COMPARISON OF DIAGNOSTIC QUALITY AND RADIATION DOSE BETWEEN TEST BOLUS AND BOLUS TRACKING PROTOCOLS FOR COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY (CTPA) AMONG PREGNANT WOMEN IN TWO TERTIARY CENTRES

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DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENT FOR MASTER OF MEDICINE (RADIOLOGY)

UNIVERSITI SAINS MALAYSIA

2023

ACKNOWLEDGEMENT

I would like to express my utmost gratitude to God for giving us the opportunity and helping me endlessly finish the Module of Dissertation formatting with Microsoft Word. The masterpiece has led to the development of a Dissertation that is readily used and applied to all USM community networks. Special thanks to my supervisor Dr Noor Khairiah A. Karim, for guiding me and correcting the proposal until the completion of this dissertation. Special gratitude goes out to all in the team – Dr Rositaa Mohd Ibrahim and Dr Roslina Abd Halim, patience in overcoming numerous obstacles in finishing the task. Moreover, in completing the Dissertation, I had to take the help of some respected persons who deserve our most incredible gratitude, Dr Kueh Yee Cheng (Biostatistics and Research Methodology, HUSM), Dr Nurul Akhmar Omar (Head of the department, Radiology Hospital Pulau Pinang), Dr Tan Yuan Ying (Radiologist, Radiology Department Hospital Seberang Jaya), Pn Kartini (Radiographer, Radiology Department Hospital Seberang Jaya) and Pn Mashita (Physicist, Radiology Department Hospital Seberang Jaya) for guiding and helping us in numerous consultations. In addition, special thanks to the Director of Hospital Pulau Pinang, Dato' Dr Teo Gim Sian and the Director of Hospital Seberang Jaya, Dr Hj Saiful Azlan bin Hj Sharif for permitting to review the old records and PACS of both hospitals. Last but not least, I appreciate my family and wife, Lee Chew Hun, for supporting me.

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LIST OF SYMBOLS, ABBREVIATIONS, AND ACRONYMS

≥	more than or equal to
>	more than
<	less than
≤	less than or equal to
±	plus or minus, used to indicate the precision of an approximation

CM	Contrast Media
CT	Computed Tomography
CTPA	Computed Tomography Pulmonary Angiogram
ECG	Electrocardiography
HSJ	Hospital Seberang Jaya
HPP	Hospital Pulau Pinang
HU	Hounsfield units
LV	Left ventricle
MOH	Ministry of Heath
n	number
PA	Pulmonary Artery
PACS	Picture archiving and communication system
SD	Standard Deviation
SVC	Superior vena cava
ROI	Region of Interest
RV	Right ventricle
TTP	Time to Peak
VTE	Venous thromboembolism

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ABSTRAK

Latar belakang: Tomografi berkomputer angiografi pulmonari (CTPA) dalam kalangan wanita hamil selalunya bukan diagnostik dan terdedah kepada pengulangan CTPA. Kajian ini bertujuan untuk membandingkan protokol ujian bolus dan pengesanan bolus untuk CTPA di kalangan wanita hamil dengan menganalisis purata peningkatan kontras arteri pulmonari, kualiti diagnostik dan dos sinaran, serta keputusan CTPA berulang di kalangan wanita hamil disebabkan oleh CTPA yang tidak diagnostik.

Metod: Kajian retrospektif dari dua hospital rujukan tertiari ini termasuk wanita hamil yang menjalani pemeriksaan CTPA menggunakan protokol ujian bolus dan pengesanan ujian. Kualiti CTPA, purata kontrast arteri pulmonari dan *dos length product (DLP)* telah dikumpulkan dan dibandingkan antara kedua-dua protokol. Kekerapan dan keputusan pengulangan CTPA disebabkan kualiti suboptimum telah dianalisis.

Keputusan: Seramai 69 pesakit telah dipilih daripada kedua-dua kumpulan, 34 daripada protokol ujian bolus dan 35 daripada protokol pengesanan bolus. Protokol ujian bolus menghasilkan kontrast arteri pulmonari yang sama dengan peratus CTPA kualiti diagnostik yang lebih tinggi daripada protokol pengesaan bolus, namun tidak signifikan secara statistik. Protokol pengesanan ujian mempunyai kualiti CTPA yang boleh diterima dengan signifikan berbanding protokol ujian bolus. Protokol ujian bolus mempunyai purata *DLP* yang lebih rendah, 220 mGy.cm ± 69, membanding degan protokol pengesanan ujian, 323 mGy.cm ± 34, nilai p <0.001. Separuh daripada tomografi berkomputer angiografi pulmonari yang berulang tidak menunjukkan kualiti tomografi berkomputer angiografi pulmonari yang lebih baik secara signifikan.

Kesimpulan: Tidak terdapat perbezaan yang signifikan antara protokol ujian bolus dan pengesanan ujian dalam CTPA di kalangan wanita hamil, tetapi protokol pengesanan ujian mempunyai kualiti CTPA keseluruhan yang lebih baik dengan pertukaran dos

sinaran yang lebih tinggi. Pengulangan kajian CTPA untuk suboptimum kualiti tidak selalu mendapat manfaat. Oleh itu, kami menasihatkan supaya menimbangkan risiko dan faedah pengulangan CTPA.

Kata kunci: *Tomografi berkomputer angiografi pulmonari (CTPA), hamil, ujian bolus, pengesanan ujian, dos radiasi*

ABSTRACT

Background: Computed Tomography Pulmonary Angiography (CTPA) among pregnant women is often non-diagnostic and may need the repetition of CTPA. This study aims to compare the test bolus and the bolus tracking protocols for CTPA among pregnant women by analysing the mean contrast enhancement of the pulmonary artery, diagnostic quality and radiation dosage, as well as the outcome of repeated CTPA among pregnant women due to initial non-diagnostic CTPA.

Methods: This retrospective study from two tertiary centres included pregnant women who underwent CTPA using test bolus and bolus tracking protocols. CTPA quality, mean pulmonary artery enhancement and dose length product (DLP) were collected and compared between both protocols. The frequency and outcome of CTPA repetition due to suboptimal quality were analysed.

