**Pulmonary Hypertension Questions**

**Question 1**: Epidemiology (1)

A 69 year-old male with progressive breathlessness is admitted under the medical assessment and planning unit (MAPU) with progressive breathlessness for investigation. He had an unprovoked pulmonary embolus 3 years ago that was treated with 6 months of warfarin. Since that time, he has noted his breathlessness to worsen progressively. Further complaints include intermittent dizziness and syncope. He has noted an increase in his abdominal girth with accompanying leg swelling. He is now largely bed-bound and is completely dependent on his family for his activities of daily living. He has a loud P2, an ejection systolic murmur over the tricuspid region and a right ventricular heave. His JVP is elevated without ‘a’ waves but prominent ‘v’ waves. He has shifting dullness and peripheral oedema up to mid thigh. His ECG shows signs of right ventricular hypertrophy, and his ECHO estimates a systolic pulmonary pressure of 55mmHg using the estimated tricuspid jet velocity in ‘M’ mode.

With regards to his most likely diagnosis, what is the most CORRECT statement?

(A) Idiopathic pulmonary arterial hypertension (IPAH) patients most likely carry the mutation for Bone Morphogenetic Receptor 2

(B) The expected survival of a patient who responds to inhaled nitric oxide with a drop in their mean pulmonary arterial pressure of 8mmHg is highly favourable if they are placed on high dose nifedipine or diltiazem

(C) 10% of patients will get pulmonary hypertension complicating a pulmonary embolus

(D) The treatment of patients with pulmonary artery hypertension secondary to obesity hypoventilation syndrome is similar to that of pulmonary artery hypertension secondary to chronic thromboembolic disease

(E) The mean age of diagnosis if idiopathic pulmonary arterial hypertension (IPAH) is 55 years with a median survival that is improving, however 5 year survival being only 2.8 years

**Question 2:** Epidemiology and prognostic factors

Which of these following factors is NOT a known adverse prognostic feature of pulmonary arterial hypertension

(A) Echocardiographic findings of large right atrial diameter, diastolic septal shifting and pericardial effusions

(B) Hypocapnia

(C) ECG findings of atrial fibrillation, atrial flutter or prolonged QRS duration

(D) Female gender

(E) Six minute walk test

**Question 3:** Clinical Diagnosis

On the Jugular venous pressure trace, what feature is associated with pulmonary arterial hypertension?

(A) Absent ‘a’ waves

(B) Prolonged ‘x’ and ‘y’ descent

(C) Kausmalls sign

(D) Cannon ‘a’ waves

(E) Raised ‘v’ waves

**Question 4:** Clinical Diagnosis

Which of the following clinical signs are NOT associated with pulmonary arterial hypertension?

(A) Right ventricular lift

(B) Pulsatile liver, ascites and peripheral oedema

(C) Early decrescendo diastolic murmur with pre-systolic blowing murmur

(D) Right ventricular third heart sound

(E) Paradoxically split second heart sound with palpable S2

**Question 5:** Clinical Diagnosis

What is the most common arrhythmia associated with pulmonary arterial hypertension?

(A) Atrial Fibrillation

(B) Atrial Flutter

(C) Atrio-Ventricular Nodal Re-entrant Tachycardia

(D) Idioventricular Rhythm

(E) Sinus Bradycardia

**Question 6:** Clinical Diagnosis

A 69 year-old male with progressive breathlessness is admitted under the medical assessment and planning unit (MAPU) with progressive breathlessness for investigation. He had an unprovoked pulmonary embolus 3 years ago that was treated with 6 months of warfarin. Since that time, he has noted his breathlessness to worsen progressively. Further complaints include intermittent dizziness and syncope. He has noted an increase in his abdominal girth with accompanying leg swelling. He is now largely bed-bound and is completely dependent on his family for his activities of daily living. He has a loud P2, an ejection systolic murmur over the tricuspid region and a right ventricular heave. His JVP is elevated without ‘a’ waves but prominent ‘v’ waves. He has shifting dullness and peripheral oedema up to mid thigh. His ECG shows signs of right ventricular hypertrophy, and his ECHO estimates a systolic pulmonary pressure of 55mmHg using the estimated tricuspid jet velocity in ‘M’ mode.

