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Relationships between patient characteristics and contrast agent dose for successful computed tomography venography with a body-weight-tailored contrast protocol

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Abstract

The aim of this study was to evaluate the effect of patient characteristics on the contrast agent dosage that is required to reach effective enhancement of the inferior vena cava (IVC) on computed tomography venographs (CTV).

This retrospective study included 50 patients who underwent CTV at 80 kVp. The contrast injection protocol (iodine 600 mg/kg) was tailored to their body weight. We calculated the required contrast agent volume ($CAV_{mean\text{-}IVC}$) to reach the mean enhancement of IVC. We performed univariate and multivariate linear regression analyses between the sex, age, body weight (BW), lean body weight (LBW), body surface area (BSA), height (HT), estimated glomerular filtration rate (eGFR), and $CAV_{mean\text{-}IVC}$.

The univariate linear regression analysis show that HT, BW, LBW, and BSA were significantly correlated with $CAV_{mean\text{-}IVC}$ ($P < .01$ for all). The $CAV_{mean\text{-}IVC}$ was significantly higher for males than females ($P < .01$). Multivariate regression analysis showed that BW, LBW, and BSA had a statistically significant effect on $CAV_{mean\text{-}IVC}$. There was no significant correlation of age, HT, or eGFR with $CAV_{mean\text{-}IVC}$.

BW, LBW, and BSA each had an independent significant effect on $CAV_{mean\text{-}IVC}$. The conventional BW-tailored contrast injection protocol might be insufficient for CTV.

Abbreviations: BSA = body surface area, BW = body weight, $CAV_{mean\text{-}IVC}$ = required contrast agent volume, CTPA = pulmonary CT angiography, CTV = computed tomography venography, DVT = deep vein thrombosis, eGFR = estimated glomerular filtration rate, FOV = field-of-view, GLM = generalized linear model, IVC = inferior vena cava, LBW = lean body weight, PE = pulmonary embolism.

Keywords: computed tomography, contrast agent dose, venography

1. Introduction

Deep vein thrombosis (DVT) is the most important predisposing factor for developing pulmonary embolism (PE).[1,2] To avoid PE, it is important to make a prompt diagnosis of DVT.[3] Although ultrasound (US) remains the workhorse for detection of DVT,[4] this technique is highly operator-dependent. However, previous reports have suggested the usefulness of computed tomography angiography (CTA) for the evaluation of vascular stenosis and vascular dissection.[5,6] Generally, venous enhancement is significantly lower than arterial enhancement on enhanced CT, and the degree of venous enhancement on CT venography (CTV) is important for a DVT diagnosis. Earlier reports suggested that higher venous attenuation on CTV images can be achieved with a high concentration of iodine contrast medium, a larger volume of contrast medium, or with low tube-voltage- or optimal scan-delay techniques.[7–10] However, it can be difficult to obtain diagnostic venous enhancement in some patients with suspected DVT.[11,12]

Yamashita et al[11] reported that a body weight (BW)-tailored protocol yields high-quality hepatic dynamic CT images. In addition, various body size indices, such as lean body weight (LBW) and body surface area (BSA), have been proposed to determine the contrast agent dose for dynamic CT.[12,13] Using multiple stepwise regression analyses with a fixed contrast agent protocol, a previous report[14] suggested that patient 'BW played a significant role in CT pulmonary angiography (CTPA) and venography. However, they did not evaluate the height and the estimated glomerular filtration rate (eGFR). Additionally, there have been no previous reports about the influence of the LBW and BSA on CTV and the CTPA protocol. There have been no previous reports about the validity of the contrast agent volume field-of-view determined by a BW-tailored protocol in CTV and CTPA. Additionally, there have been no previous reports about the influence of the LBW and BSA on the validity of the contrast agent volume on CTV and CTPA protocols.

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We hypothesised that the BW-tailored protocol would be suitable to keep the contrast agent volume to yield varid venous enhancement on CTV images. The purpose of this study was to evaluate the relationship between the required contrast agent dose to acquire diagnostic-quality CTV with a BW-tailored contrast dose protocol, and patient characteristics including the age, height, BW, LBW, BSA, sex, and the eGFR using univariate and multivariate linear regression analysis.

2. Material and methods

Our institutional review board approved this retrospective study and waived the requirement for informed patient consent.

