Diagnosing pulmonary arterial hypertension

PURDUE UNIVERSITY

Glossary

Sensitivity: The percentage of positive patients that a test correctly identifies as having the disease. A test that has poor sensitivity generates a high amount of "false negatives."

Specificity: The percentage of negative patients that a test correctly identifies as not having the disease. A test that has poor specificity generates a high amount of "false positives."

Genetic Screening

Procedure: Segments of patient DNA called genes are amplified and sequenced to detect mutations linked to a disease[10]. In PAH, scientists commonly look for mutations in a gene called BMPR2[11].

Sensitivity: 70%[12]

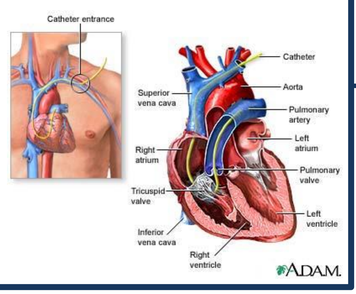
Specificity: 10-20%[12]

Other features:

- BMPR2 mutations are related to greater disease severity and earlier age-of-onset in patients that do develop PAH[13]
- Non-invasive (blood or saliva sample)
- Delayed results (must be sent to a lab for analysis)

Right Heart Catheterization

Procedure: The jugular vein serves as the point-of-entry for a catheter inserted into the right side of the heart and pulmonary arteries[14]. Because right heart catheterization directly measures the average pressure in the pulmonary arteries, it provides the definitive diagnosis for PAH.



Sensitivity: 100%

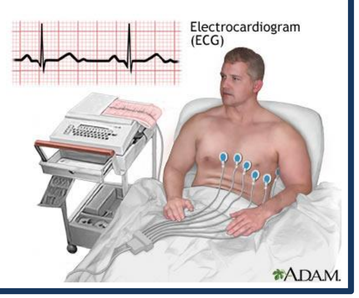
Specificity: 100%

Other features:

- Causes serious adverse events in 1.1% of cases[15]
- Minimally-invasive

Electrocardiography

Procedure: Electrodes are placed on the skin to measure the electrical activity of the heart. Signs of right heart failure, such as right bundle branch block, ventricular hypertrophy, and atrial enlargement, are used as indirect evidence of PAH[16].



Sensitivity: 55-73%[17] (for severe PAH†)

Specificity: 70%[17] (for severe PAH†)

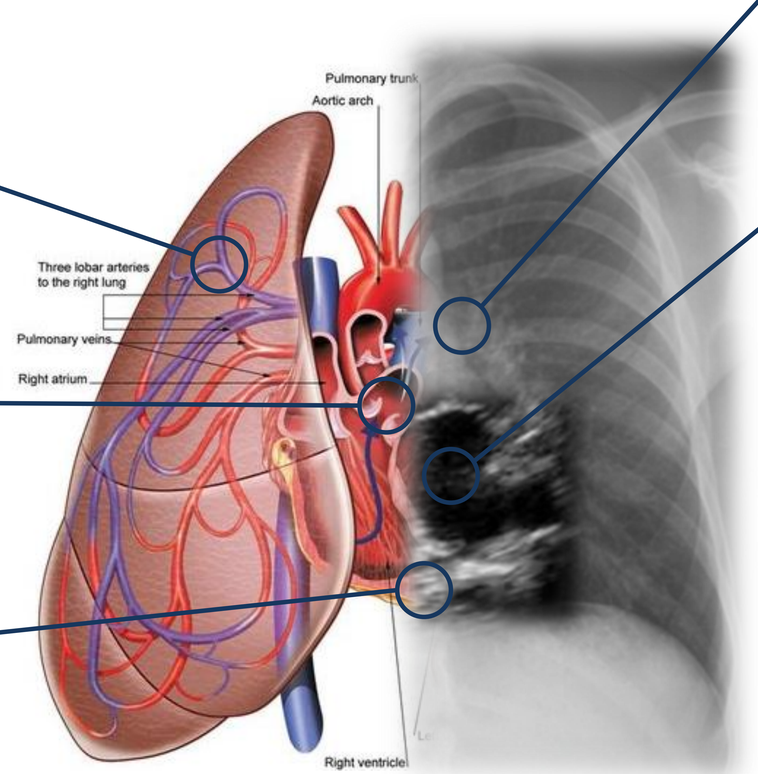
Other features:

- Non-invasive

†MPAP > 50 mmHg

Introduction

Pulmonary arterial hypertension (PAH) is a disease characterized by increased vascular resistance in the arteries that carry deoxygenated blood from the heart to the lungs[1]. Clinically, it is defined as a mean pulmonary arterial pressure (MPAP) greater than 25 mmHg. Unless treated, PAH leads to right heart failure and death. Although PAH is a rare disease with an incidence of just 1-2 per million[2], it has a high prevalence in certain populations. For example, PAH affects 23% of those with connective tissue disease[3] and 32% of those with sickle cell disease[4]. This disease-associated PAH, in addition to inherited and spontaneous forms, are collectively termed "primary pulmonary arterial hypertension" (PPAH), because their exact cause is poorly understood. Just 30 years ago, the average PPAH patient died 2.8 years after diagnosis, and only 68% survived 1 year[5]. This is similar to the current 5-year survival rate for cancer[6]. Although therapeutic advancements have since improved the 1-year survival rate to 91%[7], an average delay of 2 years from symptom onset to diagnosis has not improved[8,9]. Although this is, in part, due to the subtle signs (e.g., breathlessness) of PAH[1], improved diagnostic procedures could expedite diagnosis. The purpose of this research was to conduct a review of the current techniques and technologies used to diagnose PAH.

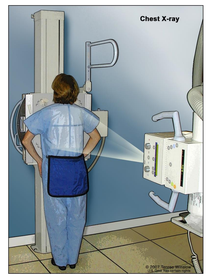


Conclusions

Currently, choosing a procedure to diagnose PAH requires making trade-offs. Those that are more accurate are also more invasive; similarly, less invasive options are less accurate. PAH has yet to find its equivalent of the drug store arm cuff, a device that can easily, inexpensively, and accurately measure MPAP. In the mean time, studies have achieved improved diagnostic success by using less invasive procedures to screen patients before using right heart catheterization to reach a definitive diagnosis[19,21].

Chest X-ray

Procedure: Small amounts of radiation are used to produce images of the heart and lungs. In X-ray images, more radiodense structures, such as the heart and pulmonary arteries, appear bright against less radiodense structures, such as lung tissue. Enlarged pulmonary arteries are used as indirect evidence of PAH[16].



Sensitivity: 50%[16]

Specificity: 100%[16]

Other features:

- Non-invasive

Echocardiography

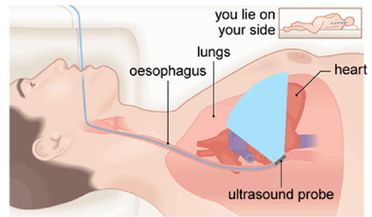
Procedure: Doppler ultrasound is used to produce moving images of the heart. These images contain useful information about the movement of blood through the heart and can be analyzed to estimate the peak pressure in the pulmonary arteries[18]. They can also be used to detect right atrial enlargement[16], a sign of right heart failure.

Sensitivity: 71%[19]

Specificity: 69%[19]

Other features:

- Overestimates pressures by more than 10 mmHg in 30-50% of patients[20]
- Non-invasive



The ultrasound probe is passed through the oesophagus to view the heart

Bupa

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