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Double low-dose computed tomography pulmonary angiography in the diagnosis of pulmonary embolism

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Abstract. The purpose of this study is to investigate the feasibility of double low-dose (low radiation and low contrast medium doses) computed tomography pulmonary angiography (CTPA) in the diagnosis of pulmonary embolism. This retrospective study involved analysis of 59 patients undergoing 64- and 128-slice CTPA examinations which were scanned with a pitch of 0.9 and 100 and 120 kVp, respectively, while flash mode of CTPA was done with a pitch of 3.2 and 120 kVp. There were no significant differences in image quality assessment between the low kVp and standard kVp or high-pitch CTPA protocols (p=0.181-0.186). The mean effective dose for the 100 kVp protocol was significantly lower than that for the120 kVp and the flash mode protocols (p<0.001). The contrast medium was between 35-45 ml for the 100 and 120 kVp protocols, and 20-30 ml for the 120 kVp flash mode protocol. Double low-dose CT pulmonary angiography is feasible for detection of pulmonary embolism with acquisition of diagnostic images.

1. Introduction

Computed tomography pulmonary angiography (CTPA) is the first line imaging modality in the diagnosis of patients with suspected pulmonary embolism (PE) owing to its high sensitivity and specificity [1, 2]. Despite high diagnostic yield of CTPA in PE, appropriate use of CTPA needs to be medically justified due to its associated high radiation dose and widespread use of CTPA in clinical practice [3-5]. Technological developments in CT scanners have allowed the CTPA to be performed widely in many clinical centres with significant reduction of radiation dose which used to be a major concern of CT imaging. Currently, low-dose CTPA is available with use of various dose-reduction strategies with resultant effective dose of less than 2.0 mSv or even less than 1.0 mSv, according to some recent studies [6-8]. Thus, significant progress has been achieved in reducing radiation dose associated with CTPA.

Another concern related to CTPA is the risk of using contrast medium during contrast-enhanced CT scans since contrast medium has potential risk of contrast-induced nephropathy (CIN). In patients with cardiovascular disease such as coronary artery disease and pulmonary embolism, reducing the risk of CIN is necessary since these patients are often associated with chronic kidney disease or with diabetes mellitus.

This has drawn increasing attention in recent years with an attempt to reduce contrast volume or lower concentration of contrast medium during CT scans. Studies have shown the feasibility of reducing radiation dose and contrast medium dose or concentration in coronary CT angiography examinations [9-11]. Similar trend has seen in CTPA protocols with regards to the recommendation of double low-dose protocols aiming to reduce both radiation and contrast medium doses. Although promising results are available in the literature, studies on the use of double low-dose CTPA protocols are still limited to certain clinical centres and are not yet widely recommended. Thus, the purpose of this study was to further investigate the clinical application of CTPA in the diagnosis of pulmonary embolism with use of double low-dose protocol in routine practice without compromising diagnostic image quality.

2 Materials and Methods

2.1 Participant recruitment

A retrospective review of patients with suspected PE who underwent CTPA examinations during January 2017 and February 2018 was performed in a tertiary clinical centre. Inclusion criteria included: confirmed presence of PE in at least one of the pulmonary artery branches and CTPA was successfully performed without any complications. Patients younger than 18 years or allergic to contrast medium were excluded. Ethics approval was obtained from the local ethics committee and Curtin University Human Research Ethics Committee. Participants were divided into three groups: Group 1 consisted of 23 patients who underwent CTPA using the 100 kVp and a pitch of 0.9 protocol as a low-dose protocol. Group 2 included 30 patients who underwent CTPA using the standard 120 kVp and a pitch of 0.9 protocol, while Group 3 comprised 6 patients who received a CTPA protocol with 120 kVp and a high pitch 3.2. Tube current modulation was applied to all patients.

