•ESC/ERS Guidelines and DETECT Algorithm Raccomandation in Pulmonary Artery Hypertension associated to Scleroderma. A real life comparison.

Walter Serra, Federica Lumetti, Flavio Mozzani, Giovanni Del Sante, Maria Alberta Cattabiani, Alarico Ariani

ESC Guidelines 2009 on PH:

1 Pulmonary arterial hypertension (PAH)

- 1.1 Idiopathic
- 1.2 Heritable
  - 1.2.1 BMPR2
  - 1.2.2 ALK1, endoglin (with or without hereditary haemorrhagic telangiectasia)
  - 1.2.3 Unknown
- 1.3 Drugs and toxins induced
- 1.4 Associated with (APAH)
  - 1.4.1 Connective tissue diseases
  - 1.4.2 HIV infection
  - 1.4.3 Portal hypertension
  - 1.4.4 Congenital heart disease
  - 1.4.5 Schistosomiasis
  - 1.4.6 Chronic haemolytic anaemia
- 1.5 Persistent pulmonary hypertension of the newborn

1' Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

2 Pulmonary hypertension due to left heart disease

- 2.1 Systolic dysfunction
- 2.2 Diastolic dysfunction
- 2.3 Valvular disease

3 Pulmonary hypertension due to lung diseases and/or hypoxaemia

- 3.1 Chronic obstructive pulmonary disease
- 3.2 Interstitial lung disease
- 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
- 3.4 Sleep-disordered breathing
- 3.5 Alveolar hypoventilation disorders
- 3.6 Chronic exposure to high altitude
- 3.7 Developmental abnormalities

4 Chronic thromboembolic pulmonary hypertension

5 PH with unclear and/or multifactorial mechanisms

- 5.1 Haematological disorders: myeloproliferative disorders, splenectomy.
- 5.2 Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, neurofibromatosis, vasculitis
- 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
- 5.4 Others: tumoural obstruction, fibrosing mediastinitis, chronic renal failure on dialysis

ALK-1 = activin receptor-like kinase 1 gene; APAH = associated pulmonary arterial hypertension; BMPR2 = bone morphogenetic protein receptor, type 2; HIV = human immunodeficiency virus; PAH = pulmonary arterial hypertension.

5th World Symposium on PH: Modified classification of PH

1. Pulmonary arterial hypertension
   - 1.1 Idiopathic PAH
   - 1.2 Heritable PAH
     - 1.2.1 BMPR2
     - 1.2.2 ALK1, ENG, SMAD9, CAV1, KCNK3
     - 1.2.3 Unknown
   - 1.3 Drug- and toxin-induced
   - 1.4 Associated with
     - 1.4.1 Connective tissue diseases
     - 1.4.2 HIV infection
     - 1.4.3 Portal hypertension
     - 1.4.4 Congenital heart disease
     - 1.4.5 Schistosomiasis

1' Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

1'' Persistent PH of the newborn (PPHN)

2. PH due to LHD
   - 2.1 LV systolic dysfunction
   - 2.2 LV diastolic dysfunction
   - 2.3 Valvular disease
   - 2.4 Congenital/acquired left heart inflow/outflow obstruction

3. PH due to lung diseases and/or hypoxia
   - 3.1 COPD
   - 3.2 Interstitial lung disease
   - 3.3 Other pulmonary diseases with mixed restrictive and obstructive pattern
   - 3.4 Sleep-disordered breathing
   - 3.5 Alveolar hypoventilation disorders
   - 3.6 Chronic exposure to high altitude
   - 3.7 Developmental lung diseases

4. CTEPH

5. PH with unclear multifactorial mechanisms
   - 5.1 Haematological disorders: chronic haemolytic anaemia, myeloproliferative disorders, splenectomy
   - 5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis
   - 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders
   - 5.4 Others: tumoural obstruction, fibrosing mediastinitis, chronic renal failure, segmental PH

COPD: chronic obstructive pulmonary disease; CTEPH: chronic thromboembolic pulmonary hypertension;

Simonneau G, *et al. J Am Coll Cardiol* 2013; 62:D34-41.

Vi sono pazienti a rischio di PAH" che richiedono uno screening

- ***Familiarità per PAH** (mutazione genetica BMPR2)*
- ***Malattie polmonari** (BPCO, enfisema, fibrosi, bronchiectasie)*
- ***Ipertensione portale***
- ***Pregresse embolie polmonari***
- ***Malattie del Tessuto Connettivo***
- ***Infezione da HIV***
- ***Cardiopatie congenite con shunt sx-dx***

M.Palazzini et al . G Ital Cardiol 2009;10(5):271-300
L.J.Rubin, W. Hopkins www.uptodate.com

Screening ESC/ERS Guidelines

Proposed criteria for referral for right heart catheterisation

TR velocity	sPAP	Additional signs of PH on echo	Symptoms
> 3.4 m/s	> 50 mmHg	Yes / No	Yes / No
2.9–3.4 m/s	37–50 mmHg	Yes / No	Yes
≤ 2.8 m/s	≤ 36 mmHg	Yes	Yes

- TR velocity forms the basis of ESC / ERS screening recommendations, but it…
  - …does not accurately reflect invasive pressures
  - …is not present in all patients[3,4]

ESC / ERS: European Society of Cardiology / European Respiratory Society; TR: tricuspid regurgitant jet

36; 20 October 2013

1. Steen VD and Medsger TA. *Ann Rheum Dis* 2007; 66:940-4.
2. Tyndall AJ, *et al. Ann Rheum Dis* 2010; 69:1809-15.
3. Fisher MR, *et al. Am J Respir Crit Care Med* 2009; 179:615-21.
4. Parent F, *et al. N Engl J Med* 2011; 365:44-53.

Echocardiography for PH in SSc

Early Detection of Pulmonary Arterial Hypertension in Systemic Sclerosis

A French Nationwide Prospective Multicenter Study

Eric Hachulla,[1] Virginie Gressin,[2] Loïc Guillevin,[3] Patrick Carpentier,[4] Elisabeth Diot,[5] Jean Sibilia,[6] André Kahan,[3] Jean Cabane,[7] Camille Francès,[8] David Launay,[1] Luc Mouthon,[3] Yannick Allanore,[3] Kiet Phong Tiev,[7] Pierre Clerson,[9] Pascal de Groote,[10] and Marc Humbert[11]

- 21 SSc expert centers

- 599 SSc patients (-29 known PAH = 570)

Reliability of prospective screening of SSc patients based on:

33 patients

- TVR >2.5 m/s in symptomatic patients (25 mmHg+RAP)

Right heart catheterization. All of the 33 patients in whom PAH was suspected underwent RHC. Among them, PAH was confirmed in 18 cases g+RAP).

