Supportive module 3 "Basics of diagnosis, treatment and prevention of major pulmonary diseases "

Cor Pulmonale

LECTURE IN INTERNAL MEDICINE FOR IV COURSE STUDENTS

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Plan of the Lecture

- Definition
- Epidemiology
- Risk Factors and Etiology
- Mechanisms
- Classification
- Clinical presentation
- Diagnosis
- Treatment
- Prognosis
- Prophylaxis
- Abbreviations
- Diagnostic guidelines

http://img.tfd.com/MosbyMD/thumb/cor-pulmonale.jpg

Definition

Cor pulmonale (pulmonary heart disease, right hear failure) is the enlargement and failure of the right ventricle of the heart as a response to increased vascular resistance (such as from pulmonic stenosis) or high blood pressure in the lungs.

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

Epidemiology

- Cor pulmonale is estimated to account for 6-7% of all types of adult heart disease in the United States, with chronic obstructive pulmonary disease (COPD) due to chronic bronchitis or emphysema the causative factor in more than 50% of cases
- In addition, cor pulmonale accounts for 10-30% of decompensated heart failure–related admissions in the United States
- In contrast, acute cor pulmonale is usually secondary to massive pulmonary embolism that is the most common cause of acute life-threatening cor pulmonale in adults (50,000 deaths in the United States)
- Globally, the incidence of cor pulmonale varies widely among countries, depending on the prevalence of cigarette smoking, air pollution, and other risk factors for various lung diseases.

http://emedicine.medscape.com/article/154062-overview?pa=yxfMHIhqouVY2QjSZ271hAHLlIINrXw0FEuNAGQj9d45R6qiJxgtX19AtDT%2B5dxG8SIvl8zjYv73GUyW5rsbWA%3D%3D#a

Risk Factors and Etiology

- Acute respiratory distress syndrome (ARDS)
- Chronic obstructive pulmonary disease (COPD)
- Primary pulmonary hypertension
- Blood clots in lungs
- Kyphoscoliosis
- Interstitial lung disease
- Cystic fibrosis
- Sarcoidosis
- Obstructive sleep apnea (untreated)
- Sickle cell anemia
- Bronchopulmonary dysplasia (in infants)

https://en.wikipedia.org/wiki/Pulmonary_heart_disease#Causes

Mechanism 1

- Pulmonary hypertension is the “sine qua non” of cor pulmonale
- In chronic respiratory diseases pulmonary hypertension results from increased pulmonary vascular resistance (PVR) whereas cardiac output and pulmonary “capillary” wedge pressure are normal; pulmonary hypertension is said to be precapillary
- The factors leading to an increased PVR in chronic respiratory disease are numerous but alveolar hypoxia is by far the most predominant, at least in COPD, kyphoscoliosis, and the obesity–hypoventilation syndrome
- Two distinct mechanisms of action of alveolar hypoxia must be considered: acute hypoxia causes pulmonary vasoconstriction, and chronic longstanding hypoxia induces structural changes in the pulmonary vascular bed (pulmonary vascular remodelling)

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1767533/

Mechanism 2

- Hypoxic pulmonary vasoconstriction (HPV) explains the rise of PVR and pulmonary arterial pressure (PAP) during acute hypoxia
- Pulmonary hypertension is generally observed in respiratory patients exhibiting pronounced chronic hypoxaemia (PaO_2 < 55–60 mm Hg)
- Chronic alveolar hypoxia leads to remodelling of the pulmonary vascular bed (hypertrophy of the muscular media of the small pulmonary arteries, muscularisation of pulmonary arterioles, and intimal fibrosis) comparable to that observed in natives living at high altitude
- Other functional factors must be considered, namely hypercapnic acidosis and hyperviscosity caused by polycythemia, but their role seems small when compared to that of alveolar hypoxia

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1767533/

Mechanism 3

- In idiopathic pulmonary fibrosis the increase of PVR is caused by anatomical factors: loss of pulmonary vascular bed or compression of arterioles and capillaries by the fibrosing process
- Pulmonary hypertension increases the work of the right ventricle, which leads more or less rapidly to right ventricular enlargement (associating hypertrophy and dilatation) which can result in ventricular dysfunction (systolic, diastolic)
- Cor pulmonale characterised by the presence of peripheral edema can be observed, at least in some respiratory patients
- The interval between the onset of pulmonary hypertension and the appearance of cor pulmonale is not known and may vary from one patient to another
- There is a relation between the severity of pulmonary hypertension and the development of cor pulmonale.

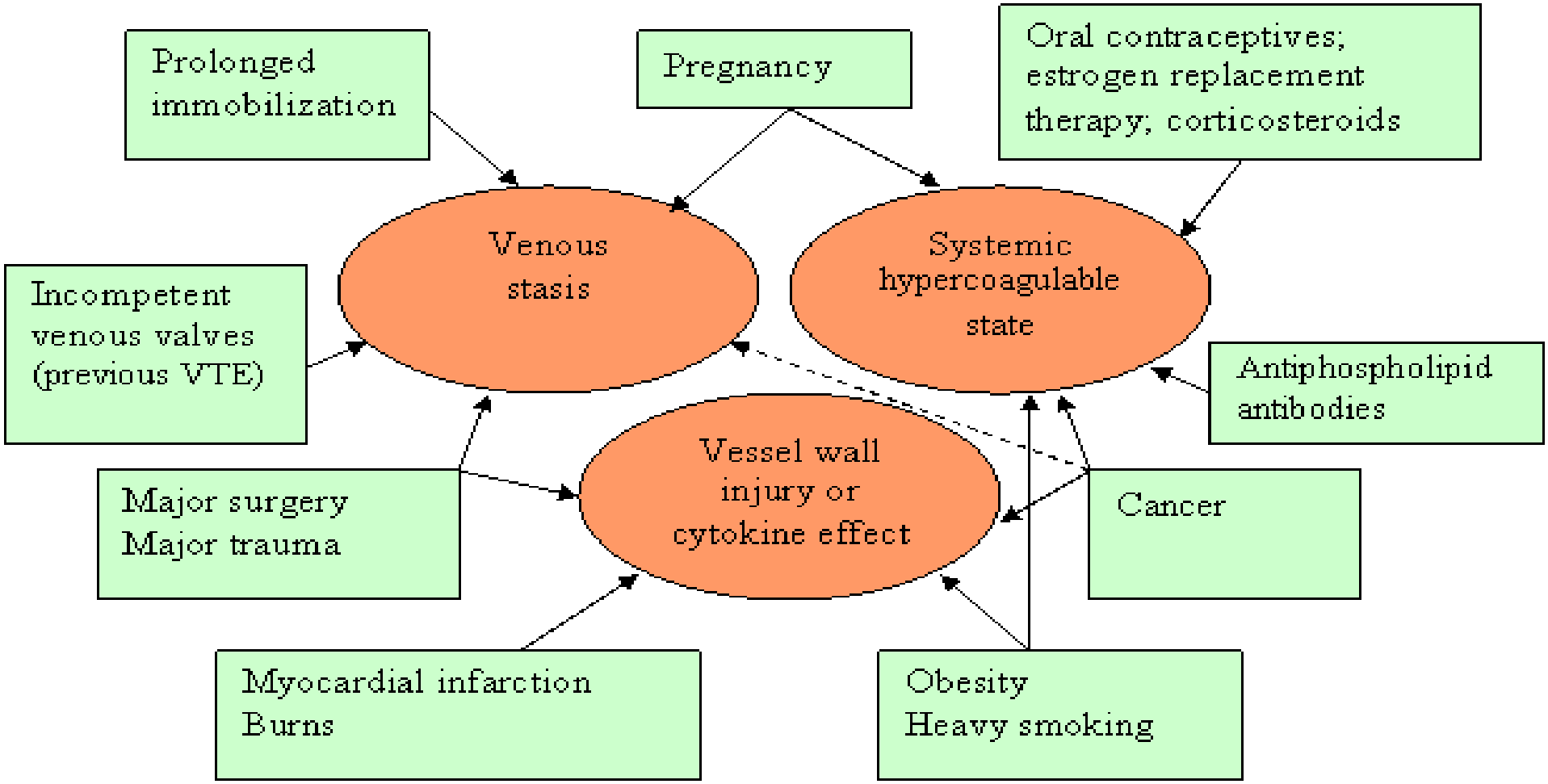
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1767533/