Results: A total of 69 patients were selected from both groups, 34 from test bolus protocol and 35 from bolus tracking protocol. Test bolus protocol yields similar contrast enhancement with slightly higher percentage of CTPA with diagnostic quality than bolus tracking protocol; but not statistically significant. However, bolus tracking protocol had significantly better acceptable CTPA quality than the test bolus protocol. Test bolus protocol had significantly lower mean DLP, 220 mGy.cm ± 69, than bolus tracking protocol, 323 mGy.cm ± 34, p-value <0.001. Half of the repeated CTPA did not show significantly better CTPA quality on repetition.

Conclusion: No significant difference between test bolus and bolus tracking protocol in CTPA among pregnant women, but the bolus tracking protocol had better overall CTPA quality with higher radiation dose. Repetition of CTPA studies for poor CTPA quality may not always benefit. Hence, we advise weighing the risk and benefits of study repetition.

Keywords: CTPA, pregnant, test bolus, bolus tracking, radiation dose

CHAPTER 1: BACKGROUND

1.1 Introduction

Pulmonary embolism (PE) is a morbidity during pregnancy and a cause of pregnancy-related mortality. The risk of venous thromboembolism (VTE) in pregnant women is 4 to 6 folds higher compared to non-pregnant women (Heit et al., 2005; Pomp et al., 2008). There is an increased risk of VTE passing the trimester of pregnancy, with the peak at the puerperium period up to 84-fold higher than other pregnancy periods (Pomp et al., 2008). It then declines equivalent to a non-pregnant state by 12 weeks postpartum (Pomp et al., 2008).

The overall risk of venous thromboembolism VTE in pregnancy is 1.72 per 1000 deliveries, while pulmonary embolism makes up 21% (0.36 per 1000 deliveries) (James et al., 2006). Pulmonary embolism was one per 7066 (0.014%) births in California US (Gherman et al., 1999). The prevalence of pulmonary embolism (PE) in pregnant women with suspected PE is about 2% in Canada and US (Chan et al., 2002; Shahir et al., 2010).

Pulmonary embolisms remained a significant cause of death in pregnancy, with 12 deaths or 10.1% of the total maternal deaths in Malaysia in 2018 (Ministry of Health Malaysia, 2018). However, it had been reduced from 16.2% in 2016 (Ministry of Health Malaysia, 2016). Hence, women suspected of thromboembolism must have objective testing performed to confirm or negate the diagnosis of pulmonary embolism.

Test bolus and bolus tracking are two principal techniques to perform Computed Tomography Pulmonary Angiogram (CTPA) of high diagnostic quality (Bae, 2010). The

test bolus technique is done by injecting a small test bolus (10–20 mL) of contrast medium with the following saline chaser. A time-enhancement curve is obtained by measuring the enhancement within the area of interest placed at the pulmonary trunk. Subsequently, the sum of the time to peak (TTP) contrast enhancement and an additional delay is calculated to estimate the scan delays for a full-bolus diagnostic CT scan using a full bolus of contrast medium (Bae, 2010).

Bolus-tracking technique is based on measuring contrast enhancement within the region of interest placed at the pulmonary trunk while a full diagnostic bolus of contrast medium with the following saline chaser is injected. After contrast enhancement exceeds the predetermined threshold (e.g. 150 HU), the diagnostic CT scan begins after an additional trigger delay (Bae, 2010).

1.2 Objectives

1.2.1 General Objective

To compare the quality and radiation dose between test bolus and the bolus tracking protocols for CTPA among pregnant women.

1.2.2 Specific Objectives

1. To compare the mean contrast enhancement of the pulmonary artery in CTPA among pregnant women between test bolus and bolus tracking protocols.
2. To compare the diagnostic quality of CTPA among pregnant women between test bolus and bolus tracking protocols.
3. To compare the radiation dosage (dose length product) between test bolus and bolus tracking protocols for CTPA to mother and fetus.

1.3 Hypothesis

1. Test bolus protocol had higher mean contrast enhancement of the pulmonary artery in CTPA among pregnant women than bolus tracking protocol.
2. Test bolus protocol had better diagnostic quality of CTPA among pregnant women than bolus tracking protocols.
3. Bolus tracking protocol had lower radiation dosage (dose length product) than test bolus protocol for CTPA to mother and fetus.

1.4 Research Question

1. Which technique of CTPA has significantly better pulmonary trunk enhancement in pregnant women?
2. Which technique of CTPA has significantly better diagnostic quality of CTPA in pregnant women?
3. Which technique of CTPA has a significantly lower radiation dose or a lower rate of repetition of examination in pregnant women?
4. Is it necessary to repeat the CTPA study if non-diagnostic?

CHAPTER 2: LITERATURE REVIEW

CTPA among pregnant women is often non-diagnostic , with a rate of 17 to 36%, which is higher than the non-pregnant group (Cahill et al., 2009; Revel et al., 2011; Ridge et al., 2009; U-King-Im et al., 2008). This is likely due to hyperdynamic circulation in physiological changes during pregnancy, such as increased blood volume, haemodilution and heart rate (Schaefer-Prokop and Prokop, 2008; Tromeur et al., 2019). These reduce the average enhancement of the pulmonary vasculature in CTPA, which may cause an overlook of pulmonary emboli (Schaefer-Prokop and Prokop, 2008). The CTPA examination might need to be repeated to exclude PE, which increases radiation to the mother and fetus. Thirty seven percent of pregnant women required repetition of CTPA examinations due to non-diagnostic CTPA using bolus tracking, but sometimes repetition might not solve this problem (Ridge et al., 2009). Lower limb compression duplex ultrasound is recommended if the patient is clinically suspicious of deep vein thrombosis (DVT), as an anticoagulant could be started without CTPA in a stable patient (Zurkurnai Yusof et al., 2018).

Enhancement of the pulmonary trunk in CTPA with at least 100 HU is required to identify acute emboli, and at least 200 HU is necessary to identify chronic emboli from enhancing vessels (Castañer et al., 2009; Trainer et al., 2013; Wittram et al., 2005). The suggested contrast enhancement of the pulmonary arteries for diagnostic CTPA is at least 250 HU (Chen et al., 2017; Leitman and McDermott, 2019; Uysal Ramadan et al., 2010). However, some studies consider at least 200 HU as diagnostic studies (Mortimer et al., 2011; Rodrigues et al., 2012).

