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Original Article

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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Abstract

Introduction: 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 guality, 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: Test bolus protocol yields a slightly higher number of diagnostic qualities CTPA than bolus tracking protocol; however not statistically significant. The 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 guality with higher radiation dose. Repetition of CTPA studies for poor CTPA guality may not always benefit. Hence, we advise weighing the risk and benefits of study repetition.

Keywords: CTPA; Pregnant; Test Bolus; Bolus Tracking

Introduction

Pulmonary embolism (PE) is a morbidity and mortality during pregnancy. The risk of venous thromboembolism (VTE) in pregnant women is 4 to 6 folds higher compared to non-pregnant women (<u>Heit *et al.*</u>, 2005; <u>Pomp *et al.*</u>, 2008). There is an increased risk of VTE passing the trimester of

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pregnancy, with a peak at the puerperium period up to 84-fold higher than other pregnancy periods (<u>Pomp *et al.*, 2008</u>). It then declines equivalent to a non-pregnant state by 12 weeks postpartum (<u>Pomp *et al.*, 2008</u>).

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) (<u>James *et al.*</u>, 2006). 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 although it had been reduced from 16.2% in 2016 (<u>Ministry of Health Malaysia</u>, 2016, 2018). Hence, women suspected of thromboembolism were required to have objective testing to confirm or negate the diagnosis of pulmonary embolism.

Computed Tomography Pulmonary Angiography (CTPA) among pregnant women is often nondiagnostic, with a rate ranging between 17 to 36%, which is higher than non-pregnant group (<u>Cahill *et al.*</u>, 2009; <u>Revel *et al.*</u>, 2011; <u>Ridge *et al.*</u>, 2009; <u>U-King-Im *et al.*, 2008). This is likely due to hyperdynamic circulation in physiological changes during pregnancy, such as haemodilution and increased heart rate (<u>Schaefer-Prokop & Prokop, 2008</u>; <u>Tromeur *et al.*</u>, 2019</u>). These reduce the average enhancement of the pulmonary vasculature in CTPA (<u>Schaefer-Prokop and Prokop, 2008</u>). The study might need to be repeated due to suboptimal to exclude PE, which increases radiation to the mother and fetus.

Reduced average enhancement of the pulmonary vasculature in CTPA may cause an overlook of pulmonary emboli (Schaefer-Prokop & Prokop, 2008). The attenuation of chronic pulmonary emboli (PE) is higher than acute PE, in which chronic PE may have an attenuation of 87 HU ± 30 and 33 HU ± 15 in acute PE (Wittram et al., 2005). Therefore, opacification of the pulmonary trunk in CTPA with at least 100 HU is required to identify acute emboli, and at least 200 HU is needed to identify chronic emboli from enhancing vessels (Castañer et al., 2009; Trainer et al., 2013). Given that contrast enhancement is usually lower in peripheral vessels, a higher level of contrast enhancement in the main pulmonary artery is needed for acceptable enhancement (Michelle Muller et al., 2022). There is no overall consensus on the threshold of diagnostic CTPA, and various other figures have been suggested in the literature (Chen et al., 2017). The suggested contrast attenuation of the pulmonary arteries for diagnostic CTPA is at least 250 HU(Chen et al., 2017; Leitman & McDermott, 2019; Nazaroĝlu et al., 2009; Nguyen et al., 2022; Uysal Ramadan et al., 2010). However, some studies consider at least 200 HU to be optimal (Mortimer et al., 2011; Rodrigues et al., 2012; Trainer et al., 2013) or at least 210 HU (Basson et al., 2022). A higher contrast attenuation of the main pulmonary artery is necessary to prevent overlooking PE at distal pulmonary artery branches, as the contrast opacification commonly faints out distally.

Optimal CTPA study among pregnant women is necessary to avoid overlooking pulmonary emboli or repeated study, increasing the unnecessary dose to the fetus and mother. 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.