Mechanism 4

- Acute cor pulmonale is result of pulmonary embolism (more common) and ARDS
- The underlying pathophysiology in a massive pulmonary embolism causing cor pulmonale is the sudden increase in pulmonary resistance
- In ARDS, RV overload can occur due to mechanical ventilation and the pathologic features of the syndrome itself
- Mechanical ventilation, especially higher tidal volumes, requires a higher transpulmonary pressure.
- In the case of ARDS, cor pulmonale is associated with an increased possibility of right-to-left shunting through a patent foramen ovale, which carries a poorer prognosis.

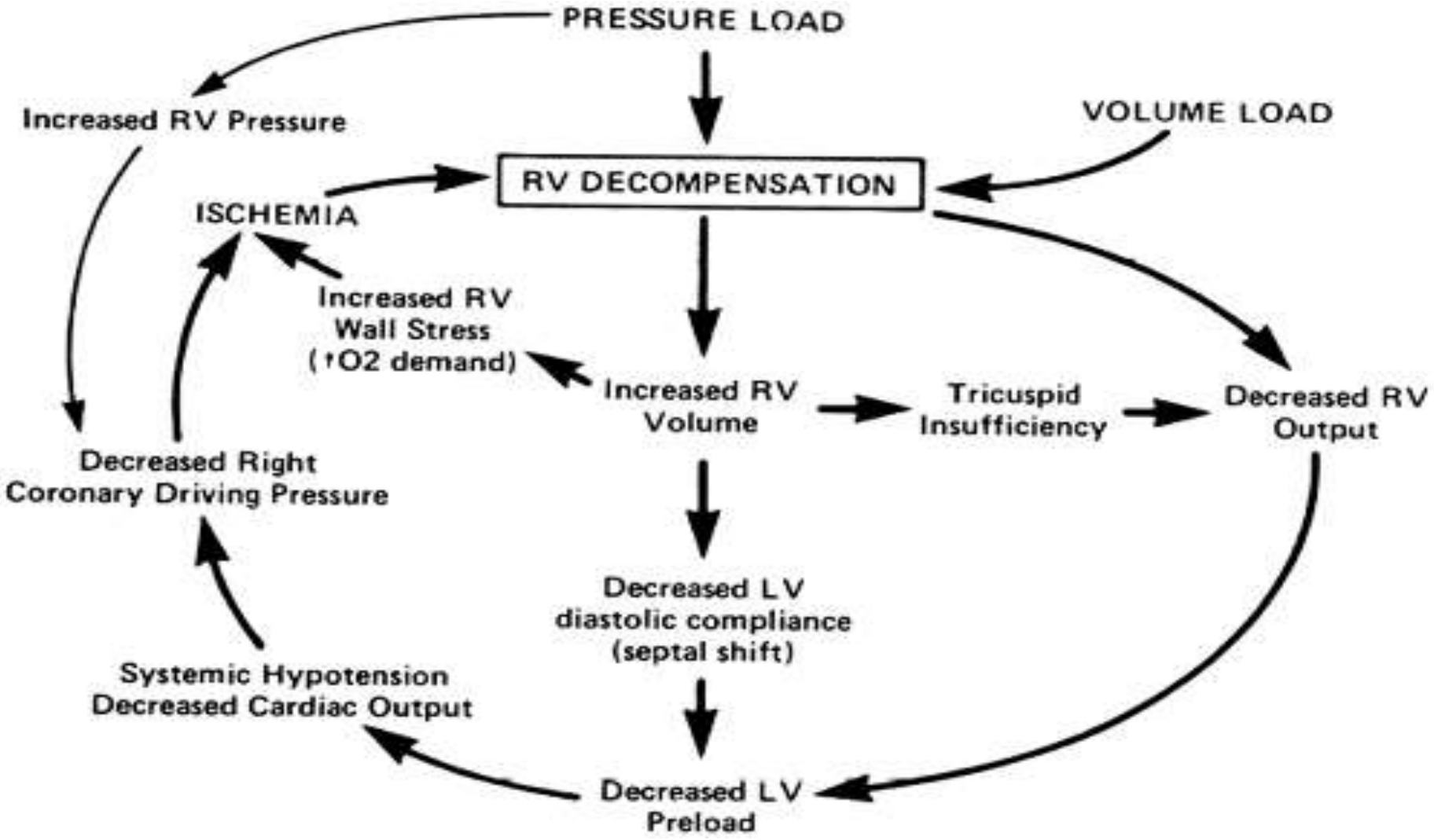
http://emedicine.medscape.com/article/154062-overview?pa=yxfMHIhqouVY2QjSZ271hAHLllINrXw0FEuNAGQi9d45R6qiJxgtX19AtDT%2B5dxG8SIvl8zjYv73GUyW5rsbWA%3D%3D#a2

Mechanism 5



Cor pulmonale and pulmonary embolism.