2.1. Patients

We enrolled 50 patients with suspected DVT or PE owing to elevated D-dimer levels (>5 μg/mL) or clinical symptoms (swelling of the calf or thigh, or dyspnea). They underwent CTV and CTPA between November 2015 and May 2016. They were 26 men and 24 women ranging in age from 19 to 89 years (mean 69.4 years); their BW ranged from 38 to 82 kg (mean 59.2 kg).

2.2. Body size parameter

We adopted BW, LBW, and BSA as the body size indexes. We calculated the LBW using the following formular in men;[14] $LBW = (1.10 \times BW) - 128 \times (BW^2/[100 \times HT]^2)$. In addition, we calculated the LBW using a similar equation in women: $LBW = (1.07 \times BW) - 148 \times (BW^2/[100 \times HT]^2)$.

We also calculated the BSA using the following; $BSA = BW^{0.425} \times HT^{0.725} \times 0.007184$.[15]

2.3. CT scanning and contrast infusion protocols

Of the 50 patients, 29 underwent precontrast CT-, CTV-, and CTPA studies on a 64-detector CT scanner (Brilliance-64; Philips Medical Systems, Cleveland, OH). The other 21 were scanned on a 128-detector CT scanner (Brilliance-iCT; Philips Medical Systems). Precontrast CT- and CTPA scans were acquired in the caudocranial direction during a single inspiratory breath-hold.

The parameters for 64-detector CTV scanning were 80 kVp, detector collimation 64 × 0.625 mm, 750-ms tube rotation time, and 0.49 helical pitch (beam pitch). For 128-detector CTV studies, they were 80 kVp, detector collimation 128 × 0.625 mm, 750-ms tube rotation time, and 0.61 helical pitch (beam pitch). The CT dose index of CTV for 64- and 128-detector CT scanning was 14.2 and 11.7 mGy, respectively. The range of precontrast CT was from the diaphragm to the pelvis. CTV scanning was from just above the diaphragm to the end of the feet in a caudocranial direction.

For all studies, the contrast medium (BW 600 mgI/kg; iopamidol,370 mg/mL [Iopamiron-370; Bayer Yakuhin Ltd., Osaka, Japan]; iomeron, 350 mg/mL [Iomeron-350; Bracco-Eisai Co Ltd., Tokyo, Japan]; or omnipaque, 300 mg/mL [omnipaque 300; GE Healthcare Inc., Princeton, NJ]) was injected with a power injector (DUAL SHOT GX; Nemoto-Kyorindo, Tokyo, Japan) in the course of 30 seconds via a 20-gauge catheter inserted into the antecubital vein.

CTPA was at 80 kVp; the scan start time was determined with a computer-assisted bolus tracking program (Bolus Pro Ultra; Philips Medical Systems) with a trigger threshold of 175 Hounsfield units (HU) in the pulmonary trunk. Real-time serial monitoring studies began 5 sec after the start of contrast injection.

Scanning started 10 seconds after triggering; 80-kVp CTV scans were acquired 270 seconds after contrast injection.

2.4. CT image reconstruction

The field of view (FOV) ranged from 30 to 45 cm depending on the patient physique. All CTV images were reconstructed with a slice thickness of 2.5 mm and slice interval of 2.5 mm. All CTV images were reconstructed with hybrid iterative reconstruction (HIR) (iDose4, Philips Healthcare). The iDose level was a parameter to adjust the image noise; the higher its level, the greater the noise reduction. Based on the results of preliminary studies, we selected an HIR level of 50% (iDose level 4) for image reconstruction.

2.5. Data analysis (CTV)

We acquired the patients' age and sex from their electronic health records. Their BW and HT were measured just before CT scanning. For all patients, we recorded the eGFR obtained within 3 days before CT.

A radiologist with 6 years of experience with CTV on BW-tailored contrast injection protocol performed quantitative image analysis using reconstructed 2.5-mm-thick axial CTV images. For each patient, images above the level of the inferior vena cava (IVC) bifurcation were selected. The average venous attenuation of two circular regions of interest (ROI) on 2 slices above the level of the IVC bifurcation on precontrast and CTV images ($ROI_{plain\text{-}IVC}$ and $ROI_{CTV\text{-}IVC}$) was measured. Attempts were made to select an ROI in the IVC that was as large as possible and was unaffected by pixel variability and small enough to exclude the vessel wall or perivascular fat. We assessed the effects on venous contrast enhancement; its degree was expressed as the change in the venous CT number (ΔHU_{IVC}), calculated by subtracting ROI_{plain} from ROI_{CTV}. We also calculated the mean ΔHU_{IVC} of this study' patients ($\Delta HU_{IVC\text{-}mean}$).

