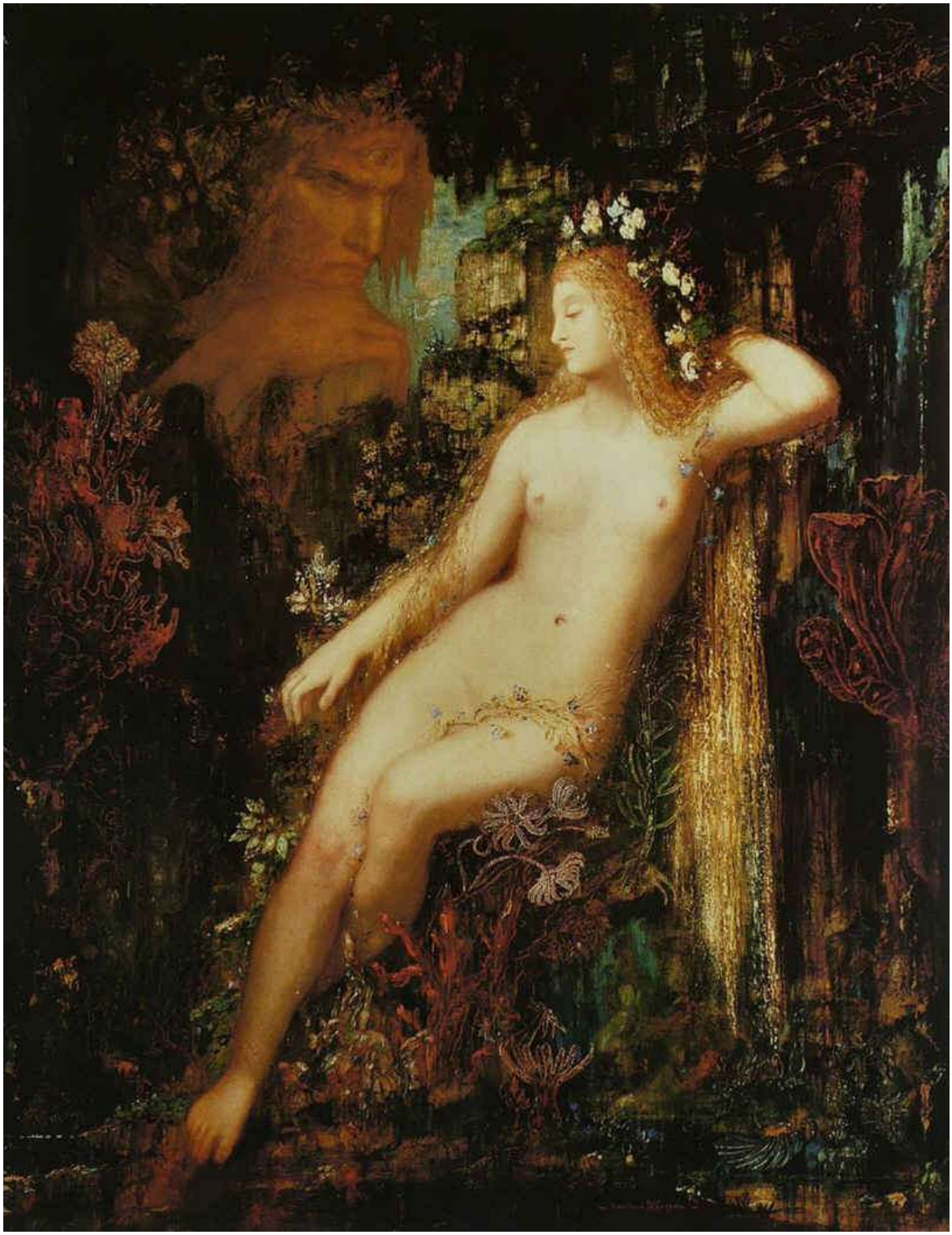
THE NORTHERN HOSPITAL

PULMONARY EMBOLISM (IN PREGNANCY)



"Galatea", oil on wood, Gustave Moreau c. 1880, Musée d'Orsay, Paris.