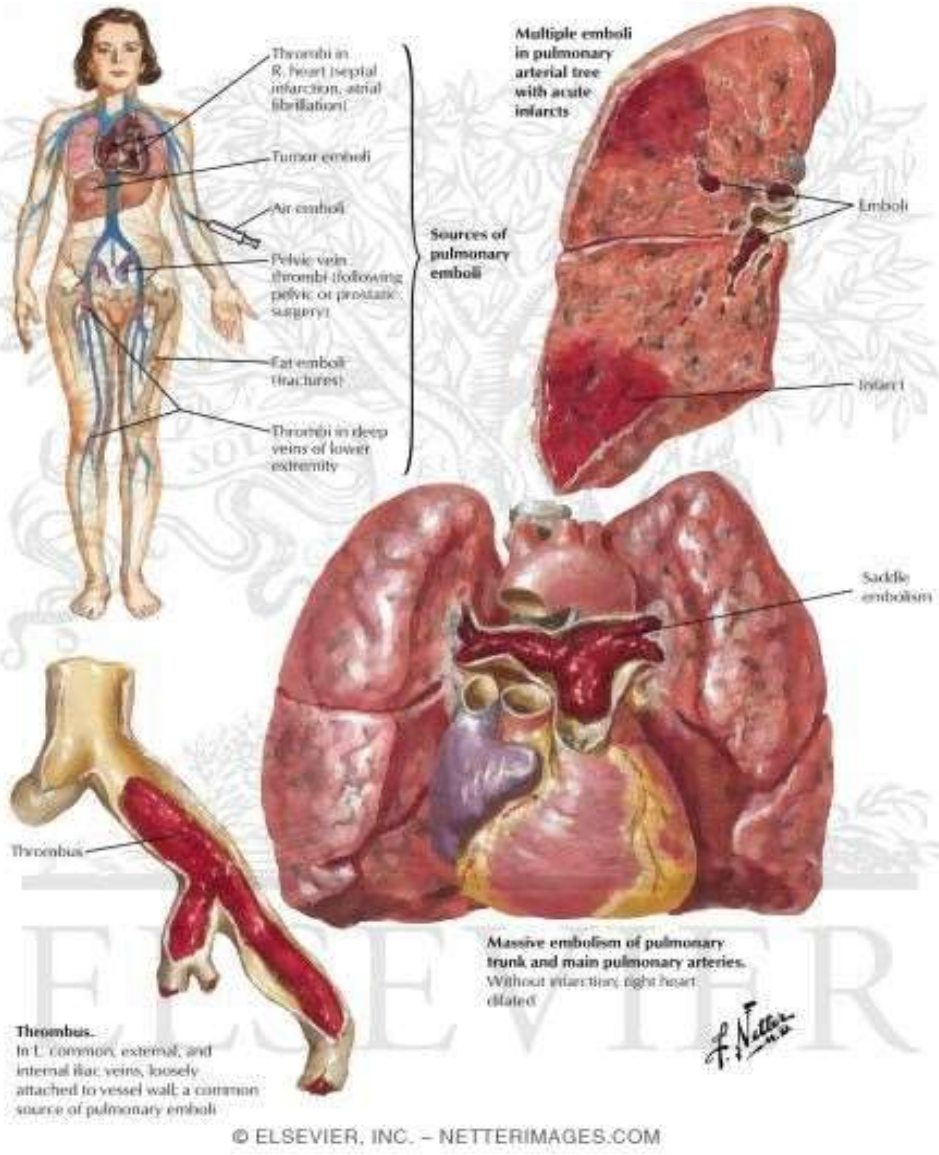
Mechanism 6



Mechanism of acute right heart failure: the vicious cycle.

http://img.medscape.com/fullsize/migrated/458/659/src458659.fig4.gif

Mechanism 7



Acute Cor Pulmonale

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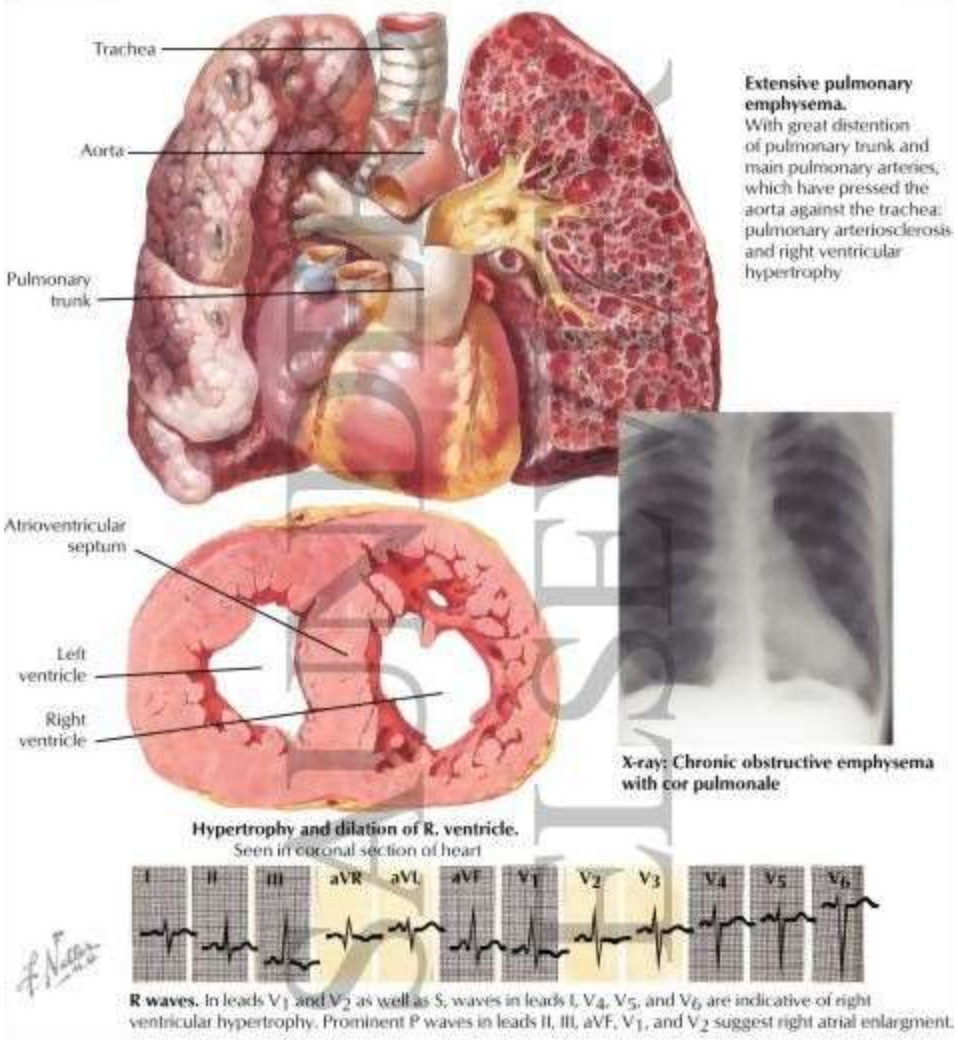
https://www.netterimages.com/images/vpv/000/000/010/10281-0550x0475.jpg

