MODIFIED CONTRAST VOLUME AND SALINE CHASER TO REDUCE ARTIFACTS IN COMPUTED TOMOGRAPHY PULMONARY ANGIOGRAPHY (CTPA)

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

CT	Computed tomography
CTPA	Computer tomography pulmonary angiography
PE	Pulmonary embolism
SVC	Superior vena cava
BMI	Body mass index
PACS	Picture archiving and communication system
Kg	Kilogram
m	Meter
IV	Intravenous
kV	Kilovolt

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ABSTRAK

Latar belakang: Angiografi pulmonari tomografi berkomputer (CTPA) adalah teknik pengimejan yang utama dalam diagnostik embolisme pulmonari (PE). Oleh itu, kualiti pengimejan memainkan peranan yang besar dalam diagnosis dan rawatan pesakit nanti. Kualiti imej terutamanya dinilai oleh peningkatan Hounsfield Unit (H.U) dalam arteri pulmonari dan kesan artifak daripada kepekatan kontras yang tinggi di dalam salur darah bersebelahan. Di Hospital Universiti Sains Malaysia (HUSM), masalah utama yang kami hadapi ialah kualiti imej disebabkan kurang peningkatan H.U. pada arteri pulmonari kerana kebanyakan kontras masih berada di dalam vena subclavia, vena brachiocephalic dan vena cava superior (SVC). Terdapat banyak faktor yang menyumbang kepada masalah ini, ianya dibahagikan kepada dua kategori: protokol pengimbasan dan faktor berkaitan pesakit. Faktor berkaitan pesakit adalah komponen yang sukar dan hampir mustahil untuk diubahsuaikan. Oleh itu, tujuan kajian adalah untuk mengubah suai protokol pengimbasan CT untuk meningkatkan kualiti imej dan untuk menentukan perkaitan dengan faktor indeks jisim badan (BMI).

Metod: Kajian prospektif telah dijalankan di HUSM, Kota Bharu, Kelantan, Malaysia terhadap pesakit yang disyaki menghidap PE dan menjalani CTPA menggunakan pengimbas CT Toshiba Aquilion PRIME. Kesemua pesakit menjalani CTPA dari 1 Jun 2020 hingga 14 Februari 2021 menggunakan protokol standard (isipadu kontras 40 ml dan isipadu saline 60 ml). Manakala mereka yang menjalani CTPA dari 15 Februari 2021 hingga 31 Oktober 2021, menggunakan protokol terubahsuai (isipadu kontras 30 ml dan isipadu saline 70 ml). Ia adalah pensampelan secara tanpa rawak, mudah berdasarkan kriteria kemasukan dan pengecualian. Semua imbasan CT

dilakukan menggunakan teknik pengesanan bolus. Kedua-dua pengimejan protokol dibandingkan dari segi peningkatan H.U. arteri pulmonari dan kadar artifak dari SVC dan vena subclavia. Peningkatan arteri pulmonari juga berkait dengan indeks jisim badan pesakit (BMI).

Keputusan: Seramai 254 pesakit disyaki menghidap pulmonary embolism dan menjalani CTPA. Selepas mempertimbangkan kriteria kemasukan dan pengecualian, 199 pesakit didaftar, di mana 83 daripada mereka menjalani CTPA dengan protokol standard dan 116 daripada mereka menjalani protokol terubahsuai. Julat umur subjek untuk protokol standard adalah dari 13 hingga 86 (min umur 50.5) tahun, manakala protokol terubahsuai adalah dari 13 hingga 95 (min umur 52.7) tahun. Purata BMI untuk protokol standard ialah 26.0 (julat 14.3 hingga 43.0) dan protokol terubahsuai ialah 24.8 (15.6 hingga 43.8). Min H.U. arteri pulmonari menunjukkan perbezaan yang ketara antara dua protokol, yang mana ianya lebih tinggi dalam protokol terubahsuai [perbezaan min (95% CI) = -41.97 (-80.60, -3.34), p = 0.033], Walau bagaimanapun, perbezaan min H.U. arteri pulmonari antara dua protokol tidak menunjukkan perbezaan yang ketara selepas diselaraskan dengan BMI dan HR sebagai kovariat. Majoriti subjek mempunyai gred artifak 3 untuk SVC (75.4%) dan vena subclavian (62.8%). Protokol terubahsuai mempunyai kadar artifak gred 3 yang lebih rendah untuk kedua-dua SVC dan vena subclavian ($p<0.001$). BMI dan H.U. arteri pulmonari mempunyai korelasi yang ketara, secara keseluruhan ($r=-0.4$) dan mengikut setiap jenis protokol (protokol standard $r=-0.3$, protokol terubahsuai $r=-0.4$).

Kesimpulan: Protokol terubahsuai menunjukkan peningkatan kontras yang lebih baik dalam arteri pulmonari dan kadar artifak yang lebih rendah daripada protokol standard dalam kajian ini. BMI adalah faktor pengasas bersama dan menunjukkan korelasi ketara dengan peningkatan H.U. arteri pulmonari.

Kata kunci: imbasan CT, Angiografi pulmonari tomografi berkomputer (CTPA), embolisme pulmonari, indeks jisim badan pesakit (BMI).