45% of cases of echocardiographic diagnoses of PH were falsely positive!

Echocardiography may help detect pulmonary vasculopathy in the early stages of pulmonary artery hypertension associated with systemic sclerosis

Cardiovascular Ultrasound 2010, 8:25 doi:10.1186/1476-7120-8-25

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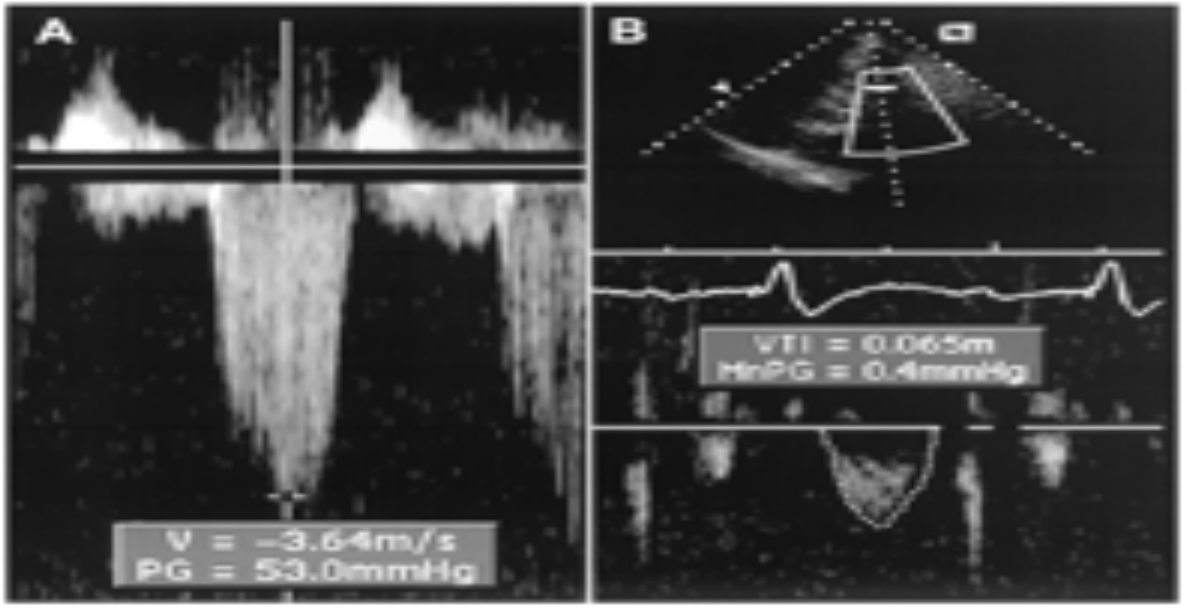
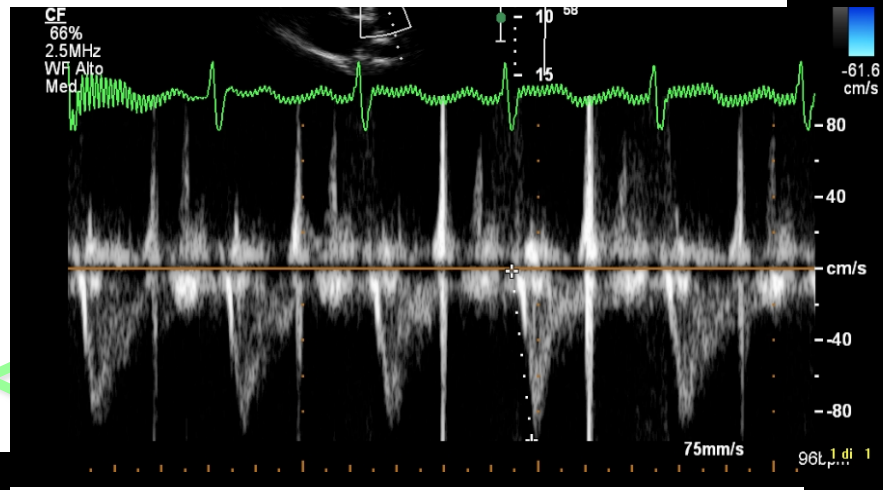
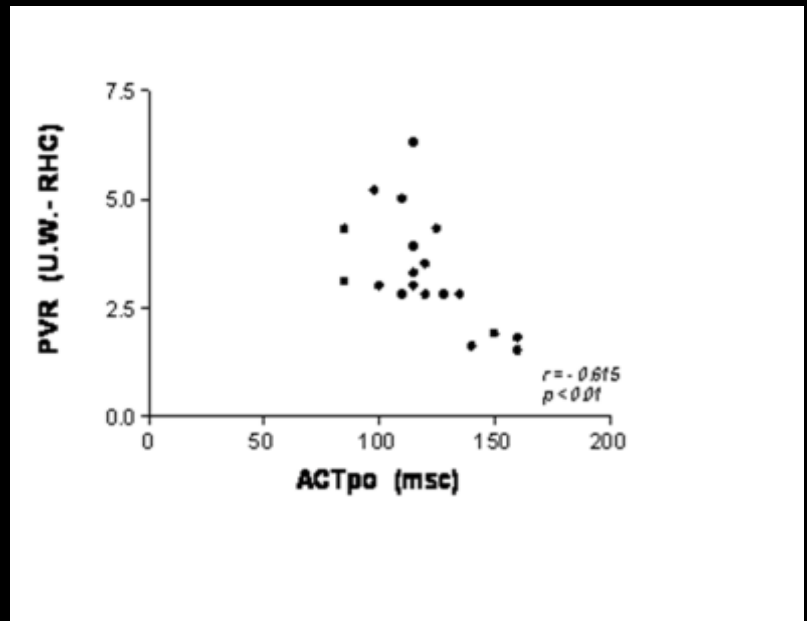
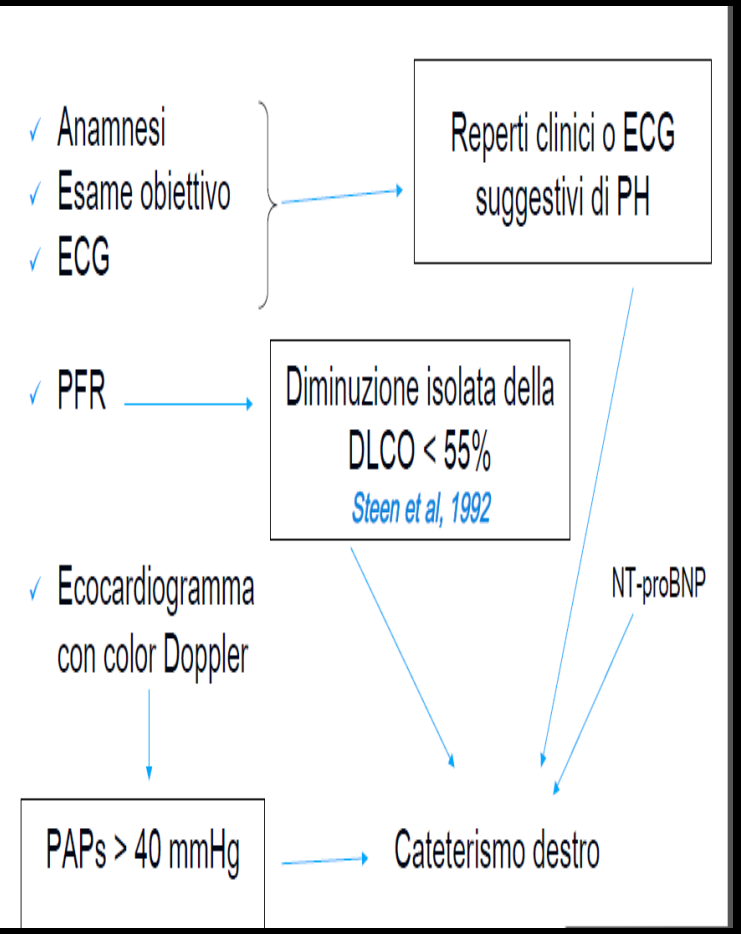
NUOVI PARAMETRI