The contrast agent dose (gram of iodine) to elevate mean enhancement of IVC ($[gI/\Delta HU_{IVC}] \times \Delta HU_{IVC\text{-}mean}$) were calculated to evaluate the effect of these factors on venous contrast enhancement ($CA_{IVC\text{-}mean}$). We calculated that contrast agent volume for 300 mg/mL, as follows; $CA_{IVC\text{-}mean}/0.3$ ($CAV_{IVC\text{-}mean}$).

Figure 1 shows the lesions of each ROI for CTV images.

2.6. Statistical analysis

All statistical analyses were performed with the free statistical software "R" (R, version 3.2.2; The R Project for Statistical Computing; http://www.r-project.org/). Univariate linear regression analysis was used and Pearson correlation coefficients (r) were determined to compare the patient characteristics (age, sex, one body size parameter [BW, LBW, or BSA], height, and eGFR) and the required contrast agent volume ($CAV_{IVC\text{-}mean}$). The absolute of r was determined as follows: a correlation of 0 to 0.19 was rated very weak, 0.2 to 0.39 was rated weak, 0.40 to 0.59 was rated moderate, 0.6 to 0.79 was rated strong, and 0.8 to 1 was rated very strong. We also compared ΔHU/gI and ROI_{IVC} between males and females using Student t test.

We also performed multivariate linear regression analysis to determine which of the patient characteristics (age, sex, one body size parameter [BW, LBW, or BSA], height, and eGFR) affected

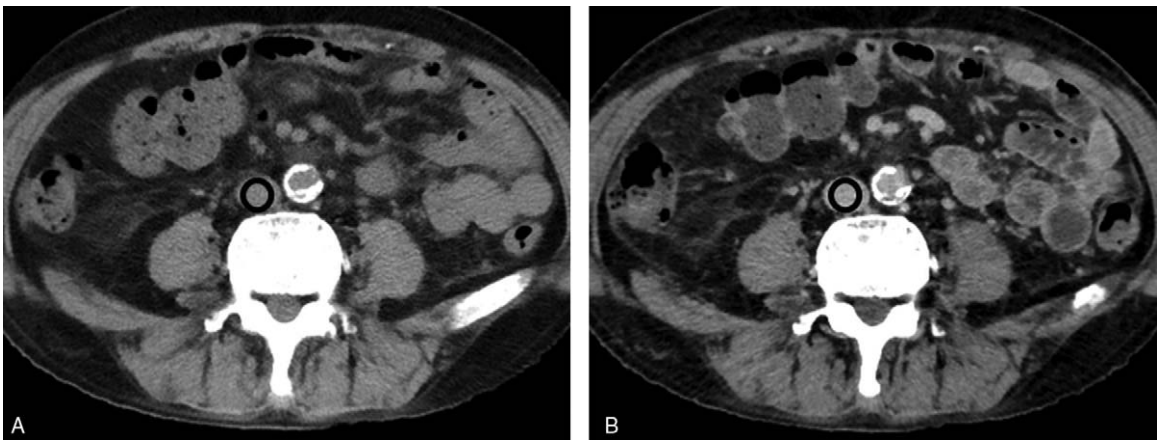

Figure 1. A and B show the precontrast CT and CT venography images above the level of the inferior vena cava (IVC) bifurcation. We measured the venous attenuation using circular regions of interest (ROIs) ($ROI_{plain\text{-}IVC}$ and $ROI_{CTV\text{-}IVC}$).

the $CAV_{IVC\text{-}mean}$. P values <.05 were considered to indicate a significant difference. If there was a significant difference between a patient characteristic and the $CAV_{IVC\text{-}mean}$, we created an optimized linear regression model of that characteristic for the $CAV_{IVC\text{-}mean}$. To assess the magnitude of association, we calculated the squared coefficients of determination (R^2 and adjusted R^2) between the patient characteristic(s) and the $CAV_{IVC\text{-}mean}$.