"*While I pursued Acis with a passionate love, the Cyclops pursued me just as passionately . And, should you ask me... I could not declare whether my hatred of him, or my love of Acis was the stronger - they were equal...*

That savage, dreaded by the forest trees, feared by the stranger who beholds his face, creature of Olympus and the gods, now he can feel what love is. He is filled with passion for me. He burns hot for me, forgetful of his cattle and his caves. Now, Polyphemus, wretched Cyclops, you are careful of appearance, and you try the art of pleasing. You have even combed your stiffened hair with rakes: you to trim your shaggy beard with sickles, while you gaze at your fierce features in a pool so earnest to compose them. Love of flesh, ferocity and your thirst for blood have ceased. The ships may safely come and go! "

...While all this happened, Telemus arrived at the Sicilian Etna - Telemus, the son of Eurymus, who never once mistook an omen, met the dreadful Cyclops, Polyphemus, and said: "*That single eye in your brow; Ulysses will take from you". In reply, the Cyclops only laughed at him and said, "Most ignorant of the prophets! You are wrong, a maiden has already taken it!* "

He said to Galatea, "*you must know, my father Poseidon is the ruler of all the seas, and therefore I now offer him to you as your own father-in-law - But, do take some pity on a suppliant and hear his prayer, for only unto you my heart is given. I, who despise the power of Zeus, his heavens and piercing lightning bolts, am afraid of you - your wrath more fearful to me than the lightning's flash - but I should be more patient under slights, if you avoided all men: why reject the Cyclops for the love that Acis gives? And why prefer his smiles to my embraces...I will pull out his palpitating entrails, and scatter his torn limbs about the fields and over and throughout your salty waves; and then let him unite himself to you that way. I burn so, and my slighted passion raves with greater fury and I seem to hold and carry Etna in my breast - transferred there with its flames - Galatea! can you listen to my passion thus unmoved!*"

...I saw all this; and, after he in vain had uttered such complaints, he stood up like a raging bull whose heifer has been lost, that cannot stand still, but must wander on through brush and forests, that he knows so well: when that fierce monster saw me and my Acis - we neither knew nor guessed our fate - he roared: "*I see you both! Never again will you parade your love before me!*" *In such a voice as matched his giant size, all Etna shook and trembled at the noise; and I amazed with horror, plunged into the adjoining sea. My loved one, Acis turned his back and fled and cried out,* "*Help me Galatea, help!, let your parents help me, and admit me safe within their realm; for I am now near my destruction!* " *But the Cyclops rushed at him and hurled a fragment he had torn out from the mountain, and although the extreme edge only of the rock could reach him there, it buried him entirely.*

...Then I did the only thing the Fates permitted me: I let my Acis take the ancestral power of the river deities. The purple blood flowed from beneath the rock, but soon the sanguine richness faded and became at first the colour of a stream, disturbed and muddied by a shower. And presently it cleared. The rock that had been thrown by Polyphemus then split in two, and through the cleft a reed, stately and vigorous, arose to life. And soon the hollow mouth in the great rock, resounded with the waters gushing forth. And wonderful

to tell, a youth emerged, the water flowing clear about his waist, his new horns circled with entwining reeds, and the youth certainly was Acis, though he was of larger stature and his face and features all were azure. Acis changed into a stream which ever since that time has flowed there and retained its former name.