ABSTRACT

Background: Computer tomography pulmonary angiography (CTPA) is the gold standard imaging for the diagnosis of pulmonary embolism (PE). Therefore, the quality of the images plays a big role in the diagnosis and patient's management later. The image quality is mainly assessed by the pulmonary artery enhancement in the Hounsfield Unit (H.U.) and the impact of the streak artifacts from the high concentration of contrast in the adjacent vessels. In Hospital Universiti Sains Malaysia (HUSM), the major problem that we faced was poor enhancement of the pulmonary artery as most of the contrast remained in the subclavian vein, brachiocephalic vein, and superior vena cava (SVC). Many factors contributed to these problems, which were divided into 2 categories: scanning protocol and patient-related factors. The patient-related factor is a component that is difficult and almost impossible to adjust. Thus, the purpose of the study is to modify the CT protocol to improve the image quality and correlate with the body mass index (BMI) factor.

Methods: A prospective study was conducted in HUSM, Kota Bharu, Kelantan, Malaysia on patients who were suspected to have PE and underwent CTPA using Toshiba Aquilion PRIME computer tomography (CT) scanner. All the patients who underwent CTPA from 1st June 2020 to 14th February 2021 used a standard protocol (contrast volume 40 ml and saline flush 60 ml). While those who underwent CTPA from 15th February 2021 to 31st October 2021, used a modified protocol (contrast volume 30ml and saline flush 70ml). It is a non-randomized, convenient sampling based on inclusion and exclusion criteria. All the scans were performed using the bolus tracking technique. Both protocols were compared for pulmonary trunk enhancement

and degree of artifacts from the SVC and subclavian vein. The pulmonary trunk enhancement was also correlated with patient's BMI.

Results: A total of 254 patients with suspected PE underwent CTPA. Based on the inclusion and exclusion criteria, 199 patients were enrolled. Of these, 83 patients underwent CTPA with standard protocol and 116 patients underwent modified protocol. The age range of the subjects for standard protocol was 13 to 86 (mean age 50.5) years old, and the modified protocol was 13 to 95 (mean age 52.7) years old. The mean BMI for standard protocol was 26.0 (range 14.3 to 43.0) and for modified protocol was 24.8 (15.6 to 43.8). The mean H.U. of pulmonary trunk showed significant difference between the two protocols, which was higher in the modified protocol [Mean difference (95% CI) = -41.97 (-80.60, -3.34), p = 0.033]. However, the difference in mean H.U. of pulmonary trunk between the protocols showed no significant difference after adjusted to BMI and HR as covariates. Majority of subjects had artifact grade 3 for SVC (75.4%) and subclavian vein (62.8%). The modified protocol had a lower proportion of grade 3 artifacts for both SVC and subclavian vein ($p<0.001$). BMI and H.U. of pulmonary trunk revealed a significant correlation, overall (r=-0.4) and by each type of protocol (standard protocol r=- 0.3, modified protocol r=-0.4).

Conclusion: The modified protocol showed better contrast enhancement in pulmonary trunk and lower artifacts than the standard protocol in this study. BMI was a cofounding factor and showed significant correlation with pulmonary trunk enhancement.

Keywords: CT Scan, Computer tomography pulmonary angiography, pulmonary embolism, body mass index (BMI).

CHAPTER 1: BACKGROUND

1.1 Introduction

Pulmonary embolism (PE) occurs when thrombosis in the systemic venous system break free and migrate to the pulmonary arteries, totally or partially occluding the blood flow to the lung parenchymal (Mayo and Thakur, 2013). PE is the third most common acute cardiovascular disease after myocardial infarction and stroke (Mayo and Thakur, 2013). It is a life-threatening clinical diagnosis with nonspecific signs and symptoms which can be mimicked by other medical conditions.

Computed tomography (CT) has practically become the first-line imaging modality for pulmonary circulation in patients suspected of having PE (Schoepf and Costello, 2004). Computed tomography pulmonary angiography (CTPA) was reported to have sensitivity and specificity of 89% and 95%, respectively (Marshall et al., 2019). However, significant suboptimal CTPA image quality may interfere with the diagnosis of PE. The most common causes are streak artifacts from contrast, motion artifacts caused by cardiac pulsation or respiratory movements, and poor contrast enhancement (Hu *et al.*, 2017). Therefore, factors affecting the image quality of CTPA can be divided into scanning protocol and patient-related factors.

Scanning protocol involves contrast concentration, contrast injection rate, contrast volume, scan timing – bolus tracking or test bolus and delay time in scanning. All these parameters are easily adjustable. Patient-related factor involves gender, patient's BMI, cardiac output, venous access, and underlying illness. Body

weight affects intravenous contrast attenuation; as the patient's body weight increases the blood volume increases which thus reduces the intravascular attenuation of iodine (Hendriks *et al.*, 2018). Therefore, one of the easier methods to modify and optimise patient-related factors is by adjusting the contrast volume according to patient weight.

1.2 Objectives

1.2.1 General Objective

To compare the pulmonary trunk enhancement and artifacts between standard protocol and modified protocol (lower contrast volume and higher saline flush volume) in CTPA, and to correlate with BMI.