Mechanism 8



Chromic Cor Pulmonale.

https://www.netterimages.com/images/vpv/000/000/010/10281-0550x0475.jpg

Classification

International Classification of Diseases

- X Diseases of the respiratory system
- Pulmonary heart disease and diseases of pulmonary circulation
  (I26-I28)
- 126 Pulmonary embolism
- 127 Other pulmonary heart diseases
- 127.0 Primary pulmonary hypertension
- 127.1 Kyphoscoliotic heart disease
- 127.2 Other secondary pulmonary hypertension
- 127.8 Other specified pulmonary heart diseases
- 127.9 Pulmonary heart disease, unspecified

http://apps.who.int/classifications/icd10/browse/2016/en#/J45

Classification

Clinical 1

1. Pulmonary arterial hypertension
   1.1 Primary pulmonary hypertension
      (a) Sporadic, (b) Familial
   1.2 Related to:
      (a) Collagen vascular disease
      (b) Congenital systemic to pulmonary shunts
      (c) Portal hypertension
      (d) HIV infection
      (e) Drugs/toxins: (1) Anorexigens, (2) Other
      (f) Persistent pulmonary hypertension of the newborn
      (g) Other

Classification

Clinical 2

2. Pulmonary venous hypertension: 2.1 Left sided atrial or ventricular heart disease, 2.2 Left sided valvar heart disease, 2.3 Extrinsic compression of central pulmonary veins: ((a) Fibrosing mediastinitis, (b) Adenopathy/tumours), 2.4 Pulmonary veno-occlusive disease, 2.5 Other
3. Pulmonary hypertension associated with disorders of the respiratory system and/or hypoxaemia (3.1 Chronic obstructive pulmonary disease, 3.2 Interstitial lung disease, 3.3 Sleep disordered breathing, 3.4 Alveolar hypoventilation disorders, 3.5 Chronic exposure to high altitude, 3.6 Neonatal lung disease, 3.7 Alveolar capillary dysplasia 3.8 Other

Classification

Clinical 3

4. Pulmonary hypertension caused by chronic thrombotic and/or embolic disease
   4.1 Thromboembolic obstruction of proximal pulmonary arteries
   4.2 Obstruction of distal pulmonary arteries ((a) Pulmonary embolism (thrombus, tumour, ova and/or parasites, foreign material), (b) In situ thrombosis, (c) Sickle cell disease)
5. Pulmonary hypertension caused by disorders directly affecting the pulmonary vasculature
   5.1 Inflammatory ((a) Schistosomiasis, (b) Sarcoidosis, (c) Other)
   5.2 Pulmonary capillary haemangomatosis.

Symptoms and Signs 1

- Shortness of breath
- Wheezing
- Cyanosis
- Ascites
- Jaundice
- Hepatomegaly
- Raised jugular venous pressure (JVP)
- Third heart sound
- Intercostal recession
- Presence of abnormal heart sounds
- Peripheral edema

https://en.wikipedia.org/wiki/Pulmonary_heart_disease#Signs_and_symptoms

Symptoms and Signs 2

https://s-media-cache-ak0.pinimg.com/originals/8c/b6/8b/8cb68b7c03b87a61906effb5eea9b4d8.jpg

Clinical Manifestations

- The clinical manifestations of cor pulmonale may be nonspecific
- The symptoms may be subtle, especially in early stages of the disease, and they may be mistakenly attributed to the underlying pulmonary pathology
- Clinical signs are not sensitive indicators of pulmonary hypertension or right ventricular hypertrophy
- Peripheral edema is the best sign of right heart failure, but it is not specific and can arise from other causes.v

Complications

- Life-threatening shortness of breath
- Severe edema
- Shock
- Death.

https://medlineplus.gov/ency/article/000129.htm

Diagnosis

- A general approach to diagnose cor pulmonale starts with routine laboratory tests, chest radiography, and electrocardiography
- Echocardiography gives information about the disease and right ventricular function
- Right heart catheterization is the most accurate but invasive test to confirm the diagnosis
- Pulmonary function tests may be required to confirm the presence of other lung pathologies
- Ventilation/perfusion scanning or chest computed tomography scanning may be performed if the patient's history and physical examination suggest pulmonary thromboembolism
- Imaging studies may show evidence of underlying cardiopulmonary diseases, pulmonary hypertension, or right ventricle enlargement

http://emedicine.medscape.com/article/154062-overview?pa=yxfMHIhqouVY2QjSZ271hAHLlINrXw0FEuNAGQi9d45R6qiJxgtX19AtDT%2B5dxG8SIvl8zjYv73GUyW5rsbWA%3D%3D#a5

Diagnosis
Tests 1

- Laboratory investigations: 1) hematocrit for polycythemia, which can increase pulmonary arterial pressure by increasing viscosity, 2) serum alpha1-antitrypsin, if deficiency is suspected, 3) antinuclear antibodies level for collagen vascular disease, and scleroderma, 4) coagulations studies to evaluate hypercoagulability states
- Arterial Blood Gas Analysis (level of oxygenation and type of acid-base disorder)
- Brain natriuretic peptide (BNP): both congestive heart failure due to left ventricular failure and cor pulmonale can lead to elevations in plasma BNP
- Chest radiography: enlargement of the central pulmonary arteries and the right ventricle (these findings have reduced sensitivity in the presence of kyphoscoliosis or hyperinflated lungs)