Ovid,
Galatea and Polyphemus;
The Metamorphoses
Bk 13,
8 A.D

Galatea the beautiful river nymph was in love with Acis, but she had caught the eye of the terrifying son of Poseidon, Polyphemus, the Cyclops. The Cyclops dreadful to behold fell passionately in love with Galatea. He made a fool of himself composing loves songs to her and trying to tidy up his appearance in order to distract her from the appalling single eye placed in the middle of his forehead. Galatea was horrified and rejected his hopeless advances. Polyphemus however was well known for being "one eyed", not just in appearance, but also by stubborn temperament! When he had set his mind on something he desired it was as though he had focused his single eye on this object to the exclusion of all else. The great seer Telemus had seen omens and warned Polyphemus at this point in time of his future fate at the hands of Ulysses, but he had ignored the prophecy, metaphorically blinded by his lust for Galatea.

Polyphemus learnt that Galatea was in love with Acis, and when he encountered the lovers in a clearing he grew so angry that he grabbed an immense rock and hurled it at Acis, crushing him beneath it. Galatea, being a river nymph had semi-divine aquatic powers, and to save Acis turned him into a river that carried his spirit in order to escape entombment under the rock.

Unlike the Cyclops we must not be narrow sighted when it comes to managing our pregnant patients with suspected PE. We must always pay heed to the warning signs of possible pulmonary embolism and not ignore these dangerous omens. Should we suspect this potentially lethal condition, we must not be overly distracted from misplaced concerns over the dangers of radiation. Although some radiation exposure will be involved, steps are taken to minimise this exposure as much as possible, in the form of nuclear perfusion scanning as the preferred option for imaging and bismuth shielding for those who do require a CTPA.

PULMONARY EMBOLISM (IN PREGNANCY)

Introduction

PE in pregnancy is a significant cause of morbidity and mortality in pregnant women in Australia

Failure to investigate symptoms suggestive of pulmonary embolism (PE) is a consistent finding in maternal death enquiries, and clinical symptoms should not be relied on to exclude or diagnose VTE.

In pregnancy, the symptoms of PE (shortness of breath, pleuritic chest pain, haemoptysis and syncope) are not sufficiently specific to allow a confident clinical diagnosis.

For this reason, all pregnant or postpartum women with a clinical suspicion of PE should have appropriate imaging.

Options include:

- Nuclear medicine perfusion scanning with or without ventilation scanning
- CT pulmonary angiography (CTPA).

In **non-pregnant** patients, CTPA has become the test of choice for investigation of suspected PE because of a high rate of non-diagnostic ventilation/ perfusion (V/Q) scans and the ability of CTPA to diagnose other chest pathology.

However, in **pregnant women**, the rate of non-diagnostic V/Q scans is lower or equivalent to the rate of non-diagnostic CTPA.

The performance of isotope scanning in pregnant and postpartum women with suspected PE therefore remains the investigation of choice when available, due to reduced ionizing radiation doses, **(see appendix 1).**

Warfarin is absolutely contraindicated in pregnancy.

Treatment for PE in pregnancy will require **daily LMWH**

LMWH provides safe and effective treatment of such events with no adverse fetal effects.

All patients diagnosed with a pulmonary embolism should be admitted to hospital for at least 48 hours.

Pathophysiology

There is an extensive array of pathological risk factors for VTE in pregnancy.

These include:

- Personal history of VTE
- Family history of VTE
- Thrombophilia: Congenital or Acquired
    - ♥ In particular Antiphospholipid syndrome (APLS)
- Extended major pelvic or abdominal surgery
- Paralysis of lower limbs
- Age greater than 35 years
- Weight greater than 80 kg and / or BMI greater than or equal to 30
- Parity of four or more
- Gross varicose veins
- Current infection
- Prolonged immobility/hospitalization (greater than 4 days)
- Delivery related factors:
    - ♥ Caesarean delivery: Increased risk with emergency caesarean in labour
    - ♥ Labour longer than or equal to twelve hours
    - ♥ Assisted birth
    - ♥ Excessive blood loss
- Dehydration
- Pregnancy related medical illnesses:
    - ♥ Ovarian hyper-stimulation syndrome; Preeclampsia; Hyperemesis
- Pre-existing medical illness, for example:
    - ♥ Nephrotic syndrome; Cardiac disease; Cancer; Inflammatory bowel disease; Sickle cell disease

Clinical assessment

There is an increased risk of thrombo-embolic disease in pregnancy and in the immediate post partum period.