1.2.2 Specific Objectives

a. To compare the mean H.U. of pulmonary artery enhancement between standard protocol and modified protocol.
b. To compare the grade of streak artifacts in subclavian vein and superior vena cava between standard protocol and modified protocol.
c. To correlate the BMI with H.U pulmonary artery enhancement in standard protocol and modified protocol.

1.2 Hypothesis

a. Modified protocol with lower contrast volume and higher saline flush volume has better pulmonary artery enhancement compared to the current standard protocol.

b. Modified protocol can reduce the grade of streak artifact from subclavian and superior vena cava.

c. Higher BMI reduces the pulmonary artery enhancement.

.4 Research Question

Will the modified protocol produce better pulmonary trunk enhancement and reduce the streak artifact compared with the standard protocol?

CHAPTER 2: LITERATURE REVIEW

2.1 Quantitative analysis of pulmonary artery enhancement.

The quantitative analysis is mainly to assess the vascular enhancement of the pulmonary trunk, right main pulmonary artery, left main pulmonary artery, and peripheral pulmonary arteries, which include the left upper lobar, left posterobasal segmental and its subsegmental branches. A study by Kim *et al.*(2017), assessment of pulmonary artery enhancement was based on venous routes of contrast administration. They have stated that diagnostic image quality needed pulmonary artery enhancement of more than 250 H.U. Similar value of pulmonary artery enhancement as a diagnostic image quality was also mentioned in a study by Ramadan *et al*.(2010).

The method of measuring the H.U was explained by Lu *et al.*(2014). It was measured on axial images using a manually defined circular region of interest (ROI) with a size of 2 cm^2 in the main pulmonary artery and 0.5-0.7 cm^2 in the left pulmonary artery and right pulmonary artery. Measurements were performed three times and the average values were calculated.

2.2 Image artifacts.

CTPA image artifacts are mainly due to the respiratory artifact, streak artifact, pulsation artifact, motion artifact, or the presence of foreign bodies/ devices. Hutchinson *et al.*(2015) stated that 42.2% of CTPA cases have motion artifacts due to breathing. The second major artifact was beam hardening (streak artifact) from high-density structures such as pooled contrast in SVC or adjacent vessels, foreign bodies/ pacemaker device, and the patient's arm when not elevated above the chest. It also explained the ways to overcome these artifacts, with caudocranial scanning direction and saline flush.

Hargaden *et al.*(2006) explained the comparison between craniocaudal and caudocranial directions of CTPA scan based on the diagnosis and image quality. Their study showed a significant difference with higher upper lobe artery opacification in cranio-caudal direction scan ($p=0.02$), but the overall image quality is not significantly different ($p=0.07$). Besides that, there is no significant difference in the prevalence of emboli in both groups ($p=0.76$). However, this study did not mention the impact of direction of the scan on the breathing motion artifact.

Few studies defined the beam hardening artifact from SVC or adjacent vessel as a perivenous artifact. The study by Ramadan *et al.*(2010) explained how the perivenous artifact was assessed based on a four-point scale: grade 0 (no artifact), grade 1 (negligible artifacts), grade 2 (moderate artifacts but all vessel portions diagnostic), and grade 3 (severe or extensive artifacts that might lead to misinterpretation in some vessel portions). They suggested to use saline flush technique to overcome the artifact.

2.3 Scanning protocol and contrast medium.

There are two main methods of scanning CTPA: bolus tracking and test bolus. Many studies had been done before this to compare both methods. In a study by Cademartiri *et al.*(2007), a test bolus versus bolus tracking techniques in 16-detector row helical CT coronary angiography was compared. Both methods scanning of ROI was set at the aortic root and attenuation at ascending aorta, descending aorta and main pulmonary artery were compared. The results showed significantly higher attenuation of the pulmonary artery in the bolus tracking technique compared to the test bolus ($p<0.05$) and more homogeneous enhancement. No significant differences in ascending and descending aorta attenuation in both methods. However, this study was done using a CT scanner of 16 detector rows. Nowadays, most of the hospitals in Malaysia already have CT scanners with better detector row. Another study by Moradi and Khalili, 2016) also compared both scanning methods using light speed 64 detector row CT scanner. It showed no significant statistically difference between both methods in pulmonary artery enhancement ($p=0.547$), but the radiation dose was higher in the test bolus technique compared to bolus tracking ($p=0.012$).

Hendriks *et al.*(2018) mentioned that both bolus tracking and test bolus techniques were examples of integrated individualization techniques which took into consideration of each's patient individual cardiac output to achieve diagnostic pulmonary artery enhancement. They also explained the need to more personalised approach in terms of contrast medium and scanning protocol in CTPA. In their study, the contrast injection protocol was modified according to patient body weight and kV selection via a predefined formula based on previous research. Total contrast volume used for each patient was based on the 2.5 second injection time of test bolus

multiplied by flow rate, which was calculated by body weight-dependent value adapted per kV. Then followed by a 30 ml saline flush with the same flow rate. They concluded patients with lower BMI used lesser contrast medium volume ($p<0.001$).

