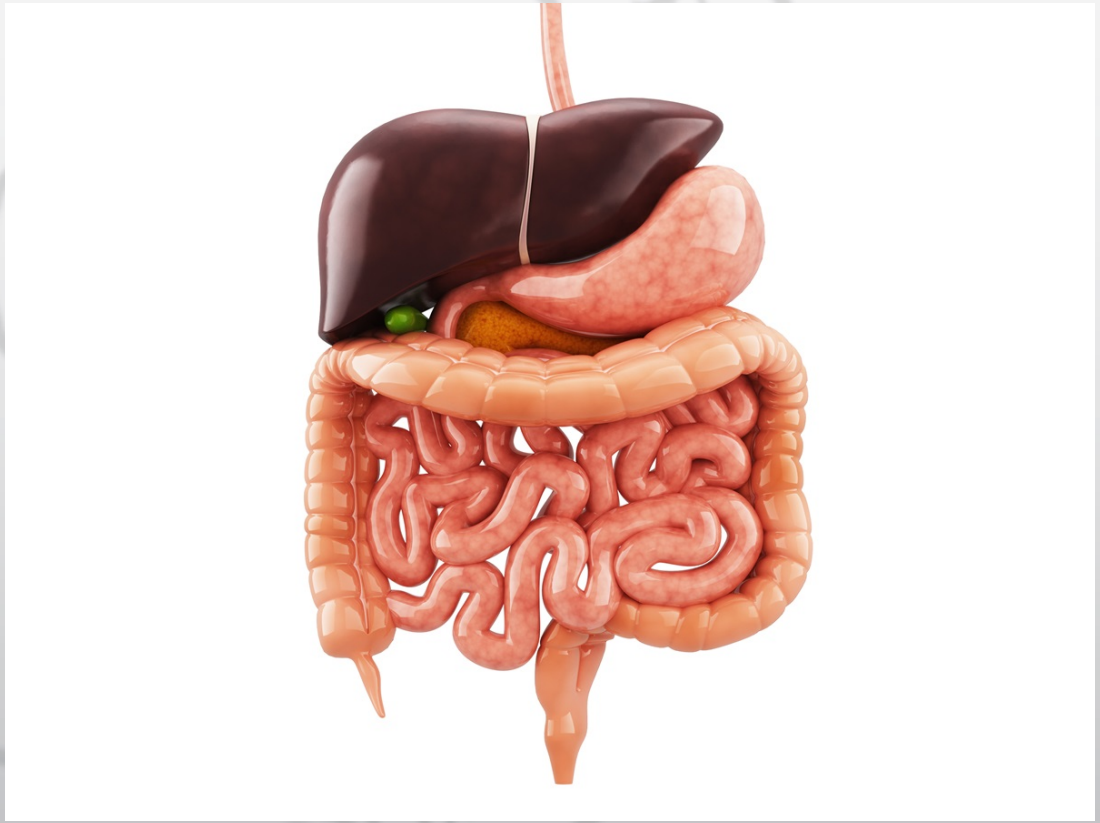
Università degli Studi di Padova

DiSCOG

Scuola di Specializzazione
in Malattie dell'Apparato
Digerente

UNA STENOSI INUSUALE

Dott.ssa ***Costanza Orlando***



F ♀
65 y.o.

GI EVALUATION

16
NOV
17

Dysphagia to solids, not liquids (1 year), rigurgitis:

COMORIBIDITIES

- *Scleroderma*
- *Multinodular goiter in euthyroidism*
- *Vitiligo*
- *Left DVT*

IN THERAPY WITH

- *Nifedipine*
- *Antiacids*
- *IPP*

Familiarity for CRC (1° grade: mother)

1°

GI EVALUATION

16 NOV 17

BARIUM SWALLOW TEST 05 JUL 2017

Esofago pervio sino in sede sottocarenale, ampio il suo calibro con aspetti di ipotonia e ipocinesia.

Subito a valle si evidenzia riduzione di calibro con pervietà però conservata e con aspetti discinetici con alternanza di tratti di calibro ridotto e tratti di calibro aumentato. Abbondante il reflusso di bario a monte. Piloro pervio.

Lo stomaco forma ernia transjatale, in corrispondenza le pliche mucose appaiono più rilevate e disordinate.

Stomaco ad uncino, un po' ipotonico ed ipocinetico, si svuota lentamente.

Bulbo duodenale discinetico con prevalenza di ipertonia.

1°

GI EVALUATION

16 NOV 17

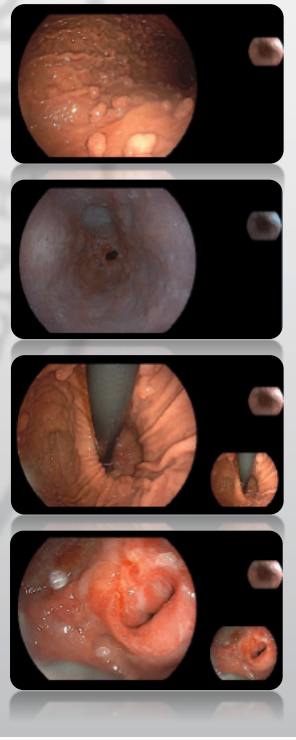
EGDS 10 OCT 2017

ESOFAGO
Regolare per calibro e rilievo mucoso fino a 25 cm dall'AD da dove dipartono erosioni longitudinali anche di 10mm. Cardias a 29 cm dalla AD, ipertonico, rivestito da mucosa iperemica ed edematosa, congesta e facilmente sanguinante al contatto con lo strumento, valicabile con strumento standard con scatto (biopsie). Dal cardias partono lingule di mucosa arancione he si estendono fino a 27 cm dall'AD (biopsie). Impronta dei pilastri diaframmatici a 35 cm dall'AD. Si eseguono biopsie a 33 cm dall'AD (giunzione esofago-gastrica).

STOMACO
Ben distensibile, contiene normale quantità di succo gastrico limpido.
La mucosa gastrica si solleva in pliche regolari.
Fondo e corpo appaiono rivestiti da mucosa edematosa e livemente iperemica, presentanto numerosi polipi anche di 8-10 mm rivestiti da mucosa translucida (biopsie). Antro iperemico. Piloro regolare.
In retroversione si conferma voluminosa ernia jatale. Eseguite biopsie ad antro, angulus e corpo (biopsie totali n. 5).

DUODENO
Bulbo rivestito da mucosa regolare. Non si riesce a visualizzare seconda porzione duodenale per brusca angolazione del viscere.

CONCLUSIONI
Esofagite di grado B sec Los Angeles
Voluminosa ernia jatale
Sospetto esofago di Barrett
Cardias ipertonico con substenosi
Gastropatia diffusa non erosiva
Polipi dello stomaco (verosimilmente ossintici)
Esame istologico in corso



1°

GI EVALUATION

16 NOV 17

HYSTOLOGICAL EXAM

DIAGNOSI

Gastrite (+--) non-atrofica dell'area di transizione ossintico-antrale con iperplasia delle foveole (1).
Campioni di mucosa gastrica ossintica con minima flogosi linfomonocitaria, anche di tipo nodulare, della lamina propria (2,3).
Polipo della mucosa ossintica (3).
Campione di mucosa gastrica cardiale con flogosi linfomonocitaria di basso grado della lamina propria ed estesa alla *muscularis mucosae* (4).
Campioni superficiali di mucosa della giunzione squamo-colonnare con erosione dell'epitelio di superficie associata a flogosi linfomonocitaria/granulocitaria e a tessuto di granulazione infiammatorio della lamina propria, reperto focale di metaplasia intestinale delle ghiandole e con iperparacheratosi ed esocitosi leucocitaria dell'epitelio pavimentoso (5).
Campione di mucosa di tipo gastrico con angiectasie e flogosi linfomonocitaria/granulocitaria della lamina propria (6).