2.2 CTPA scanning protocols

CT scans were performed on 64- and 128-slice CT scanners with details as follows: 52 patients were scanned on a 128-slice dual-source CT (Siemens Definition Flash, Siemens Healthcare, Forchheim, Germany), 4 patients were on a 64-slice scanner (GE VCT, GE Healthcare, USA) and 3 cases on a 64-slice GE Revolution (GE Medical Systems, Waukesha, USA), respectively. Contrast medium Iohexol (Omnipague 350, GE Healthcare, USA) was injected using a power injector with a flow rate of 5 ml/s, followed by a saline flush of 40 ml at the same injection rate. The volume of contrast medium was determined by each group's scanning protocol, ranging from 20-30 ml to 35 to 45 ml. A test bolus technique was used in all patients with a threshold of 150 HU in the pulmonary trunk used as the triggering threshold to initiate scans. All images were reconstructed with a soft tissue kernel using the standard filtered back projection. The slice thickness was 1 mm with 0.5 mm reconstruction interval.

2.3 Quantitative image quality assessment

Original images in digital imaging and communications in medicine (DICOM) format were transferred to a workstation with Analyze 12.0 (AnalyzeDirect, Inc., Lexana, KS, USA) of image post-processing and measurement. Quantitative assessment of image quality was determined by measuring signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) in the main pulmonary arteries. CT attenuation in the background was measured in the paravertebral muscle. A region of interest (ROI) (containing minimum 150 voxels) was placed in the pulmonary trunk with SNR and CNR calculated as follows: SNR=CT attenuation in pulmonary trunk/SD (image noise); CNR=(CT attenuation in pulmonary trunk-background CT attenuation)/SD (image noise). The standard deviation (SD) refers to the image noise measured in the pulmonary trunk.

2.4 Qualitative image quality assessment

Qualitative assessment of image quality was performed by two independent experienced radiologists (each with more than 5 years' experience in reporting CTPA) using a 5-point scale: 5: excellent image quality, 4: good image quality, 3: moderate image quality, 2: suboptimal image quality and 1: poor image quality. Both observers were blinded to CTPA scanning protocols and clinical information and they scored the images separately. Inter-observer agreement was assessed by Cohen's kappa statistics. A score of 3 or more indicates acceptable image quality.

2.5 Radiation dose and data analysis

Volumetric dose index (CTDIvol) and dose length product (DLP) were available in CT console from each scanning protocol. Effective dose was calculated by multiplying the DLP with a tissue conversion factor of 0.014 mSv/mGy/cm [12]. One way analysis of variance (ANOVA) was used to determine if there is any significant difference in SNR and CNR between groups and within groups using different CTPA protocols. Kruskal-Wallis test was used to determine any significant difference in CTPA protocols with respect to image quality as assessed by two radiologists. A k value was calculated to determine inter-observer agreement $k \leq 0.20$ as poor, k =0.21-0.40 fair, k =0.41-0.60 moderate, k =0.61-0.8 good and $k > 0.81$ excellent. A p value less than 0.05 was considered statistically significant.

3 Results

There were no significant differences in patient's age and gender among these three CTPA protocols (all p>0.05) (Table 1). The patient's body weight in the 100 kVp protocol was significantly smaller than that in the 120 kVp protocols (p<0.001), while there was no significant difference in the body weight between 120 kVp standard pitch and high pitch protocols (p=0.27). Pulmonary embolism was presented in all cases with both sides of pulmonary arteries having emboli in more than half of the patients (54%). Inter-observer agreement was good (k=0.78) for the diagnosis of pulmonary embolism.

Table 1. Measurements of SNR and CNR associated with different CTPA protocols.

