnan Skin Score (MRSS)



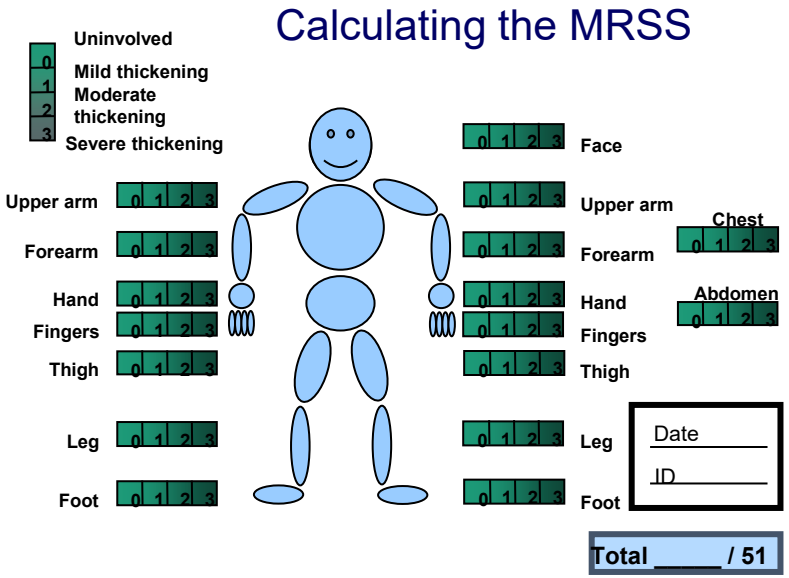
Skin score grade 1 2 3

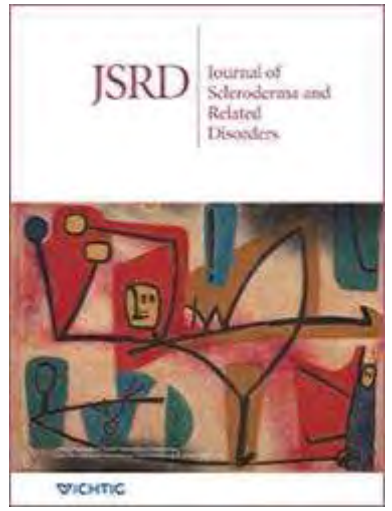
Histological correlation of skin score



Denton and Silver, 2011

Calculating the MRSS





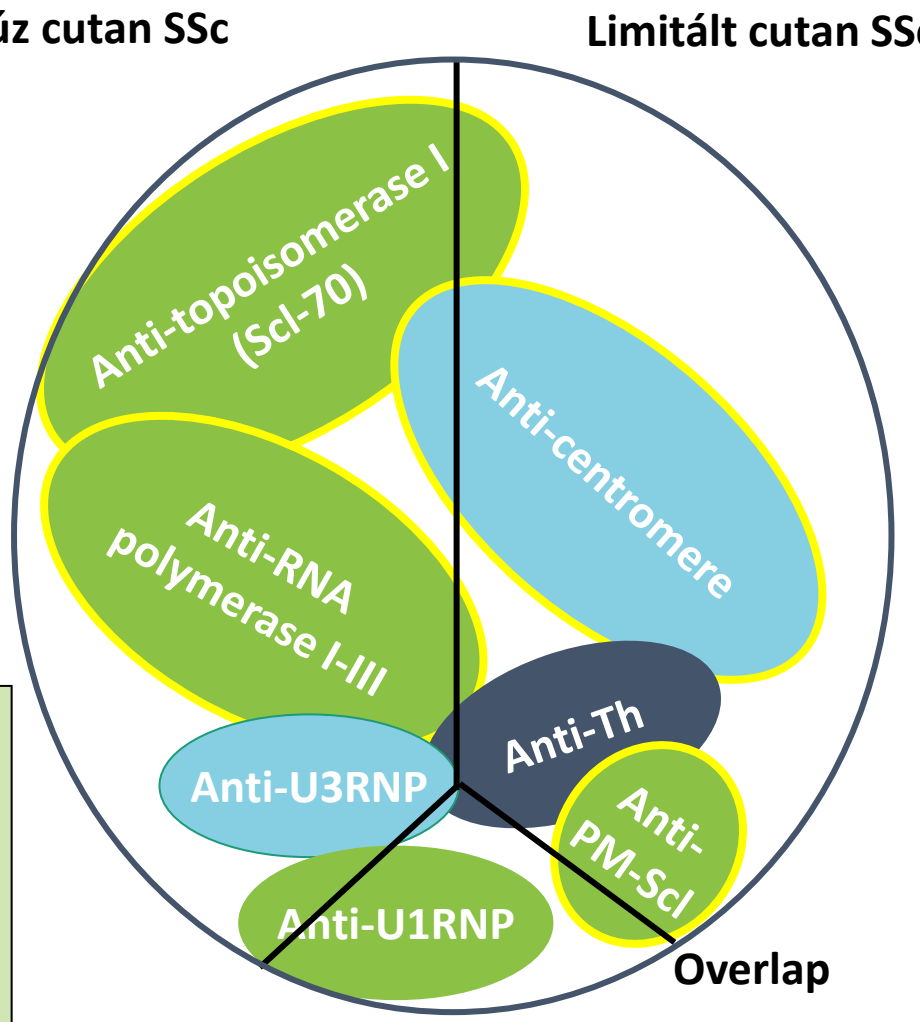
Standardization of the mRSS for use in clinical trials of SSc.

Khanna D, .. Denton CP. **J Scleroderma Relat Disord**. 2017;2:11-18.

Szerológiai alcsoportok SSc-ben

50-60%:

anti-centromer,
anti-Scl70,
anti-RNA polimeráz III

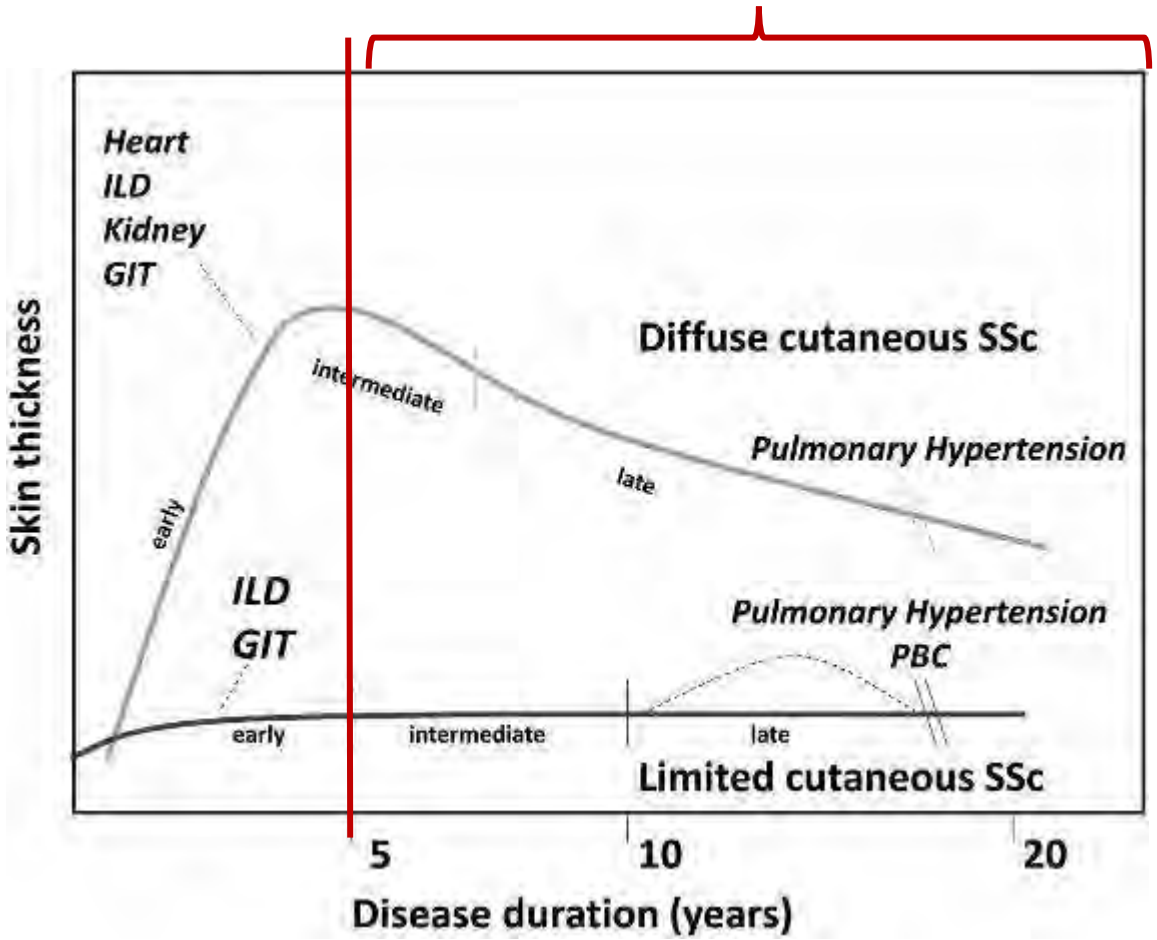


Anti- Scl-70 = ILD
Anti-centromere = PAH
Anti-RNA pol III = renalis crisis, malignitás, rapid bőr progresszió
Anti-PM-Scl = SSc-myositis
Anti-Ro52 – súlyosabb ILD
Anti-U3RNP = ILD, PAH, myositis
Anti-Th/To = ILD, PAH

Clements PJ and Furst DE. *Systemic Sclerosis*. Lippincott, Williams & Wilkins, Baltimore, 2004.

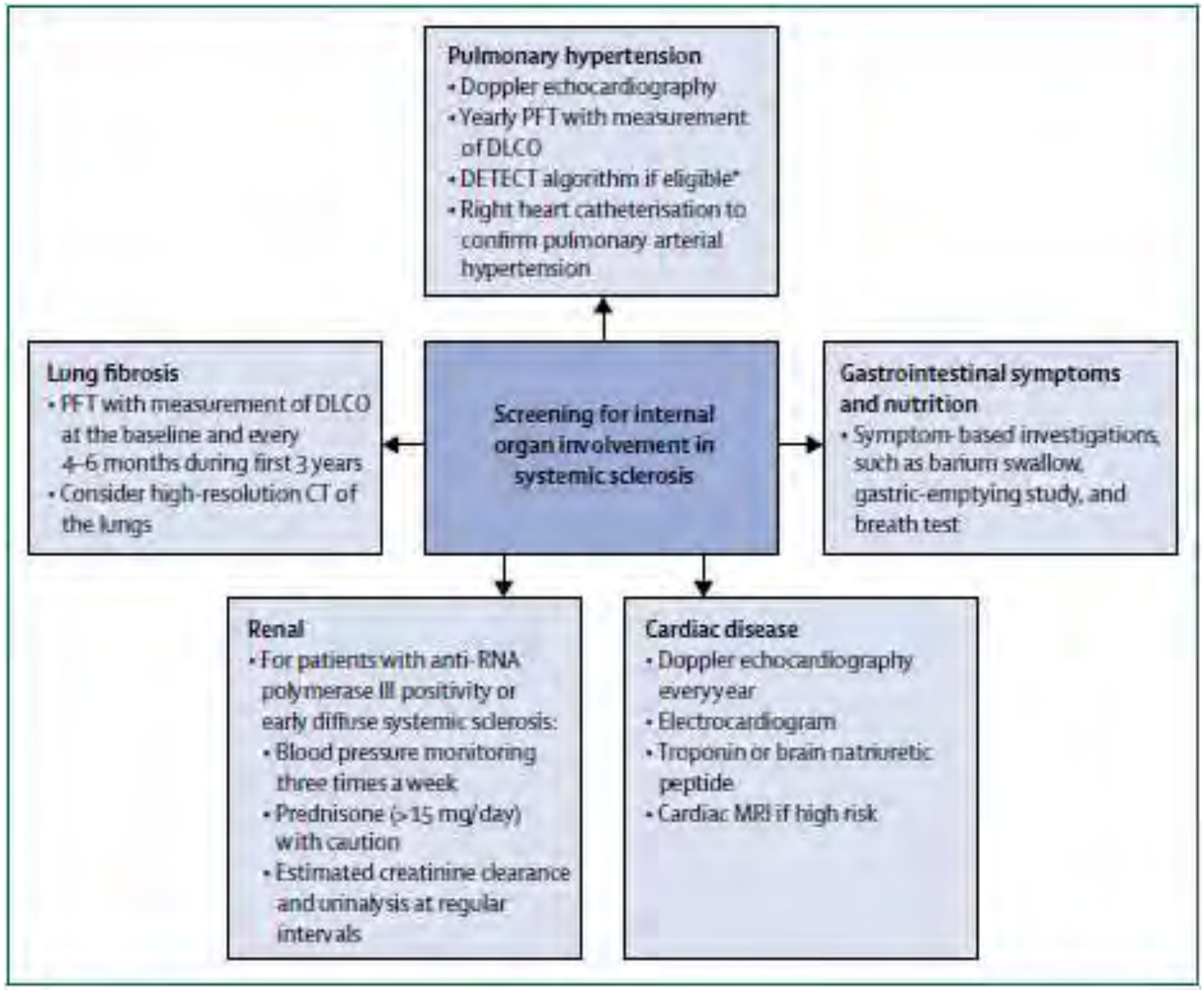
Terápiás sürgősség – Korai progresszorok

Hosszútávú progresszió és tartós tünetek



Arthritis & Rheumatology, Volume: 72, Issue: 7, Pages: 1049-1058, First published: 05 March 2020, DOI: (10.1002/art.41246)

Belső szervi manifesztációk



Denton CP et Kanna D. Systemic sclerosis Published online April 13, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30933-9

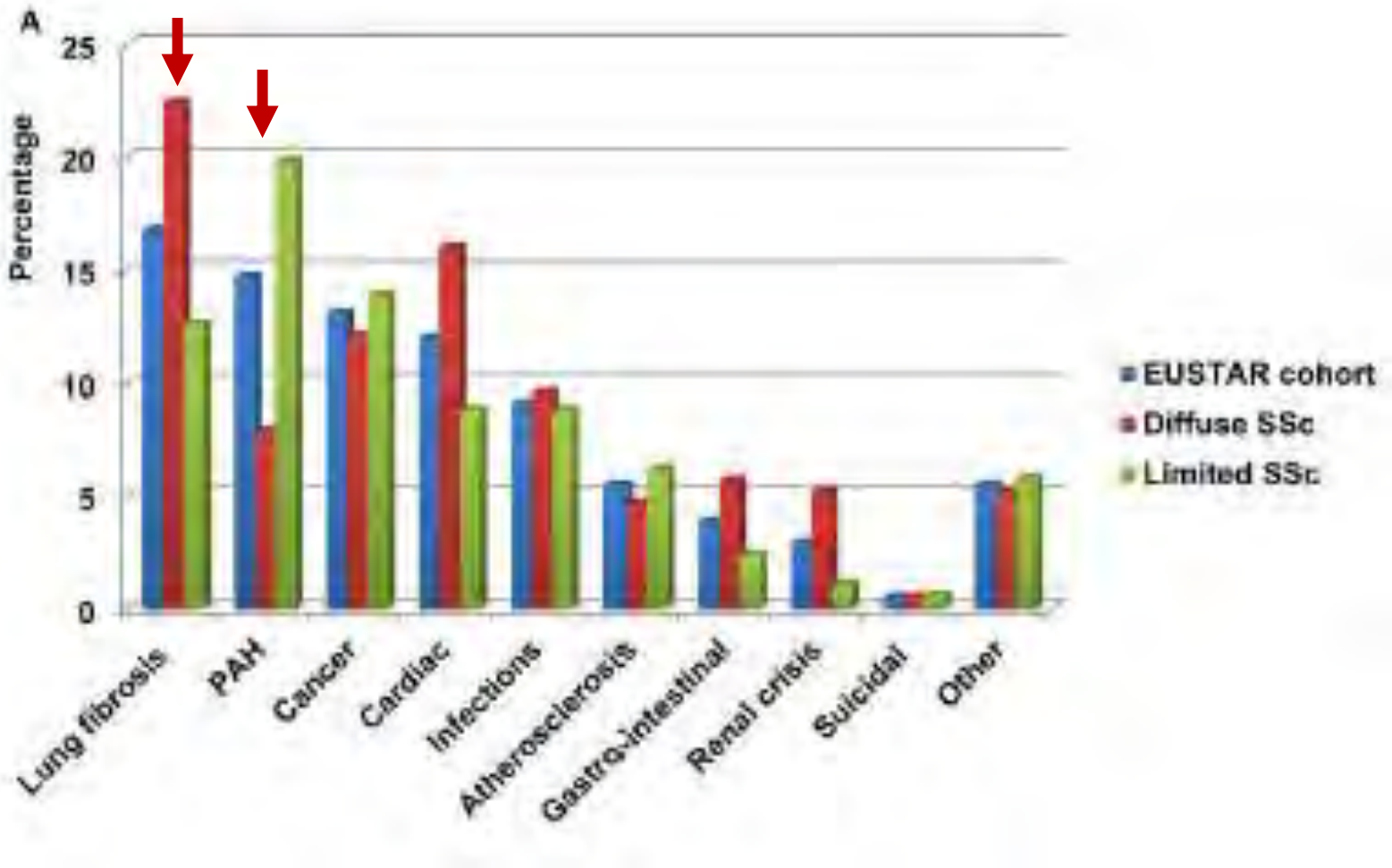


Figure 2 (A) Causes of death in the entire EUSTAR sample and in the limited and diffuse cutaneous forms. (B) Comparison of causes of death in the EUSTAR and in the death certificates samples. The results are presented as % of deaths. EUSTAR, European Scleroderma Trials and Research; PAH, pulmonary arterial hypertension; SSc, systemic sclerosis.

Elhai M, et al. Ann Rheum Dis 2017;**76**:1897–1905. doi:10.1136/annrheumdis-2017-211448

Ann Rheum Dis 000 (2025) 1–39

Contents lists available at ScienceDirect

Annals of the Rheumatic Diseases

journal homepage: https://www.sciencedirect.com/journal/annals-of-the-rheumatic-diseases

Version of Record

ERS/EULAR clinical practice guidelines for connective tissue diseases associated interstitial lung disease

Katerina M. Antoniou[1,36], Oliver Distler[2,36], Ana-Maria Gheorghiu[3],

Table 3

Risk factors in patients with connective tissue disease and rheumatoid arthritis (RA) defining an at-risk patient population that should be screened for interstitial lung disease

	SSc	RA	IIM	SjD
Demographics	• Longer disease duration	• Older age • Male sex • Smoking	• Older age	• Older age • Male sex
Circulating markers	• Increased KL-6 • Presence of ATA-I	• Increased ESR • Presence of anti-CCP, RF	• Increased CRP, ESR • Presence of anti-Jo1, anti-MDA-5, anti-Ro52	• Increased CRP • Presence of anti-Ro52
Extrapulmonary involvement	• Diffuse cutaneous SSc • Higher mRSS	• Higher articular disease activity	• Anti-synthetase syndrome • Clinical amyopathic dermatomyositis • Skin involvement[#] • Arthritis/arthralgia	• Presence of extrapulmonary involvement

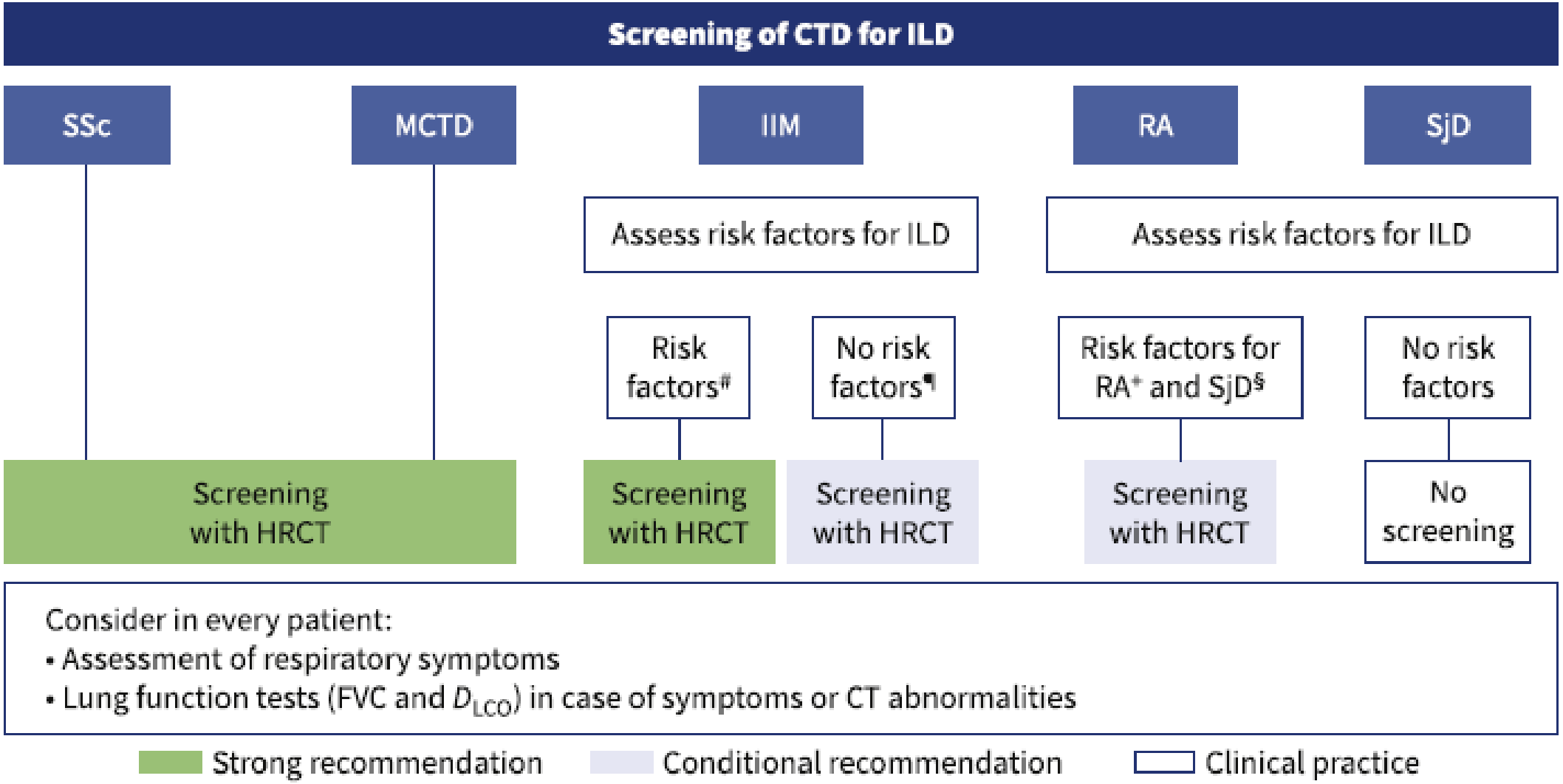
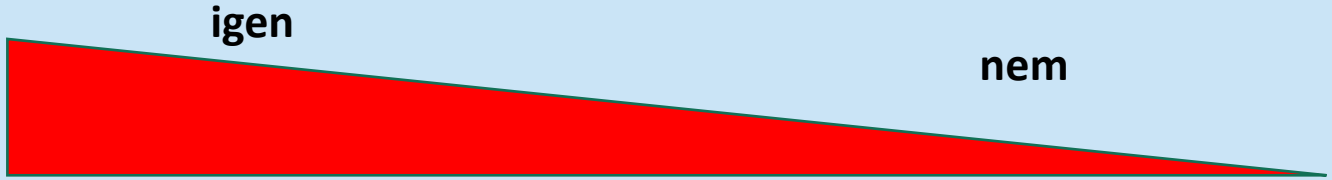