CTPA techniques using bolus tracking with short start delays, high flow rates of 4 to 6 ml/s, high contrast medium concentration (350-400 mg/ml), preferential use of fast CT scanner and the use of low kVp CT techniques are recommended for pregnant women to minimise non-diagnostic CTPA examination (Schaefer-Prokop and Prokop, 2008). Deep inspiration in pregnant women may precipitate more non-opacified blood via the inferior vena cava into the right heart, causing dilution of contrast. This effect can be reduced by Valsalva manoeuvre or shallow respiration as an alternative to suspended breathing during exposure (Schaefer-Prokop and Prokop, 2008).

Pulmonary ventilation-perfusion (V/Q) scan has a lower radiation dose, approximately 0.11–0.31 mGy, compared to 20 mGy in CTPA (Shahir et al., 2010). V/Q scan also has a higher negative predictive value than CTPA in the non-pregnant patient. However, a V/Q scan has the disadvantage of a higher fetal dose due to radiotracer being injected intravenously, leading to direct fetal exposure (Moradi, 2013). The carcinogenic potential is still unknown. Furthermore, V/Q scan may not provide alternative diagnoses such as pneumonia, pulmonary oedema and aortic dissections compared to CTPA (Konstantinides et al., 2020; MOH, 2018). CTPA, the current gold standard, provides accurate diagnosis for pulmonary embolism with sensitivity and specificity between 94% and 100% (Matthews, 2006; Moore et al., 2018). The negative predictive value of a normal CTPA is approximately 99%. The advantage of CTPA is directly visualising emboli, unlike V/Q scanning (Matthews, 2006). However, CTPA may predispose the fetus to risk of iodine-induced hypothyroidism, but unproven (Shahir et al., 2010).

The advantages of bolus tracking are fast and easy to use with real-time imaging at the region of interest, the pulmonary artery. However, it has a limitation of an additional

delay time for patient instruction and unpredictable poor contrast opacification (Yamaguchi and Takahashi, 2010). The advantages of test bolus are the ability to predict poor contrast opacification and setting the scanning time interval as the time to peak contrast opacification is calculated. Unfortunately, the haemodynamic might differ between the test and the main bolus, which may cause suboptimal contrast opacification (Yamaguchi and Takahashi, 2010).

Both bolus tracking and test bolus protocol may have varied outcomes on the diagnostic quality of CTPA, especially in pregnant women, with no previous statistical study. Test bolus protocol showed significantly better opacification of the pulmonary trunk than the bolus tracking protocol among non-pregnant patients (Rodrigues et al., 2012; Suckling et al., 2013). However, another study showed no statistically significant difference between bolus tracking and test bolus techniques (Moradi and Khalili, 2016).

Fetal radiation from diagnostic imaging may cause prenatal death, malformation, or impaired mental development. Still, the probability of cancer risk in the first and second decades caused by low-level radiation is more worrying (Valentin and Protection, 2003). Hence, a lower radiation dose CTPA protocol should be determined to reduce the risk of fetal radiation. Radiation dose in CTPA is our concern, especially for the fetus. The fetal radiation exposure for CTPA varies from 3.3 μGy to 130.0 μGy as the dose increases during each trimester when the fetus grows and approaches the imaged area in the upper abdomen (Winer-Muram et al., 2002). However, the fetal radiation dose for V/Q scanning is estimated as 100–370 μGy, which may be three times greater than for CTPA (Matthews, 2006).

The median of radiation dose in test bolus was higher than bolus tracking [553.5 (519.2-593.7) vs 469.8 (407.7-585.5), respectively] (Moradi and Khalili, 2016). However, another study found no significant difference (P = 0.8287) between the effective radiation doses of the test bolus protocol CTPA scans compared to the bolus tracking scans (Rodrigues et al., 2012).

The mean diameter and standard deviation (SD) of the main pulmonary artery in pregnancy were larger than in non-pregnant, measuring 28 mm ± 3.5 mm, with a range of 20 – 40 mm. This also causes a pitfall of pulmonary artery to aorta (PA/A) ratio > 1.0, which may not be as predictive of pulmonary hypertension among pregnant women (Khalil et al., 2009).