Automated tube voltage selection (ATVS) software was used to adapt tube voltage (from 70 kV to 120 kV) to the individual patient based on anterior-posterior and lateral scout scan (Hendriks *et al.*, 2018). They explained regarding the beam hardening mechanism that the low-energy photons were easily absorbed when the x-rays passed through the body and leaving an x-ray beam with higher mean energy. Increased mean energy also meaned the x-rays were moving away from the K-edge of iodine and the attenuation of iodine decreased. Their conclusion was the attenuation of iodine increased when tube kV moved closer toward the K-edge of iodine (33 kV).

Boos J, Kropil P, Lanzman RS, (2016) also studied on reducing kV and contrast volume in CTPA scans. They divided all the patients into 2 groups: group A (70 kV, 40 ml contrast volume and 0.9 pitch) while group B (100 kV/ 120 kV and 70 ml contrast volume and 2.2 pitch). However, this study was only done on patients with BMI less than 35 kg/m². Technique of saline flush (40 ml at rate of 3ml/s) and bolus tracking were used. It used breath holding instead of deep inspiration. The image quality was assessed by signal-to-noise ratio (SNR) and contrast to noise ratio (CNR) at the pulmonary trunk and left lower lobe segmental pulmonary artery. Subjective image quality was assessed using 4 points scales, based on vascular attenuation, image noise, artifact, and diagnostic confidence. The result showed group A had better pulmonary trunk ($p<0.0001$) and left lower lobe segmental pulmonary artery enhancement ($p<0.0001$). But there was no statistical difference between both groups on SNR, CNR, and subjective image quality ($p>0.05$). They concluded that it is

feasible to use 70kV, 40ml contrast volume with low pitch as it reduced the radiation dose by almost 50%. They explained that dose reduction can only be reduced by kV reduction if the tube current product does not completely counterbalance the dose reduction. However, this study involved a small number of patients, a total of 35 patients for each group.

Lu *et al.* (2014) also used the similar CTPA protocol concept of lower contrast volume with lower kV and higher pitch. They used test bolus method with 10 ml contrast and 20 ml of saline flush. They divided patients into two groups. Group A used 60 ml contrast 300 mg I/ml at injection rate 4 ml/s, 30 ml saline chase/flush, 100 kVp and routine pitch 1.2. Group B used 20 ml contrast 300 mg I/ml at injection rate 4 ml/s, 30 ml saline chase/flush, 80 kVp and pitch 2.2. Their result showed group B had higher enhancement of pulmonary trunk, bilateral main pulmonary, lobar, segmental and subsegmental pulmonary arteries compared to group A. They concluded that high pitch CTPA with 80 kV protocol can achieved adequate enhancement with 20 ml of contrast volume. However, their study was only involved patient with body weight below 80 kg.

Contrast medium concentration and the injection rate also played important role in the pulmonary artery enhancement in CTPA. Faggioni *et al.* (2012) studied on the pulmonary artery enhancement by using two different concentration of contrast medium. In their study, patients were divided into two groups: moderate concentration iso-osmolar contrast (iodixanol, 320 mg I/ml) with injection rate 5 ml/s and high concentration low-osmolar (iomeprol, 400 mg I/ml) with injection rate 4 ml/s. The contrast volume (40 ml) and saline flush (40 ml) was same in both groups. Their result showed pulmonary arteries down to segmental level was significantly higher with

iodixanol (320 mg I/ml) compared to iomeprol (400 mg I/ml) ($p = 0.036$). However, the enhancement homogeneity had no significant differences between both groups ($p = 0.8966$). Thus, they concluded that good pulmonary artery enhancement down to segmental level can achieved by using 40 ml of iodixanol (320 mg I/ml). They also mentioned that this can help reduce the risk of contrast induced nephropathy and health care cost.

In study by Bae *et al.*(2007), the amount of contrast required for a given patient weight to achieve diagnostic CTPA pulmonary artery attenuation with 16-detector and 64-detector CT scanners was evaluated. They used contrast volume based on the calculation of injection rate multiplied by the sum of scanning delay and scanning duration. Contrast enhancement is measured at the pulmonary trunk and aorta. They calculated each patient's contrast volume per body weight index. Subsequently, linear regression analysis was performed to assess the differences between the two CT scanners. The derived regression equation 64 detector CT scanner was: pulmonary artery enhancement H.U = 211 x contrast volume per body weight index. The result showed 1.2ml per kilogram of body weight of contrast is needed to achieve 250 H.U attenuations of the pulmonary artery. The 64 detector CT scanner had a shorter scanning time, so it required lesser contrast volume than the 16 detector CT scanner ($p<0.001$). The difficulty they faced was variation of cardiac output among patients which caused difficulty to individualise the scanning delay. However, this problem can be overcome by using test bolus or bolus tracking technique. These studies regarded the CTPA protocols were summarised in Table 1.