3. Results

The patient characteristics are presented in Table 1. The age of the 26 males and 24 females ranged from 19 to 89 years, their BW from 37.5 to 81.7 kg, their LBW from 40.7 to 60.9 kg, their BSA from 1.33 to 1.88 m^2, their HT from 141.2 to 179.3 cm, and their eGFR from 37.0 to 123.4 mL/min/1.73 m^2. ROI_{IVC} ranged from 93.7 to 202.8 HU, ΔHU_{IVC} from 195 to 601 HU, $CA_{IVC\text{-}mean}$ from 22.0 to 49.8 gI and $CAV_{IVC\text{-}mean}$ from 73.3 to 166.0 mL. $\Delta HU_{IVC\text{-}mean}$ is 104.1 HU.

Table 1

Patient characteristics and venous enhancement.

Number of patients	50
Males: females	24:26
Age, y	69.4 ± 15.8
Body weight, kg	59.2 ± 11.8
Lean body weight, kg	55.3 ± 6.4
Body surface area, m^2	1.59 ± 0.14
Height, cm	158.6 ± 9.9
eGFR, mL/min/1.73m^2	66.1 ± 16.5
Mean venous enhancement ($\Delta HU_{IVC\text{-}mean}$) (HU)	104.1 ± 18.1
Venous enhancement per gram of iodine, HU/gI	3.0 ± 0.7
Required contrast agent volume to success the mean enhancement of IVC ($CA_{IVC\text{-}mean}$), mL	120.9 ± 24.8
Mean pumonary arterial enhancement ($\Delta HU_{PA\text{-}mean}$), HU	369.6 ± 126.3
Pulmonary arterial enhancement per gram of iodine, HU/gI	0.11 ± 0.05
Required contrast agent volume to success the mean enhancement of PA ($CA_{PA\text{-}mean}$), mL	133.9 ± 56.0

Values are the mean ± standard deviation. eGFR = estimated glomerular filtration rate, IVC = inferior vena cava, PA = pulmonary artery.

3.1. Effect of patient characteristics on $CAV_{IVC\text{-}mean}$

On univariate liner regression analysis, significant inverse correlations were seen between $CAV_{IVC\text{-}mean}$ and BW ($r = 0.59$), height ($r = 0.55$), BSA ($r = 0.63$), and LBW ($r = 0.64$) ($P < .01$ for all). There are significantly different in the $CA_{IVC\text{-}mean}$ between male and female ($P < .01$). Multivariate linear regression analysis showed that only BW maintained their independent predictive value ($B = 0.27$, $P = .03$). The regression formula ($CAV_{IVC\text{-}mean}$[mL] = 57.5 + BW [kg]) suggests that for each 1-kg increase in BW, contrast agent volume is increased by about 1.0 mL.

We also create the regression formula of the BSA and LBW as follows: ($CAV_{IVC\text{-}mean}$[mL] = 17.7 + 53.4 × BSA [m^2]) and ($CAV_{IVC\text{-}mean}$[mL] = 47.3 + 1.7 × LBW [kg]).

Tables 2 to 4 showed the relationship between patient characters including each 3 body size parameters and $CAV_{IVC\text{-}mean}$.

4. Discussion

Our result suggested that BW, LBW, and BSA were independent predictive values at multivariate linear regression analysis for affecting the $CAV_{IVC\text{-}mean}$. Our most important finding is that our BW-tailored contrast injection protocol (2 mL/kg [300 mg/mL]) is unsuitable for CTV. The regression formula $CAV_{IVCmean}$ was as follows, $CAV_{IVCmean}$ mL] = 57.5 + BW [kg] for 300 mg/ml. Therefore, our BW-tailored protocol showed that excessive contrast agent might be given in heavy patients to keep the mean

Table 2

Multivariate GLM analysis of the effect of patient characteristics including body weight on $CA_{IVC\text{-}mean}$ (mL).

	Optimized model	
	β coefficients	*P*
Intercept	57.49	<.01
Age	—	—
Body weight	1.00	<.01
eGFR	—	—
Height	—	—
Sex	—	—
Adjusted R^2	0.31	

eGFR = estimated glomerular filtration rate, GLM = generalized linear model.

Table 3

Multivariate GLM analysis of the effect of patient characteristics including lean body weight on $CA_{IVC\text{-}mean}$ (mL).