2.1 Conceptual framework

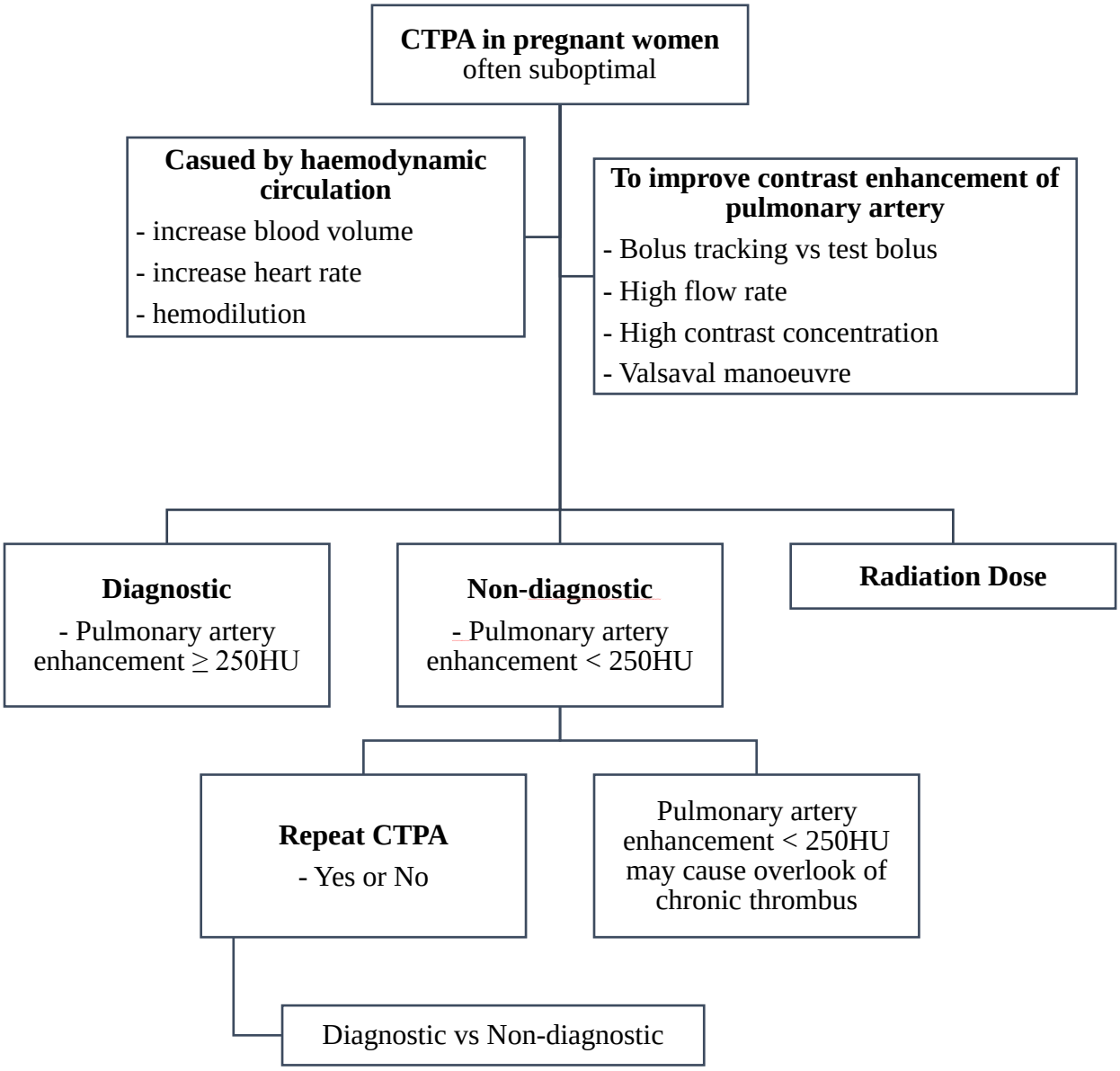


Figure 1: Conceptual framework

2.2 Rationale of Study

CTPA among pregnant women is often suboptimal due to hyperdynamic circulation in physiological changes that occur during pregnancy, such as haemodilution and increased heart rate (Schaefer-Prokop and Prokop, 2008; Tromeur et al., 2019). These reduce the average enhancement of the pulmonary vasculature in CTPA (Schaefer-Prokop and Prokop, 2008). The study might need to be repeated to exclude PE, which increases radiation to the mother and fetus.

The quality of repeated CTPA study has to be figured out to determine the necessity of repeating the CTPA study in the non-diagnostic CTPA study, as sometimes repetition might not solve this problem. A V/Q scan may be used to exclude pulmonary embolism.

Optimal CTPA study among pregnant women is necessary to avoid overlooking pulmonary emboli or repetition of study, which increases the unnecessary dose to the fetus and mother.

CHAPTER 3: METHODOLOGY

3.1 Study Design

This was a retrospective study. Secondary data were reviewed.

3.1.1 Study Location

1. Department of Radiology, Hospital Pulau Pinang, Ministry of Health Malaysia, Jalan Residensi, 10990 George Town, Pulau Pinang, Malaysia.
2. Department of Radiology, Hospital Seberang Jaya, Ministry of Health Malaysia, Jalan Tun Hussein Onn, Seberang Jaya, 13700 Permatang Pauh, Pulau Pinang, Malaysia.

3.1.2 Data collected period: 2 years

1. 1st of January 2019 to 31st of December 2020 in Hospital Pulau Pinang (HPP). HPP had another prospective study that modifies the scanning parameters of CTPA in pregnant women starting 1st of January 2021

2. 1st of January 2020 to 31st of December 2021 in Hospital Seberang Jaya (HSJ). HSJ had 128 slices CT scan machine (GE health care 128 evaluation) since December 2019. Data performed by previous CT machines was not included as there were differences in CT scan slices and parameters.

3.2 Study Population

i. Reference population: All pregnant women who required CTPA examination.

ii. Target population: All pregnant women who have successfully undergone a CTPA examination.

iii. Sampling population: All pregnant women who successfully underwent CTPA examinations in the Department of Radiology, Hospital Pulau Pinang (HPP) and Hospital Seberang Jaya (HSJ).

3.3 Sample Size Calculation

Sample size estimation was calculated using Sample Size Calculator by Wan Nor Arifin (Web), with 95% CI and power of study 80% (Wan Nor Arifin, 2017).

For objective 1, two-means hypothesis testing was used to compare the contrast opacification of the pulmonary artery in CTPA among pregnant women between test bolus and bolus tracking protocols.

Based on preliminary data, the standard deviation was 89.3, and the expected difference was 104.4 (Rodrigues et al., 2012). With the significant level (α) of 0.050 and Power (1−β) of 0.8, the estimated minimum sample size required was 12 per group.

For objective 2, two-proportion comparison (independent) testing were used to compare the diagnostic quality of CTPA among pregnant women between test bolus and bolus tracking protocols.

Based on prior data, the proportion in control (p0) was 82%, and the balance in case (p1) was 18% (Rodrigues et al., 2012). With the significant level (α) of 0.050 and Power (1−β) of 0.8, the estimated minimum sample size required was 9 per group.

For objective 3, two means of hypothesis testing were used to compare the radiation dosage between test bolus and bolus tracking protocols for CTPA to mother and fetus. Based on prior data, the standard deviation was 44.45, and the expected difference was 71.7 (Moradi and Khalili, 2016). With the significant level (α) of 0.050 and Power (1−β) of 0.8, the estimated minimum sample size required was 7 per group.

Hence, the estimated minimum sample size required was 12 per group.

3.4 Sampling Method

Data was collected retrospectively from two tertiary centres of pregnant women who underwent CTPA examination using a different protocol. Group A from Hospital Pulau Pinang (HPP), Ministry of Health Malaysia, used test bolus protocol, and Group B from Hospital Seberang Jaya (HSJ), Ministry of Health Malaysia, used bolus tracking protocol.