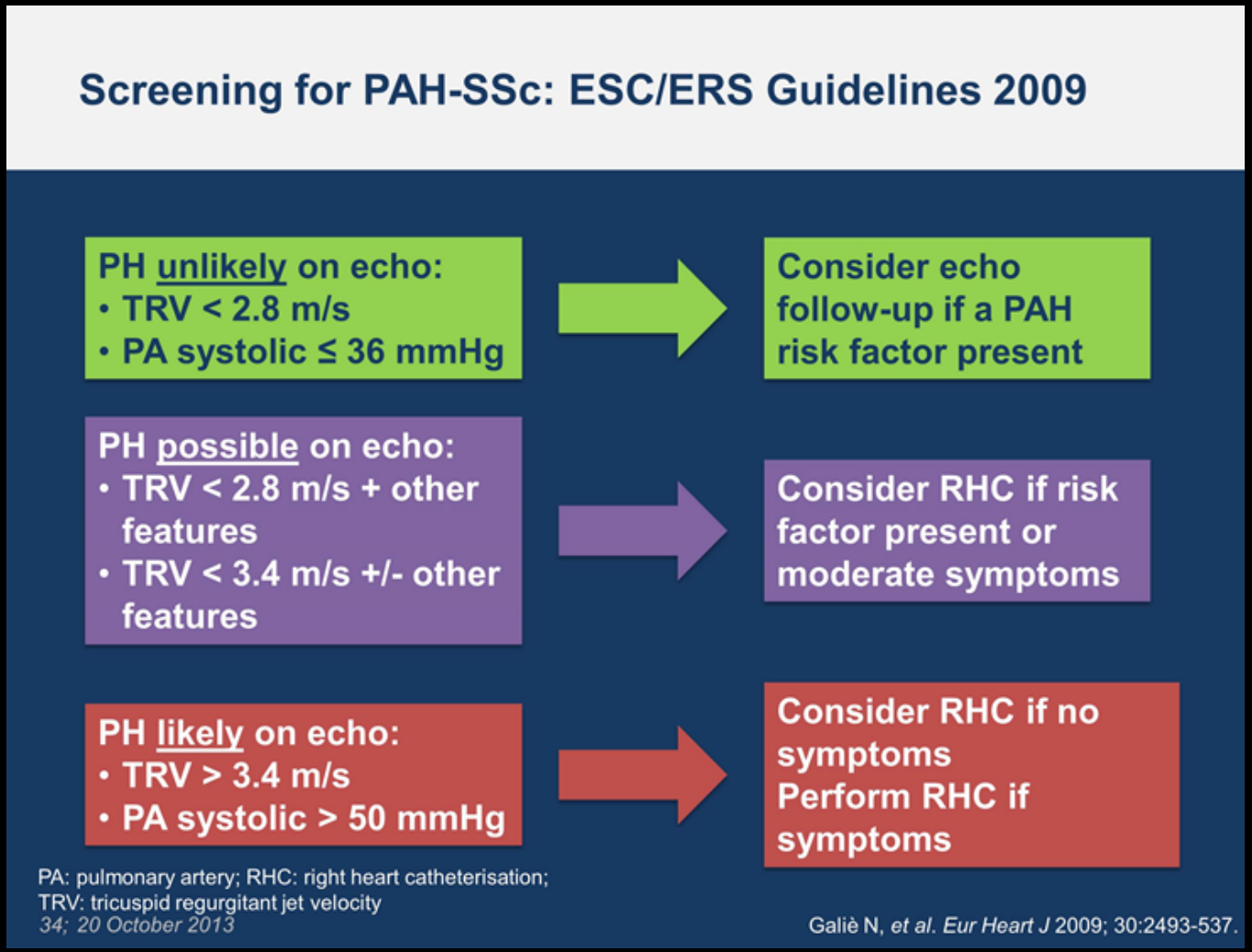




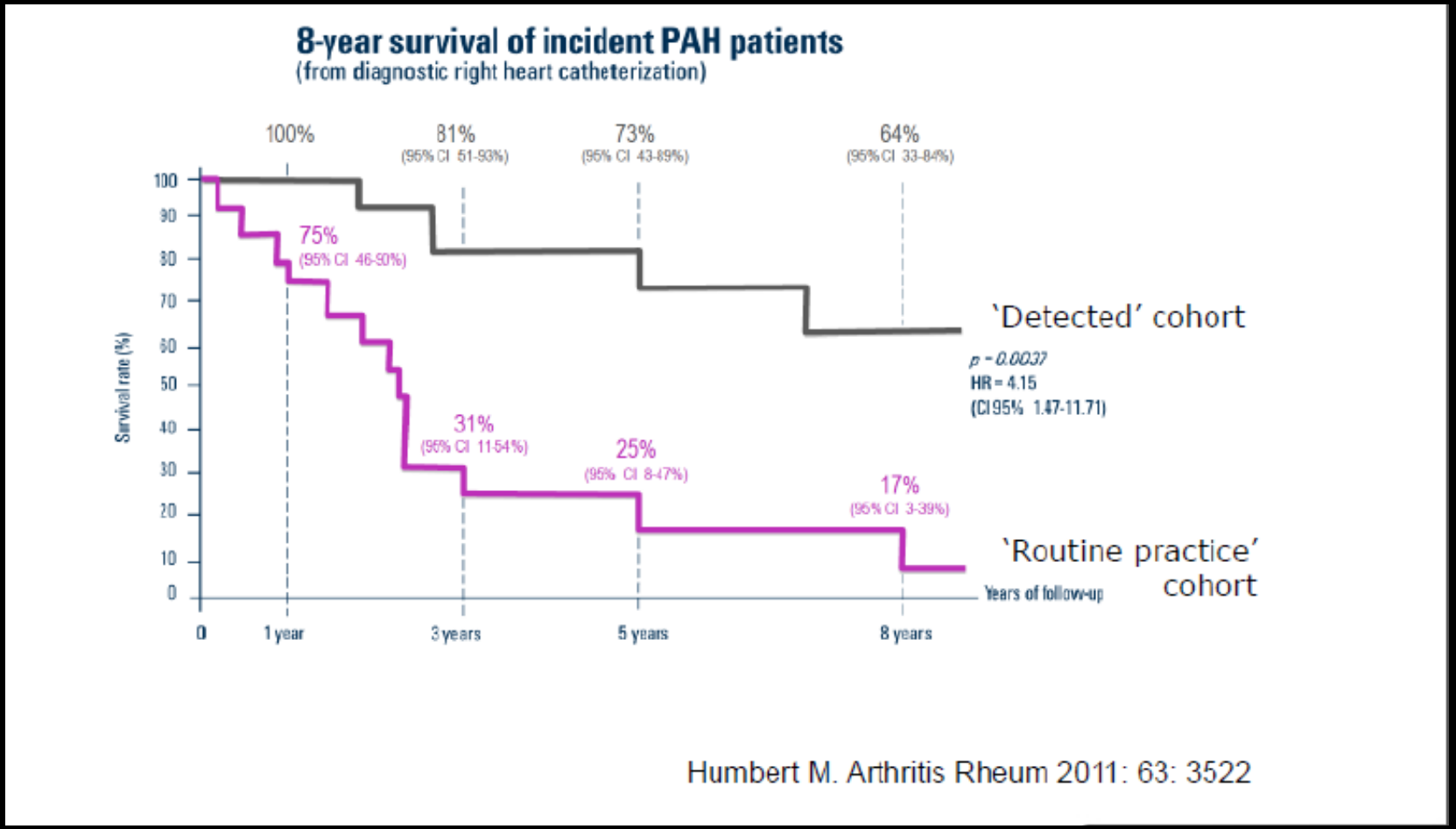


Early detection of PAH in SSc





Early detection of PAH in SSc



Humbert M. Arthritis Rheum 2011: 63: 3522

5th World Symposium on PH: Updated recommendations on screening for PAH

Recommendations on screening of high-risk populations for PAH
Annual screening for PAH is recommended in asymptomatic patients with the SSc spectrum of diseases
Screening should include a two-step approach using clinical assessment in the initial stage, followed by echocardiography and consideration of RHC in patients with abnormal findings*†
