Optimizing Pulmonary Embolism Computed Tomography in the Age of Individualized Medicine A Prospective Clinical Study

Optimizing Pulmonary Embolism Computed Tomography in the Age of Individualized Medicine

A Prospective Clinical Study

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Purpose: The aim of the study was to simultaneously optimize contrast media (CM) injection and scan parameters for the individual patient during computed tomography pulmonary angiography (CTPA).

Methods: In this study (NCT02611115), 235 consecutive patients suspected of having pulmonary embolism were prospectively enrolled. Automated kV selection software on a third-generation multidetector computed tomography adapted tube voltage to the individual patient, based on scout scans. The contrast injection protocol was adapted to both patient body weight and kV-setting selection via a predefined formula, based on previous research. Injection data were collected from a contrast media and radiation dose monitoring software. Attenuation was measured in Hounsfield units (HU) in the pulmonary trunk (PT); attenuation values 200 HU or greater were considered diagnostic. Subjective image quality was assessed by using a 4-point Likert scale at the level of the PT, lobar, segmental, and subsegmental arteries. Results between groups were reported as mean ± SD.

Results: Two hundred twenty-two patients (94%) were scanned at a kV setting below 100 kV: n = 108 for 70 kV, n = 82 for 80 kV, and n = 32 for 90 kV. Mean CM bolus volume (in milliliters) and total iodine load (in grams of iodine) for 70 to 90 kV were as follows: 24 ± 3 mL and 7 ± 1 g I, 29 ± 4 mL and 9 ± 2 g I, and 38 ± 4 mL and 11 ± 1 g I, respectively. Mean flow rates (in milliliters per second) and iodine delivery rates (in grams of iodine per second) were 3.0 ± 0.4 mL/s and 0.9 ± 0.1 g I/s (70 kV), 3.6 ± 0.4 mL/s and 1.0 ± 0.1 g I/s (80 kV), and 4.7 ± 0.5 mL/s and 1.3 ± 0.1 g I/s (90 kV). Mean radiation doses were 1.3 ± 0.3 mSv at 70 kV, 1.7 ± 0.4 mSv at 80 kV, and 2.2 ± 0.6 mSv at 90 kV. Mean vascular attenuation in the PT for each kV group was as follows: 397 ± 101 HU for 70 kV, 398 ± 96 HU for 80 kV, and 378 ± 100 HU for 90 kV, $P = 0.59$. Forty-six patients (21%) showed pulmonary embolism on the CTPA. One scan (90 kV) showed nondiagnostic segmental pulmonary arteries, and 5% of subsegmental arteries were of nondiagnostic image quality. All other segments were considered diagnostic-excellent subjective image quality.

Conclusions: Simultaneously optimizing both CM injections and kV settings to the individual patient in CTPA results in diagnostic attenuation with on average 24 to 38 mL of CM volume and a low radiation dose for most patients. This individualized protocol may help overcome attenuation-variation problems between patients and kV settings in CTPA.

Key Words: contrast media, individualized medicine, multidetector computed tomography, pulmonary embolism, radiation dosage

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Ever since the introduction of multidetector computed tomography (CT), computed tomography pulmonary angiography (CTPA) has become and remained the number one diagnostic imaging test for confirming or ruling out pulmonary embolism (PE).[1–3] With CTPA already firmly established in the current diagnostic algorithm, recent research has focused on lowering radiation dose and iodinated contrast media (CM) volume.[4–6] The primary aim of lowering these doses is to reduce any risks, albeit hypothetical, of both radiation-induced malignancies and contrast-induced nephropathy (CIN). Although there is some controversy around the existence of CIN after intravenous injection of iodinated CM,[7] the European Society of Urogenital Radiology guidelines state a relationship between the dose of CM and the incidence of CIN and recommend avoiding unnecessarily large doses of CM.[8] Lowering CM doses has an additional purpose in the patient group with suspected PE. The right ventricle of the heart provides a continuous low-pressure perfusion of the pulmonary vasculature, but is sensitive to changes in loading conditions and intrinsic contractility.[9] Especially in an already overloaded right ventricle in the case of PE, right ventricular failure or ischemia may be induced or worsened by rapid infusion of large volumes of saline, or CM for that matter.[10]

Mostly, the optimization of CTPA has revolved around using low-tube-voltage settings and minimizing CM, either for a predefined selected group (eg, low-weight patients) or for the entire population.[11] Comparatively little attention has been given to strategies for optimizing CTPA protocols for each individual patient, even though the effects of patient characteristics on CTPA contrast enhancement have repeatedly been shown.[12–14] Both bolus triggering and test bolus technique are examples of already integrated individualization techniques. These timing methods account for each patient's individual cardiac output; both achieve good diagnostic enhancement of the pulmonary vascular tree.[15,16] The current trend of individualized diagnostics asks for a more personalized approach, not only in terms of CM timing but encompassing all other factors in CM and scan protocols. Importantly, this should remain simple and quick to perform in daily clinical practice.