http://emedicine.medscape.com/article/154062-overview#a6

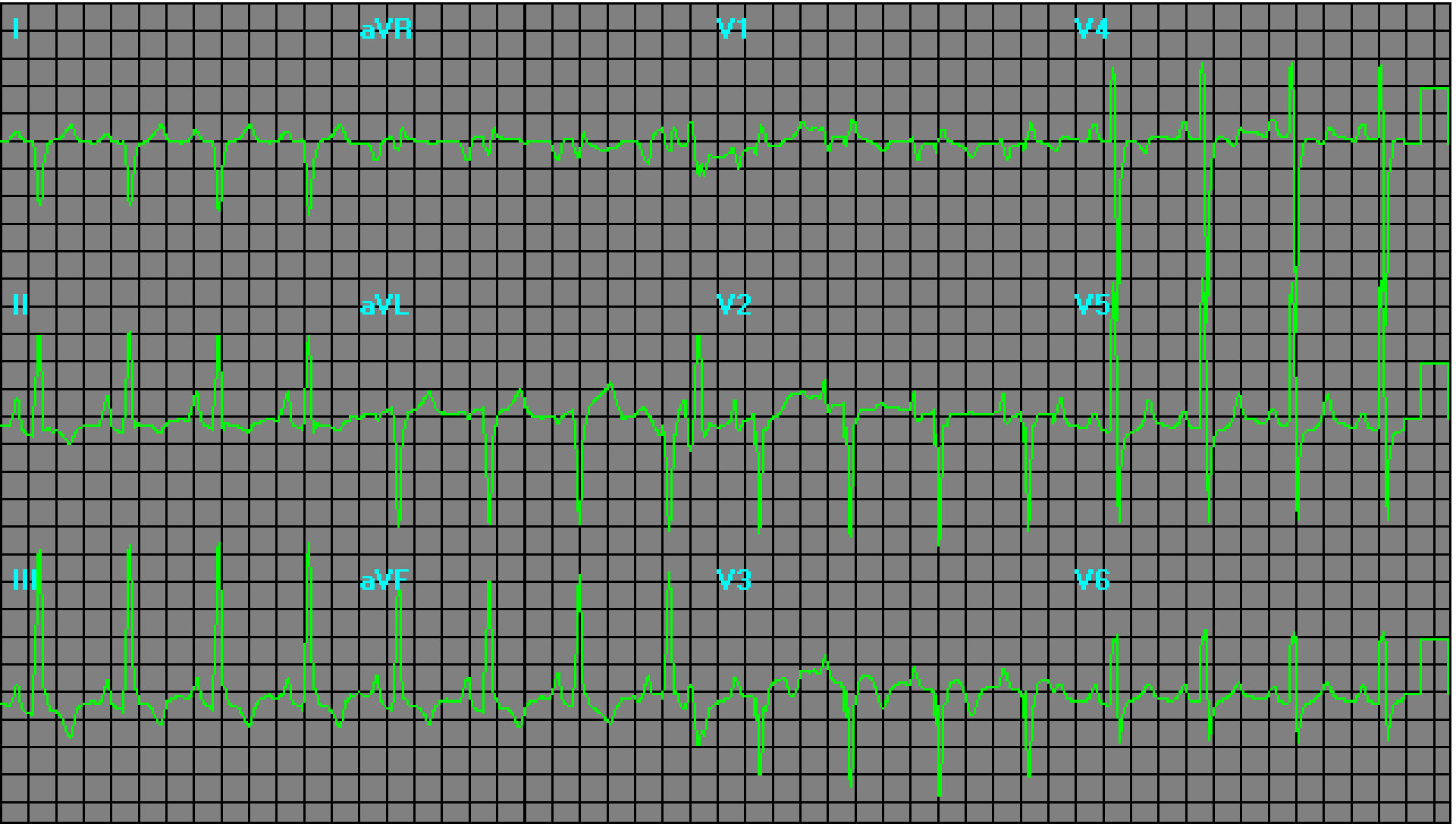
Diagnosis
Tests 2

- Electrocardiographic abnormalities: right axis deviation, R/S amplitude ratio in V1 greater than 1; R/S amplitude ratio in V6 less than 1; an increase in P wave amplitude in leads 2, 3, and aVF; $S_1 Q_3 T_3$ pattern and right bundle branch block, low-voltage QRS , many rhythm disturbances
- Two-dimensional echocardiography: signs of chronic right ventricular pressure overload
- Doppler echocardiography: increased pulmonary arterial pressure
- Pulmonary Thromboembolism Imaging Studies: pulmonary angiography, computed tomography pulmonary angiography
- Ultrafast, electrocardiographically-gated computed tomography: right ventricular function.