In pregnancy, the symptoms of PE are not sufficiently specific to allow a confident clinical diagnosis.

Ultimately an imaging test will be required to make or rule out the diagnosis.

Investigations

A concerning feature in reports of maternal mortality and morbidity is that women who present with symptoms suggestive of PE and DVT are often inadequately investigated. Commonly this is either because of a failure to recognise that women's symptoms may be due to DVT or PE or because appropriate investigations are not carried out because of misplaced concerns about the fetal effects of radiation used in imaging studies.

Radiation risk

The maternal and fetal risks of exposure to ionising radiation are often a cause for concern for both clinicians and their patients.

However, the radiation doses associated with the radiological investigations mentioned above are well below the threshold of 50 mGy above which the risk of adverse fetal effects begins to rise.

The usual doses of the radioisotopes used in V/Q scanning do not deliver high doses to the fetus.

D-Dimer testing:

In **non-pregnant** patients, the addition of D-dimer testing to clinical assessment is useful in evaluating suspected DVT.

In **pregnancy,** D-dimer levels are elevated leading to a high rate of false-positive results if standard cut-off values are used, irrespective of the laboratory assay used.

D-dimer testing is **not recommended** for the evaluation of suspected DVT or PE in pregnancy or the early postpartum period.

Thrombophilia screen:

Antiphospholipid antibodies should be checked in all patients. This includes lupus anticoagulant, anti-cardiolipin antibodies and B2-glycoprotein antibodies.

A general Thrombophilia screen should also be performed in **all** pregnant women.

Thrombophilia screening includes:

- Factor V Leiden
- Prothrombin Gene Mutation
- Protein S
- Protein C
- Anti-thrombin III

Thrombophilia screen should be done **prior** to the commencement of anticoagulation as it may affect results.