Non sono stati istologicamente documentati (colorazione *Giemsa*-modificata) batteri con morfologia compatibile con *Helicobacter pylori*.

Stadiazione della gastrite: A=0; C=0: Stadio 0 (*OLGA system*, 2005);
Caratterizzazione eziologica: *Hp*-vo.

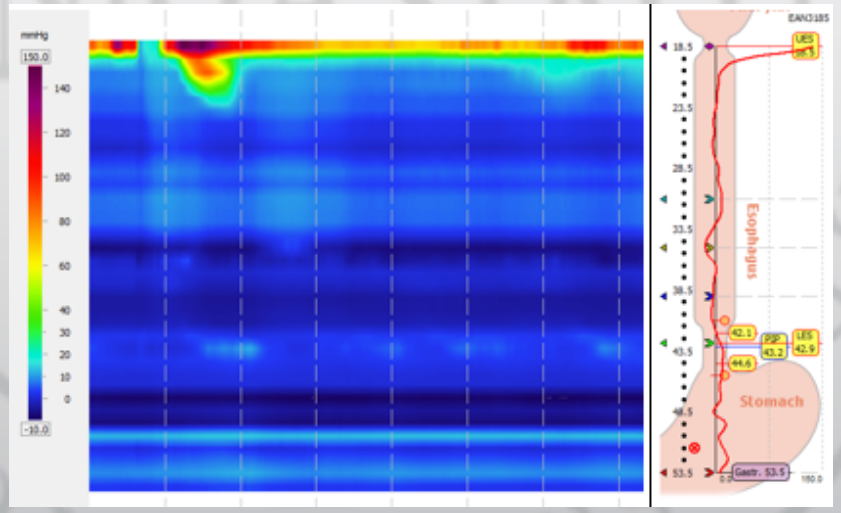
2°

GI EVALUATION

05
MAR
18

MANOMETRY 20 DEC 2017

Sfintere esofageo inferiore ipotonico, normorilasciantesi, di lunghezza ridotta; assenza di onde peristaltaltiche nel 100% delle deglutizioni liquide; SES liev. ipertonico.



2°

GI EVALUATION

05 MAR 18

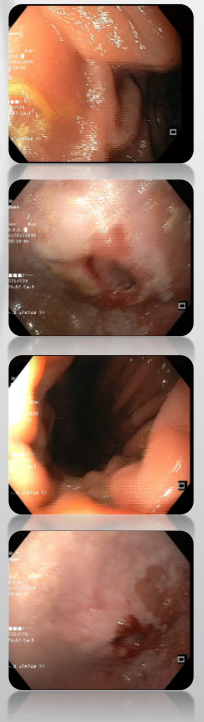
EGDS 27 FEB 2018

ESOFAGO
Calibro aumentato e decorso distorto, con aspetto dilatato soprattutto in sede distale. A partire da circa 26 cm dall'a.d. presenza di lingua ectopica che si estende fino alla verosimile regione cardiale (29 cm): si inizia mappaggio bioptico interrotto per intolleranza della paziente. Linea Z non bene visualizzabile apparentemnte a 29 cm.
La regione cardiale appare substenotica, ma ben valicabile, con mucosa eritematosa ectopica e gettone di mucosa rilevata ectopica (multiple biopsie). Dalla regione cardiale si assiste ad erniazione di mucosa gastrica. L'esofago è verniciato da residui liquidi di ingesti.

STOMACO
Ben distensibile, contiene normale quantità di succo gastrico limpido.
La mucosa gastrica si solleva in pliche regolari.
Fondo, corpo ed antro appaiono rivestiti da mucosa eritematosa. Presente qualche rilevatezza polipoide.
Piloro regolare.
In retroversione evidente ampia ernia jatale.

DUODENO
Bulbo rivestito da mucosa regolare. Seconda porzione duodenale con normale rappresentazione plicale e dei villi.

CONCLUSIONI
- Dilatazione dell'esofago
- Quadro macroscopico compatibile con esofago di Barrett
- Substenosi del cardias (MM?)
- Ernia jatale
- Polipi del corpo gastrico



2°

GI EVALUATION

05 MAR 18

HYSTOLOGICAL EXAM

Materiale inviato in esame come:
1) n. 2 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 26 dall'arcata dentaria)
2) n. 3 campioni bioptici della mucosa dell'esofago (prelievo operato a cm 29 dall'arcata dentaria).

Informazioni cliniche (come segnalate in richiesta):
- Odinofagia e disfagia persistente in sclerodermia e recente diagnosi di esofago di Barrett.
- Reperto endoscopico: Esofago di Barrett. Substenosi del cardias, Ernia iatale.

DIAGNOSI

Campioni di mucosa di tipo gastrico con minima flogosi linfogranulocitaria e edema della lamina propria (1).
Campione di mucosa del tipo della giunzione squamo-colonnare con iperparacheratosi, flogosi linfogranulocitaria (+--; anche eosinofila) della lamina propria e intraepiteliale e con reperto focale di metaplasia intestinale delle ghiandole (MI +--) (1).
Campioni di mucosa della giunzione squamo-colonnare e di tipo gastrico-cardiale (polipoide) con spongiosi e angiectasie interpapillari dell'epitelio pavimentoso e con minima flogosi linfocitaria e angiectasie della lamina propria, iperplasia delle foveole e reperto plurifocale di metaplasia intestinale delle ghiandole (MI +--) (2).

2° GI EVALUATION

05 MAR 18

CHEST X-RAY 13 DEC 2017

Campi polmonari bene espansi.
Più accentuato l'interstizio polmonare bilateralmente più evidente alle basi, su fondo enfisematoso.
Ombre ilari, cuore nei limiti. Aortosclerosi.
Emidiaframmi liberi.

HRTC 12 JAN 2018

*Esofago toracico distonico e dilatato sin dall'origine (calibro assiale massimo del tratto preterminale: 50 x 35 mm), pieno di ingesti, compatibilmente con acalasia inveterata.
Concomitante ernia transiatale toracica da scivolamento di parte dello stomaco (diametri assiali: 46 x 39 mm).
Splenulo di 15 mm in prossimità dell'ilo splenico.

2°

GI EVALUATION

05
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18

REUMATOLOGICAL EVALUATION 11 JAN 2018

Conclusioni: sclerodermia con impegno esofageo e polmonare; per completare la stadiazione della paziente è necessario eseguire un eco cuore con studio della pressione polmonare.

F ♀
65 y.o.

TO SUM UP

SUM
MA
RY

Systemic sclerosis with gastrointestinal and pulmonary involvement

→ Esophagitis

→ Barrett's esophagus

→ Cardial substenosis

Focus

SCLERODERMA DISORDERS

Heterogeneous group of conditions linked by the presence of thickened, sclerotic skin lesions.

LOCALIZED

- Linear scleroderma
- Localized and generalized morpheae

SYSTEMIC FORMS (SYSTEMIC SCLEROSIS, SSc):

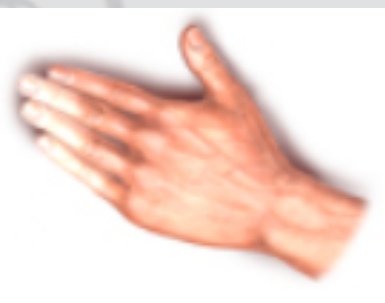
a multisystem disease characterized by widespread vascular disfunction and progressive fibrosis of the skin and internal organ.