3.5 Inclusion Criteria

1. Pregnant women who successfully underwent CTPA using bolus tracking or test bolus protocol.
2. Age from 18 – 50 years old.

3.6 Exclusion Criteria

1. Patients with underlying shock, renal impairment, heart diseases such as the right to left shunt, valvular heart disease or heart failure
2. Patient with IV access from the lower limb.
3. Unsuccessful CTPA, such as extravasation.
4. Images of CTPA are severely degraded by artefacts such as breathing or motion that interfere with the measurement.
5. No images in PACS

3.7 Research Tools

CTPA in HPP were done using 128 slices CT scanner SOMATOM definition plus, Siemens, meanwhile CTPA in HSJ were done using 128 slices CT scanner (GE health care 128 evaluation). Dicom files were obtained after scan and viewed using OsiriX DICOM viewer (Bernex, Switzerland).

3.8 CT imaging technique

CTPA technique among pregnant women used in HPP was a test bolus protocol. Patients were administered with non-ionic contrast media (Ultravist) of 370 mgI/ml. The test bolus protocol was carried out by injecting 10mL of contrast media followed by 20ml of saline chaser. A time-enhancement curve was obtained by measuring the enhancement within the region of interest (ROI) placed at the pulmonary trunk. The time to peak (TTP) contrast enhancement with an additional delay of 2 seconds was calculated as the scan delays for full-bolus CTPA.

For patients from HSJ, the scanning technique used was bolus tracking protocol using the same contrast media (Ultravist) of 370 mgI/ml. The bolus tracking protocol was done by measuring contrast enhancement within the ROI placed at the pulmonary trunk while a full diagnostic bolus of contrast medium with the following saline chaser was injected. After contrast enhancement exceeded the threshold of 150 HU, the diagnostic CTPA scan began after 3 seconds delay.

Both centres used a fixed volume of contrast media injected using a dual injector at a rate of 5.0 ml/s through an 18-gauge cannula into an arm vein using a power injector.

Immediately after the administration of CM, a 40-mL saline bolus was injected at the same rate.

All pregnant women wore abdominal shields as a protective cover for the fetus during the CT scan. All images were obtained in a cranial-caudal direction from the thoracic inlet level to the lung bases with both arms extended above the head during a single inspiratory breath-hold. Automated verbal breathing instructions were used during the scanning. Patients were instructed to take a deep breath and hold it just before the scan started. Although both groups used different company CT scan machines and triggering techniques, the rest of the parameters were similar to minimise the potential differences that would affect the study result. Summary of the parameters as stated below:

Table 1: CTPA parameters

	Group A (HPP)	**Group B (HSJ)**
CT scan slices	128 slices	128 slices
CT Parameters		
a) Tube voltage	120kVp	120kVp
b) Tube current	Tube current modulation	Tube current modulation
Contrast media		
a) Concentration	370mgI/ml	370mgI/ml
b) Volume	80ml	80ml
c) Injection rate	5.0ml/s	5.0ml/s
Protocol	Time to peak (TTP) + 2 seconds delay	Bolus tracking + 3 seconds delay

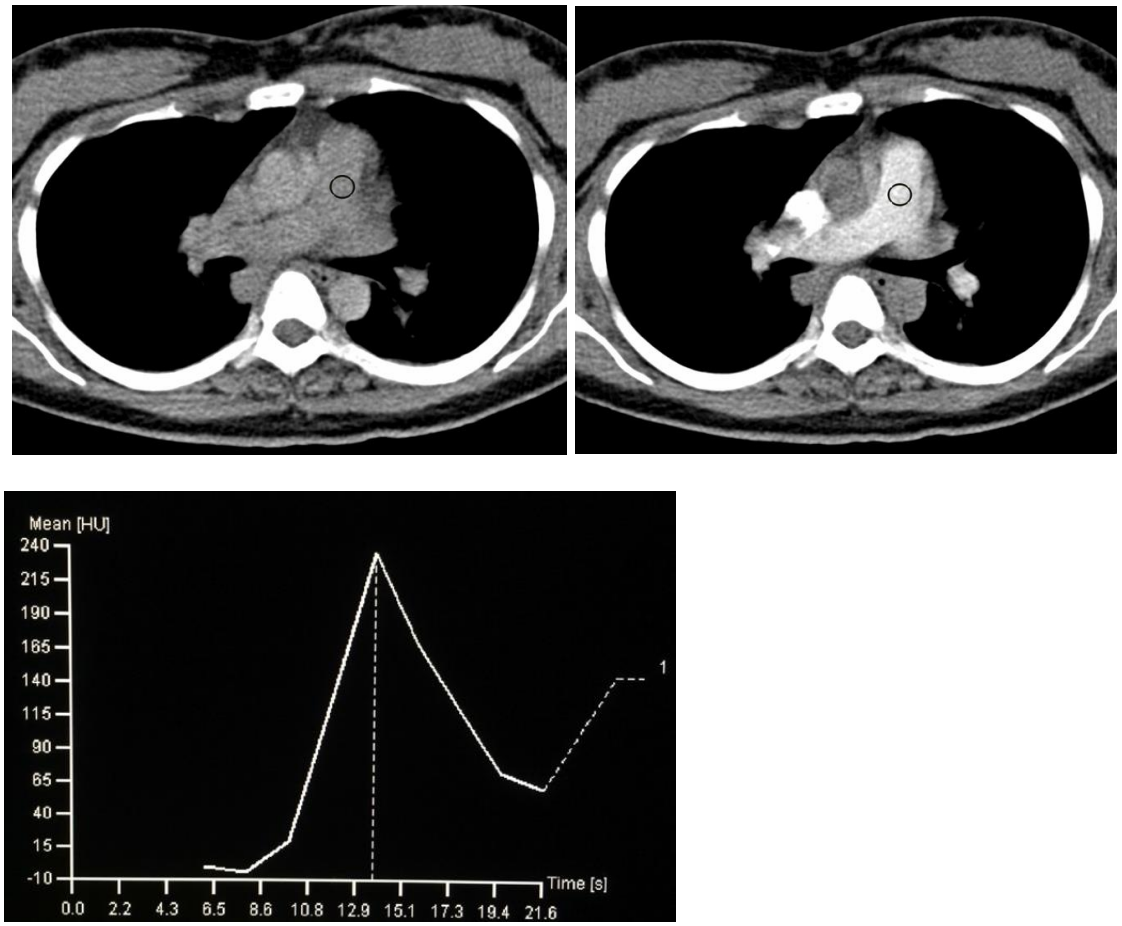


Figure 2: Test bolus protocol using time to peak with ROI placed at the pulmonary trunk by scaning at subcarinal region.