Screening of CTD for ILD
SSc
MCTD
IIM
RA
SjD
Assess risk factors for ILD
Assess risk factors for ILD
Risk factors#
No risk factors¶
Risk factors for RA* and SjD§
No risk factors
Screening with HRCT
Screening with HRCT
Screening with HRCT
Screening with HRCT
No screening
Consider in every patient:
• Assessment of respiratory symptoms
• Lung function tests (FVC and D_{LCO}) in case of symptoms or CT abnormalities
Strong recommendation
Conditional recommendation
Clinical practice

Table 4

Risk factors for poor outcome, defined as disease progression and death, in patients with connective tissue disease (CTD)-associated interstitial lung disease (ILD) and rheumatoid arthritis (RA)-associated ILD

	SSc[#]	RA[#]	IIM[#,¶]
Demographics	• Older age • Male sex • African American ethnicity	• Older age at RA onset • Male sex	
Circulating markers	• Elevated ESR, CRP • ATA-I	• Anti-CCP, RF	• Elevated ferritin • Anti-MDA-5, anti-synthetase
Pulmonary function/markers	• Baseline PFTs (FVC, D_{LCO})	• Baseline PFTs (low FVC and/or D_{LCO})	
Imaging/histology	• Higher extent of ILD on HRCT	• UIP and probable UIP HRCT/histological patterns • Higher extent of ILD on HRCT	• Higher extent of ILD on HRCT and ILD pattern on HRCT
Extrapulmonary involvement	• Recent onset of SSc with rapid skin progression, more extensive skin fibrosis (mRSS)	• Higher articular disease activity	

Progresszió megítélése és monitorozás



HRCT kiterjedés	**>20%**	**<10%**
FVC kiindulás	**<normál**	**normál**
Dlco kiindulás	**<normál**	**normál**
FVC változás 12 hónap	**≥ 10%**	**<5%**
Dlco változás 12 hónap	**≥ 15%**	**<15%**
Tünetek	**igen**	**nem**
Akut kezdet	**igen**	**nem**

CTD-ILD beteg monitorozása

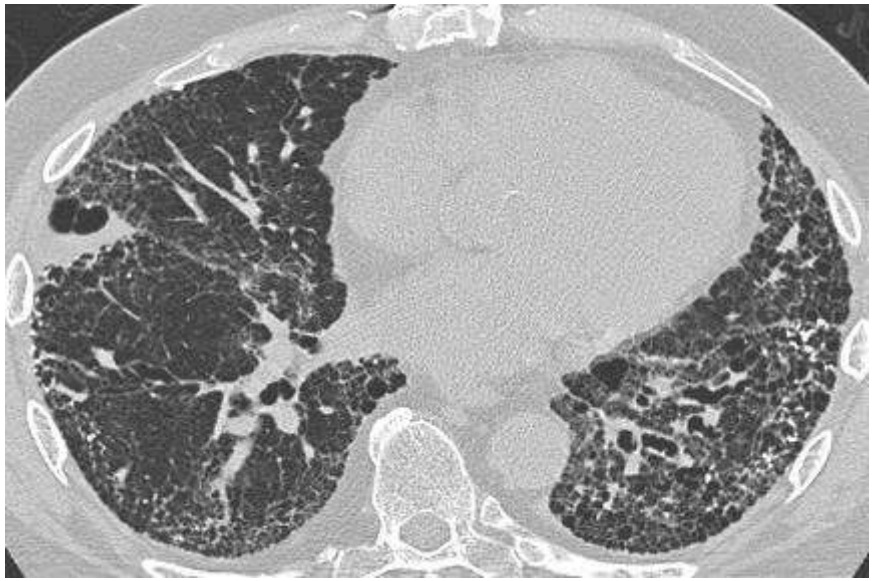
FVC és Dlco
- Alacsony rizikó esetén 6 havonta
- Magas rizikó esetén 3 havonta

HRCT
- Alacsony rizikó esetén 24 havonta
- Magas rizikó esetén 12 havonta

Új légzőszervi panasz
Azonnali vizsgálat!

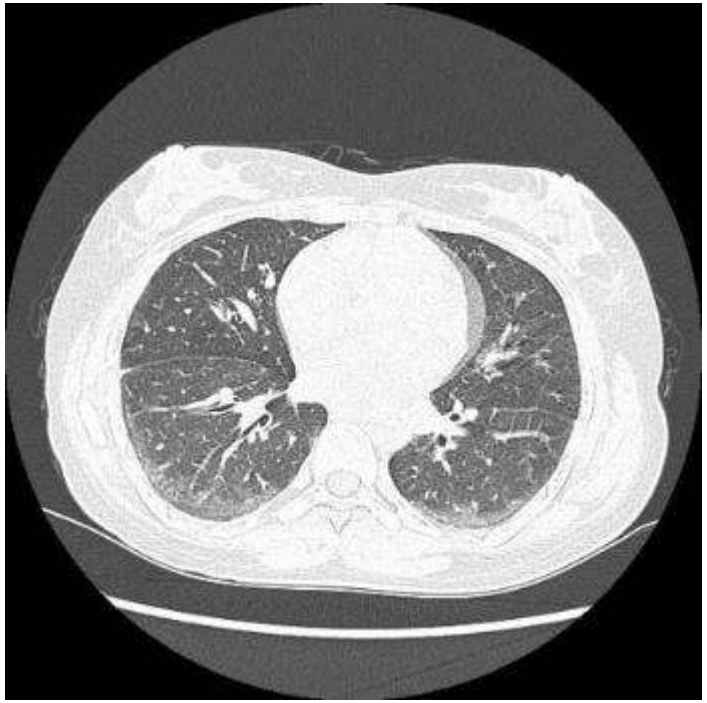
- **Tüdő HR-CT**
-
  - **Technikai nehézségek**
  - **Kiértékelés nehézségei**

UIP pattern



https://en.wikipedia.org/wiki/Usual_interstitial_pneumonia

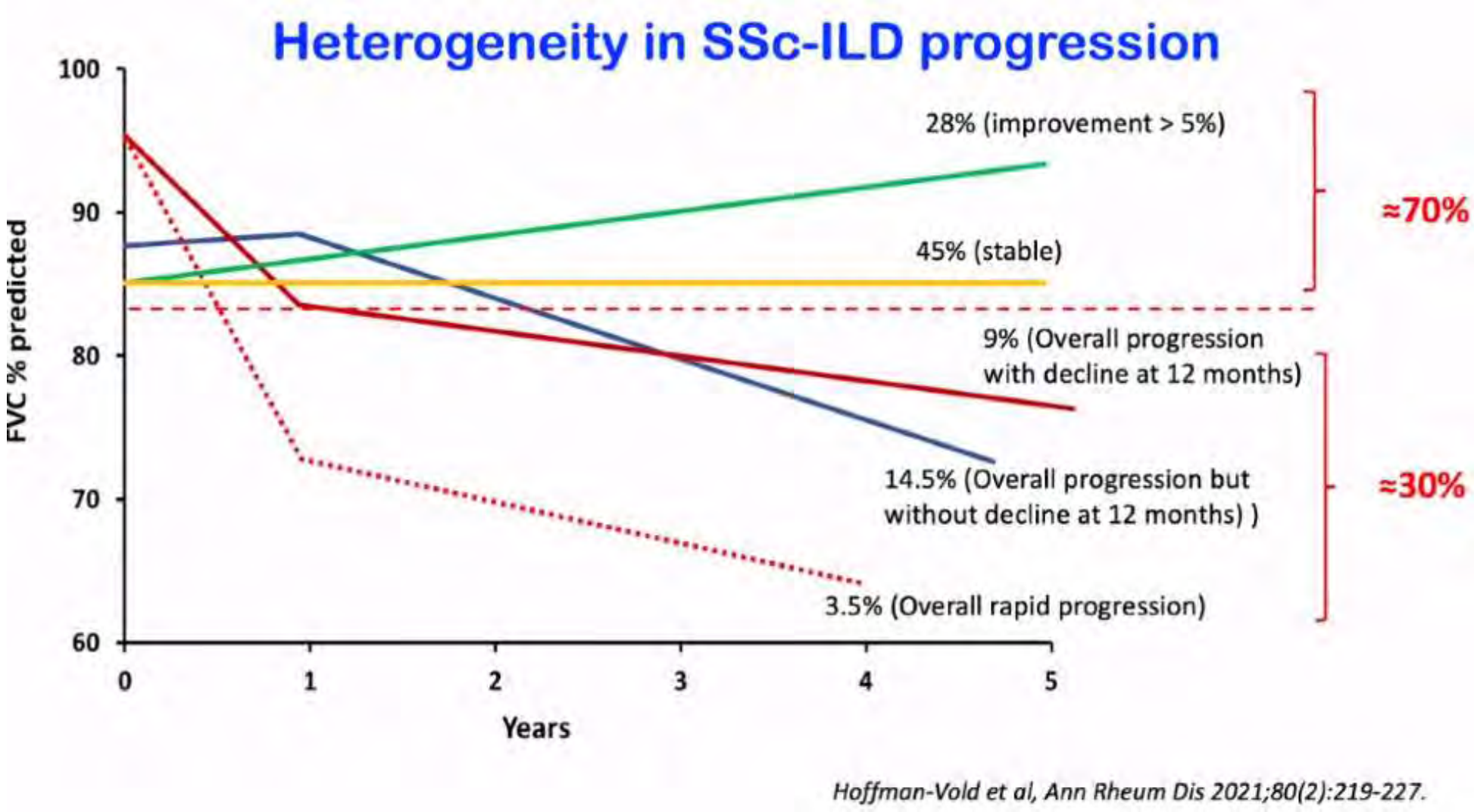
NSIP pattern



https://radiopaedia.org/articles/non-specific-interstitial-pneumonia-1?lang=us

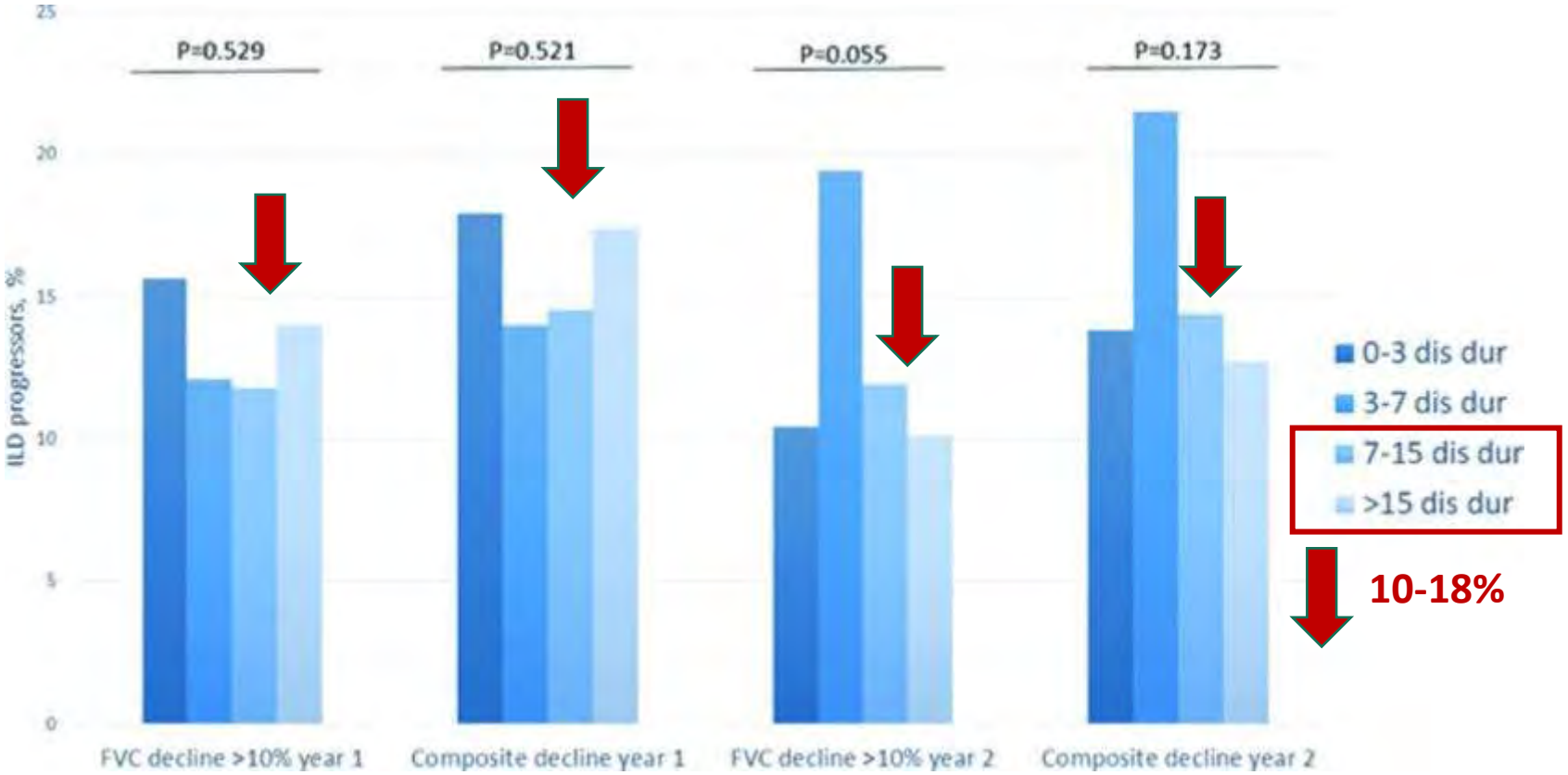

SSc-ILD monitoring
Assess prognosis, risk of progression and disease severity at every visit
High risk
Low risk
Indication of progression
Disease duration
<3–5 years
>3–5 years
<3–5 years
>3–5 years
Anytime
Lung function test (FVC and D_{LCO})
Every 3–6 months
Every 6–12 months
Every 6–12 months
Every 12 months
Conduct
HRCT (pattern and extent)
Every 12 months
Every 12 months
After 2 years
Clinical indication
Conduct
6MWD and O_2 desaturation
Every 6–12 months
Every 6–12 months
Every 12 months
Every 12 months
Conduct
Patient-reported outcome measures
Every 6–12 months
Every 6–12 months
Every 12 months
Every 12 months
Conduct
Conditional recommendation
Usual clinical practice

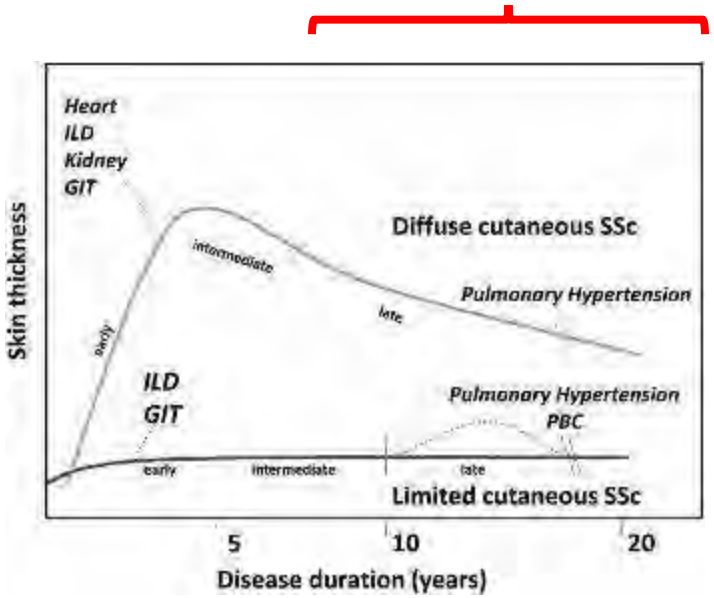
EUSTAR database



Hoffman-Vold et al, Ann Rheum Dis 2021;80(2):219-227.

FVC decline >10% and composite FVC and DLCO decline in the first and second 12+/-3 months within the four subgroups segregated by disease duration.





2258 SSc-ILD beteg

Betegség fennállási idő: (20.8%) ≤3 év, 550 (24.4%) >3- ≤7 év, 752 (33.3%) >7- ≤15 év, 488 (21.6%) >15 év

Ann Rheum Dis 2022;81:248; Arthritis & Rheumatology, Volume: 72, Issue: 7, Pages: 1049-1058, 2020

ILD team

Alapbetegség diagnózisának felállítása (Alcsoport besorolás)

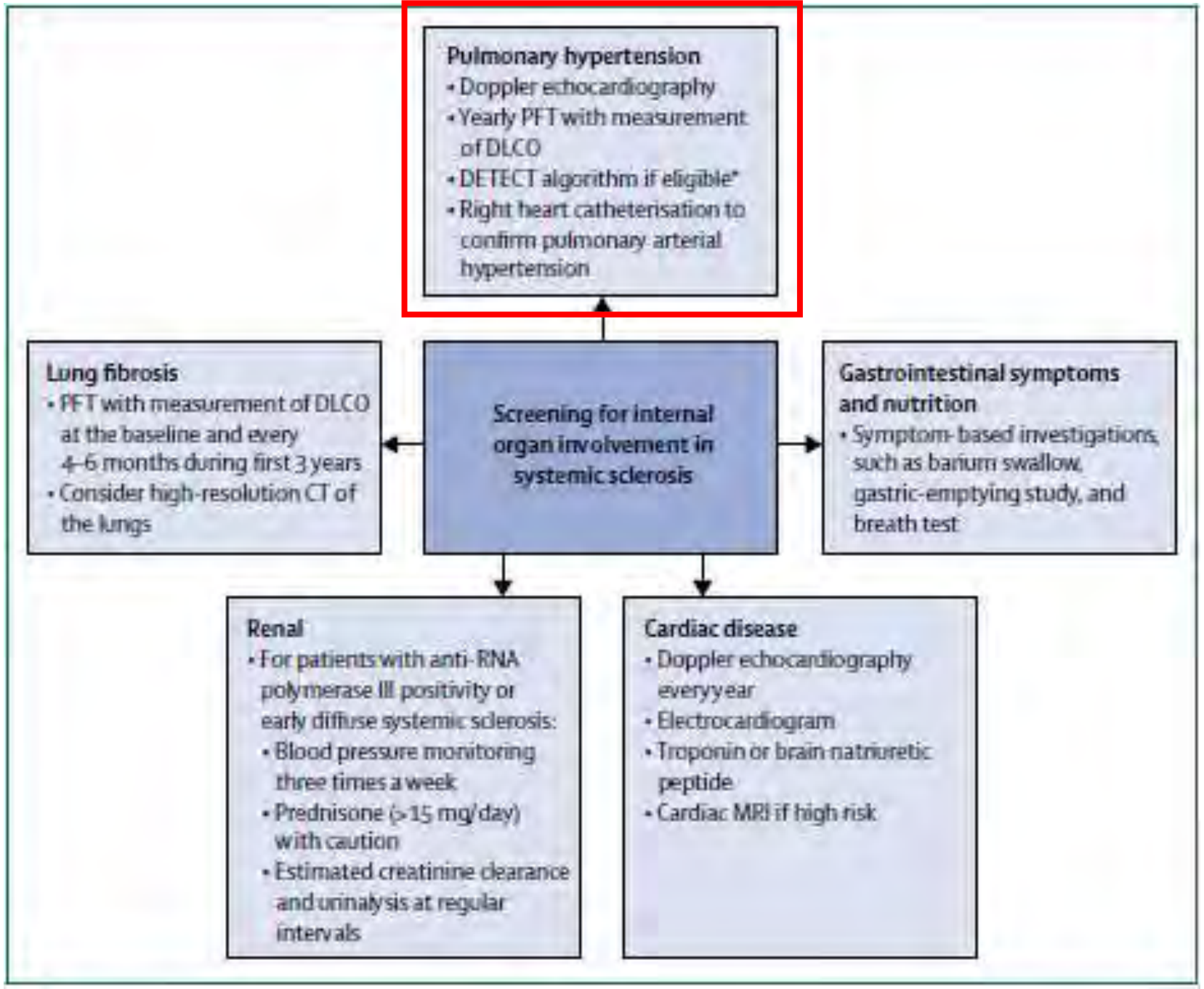
ILD szűrővizsgálatok

Progresszív ILD predikciója

Vizsgálatok a követés során

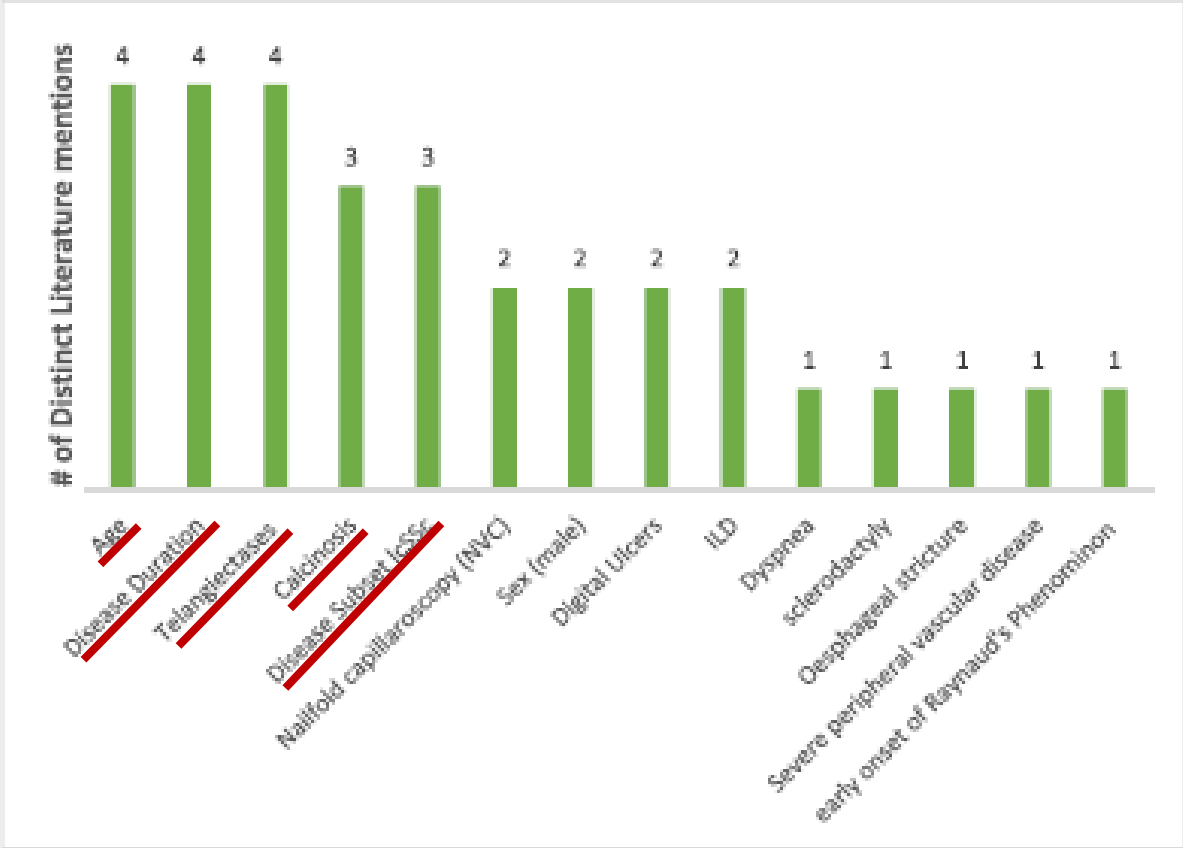
(klinikai tünetek, légzésfunkció, képalkotó)