Previous research has shown body weight–based CM injection protocols for CTPA to deliver a more uniform, predictable enhancement of the pulmonary arteries.[13] Recent developments such as postprocessing with iterative reconstruction and the latest generations of CT scanners with more tube current potential (eg, implemented in third-generation dual-source CT [DSCT] scanners) have lowered CTPA kV settings to the point where now light-weight patients might even be scanned at tube voltages of 70 to 80 kV.[17–20] However, not only

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light-weight patients, but all patients should receive optimal, individualized diagnostics. The necessary iodine delivery rate (IDR) for diagnostic enhancement of the pulmonary arteries per body weight, however, has so far been investigated only for 100 kV scans.[13]

In a quest for an individualized CTPA protocol that would be workable in clinical practice, this study aimed to combine previous strategies. When aiming to combine these strategies, it is important to realize that tube voltage influences enhancement of iodinated CM; when tube voltage moves closer toward the k-edge of iodine (at 33 kV), the attenuation of iodine rises and vice versa.[21] The exact effect was quantified in previous research using an identical IDR at different kV settings in a vascular circulation phantom.[22] Patient body weight also effects attenuation; as a patient's body weight becomes higher and blood volume increases, the intravascular attenuation of iodine goes down.[12,14,23] The second mechanism is through beam hardening; when the x-rays travel through the body, low-energy photons are absorbed more readily, leaving an x-ray beam with an increased mean energy. As previously explained, this increased mean energy means the x-rays are moving away from the k-edge of iodine, so the attenuation of iodine decreases. This effect is more pronounced in patients with a higher body weight.[24]

Automated tube voltage selection (ATVS), supplied on a third-generation DSCT scanner, was used to adapt tube voltage to the body habitus of each patient. The IDR of the CM was consequently adapted to both patient body weight and tube voltage. We hypothesized that this level of individualizing would create robust, homogeneous enhancement throughout the whole patient population, while using only the radiation and CM dose needed for each individual. This study aimed to evaluate diagnostic image quality, radiation dose, and CM dose when using a completely individualized CTPA protocol.

MATERIALS AND METHODS

Patient Population and Ethics

Consecutive patients referred for CTPA with a clinical suspicion of PE were included between September 2015 and November 2016. Informed consent was waived by the local medical ethical commission (no. 15-4-167) and the board of directors. This study is registered on ClinicalTrials.gov under reference number NCT02611115. An estimated glomerular filtration rate (eGFR) equal to or greater than 30 mL/min was required. Patients with an eGFR of less than 60 mL/min but greater than 30 mL/min received prehydration and posthydration according to the recommendations of the hospital protocol and were also included.

Our institutional exclusion criteria for CT angiography (CTA) were applied: known severe iodine allergy and severe renal insufficiency defined as eGFR of less than 30 mL/min. Patients receiving combined CT scan protocols, such as a CTPA in combination with an abdominal scan or triple-rule-out tests, and therefore required a long CM bolus were also excluded.

Before each scan, the patients were weighed to determine body weight in kilograms because this information in combination with the kV selection determined the CM injection protocol. When patients could not be weighed (eg, in case of immobility), the last known body weight was used. Patient diameters, anterior-posterior and lateral, were measured on scout views for later correlation with kV selection as performed by ATVS.

Scan Technique

All patients were scanned on a third-generation DSCT (Somatom Force; Siemens Healthineers, Forchheim, Germany) with ATVS capabilities and automated exposure control (CareDose 4D; Siemens). See Table 1 for an overview of the acquisition parameters. The scan was executed in single source mode. Reference tube voltage was set to 100 kV_{ref}, and the quality reference tube current was set to 105 mAs_{ref}; the image quality slider was set to vascular mode. All other kV settings had a corresponding reference mAs; for 70 kV, this was 247 mAs_{ref}, 80 kV at 164 mAs_{ref}, 90 kV at 124 mAs_{ref}, 110 kV at 95 mAs_{ref}, and finally 120 kV at 88 mAs_{ref}.