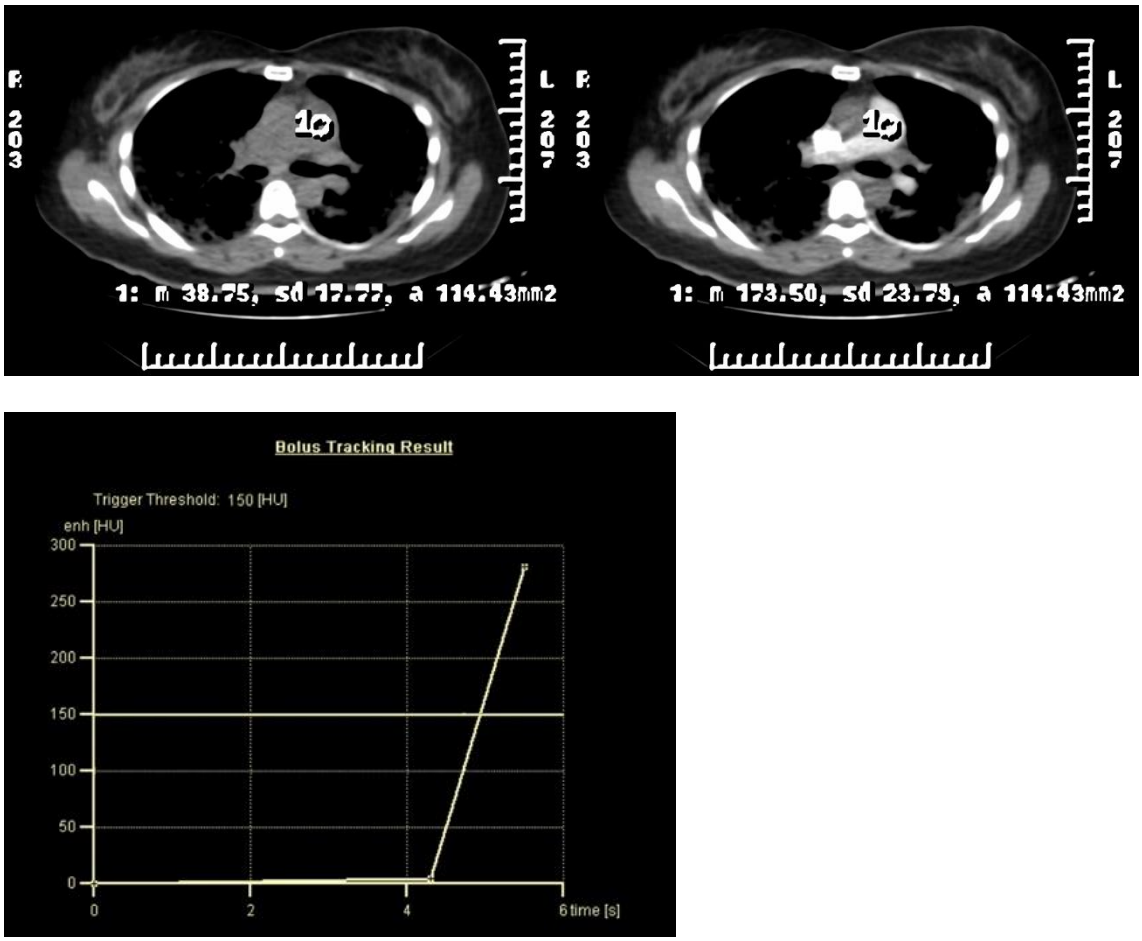


Figure 3: Bolus tracking protocol with ROI placed at pulmonary trunk. Scanning and image acquired

3.9 Data Collection

Permission to retrieve, review and data collection consent were obtained from each Hospital Director. All images were retrieved from picture archiving and communication system (PACS) in both HPP and HSJ. After sample identification, all images were labelled with the study ID number to maintain the subject's privacy and confidentiality. Data obtained were calculated by the investigator and then validated by Radiologist. Data collected were kept in the subject data collection form (see appendix A). Medical records were reviewed to record the patient’s weight, heart rate and period of amenorrhea (POA)/ gestation (POG).

3.10 Data analysis & Operational definition

All images were retrieved from PACS storage. The enhancement readings in Hounsfield unit (HU) values were measured by manually placing round-shaped regions of interest (ROI) of 1.0cm in diameter at the main pulmonary trunk (PT), right pulmonary artery (RPA), left pulmonary artery (LPA), Arch of aorta (AoA), and descending aorta (DA) using OsiriX DICOM viewer (Bernex, Switzerland). Each ROI were placed, avoiding partial-volume and streak artefacts. Mean aorta contrast enhancement were measured to determine early or late scan timing. Early scan timing was defined as no aorta enhancement in the suboptimal pulmonary artery enhancement. Late scan timing was defined as mean aorta enhancement was higher than pulmonary artery enhancement with contrast washout in superior vena cava (SVC).