What chest X-ray imaging sign would be LEAST associated with pulmonary hypertension

(A) Cardiomegaly

(B) Pulmonary Arterial Pruning

(C) Right Upper Lobe consolidation with air-bronchograms

(D) Bi-basal predominant interstitial infiltrates resembling fibrosis

(E) Hampton’s hump

**Question 7:** Clinical Diagnosis

A 28 year-old man is suspected of having idiopathic pulmonary artery hypertension with a JVP measuring 5cm above sternal notch. He has an echocardiogram performed. The views were of sufficient quality, enabling the sonographer to calculate the following parameters:

Tricuspid regurgitant jet velocity: 4m.s-1

Left ventricular Ejection Fraction using Simpsons Method: 58%

Fractional shortening: 37%

What is the BEST fit for calculated parameters

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Answer | Pressure gradient (δP) | Right Atrial Pressure | Systolic Pulmonary Arterial Pressure | Diagnosis |
| A | 64 | 10 | 54 | Pulmonary hypertension |
| B | 64 | 10 | 74 | Undetermined |
| C | 64 | 5 | 69 | Undetermined |
| D | 48 | 5 | 53 | Pulmonary hypertension |
| E | 48 | 10 | 58 | Pulmonary hypertension |

**Question 8:** Clinical Diagnosis

A 24 year-old female with uncontrolled HIV presents with progressive breathlessness. An echocardiogram is performed showing raised pulmonary systolic pressures of 70 mmHg. A right heart catheterisation study is organised. Which answer of the following trace best identifies the correct sequence of waveforms?

A

B

C

D

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Answer | A | B | C | D |
| A | Wedge pressure | Right atrial Pressure | Right ventricular pressure | Pulmonary artery pressure |
| B | Right ventricular pressure | Wedge pressure | Pulmonary artery pressure | Right atrial Pressure |
| C | Right atrial Pressure | Right ventricular pressure | Wedge Pressure | Pulmonary artery pressure |
| D | Right atrial Pressure | Right ventricular pressure | Pulmonary artery pressure | Wedge pressure |
| E | Right atrial Pressure | Pulmonary artery pressure | Right ventricular pressure | Wedge pressure |

**Question 9:** Categories of pulmonary hypertension

Once the diagnosis of pulmonary arterial hypertension is distinguished from pulmonary venous hypertension, which of the below options does NOT adequately help distinguish a cause

(A) ANA and interstitial lung disease

(B) V/Q and CTPEH

(C) anti-scl70 and diffuse scleroderma

(D) anti-centromere and limited scleroderma

(E) HIV third generation antigen/ antibody and HIV

**Question 10:** Causes

Which of the following medications are NOT associated with idiopathic pulmonary arterial hypertension

(A) dasatinib

(B) appetite suppressants

(C) St Johns wort

(D) chronic cocaine use

(E) obinutuzumab

**Question 11:** Treatment

A 68 year-old male with idiopathic pulmonary hypertension is undergoing consideration for treatment. Which of the following statements is FALSE about the role of anti-coagulation.

(A) Warfarin is the anticoagulation of choice because other studies are lacking

(B) A meta-analysis of seven observational studies has shown a benefit favouring anti-coagulation in terms of mortality

(C) There is no difference in bleeding risk in patients with PAH secondary to connective tissue disease in comparison to patients with idiopathic pulmonary hypertension

(D) There is no evidence for use of anticoagulation in PAH due to anorexigens

(E) The rationale for anti-coagulation is due to sluggish pulmonary blood flow leading to a predisposition for thrombosis on the background of poor physiological reserve

**Question 12:** Treatment

Which patient group is most likely to respond to the nitrous oxide vasoreactivity test?