TABLE 1. Acquisition Parameters

Scan Technique	Scanner	2∗2∗96-Slice DSCT
	ATVS	On (CarekV)
	Tube voltage	100 kV_{ref}
	Tube voltage range	70–150 kV
	Tube current modulation	On (CareDose)
	Tube current	105 mAs_{ref}
	Pitch	1.2
	Collimation	0.6 mm
CM injection	Concentration	300 mg I/mL
	Timing	Test bolus 2.5-s Injection time at individual flow rate
	Main bolus volume Flow rate	Individualized to kV and body weight
	Total iodine load	
Reconstruction	IR	ADMIRE,* strength level 3
	Slice thickness	1.0 mm
	Increment	0.7 mm
	Kernel	Bv40

*ADMIRE is an advanced model-based IR algorithm.
IR indicates iterative reconstruction.

Patients were assigned by the scanner to 1 of the 6 study groups: 120, 110, 100, 90, 80, or 70 kV, based on anterior-posterior and lateral scout views (CarekV; Siemens). A pitch of 1.2 was selected along with a gantry rotation time of 0.25 second and a slice collimation of 192 × 0.6 mm; scan time was 1.33 seconds. One-millimeter slices with 0.7-mm overlapping increment were reconstructed using the advanced model-based iterative reconstruction algorithm (IR; ADMIRE) at strength level 3 and a Bv40 vascular kernel, with a standard clinical addition of 2-mm slices with a 1.4-mm increment on a lung kernel (Br54).

A short-breath-hold command was applied; technicians took special care instructing the patient before the scan, to prevent artifacts caused by deep inspiration or Valsalva maneuvers. Table height at the moment of the scan was taken from the DICOM header. It is measured from the table surface until the gantry isocenter, in millimeters below the isocenter.

Contrast Media Injection Protocol

All patients received prewarmed CM at body temperature (37°C [99°F]) (iopromide [Ultravist]; Bayer Healthcare, Berlin, Germany) with an iodine concentration of 300 mg I/mL. The CM was injected through an 18- to 20-gauge catheter in an antecubital vein or through a central venous catheter, using a dual-head power injector (Stellant; Bayer).

The CM flow rate was calculated using kV-dependent IDR reduction percentages and body weight–adapted IDR values taken from P3T software (Bayer), which have been validated in previous studies.[13,22] The body weight–dependent values were adapted per kV setting as follows: IDR (120 kV) × 0.9 for 110 kV, IDR (120 kV) × 0.8 for 100 kV, IDR (120 kV) × 0.7 for 90 kV, and so on. This strategy

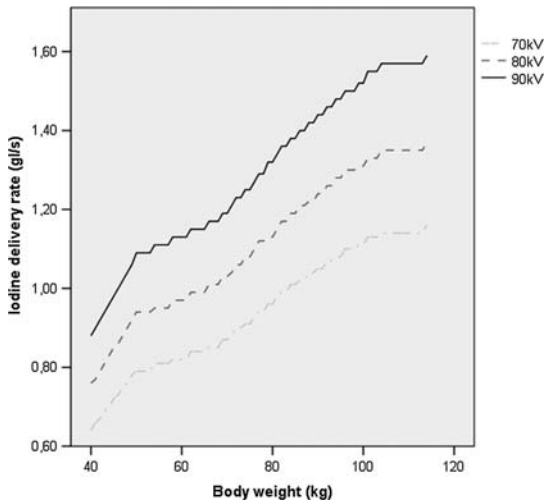

FIGURE 1. The line graph is a visual representation of the adaptation of the IDR to both patient body weight and kV setting. A specialized CM injection software (P3T; Bayer) adapts IDR to body weight. Next, a correction for the influence of kV on iodine attenuation was performed, resulting in the IDR values as displayed in this graph.

resulted in the formula considering body weight, kV setting, and concentration of CM to create an individually optimized IDR (Fig. 1).

The CM protocol consisted of a test bolus at the precalculated flow rate in order to determine scan delay, followed by a main CM bolus with 8-second injection time at the same flow rate. The volume of the test bolus was determined by a 2.5-second injection time, multiplied by the flow rate. The CM boli were followed by a 30-mL saline chaser, again at the same flow rate.

Data Collection and Processing

Information on effective dose was collected and analyzed using dedicated software (Radimetrics; Bayer), which takes into account the patient parameters, scanner technology, dose length product (DLP), and CT dose index to accurately estimate the effective dose in millisieverts. Contrast media–related factors including bolus volume, injection pressure, and flow rate were monitored on a data acquisition software and read out after injection. The IDR and the total iodine load were calculated.