Screening programs for patients with SSc should be part of a scientific protocol, or a registry, whenever possible
Patients with SSc and other CTDs with clinical signs and symptoms of PH should be evaluated by RHC

*Based on the DETECT study

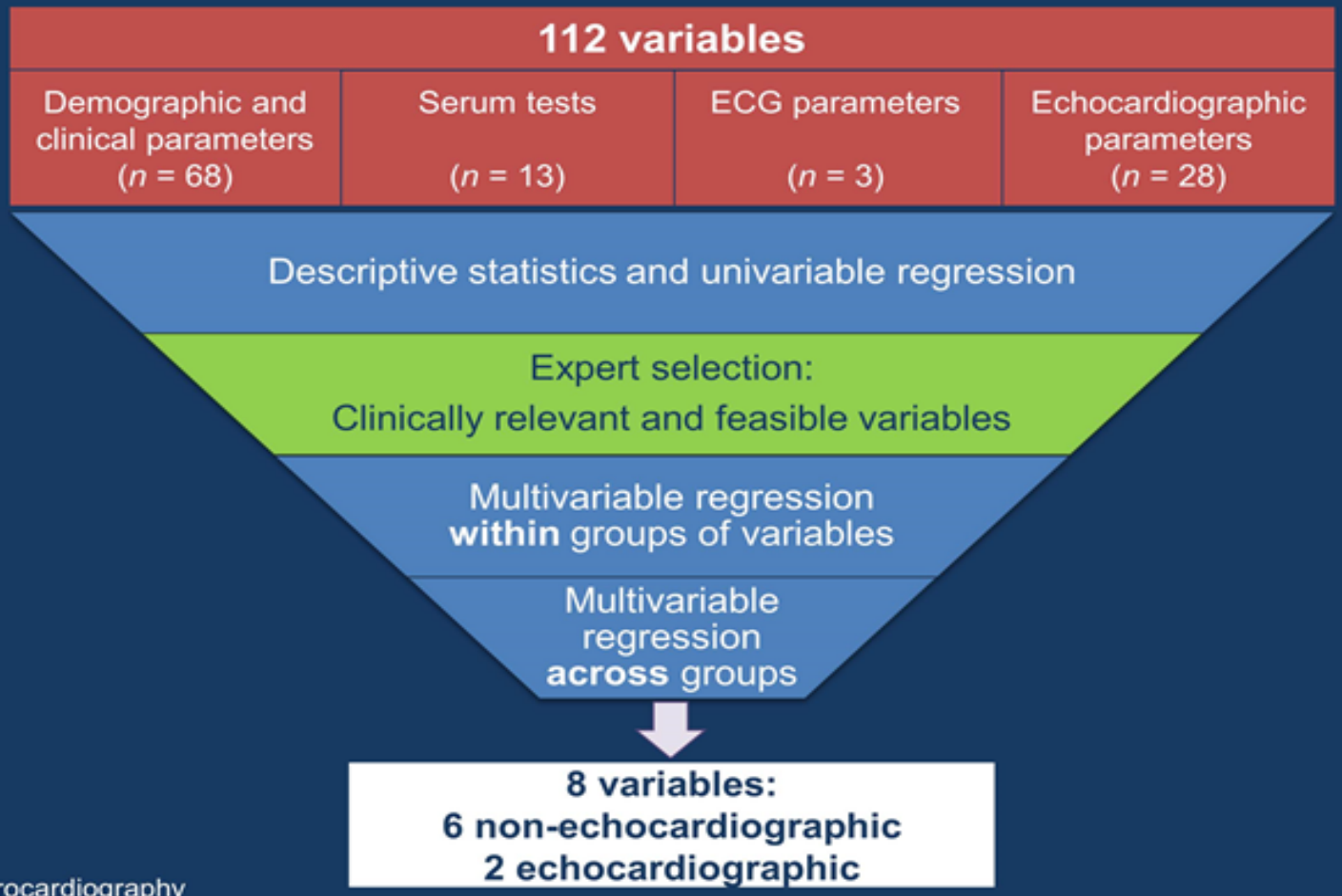
†There is a lack of data with DLCO > 60%

CTD: connective tissue disease; DLCO: carbon monoxide diffusing capacity; RHC: right heart catheterisation; SSc: systemic sclerosis

Adapted from Hoeper MM, *et al. J Am Coll Cardiol* 2013; 62:D42-50.