Table 1: Summary of studies on CTPA protocols

Title/ authors/ country	CT machine	Protocol/ contrast	Result (mean Pulmonary trunk enhancement in HU)	Conclusion
Optimising pulmonary embolism computed Tomography in age of individualised medicine (Hendriks *et al.*, 2018) Germany	MDCT Dual Source (Somatom Force, Siemens Healthineers, Forchheim, Germany)	Test bolus, Automated tube voltage selection (ATVS) *Initial plan to divide into 6 group with kV 70 – 120 based on patient body scout view. kV: 70, mAs: 247 kV:80, mAs: 164 kV:90, mAs: 124 kV:100, mAs: 105 kV: 110, mAs:95 kV: 120, mAs: 88 However, all the patients only fall into group 70 – 90 kV. Group 1: 70 kV, 24 +/-3 ml Contrast 300 mg I/ml Mean radiation dose: 1.3 +/- 0.3 mSV Saline chase: 30ml Group 2: 80 kV, 29 +/-4 ml Contrast 300 mg I/ml Mean radiation dose: 1.3 +/- 0.3 mSV Saline chase: 30ml Group 3: 90 kV, 38 +/-3 ml Contrast 300 mg I/ml Mean radiation dose: 1.3 +/- 0.3 mSV Saline chase: 30ml	Group 1: 397 +/- 101 Group 2: 398 +/- 96 Group 3: 378 +/- 100 1 scan with 90 kV non diagnostic segmental pulmonary arteries.	The diagnostic CTPA scan (H.U > 200) was achieved with 24-38 ml contrast volume and a low radiation dose.

CT pulmonary angiography: stimultaneous low-pitch dual-source acquisition mode with 70 kVp and 40 ml of contrast medium and comparison with high-pitch spiral dual-source acquisition with automated tube potential selection (Boos J, Kropil P, Lanzman RS, 2016) Germany	64-MDCT Dual source CT scanner (Siemens Definition Flash; Siemens Healthcare GmbH, Erlanger, Germany)	Trigger H.U: 130 ROI: pulmonary trunk *Breath hold command (no deep inspiration) Protocol A: Dual source, simultaneous acquisition mode, 70 kV 40ml contrast 300 mg I/ml at 3 ml/s 40ml saline at 3 ml/s Protocol B: Dual source acquisition mode, high pitch, 118 kV 70ml contrast 300mg I/ml at 3 ml/s 40ml saline at 3 ml/s	Protocol A: 414.3 +/- 149.4 Protocol B: 259.6 +/- 69.7 ($p<0.0001$)	Protocol A was feasible to provide diagnostic image quality with lower radiation dose and contrast medium.
80-kV pulmonary CT angiography with 40 mL of iodinated contrast material in lean patients: Comparison of vascular enhancement with iodixanol (320 mg I/mL) and iomeprol (400 mg I/mL) (Faggioni *et al.*, 2012) Italy	64-MDCT scanner (LightSpeed VCT, GE Healthcare)	Trigger H.U: 250 ROI: SVC KV: 80 Rotation time: 0.5s Delay time: 5-6s Group 1: 40 ml contrast 320 mg I/ml 40ml saline Rate 5 mL/s Group 2: 40ml contrast 400mgI/ml 40ml saline Rate 5 mL/s	Group 1: 704.5 ± 37.2 Group 2: 614.5 ± 39.6	High pulmonary trunk enhancement can be achieved using 40 ml contrast 320 mg I/ml than using 40ml contrast 400mgI/ml.

Optimisation of contrast medium volume and injection-related factors in CT pulmonary angiography: 64-slice CT study (Ramadan *et al.*, 2010) Turkey	64-slice CT (Aquillion 64, Toshiba Medical Systems,	ROI: pulmonary trunk KV: 80 Pitch: 0.8 Rotation time: 0.5s Delay time: 7-8s Protocol 1: Trigger H.U: 120 60 ml contrast 300 mg I/ml at 5ml/s, 20ml saline chase Protocol 2: Trigger H.U: 90 55ml contrast 300 mg I/ml at 5ml/s, 20ml saline chase Protocol 3: Trigger H.U: 75 50ml contrast 300 mg I/ml (75ml- First 25 ml at 5 ml/s the remaining 25 ml at 4 ml/s) 20ml saline chase	Protocol 1: 390 ± 144 Protocol 2: 401 ± 102 Protocol 3: 386 ±97	CTPA protocol with low trigger level and high flow rate with saline chase can decreased the contrast volume can achieve diagnostic pulmonary trunk enhancement.
Effect of patient weight and scanning duration on contrast enhancement during pulmonary multidetector CT angiography (Bae *et al.*, 2007) Turkey	16-section (sensation 16; Siemens Medical Solution, Forchheim, Germany) and 64-section (Sensation 64; Siemens Medical Solutions	Trigger H.U: 150 ROI: pulmonary trunk KV: 120 Pitch: 0.8 Rotation time: 0.5s Delay time: 15s 350mgI/ml at 4ml/sec 20G cannula size *Amount of contrast volume: injection rate multiplied sum scan delay plus scanning duration. - range patient weight 45.3 to 153 kg. - range contrast volume 76 – 125 ml.	16-section CT: 282.9, 103.6ml contrast 64-section CT: 257.7, 85.4ml contrast	Amount of contrast volume used can be adjusted according paitent's body weight. The regression formula is 1.2 ml/kg of contrast medium need to achieve 250 H.U. pulmonary trunk enhancement.