Diagnostic images were viewed and analyzed on a dedicated workstation (Syngo.Via; Siemens). Image quality was objectified by measuring vascular attenuation, signal-to-noise (SNR) and contrast-to-noise ratio (CNR) in the pulmonary trunk (PT) and both main pulmonary arteries via manually drawn regions of interest. The following equations were used to define SNR and CNR:

$$\mathrm{SNR} = \frac{\text{Mean pulmonary enhancement (HU)}}{\text{Mean pulmonary enhancement SD (HU)}}$$

$$\mathrm{CNR} = \frac{\text{Mean pulmonary enhancement (HU) - paraspinal muscle enhancement (HU)}}{\text{Paraspinal muscle enhancement SD (HU)}}$$

Diagnostic enhancement was empirically defined as pulmonary artery enhancement over 200 Hounsfield units (HU). Subjective image quality was determined by 2 experienced readers, blinded to each other's scores. A 4-point Likert scale was used at the level of the PT and main pulmonary arteries ("central"), lobar arteries, segmental arteries, and subsegmental arteries. The scale was defined as follows: 0 = nondiagnostic, 1 = diagnostic image but severe artifacts are present, 2 = good image quality with minor artifacts, and 3 = excellent image quality with no relevant artifacts.

Pulmonary Embolism

All scans were viewed by experienced radiologists immediately after completion. The presence of PE and most central location of the emboli were noted in the clinical CTPA report. An experienced researcher, blinded to the radiologist's report, viewed the images and noted the presence, location, and extent of PE. Any incongruent results were then resolved via a consensus meeting between the original reporting radiologist and the researcher.

Statistical Analysis

An initial power calculation was performed to determine the number of patients per possible kV group; in order to detect the thrombi on a CTPA, the intravascular attenuation of the injected CM should reach at least 180 HU.[25] Results from previous studies using body weight–adapted injection protocols (300 mg I/mL) in standard 100-kV scan protocols show that an overall mean attenuation of 280 ± 90 HU can be achieved. As attenuation greater than 180 HU can be considered diagnostically sufficient,[26] a mean decrease by 100 HU (difference between 280 and 180 HU) is considered the largest difference that is clinically acceptable.

Based on a noninferiority margin of 100 HU and an SD of 90 HU, 14 patients are required in each kV group to be 90% sure that the lower limit of a 1-sided 95% confidence interval (or equivalently

TABLE 2. Patient Characteristics and Table Height, Overall and per kV Group

		70 kV (n = 108)	80 kV (n = 82)	90 kV (n = 32)	*P*
Sex, % male		38%	44%	66%	*0.022*
Age, y (range)		61 ± 15 (19–92)	60 ± 18 (16–93)	62 ± 14 (23–83)	0.772
BW, kg (range)		73 ± 15 (42–125)	74 ± 15 (45–117)	91 ± 15 (64–118)	*<0.001**
BMI, kg/m^2 (range)		25 ± 5 (16–46)	26 ± 4 (16–38)	31 ± 6 (22–55)	*<0.001**
Diameter, cm	Anterior-posterior	27 ± 4	25 ± 4	28 ± 3	*0.001*†
	Lateral	37 ± 5	37 ± 4	41 ± 7	*<0.001**
Table height, cm (range)		17.7 ± 2.4 (12.5–25.9)	17.7 ± 2.8 (13.2–26.8)	19.2 ± 23 (15.1–23.1)	*0.009*‡

Notice the significant differences in body weight and BMI for the different groups; body weight and BMI were different between 70/80 kV and 90 kV. Pulmonary embolism was diagnosed in 22% of patients.

*The lateral diameter, BMI, and body weight are significantly larger and higher in the group of 90 kV compared with the 70/80 kV groups.

†Post hoc analysis showed a significant difference in patients' anterior-posterior diameter between 80 kV and 70/90 kV.

‡The mean table height is significantly different between the 90 kV group and the other groups.

BMI indicates body mass index.