Imaging

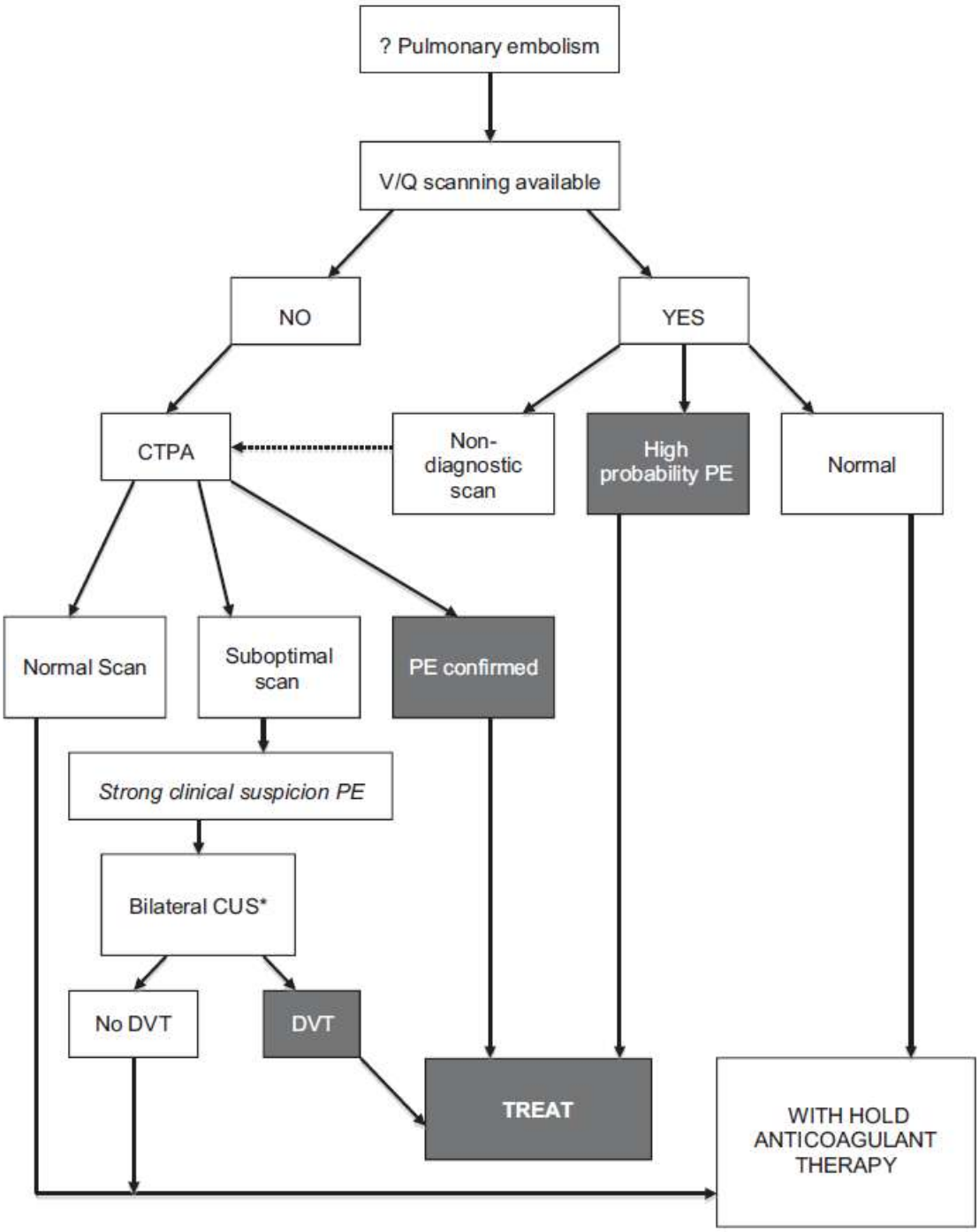
CXR should be the initial imaging investigation. This may suggest an obvious alternative diagnosis, but is also necessary to assist in determining the optimal subsequent imaging investigation.

Radioisotope (V/Q) scanning is the preferred investigation in pregnant or postpartum women with suspected PE who have a *normal chest X-ray.*

CTPA should be used in women with an abnormal CXR or where V/Q scanning is inconclusive or not available.

The fetal and maternal radiation dose with either V/Q scanning or CTPA is within acceptable limits, and neither test should be withheld in a pregnant woman who has clinical symptoms that raise the suspicion of PE.

Bilateral total limb compression ultrasound scanning has a role in patients who have had CTPA scan with inconclusive results.



*Pathway for investigation of suspected PE in the pregnant patient and in the immediate post part partum period. * CUS = compression ultrasound.*

V/Q Scanning

In women investigated for PE using isotope scanning, **a normal perfusion scan** is generally considered sufficient to exclude thrombosis and a ventilation scan is not required. This approach is reasonable in women with a *low clinical probability* of a PE.

Women with an abnormal perfusion scan require confirmation of ventilation/ perfusion mismatch and so will need a follow-up ventilation scan.

CTPA

Maternal radiation exposure, in particular to the breasts, can be up to 40 times higher with CTPA (16 - 50 mGy) than with V/Q scanning.

The major concern with this is a potential to increase the lifetime risk of breast cancer, especially given the increased radiosensitivity of proliferating breast tissue in pregnancy or during lactation.

Bismuth breast shielding reduces breast radiation exposure by > 50% (without degrading the images) and is recommended with CTPA.

Breastfeeding:

Women investigated for PE who are breastfeeding do not need to discard milk following CTPA (or MRI).

Following V/Q scan, breast milk should be discarded for a period of **12 hours.**

Management

Warfarin is absolutely contraindicated in pregnancy

Warfarin may be used safely in the postpartum period and is safe for breastfeeding.