High pitch CTPA with iterative recontruction at 80kVp and 120 ml contrast agent volume (Lu *et al.*, 2014) China	Dual source CT scanner system (Definition Flash, Siemens Medical Solution, Forchheim, Germany)	Trigger H.U: 100 ROI: pulmonary trunk Cranicaudal direction at end inspiration Test bolus 10ml contrast and 20ml saline chase Group A: 100 kVp routine pitch 1.2 Gantry rotation time: 0.5s, 60 ml contrast 300 mg I/ml at 4 ml/s. 30 ml saline chase/flush Group B: 80 kVp pitch 2.2 Gantry rotation time: 0.28s. 20 ml contrast 300 mg I/ml at 4 ml/s. 30ml saline chase/flush.	Group A: 320.0 +/- 75.6 Group B: 416.3 +/- 108.6 *Group B had higher enhancement of pulmonary trunk, bilateral main pulmonary, loba, segmental and subsegmental pulmonary arteries.	High pitch CTPA at 80 kVp can achieve diagnostic CTPA with 20 ml contrast volume in normal weight patient (<80kg)

Regarding the contrast medium administration (vascular assess) usually intravenous (IV) through the antecubital vein of the arm as explained by Kim *et al.*(2017). The administration of contrast medium through the arm vein is higher diagnostic rate of pulmonary artery enhancement compared to the leg vein ($p<0.01$). But this study did not mention the size of the IV cannula used at the arm and leg. However, the preferred IV cannula size is 18- gauge (Wittram, 2007).

Another important factor in the scanning protocol is saline flush following contrast medium administration. As there are many studies show that high vascular enhancement in subclavian vein in CTPA. Therefore, the saline flush technique was used to push contrast medium located in the upper arm and superior vena cava towards the heart. This helped reduced the perivenous artifacts. Indirectly also reduced the contrast volume to be used in CTPA. Many studies stated that with the saline chase/ flush technique, the volume of contrast used can be reduced. Included aforementioned studies such as Hendriks *et al.* (2018), Boos J, Kropil P, Lanzman RS (2016), (Faggioni *et al.*, 2012) and Ramadan *et al.* (2010). Saline flush technique was used to reduce contrast volume in CT coronary angiogram and aortogram as explained in studies by Schoellnast *et al.* (2004) and Cademartiri *et al.*(2004). There were many other studies that compared CTPA protocols of no saline flush given versus saline flush given, which were summarised in Table 2.

Table 2: Summary of studies regarding saline flush/ chase

Titles, authors	Contrast and saline volume used.	Conclusion
Artifact reduction in bolus-enhanced spiral CTPA using saline push. (Vogel *et al.*, 2001)	Group 1: 120ml contrast and no saline. Group 2: 120ml contrast and 60ml saline	Protocol with saline push significantly reduces artifacts mainly by washout of contrast medium in superior vena cava ($p<0.05$).
Use of saline chaser in the intravenous, administration of contrast material in non-invasive coronary angiography with 16-row multislice computed tomography. (Cademartiri *et al.*, 2004)	Group 1: 140ml contrast and no saline. Group 2: 100ml contrast and 40ml saline	No significant different of CT coronary enhancement between 2 groups. Saline chase reduce contrast volume.
Developments and Instrumentation; Thoracic spiral CT: Delivery of contrast material pushed with injectable saline solution in a power injector (Hopper, Tenhave and Tully, 1997)	Group 1: 50ml contrast Group 2: 75ml contrast Group 3: 75ml contrast Group 4: 100ml contrast Group 5: 100ml contrast Group 6: 125ml contrast Group 3,4,6 – no saline Group 1,2,4 – saline 50ml	Vascular opacification by 75ml contrast and 50ml saline is equivalent with opacification provided by 125ml contrast.
Reduction of Contrast Material Dose and Artifacts by a Saline Flush Using a Double Power Injector in Helical CT of the Thorax (Haage, Schmitz-rode and Günther, 2000)	Group 1: 60ml contrast, 30ml saline. Group 2: 75ml contrast, no saline.	Saline flush/ chase allow reduction of 20% contrast volume with similar degree of enhancement.

2.4 Patient's weight.

The weight of the patient was found to be an effective parameter for enhancement in all pulmonary arteries as in the aforementioned studies by Ramadan et al. (2010) and Hendriks *et al.*(2018). They found that as the patient's body weight increased, the blood volume increased which thus reduced the intravascular attenuation of iodine. As conclusion, more contrast volume was needed in patient with high body weight to achieve diagnostic pulmonary artery enhancement.

Besides that, high body weight patient also needs higher kV in CTPA. As Low kV will cause near complete attenuation of photon beam, leading to noisy images which are not diagnostic quality images. Same concept, lower body weight patients will receive substantial radiation dose reduction using this method (Mayo and Thakur, 2013).