TABLE 3. Radiation Dose and CM Parameters

Scan and CM Injection Outcomes		70 kV (n = 108)	80 kV (n = 82)	90 kV (n = 32)	*P*
Radiation dose					
DLP,* mGy/cm		79.5 ± 17.4	105.7 ± 23.4	178.8 ± 61.3	*<0.001*
$CTDI_{vol}$,* mGy		2.1 ± 0.5	2.8 ± 0.6	4.6 ± 1.0	*<0.001*
Effective dose,* mSv		1.3 ± 0.3	1.7 ± 0.4	2.2 ± 0.6	*<0.001*
CM injection					
Flow rate,* mL/s		3.0 ± 0.4	3.6 ± 0.4	4.7 ± 0.5	*<0.001*
CM volume, mL	Test bolus	7.6 ± 0.9	8.6 ± 1.8	11.8 ± 1.0	*<0.001*
	Main bolus	24.1 ± 2.8	28.7 ± 3.5	37.8 ± 3.5	*<0.001*
IDR, g I/s		0.9 ± 0.1	1.0 ± 0.1	1.3 ± 0.1	*<0.001*
Iodine per kg, g		0.10 ± 0.0	0.12 ± 0.0	0.13 ± 0.0	*<0.001*
TIL, g		7.2 ± 0.8	8.6 ± 1.8	11.3 ± 1.0	*<0.001*
Peak pressure, psi		70.5 ± 23.0	73.6 ± 27.2	83.7 ± 16.0	*0.026*†

*A Welch test was used to correct for nonnormal distribution.

†Post hoc comparison showed that peak pressure was significantly higher in the 90 kV group compared with 70 kV, which can be explained with the higher flow rates. However, the peak pressure did not approach the maximum pressure of 325 psi.

CTDI indicates CT dose index.

a 90% 2-sided confidence interval) of the difference between injection protocols will be above the noninferiority limit of 100 HU. To create a 10% safety margin in the study population, a minimum of 16 patients per kV group (70, 80, 90, 100, 110, and 120 kV) should be included.

Statistical data analysis was performed using the Statistical Package for the Social Sciences version 23.0 (SPSS Inc, Chicago, IL). Levene's test was used to check for normal distribution of variances; where applicable, a Welch test was used to correct for the difference in variances. Continuous variables between groups were analyzed using 1-way analysis of variance; a post hoc Scheffé test was used to compare significant differences. Continuous variables are reported as mean ± SD. Likert scale data were reported and therefore also analyzed as continuous variables. Categorical variables were reported as percentages, and again a χ^2 test was performed to check for differences between groups. Interrater agreement was calculated in percentages. All *P* values are 2-sided, and $P < 0.05$ was considered statistically significant.

RESULTS

Patient Characteristics

A total of 235 patients were included; 222 patients (94%) were scanned sub-100 kV. Automated tube voltage selection selected 70 kV in 108 cases, 80 kV in 82 cases, 90 kV in 32 cases, and 100, 110, and 120 kV, respectively, in 6, 2, and 5 cases. Because the 3 kV groups of 100, 110, and 120 kV did not meet a minimum of 16 patients (as calculated by the aforementioned power calculation), these groups were excluded from further statistical analysis. No patients or scans were excluded because of insufficient enhancement or improper CM timing. There were no CM injection–related complications.

Fifty-five percent of the population was female; the average age was 60 ± 17 years, with a range of 14 to 93 years. Mean body weight was 77 ± 17 kg, with a range of 42 to 130 kg. For an overview of patient characteristics per kV group, see Table 2.

Radiation and CM Dose

The average DLP ranged from 80 ± 17 mGy·cm in the 70 kV group to 106 ± 23 mGy·cm in the 80 kV group and up to 179 ± 61 mGy·cm in the 90 kV group. For a complete overview of dose parameters, see Table 3. The effective doses were on average 1.3 ± 0.3 mSv at 70 kV, 1.7 ± 0.4 mSv at 80 kV, and 2.2 ± 0.6 mSv at 90 kV (Fig. 2).

The individually tailored CM protocols resulted in mean main bolus volumes of 24 ± 3 mL at 70 kV, 29 ± 4 mL at 80 kV, and 38 ± 4 mL at 90 kV. The mean flow rates for the respective kV groups were 3.0 ± 0.4, 3.6 ± 0.4, and 4.7 ± 0.5 mL/s. Table 3 also shows that the injection pressure remained well below the maximum injection pressure of 325 psi.

Image Quality

Diagnostic enhancement of the pulmonary arteries was reached for all scans in all 3 kV groups, with an average of 397 ± 101 HU for 70 kV, 398 ± 96 HU for 80 kV, and 378 ± 100 HU for 90 kV. The attenuation was comparable between groups ($P = 0.590$), indicating that the formula corrected for the attenuation differences that kV settings and patient characteristics can create. Table 4 and Figure 3 show the attenuation per kV group in the PT and both left and main pulmonary artery. Image noise and CNR also remained relatively constant throughout all groups, with $P > 0.05$ (see Table 4 for the exact values).