*Coghlan JG, *et al. Ann Rheum Dis* 2013; 73:1340-9.

Selection of screening variables in the DETECT study

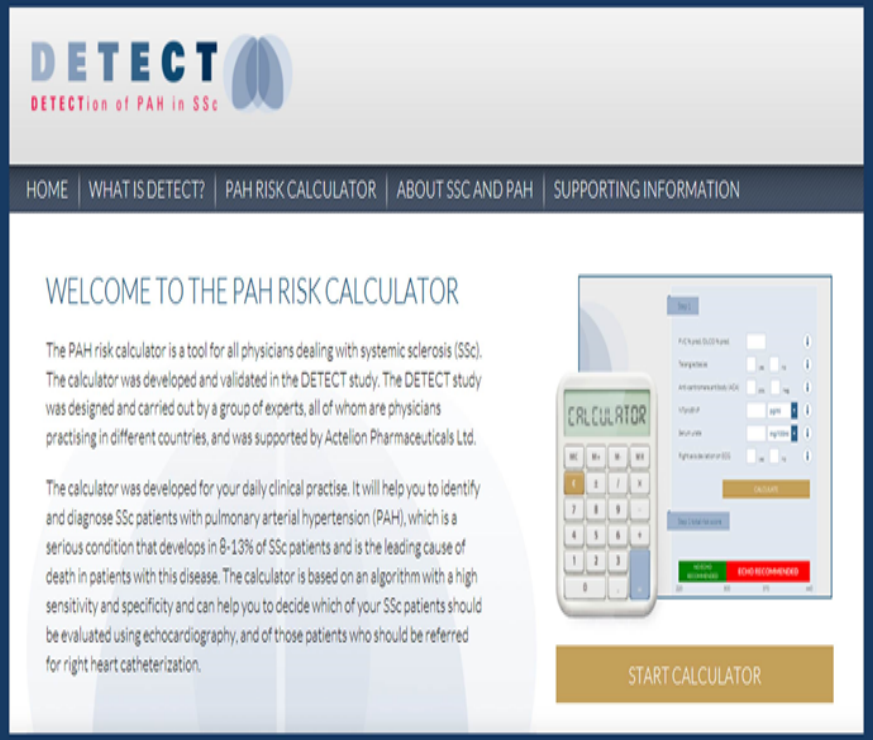


ECG: electrocardiography

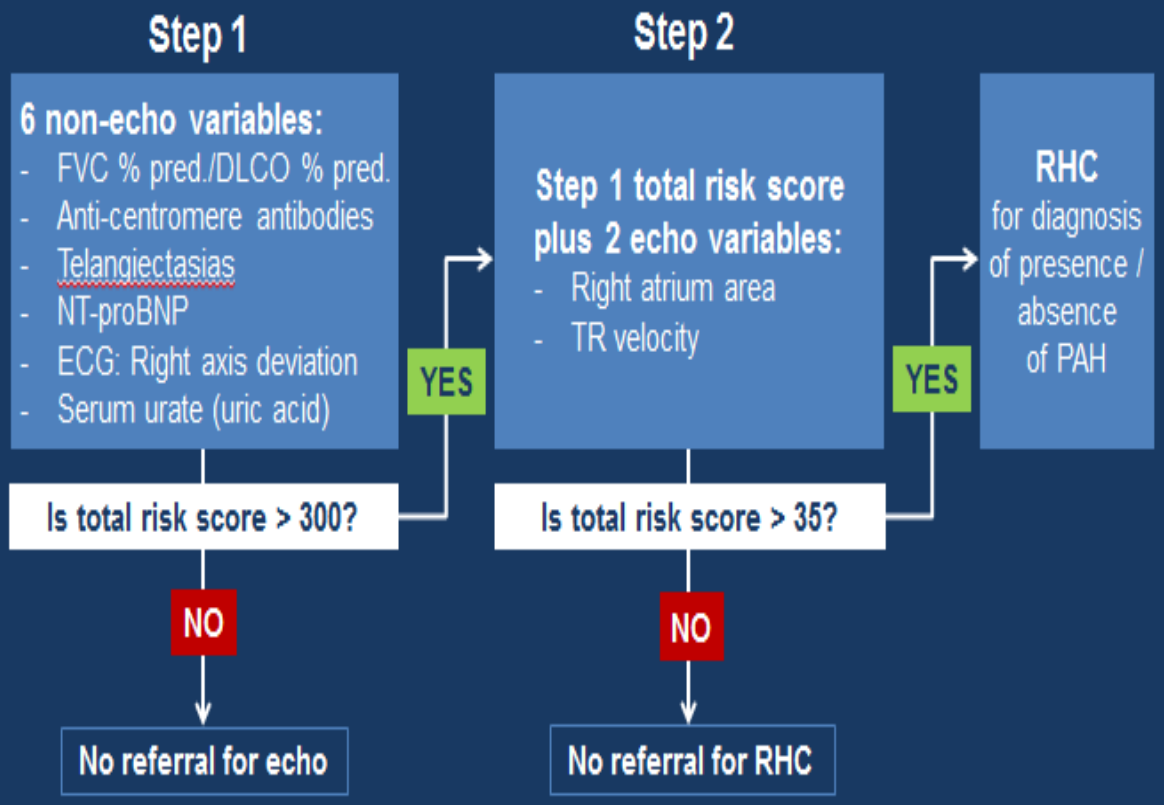
38; 20 October 2013

Coghlan JG, *et al. Ann Rheum Dis* 2013; Epub ahead of print.