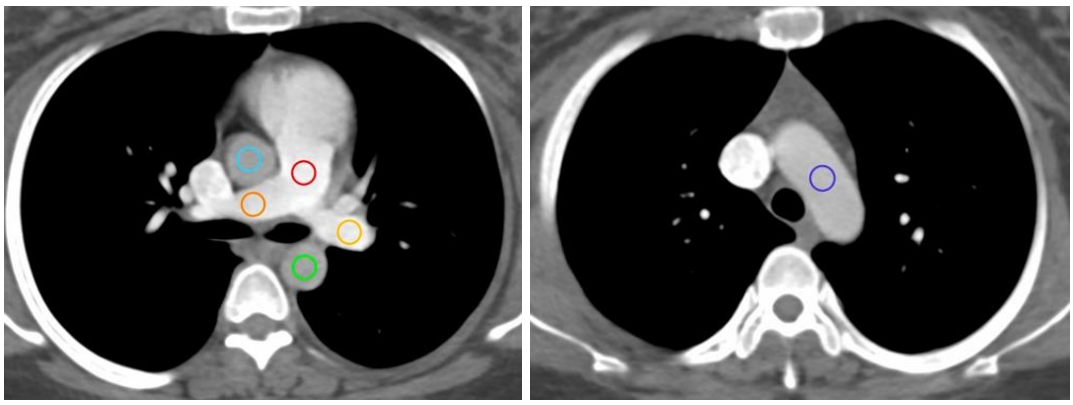


Figure 4: ROI placement using OsiriX DICOM viewer

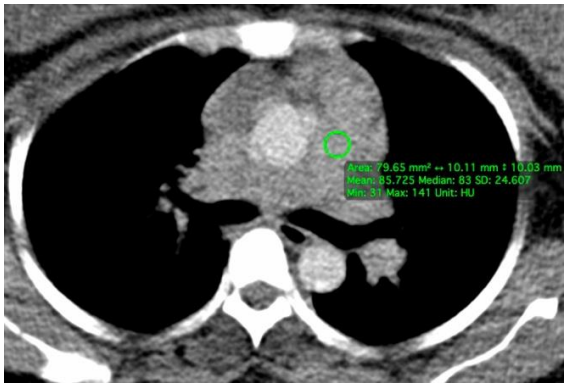
After each anatomical area was measured, the mean PA enhancement were calculated using the average of main pulmonary trunk, right and left PA average enhancement. The mean aortic enhancement also were calculated by averaging the enhancement in the ascending aorta, aortic arch, and descending aorta. 10% of the data were validated by radiologists.

CTPA quality was assessed by the degree of mean PA enhancement summarised in Table 2 as suggested by a few studies (Chen et al., 2017; Leitman and McDermott, 2019; Nazaroğlu et al., 2009; Uysal Ramadan et al., 2010). A different threshold of mean PA enhancement for diagnostic CTPA was also used to analyse as suggested by some studies, whereby the diagnostic CTPA had mean PA enhancement of ≥ 200 HU and non-diagnostic CTPA had mean PA enhancement of < 200 HU (Mortimer et al., 2011; Rodrigues et al., 2012; Trainer et al., 2013). The signal-to-noise ratio was not included in our criteria as it varies with the patient body habitus.

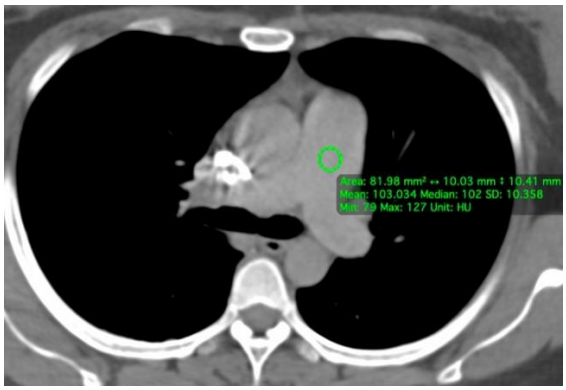
Table 2: CTPA Quality

CTPA Quality		**Mean PA Enhancement**
Diagnostic CTPA		≥ 250 HU
Non-diagnostic CTPA	Acceptable	200 – 249 HU
	Poor	100 – 199 HU
	Very Poor	<100 HU

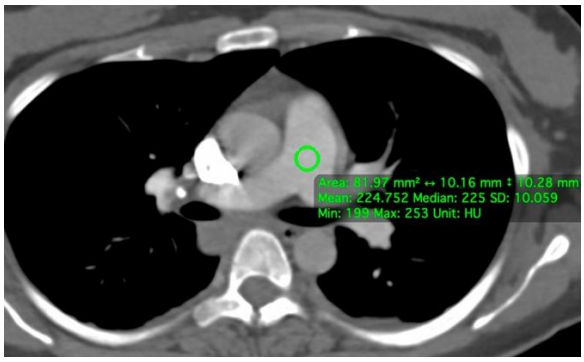
The total CT dose length product of each CTPA examination were recorded as mGy.cm in PACS. The frequency of repeated CTPA examination due to nondiagnostic pulmonary artery contrast enhancement were recorded for each protocol. Pulmonary embolism was defined by the presence of filling defect in the pulmonary arterial system, as reported by radiologist documented in the report.



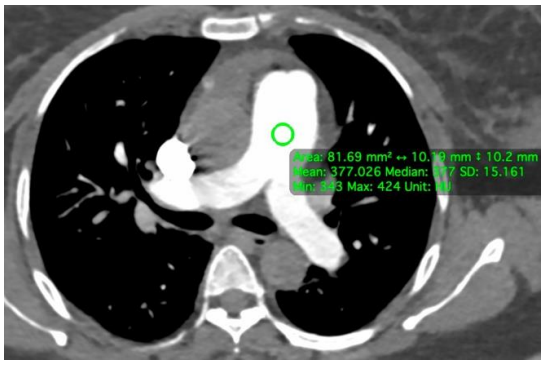
(a) Mean PA enhancement < 100 HU



(b) Mean PA enhancement 100 – 200 HU

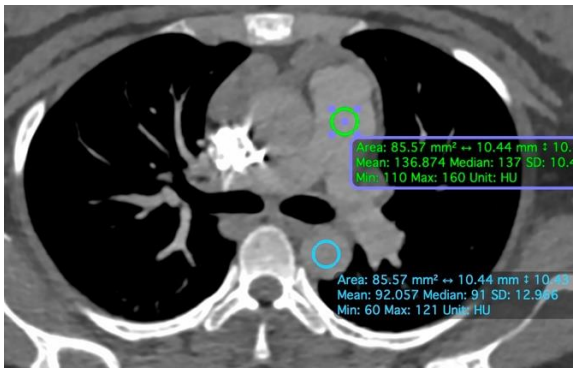


(c) Mean PA enhancement 200 – 249 HU

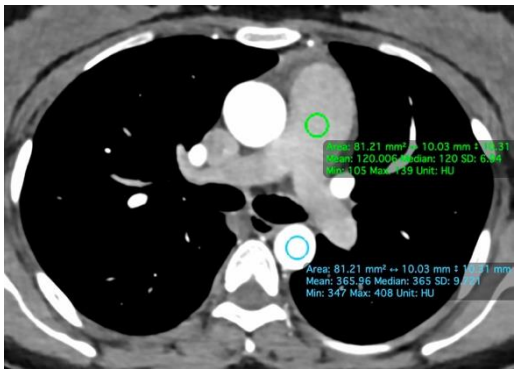


(d) Mean PA enhancement ≥ 250 HU

Figure 5: Example of mean PA enhancement.