Terápia tervezése - gyógyszerválasztás

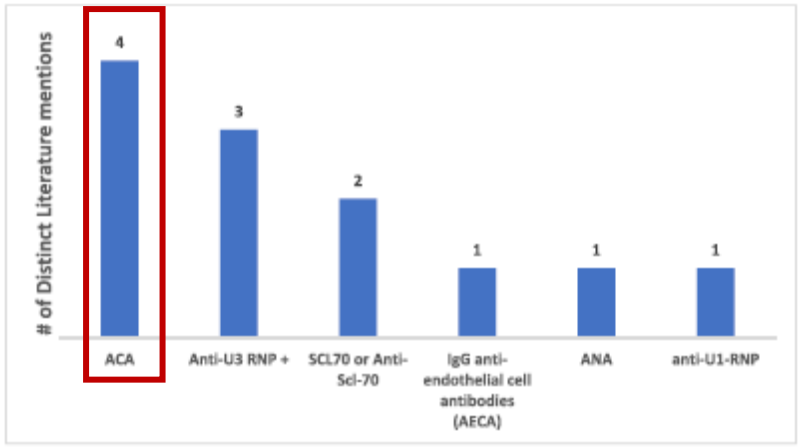


Denton CP et Kanna D. Systemic sclerosis Published online April 13, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30933-9

SSc-PAH



e. Patient characteristics associated with SSc-PAH as reported in literature



d. Antibody profiles associated with SSc-PAH as reported in literature

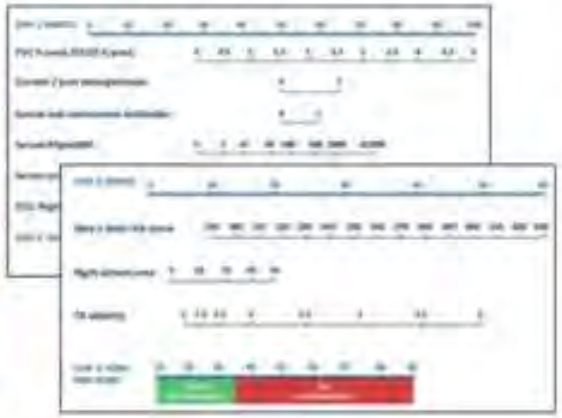
Pope J. Factors associated with pulmonary arterial hypertension (PAH) in systemic sclerosis (SSc). Autoimmunity Reviews 19 (2020) 102602

SSc-PAH szűrése

Peak TRV, m/s	Presence of other echocardiographic PH signs	Echocardiographic probability of PH
≤ 2.8 or not measurable	No	Low
≤ 2.8 or not measurable	Yes	Intermediate
2.9–3.4	No	
2.9–3.4	Yes	High
> 3.4	Not required	

Echo[a] (TTE)

ESC/ERS 2015 guidelines recommend the use of annual resting TTE as a screening test in asymptomatic patients with SSc and in symptomatic patients with other CTDs

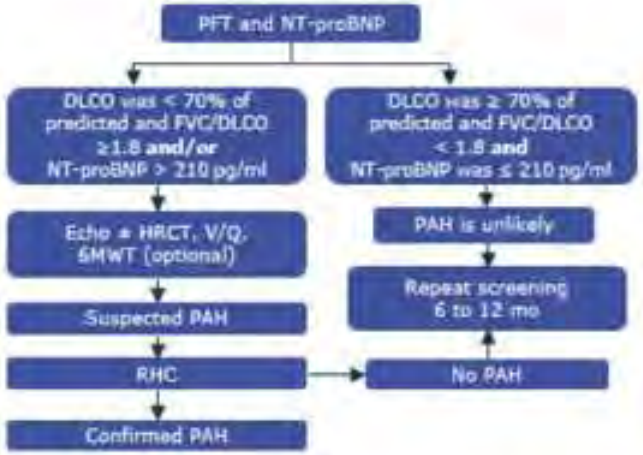


DETECT[b]

A 2-step algorithm using nonechocardiographic and echocardiographic variables to screen for PH

Delphi-based expert consensus[c]

Consensus on strongly suggested and easily applicable tools for annual systemic assessment of organ involvement in SSc

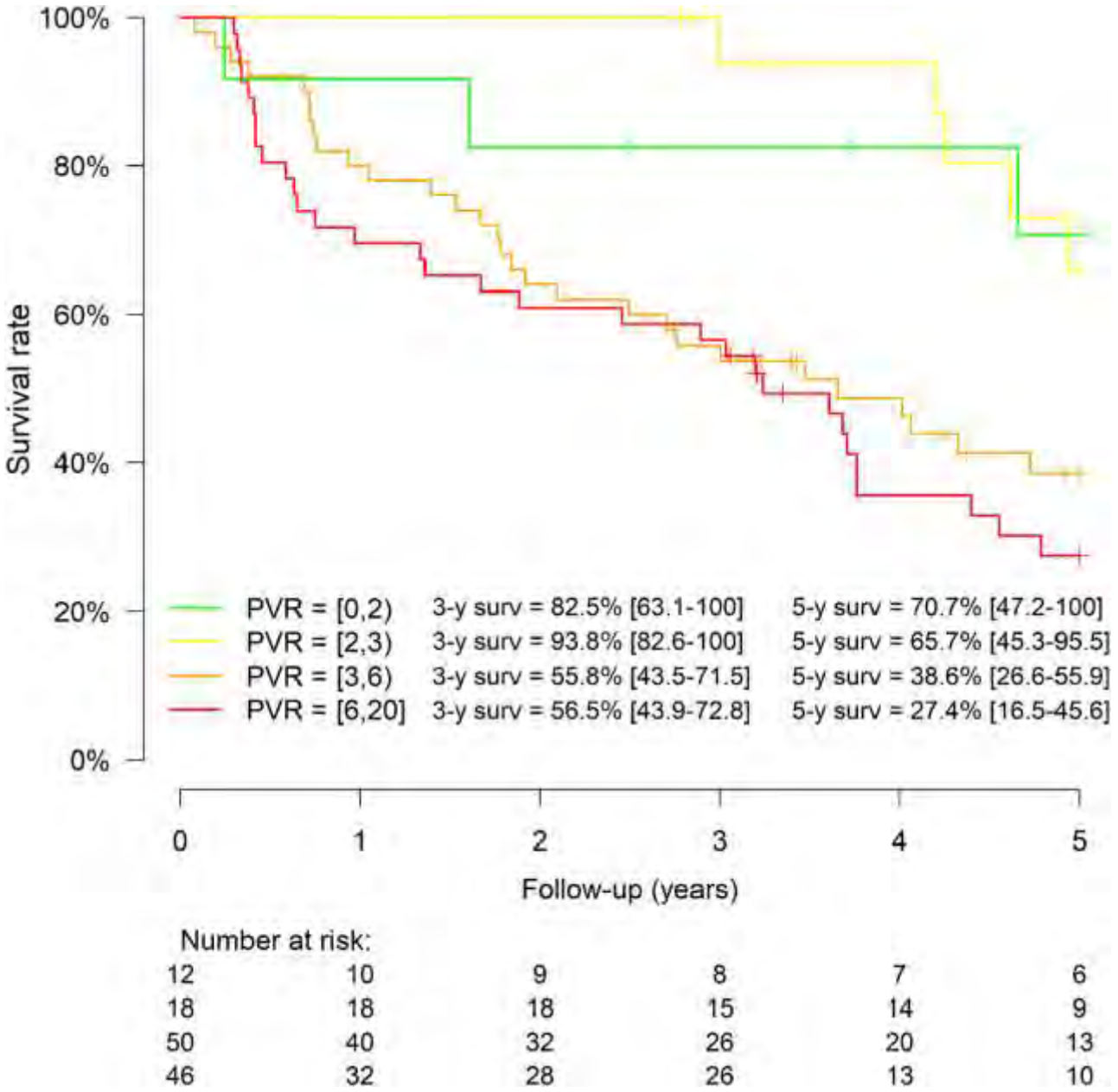


Australian Scleroderma Interest Group[d][e]

An Australia-wide screening program where enrolled patients were recommended to have PFTs, EKG, TTE, and NT-proBNP measurement; and if abnormal, RHC and 6MWD

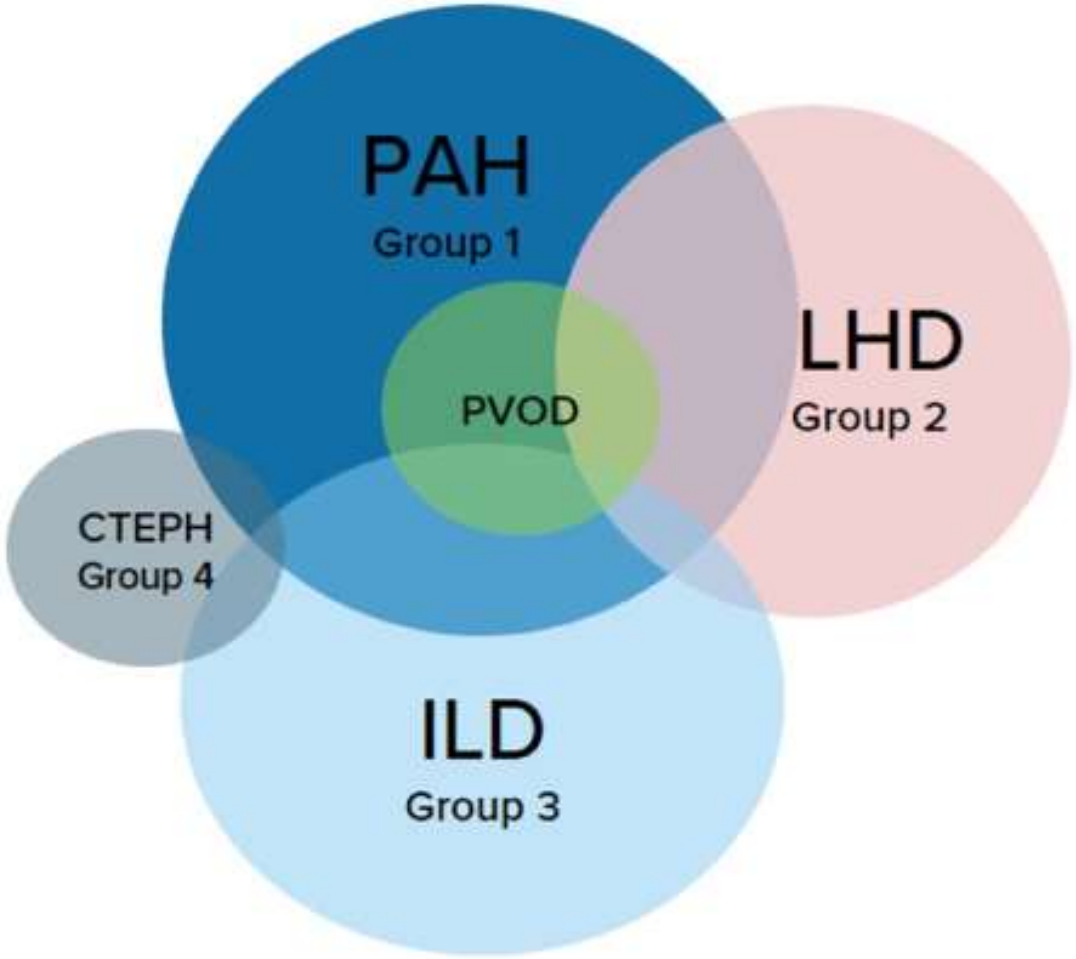
a. Galiè N, et al. *Eur Heart J.* 2016;37:67-119; b. Coghlan JG, et al. *Ann Rheum Dis.* 2014;73:1340-1349; c. Hoffmann-Vold A-M, et al. *RMD Open.* 2019;5:e000826; d. Morrisroe K, et al. *Arthritis Res Ther.* 2017;19:42; e. Thakkar V, et al. *Arthritis Res Ther.* 2013;15:R193.

- **Precapillaris PH: új 2022-es ESC/ERS definíció:**
  - **mPAP küszöbérték: 25 → 20 Hgmm + pulmonális vascularis rezisztencia (PVR) ≥ 2 Wood units (WU).**
- **SSc betegek reklasszifikációja!**
- **Korai PAH-kezelés, jobb túlélés**



Puigrenier *et al. Respiratory Research (2022) 23:284*

PAH fenotípusok SSc-ben

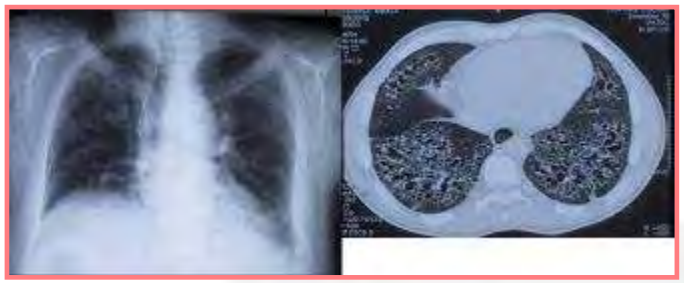


Pre-capillary PH	Mean PAP > 20 mmHg *plus* PAWP ≤ 15 mmHg *plus* PVR > 2 Wood units
IpcPH	Mean PAP > 20 mmHg *plus* PAWP > 15 mmHg *plus* PVR ≤ 2 Wood units
CpcPH	Mean PAP > 20 mmHg *plus* PAWP > 15 mmHg *plus* PVR > 2 Wood units
PH due to chronic lung disease	Severe PH: PVR ≥ 5

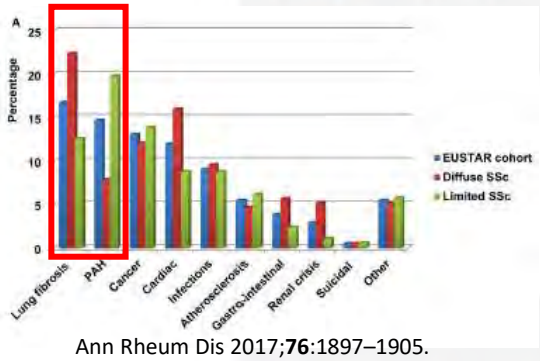
Almaaitah S et al. Integrated Blood Pressure Control 2020:13 15–29

2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension
Humbert M et al. European Heart Journal (2022) 43, 3618–3731