Clinical and imaging characteristics	**Group 1 100 kVp pitch 0.9 (n=23)**	**Group 2 120 kVp pitch 0.9 (n=30)**	**Group 3 120 kVp pitch 3.2 (n=6)**	***P* values**
Age (years) (range, mean ± SD)	16-93 52.77 ± 21.28	15-72 47.53 ± 16.78	18-67 48 ± 13.17	0.31-0.94
Gender (M/F)	8/15	14/16	2/4	-
Body weight (kg) (range, mean ± SD)	68-88 76.34 ± 4.38	75-117 95.6 ± 11.09	85-95 90.5 ± 3.61	<0.001/0.27*
SNR	21.56 ± 6.40	22.06 ± 8.21	15.99 ± 4.99	0.09-0.96
CNR	19.82 ± 5.88	19.71 ± 7.44	14.42 ± 4.75	0.06-0.77
Qualitative assessment of image quality	4.61 ± 0.45	4.76 ± 0.48	4.58 ± 0.49	0.23-0.90
Contrast medium (ml)	35-45	35-45	20-30	-
CTDIvol (mGy)	6.09 ± 1.14	10.06 ± 3.20	7.46 ± 0.69	<0.05
DLP (mGy.cm)	173.83 ± 29.18	332.73 ± 126.24	238.08 ± 42.88	<0.001*/ 0.06-0.08#
Effective dose (mSv)	2.43 ± 0.41	4.66 ± 1.76	3.33 ± 0.60	<0.001/0.08*

* significant differences in CTDIvol and effective dose between 100 kVp and 120 kVp protocols, # but no significant difference between 120 kVp low pitch and high pitch protocols. SD-standard deviation

All images were scored as diagnostic with a score of 3 given by one assessor and a score of 4 by another assessor in two cases. In the remaining cases, a score of 4 or 5 was given in 13 and 44 cases by these two assessors, respectively. No significant difference was found in the qualitative assessment of image quality among the three groups ($p>0.05$) (Table 1). Kruskal-Wallis test indicates that neither radiologist (observer) 'sees' any significant difference in CTPA protocols with respect to image quality scores ($p=0.135$ and 0.621 for Radiologists 1 and 2, respectively). Radiation dose was significantly lower in the 100 kVp and standard pitch protocol than those in the 120 kVp with standard and high pitch protocols ($p<0.05$) as shown in the Table 1.

Similarly, there were no significant differences in SNR and CNR among these CTPA protocols, although the SNR and CNR measured with the 120 kVp and high pitch 3.2 protocol were lower than those with the 100 and 120 kVp with standard pitch protocols ($p=0.181$ and 0.186 for SNR and CNR, respectively) (Table 1). The contrast medium ranged from 35 to 45 ml in the 100 and 120 kVp with standard pitch protocols, 20 to 30 ml in the 120 kVp with high pitch protocol, as shown in Table 1. Figures 1-3 are examples of image quality for Groups A-C with use of different CTPA protocols for demonstration of pulmonary embolism in 2D axial and coronal reformatted images with acceptable image quality.