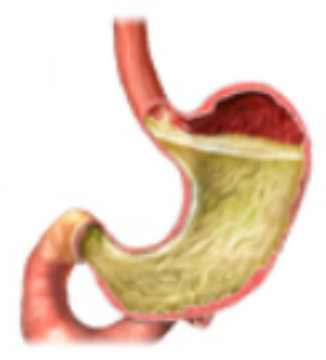
- Diffuse cutaneous SSc
- Limited cutaneous SSc (CREST)
- SSc sine scleroderma
- Environmentally induced- scleroderma
- Overlap syndromes

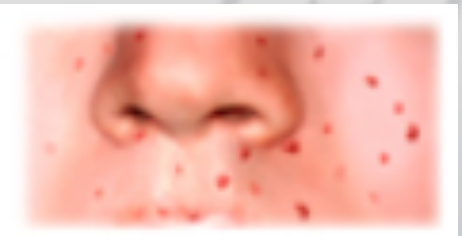
Focus

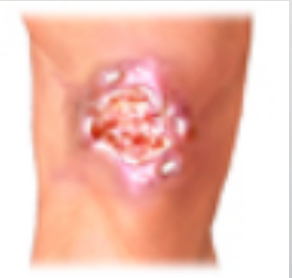
CREST

- Calcinosis: calcium deposits in the skin
- Raynaud's phenomenon
- Esophageal dismotylity
- Sclerodactily: thickening and thightening of the skin on the fingers and hands
- Telangiectasias: dilatation of capillaries causing red marks onsurface of the skin









Focus

EPIDEMIOLOGY

Prevalence from 50 to 300 cases per 1 million persons

Incidence fron 2.3 to 22.8 cases per 1 million persons per year

Ratio Women- Men = 3-4:1

A increased susceptibility among blacks

60% Limited cutaneous SSc

35% Diffuse cutaneous SSc

5% SSc sine scleroderma

Gabrielli et al, N Engl J Med 2009; 360: 1989-2003.
Hinchcliff et al, Am Fam Physician 2008; 78(8): 961-8

Focus

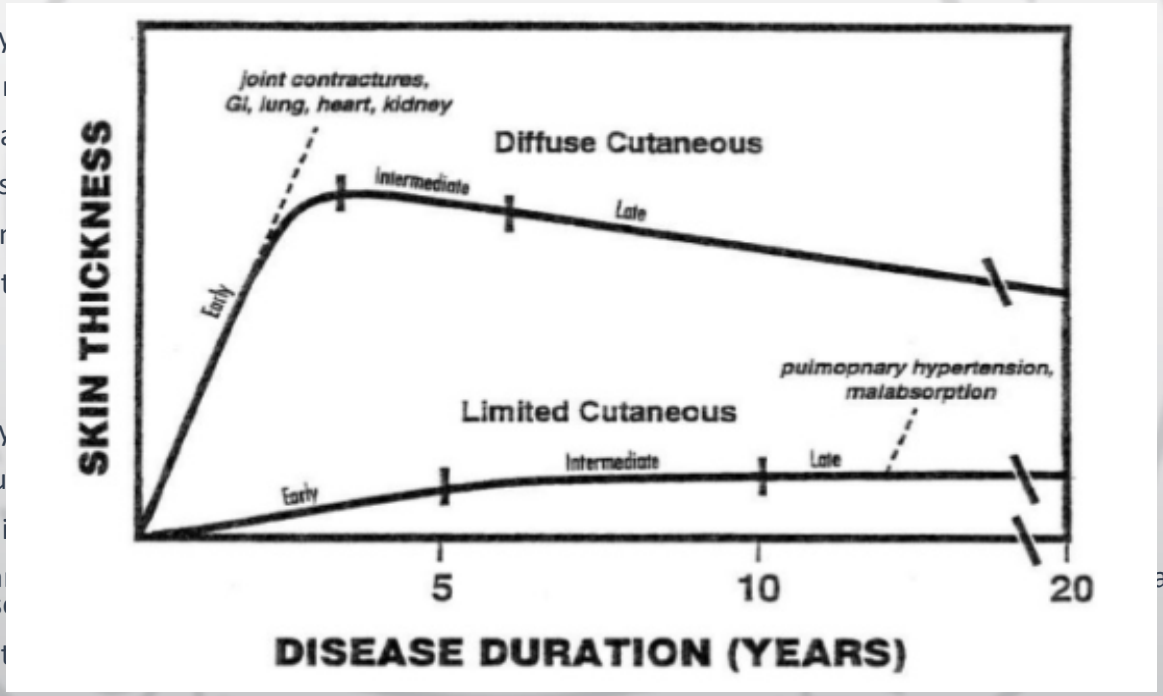
LIMITED VS DIFFUSE

LSSc

- Ray
- Ski
- Dil
- A s
- Rer
- Ant

DSSc

- Ray
- Tru
- Nai
- Ea
  dis
- Ant



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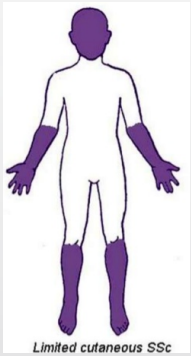


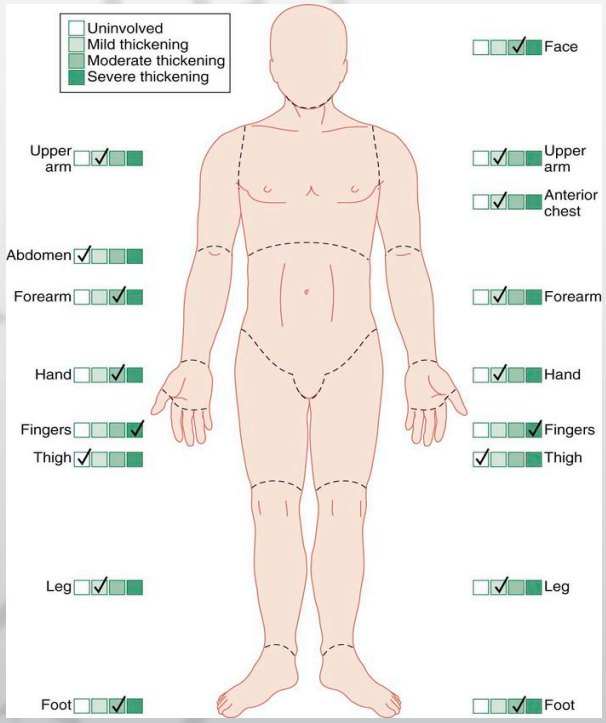
Le Roy et al, J Rheumatol 1988; 15(2): 202-5c
Medsger et al; Rheum Dis N Am 2003; 29(2): 255-73