Initial agreement percentages on the subjective image quality scoring between the 2 readers were 82%, 77%, 74%, and 97% for the

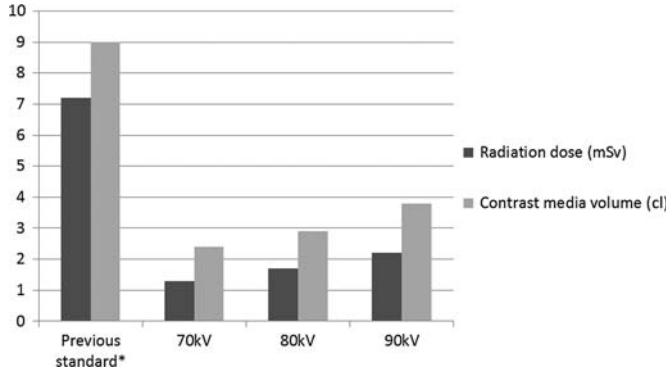

FIGURE 2. The graph shows the radiation dose and CM use per kV group, offset against the institutional previous standard of 100 kV CTPA with standard CM injection protocols. *The reference data on CM and radiation dose were taken from a previous study in a comparable patient group, with a standard injection protocol and a high pitch 100 kV CTPA on a second-generation DSCT scanner.[13]

TABLE 4. Image Quality of the Scans, per kV Group and per Segment

Image Quality		70 kV (n = 108)	80 kV (n = 82)	90 kV (n = 32)	*P*
Attenuation, HU	PT	397 ± 101	398 ± 96	378 ± 100	0.588
	Left main artery	377 ± 97	367 ± 86	369 ± 81	0.739
	Right main artery	383 ± 94	369 ± 94	367 ± 83	0.485
SNR	PT	14 ± 4	14 ± 4	13 ± 4	0.393
	Left main artery	14 ± 5	13 ± 4	13 ± 4	0.602
	Right main artery	14 ± 4	13 ± 4	14 ± 5	0.500
CNR	PT	13 ± 6	16 ± 6	14 ± 7	0.066
	Left main artery	13 ± 6	14 ± 6	14 ± 6	0.146
	Right main artery	13 ± 6	14 ± 6	14 ± 6	0.304

respective levels (central-subsegmental). For an overview of all the scores per level and per reader, see the Supplementary Table, Supplemental Digital Content, http://links.lww.com/RLI/A367, on subjective image quality. After averaging the Likert score percentages, the subjective image quality was as follows: the PT segment was rated excellent in 84% at 70 kV, in 72% at 80 kV, and in 77% at 90 kV. Similar results were reported at the lobar level with 80% at 70 kV, 69% at 80 kV, and 74% at 90 kV. The segmental level was also rated excellent on average (in 70% at 70 kV, 61% at 80 kV, and 59% at 90 kV). The subsegmental arteries could only be scored diagnostic or nondiagnostic, which resulted in 96% diagnostic scans at 70 kV, 94% at 80 kV, and 93% at 90 kV. For a complete overview of the Likert scores, see the additional content. Figure 4 shows examples of CTPA image quality in each kV group.

Pulmonary Embolism

A total of 46 patients showed PE on the CTPE, representing 21% of all patients in this study. The 70 kV group showed 24 PE cases (22%), the 80 kV group showed 17 cases (21%), and in the 90 kV group, there were 5 cases (16%). The χ^2 test showed no significant difference between groups, with $P = 0.72$. When looking specifically at central PE, the numbers were as follows: 7 cases (6%) at 70 kV, 5 cases (6%) at 80 kV, and 4 cases (13%) at 90 kV. $P = 0.33$ indicates no statistical difference; nevertheless, the percentage of centrally located PE is doubled in the 90 kV group. This difference is most likely due to coincidence; no other valid reason could be hypothesized.

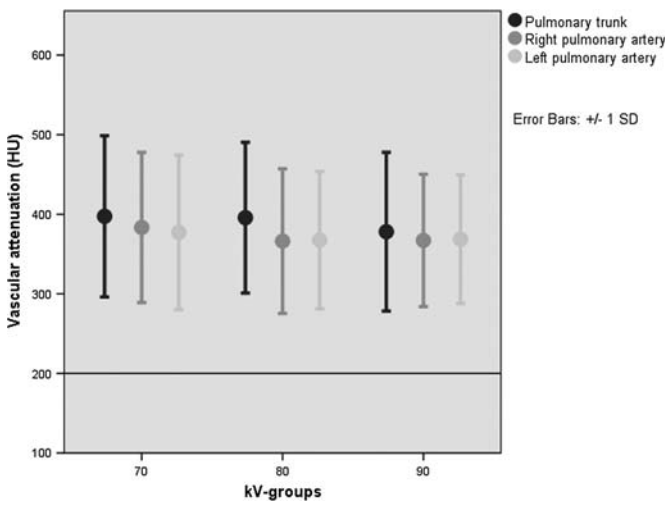

FIGURE 3. This graph shows the comparable intra-arterial attenuation of the pulmonary vasculature per kV group. Note the similar SDs. The horizontal black reference line indicates an empirical diagnostic attenuation threshold at 200 HU.