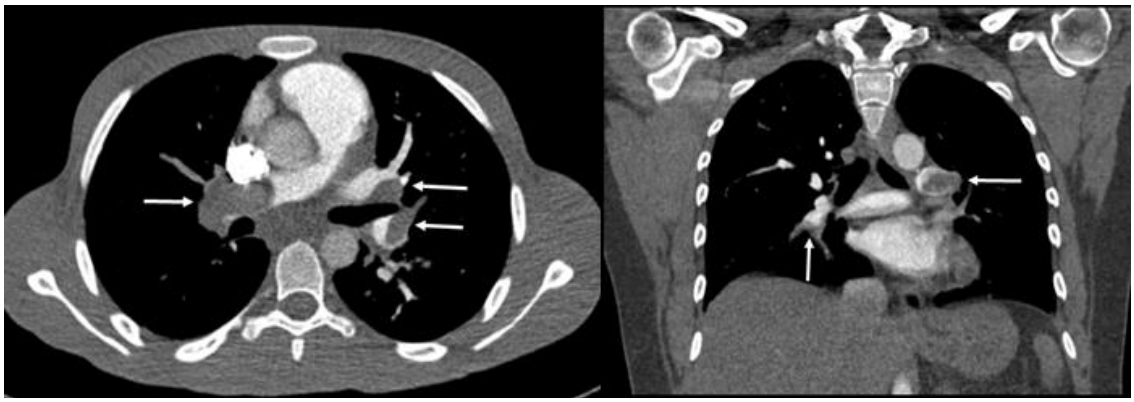

Figure 1. CTPA with use of 100 kVp, pitch 0.9 and 40 ml contrast medium in a 26-year-old male with diagnosed PE. Multiple emboli are seen at both sides of pulmonary arteries (arrows).

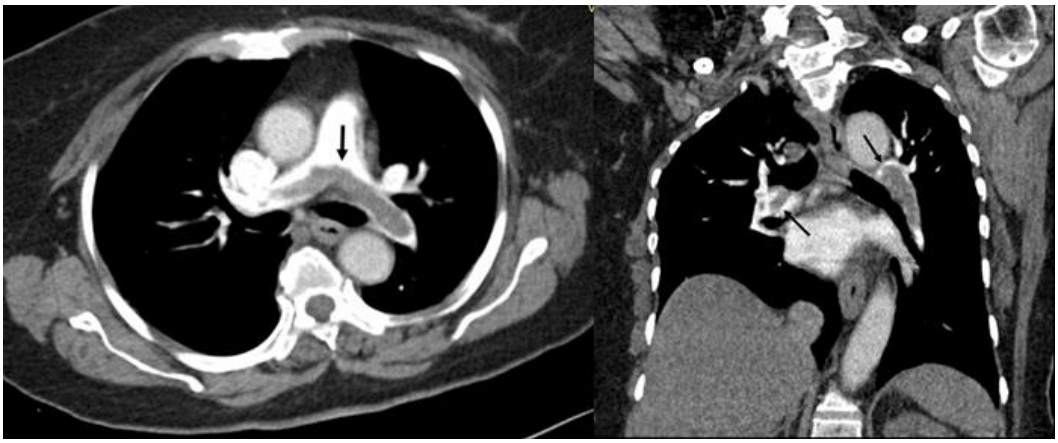

Figure 2. CTPA with use of 120 kVp, pitch 0.9 and contrast medium 45 ml in a 71-year-old female with PE in the main pulmonary trunk extending to both pulmonary arteries (arrows).

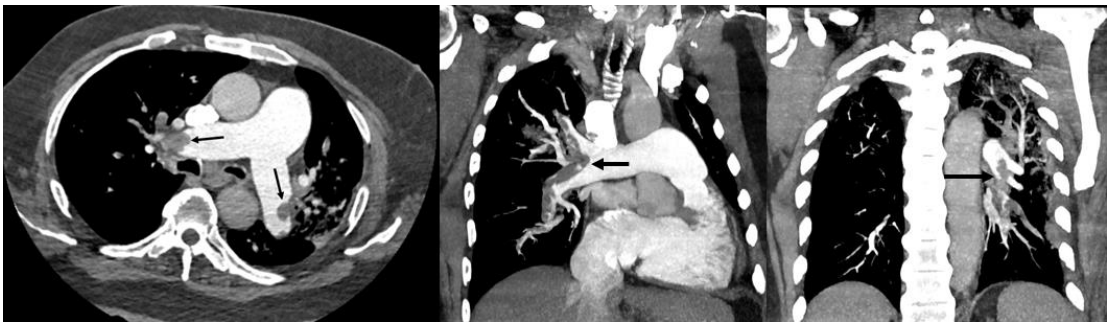

Figure 3. CTPA with use of 120 kVp, pitch 3.2 and 25 ml contrast medium in a 59-year-old man with PE on both sides of pulmonary arteries (arrows).