	Optimized model	
	β coefficients	*P*
Intercept	47.25	<.01
Age	—	—
Lean body weight	1.67	<.01
eGFR	—	—
Height	—	—
Sex	—	—
Adjusted R^2	0.38	

eGFR = estimated glomerular filtration rate, GLM = generalized linear model.

attenuation of the IVC on CTV. In our BW tailored-protocol, the contrast agent might be insufficient in thin patients to keep the mean attenuation of IVC on CTV.

Multivariate linear regression analysis for $CA_{IVC\text{-}mean}$ revealed that only the BW was of independent predictive value. Some studies addressed the relationship between venous enhancement and patient characteristics on CTV images[16,17]; Arakawa et al[16] suggested that BW and the contrast material dose are important factors associated with venous enhancement when the dose is fixed. Our findings are consistent with theirs. To our knowledge, there are no reports on the relationship between the eGFR and $CA_{IVC\text{-}mean}$. We detected no significant relationship between the eGFR and $CA_{IVC\text{-}mean}$. The scan delay time is relatively long (2–4 minutes) at CTV studies.[18] Although we expected an increase in IVC attenuation in patients with renal dysfunction, we observed no relationship between their eGFR and venous enhancement.

Our study suggested that our BW-tailored protocol in this study (600 mgI/kg) failed to yield the contrast agent volume to success the valid enhancement of IVC on CTV for all patients. Others[19–23] suggested that a BW-tailored protocol resulted in consistent enhancement on various CT examination. The BW is the most important patient-related factor for the estimation of the contrast agent dose required for consistent enhancement, although it may not be the most precise body size index. In obese patients, the BW-tailored contrast agent dose may be excessive because they harbor a large proportion of adipose tissue in which the medium is distributed poorly.[21,23–25] Consequently, various body size indices such as the LBW and the BSA have been introduced to determine the optimal contrast agent dose for cardiac CT- and hepatic dynamic CT studies and for CTA.[26–29] Awai et al[28] suggested that the LBW exhibited the strongest correlation with aortic and hepatic enhancement and Yanaga et al[29] reported that an LBW-tailored dose yielded more consistent aortic enhancement with reduced interpatient variability than the CTA protocol that delivered a BW-tailored dose. According to Bae et al,[26] a contrast dose based on the BSA was useful for obtaining consistent contrast enhancement on cardiac CT angiographs. However, the intercept of our optimized linear model using the BSA and LBW was also not zero. Therefore, the simple BSA- and LBW-tailored protocol cannot offer the stable enhancement of IVC. The intermediate protocol between the fixed- and body-size tailored contrast injection protocol might be well suited for the CTV.

Table 4

Multivariate GLM analysis of the effect of patient characteristics including BSA on $CA_{IVC\text{-}mean}$ (mL).

	Optimized model	
	β coefficients	*P*
Intercept	17.74	.36
Age	—	—
Body surface area	53.44	<.01
eGFR	—	—
Height	—	—
Sex	—	—
Adjusted R^2	0.37	

eGFR = estimated glomerular filtration rate, GLM = generalized linear model.

Our study has some limitations. First, it was a single-center study and the small sample size may limit the statistical significance of our findings. Second, we did not evaluate the relationship between CO, which may affect the blood volume and blood pooling, and venous attenuation. According to Bae et al,[26] the CO directly affects vessel enhancement by contrast media. Third, because our precontrast CT scan range covered mainly the chest to the pelvis, we only evaluated CT attenuation of the IVC; we did not study attenuation of veins in the lower and upper thigh. We will address these issues in future studies. Last, we did not use the optimized protocol in clinical practice. Theoretically, the optimized protocol yields the contrast agent volume to success the valid enhancement of IVC on CTV for all patients. However, it might affect the CTPA protocol. Previous report suggested that 1.2 mL/kg for 350 mg/mL (about 1.5 mL/kg for 300 mg/mL) can yield varied contrast enhancement of PA on CTPA.[30] Therefore, we can use the loose slope to determine the contrast agent volume to success the valid enhancement of IVC and PA on CTV and CTPA.

5. Conclusion

In conclusion, BW, LBW, and BSA each had an independent significant effect on $CAV_{mean\text{-}IVC}$. The conventional BW-tailored contrast injection protocol might be insufficient for CTV.

Author contributions

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