http://emedicine.medscape.com/article/154062-overview#a10

Diagnosis

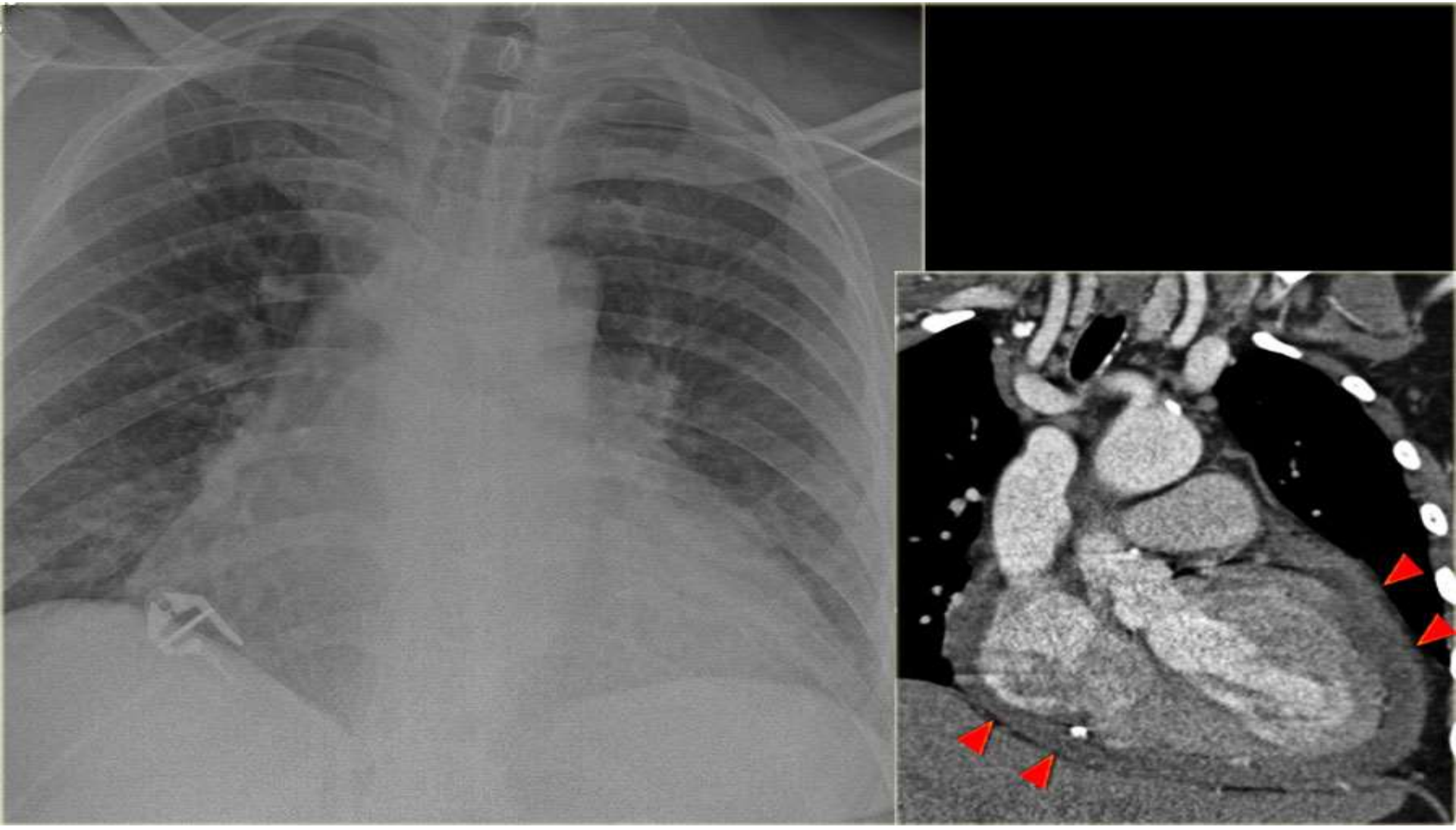
Tests 3



http://int-prop.lf2.cuni.cz/heart_sounds/ekg1/ekg-copd.gif

Diagnosis

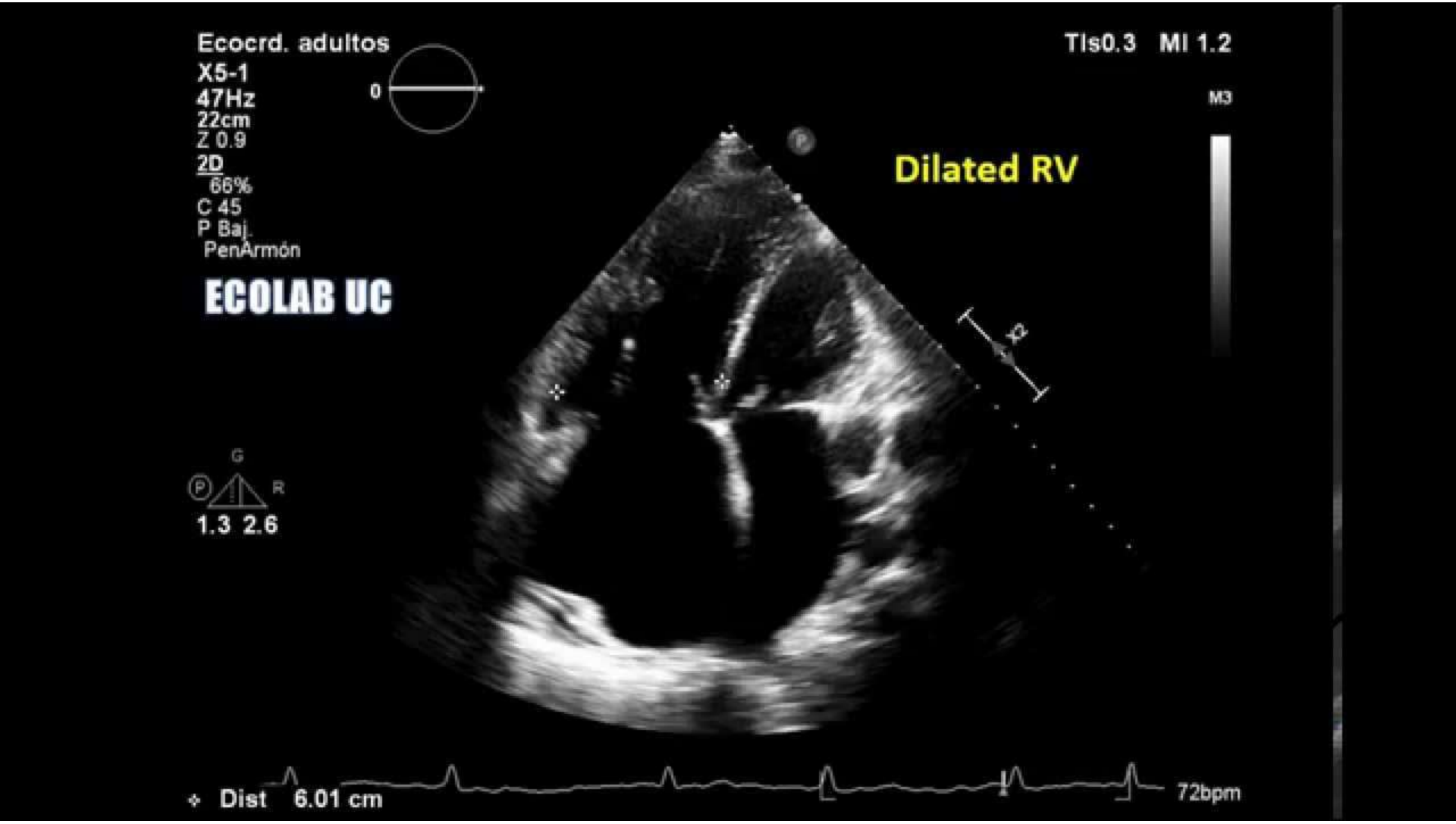
Tests 4



http://www.radiologyassistant.nl/data/bin/a509797a67fe0d_groot-cor-pericard.jpg

Diagnosis

Tests 5



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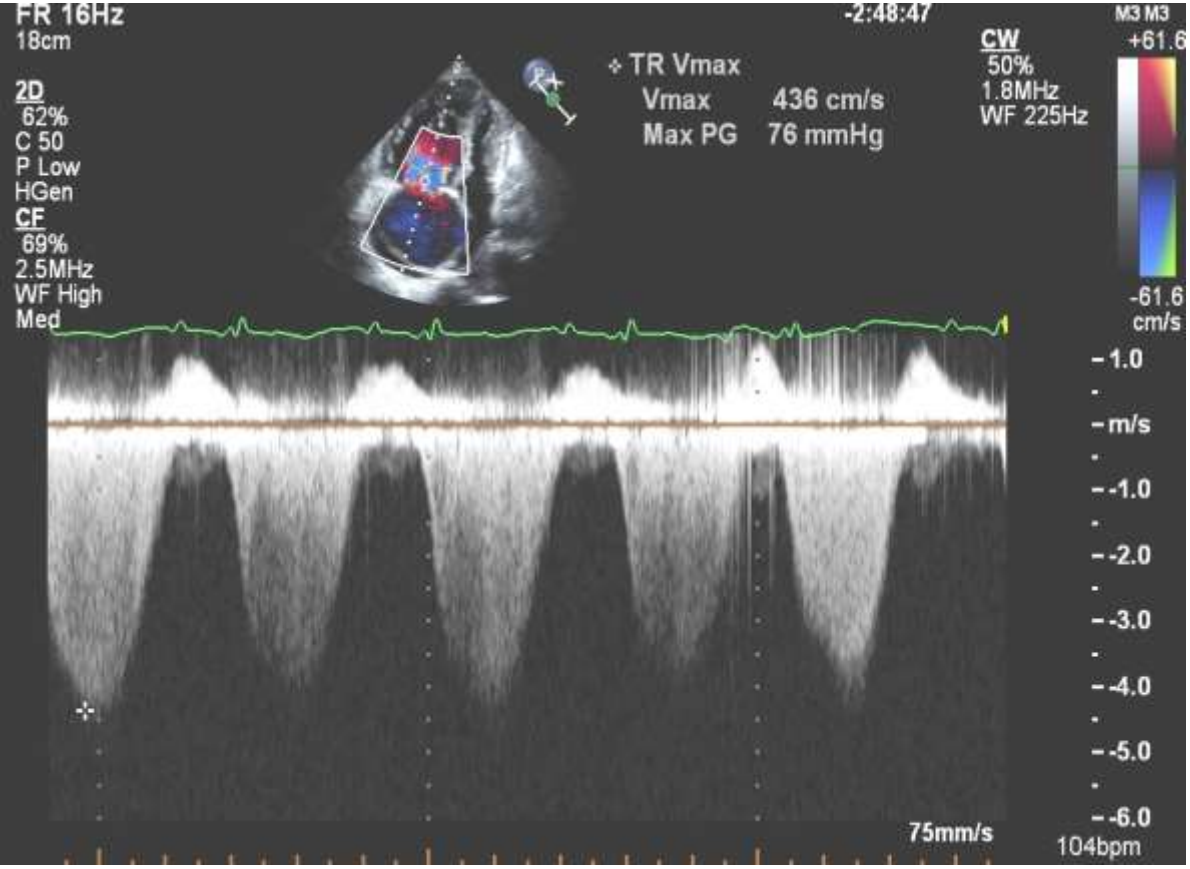
Diagnosis

Tests 6



Doppler shows a thick dense regurgitated jet. The estimated pulmonary artery systolic pressure is markedly elevated Adding on an right atrium. pressure of 15, which this individual had, yields a pulmonary artery systolic pressure of nearly 90 mmHg.