Focus

SKIN THICKENING IN SSC

Modified Rodnan Skin Score

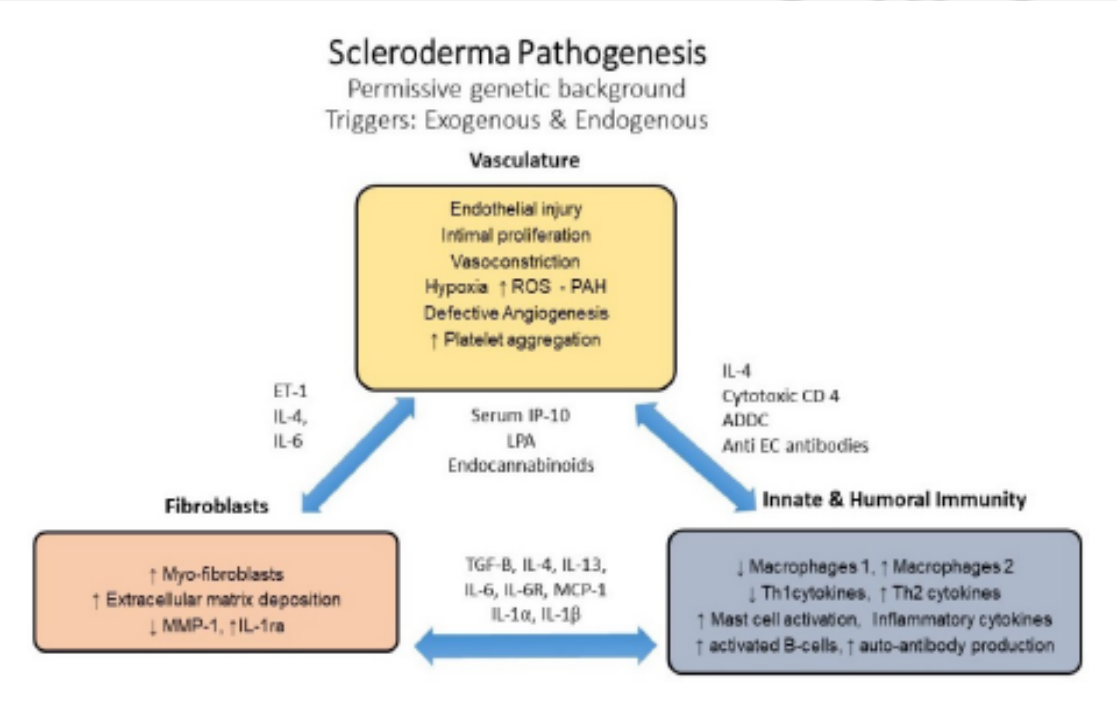
- Validated measure of skin thickening in clinical trials
- Correlates with internal organ involvement and survival in diffuse patients
- Thickening assessed in 17 body areas: face/neck, anterior chest, abdomen, bilateral fingers,, dorsal hands, forearms, upper arms, feet, lower legs and thighs
- Each area scored and summed for total score (0-51):
  - ***0 = normal;***
  - ***1 = mild thickening,***
  - ***2 = moderate thickening, unable to move***
  - ***3 = hidebound, unable to pinch***



Kaldas et al; Rheumatology 2009; 48: 1143-46
Clements et al; Arthritis Rheum 2000; 43: 2445-54

Focus

PATHOGENESIS



McFarlane et al., Rheumatology 2018; 8(1)

Focus

AUTOANTIBODIES

Antinuclear antibody (ANA)

- Positive in 95% of patients with SSc

Antitopoisomerase I (anti Scl-70) antibody

- Associated with diffuse cutaneous SSc
- Higher risk of severe intertitial lung disease

Anticentromere antibody (ACA)

- Usually associated with limited cutaneous SSc
- Only 5% of patients with dcSSc

Anti RNA polymerase III antibody

- In patients with dcSSc
- Associated with rapidly progressive skin involvement and an increased risk for scleroderma renal crisis

Anti Scl 70, ACA, anti RNA polymerase III are highly specific (>99.5%) but are moderately sensitive (20 to 50%).

The autoantibodies are almost always mutually exclusive.

Focus

CLASSIFICATION CRITERIA

Reference	SSc classification criteria
ARA criteria 1980 [2]	1 major criterion: proximal scleroderma defined as tightening, thickening, and non-pitting induration proximal to the metacarpophalangeal or metatrasophalangeal joints or 2 or more minor criteria: (1) sclerodactyly, (2) digital pitting scars of the fingertips or loss of the substance of the distal pad, (3) bilateral basilar pulmonary fibrosis
Nadashkevich et al. 2004 [4, 5]	Any 3 of ABCDCREST: (1) *a*utoantibodies to: centromere proteins, ScL-70 (topoisomerase-1, fibrillin), (2) *b*ibasilar pulmonary fibrosis, (3) *c*ontractures of the digital joints or prayer sign, (4) *d*ermal thickening proximal to the wrists, (5) *c*alcinosis cutis, (6) *R*aynaud's phenomenon, (7) *e*sophageal distal hypomotility or reflux esophagitis, (8) *s*clerodactyly or non-pitting digital edema, (9) *t*elangiectasia
LeRoy and Medsger 2001 [6]	Limited SSc (lSSc) (1) Raynaud's phenomenon And (2) abnormal wide-field nailfold capillaroscopy or (3) SSc selective autoantibodies; limited cutaneous (lcSSc); Criteria for lSSc and cutaneous changes distal to the elbow, knees, and clavicles; Diffuse cutaneous (dcSSc); Criteria for lSSc and cutaneous involvement of the arms, chest, abdomen, back, or thighs
Avouac et al. 2011, VEDOSS criteria [7]	(1) Raynaud's phenomenon, (2) puffy fingers, (3) antinuclear antibodies, and (4) capillaroscopy or (5) SSc-specific antibodies

Johnson; Curr Rheumatol Rep 2015; 17: 32-8

Focus

NEW ACR EULAR CRITERIA 2013

Item	Sub-items(s)	Weight/score †
Skin thickening of the fingers of both hands extending proximal to the metacarpophalangeal joints *(sufficient criterion)*	-	9
Skin thickening of the fingers *(only count the higher score)*	Puffy fingers	2
	Sclerodactyly of the fingers (distal to the metacarpophalangeal joints but proximal to the proximal interphalangeal joints)	4
Fingertip lesions *(only count the higher score)*	Digital tip ulcers	2
	Fingertip pitting scars	3
Telangiectasia	-	2
Abnormal nailfold capillaries	-	2
Pulmonary arterial hypertension and/or interstitial lung disease *(maximum score is 2)*	Pulmonary arterial hypertension	2
	Interstitial lung disease	2
Raynaud's phenomenon	-	3
SSc-related autoantibodies (anticentromere, anti–topoisomerase I [anti–Scl-70], anti–RNA polymerase III) *(maximum score is 3)*	Anticentromere 3 Anti–topoisomerase I Anti–RNA polymerase III	3

* The criteria are not applicable to patients with skin thickening sparing the fingers or to patients who have a scleroderma-like disorder that better explains their manifestations (e.g., nephrogenic sclerosing fibrosis, generalized morphea, eosinophilic fasciitis, scleredema diabeticorum, scleromyxedema, erythromyalgia, porphyria, lichen sclerosis, graft-versus-host disease, diabetic cheiroarthropathy).

† The total score is determined by adding the maximum weight (score) in each category.
Patients with a total score of ≥ 9 are classified as having definite scleroderma.