DETECT online PAH risk calculator



DETECT two-step decision tree for screening SSc patients

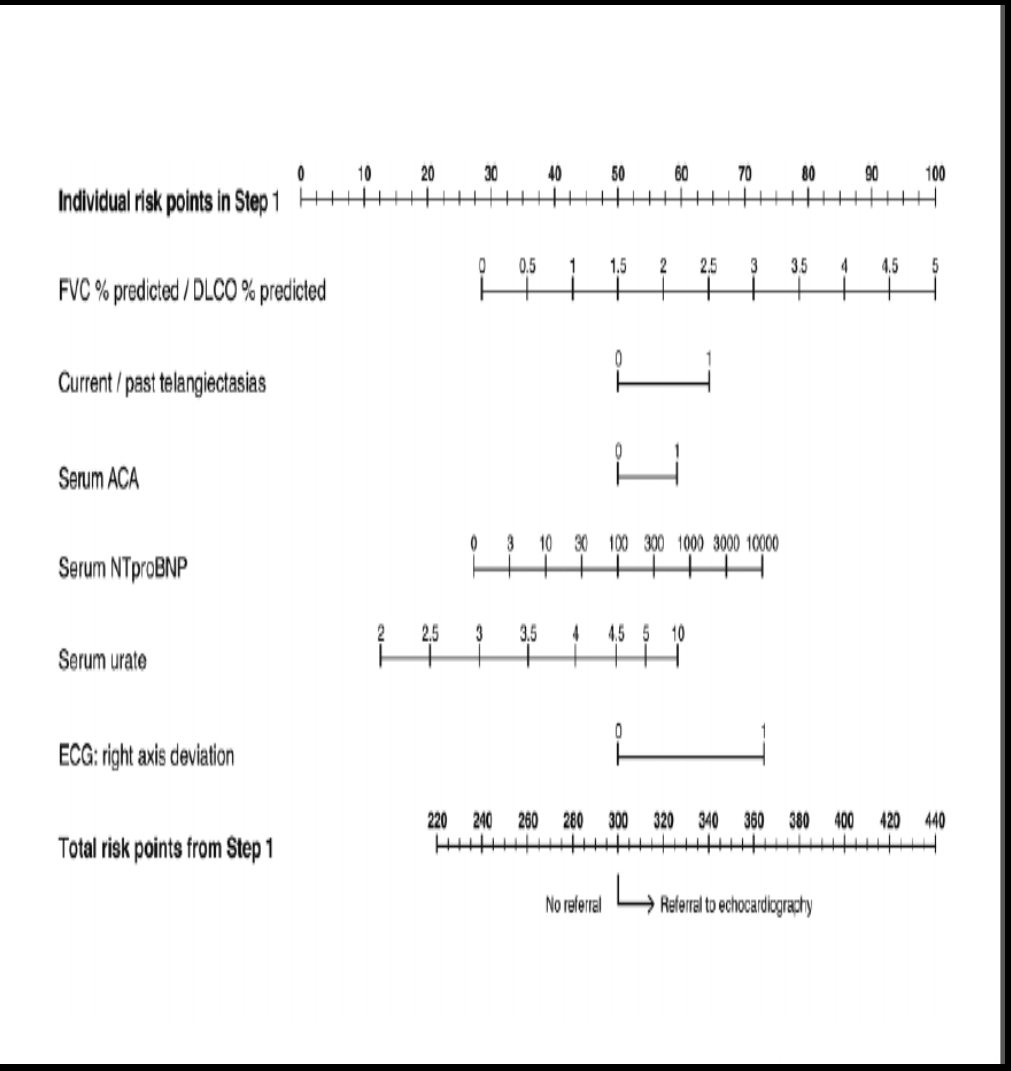


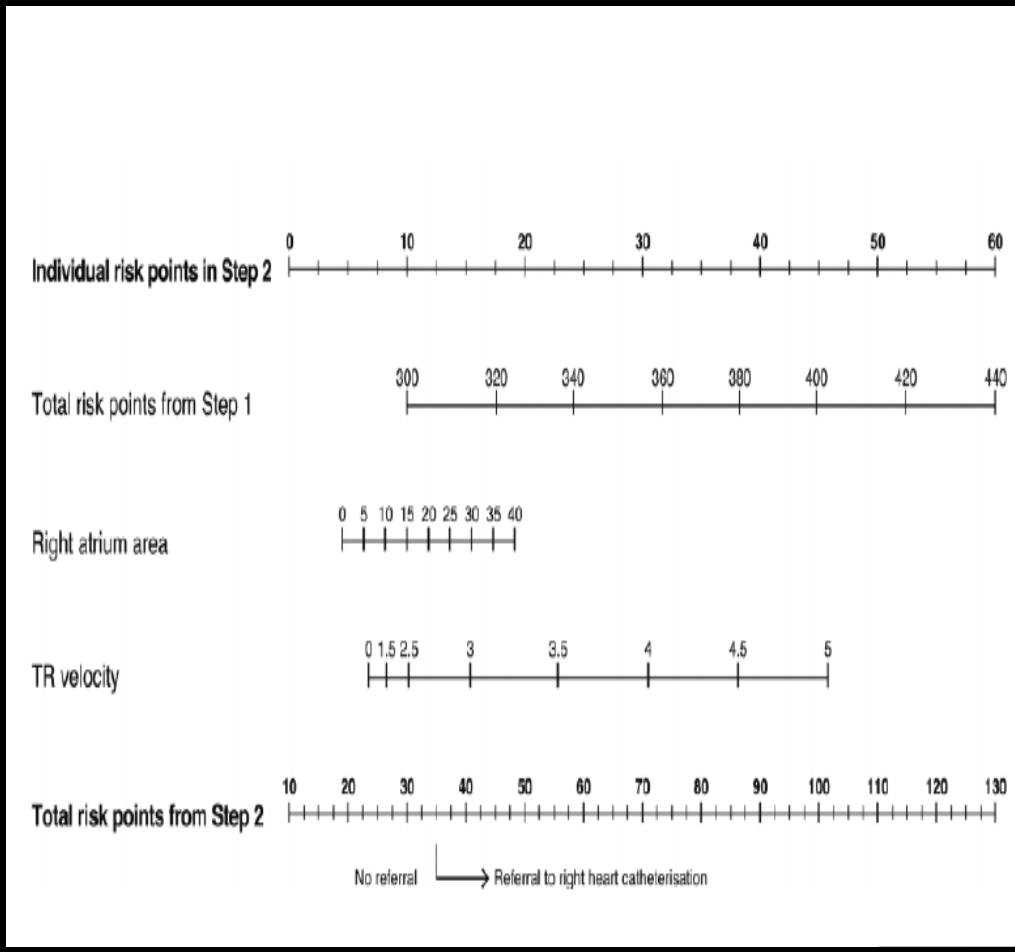
DLCO: Diffusing capacity of the lungs for carbon monoxide; ECG: Electrocardiogram; FVC: Forced vital capacity; NT-proBNP: N-terminal prohormone brain natriuretic peptide; RHC: Right heart catheterisation; SSc: Systemic Sclerosis; TR: Tricuspid regurgitation