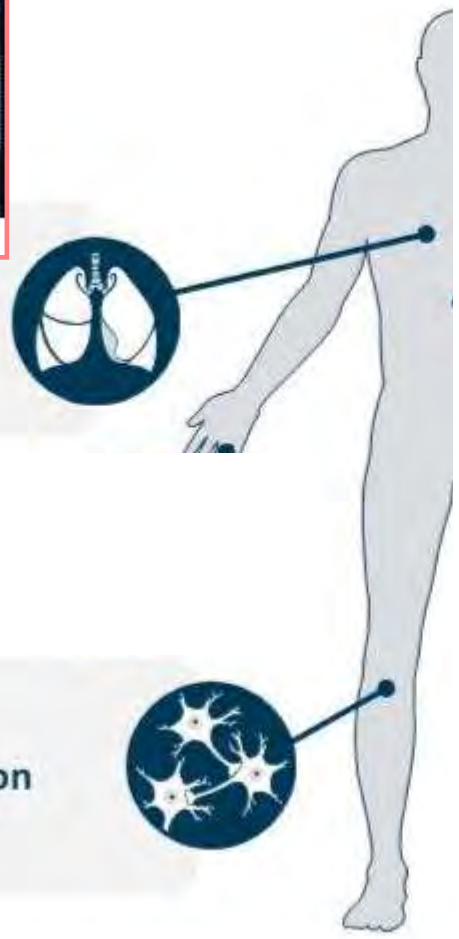
SSc-ILD, SSc-PAH



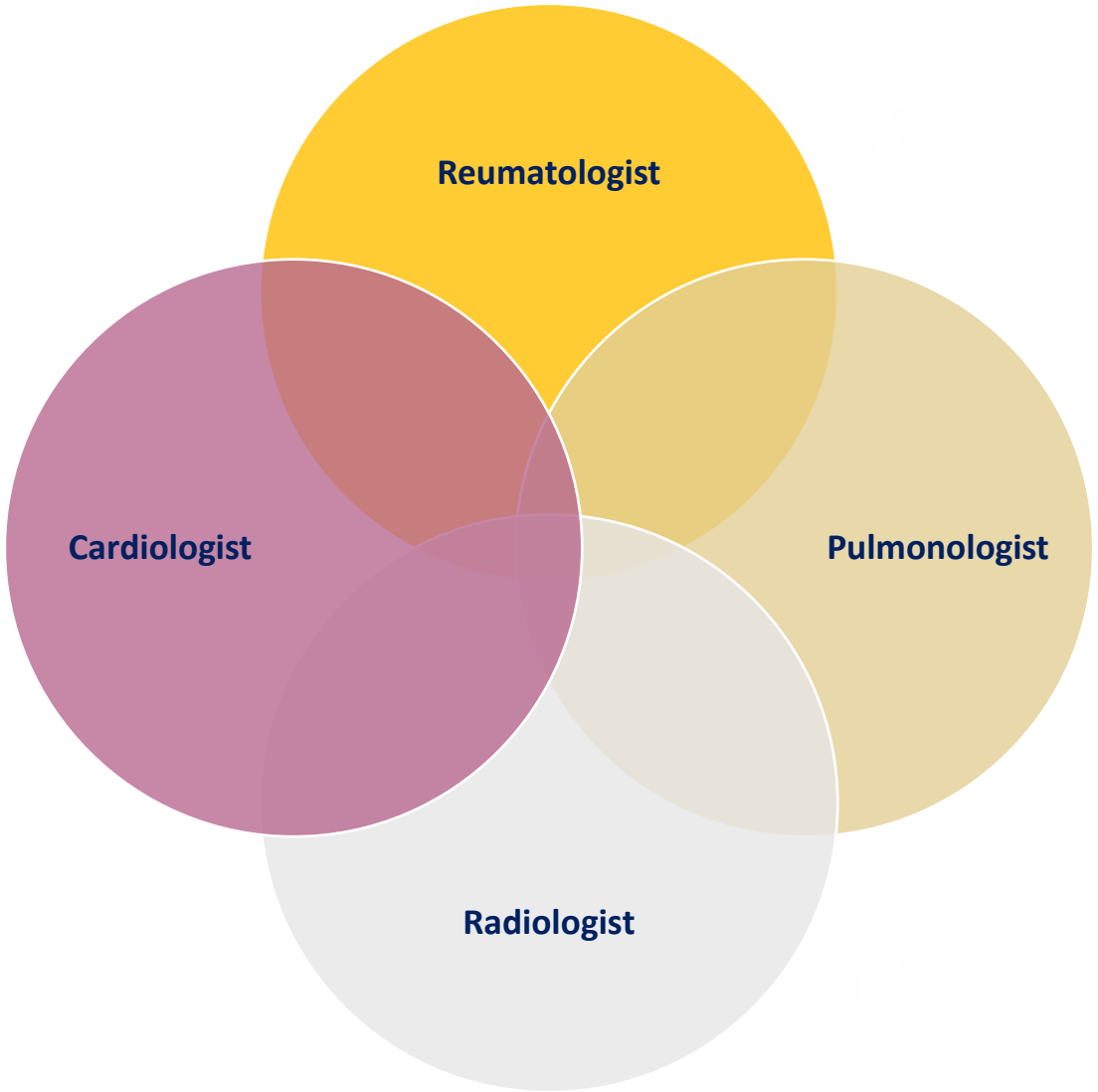
Lung Fibrosis

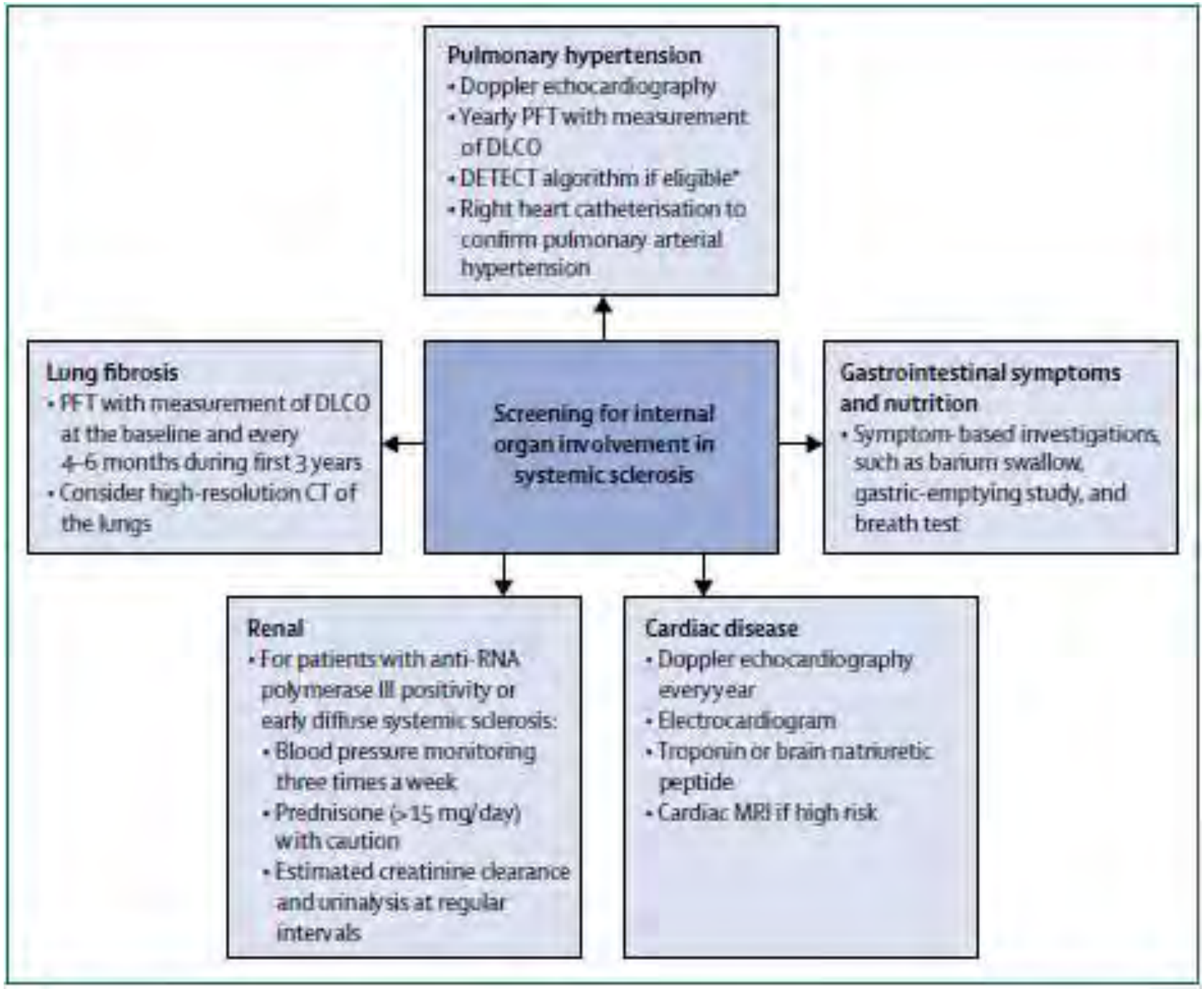


Ann Rheum Dis 2017;**76**:1897–1905.



Pulmonary Hypertension





Denton CP et Kanna D. Systemic sclerosis Published online April 13, 2017 http://dx.doi.org/10.1016/S0140-6736(17)30933-9

RHEUMATOLOGY

Rheumatology 2015;54:647–654
doi:10.1093/rheumatology/keu350
Advance Access publication 18 September 2014

Original article

Assessment of myocardial fibrosis and microvascular damage in systemic sclerosis by magnetic resonance imaging and coronary angiotomography

Tatiana S. Rodríguez-Reyna[1], Martha Morelos-Guzman[2], Pablo Hernández-Reyes[3], Karla Montero-Duarte[2], Cynthia Martínez-Reyes[1], Carlos Reyes-Utrera[1], Jorge Vazquez-La Madrid[2], Jaime Morales-Blanhir[4], Carlos Núñez-Álvarez[1] and Javier Cabiedes-Contreras[1,†]

FIG. 2 Cardiac MRI in TI gradient echo sequence showing late enhancement in the anteroseptal wall of the left ventricle of a SSc patient

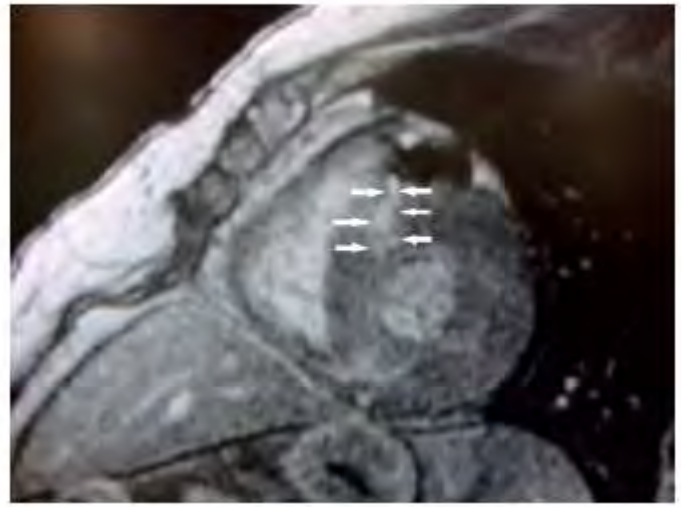
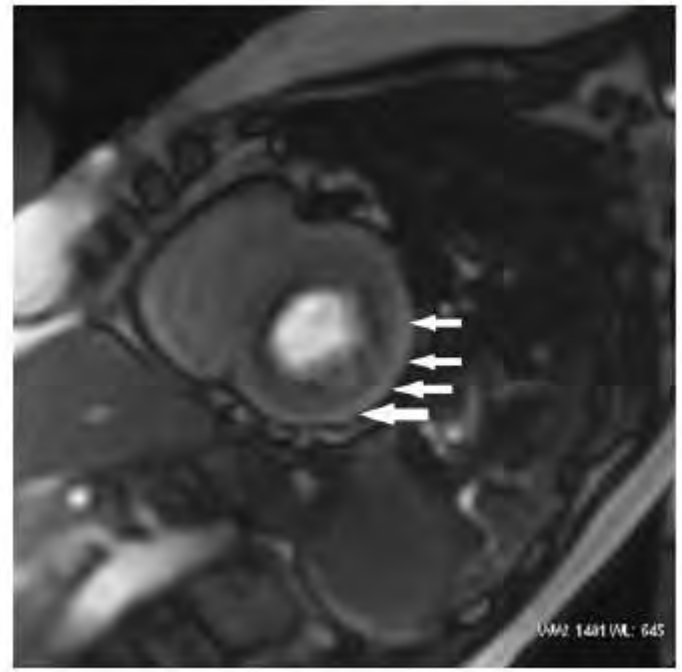


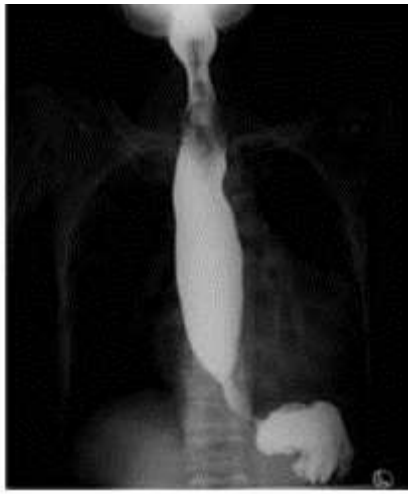
FIG. 3 Cardiac MRI in TI gradient echo/echo planar imaging pulse sequence showing a diffuse subendocardial perfusion defect in the left ventricle wall of a SSc patient

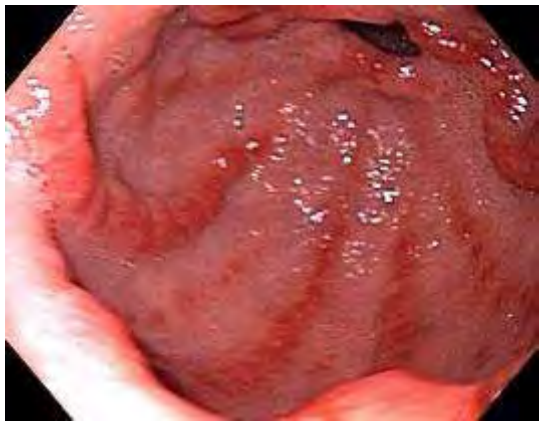


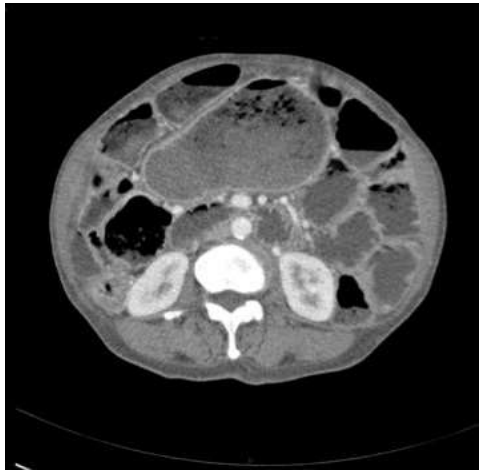
Gasztrointesztinális érintettség

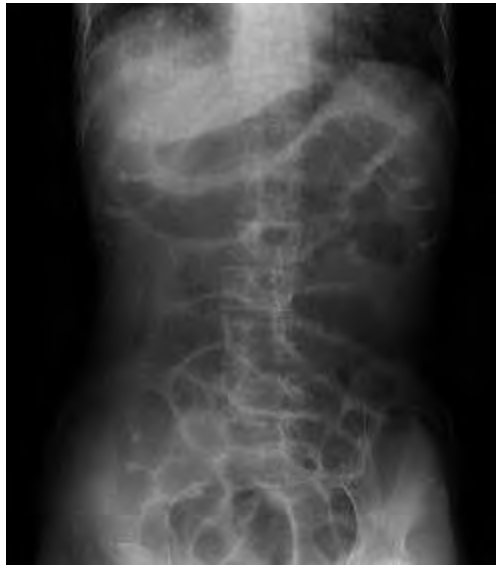
- **A betegek 90%-ában**
- **Patogenetika: fibrosis, autonóm neuropathia, vascularis malformációk**
- **Érintett szakasz: oesophagus, de a GI traktus bármelyik része**

- **Nyelőcső dysmotilitás, szűkület-tágulat, reflux oesophagitis, „görögdinnye” gyomor, intestinalis pseudo-obstrukció, bakteriális túlnövekedés, anorectalis inkontinencia, exokrin pancreas insufficiencia**



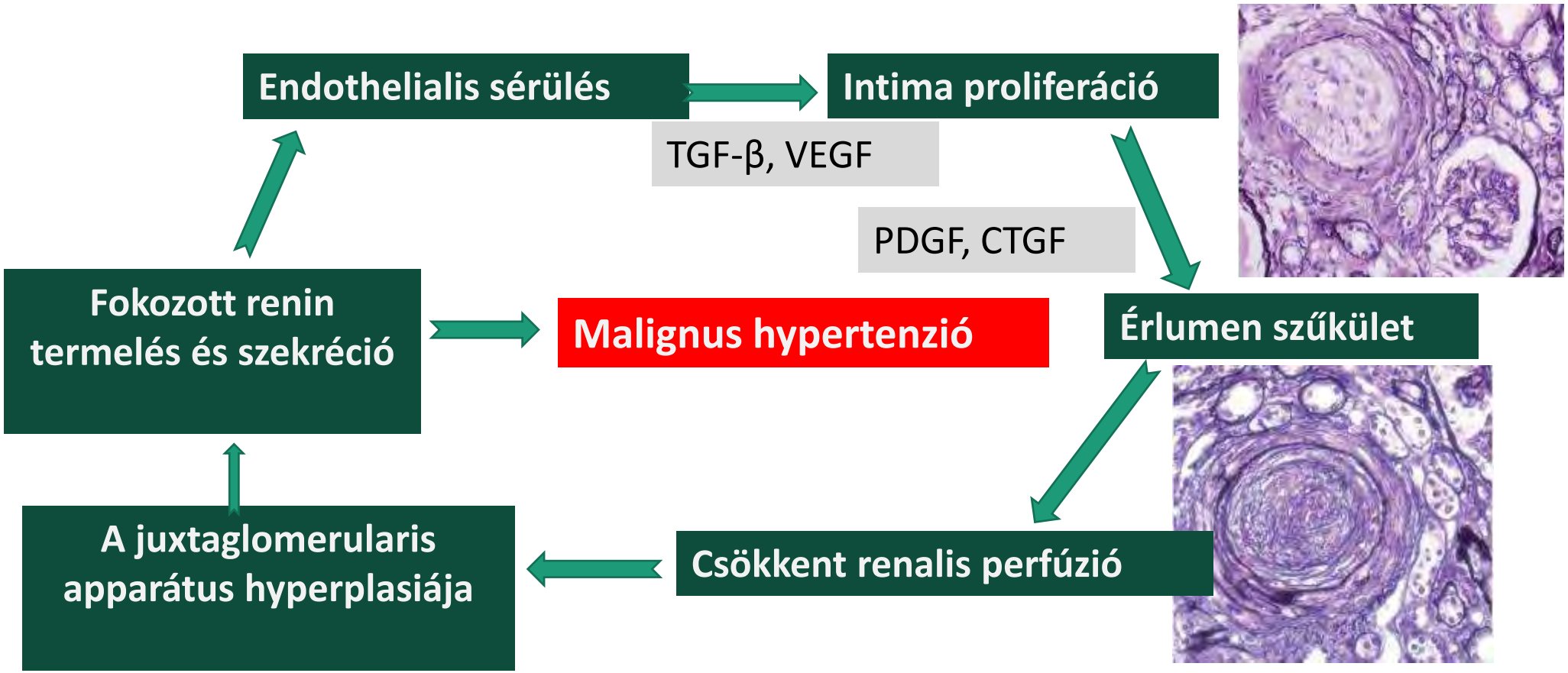




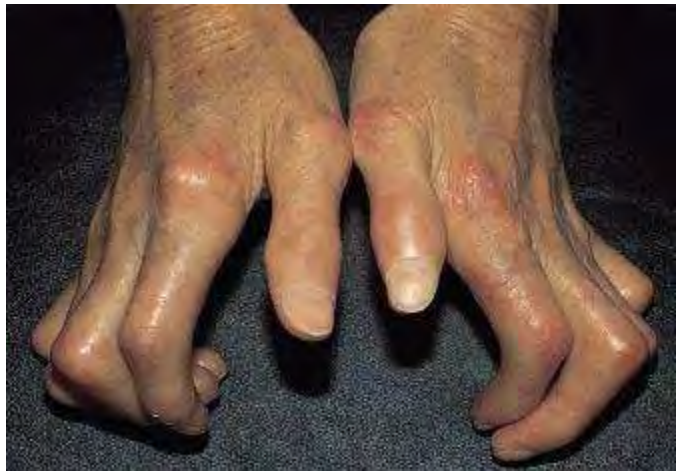


Veseérintettség

- Scleroderma renalis krízis: az SSc-s betegek 2-15%-a, dcSSc-ben az első 3-5 évben gyakoribb

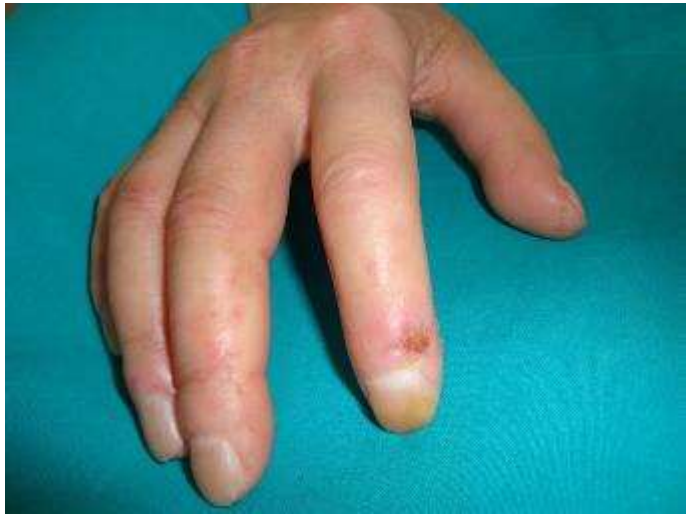


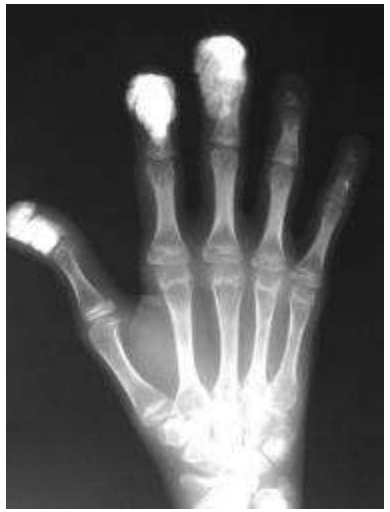
Musculoskeletális tünetek

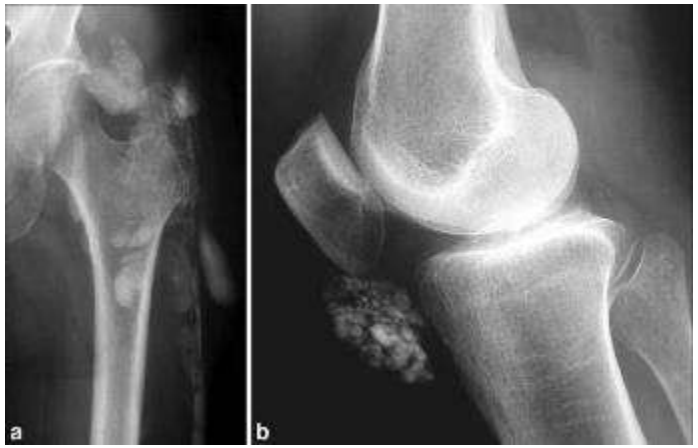


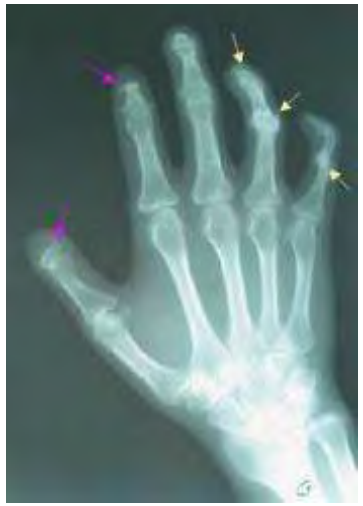
- 46-97%-ban

- Érintett területek: bőr és subcutis, ízületek, inak, vázizomzat, csontok
- Kontraktúrás ízületek, arthralgia, arthritis, tendinitis, crepitatio az ín felett („tendon friction rubs”), myalgia, myositis