Sensitivity 91% Specificity 92%

1980
- SE 0.75
- SP 0.72

2001
- SE 0.75
- SP 0.78

2013
- SE 0.91
- SP 0.92

Van de Hoogen et al; Arthritis and Rheumatism 2013; 64: 2737-47

Focus

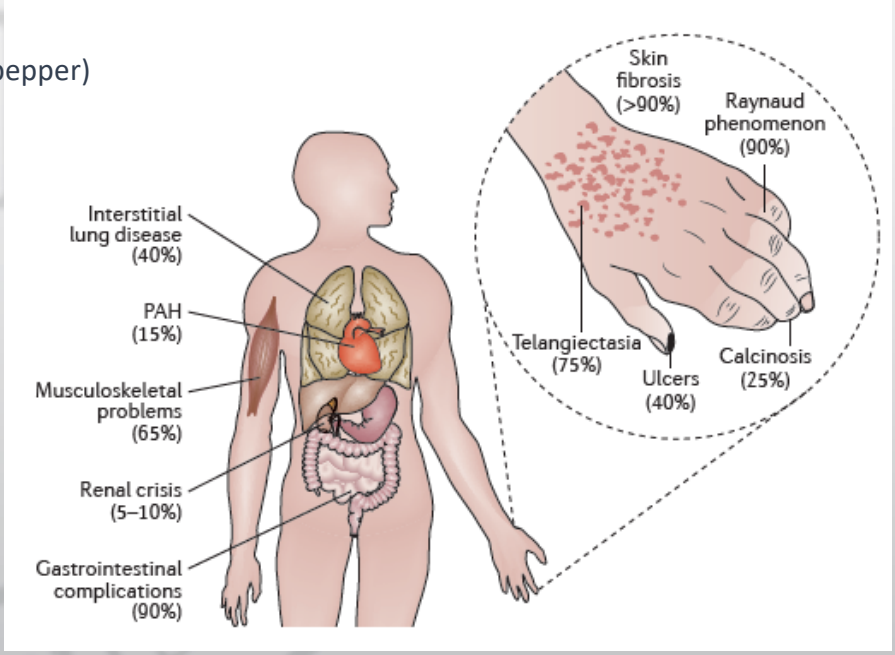
CLINICAL MANIFESTATIONS

SKIN INVOLVEMENT

- Pruritus
- Edema
- Skin hyperpogmentation or depigmentation (salt and pepper)
- Loss of appendicular hair
- Sclerodactyly
- Digital ulcers
- Pitting at the fingertips
- Telangiectasia
- Calcinosis cutis

VASCULAR DISEASE

- Raynaud phenomenon
- Thromboemobolic disease



Hinchcliff et al, Am Fam Physician 2008; 78(8): 961-8

Focus

CLINICAL MANIFESTATIONS

PULMONARY INVOLVEMENT

- Interstitial lung disease
- Pulmonary vascular disease (PAH)

RENAL DISEASE

- Scleroderma renal crisis

CARDIAC DISEASE

- Pericarditis; pericardial effusion
- Myocardial fibrosis, myocarditis
- Heart failure
- Myocardial infarction
- Conduction disturbances/ arrhythmias

MUSCULOSKELETAL DISEASE

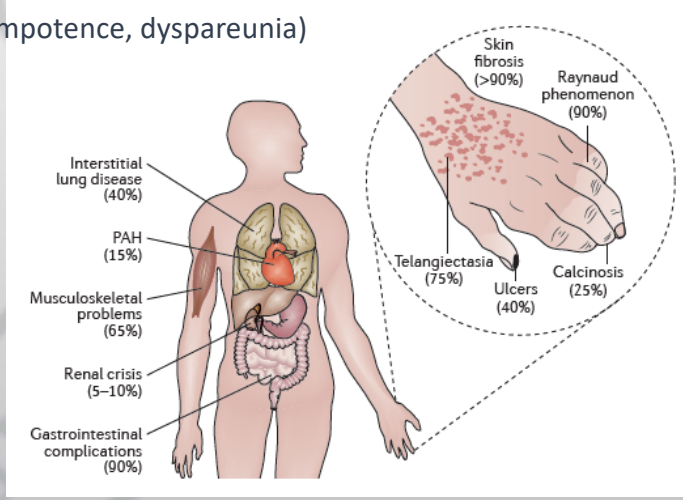
- Swelling of the hands, arthralgia, myalgia, fatigue

NEUROMUSCULAR INVOLVEMENT

- Cranial, entrapment, peripheral cutaneous and autonomic neurophathies
- Myopathy and infiammmatory myositis
- Headache, seizures, stroke, radiculopathy, myelopathy

GENITOURINARY

- Sexual Dysfuction (impotence, dyspareunia)



Hinchcliff et al, Am Fam Physician 2008; 78(8): 961-8

Focus

GASTROINTESTINAL MANIFESTATIONS

- 90% of patients with SSc have some degree of GI involvement (Schmeiser et al. 98.9%)
- One half are symptomatic
- Equal frequency among patients with the diffuse and limited subtypes of SSc
- Any part of the GI tract may be involved (Esophagus +++)

SJOGREN THEORY: SSc affects GI tract by an orderly series of steps that result in progressive dysfuction

1. Neural dysfunction, a consequence of collagen deposits causing vascular derangement, compression of the nerves, or autoimmune-mediated injury
2. Smooth muscle atrophy (most patients present with symptoms at this stage)
3. Muscle fibrosis, the muscle is unable of responding to stimuli and pharmacologic restoration of funcion is no longer possible

GI HISTOPATHOLOGY:

1. *Smooth muscle atrophy*
2. *Gut wall fibrosis*

Tian et al, WJG 201; 19(41): 7062-8
Sjogren, Arthritis Rheum 1994; 37: 1265-82

Focus

OROPHARYNGEAL INVOLVEMENT

OROPHARYNGEAL DYSPHAGIA (25%)

Involvement of the oral an perioral tissues

- Reduced oral aperture from skin thickening, rigidity and thinning of the soft palate and oral mucosa
- Resorption of alveolar bone and malalignment of teeth

May lead to

- swalloning difficulties,
- xerostomia
- sensation of residual food remaining in pharinx,
- nasal regurgutation
- coughing after swallowing
- oral leakage, retention and aspiration

Tian et al, WJG 201; 19(41): 7062-8
Forbes et al, Rheumatology 2008; 48: 36-39
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