This study aims to compare the test bolus and the bolus tracking protocols for CTPA among pregnant women by analysing the mean contrast opacification of the pulmonary artery, diagnostic quality and radiation dosage.

Methodology

Study population

Data were collected retrospectively from two tertiary centres consisting of pregnant women who underwent CTPA examination using different protocols; Group A used test bolus protocol from Hospital Pulau Pinang (HPP), Ministry of Health (MOH) Malaysia, and Group B used bolus tracking protocol from Hospital Seberang Jaya (HSJ), MOH Malaysia. Data from pregnant patients 18 years old to 50 years old who successfully underwent CTPA examination using a 128-slice CT scanner in each centre was included in this study. Data on the patient's age, documented heart rate before the CT scan, gravidity, period of amenorrhea (POA) or period of gestational (POG) and body weight were collected

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from either request form or medical record. Patients with underlying shock, renal impairment, heart diseases such as the right to left shunt, valvular heart disease or heart failure, and patients with IV access from the lower limb or unsuccessful CTPA due to extravasation were excluded from this study.

CT imaging technique

CTPA technique of Group A was test bolus performed using 128 slices CT scanner (SOMATOM definition plus, Siemens). Patients were administered non-ionic contrast media Ultravist of 370 mgl/ml. The test bolus protocol was done 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 main pulmonary artery (PA). The time to peak (TTP) contrast enhancement with an additional delay of 2 seconds was calculated as the scan delay time for full-bolus CTPA.

For patients from Group B, the scanning technique was bolus tracking using 128 slices CT scanner (GE health care 128 evaluation) with the same contrast media 370 mgl/ml. The bolus tracking protocol measured contrast enhancement with 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 80ml contrast media injected using a dual injector at the 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, 40ml of saline chaser was injected at the same rate.

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 were using a different brand of CT scan machine, besides triggering techniques, the rest of the parameters were similar to minimise the potential differences that would affect the study result. A summary of the parameters is stated in Table 1:

	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	370mgl/ml	370mgl/L
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
Data analysis 8 Onora	ional definition	

Table 1: CTPA Protocol Parameters

Data analysis & Operational definition

All images were retrieved from picture archiving and communication system (PACS) storage. Data obtained were calculated by the investigator. The attenuation readings in Hounsfield Unit (HU) values were measured by manually placing round-shaped regions of interest (ROI) of 1.0cm in diameter centrally at the main pulmonary artery (MPA), Right pulmonary artery (RPA), left pulmonary artery (LPA), Arch of the aorta (AoA), and descending aorta (DA) using OsiriX DICOM viewer (Bernex, Switzerland) as shown in Figure 1. Each ROI was placed, avoiding partial-volume and streak artefacts.

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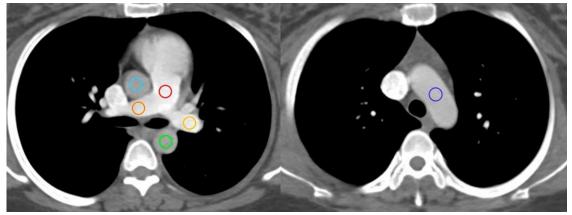


Figure 1: ROI Placement for Attenuation Measurement.

The mean PA attenuation was calculated using the average attenuation of the main pulmonary trunk and the right and left PAs. The mean aortic attenuation also was calculated by averaging the attenuation in the ascending aorta, aortic arch, and descending aorta. CTPA quality was assessed by the degree of mean PA attenuation in HU summarised in Table 2 as suggested by a few studies (<u>Chen *et al.*</u>, 2017; <u>Leitman & McDermott</u>, 2019; <u>Nazaroĝlu *et al.*</u>, 2009; <u>Nguyen *et al.*</u>, 2022; <u>Uysal Ramadan *et al.*, 2010). The signal-to-noise ratio is not included in our criteria as it varies with the patient body habitus.</u>

Table 2: CTPA Quality

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

The respiratory phase of the patient was identified by looking at the concavity of the posterior tracheal membrane, whereby concave or bowing is the expiratory phase, and rounded trachea is an inspiratory phase. The presence of breathing motion artefact indicated the patient was not breath-holding. Lung pathology such as pleural effusion and infective changes were identified. Pulmonary embolism is defined by the presence of a filling defect in the pulmonary arterial system, confirmed by a radiologist documented in the report.