(A) Pulmonary arterial hypertension secondary to non-specific interstitial pneumonia

(B) Pulmonary arterial hypertension secondary to drugs such as anorexigen

(C) Pulmonary arterial hypertension secondary to HIV

(D) Pulmonary arterial hypertension secondary to schistosomiasis

(E) Pulmonary arterial hypertension secondary to PTPN22a mutation

**Question 13:** Treatment

What is the mortality of a patient who has pulmonary arterial hypertension who falls pregnant?

(A) 17 – 33%

(B) 2 – 12%

(C) 35 – 60%

(D) 50 – 70%

(E) 60 – 85%

**Question 14:** Treatment

Which of the following statements is INCORRECT

(A) Bosentan and ambrisentan are endothelin receptor antagonists, functionally causing a pulmonary vasodilated state, with Bosentan causing reversible liver function abnormalities in 10% requiring monthly LFT monitoring

(B) Sildanefil and tadalafil inhibit phosphodiesterase 5, which causes increased cyclic GMP via nitrous oxide therefore causing pulmonary smooth muscle vasodilation. Its use is contra-indicated with other nitrates

(C) One criterion of the PBS states that right heart catheterisation should be used and the criterion is that the mean pulmonary arterial pressure is greater than 25 mmHg with the pulmonary capillary wedge pressure less than 15mmHg

(D) Prostanoids are prostacyclins that cause pulmonary arterial vasodilation with added anti-proliferative effects

(E) Riociguat cannot be used for the treatment of pulmonary artery hypertension secondary to chronic thromboembolic disease