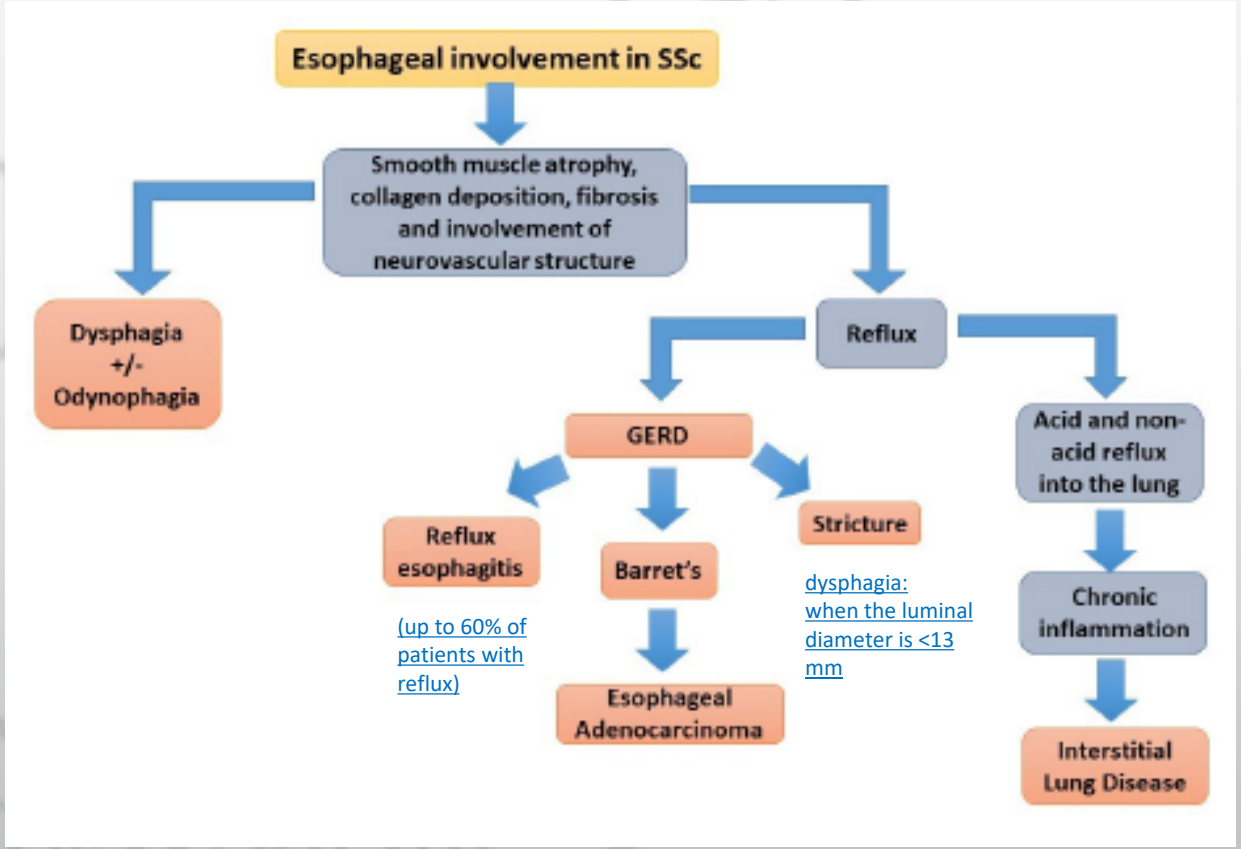
ESOPHAGEAL INVOLVEMENT

50-80% of patients with SSc; the most common target

Atrophy of the smooth muscle in the lower two-thirds of the tubular esophagus and the lower esophageal spincter

Abnormal esophageal motility present in 70-96% (manometry); 30% of these patients are asymptomatic

GERD severity in associated with ILD



Tian et al, WJG 201; 19(41): 7062-8
Forbes et al, Rheumatology 2008; 48: 36-39
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

ESOPHAGEAL INVOLVEMENT

UPPER ENDOSCOPY

ESOPHAGEAL MANOMETRY

- Hypotensive lower esophageal sphincter with a low resting sphincter pressure (<10 mmHg)
- Low amplitude (<30 mmHg) contractions in the distal smooth muscle portion of the esophagus or aperistalsis → uneffective esophageal transit

BARIUM ESOPHAGRAM

- Air- filled esophagus on plain radiograph, impaired or absent peristalsis with dilatation of the esophagus, and a rapid flow of contrast medium in upright position

Focus

GASTRIC INVOLVEMENT

GASTROPARESIS

- Rare
- The result of chronic gastric motility alterations → delayed gastric emptying or complete gastric paralysis
- Abdominal pain, early saziety, bloating, nausea, vomiting, which may cause weight loss and nutritional deficiences
- Delayed gastring emptying can make GERD even worse

GASTRIC ANTRAL VENOUS ECTASIA (GAVE; Watermelon stomach)

- 5.7-14%
- Diagnosis made by upper endoscopy: multiple, parallel longitufdinal columns of red vessels within the gastric antrum radiating to the pylorus, resembling the stripes on a watermelon.
- Acute bleeding, low grade GI bleeding, iron deficiency anemia

Tian et al, WJG 201; 19(41): 7062-8
Forbes et al, Rheumatology 2008; 48: 36-39
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

SMALL INTESTINAL INVOLVEMENT

The second most common target inSSc (20-60%)

Pathophysiology: reduced peristalsis → stasis and intestinal dilatation → symptoms

SIBO (Small intestinal Bacterial overgrowth)

- 10-30%, > LcSSc
- Presence of more than 1 x 10^5 organisms per millimeter of duodenal apirate fluid
- Nonspecific symptoms: bloating, flatulence or abdominal discomfort, diarrhea (stasis)
- Malabsorption

HYPOMOTILITY and INTESTINAL PSEUDO-OBSTRUCTION

- Reccurent or chronic abdominal pain and bloating
- Acute symptoms of abdominail pain, nausea and vomiting with marked abdominal distension

Tian et al, WJG 201; 19(41): 7062-8
Forbes et al, Rheumatology 2008; 48: 36-39
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

SMALL INTESTINAL INVOLVEMENT

PCI (PneumatosiS cystoides intestinalis)

- Intramural gas in GI tract
- Complications: intestinal ischemia and pneumoperitoneums (rupture of air filled cysts in the bowel)

MALNUTRITION

- 15-20%, associated with a higher disease activity
- Multifactorial:
  - loss of appetite
  - physical challenges of eating
  - Gastroparesis
  - malabsorption secondary to SIBO → *bacteria overgrowth competes with the host for nutrition and causes malabsorption*
  - oral symptoms
  - drug side effects

Tian et al, WJG 201; 19(41): 7062-8
Forbes et al, Rheumatology 2008; 48: 36-39
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

COLON AND ANORECTAL INVOLVEMENT

10-50%

Pathophysiology: gastrocolic reflex in which ingested food leads to significnt spike and contractile activity in the colon is absent early in SSc

COLONIC INERTIA

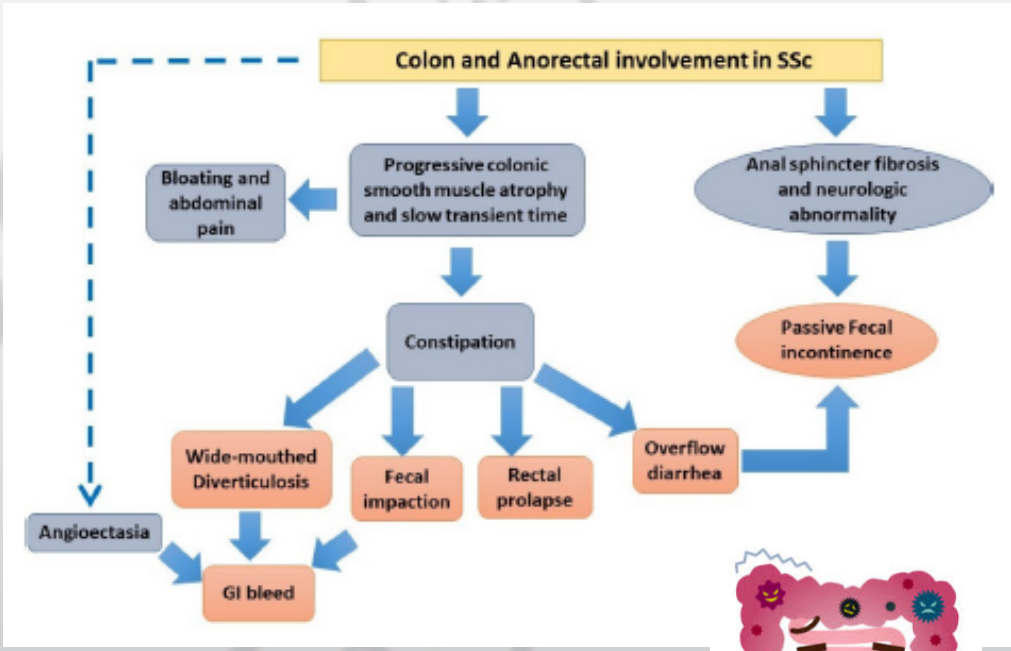
- Slow transit → constipation, bloating, abdominal pain