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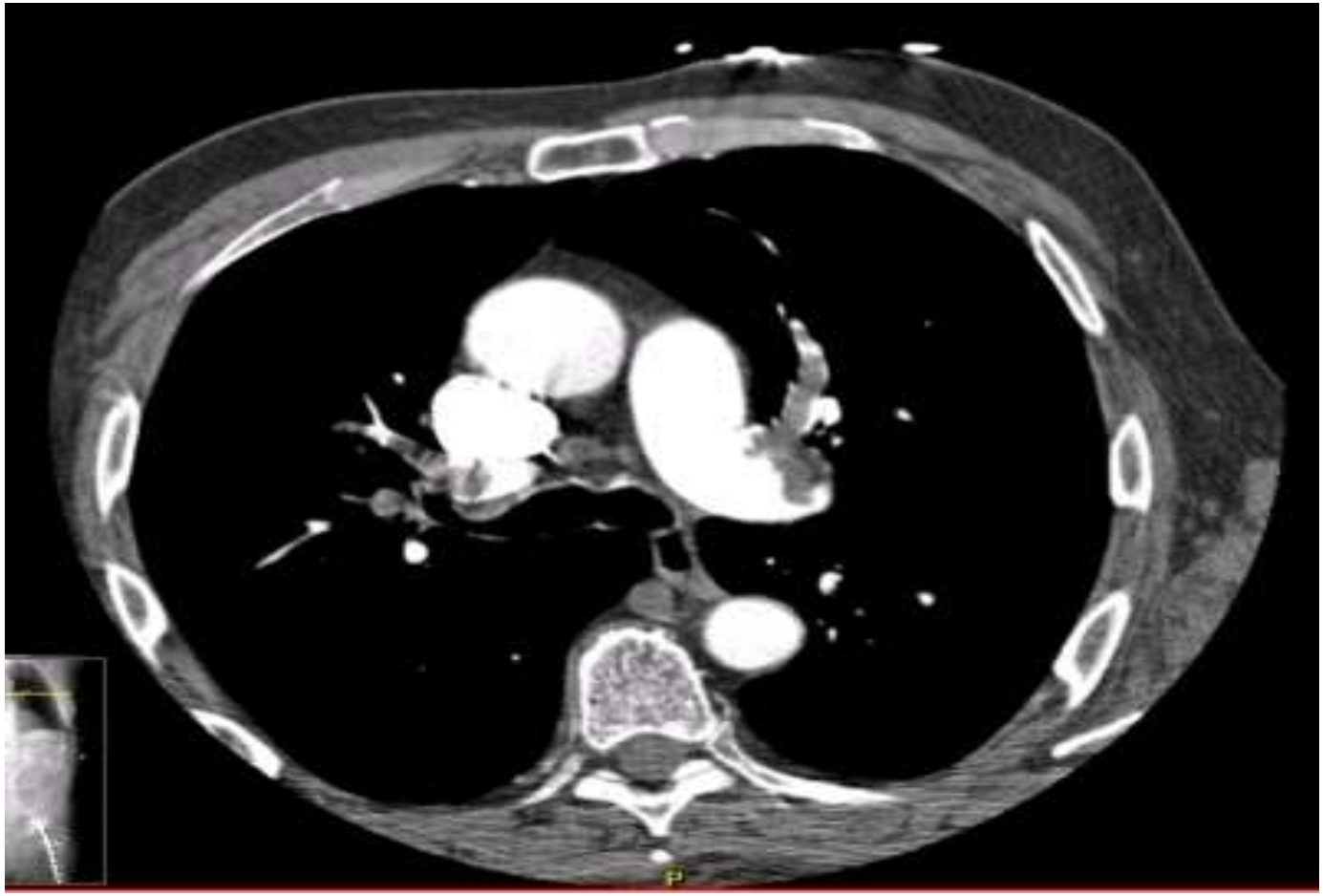
Diagnosis

Tests 7



Computerized axial tomography demonstrating bilateral main pulmonary artery emboli.

https://i.ytimg.com/vi/zaYxtKYthDk/maxresdefault.jpg

Diagnosis
Differentiation

- Atrial myxoma
- Blood disorders that are associated with increased blood viscosity
- Congestive (biventricular) heart failure
- Constrictive pericarditis
- High-output heart failure
- Infiltrative cardiomyopathies
- Primary pulmonic stenosis
- Right heart failure due to right ventricular infarction
- Right heart failure due to congenital heart diseases
- Ventricular septal defect.