The total CT dose length product of each CTPA examination was recorded in mGy.cm. The frequency of repeated CTPA examination due to non-diagnostic pulmonary artery contrast opacification was recorded for each protocol, with its PA contrast opacification. **Statistical analysis**

CTPA quality and mean pulmonary artery attenuation were assessed and compared between groups A and B, using Pearson chi-square. The maximum mean contrast attenuation of all measured structures was identified. Each group's total CT dose length product was assessed and compared using an independent T-test. Demographic data association with diagnostic quality CTPA were analysed using independent T-test and Pearson correlation coefficient for association with mean PA attenuation. All statistical analyses 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 is considered significant.

Ethical Approval

This study received ethical approval from Medical Research and Ethics Committee (MREC) National Institutes of Health (NIH) Malaysia and Jawatankuasa Etika Penyelidikan Manusia Universiti Sains Malaysia (JEPeM-USM).

Results

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A total of 73 patients who performed CTPA during pregnancy were obtained from both groups, 38 from group A (Test bolus protocol) and 35 from group B (Bolus tracking protocol). Image data in PACS of 3 patients were lost to retrieved from group A and a patient with congestive cardiac failure from group A were excluded (Figure 2).

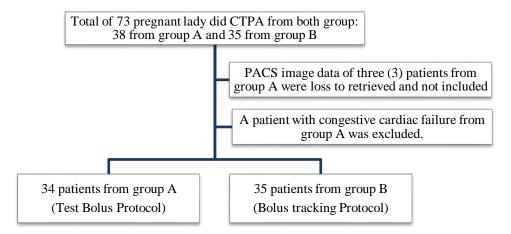


Figure 2: Data Sampling Flow Chart

The study population is described in Table 3. There was no statistical association of age, documented heart rate, gravida, POA/POG and body weight with diagnostic quality of CTPA, p-value >0.05. Two patients out of 69 (2.9%) were diagnosed with pulmonary embolism during pregnancy within two years of data but within a limited sample size. Three patients (4.3%) had pneumonia, three patients (4.3%) had pleural effusion, a patient (1.4%) had non-specific bi-apical ground glass opacity, three patients (4.3%) had COVID-19 pneumonia, and the rest of the patients (82.6%) had clear lung fields.

Table 3: Study Population Demographic

		Diagnostic	Non-diagnostic
		Mean ± SD	Mean ± SD
Age		28.7 ± 6.8	30.6 ± 5.1
Heart Rate befo	ore CT scan	110.1 ± 19.6	117 ± 15.1
Gravidity		2.7 ± 2.0	2.4 ± 1.8
POA/POG		30.4 ± 6.1	31.0 ± 7.8
Weight (kg)		64.7 ± 14.5	70.2 ± 14.4
		Count, n (%)	Count, n (%)
Respiratory	Inspiratory, n = 51	32 (82.1%)	19 (63.3%)
Phase	Expiratory, n= 18	7 (17.9%)	11 (36.7%)

A total of 39 pregnant patients (56.5%) had diagnostic quality CTPA, 12 patients (17.4%) had acceptable quality, and 18 patients (26.1%) had poor quality CTPA. No patients had very poor CTPA quality. The number of patients for each diagnostic quality, mean PA attenuation and DLP for both protocols are summarised in Table 4.