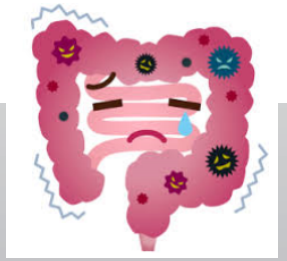
DIARRHEA

- Multifactorial: SIBO, pancreatic exocrine insufficiency or overflow from constipation

FECAL INCONTINENCE

- Result from involvement of the anal sphincter
- Manometric abnormalities: absent or diminished rectoanal inhibitory reflex and decrease in internal anal resting pressure





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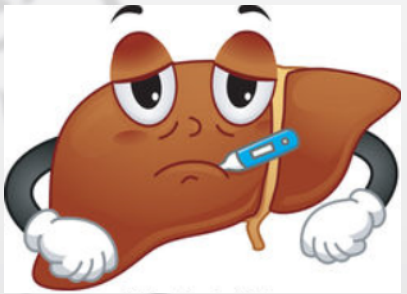
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

LIVER, BILIARY TREE AND PANCREATIC INVOLVEMENT

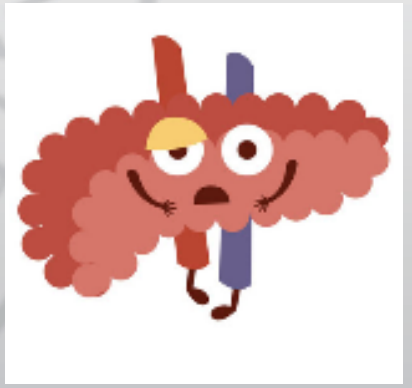
PBC

- occurs in 2-18% of patients with SSc (Lc SSc)
- patients with lcSSc tend to have a slower progression of hepatic disease compared with patients with PBC but without SSc



PANCREATIC EXOCRINE INSUFFICIENCY

- maldigestion of fat and protein leading to steatorrhea and weight loss
- steatorrhea occur until approximately 90% of glandular fuction has been lost



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Forbes et al, Rheumatology 2008; 48: 36-39
Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

Focus

THERAPY

Location	Features	Investigations	Complications	Treatments
Mouth	– Limitation of opening contributes to poor dental hygiene – Atrophy of the lips and gums	– Measurement of maximal interdental and interlabial distance	– Dental malocclusion and dysfunction of masticator system – Dental caries	Physical therapy Dental hygiene with application of fluorine
Salivary glands	– Association with Sjögren's syndrome reducing the salivary flow	– Measurement of stimulated salivary flux – Scoring analysis of salivary gland scintigraphy – Salivary labial gland biopsy	– Dental caries	– Humidification of the mouth – Chewing gum – Non-selective or selective muscarinic receptor agonist – Artificial saliva
Esophagus	– Gastro-esophageal reflux (GER) due to impaired esophageal clearance and reduced low esophageal sphincter pressure – Epithelial changes resulting from chronic acid GER	Endoscopy is the better examination to evaluate the presence of esophagitis or Barret's metaplasia Manometry pH metry	– Esophagitis – Esophageal erosion, stenosis or bleeding – Barret's esophagus – Adenocarcinoma – Recurrent pneumonia	– Behavior modification (elevation of head during sleep) – Proton pump inhibitor – Prokinetic drugs (domperidone, cisapride and erythromycin) In severe and resistant GER – Surgical Nissen fundoplication or laparoscopic fundoplication

GERD

Lifestyle and dietary modification

Calcium channel blokers and anticholinergic agents can potentially worsen reflux

PPI

H2 receptor antagonist

Prokinetic agents

Surgery (?)

Esophageal motility disorders → Prokinetic agents

Stricture → endoscopic dilation

Tiev et al, Autoimmunity Reviews 2011; 11: 68-73

F ♀
65 y.o.

TO SUM UP

SUM MA RY

Distal esophageal stricture in SSc

→Peptic stricture (GERD)?

→Neoplastic stricture (Barrett)?

Pulmonary involvement GERD related?

Gastroesophageal Reflux and Pulmonary Fibrosis in Scleroderma

A Study Using pH-Impedance Monitoring

Edoardo Savarino[1], Marco Bazzica[2], Patrizia Zentilin[1], Daniel Pohl[3], Andrea Parodi[1], Giuseppe Cittadini[4], Simone Negrini[2], Francesco Indiveri[2], Radu Tutuian[3], Vincenzo Savarino[1], and Massimo Ghio[2]

Measurements and Main Results: Forty consecutive patients with SSc (35 female; mean age, 53 yr; range, 24–71; 15 patients with diffuse and 25 with limited SSc) were investigated; 18 (45%) patients with SSc had pulmonary fibrosis (HRCT score ≥ 7). Patients with SSc with ILD had higher ($P < 0.01$) esophageal acid exposure (10.3 [7.5–15] vs. 5.2 [1.5–11]), higher ($P < 0.01$) number of acid (41 [31–58] vs. 19 [10–23]) and nonacid (25 [20–35] vs. 17 [11–19]) reflux episodes, and higher ($P < 0.01$) number of reflux episodes reaching the proximal esophagus (42.5 [31–54] vs. 15 [8–22]) compared with patients with SSc with normal HRCT scores. Pulmonary fibrosis scores (HRCT score) correlated well with the number of reflux episodes in the distal ($r^2 = 0.637$) and proximal ($r^2 = 0.644$) esophagus.

Conclusions: Patients with SSc with ILD have more severe reflux (i.e., more reflux episodes and more reflux reaching the proximal esophagus). Whether or not the development of ILD in patients with SSc can be prevented by reflux-reducing treatments needs to be investigated.

Interstitial lung disease (ILD) is reported in 57–86% of patients with SSc

GERD is a risk factor for ILD

S<v<rino et al, Am j Respr Crit Care Med 2009; 179: 408-13

Focus

SSC AND CANCER

LUNG CANCER

	SIR	Number of patients	Years of follow-up
Kuo et al [25]	4.2	2,053	1996 - 2008
Hill et al [26]	5.9	441	1993 - 2000
Rosenthal et al [27]	4.9	917	1965 - 1983
Chatterjee et al [28]	1.23	538	1973 - 2004

BREAST CANCER

increased risk (OR=2.6), but only few studies have suggested a possible causal relationship between the two

ESOPHAGEAL ADENOCARCINOMA

Zeineddine et al, J Clin Med Res 2016; 8(9): 625-32

Focus

ESOPHAGEAL ADENOCARCINOMA

Barrett's esophagus (due to crtonic reflux), particularly with high grade dysplasia, is the most risk factor

BE = presence of intestinal architecture in the lower esophagus dysplaying a villiform columnar-lined mucosa with goblet cells

Only a few studies have determined the prevalence of BE and EAC in SSc with conflicting results

Incidence of BE 6.8-12.7% in SSc (population risk of BE <1%)

Wipff 2005: Barrett's risk in SSc

- 14/110 (12.7%)
- Dysplasia 3/14

Wipff 2011: Cancer risk in SSc

- 50 individuals with BE
- 3 years of follow up

Wipff et al, Rheumathology 2011; 50: 1440-45
Wipff et al, Arthritis and Rheumatism 2005; 52: 2882-8

Focus

ESOPHAGEAL ADENOCARCINOMA

Outcomes of Barrett's oesophagus related to systemic sclerosis: a 3-year EULAR Scleroderma Trials and Research prospective follow-up study

Julien Wipff[1], Romain Coriat[2], Michela Masciocchi[3], Paola Caramaschi[4], Chris T. Derk[5], Eric Hachulla[6], Valeria Riccieri[7], Luc Mouthon[8], Dorota Krasowska[9], Lidia P. Ananyeva[10], André Kahan[1], Marco Matucci-Cerinic[11], Stanislas Chaussade[2] and Yannick Allanore[1]

Abstract

Objective. Barrett's oesophagus (BE) is the major risk factor for oesophageal adenocarcinoma (EAC). SSc is associated with an increased risk of BE related to chronic reflux. The aim of this study is to determine the outcomes of BE and estimate the EAC risk in SSc patients over a 3-year prospective study.