DISCUSSION

This clinical trial demonstrates the feasibility of combined individualizing CTPA scan and injection protocols in a prospective manner and in a large, clinical patient cohort. The individualization as seen in this protocol allowed for convincing dose reductions in both radiation dose and CM compared with standard CM injection 100-kV protocols (Fig. 2) while homogenizing image quality throughout all kV settings. The described method of optimizing injection protocols for both body weight and kV setting may serve as a guide for future implementation of individualized CT protocols in other CTA areas.

This study protocol was performed 24/7 with consecutive patients during a period of 1 year. Both experienced and new CT-qualified technicians performed this protocol. This study design was chosen to test the protocol under all emergency conditions, ensuring a robust CTPA protocol.

Virtually no patients were selected to undergo a CTPA with a tube voltage greater than 90 kV, and no clear weight limit was seen. This finding was regarded as very interesting because 100 kV is currently widely used for this protocol. It seems that new technology could lead to a new standard of 90 kV or even 80 kV in the future. The kV-selection process is a multifactorial one, based on the desired image quality (more precisely, on the relative important of iodine contrast), the tube capabilities in terms of photon flux, and the patient attenuation. This last one is being influenced by the size of the patient (eg, diameter), the presence of pulmonary pathology (eg, pleural effusion, masses, or depth inspiration), and the scanner table height, which are some of the influencing factors that were observed in this study. The table height is relevant because geometrical magnification makes the patient appear larger on the scout scan if he/she is closer to the x-ray source. Ergo, the higher the table position, the more dose the scanner will try to apply. When using ATVS, one should take care to keep the patient in the gantry isocenter, either by adjusting the table height or by using a second lateral scout view as was performed in this study. A recent retrospective study of ATVS by Suntharalingam et al[27] in abdominal CT revealed scan length (*z* axis) and table height to be of influence.

In the most frequently chosen kV settings (70–90 kV) in this study, the effective dose was low at 0.8 to 3.7 mSv, even in patients up to 125 kg. Comparison with a previously published study clearly shows the marked effective dose reduction that this protocol can create, when compared with the currently widely performed 100 kV with automated exposure control scanning.[13] The SNR and CNR levels proved constant throughout the kV settings, showing how ATVS in combination with IR can aid in maintaining constant image quality throughout a real-world patient population.

Kok et al[28] already described in 2015 a 77% dose reduction in CTA using ATVS, compared with the standard 120-kV protocol. Several