(a) Early scan timing



(b) Late scan timing

Figure 6: Suboptimal scan timing

3.11 Statistical Analysis

CTPA quality and mean pulmonary artery enhancement were assessed and compared between test bolus and bolus tracking protocol, using Pearson chi-square. Maximum mean contrast enhancement of all measured structures was identified. Each group's total CT dose length product were assessed and compared using an independent T-test. All statistical analysis were performed using the commercial software Statistical Package for Social Sciences version 26 (SPSS, IBM, Chicago, IL, USA). A P-value less than 0.05 was considered significant.

3.12 Confidentiality and Privacy

The subjects were identified using a unique serial number. No identifiable data was shared publicly. Only research team members could access the data. The data were presented as grouped data and will not identify the responders individually.

Upon completion of the study, all data were stored on CDs, and the database on the computer was erased. The researchers retained the data for knowledge purposes only. Neither the name nor identifying information was used in any publication or presentation resulting from this study.

3.13 Ethical Consideration

The study was approved by the Human Research Ethics Committee of Universiti Sains Malaysia (USM/JEPeM/ 21100696) and is valid from 8th March 2022 until 7th March 2023. This study also obtained approval from Medical Research & Ethics Committee, Ministry of Health Malaysia (NMRR ID-22-01270-CYJ), valid until 04-August-2023. Site approval was also obtained from the Hospital Director of both Hospital Pulau Pinang and Hospital Seberang Jaya.

3.14 Study Flow Chart

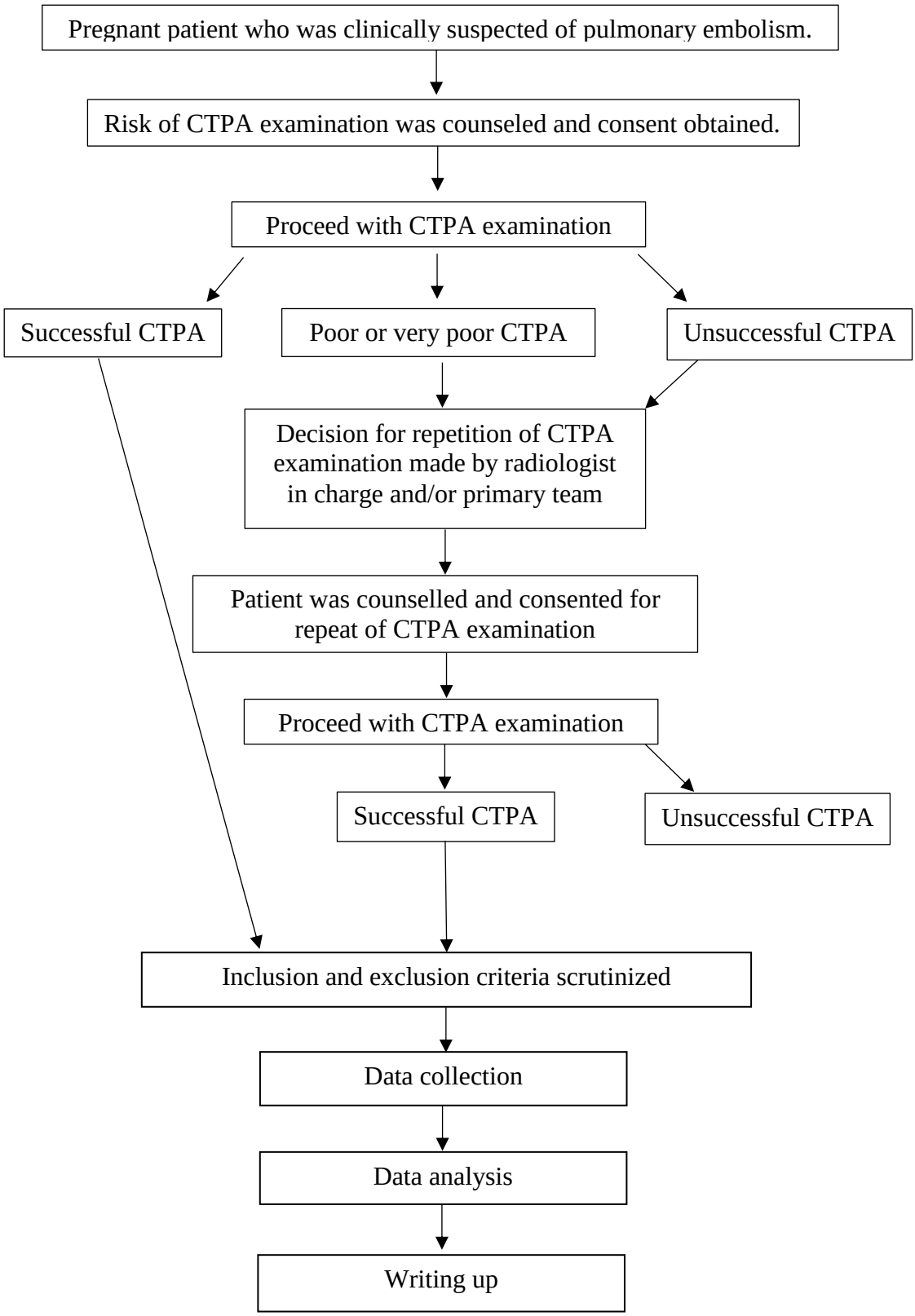


Figure 7: Study Flow Chart

CHAPTER 4: MANUSCRIPT