Methods. SSc patients were recruited through EUSTAR network centres. Inclusion criterion was a recent histological finding of BE. The patients were then prospectively followed and, as recommended, a second oesophageal endoscopy was performed according to the presence of BE-related dysplasia at baseline.

Results. A total of 50 SSc patients with BE (40 without and 10 with dysplasia) were included and 46 completed the follow-up (138 patient-years). During the 3-year follow-up, 4 of the 46 BE patients (3% per year) were diagnosed with high-grade dysplasia/EAC, of which one developed cardial EAC. EAC incidence in the BE subgroup with dysplasia increased to 4% per year compared with the absence of EAC cases in the BE subgroup without dysplasia at baseline.

Conclusion. Our results, in accordance with previous published data suggesting an increased risk of EAC or cardial adenocarcinoma in SSc, highlight the need for accurate follow-up of BE SSc patients at risk of developing adenocarcinoma.

Wipff et al, Rheumathology 2011; 50: 1440-45

Incidence of EAC in SSc with BE: 0.7% per year (vs 0.45% per year in BE population)

No patients developed EAC if BE without dysplasia occurred at baseline

Focus

ESOPHAGEAL ADENOCARCINOMA

ENDOSCOPIC SURVILLANCE GUIDELINES

STATEMENT 7

Surveillance intervals for nondysplastic BE should be stra-
tified according to the lengt
i. Irregular Z-line/columna
endoscopic surveillance
ii. Maximum extent of BE ≥ 1
iii. Maximum extent of BE ≥
Patients with BE with a ma
be referred for surveillance
center.
If a patient has reached 75 y
her last surveillance endosc
dence of dysplasia, no subs
pies should be performed.

STATEMENT 12

Patients with LGD on random biopsies confirmed by a
second expert GI pathologis
expert center. A surveillanc
confirmed LGD diagnosis is
i. If no dysplasia is found at
interval can be broadened
quent endoscopies negative
veillance for patients with n
ated.
ii. If a confirmed diagnosis
quent endoscopies, endosc
fered.

STATEMENT 13

Patients with HGD confirmed by a second expert GI pathologist should be referred to a BE expert center. In the expert center, a high-definition endoscopy should be repeated according to the following guidelines.
i. All visible abnormalities should be removed by endoscopic resection techniques for adequate histopathological staging.
ii. If no lesions suspicious for dysplasia are seen, random 4-quadrant biopsies should be taken; if these biopsies are negative for dysplasia, endoscopy should be repeated at 3 months. If these biopsies confirm the presence of HGD, endoscopic ablation is recommended, preferably with RFA.

Weusten et al, Endoscopy, 2017;49(2):191-198

3°

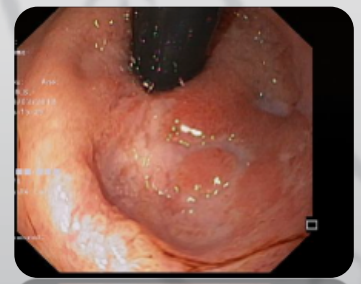
US ENDOSCOPY

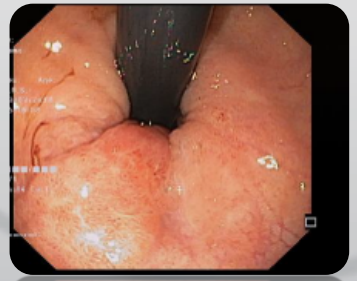
13 MAR 18

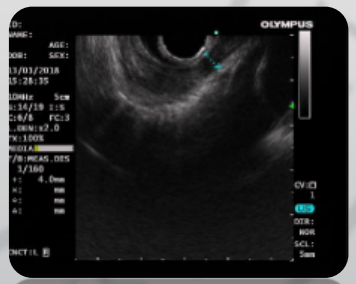
Alla preliminare EGDS si conferma stenosi con mucosa congesta a livello di esofago inferiore al passaggio esofago-gastrico con dilatazione dell'esofago a monte ed ernia jatale sottostante (biopsie multiple con pinza).

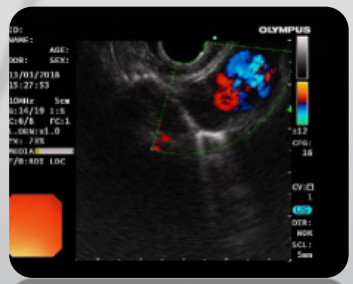
L'esame ecoendoscopico viene condotto unicamente dal versante sovraanastomotico non consentendo la stenosi il passaggio dello strumento. A tale livello si evidenzia solo lieve ispessimento parietale (3,9 mm) a profili lisci in assenza di chiare nodulazioni. Non linfoadenopatie mediastiniche.

Conclusioni: stenosi in soggetto con sclerodermia in corso di definizione istologica.









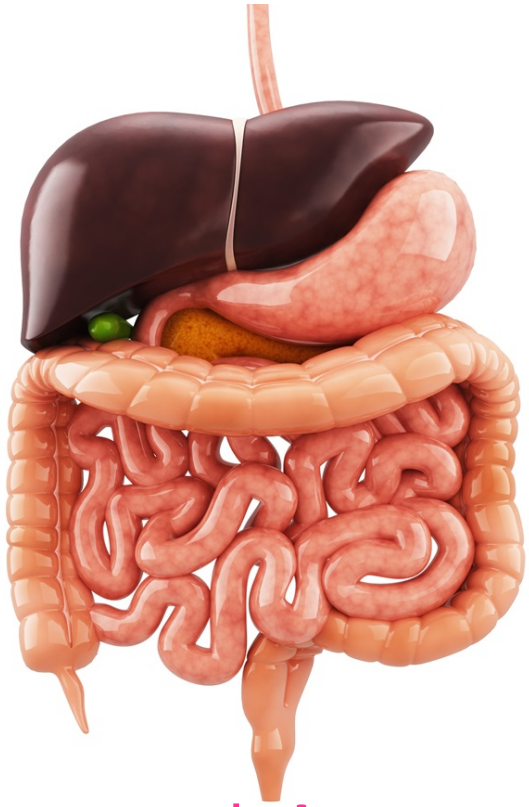
3°

HYSTOLOGICAL EXAM

13 MAR 18

Campioni di mucosa della giunzione squamo-colonnare e di tipo gastrico con paracheratosi e iperplasia del compartimento proliferativo basale dell'epitelio pavimentoso, flogosi linfomonocitaria (+--), edema e angiectasie della lamina propria, associata a metaplasia intestinale delle ghiandole (MI +++).

→ **DILATATION**



THANKS :-

Dott.ssa ***Costanza Orlando***