|  |  |
| --- | --- |
| Question | Answer |
| 1 | **A:** Out of all the genetic mutations present, BMPR2 confers the highest risk. 10 – 40% are carriers, 7% of familial PAH carry the mutation, however there is low penetrance – lifetime risk for a carrier is 20%. Other mutations include 5HTT, SMAD9 and endoglin. The pathogenesis of BMPR2 mutation is yet unknown, although a viable hypothesis is that it decreases apoptosis of endothelial cells, thereby favouring cellular endothelial proliferation. Inhaled nitrous oxide responsiveness is predictive of a favourable response to calcium channel blockers and overall good prognosis however the criterion is a reduction in more than 10mmHg in the *m*PAP pressures AND < 40mm Hg WITHOUT a fall in cardiac output. Between 0.5 – 4% of patients with a pulmonary embolus develop pulmonary arterial hypertension. Identifying a cause for PAH is important as it dictates treatment. The majority of causes are that secondary to left sided heart disease or lung disease, therefore addressing the primary cause is important. The mean age of diagnosis of idiopathic pulmonary hypertension used to be 35 years of age, and the untreated 5 year survival was 2.8 yrs but treated patients can expect a 5-year survival of 75% (1) |
| 2 | **D:** Interestingly, Hoeper and colleagues showed that PaO2 is not a prognostic indicator, yet decreased PaCO2 is a strong and independent prognostic marker (2). Echocardiographic features are important and are correlated with the extent of pulmonary hypertension, as is mixed venous oxygen saturations and six- minute walk tests (3). ECG findings mentioned above are also predictive of poor prognosis, and atrial flutter in particular may predispose to circulatory collapse (1). Other factors include co-morbid conditions, age >45, male gender, WHO functional class 3 or 4, failure to improve WHO functional class during treatment, increased NT-pro-BNP and SSRIs (uptodate) |
| 3 | **C:** Pulmonary arterial hypertension leads to signs related to tricuspid regurgitation, which would include elevated JVP with raised v waves. Absent a waves occurs in atrial fibrillation, and cannon a waves occur in tricuspid stenosis. Prolonged x and y descent occurs with constrictive pericarditis, and Kausmalls sign is a feature of both constrictive pericarditis and cardiac tamponade. It relates to the inspiratory rise in JVP that occurs due to raised right atrial pressures and a restricted physiology.  |
| 4 | **B:** Early decrescendo diastolic murmur occurs with aortic regurgitation, and pre-systolic murmur occurs with mitral regurgitation producing a functional mitral stenosis, known as the Austin flint murmur.  |
| 5 | **B:** According to Reference (1) |
| 6 | **C:** Right upper lobe consolidation occurs with pneumonia. Unless the cause is complicated by cryptogenic organising pneumonia left untreated, it is highly unlikely that pneumonia would lead to pulmonary hypertension. Pulmonary arterial pruning is a feature seen in pulmonary hypertension. Cardiomegaly may lead to pulmonary hypertension through elevated left sided pressures. Hampton’s hump is a feature of pulmonary embolus, and bi-basal predominant fibrosis may be a sign of idiopathic interstitial pneumonia that may cause pulmonary hypertension (Radiopedia.org) |
| 7 | **B:** using dP = 4v2 to calculate the pressure gradient between RA and RV gives 64 mm Hg. Using RAP = 5 + JVP gives RAP = 10 mmHg. Assume RV pressure approximates Pulmonary arterial pressure (not true if pulmonary stenosis present), then RV = dP (64) + RAP (10) = 74 mm Hg. Pulmonary arterial hypertension cannot be diagnosed through echocardiography therefore the diagnosis is yet to be determined.  |
| 8 | **D:** Other options do not make physiological sense! |
| 9 | **A:** V/Q scanning is indicated, and even better would be CTPA, as it helps to distinguish anatomy, guide management (2/3 of patients may be eligible for pulmonary endarterectomy), and help distinguish the possibility of other underling aetiologies (eg UIP radiological pattern). HIV is a well known cause of WHO Category 1 PAH, affecting 0.5% of the HIV effected population. Porto-pulmonary hypertension and schistosomiasis are also grouped into the idiopathic category. ANA is non-specific, however a raised titre may point towards a connective tissue disease as the cause, eg SLE, scleroderma or dermatomyositis/ polymyositis.  |
| 10 | **E**: obinutuzumab is a monoclonal antibody against CD20, binding at a different portion than rituximab. It is not associated with PAH. Note: SSRI’s have incidental evidence that they cause persistent pulmonary hypertension of the newborn (uptodate) |
| 11 | **C:** There is a signal showing that bleeding risk (upto 23%) is elevated in patients with PAH-CTD receiving anticoagulation. The other NOACS have not been studied, 5 out of 7 observational studies supported a mortality benefit (within the limits of observational studies). Other categories include PAH-heritable and CTPEH (4).  |
| 12 | **B**: All the others do not have as much of an effect. If there is a favourable response to nitrous oxide, with the pulmonary arterial pressure dropping 10mmHg AND below 40mm Hg mPAP AND there is no change in cardiac output THEN the patient is suitable for high dose calcium channel blockers. 10% of patients will be vasoreactive. PTPN22a mutation is not associated with PAH.  |
| 13 | **A:** There is a significant mortality due to increased pregnancy related physiological blood flow exacerbating right ventricular failure. The mortality is as high as 33%, and pregnancy should be avoided with appropriate contraception. Guidelines suggest progesterone only pills. Termination should be offered (5) |
| 14 | **E:** Riociguat is a guanyl cyclase stimulator. In a phase 3 RCT published in NEJM, Riociguat increased exercise tolerance (6MWT increase 39m compared to 6m decrease in placebo), WHO functional class, NT-pro-BNP and improved pulmonary vascular resistance when compared to placebo in patients with CTPEH who were non-operative candidates or who were re-offenders after endarterectomy (6). Another breakthrough is the combination use of ambrisentan (endothelin receptor antagonist) with tadalafil (PDE5 inhibitor) when compared to either agent alone in patients who are treatment naïve, which showed a favourable treatment response (7).  |

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