		Group / Protocol		P value
		Test Bolus	Bolus Tracking	
CTPA Quality (count, percentage)	Diagnostic (≥250HU)	20 (58.8%)	19 (54.3%)	0.704
	Non-diagnostic (<250HU)	14 (41.2%)	16 (45.7%)	
	Acceptable (200-249 HU)	2 (5.9%)	10 (28.6%)	0.025
	Poor (100-199HU)	12 (35.3%)	6 (17.1%)	
	Very Poor (<100 HU)	0 (0.0%)	0 (0.0%)	
Mean	Mean PA	266 ± 126	265 ± 68	0.955
Attenuation (HU) ± SD	Main PA	282 ± 136	269 ± 71	0.628
	Right PA	260 ± 122	259 ± 69	0.980
	Left PA	257 ± 122	266 ± 72	0.704
	Mean Thoracic Aorta	186 ± 91	201 ±55	0.423
DLP (mGy.cm)	1	220 ± 69	323 ± 34	<0.001

Malaysia Journal of Medical Research Volume 7(3) 34-40 Table 4: Comparison between Test Bolus and Bolus Tracking Protocol.

MPA: Main pulmonary artery/trunk, RPA: Right pulmonary artery, LPA: Left pulmonary artery. Mean enhancement and DLP analysed using independent T-Test. Test bolus protocol yields a slightly higher number of diagnostic quality CTPA than bolus tracking protocol; however not statistically significant with a p-value of 0.704. The bolus tracking protocol showed significantly better acceptable CTPA than the test bolus protocol, with a p-value of 0.025 (Table 4). Test bolus protocol had a higher rate of poor-quality CTPA (35.3%). Most diagnostic CTPA was in the inspiratory phase (82.1%) but not statistically significant. There were no significant differences in the mean PA enhancement between inspiratory and expiratory phases (Figure 3c), with a p-value of 0.117.

The mean PA, main pulmonary trunk and right pulmonary artery attenuation of test bolus protocol were slightly better than bolus tracking protocol, but with a high standard deviation of 126HU and not statistically significant with p-value >0.05 (Table 4). Test bolus protocol had significantly lower mean DLP, 220 mGy.cm \pm 69, than bolus tracking protocol, 323 mGy.cm \pm 34, p-value <0.001 (Table 4 and Figure 3b). However, the test bolus protocol had a higher standard of deviation.

Six patients (8.7%) had repeated CTPA given poor CTPA quality, and half did not show significantly better CTPA quality on repetition (Table 5). A patient had diagnostic CTPA quality, and two patients had acceptable quality after repetition of the study. Five patients from the Test bolus group had repeated CTPA (14.7%), which was higher than the bolus tracking group, however not significant, with a P-value of 0.081.

 Table 5: Comparison of CTPA Repetition and Its Quality Post Repetition between Test Bolus and
 Bolus Tracking Protocol

		Group / Protocol	
		Test Bolus	Bolus Tracking
Repetition	Frequency, n (percentage)	5 (14.7%)	1 (2.9%)
Repeated I	mean PA (HU) ± SD	244 ± 101	124
Repeated	Diagnostic (≥ 250 HU)	1 (20%)	0 (0%)
CTPA	Non-diagnostic (< 250 HU)	4 (80%)	1 (100%)
Quality	Acceptable (200 - 249 HU)	2 (40%)	0 (0%)
	Poor (100 – 199 HU)	2 (40%)	1 (100%)
	Very Poor (< 100 HU)	0 (0.0%)	0 (0.0%)

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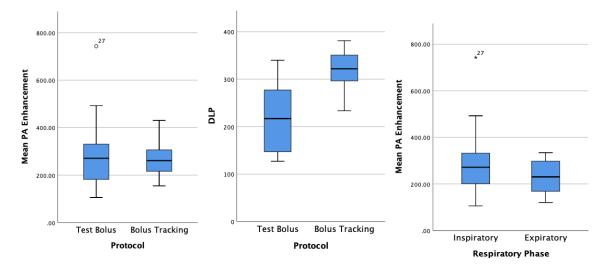


Figure 3: (a) Boxplot of mean PA attenuation comparing between test bolus and bolus tracking protocol, (b) Boxplot of radiation dosage comparing between test bolus and bolus tracking protocol, (c) Boxplot of mean PA attenuation comparing between inspiratory and expiratory phase.