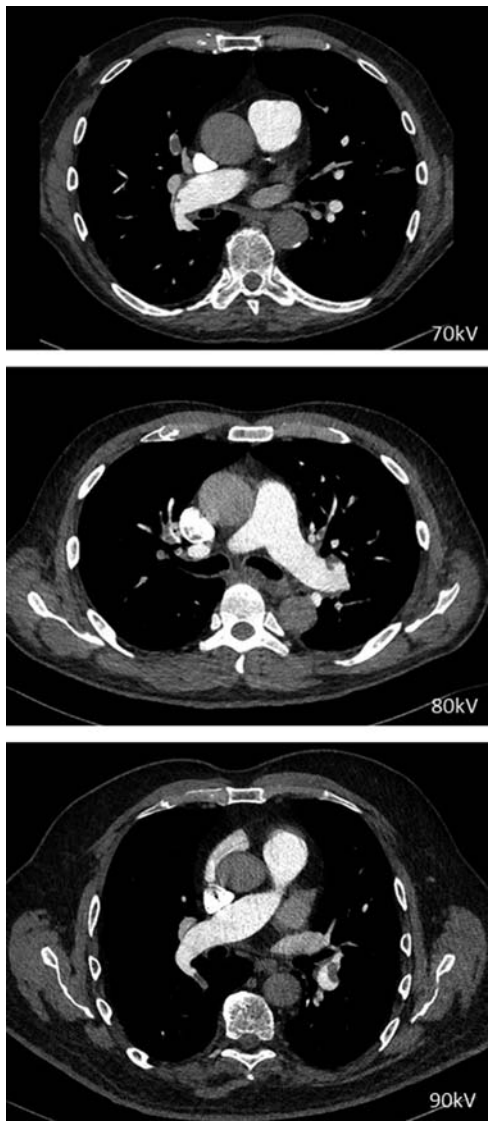

FIGURE 4. The images show the comparable image quality attained throughout the kV groups. 70 kV: male, 81 years old, 1.70 m, 70 kg, with Wells score of 8.5; scan showed bilateral lobar PE; IDR 0.87 g I/s, flow rate 2.9 mL/s, total iodine dose (TIL) 6.9 g I, attenuation PT 350 HU, effective dose 1.1 mSv. 80 kV: male, 62 years old, 1.83 m, 83 kg, with Wells score of 7; scan showed bilateral lobar PE, extending to the subsegmental level; IDR 1.1 g I/s, flow rate 3.9 mL/s, TIL 9.3 g I, attenuation PT 311 HU, effective dose 1.4 mSv. 90 kV: male, 73 years old, 1.80 m, 116 kg, with Wells score of 7.5; scan showed central PE extending into the subsegmental branches; IDR 1.6 g I/s, flow rate 5.3 mL/s, TIL 12.7 g I, attenuation PT 330 HU, effective dose 2.0 mSv.

studies have been performed using the ATVS technology in various CTA protocols, all describing a great dose reduction benefit for the patient while maintaining diagnostic image quality.[29–33] However, to the best of our knowledge, this is the first study to investigate the application of ATVS in CTPA, specifically combined with an optimized CM injection protocol.

Previously, possible CM dose reductions per kV setting have been investigated for coronary CTA,[22] and Vasconcelos et al[34] recently published a study that evaluated a kV- and body weight–adapted protocol for abdominal CTA and found that a 63% CM dose reduction was possible. In their study, the total volume of the CM was adapted to body weight by using 4 weight categories; however, it has previously been proven that the IDR is a more influential CM factor than total volume in terms of vascular enhancement on CTA studies.[35,36] The current study is the first study to simultaneously adapt the IDR for both kV and patient body weight in CTPA studies. Using IDR has the added advantage that the methods could be easily translated for other centers using different concentrations of CM.

The CM use in this study can be considered very low, with a mean of 28 ± 6 mL for the main bolus in the sub-100 kV groups. It still proved sufficient for achieving reliable diagnostic image quality. This approach of optimizing CM for kV setting and patient body weight was not primarily designed to minimize CM dose; rather, the idea was to optimize CM use for each individual patient. Even though today's low volumes of iodinated CM might not be as toxic to the renal system as previously feared, one should always practice caution when dealing with high-risk patients.[7,37] Next to the well-described phenomenon of CIN, concerns have been raised regarding the effect of iodinated CM on thyroid function. Gartner and Weissel[38] found a thyroid-stimulating hormone increase in most euthyroitic patients, and Lee et al[39] showed an abnormal thyroid-stimulating hormone level in 22% of patients after iodine administration, all of which was of a transient nature. The European Society of Urogenital Radiology stated in 2004 that monitoring of thyroid function after iodinated CM administration is recommended for patients with Graves disease and patients with multinodular goiter with thyroid autonomy, especially elderly patients and patients living in areas with iodine deficiency.[40]

Second, optimizing CM will homogenize image quality throughout the patient population and all kV settings, which aids the interpretation of the CT images by radiologists. Using a wide range of kV settings is becoming more and more standard practice in CT scanning. However, the clinical images can become difficult to interpret and nearly impossible to compare in, for example, a follow-up situation. It is therefore important to find solutions, such as the one provided by this article, that can help reduce the visible differences in CTPA image quality with the different kV setting. Lastly, CM reduction should translate into health care cost reduction in the future. This should not be underestimated because any cost reduction is vital in an age where ever-increasing health care costs threaten the availability of high-standard health care for the general population.

LIMITATIONS

The initial power calculation resulted in a population of 16 patients per kV group; however, ATVS did not select all kV options on a regular basis. Because 16 patients per group were not achievable within a reasonable amount of time, the study enrolled patients for 1 full year. As a result, in some kV groups (100, 110, and 120 kV), the statistical power was not strong enough to make any conclusions.

CONCLUSIONS

Simultaneously optimizing both CM injections and kV settings to the individual patient in CTPA results in diagnostic attenuation with, on average, 24 to 38 mL of CM volume and a low radiation dose for most patients. This individualized protocol may help overcome attenuation-variation problems between patients and kV settings in CTPA.

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