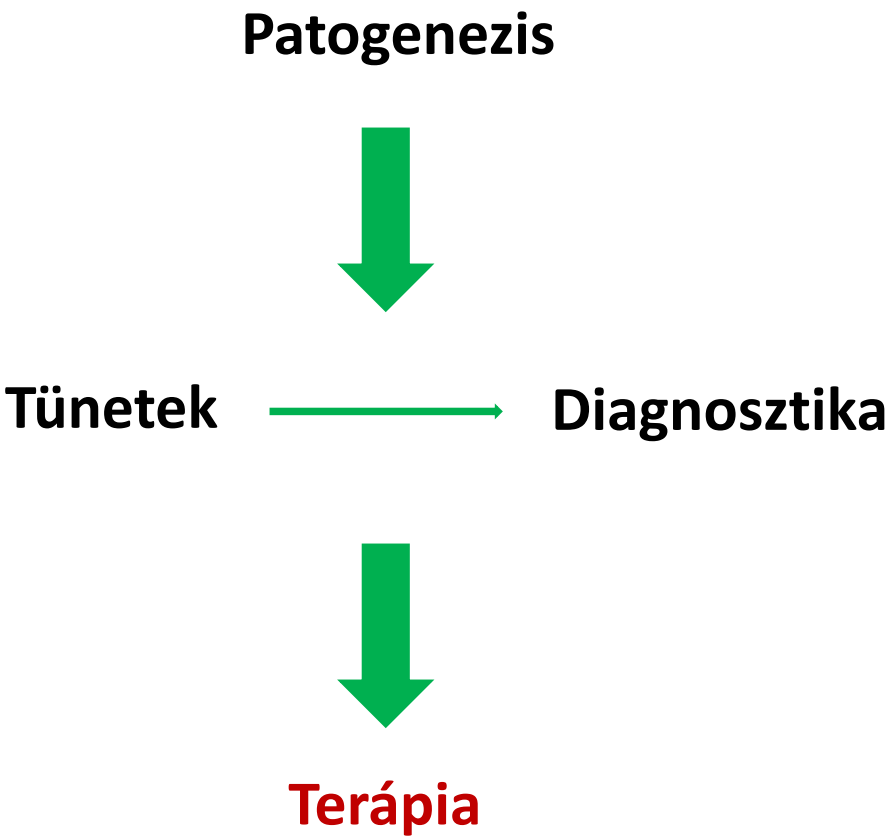








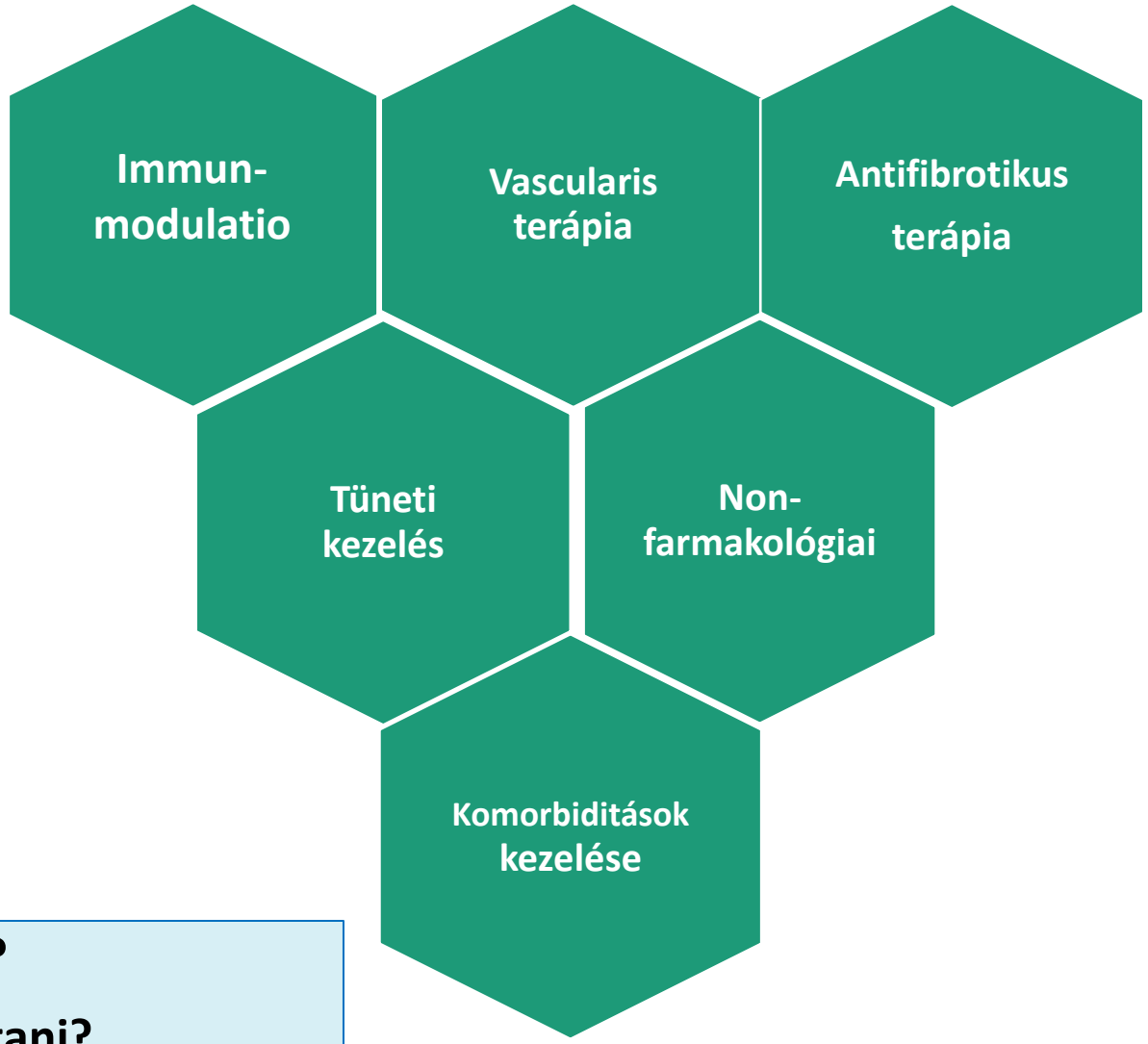
Szisztémás sclerosis



- Bőrtünetek kiterjedtsége
- Autoantitest profil
- Szervi érintettség
- Betegség progresszió és kimenetel

Lancet. 2017 Oct 7;390(10103):1685-1699

SSc- menedzsment



- **Kit kell kezelni?**
- **Mikor kell indítani?**
- **Milyen terápiát?**
- **Meddig?**

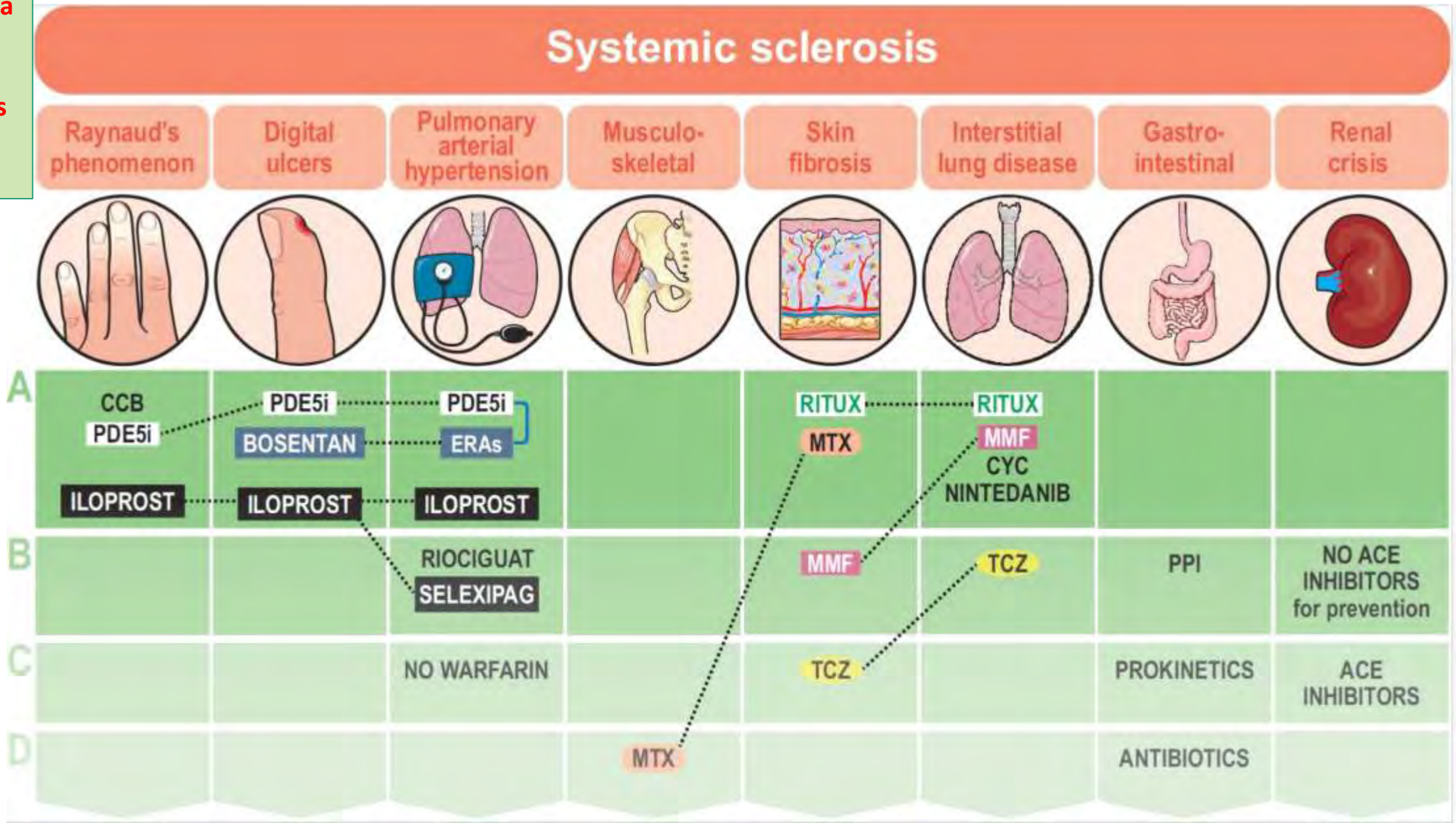
Kezelés:

Vascularis terápia

Immunszuppr./ Immunmoduláns

Antifibrotikus

SSc terápiás ajánlás – EULAR 2023



Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430

Kezelés:

Vascularis terápia

Immunszuppr./ Immunmoduláns

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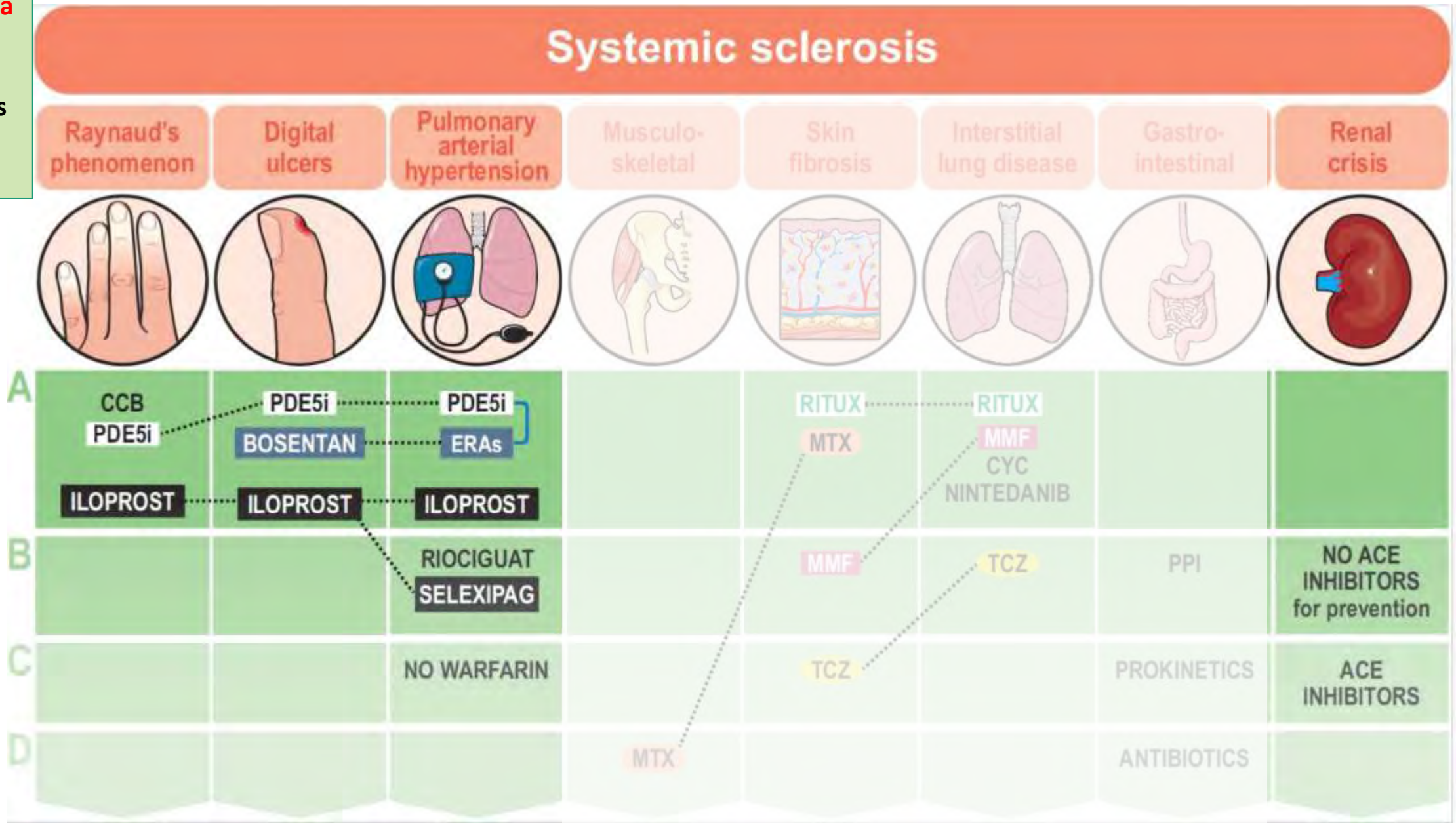
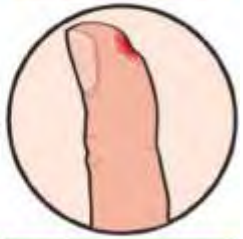
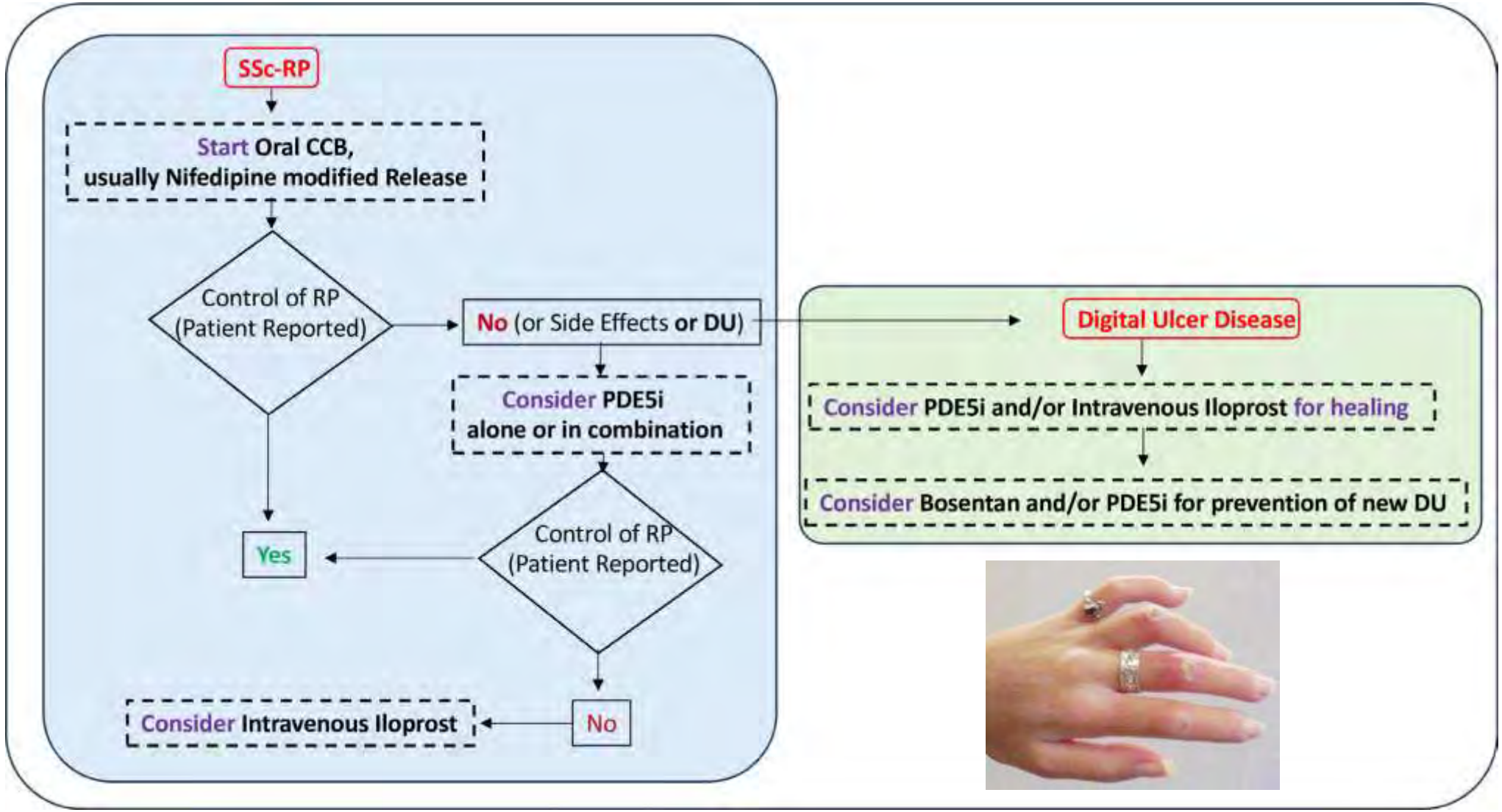
SSc terápiás ajánlás – EULAR 2023



Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430

SSc terápiás ajánlás – EULAR 2023

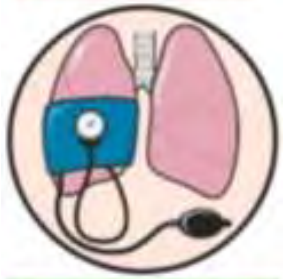
Raynaud's phenomenon	Digital ulcers
	
CCB PDE5i	PDE5i BOSENTAN ILOPROST



Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430

SSc terápiás ajánlás – EULAR 2023

Pulmonary arterial hypertension



PDE5i

ERAs

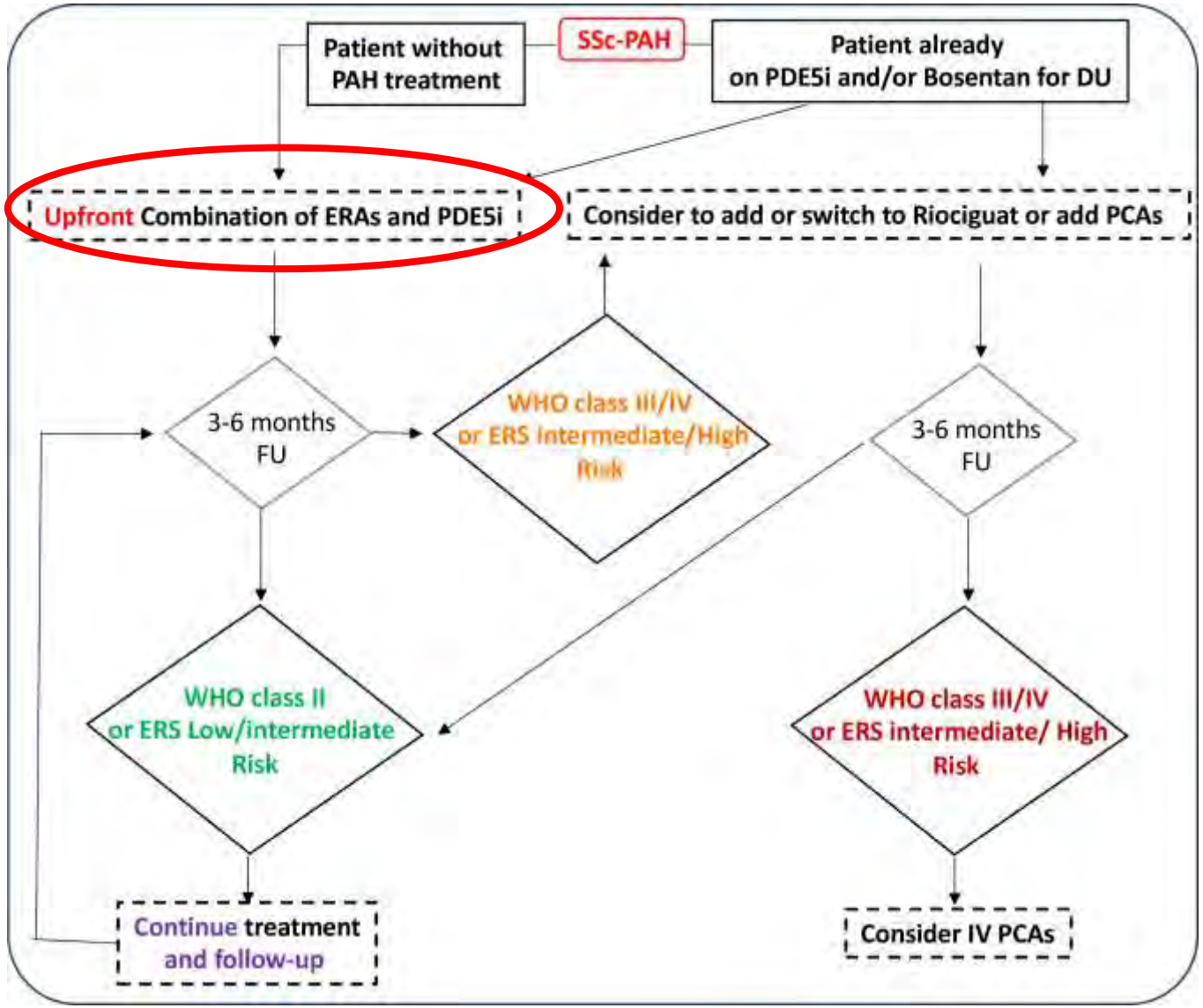
ILOPROST

RIOCIGUAT

SELEXIPAG

NO WARFARIN

+
Iv epoprostenol



Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430

SSc – PAH kezelés

https://emcrit.org/ibcc/pah/

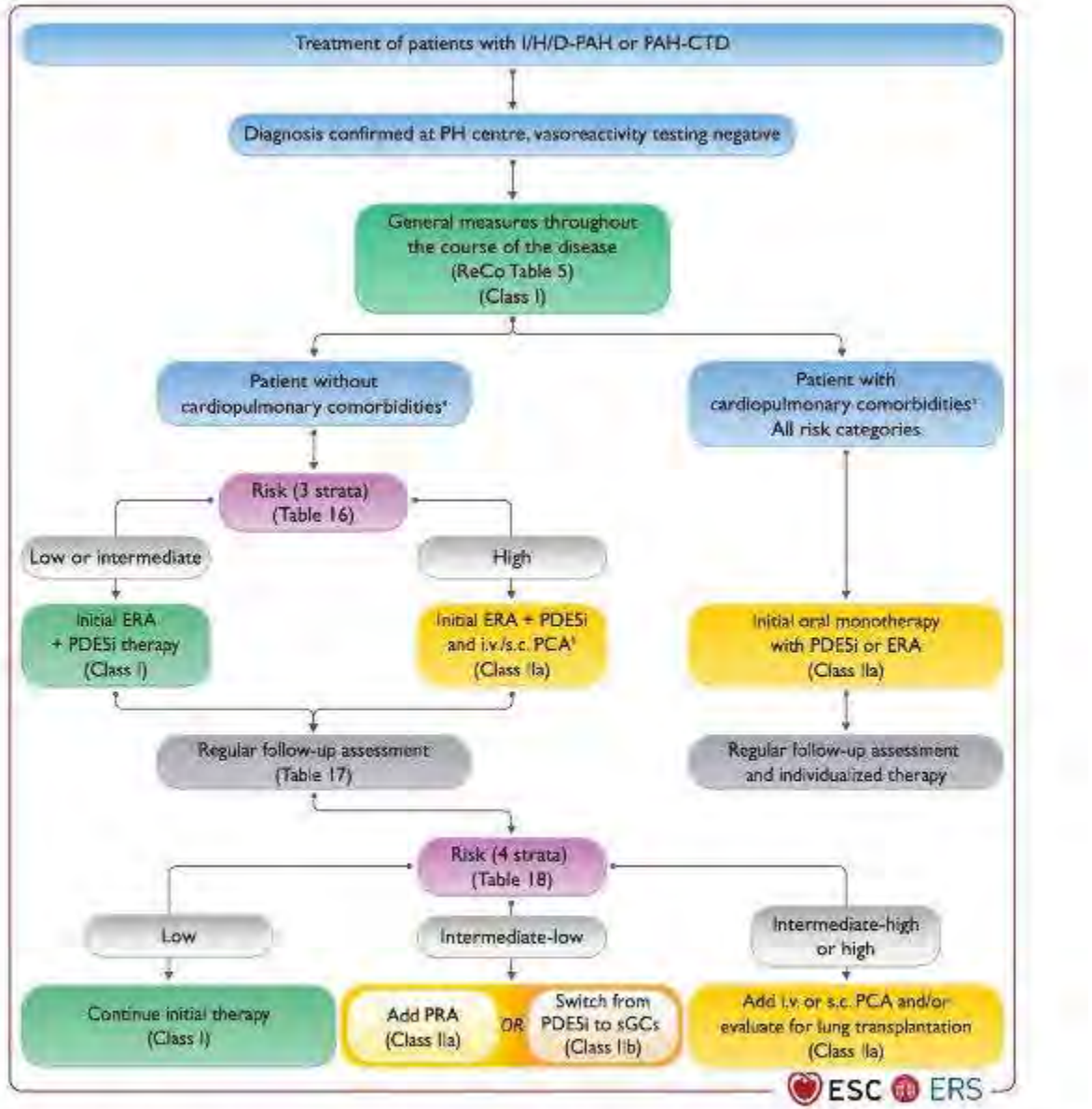
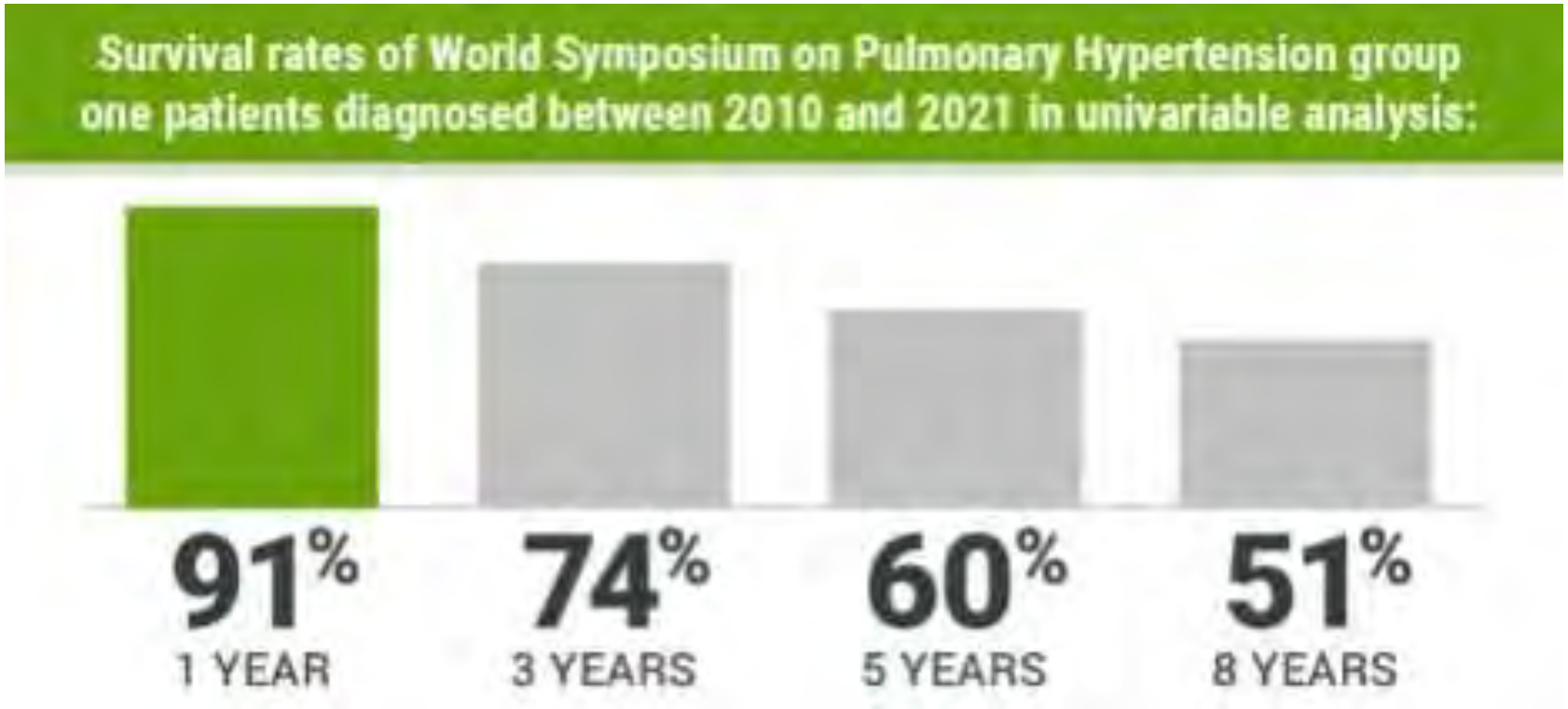


Figure 9 Evidence-based pulmonary arterial hypertension treatment algorithm for patients with idiopathic, heritable, drug-associated, and connective tissue disease-associated pulmonary arterial hypertension. DLCO, Lung diffusion capacity for carbon monoxide; ERA, endothelin receptor antagonist; I/H/D-PAH, idiopathic, heritable, or drug-associated pulmonary arterial hypertension; i.v., intravenous; PAH-CTD, PAH associated with connective tissue disease; PCA, prostacyclin analogue; PDE5i, phosphodiesterase 5 inhibitor; PH, pulmonary hypertension; PRA, prostacyclin receptor agonist; ReCo, recommendation; s.c., subcutaneous; sGCs, soluble guanylate cyclase stimulator. *Cardiopulmonary comorbidities are conditions associated with an increased risk of left ventricular diastolic dysfunction, and include obesity, hypertension, diabetes mellitus, and coronary heart disease; pulmonary comorbidities may include signs of mild parenchymal lung disease and are often associated with a low DLCO (<45% of the predicted value). †Intravenous epoprostenol or i.v./s.c. treprostinil.

Humbert M et al. PMID 36017548

Hassan HJNM et al. Improved survival for patients with systemic sclerosis–associated pulmonary arterial hypertension: the Johns Hopkins Registry.



Am J Respir Crit Care Med 2023;207:312–322.

Renalis manifesztáció

: Classification criteria of scleroderma renal crisis, from [76].

ISRCS	Expert consensus
Hypertensive SRC Any one of the following a.) Systolic BP >140 mmHg or b.) Diastolic BP >90 mmHg or c.) Rise in systolic BP >30 mmHg compared to baseline or d.) Rise in diastolic BP >20 mmHg compared to baseline AND One of the folowing features: a.) Increase in sCr >50% over baseline ors Cr >120% ULN for local laboratory b.) Proteinuria >2+ on dipstick and confirmed by uPCR > ULN c.) Hematuria: >2+ by dipstick or > 10 RBC/HPF (without mensuration) d.) Thrombocytopenia <100 G/L e.) Hemolysis on blood smear or increased reticulocyte count f.) Hypertensive encephalopathy	A. Hypertensive SRC (fullfills both A1 and A2) 1. New onset hypertension, defined as any oft he following: a.) Systolic BP ≥ 140 mmHg b.) Diastolic BP ≥ 90 mmHg c.) Rise in systolic BP ≥ 30 mmHg d.) Rise in diastolic BP ≥ 20 mmHg AND 1. One (1) oft he following five (5) features a.) Increase in sCr by >50% over baseline OR SCr ≥120% of ULN for local laboratory b.) Proteinuria ≥2+ by dipstick c.) Hematuria ≥2+ by dipstick or ≥ 10 RBC/HPF d.) Thrombocytopenia <100 G/L e.) Hemolysis defined as anemia not due to other causes and either of the following i.) Schistocytes or other RBC fragments on blood smear ii.) Increased reticulocyte count
Normotensive SRC Increase in sCr >50% over baseline or sCr >120% of ULN for local laboratory AND One of the following features: a.) Proteinuria >2+ on dipstick and confirmed by uPCR > ULN b.) Hematuria: >2+ by dipstick or > 10 RBC/HPF (without mensuration) c.) Thrombocytopenia <100 G/L d.) Hemolysis on blood smear or increased reticulocyte count e.) Hypertensive encephalopathy	B. Normotensive SRC (fullfills both B1 and B2) 1. Increase in sCr ≥50% over baseline OR sCr ≥120% ULN for local laboratory AND 2. One (1) of the following five (5) features: a.) Proteinuria ≥2+ by dipstick b.) Hematuria ≥2+ by dipstick or ≥ 10 RBC/HPF c.) Thrombocytopenia <100 G/L d.) Hemolysis defined as anemia not due to other causes and either of the following i.) Schistocytes or other RBC fragments on blood smear ii.) Increased reticulocyte count e.) Renal biopsy findings consistent with scleroderma renal crisis (microangiopathy)

SSc terápiás ajánlás – EULAR 2023

+ egyéb antitenzív terápia

ET-1Ra – nem hatékony

PEX:? – SSc+MAHA

eculizumab

Scheen M et al. Autoimmunity Reviews 22 (2023) 103330

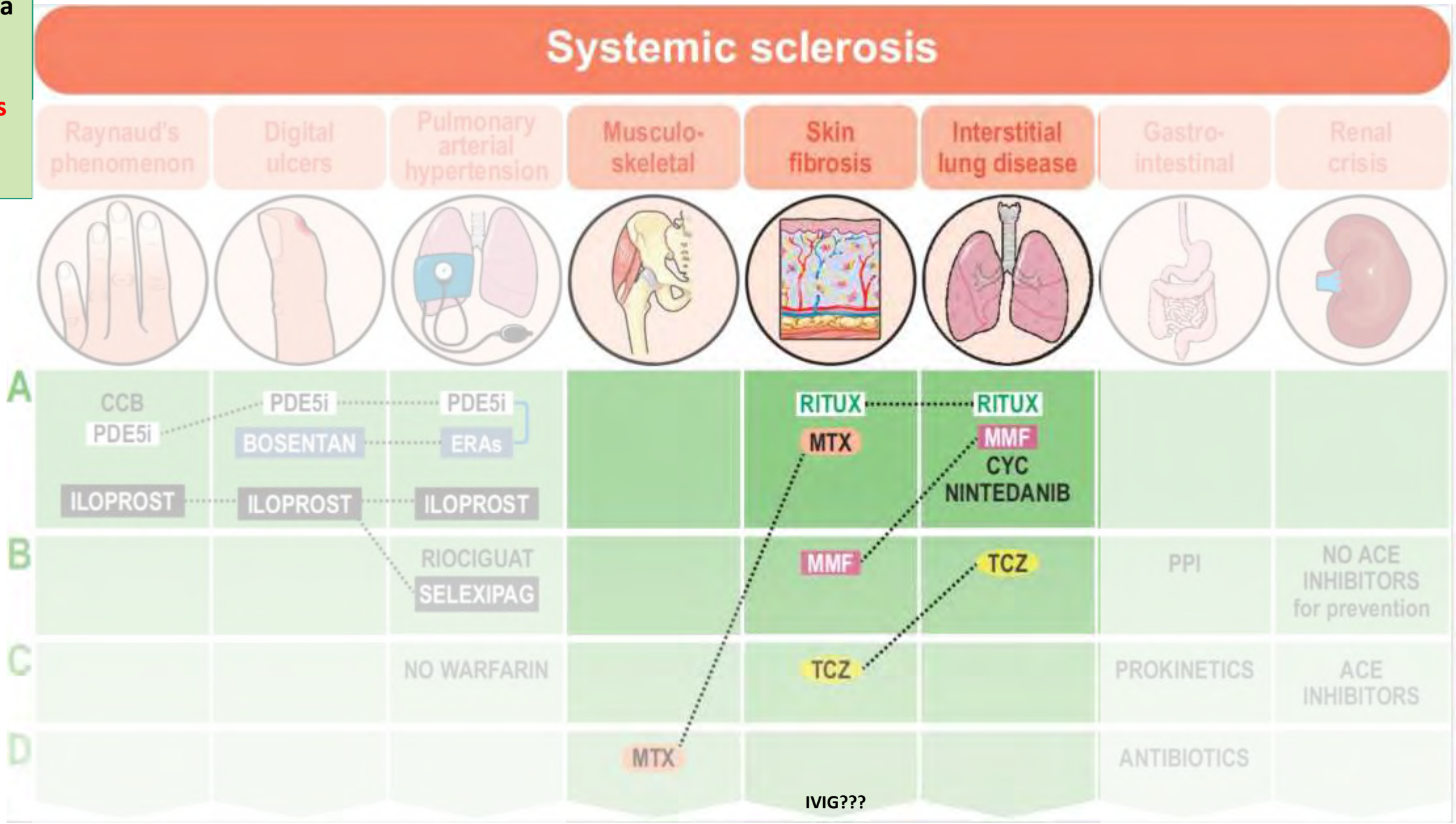
Kezelés:

Vascularis terápia

Immunszuppr./ Immunmoduláns

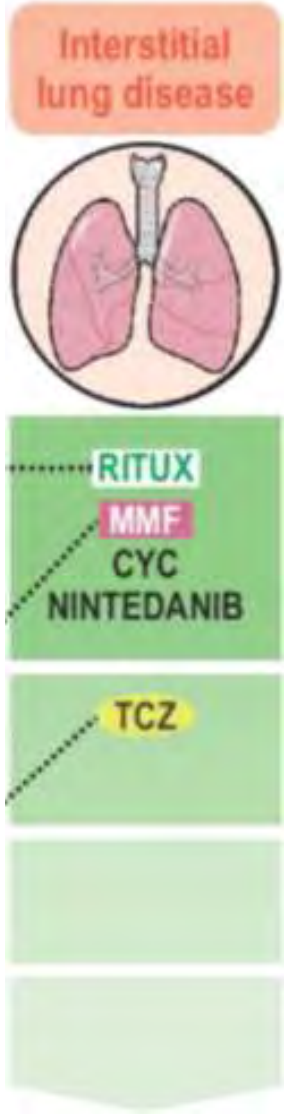
Antifibrotikus

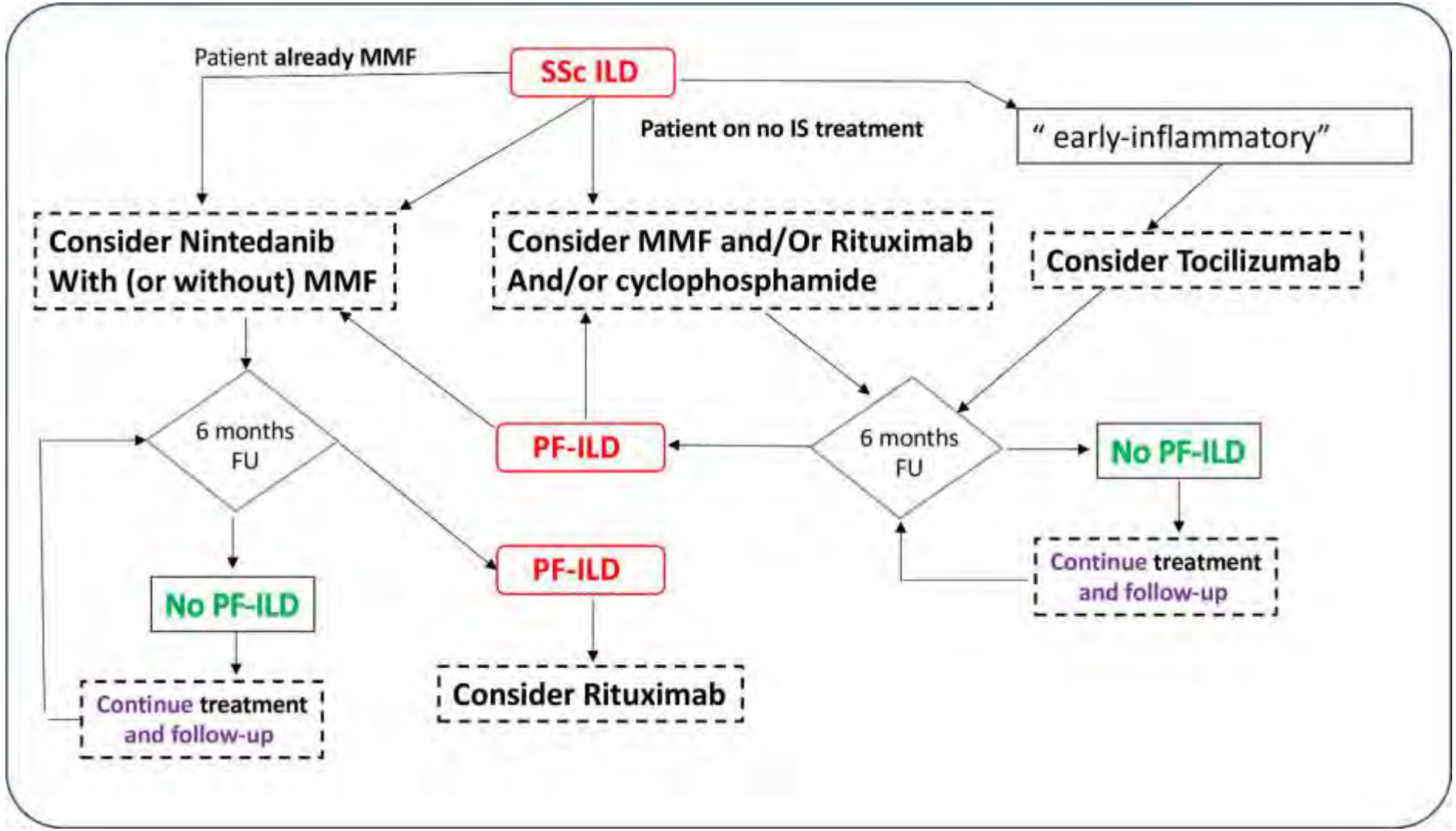
SSc terápiás ajánlás – EULAR 2023



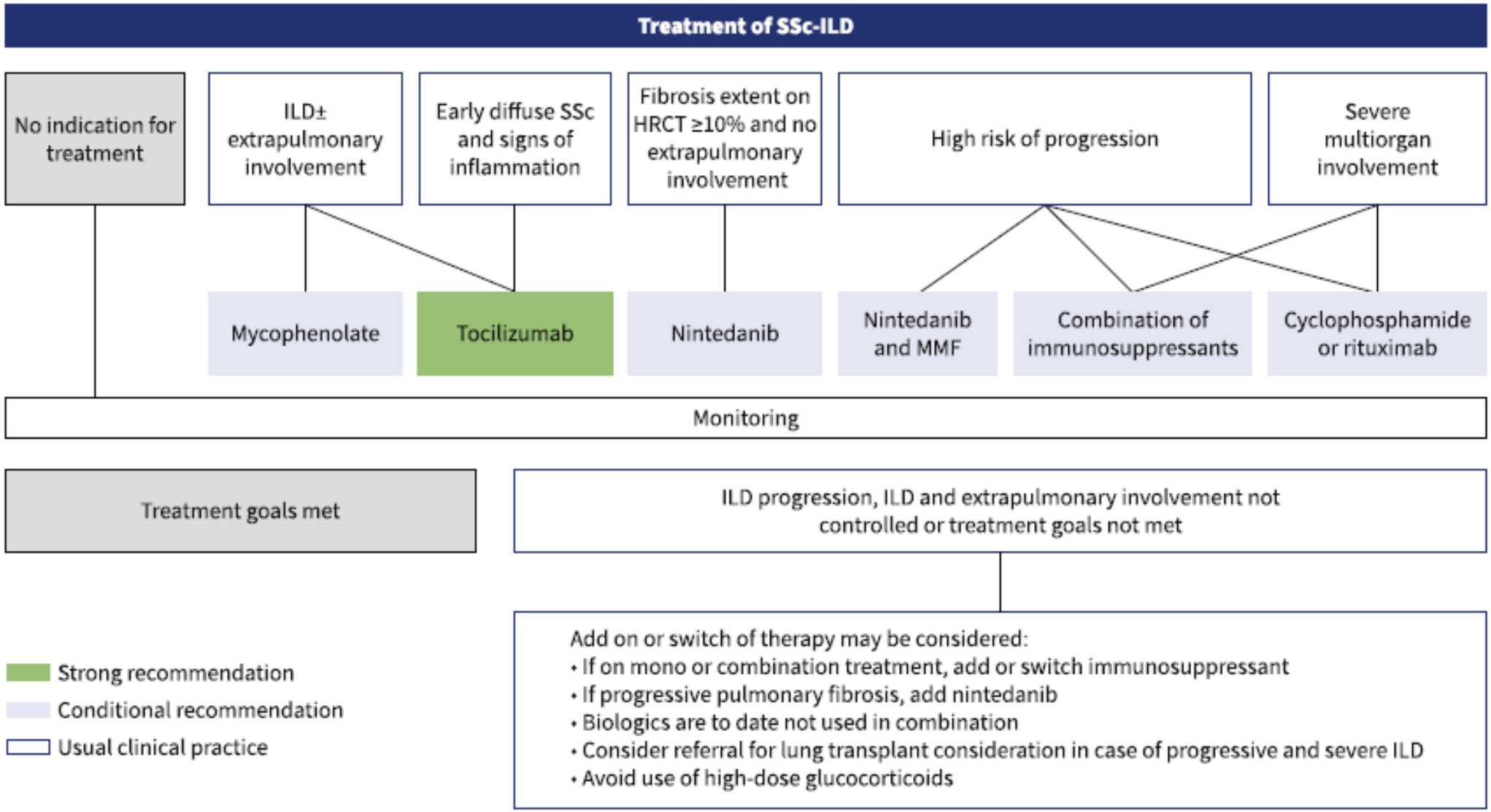
Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430