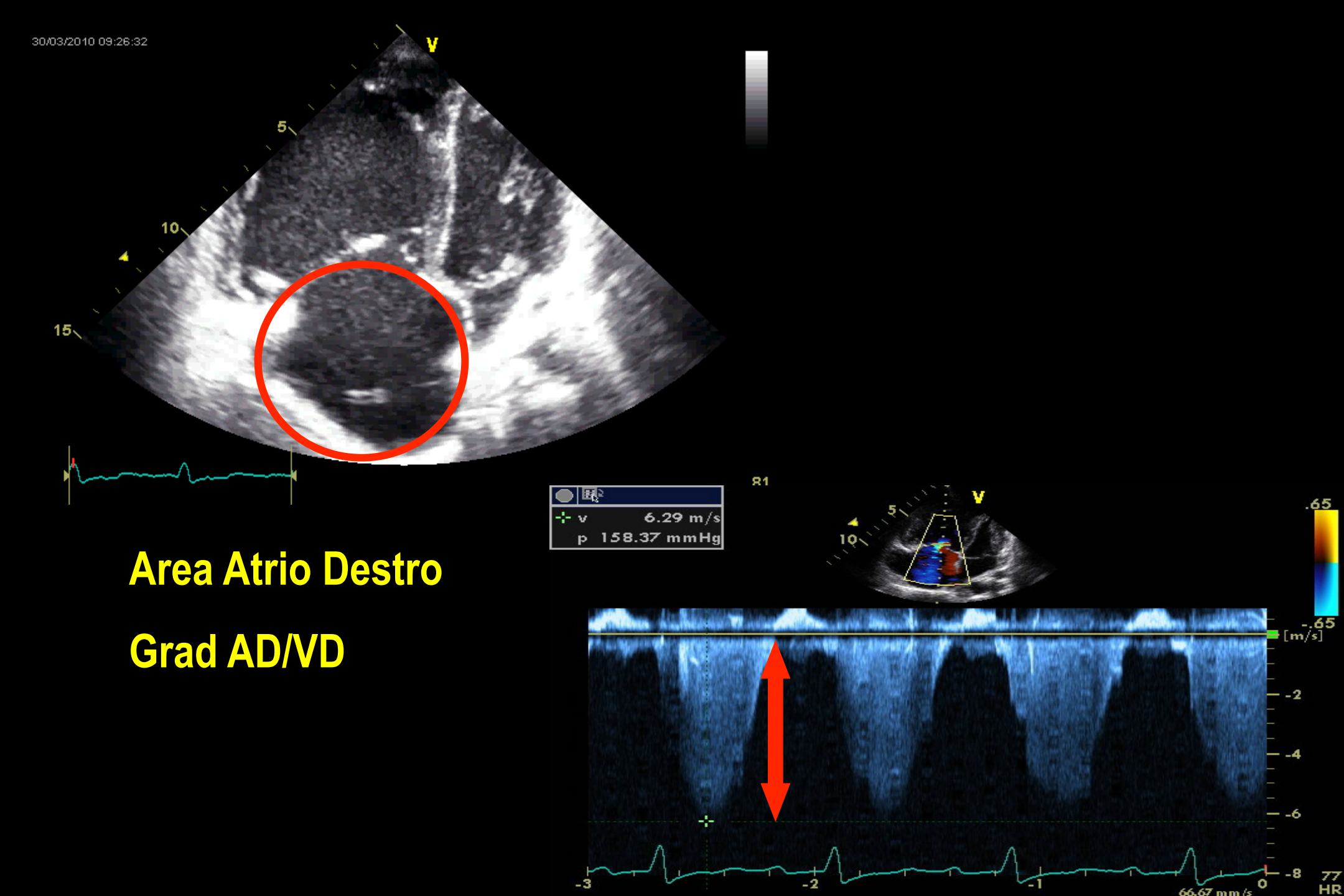
15; 29 March 2015

Coghlan JG, *et al. Ann Rheum Dis* 2014; 73:1340-9.

Evidence-based detection of Pulmonary Arterial Hipertension in Systemic Sclerosis
DETECT STUDY Coghan 2013



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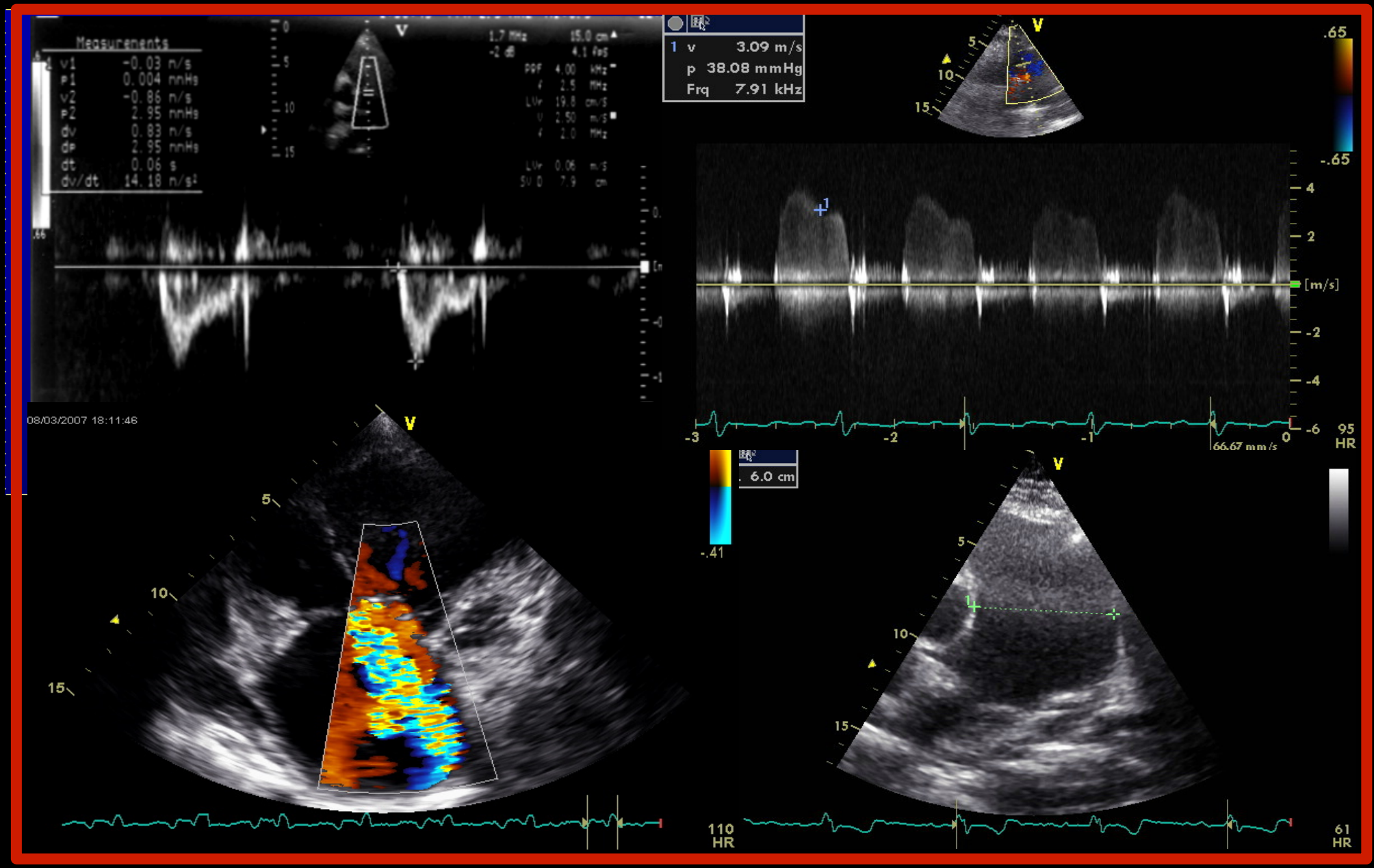