4. Discussion

This study further confirms the usefulness of low kVp for radiation dose reduction in CTPA examinations. A significant dose reduction of 48% was achieved in the 100 kVp and standard pitch protocol with use of less than 45 ml of contrast medium. Further, low contrast medium of less than 30 ml was found to be feasible in the 120 kVp and high pitch CTPA protocol with acquisition of diagnostic images.

With use of these combined dose saving methods, low-dose or ultra low-dose CTPA is available with effective dose less than 2 or lower than 1 mSv reported in some recent studies, mainly due to the use of high-pitch in 70 or 80 kVp protocol [6-8]. Use of high pitch 2.2 or 3.2 in the 120 kVp CTPA does not lead to dose reduction as opposed to the use of low kVp and high pitch CTPA protocol. This has been confirmed in our previous phantom experiments and other studies. Schafer et al compared CTPA protocol of 120 kVp and pitch 3.0 with 70 kVp and pitch 3.0 in patients scanned with 2nd and 3rd generation dual-source CT, respectively [13]. The overall effective dose was 4.40 and 2.06 mSv for the 120 kVp and 70 kVp with high pitch protocols, indicating the important role of kVp in dose reduction. Our phantom experiments are consistent with their findings [14, 15]. The highest radiation dose was noted in the 120 kVp with pitch of 2.2 or 3.2 protocols, while the lowest dose was seen in the 80 or 70 kVp with pitch of 2.2 or 3.2 protocols (up to 80% dose reduction) without compromising diagnostic image quality. The current study shows that up to 27% dose reduction was achieved when comparing 120 kVp with pitch 3.2 to 100 kVp and pitch 0.9 protocols.

Double low-dose CTPA represents the current research direction in CTPA and this has been confirmed by our recent systematic review [16]. The traditional approach of using 80-100 ml contrast medium has been replaced by low contrast medium such as 40-60 ml, followed by 30-60 ml saline flush [17]. Some studies have reported that contrast medium can be even lowered to 20 ml with high-pitch CTPA protocol with acquisition of similar image quality when compared to the standard pitch CTPA, but with significant radiation and contrast medium dose reduction [18, 19]. Our findings are in align with these reports as 20-30 ml contrast medium was used in the high-pitch CTPA protocol with resulting similar image quality as opposed to the 35-45 ml contrast medium used in the standard pitch protocols. This confirms the double low-dose CTPA protocol in routine diagnosis, although more cases are needed to validate these findings.

This study has some limitations. First, this is a single centre experience with a small number of participants. Prospective studies with inclusion of large cohorts comprising different CTPA protocols are desirable to confirm our findings. Second, CTPA scans were done on 64- and 128-slice scanners, without implementing iterative reconstruction (IR) in image reconstruction, which leads to relatively high radiation dose. Use of IR has been a common approach in many CT applications [20-22], thus further studies should include data analysis of images reconstructed with IR algorithms for more dose reduction. Third, low kVp such as 70 or 80 was not used in our cohort due to relatively large body mass. Furthermore, body mass index (BMI) was not available in most of the patients due to the retrospective nature of the study without recording

BMI, although body weight was available in these patients. Using BMI to adjust kVp is a routine protocol and this should be followed in daily practice. Finally, we only included patients with confirmed pulmonary embolism, which could introduce bias in image analysis. Inclusion of patients with small or peripheral embolism is desirable for determining low-dose CT protocol, and this needs to be addressed in future studies.

In conclusion, despite small sample size and retrospective nature, this study further confirms the feasibility of double low-dose CT pulmonary angiography in the diagnosis of pulmonary embolism. Low radiation dose can be achieved with use of 100 kVp and standard pitch when compared to 120 kVp and standard or high pitch protocol, with dose reduction of nearly 50% while maintaining diagnostic image quality. Contrast medium can be reduced to 20-30 ml in the high-pitch CTPA protocol producing similar image quality. Further research should focus on including more patients with testing different CTPA protocols with diagnostic value assessed as well in the prospective multi-centre study.

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