Management

General

- Medical therapy for cor pulmonale is focused on treatment of the underlying pulmonary disease and improving oxygenation and right ventricular function
- Oxygen therapy, diuretics, vasodilators, digitalis, theophylline, and anticoagulation therapy are all different modalities used in the long-term management of chronic cor pulmonale
- Cardiopulmonary support for acute cor pulmonale additionally includes fluid loading and vasoconstrictor (e.g., epinephrine) administration to maintain adequate blood pressure
- For massive pulmonary embolism in patients with acute cor pulmonale, consider administration of anticoagulation, thrombolytic agents or surgical embolectomy, especially if circulatory collapse is impending.

http://emedicine.medscape.com/article/154062-overview#a18

Management

Oxygen Therapy

- Oxygen therapy is of great importance in patients with underlying chronic obstructive pulmonary disease (COPD), particularly when administered on a continuous basis (the partial pressure of oxygen (PaO_2) is likely to be below 55 mm Hg and decreases further with exercise and during sleep)
- Oxygen therapy relieves hypoxemic pulmonary vasoconstriction, lessens sympathetic vasoconstriction, alleviates tissue hypoxemia, and improves renal perfusion
- Although the impact of oxygen therapy on survival in patients with cor pulmonale is unclear, it may provide some degree of symptomatic relief and improvement in functional status
- Oxygen therapy plays an important role in the immediate setting and long-term management, especially in patients who are hypoxic and have COPD.

http://emedicine.medscape.com/article/154062-overview#a19

Management
Pharmacotherapy 1

- Diuretics are used when the right ventricle filling volume is markedly elevated and in the management of associated peripheral edema
- Vasodilators have been advocated in the long-term management of chronic cor pulmonale
- Calcium channel blockers (nifedipine, diltiazem), can lower pulmonary pressures, although these agents appear more effective in primary rather than secondary pulmonary hypertension
- Beta-selective agonists have an additional advantage of bronchodilator and mucociliary clearance effect
- Epoprostenol, treprostinil, and bosentan are prostacyclin analogues and have potent vasodilatory properties

Management
Pharmacotherapy 2

- The endothelin receptor antagonists are indicated in idiopathic pulmonary artery hypertension as well as pulmonary hypertension secondary to connective tissue disorders
- The PDE5 inhibitors (sildenafil, tadalafil) function by preventing the degradation of cyclic GMP and subsequently prolonging the vasodilatory effect of nitric oxide; there are not enough data available yet regarding the efficacy of these drugs in patients with secondary pulmonary hypertension, such as in patients with COPD
- Riociguat (a soluble guanylate cyclase stimulant that mimics the function of nitric oxide as well as acts synergistically with it to promote vasodilation) has been FDA approved for the treatment of group I pulmonary hypertension as well as group 4 pulmonary hypertension (chronic thromboembolic pulmonary hypertension)

http://emedicine.medscape.com/article/154062-overview#a20

Management
Pharmacotherapy 3

- The use of cardiac glycosides, such as digitalis, must be used cautiously, and should not be used during the acute phases of respiratory insufficiency when large fluctuations in levels of hypoxia and acidosis may occur
- Theophylline has been reported to reduce pulmonary vascular resistance and pulmonary arterial pressures acutely in patients with chronic cor pulmonale secondary to COPD
- Anticoagulation with warfarin is recommended in patients at high risk for thromboembolism
- Thrombolytic therapy is indicated in patients with acute cor pulmonale due to a pulmonary embolism resulting in hemodynamic instability.

http://emedicine.medscape.com/article/154062-overview#a20

Management
Surgical Approaches

- Phlebotomy is indicated in patients with chronic cor pulmonale and chronic hypoxia causing severe polycythemia, defined as hematocrit of 65% or more
- Uvulopalatopharyngoplasty in selected patients with sleep apnea and hypoventilation may relieve cor pulmonale
- Pulmonary embolectomy is indicated in patients with acute pulmonary embolism and hemodynamic instability when thrombolytic therapy is contraindicated, and in patients whose previous thrombolytic therapy failed, particularly if the location of the thrombus is in a more proximal location
- Single-lung, double-lung, and heart-lung transplantation are all used to salvage the terminal phases of several diseases (e.g., emphysema, idiopathic pulmonary fibrosis, cystic fibrosis).

http://emedicine.medscape.com/article/154062-overview#a21

Management
Outpatient Monitoring

- Patients with cor pulmonale generally require close attention in the outpatient setting
- It is appropriate to regularly assess the patient's oxygen needs and pulmonary function
- Consider a formal program of pulmonary rehabilitation, as many patients benefit from this therapy.

http://emedicine.medscape.com/article/154062-overview#a22

Prognosis

- The occurrence of documented cor pulmonale is an indicator of poor prognosis in respiratory patients
- It is now accepted that a prolonged survival (≥ 10 years) can be observed after the first episode of peripheral edema
- The prevalence of clinical cor pulmonale has greatly decreased with the application of long term oxygen therapy, with a resulting improvement in prognosis.

https://www.ncbi.nlm.nih.gov/pmc/artides/PMC1767533/

Prophylaxis

Avoiding behaviors, such as cigarette smoking, which lead to chronic lung disease, may prevent the development of cor pulmonale.

http://www.nytimes.com/health/guides/disease/cor-pulmonale/overview.html

Abbreviations

ARDS - acute respiratory distress syndrome

BNP - Brain natriuretic peptide

CBC - complete blood count

CNS - central nervous system

COPD - chronic obstructive pulmonary disease

HPV - hypoxic pulmonary vasoconstriction

ECMO - Extracorporeal membrane oxygenation

ICU - intensive care unit

JVP - jugular venous pressure

PAP - pulmonary arterial pressure

PVR - pulmonary vascular resistance

Diagnostic and treatment guidelines

2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension

Cor pulmonale

Cor pulmonale

The treatment of chronic cor pulmonale

Pulmonary hypertension (guidelines on diagnosis and treatment of)

Diagnosis and management of stable chronic obstructive pulmonary disease