2.5 Conceptual framework.

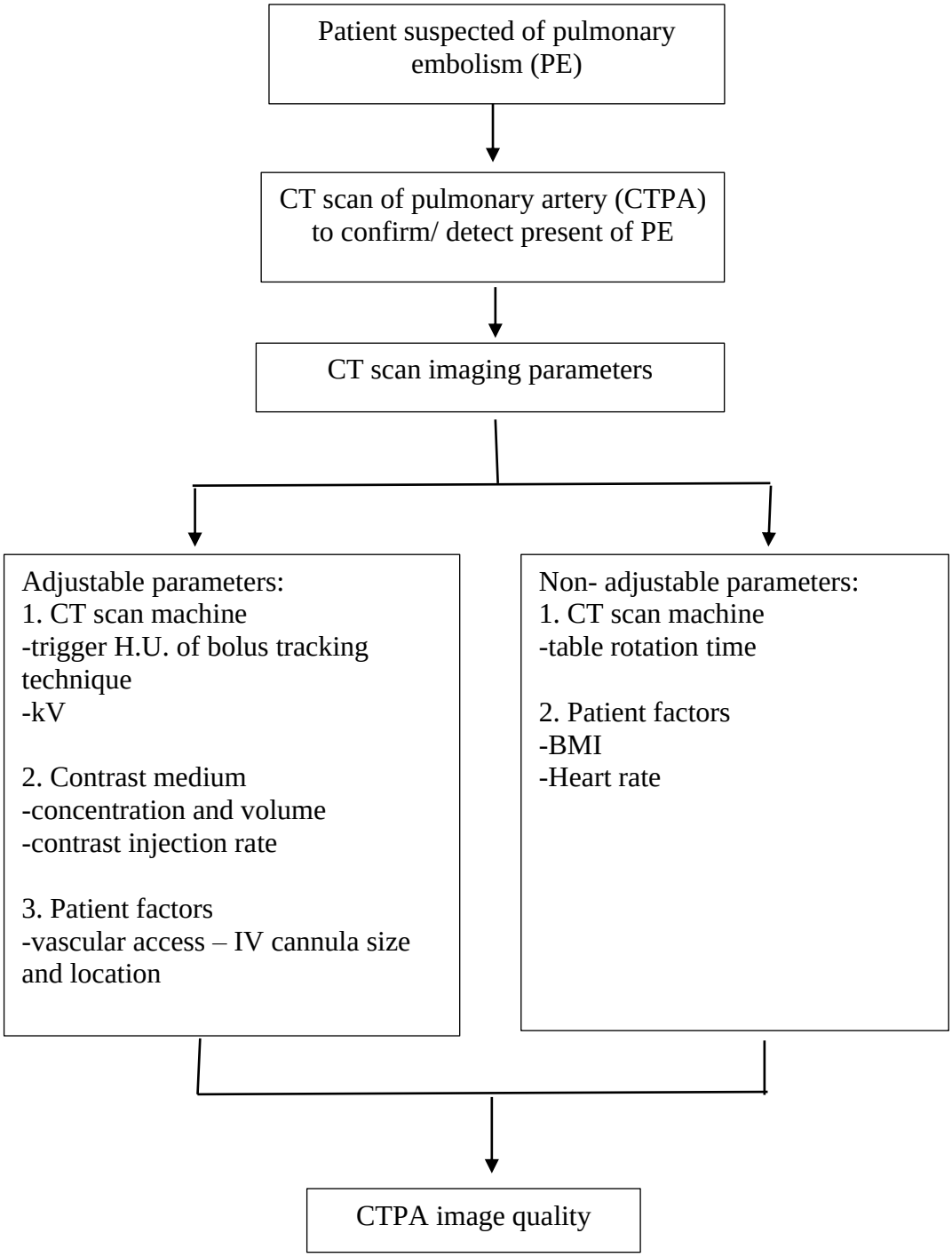

Figure 1: Conceptual framework.

2.6 Study rationale and problem statement

The main problems of imaging quality of CTPA in Hospital Universiti Sains Malaysia (HUSM) was more contrast enhancement in subclavian vein, brachiocephalic trunk, and superior vena cava (SVC) compared to pulmonary arteries, which resulted in streak artifact. This may be due to too much contrast volume, too early scanning time or patient factors such as vascular access, cardiac output, or underlying illness. As we went through the CTPA images acquired in 2019, we realised that our problems were similar to those mentioned in previous studies. Having gone other studies, we needed to optimise our standard protocol and contrast medium with our CT scanner model. In this study, we also take into consideration of our population's BMI.

Since different hospital has a different model of CT scanners and CTPA scanning protocol, a comparison of the CTPA protocol of the same CT scanner model is important in helping to improve CTPA protocol in HUSM. Using single CT scanner also remove variations caused by the table movement time, scan delay, and the number of detectors.

Applying single CTPA protocol to all patients to achieve optimum image quality is not the best practice. To our knowledge, there is no study done regarding the correlation of a patient's body mass index (BMI) with pulmonary artery enhancement in CTPA. In our setting, we were using the bolus tracking technique which is more individualised, and our CT scanner is 80 detectors with 160 slices. We believe that our CT scan machine has advanced features which enable further optimisation of the contrast volume.

It is difficult to assess patient's cardiac output and other clinical parameters just prior to the scan, as most CTPA are emergency cases. Therefore, the parameter of patient's BMI association with pulmonary artery enhancement is to be proven beneficial. It can be very useful as simple guidance in contrast volume modification in the future before a CTPA scan. Besides that, almost all the journals regarding the CTPA protocols were done in other countries as mentioned earlier. There is no published article in the English journal regarding CTPA protocol study optimization that was done in Malaysia. As in Malaysian patient factors (weight, BMI, even baseline heart rate) is different from foreigner. Apart from that, most hospitals in Malaysia have a different model of CT scanner and the age of the CT scanner. Therefore, this study can be a guideline for CTPA protocol optimization in Malaysia.