Both patients with acute pulmonary embolism had tachycardia with heart rates up to 123bpm. Both of them had normal echocardiography findings. One of them presented with chest pain and shortness of breath and had emboli at the bilateral pulmonary artery with dilated main PA measuring 3.1cm, Pulmonary artery to aorta (PA:A) ratio of 1.2. On the contrary, the other patient had pulmonary emboli at segmental branches of the bilateral lower lobe pulmonary artery and showed normal main PA of 2.4cm.

Discussion

CTPA among the pregnant women in our study has a non-diagnostic rate of 43.5% (30 of 69 patients), higher than previous studies ranging between 17 to 36% (Cahill *et al.*, 2009; Revel *et al.*, 2011; Ridge *et al.*, 2009). It is higher than the non-pregnant group ranging between 11.5 to 26.9% (Moradi & Khalili, 2016). Hyperdynamic circulation during pregnancy, such as increased blood volume and haemodilution, are the leading causes (Schaefer-Prokop & Prokop, 2008; Tromeur *et al.*, 2019). Increased heart rate and body weight did not significantly affect the CTPA diagnostic quality in our study.

The advantages of bolus tracking are fast and easy to use with real-time imaging at the region of interest, the pulmonary artery (<u>Yamaguchi & Takahashi, 2010</u>). The bolus tracking protocol had a higher sum of diagnostic and acceptable CTPA (82.9%) than the test bolus protocol (64.7%) in our study. Hence, the bolus tracking protocol showed better overall CTPA diagnostic quality CTPA than the test bolus protocol, however no significant difference between them. If considering mean PA attenuation >200 HU as the optimal study suggested by previous studies (<u>Mortimer *et al.*, 2011</u>; <u>Rodrigues *et al.*, 2012</u>; <u>Trainer *et al.*, 2013</u>), there is still no significant difference between test bolus and bolus tracking protocol, with a p-value of 0.086 (Table 6).

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		Group / Protocol		P value
		Test Bolus (n = 34)	Bolus Tracking (n = 35)	
CTPA Quality (count, percentage)	Diagnostic (≥ 200 HU)	22 (64.7%)	29 (82.9%)	0.086
	Non-diagnostic (< 200 HU)	12 (35.3%)	6 (17.1%)	

 Table 6: Comparison between Test Bolus and Bolus Tracking Protocol Using Mean PA

 Enhancement ≥ 200 HU as Diagnostic

CTPA quality analysed using Pearson chi-square.

Test bolus protocol showed a higher rate of poor CTPA quality (35.3%) with high standard deviation, likely due to the haemodynamic difference between the test bolus and the main full bolus, which may cause suboptimal contrast opacification (Yamaguchi & Takahashi, 2010). The test bolus time to peak value is based on the venous system as small amount of contrast and saline chaser were used during test bolus to determine time to peak. The increase haemodynamic in pregnancy will create variation in the actual CT scan when the main full bolus is given. The bolus tracking protocol is good in pregnancy with a lower rate of required repetition of study but with a trade-off of higher radiation dose. Our result shows that the radiation dose of bolus tracking techniques was significantly higher than test bolus. This is different from the previous study whereby the 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 between the effective radiation doses of the test bolus protocol CTPA scans compared to the bolus tracking (Rodrigues *et al.*, 2012).