Comparison of DETECT two-step algorithm with ESC/ERS guidelines

	RHC referral rate	Missed PAH diagnoses	Overall sensitivity	Overall specificity	Overall PPV	Overall NPV
ESC/ERS Guidelines*	40%	29%	71%	69%	40%	89%
DETECT algorithm	62%	4%	96%	48%	35%	98%

Coghlan JG, *et al. Ann Rheum Dis* 2013

Evidence-based detection of Pulmonary Arterial Hipertension in Systemic Sclerosis
DETECT STUDY Coghan 2013

7% dei pz con PH: rigurgito tricuspidalico assente

20% dei pz con PH: VRT<2.5 m/sec

36% dei pz con PH: VRT<2.8 m/sec

Rate of missed PAH diagnosis:

4% (n=3) DETECT algorithm

29%(n=24) ESC/ERS guidelines

- **Objectives:**
- To compare RHC recommendations according to ESC/ERS guidelines and DETECT algorithm in a group of SSc patients .

- **Methods:**
- We included 39 consecutive patients admitted to the Unit of Internal Medicine and Rheumatology of the University Hospital Parma (Italy) between April and October 2013.
- Each patient had a SSc diagnosis (according to the EULAR/ACR classification criteria) established three or more years ago and was assessed with the above mentioned non echocardiographic and echocardiographic tests.

Results:

Table 1 shows patients with RHC recommended (or not) according to ESC/ERS guidelines and DETECT algorithm.

A concordant recommendation was found in 61,5% of patients; 20,5% of patients had a RHC recommended only by ESC/ERS guidelines while 18,0% of patients had a RHC referral according to DETECT algorithm.

Moreover 15,4% of patients met ESC/ERS criteria for RHC but had not a referral to echocardiography conforming to DETECT algorithm.

Pretty much the same ESC/ERS RHC referral was noticed in patients with a DETECT Step2 score > 44.

Table 1

		DETECT algoritm	
		RHC recommended	RHC not recommended
ESC/ERS guidelines	RHC recommended	14	7
	RHC not recommended	8	10

Conclusions:

- In our cohort of patients we observed a RHC recommendation concordace between ESC/ERS guidelines and DETECT algoritm in less than two-thirds of patients. In the near future DETECT algorithm validity should be carefully assessed to have unambiguous evidence-based guidelines to identify PAH high-risk SSc patients
-
- Grazie

ESC/ERS Guidelines and DETECT Algorithm Raccomandation in ESC/ERS Guidelines and DETECT Algorithm Raccomandation in Pulmonary Artery Hypertension associated to Scleroderma.

A real life comparison.

Walter Serra, Federica Lumetti, Flavio Mozzani, Giovanni Del Sante, Alarico Ariani

Background: Pulmonary arterial hypertension (PAH) is one of the most common Sistemic Sclerosis (SSc) related cause of death.

- Right heart catheterisation (RHC) is the gold standard to detect a PAH. Nevertheless RHC is an invasive diagnostic procedure not always accepted by patients. The European Society of Cardiology/European Respiratory Society (ESC/ERS) has suggested several consensus guidelines to identify high risk PAH subjects . ESC/ERS RHC recommendation are based on patients' syntoms and echocardiographic parameters such as tricuspid regurgitant jet (TR) velocity and right atrium (RA) area. Recently the DETECT study has presented an evidence-based detection algorithm for PAH in SSc. The DETECT algorithm is divided in two steps determining referral to RHC. In the first one non ecocardiographic tests (FVC/DLCO ratio, current/past telangiectasias, serum ACA, serum NTproBNP, serum urate and right axis deviation on ECG) are taken into account. TR velocity and RA are the echocardiographic parameters assessed in step 2.
- **Objectives:** To compare RHC recommendations according to ESC/ERS guidelines and DETECT algorithm in a group of SSc patients followed up in our rheumatological clinic.
- **Methods:** We included 39 consecutive patients admitted to the Unit of Internal Medicine and Rheumatology of the University Hospital Parma (Italy) between April and October 2013. Each patient had a SSc diagnosis (according to the EULAR/ACR classification criteria) established three or more years ago and was assessed with the above mentioned nonechocardiographicand echocardiographic tests.
- **Results:** Table 1 shows patients with RHC recommended (or not) according to ESC/ERS guidelines and DETECT algorithm. A concordant recommendation was found in 61,5% of patients; 20,5% of patients had a RHC recommended only by ESC/ERS guidelines while 18,0% of patients had a RHC referral according to DETECT algorithm. Moreover 15,4% of patients met ESC/ERS criteria for RHC but had not a referral to echocardiography conforming to DETECT algorithm. Pretty much the same ESC/ERS RHC referral was noticed in patients with a DETECT Step2 score > 44.
- **Conclusions:** In our cohort of patients we observed a RHC recommendation concordace between ESC/ERS guidelines and DETECT algoritm in less than two-thirds of patients. In the near future DETECT algorithm validity should be carefully assessed to have unambiguous evidence-based guidelines to identify PAH high-risk SSc patients

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