CHAPTER 3: METHODOLOGY

3.1 Study Design.

This prospective study was conducted in Hospital Universiti Sains Malaysia (USM), Kota Bharu, Kelantan, Malaysia on patients who were suspected to have pulmonary embolism and underwent computer tomography pulmonary angiography (CTPA) using a Toshiba Aquilion PRIME CT scanner. The duration of this study was 17 months from 1st June 2020 to 31st October 2021. This study obtained approval from the Human Research Ethics Committee of USM (USM/JEPeM/20060293).

3.2 Sample Population

a. Reference population – Patients who were suspected of pulmonary embolism in HUSM.
b. Source population – Patients who were suspected of pulmonary embolism underwent CTPA in HUSM.
c. Target population – Patients who were suspected of pulmonary embolism with CTPA within the study period.
d. Sampling frame – Patients who were suspected of pulmonary embolism with CTPA done in HUSM using CT Aquilion Toshiba and full filled the inclusion criteria.

3.3 Sample Size Calculation

a. Objective 1: the sample size estimate using Two Mean estimation (Arifin, 2020). Based on (Lu et al., 2014), the standard deviation of pulmonary artery enhancement is 80.

   Total sample size of study: 92. Ratio of standard scanning protocol group to modified scanning protocol group is 1:1.

   Sample size of standard scanning protocol group: 46. Sample size of modified scanning protocol group: 46.

Measurement	SD	Expected difference	n	n + 10%	Reference
Main pulmonary artery enhancement	80	50	82	92	(Lu *et al.*, 2014)

$\alpha = 0.05$, power = 80%, Drop-out = 10%.

b. Objective 2: the sample size estimate using Two proportion estimation (Arifin, 2020). Based on (C. H. Lee et al., 2007), superior vena cava artifact: P0 = 0.97, P1 = 0.85 and subclavian vein artifact: P0 = 0.94, P1 = 0.80. [P0: Proportion of Standard Protocol with Artifact, P1: Proportion of Modified protocol with artifact].

   i) Superior vena cava artifact. Total sample size of study: 198. Ratio of standard scanning protocol group to modified scanning protocol group 1:1. Sample size of standard scanning protocol group: 99. Sample size of modified scanning protocol group: 99.

   ii) Subclavian vein artifact. Total sample size of study: 200. Ratio of standard scanning protocol group to modified scanning protocol group is

1:1. Sample size of standard scanning protocol group: 100. Sample size of modified scanning protocol group: 100.

Measurement	P_0	P_1	n	n + 10%	Reference
Superior vena cava artifact	0.97	0.85	89	198	(Lee *et al.*, 2007)
Subclavian vein artifact	0.94	0.80	180	200	(Lee *et al.*, 2007)

$\alpha = 0.05$, power = 80%, Drop-out = 10%

c. Objective 3, correlation factors for enhancement / image quality, sample size calculate using Pearson's correlation estimation (Arifin, 2020). Based on (Ramadan et al., 2010) estimated that the correlation between BMI and enhancement moderate negative. Total sample size of study: 104. Ratio of standard scanning protocol group to modified scanning protocol group is 1:1. Sample size of standard scanning protocol group: 52. Sample size of modified scanning protocol group: 52.

Variables	Expected, r	n	n + 10%	Reference
BMI (kg/m^2)	-0.4	92	104	(Ramadan *et al.*, 2010)

The expected r = -0.4, Drop-out = 10%.

3.4 Sampling Method

Non-randomized, convenient sampling was used based on inclusion and exclusion criteria.

3.5 Inclusion Criteria

a. All patients underwent CTPA using Toshiba Aquilion PRIME CT scanner.
b. Patient whose IV cannula 18G and below 18G at upper limb for contrast injection.

3.6 Exclusion Criteria

a. Patient developed complications (extravasation of contrast) during CTPA scan.
b. Patients who used central vascular catheter for contrast injection.
c. Patient with heart failure.
d. Patient who refused to participate in the study.

3.7 Research Tools

a. Data collection form.
b. Image acquisition obtained from CT Toshiba Aquilion Prime.
c. Picture Archive Communication System (PACS) series 6 in Hospital USM.
d. Patient's clinical folder.
e. SPSS for data analysis.
f. View monitor – BARCO MDNC-3421 V1.00.03.

3.8 Operational Definition

a. Hounsfield unit (HU): It is CT number that obtained from linear transformation of measures attenuation coefficients based on arbitrarily assigned densities of air and pure water.
b. Artifact: It refers to any systemic discrepancy between CT numbers in reconstructed image and the true attenuation coefficients on the object, which may obscure or mimic pathology.
c. BMI: it is a person's weight in kilograms (kg) divided by his or her height in meters squared. BMI = kg / m^2.

3.9 Methods

a. Patient Cohort

Patients who underwent CTPA from 1st June 2020 to 14th February 2021 using standard protocol were included as standard protocol group. Those who underwent CTPA from 15th February 2021 to 31st October 2021, were assigned to modified protocol group. We included a total of 199 patients with 83 patients under standard protocol and 116 patients under modified protocol. They were screened against the inclusion and exclusion criteria. All the scans were performed using the bolus tracking technique.