SSc terápiás ajánlás – EULAR 2023

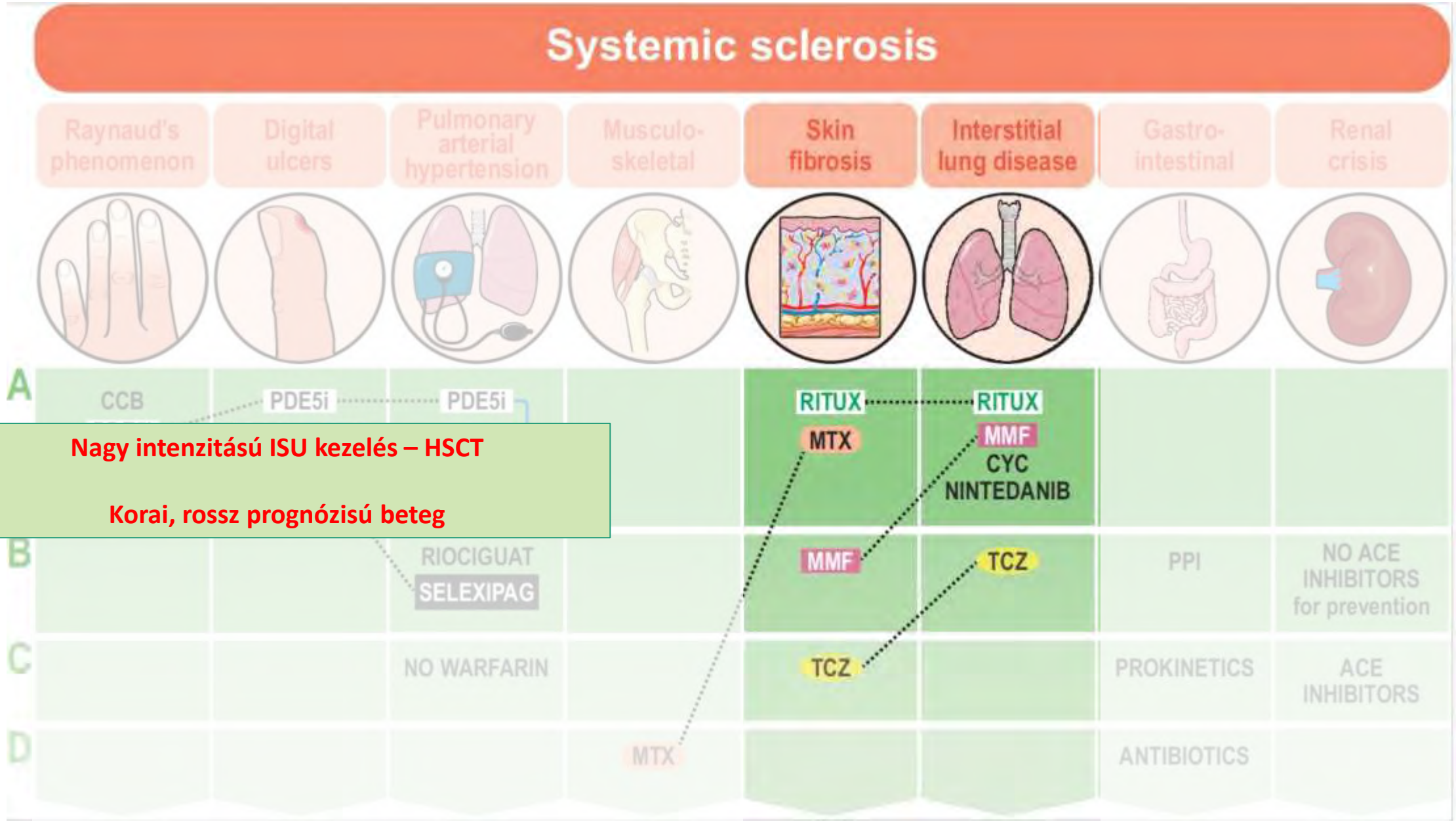




Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430


Treatment of SSc-ILD
No indication for treatment
ILD± extrapulmonary involvement
Early diffuse SSc and signs of inflammation
Fibrosis extent on HRCT ≥10% and no extrapulmonary involvement
High risk of progression
Severe multiorgan involvement
Mycophenolate
Tocilizumab
Nintedanib
Nintedanib and MMF
Combination of immunosuppressants
Cyclophosphamide or rituximab
Monitoring
Treatment goals met
ILD progression, ILD and extrapulmonary involvement not controlled or treatment goals not met
Add on or switch of therapy may be considered:
• If on mono or combination treatment, add or switch immunosuppressant
• If progressive pulmonary fibrosis, add nintedanib
• Biologics are to date not used in combination
• Consider referral for lung transplant consideration in case of progressive and severe ILD
• Avoid use of high-dose glucocorticoids
Strong recommendation
Conditional recommendation
Usual clinical practice

SSc terápiás ajánlás – EULAR 2023

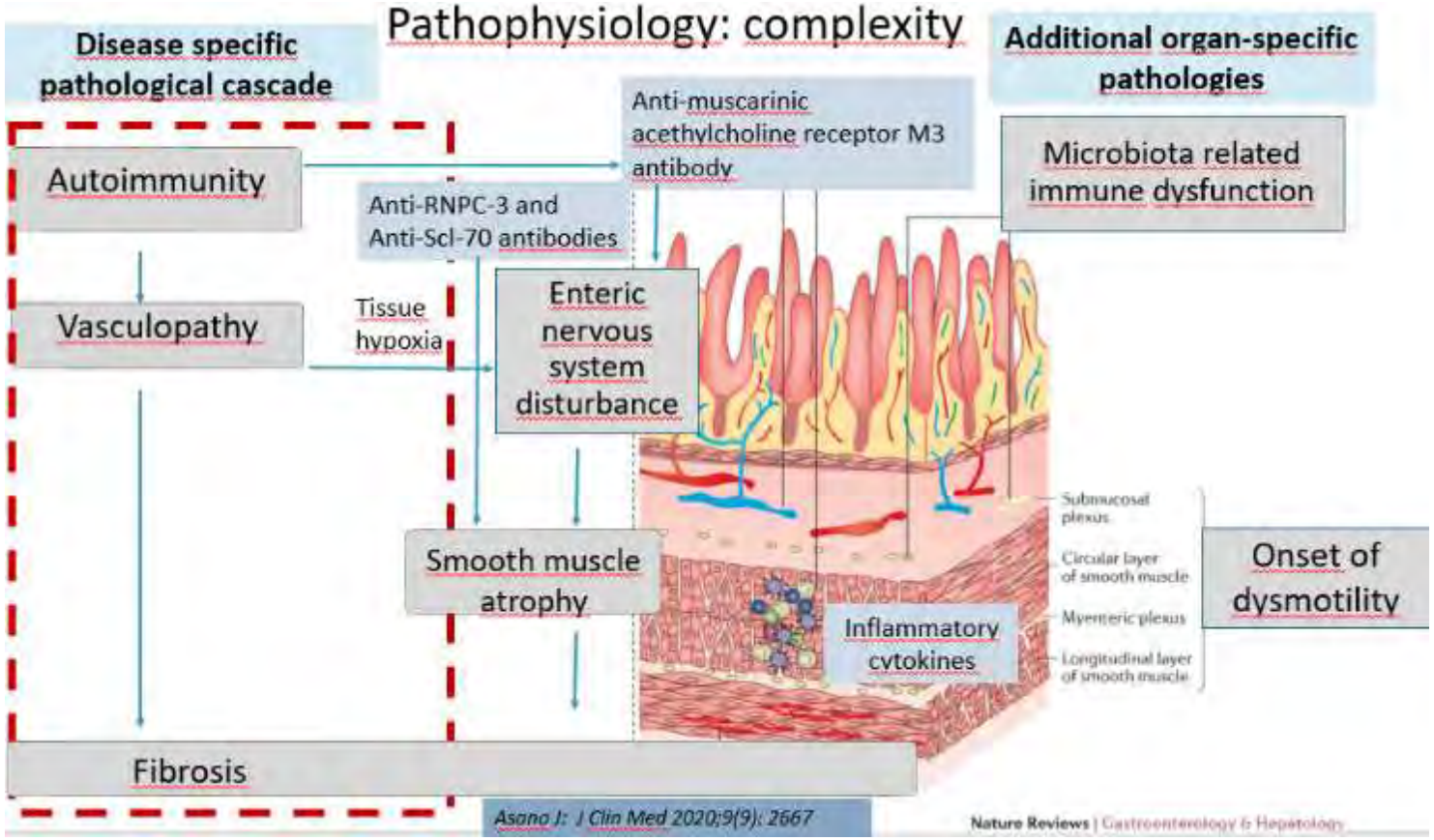


Nagy intenzitású ISU kezelés – HSCT

Korai, rossz prognózisú beteg

Del Galdo F, et al. Ann Rheum Dis 2024;**0**:1–12. doi:10.1136/ard-2024-226430

Gasztrointesztinális manifesztációk



SSc terápiás ajánlás – EULAR 2023

A kezelés csak részlegesen effektív

Itopride
dopamine és acetylcholine esterase enzim gátló
Prucalopride
5-HT_4 receptor agonista

IVIG? Autoimmun Rev 2023; 22(11): 103441.

209 SSc beteg ISU kezeléssel: alacsonyabb GIT score a követés során *RMD Open* 2024;10:e004333. doi:10.1136/rmdopen-2024-004333

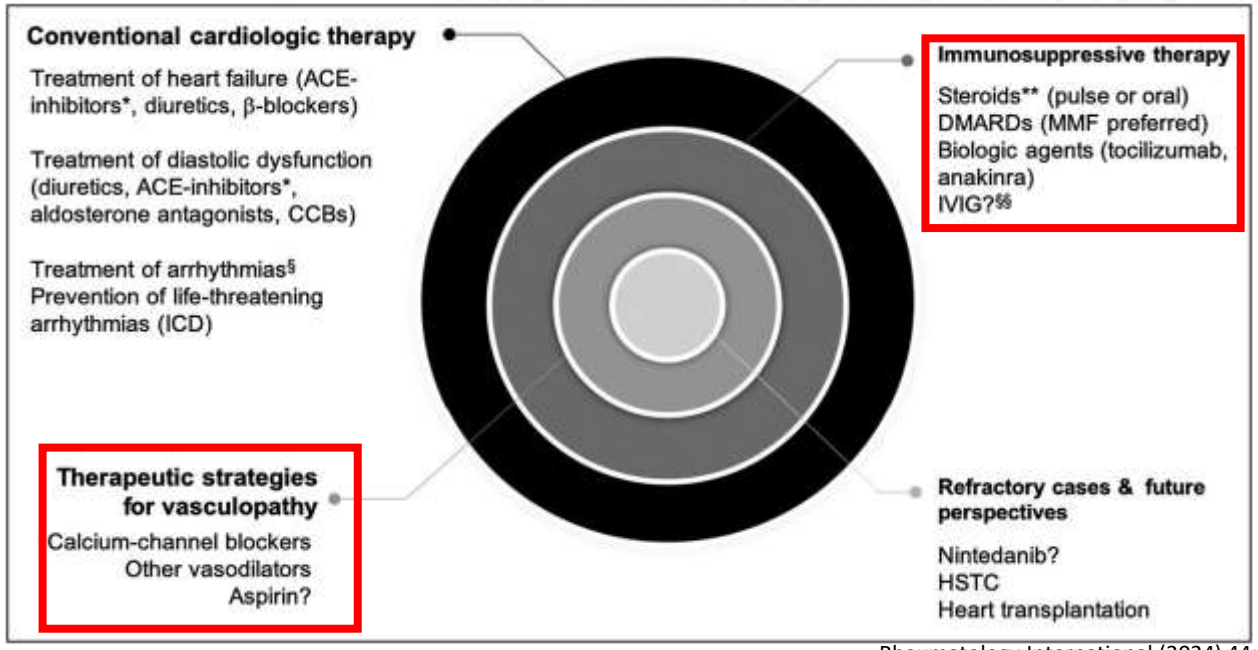
Savcsökkentő kezelés: csökkenti a MMF biohasznosulását *Semin Arthritis Rheum 2023; 63: 152270.*

Heart involvement in patients with systemic sclerosis—what have we learned about it in the last 5 years

Table 2 Current treatment options among systemic sclerosis patients with heart involvement depending on the clinical manifestation

Type of heart involvement	Treatment options
Myocarditis	DMARDs (such as: AZA, MMF, MTX, CYC) alone or with GCs [82, 83] Symptomatic treatment
Pericarditis	NSAIDs (carefully) Colchicine GCs [49]
Arrhythmia	Similar to the general population [12, 16, 82] B-blocker (carefully; cardioselective) Ivabradine (sinus tachycardia > 70/min) Oral anticoagulation, Pacemaker, ICD—if necessary [49, 82]
HFpEF	Diuretics for fluid retention Dapagliflozin/ Empagliflozin Treatment for an etiology, CV and non-CV comorbidities [49, 53, 84]
HFmrEF	Diuretics for fluid retention Dapagliflozin/ Empagliflozin ACEI/ ARNI/ ARB, MRA, B-blocker (carefully; cardioselective)—may be considered [49, 53, 84]
HFrEF	ACEI (carefully in SRC high risk patients)/ ARNI B-blocker (carefully; cardioselective) MRA Dapagliflozin/ Empagliflozin Loop diuretics for fluid retention CRT, ICD (in selected cases) [49, 53, 84]

+anti-IL6, anti-IL1, RTX?



20 SSc-ILD – nintedanib: beneficial effects of nintedanib on SSc-pHI

(Rheumatology (Oxford) 2022; 62:2550–2555.)

Rheumatology International (2024) 44:1823–1836

Curr Opin Rheumatol 2024, 36:76–93

SSc calcinosis

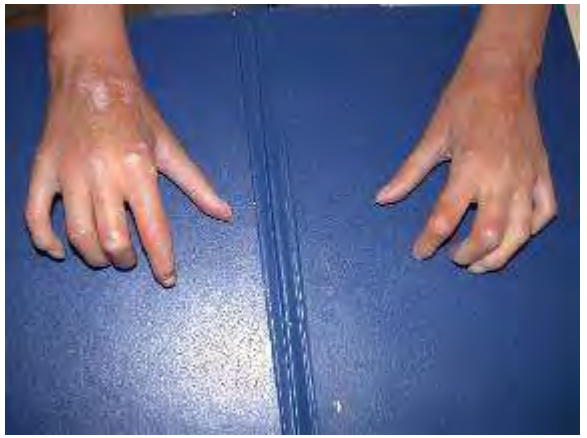
Hydroxyapatite és amorf calcium phosphate kristályok

Szignifikáns morbiditás, életminőség csökkenés

Prevalencia 18-49% (lcSSc ~ dcSSc
ACA, anti-PM/Scl + - magasabb prevalencia

Progresszió gyakoribb: ffi beteg, DU, osteoporosis, ILD

Nincs hatékony kezelés!



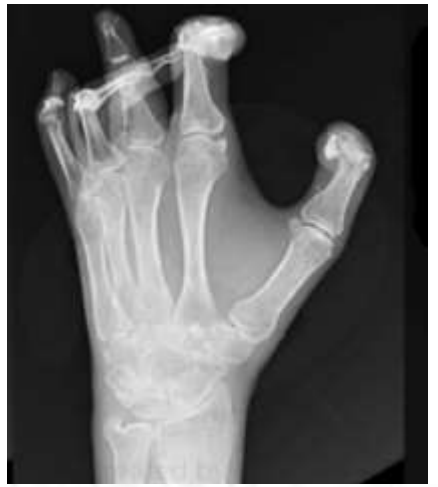


Table 2. Summary of theories for the pathophysiology of calcinosis cutis.

Mechanism	Evidence
Chronic inflammation	Increased production of TNF, IL-1, IL-6, and other proinflammatory cytokines
Vascular hypoxia (ischemia)	Hypoxia-induced imbalance between angiogenic factors (such as VEGF, platelet-derived growth factors) and antiangiogenic factors (such as angiostatin, endostatin) Increased expression of the hypoxia-associated GLUT-1 Hypoxia-induced osteoclast activity
Recurrent trauma	Presence or history of digital ulcers Calcification occurs at sites of chronic trauma/stress, suggesting a role of pressure or recurrent trauma

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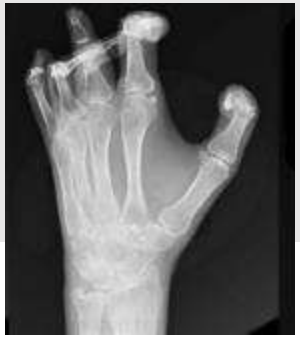
Calcinosis kezelése	level of evidence
Warfarin	IIb not recommended
Iontophoresis of acetic acid 1 ultrasound	IIB ineffective
Minocycline	IV
Diltiazem	IV
B-cell depletion therapy (Rituximab)	IV
Topical/intralesional sodium thiosulfate	IV
Intravenous sodium thiosulfate	IV not recommended
Colchicine	IV
Surgical excision/physical therapies	IV
CO2 laser	IV
Low frequency ultrasound	IV
ESWT	IV
IVIg	IV
Bisphosphonates	IV
PDE4i	
Tofacitinib	
Aluminium hydroxide	



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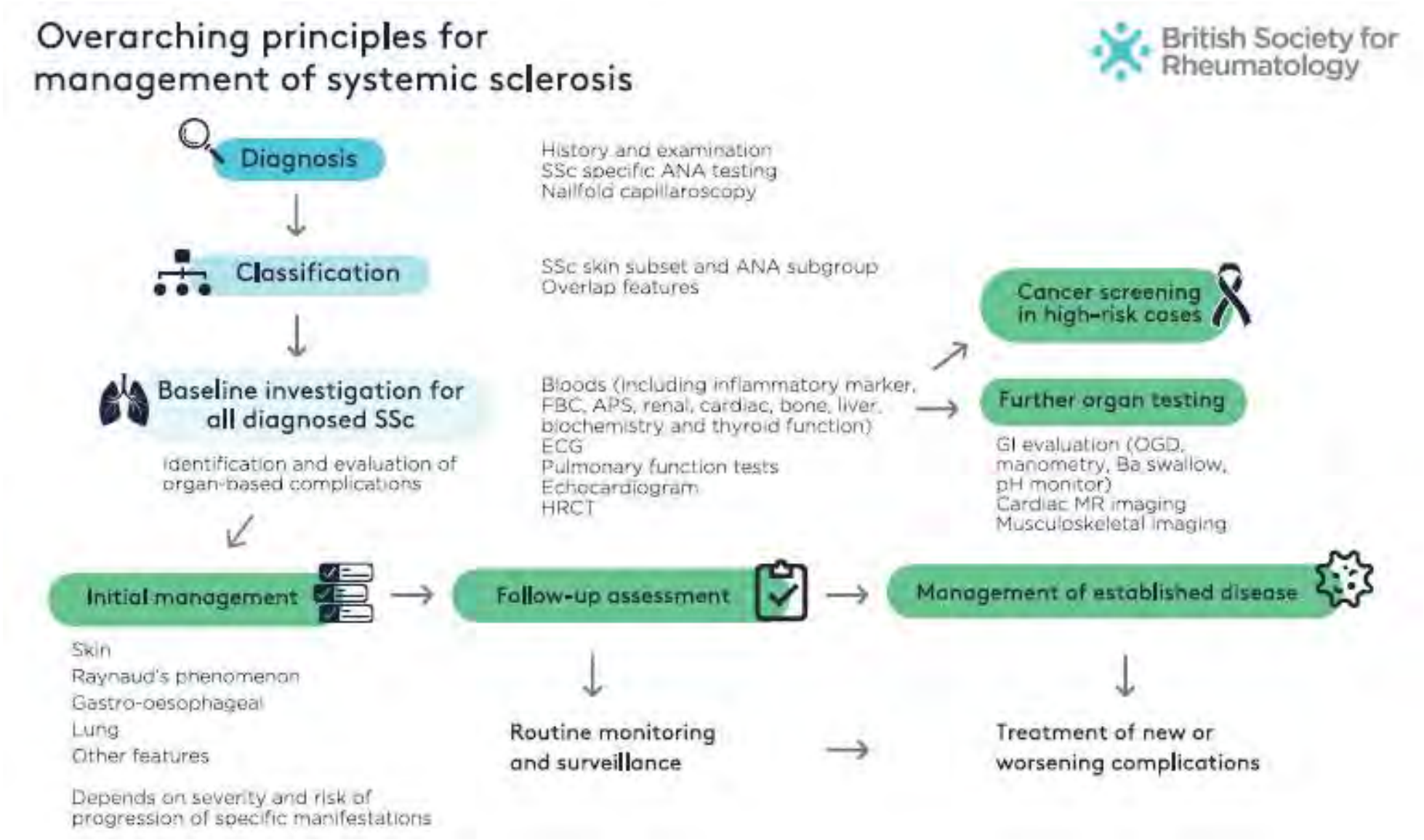
The Journal of Rheumatology 2022;49:980–9

Table 3. Management of calcinosis in rheumatic diseases.