Suboptimal CTPA among pregnant women were likely due to the influx of non-opacified blood via the inferior vena cava into the right heart, causing dilution of contrast in inspiration with underlying hyperdynamic circulation. This explains the suboptimal CTPA quality among pregnant women even using real-time ROI bolus tracking as well. Hence, this caused no significant differences between the test bolus and bolus tracking protocol among pregnant women. Valsalva manoeuvre or shallow respiration as an alternative to suspended breathing during exposure was suggested to reduce this effect (Schaefer-Prokop & Prokop, 2008). Our study showed a higher rate of diagnostic CTPA in the inspiratory phase, but it was not statistically significant. Some patients were incidentally scanned in the expiratory phase as they could not hold their breath, likely due to respiratory distress, which contributes to poor PA enhancement. The limited samples on the expiratory phase, n=18, are not generalised to represent the quality of CTPA in the expiratory phase among pregnant women. Previous studies in nonpregnant patients showed better PA enhancement in the expiratory phase but had poor lung parenchymal depiction (Mortimer et al., 2011). Breathing motion will cause artefacts, which causes an overlook of the pulmonary emboli, especially the distal pulmonary artery branches and lung bases. Hence, it is good to educate the patient about breath-holding before the study and follow the breathholding instruction during the scan.

In this study, there was no significant improvement in quality if repeat CTPA of previously poor contrast enhancement of PA among pregnant women. The sign of right heart strain is advised to be identified in the CTPA, such as main pulmonary artery size or RV:LV ratio, if both heart chambers are well opacified. However, MPA size may vary in normal pregnant women up to 3.3cm, with a mean of 2.5cm \pm 0.3cm in our study. A study by <u>Khalil et al (2009)</u> showed that the mean diameter and SD of the main pulmonary artery were 28 mm \pm 3.5 mm, with a range of 20 – 40 mm. The main pulmonary artery tends to be larger in pregnancy due to haemodynamic changes. This also causes a pitfall of pulmonary artery to aorta (PA:A) ratio >1.0, which may not be as predictive of pulmonary hypertension <u>(Khalil et al.,</u> 2009). We found that normal pregnant women could have a PA:A ratio of 1.0 \pm 0.1 with a range of 0.8 to 1.3.

Malaysia Journal of Medical Research 7(3) 34-40 Limitation

This is a retrospective study, hence we cannot eliminate factors affecting CTPA quality, such as breathholding. Some patients cannot hold their breath during the scan causing an artefact and an influx of non-opacified blood via the inferior vena cava into the right heart, causing dilution of contrast. Every patient is advised to educate on the breath holding technique prior to the CT scan. We were unable to compare the expiratory and inspiratory phases as some patients were breathless, not breath-holding properly, and were not instructed to hold their breath in the expiratory phase. Data was only obtained from a single institution in each protocol, which may not be generalised to another institute. The sample size of CTPA repetition was small and may not be representative as repetition of CTPA study will cause higher radiation dose to the mother and fetus. We were unable to retrieve some demographic data e.g. patients' weight and heart rates from the old record. The documented heart rate may not be a factor that determines the association with CTPA quality as the heart rate was documented in the ward and not recorded during the CTPA scan. A limited number of samples for patients with PE make it inaccurate to calculate the normal upper limit and its sensitivity and specificity of PA size, PA:A ratio and RV:LV ratio among pregnant women from this study.

Conclusion

No significant difference between test bolus and bolus tracking protocol in CTPA among pregnant patients. Bolus tracking protocol had better overall CTPA quality, but it had a higher estimated radiation dose to mother and fetus. The repetition of CTPA for the suboptimal study is controversial, depending on risk and benefit to the patient.

Future Recommendations

A larger study with more samples is needed to yield more representative CTPA repetition outcomes. Prospective studies are recommended to include the difference between breath-holding expiratory and inspiratory phases and short start delay time. A larger sample size of PE in pregnancy can come out with the normal upper limit and its sensitivity and specificity of PA size, PA/A ratio and RV/LV ratio among pregnant women.

Conflict of Interest

All authors declared that they have no conflict of interest.

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