Heparin does not cross the placenta and is safe to use in pregnancy and breast feeding.

NOACs are contraindicated in pregnancy.

Heparin therapy:

LMWH & UFH:

Women with PE (and/or DVT) during pregnancy should be treated with therapeutic dose low molecular weight heparin, (LMWH) in preference to unfractionated heparin (UFH).

In women judged to be at high risk of haemorrhage, UFH may be preferred because of its shorter half-life and the ability to fully reverse its anticoagulant activity if necessary.

Frequency:

Women with PE (or more extensive DVT i.e. iliofemoral thrombosis) during pregnancy should receive initial treatment with **twice-daily** LMWH for at least 8-12 weeks, after which time a reduction to a once-daily regimen may be considered.

Duration:

Anticoagulant therapy in pregnant women with acute proximal DVT and/or PE should be continued until at least six weeks postpartum or longer, if necessary, to complete a minimum total treatment period of six months.

Monitoring:

Monitoring of LMWH therapy is usually unnecessary in non-pregnant patients.

Weight-related changes in volume of distribution and increased renal clearance during pregnancy have been suggested as reasons for monitoring women on therapeutic LMWH.

However, there is no data demonstrating clinical benefit from dose adjustment of LMWH according to anti-Xa levels during pregnancy.

There is insufficient evidence to recommend monitoring of anti-Xa levels to guide dosing in women on therapeutic dose LMWH.

Anti-Xa levels are not required in women on prophylactic dose LMWH.

IVC filters:

Insertion of a temporary IVC filter should be considered in pregnant patients with:

- Recent acute venous thrombosis in whom therapeutic anticoagulation is contraindicated because of a high risk of bleeding.

- Objectively confirmed recurrent VTE despite therapeutic anticoagulation.

Compression stockings:

Post-thrombotic syndrome (PTS) is characterised by symptoms of leg, itching, cramps and pain, with physical signs of leg oedema, hyperpigmentation, new venous ectasia and, rarely, in its most severe manifestation, by the presence of a venous stasis ulcer.

Around 15-50% of patients who have suffered with DVT will develop PTS; however, regular use of an elastic compression stocking reduces the incidence of PTS by around 50%.

The rate of PTS is similar to the rate in non-pregnant women of the same age suggesting that pregnancy, per se, does not increase the risk of PTS after a DVT.

All women with a confirmed DVT should wear a below knee class 2 (i.e. 30 - 40 mmHg) compression stocking for up to two years.

Thrombolysis:

Thrombolysis should only be considered in pregnancy for women with: life or limb-threatening complications of acute VTE.

- Life threatening PE includes those who have cardiogenic shock with a systolic blood pressure of < 90 mm Hg.

- Limb threatening VTE disease includes massive iliofemoral vein thrombosis with consequent limb threatening ischemia.

Disposition:

Inpatient observation and treatment of women with PE, for the first few days following diagnosis is recommended.

Referral should be to:

- Obstetrics

- Haematology

Appendix 1

Estimated fetal and maternal radiation doses associated with radiological investigations used for diagnosis of pulmonary embolism.

Radiological procedure	Fetal dose (mSv)	Maternal dose (mSv)
Chest X-ray	0.001- 0.01	< 0.01
Ventilation scan ^{99m}Tc	0.01 - 0.1	0.5
Perfusion scan ^{99m}Tc	0.1 - 0.6	0.6 - 1.0
Single slice CTPA	0.03 - 0.06	1.6 - 4.0
Multi-slice CTPA	0.003 - 0.1	2 - 6
Pulmonary angiography	> 0.5	5 - 30

References

1. McLintock C et al; Recommendations for the diagnosis and treatment of deep venous thrombosis and pulmonary embolism in pregnancy and the postpartum period; Australian and New Zealand Journal of Obstetrics and Gynaecology 2012; 52: 14-22

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