Treatment	Dosage	Study Design	Partial Response, n (%)	Complete Response, n (%)	First Author, Year	No. of Patients (Diseases)	Outcomes
Warfarin	1 mg/d	RCT	0 (0)	0 (0)	Berger, 1987[104]	8 (4 placebo; 4 DM, SSc)	No regression of calcinosis
	1 mg/d	R	0 (0)	0 (0)	Lassoued, 1988[79]	6 (DM, SSc)	Worsening of calcinosis. 1 stable
	1 mg/d	R	0 (0)	2 (66)	Cuklerman, 2004[51]	3 (SSc)	2 complete regressions of calcinosis
	NA	R	1 (25)	0 (0)	Balin, 2012[44]	4 (SSc, DM)	1 partial response in calcinosis
	NA	R	0 (0)	0 (0)	Fredi, 2015[45]	2 (DM)	No response in calcinotic lesion
Diltiazem	60 mg tid	R	3 (25)	0 (0)	Vayssairat, 1998[8]	12 (SSc)	3 radiographic improvement
	< 480 mg/d	R	9 (53)	0 (0)	Balin, 2012[44]	17 (SSc, DM)	10 cutaneous lesion improvement
	NA	R	0 (0)	0 (0)	Fredi, 2015[45]	12 (DM)	No response in calcinotic lesion
	240-480 mg/d	CS	2 (50)	2 (50)	Palmieri, 1995[42]	4 (CTD)	Regression of calcific lesion
	120 mg bid	CR	NA	1 (100)	Dolan, 1995[43]	1 (SSc)	Remission of calcinosis
	240 mg/d	CR	1 (100)	NA	Farah, 1990[41]	1 (SSc)	Regression of calcinotic lesion
Rituximab	0.375-1 g/m² wk 0/1	RCT	NA	1 (14)	Aggarwal, 2017[105]	76 (DM), 48 (JDM)	No improvement in calcinosis
	500 mg/m² wk 0/2	P	0 (0)	3 (100)	Moazedi-Fuerst, 2015[50]	3 (SSc)	Regression of calcinotic lesion
	500mg/m² wk 0/2	P	4 (36)	NA	Narváez, 2014[75]	9 (SSc)	Reduction in calcinotic lesion
	375 mg/m²/wk × 4	P	3 (50)	NA	Giuggioli, 2015[54]	10 (SSc)	Improvement in calcinosis in 3/6 patients
	2 × 500 mg/m²	P	0 (0)	0 (0)	Bader-Meunier, 2011[77]	6 (JDM)	No calcinosis improvement in 6 patients
	375 mg/m² × 4	CR	NA	1 (100)	Daoussis, 2012[55]	1 (SSc)	Calcinosis significantly improved and pain resolved
Bisphosphonate	NA	R	1 (20)	0 (0)	Balin, 2012[44]	5 (DM, SSc)	1 partial response, 3 had no response
	IV 1 mg/kg/d	R	2 (66)	1 (33)	Marco Puche, 2010[47]	3 (JDM)	Reduction and remission of calcinosis
	IV 1 mg/kg/d	R	2 (33)	2 (33)	Tayfur, 2015[61]	6 (JDM)	Resolution of calcinosis in 4/6 patients
	10 mg/kg/d	CR	1 (100)	NA	Rabens, 1975[40]	1 (SSc)	Partial regression of calcinosis
	10 mg/d	CR	1 (100)	NA	Masza Mukamel, 2001[62]	2 (JDM)	Complete resolution of calcified lesions
	Initial dose 10 mg/kg/d, then 20 mg/kg/d	CR	0 (0)	0 (0)	Metzger, 1974[48]	6 (SSc, DM)	Progression of calcinosis
Surgical excision	NA	R	3 (27)	8 (73)	Balin, 2012[44]	11 (DM, SSc)	Complete response in 8/11 patients
Extracorporeal shock wave lithotripsy	NA	P	4 (100)	0 (0)	Blumhardt, 2016[91]	4 (SSc)	Reduction of calcinosis
	NA	P	1 (33)	0 (0)	Sultan-Bichat, 2012[90]	4 (venous insufficiency), 1 (DM), 3 (SSc)	Reduction of calcinotic lesion
Carbon dioxide laser	P	P	5 (83)	NA	Bottomley, 1996[89]	6 (SSc)	Pain reduction
Iontophoresis of acetic acid	Iontophoresis with 2-5% acetic acid at 10 microA for 20 mins[c]	P	0 (0)	0 (0)	Shetty, 2005[77]	3 (SSc)	Reduction in the intensity of calcinosis in imaging, but no clinical benefits
Surgical excision (microdrilling)	NA	P	12 (80)	NA	Fahmy, 1998[88]	15 (SSc)	Improvement of calcinosis in 12/15 digits

The 2024 British Society for Rheumatology guideline for management of systemic sclerosis



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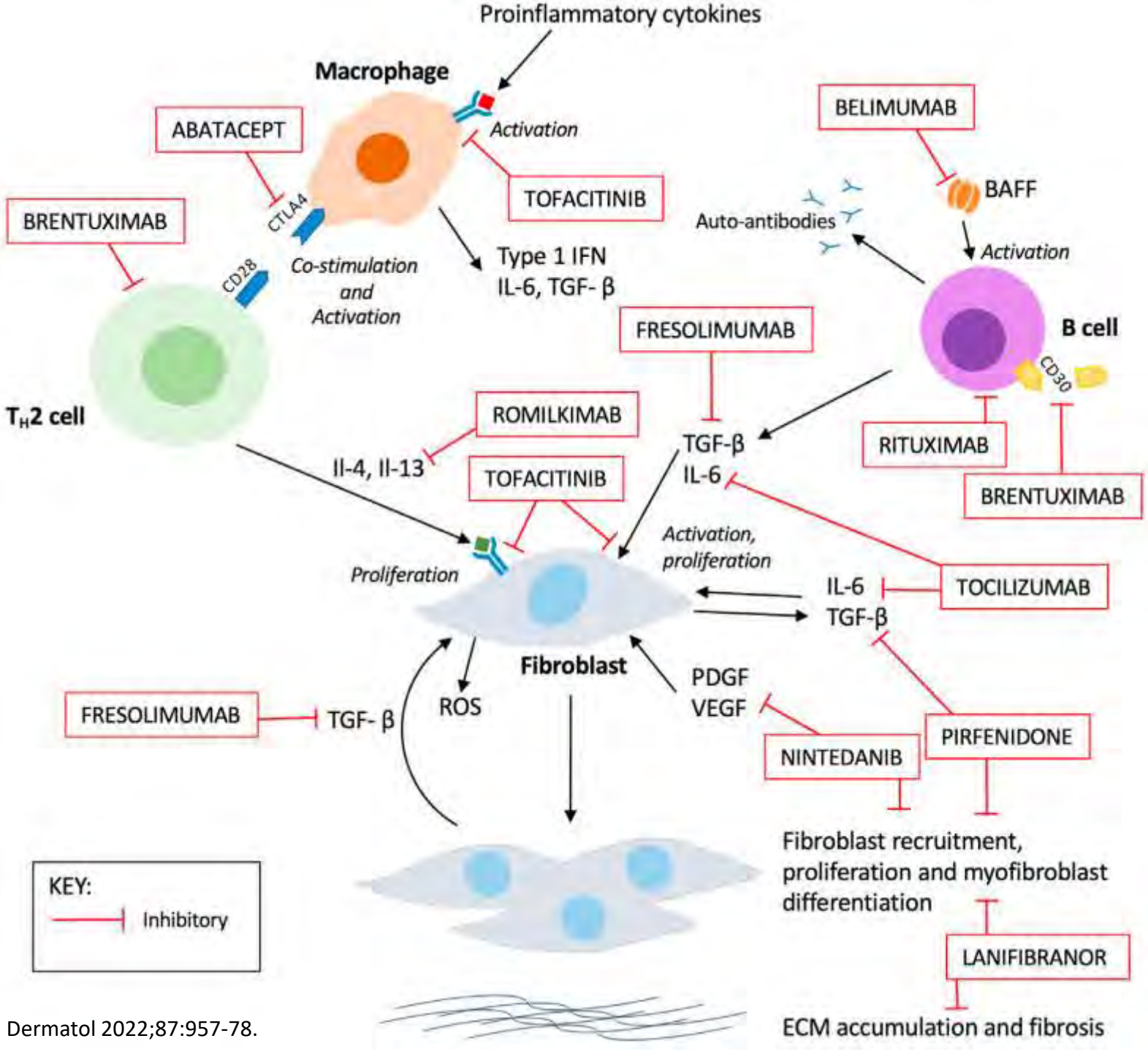

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Morgan ND et al. Curr Treatm Opt Rheumatol. 2016 March ; 2(1): 69–84. doi:10.1007/s40674-016-0038-7.

SCLERODERMA MIMICS

LOCALIZED

Morphea

Linear
Generalized
Panscleroti

SYSTEMIC

Inflammatory & Immune mediated

★ Eosinophilic fasciitis
Graft versus host disease
Lichen sclerosus et atrophicus
POEMS syndrome *

Hereditary

Congenital fascial dystrophy
Progeroid disorders
- Progeria
- Acrogeria
- Werner's syndrome

Deposition Disorders

★ Scleromyxedema
Systemic amyloidosis
★ Nephrogenic systemic fibrosis
★ Scleredema adultorum
Lipodermatosclerosis

Metabolic

Hypothyroidism (myxedema)
Phenylketonuria
Porphyria cutanea tarda

Occupational Exposure

Epoxy resins
Organic solvents
Polyvinyl chloride
Silica

Toxin & Chemical Induced

Pharmaceuticals

Balicatib
Bisoprolol
Bleomycin
Bromocriptine
Carbidopa
D-Penicillamine
L-tryptophan
Pentazocine
Postradiation fibrosis
Toxic oil syndrome

Pesticides

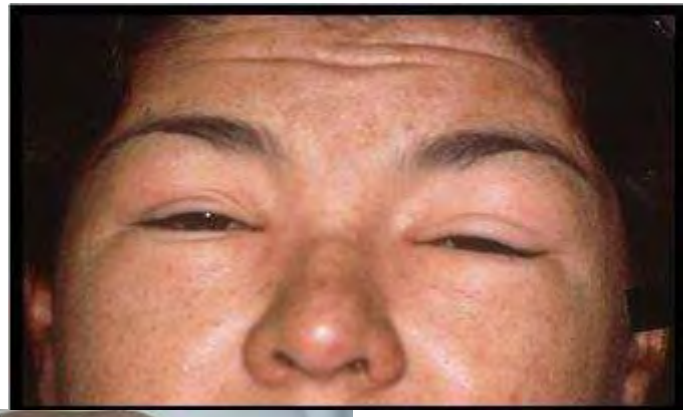
Diniconazole
Malathion

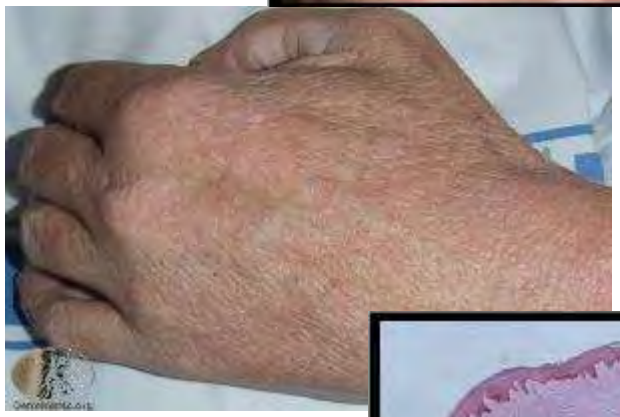
Chemicals

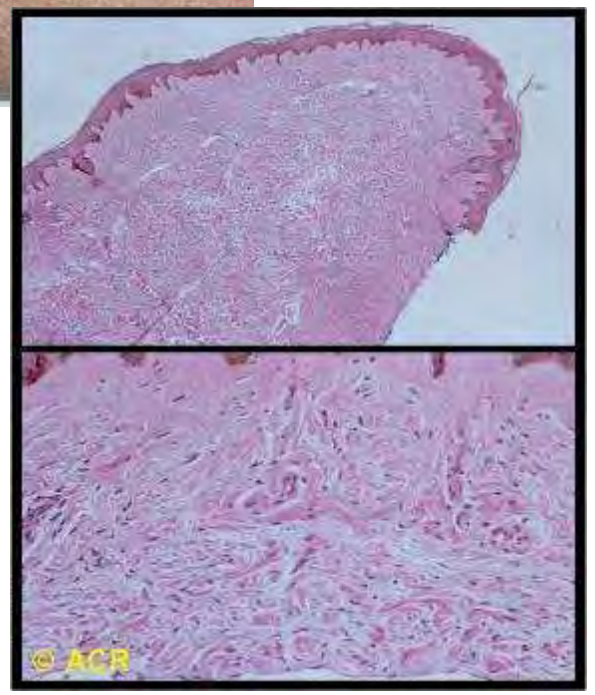
Benzene
Malathion
Naphthalene
Toluene
Trichloroethylene
Vinyl chloride monomers

Scleromyxoedema

- **30-50 éves korban, férfi:nő = 1:1**
- **monoclonalis gammopathia (IgG lambda könnyű lánc)**
- **ritkán daganatos betegség/infectiohoz társul**
- **arc, törzs, végtagok bőre érintett**
- **belszervi tünetek potenciálisan súlyosak (oesophagus dysmotilitás, veseelégtelenség, izomgyengeség)**
- **Raynaud phenomen hiányzik**
- **Mucin depositumok az érfalban és a dermisben**



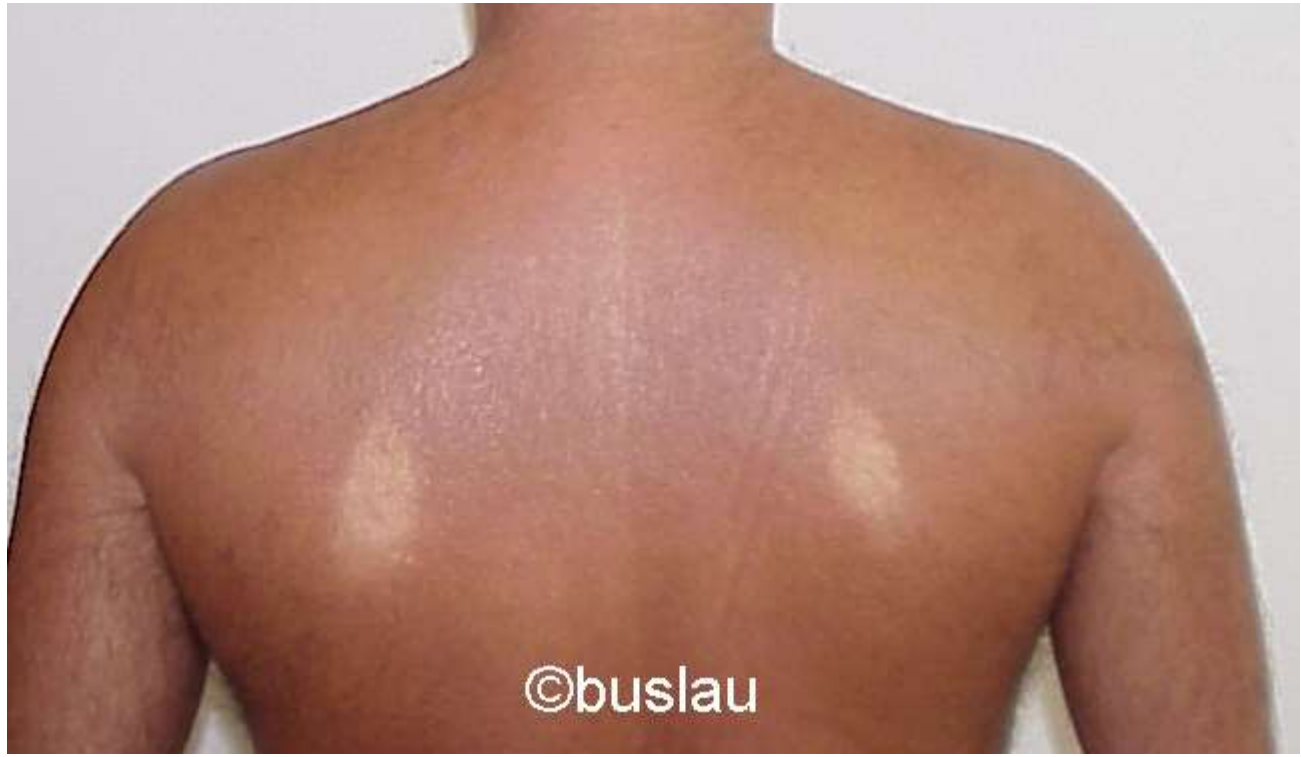




- Terápia:
- prednisolon
- melphalan
- cyclophosamid
- chloroquin
- PUVA, fotopheresis
- plasmapheresis
- IVIG

Scleredema adultorum Buschke

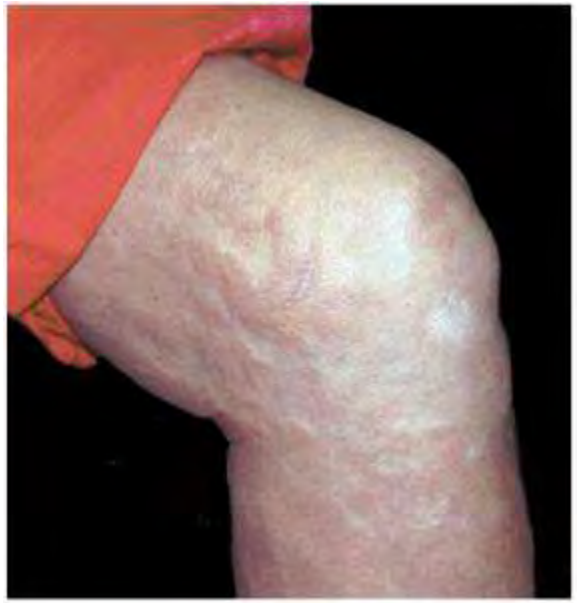
- **Diabetes mellitus**
- **Gyerekekben infectiohoz társul**
- **monoclonalis gammopathia gyakori**
- **Nyak, hát (ujjak nem)**
- **Collagen ↑↑, kevés mucin lehet**

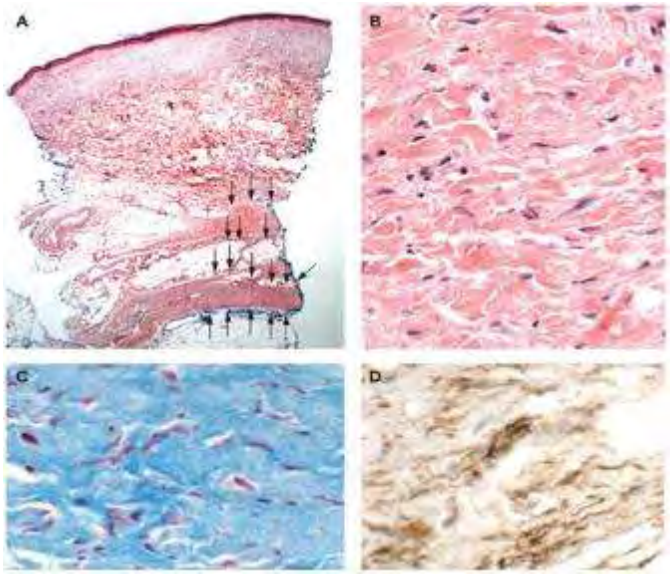


- **Terápia:**
- prednisolon
- D-penicillamin
- PUVA, fotopheresis

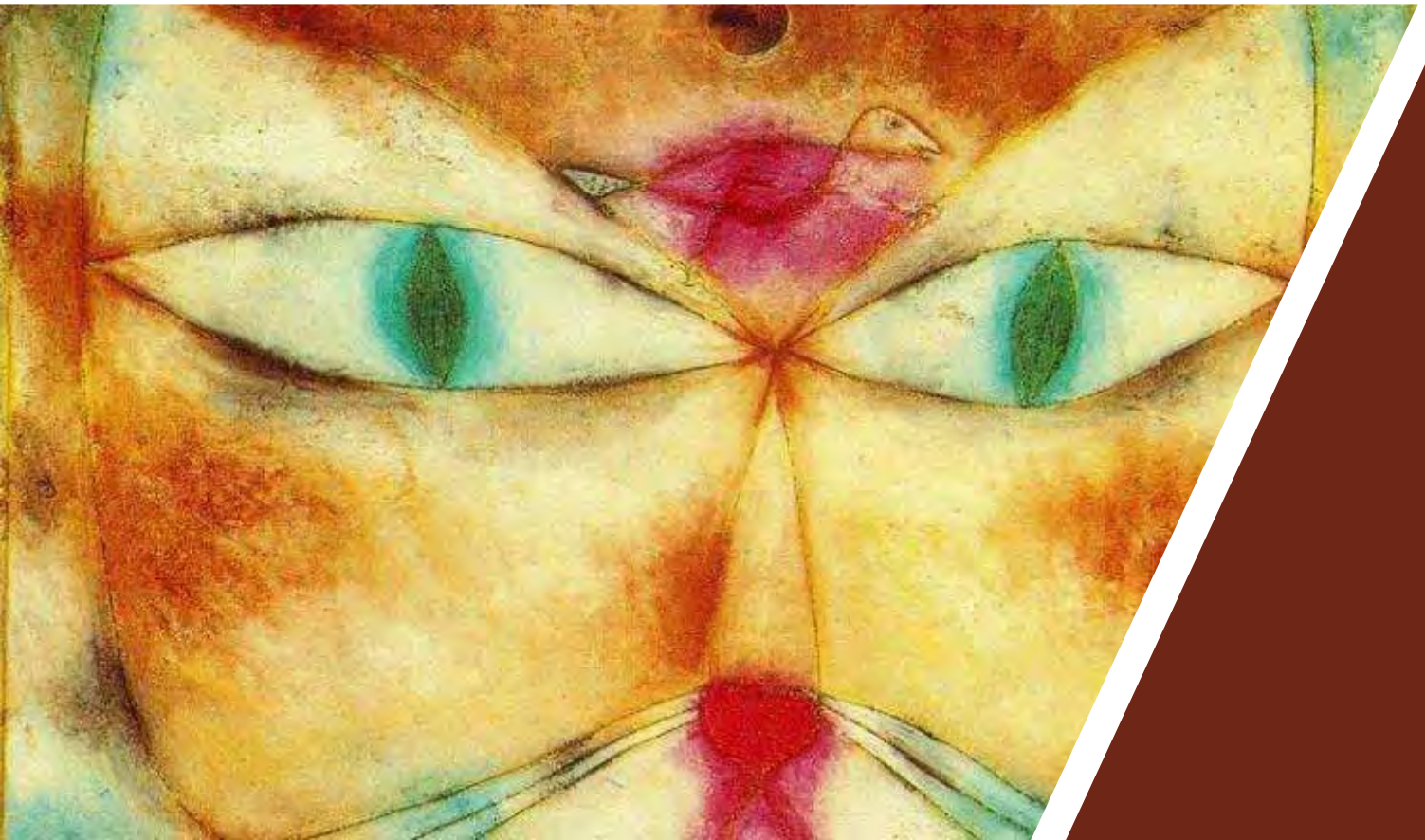
Nephrogen systemas fibrosis

- **2000-ben írták le először dializált betegekben**
- **a bőr megvastagodása, hyperpigmentáció, de az ujjak megkíméltek!) „narancsbőr” jellegű**
- **belszervek fibrosisa: izom, myocardium, tüdő**
- **trigger: nagy dózisú erythropoetin, gadolínium tartalmú kontrasztanyag (MR angio!)**
- **dg alapja a szövettan: bőr teljes vastagságára kiterjedő fibrosis, csillag alakú és osteclast-szerű óriássejtek**





1879-1940



KÖSZÖNÖM A FIGYELMET!