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Improved detectability of thromboses of the lower limb using low kilovoltage computed tomography

Tomoaki Sasaki, MD, PhD*, Yasuomi Fujimoto, MD, Shunta Ishitoya, MD, PhD, Basim Nabaa, MD, PhD, Naofumi Watanabe, MD, Toshihiro Yamaki, MD, Koji Takahashi, MD, PhD

Abstract

To determine the utility of low kilovoltage computed tomographic venography (CTV) for the detection of deep venous thrombus in the lower limbs.

Twenty-one thrombi in 19 enrolled patients were investigated in this retrospective study. Patients were initially scanned using CTV at 100 kVp, at the femur level, followed by an immediate switch to 80 kVp. We assessed the CT values of thrombi and veins and performed subjective evaluation for detecting thrombi using a 5-point scoring system: 1, unable to evaluate due to noise or artifacts; 2, equivocal venous thrombus; 3, possible venous thrombus; 4, probable venous thrombus; and 5, definite venous thrombus.

Venous density on 100-kVp images (mean ± SD [standard deviation]: 122 ± 23 HU, 95% confidence interval [CI]: 111–133 Hounsfield unit [HU]) was significantly lower than that on 80-kVp images (136 ± 24 HU, 95% CI: 125–147 HU, $P < .001$). There was no significant difference in thrombi between 100-kVp images (55 ± 14 HU, 95% CI: 49–61 HU) and 80-kVp images (57 ± 16, 95% CI: 50–64 HU, $P = .168$). The thrombus to vein ratio on 100-kVp images (0.47 ± 0.20, 95% CI: 0.39–0.56) was significantly higher than that on 80-kVp images (0.44 ± 0.16, 95% CI: 0.37–0.51, $P = .048$). The mean 5-point score was significantly higher on the 80-kVp images (4.76) than on the 100-kVp images (4.45, $P = .016$).

Lower kilovoltage CTV significantly improved thrombotic to venous contrasts in the lower limbs.

Abbreviations: CI = confidence interval, CNR = contrast-to-noise ratio, CT = computed tomography, CTDI = computed tomography dose index, CTV = computed tomographic venography, DECT = dual-energy computed tomography, DVT = deep vein thrombosis, HU = Hounsfield unit, kVp = kilovoltage peak, PE = pulmonary embolism, ROI = region-of-interest, SD = standard deviation, US = ultrasonography.

Keywords: computed tomographic venography, contrast medium, low kilovoltage, lower limbs

1. Introduction

Pulmonary embolism (PE) derived from deep vein thrombosis (DVT) can cause severe dyspnea, which increases mortality.[1–4] Detection of DVT using ultrasonography (US) and computed tomographic venography (CTV) is necessary for prevention of critical PE.[1–3,5] US is the standard method of screening for DVT, but it has several limitations in terms of detection of thrombi.[3] CTV is another powerful method for detecting DVT[1,3–6]; it has several advantages, such as providing objective results more rapidly than US and concurrently revealing additional important organ information, such as pulmonary arterial status. Therefore, CTV is the preferred examination modality, particularly in emergency cases associated with a risk of DVT.

Low kilovoltage CTV confer several examination advantages, such as increased iodine contrast[7–15] and lower radiation exposure.[7,9,14,15] Virtual monochromatic reconstruction images on dual-energy CT (DECT) can improve venous iodine contrast to a greater extent than low photon energy images can.[12,16,17] Most previous studies on low kilovoltage CTV have demonstrated increased iodine contrast in the veins, but relatively few have evaluated this with regard to DVT.[7,8,10,13–16] Moreover, the majority have made comparisons between 120 and 100 kVp,[8,11,14] or 120 and 80 kVp.[13,15] Only Cho et al[11] compared contrast of thrombi to veins in the 100 and 120 kVp settings and demonstrated higher contrast at 100 kVp in the clinical human study. Furthermore, Bongers et al[17] demonstrated that lower monoenergetic images derived from DECT provided better contrast of thrombus to iodine, in an ex vivo phantom study. In addition, there was no evidence to compare the contrast of thrombi to veins in the lower limbs between 100 and 80 kVp images.

We hypothesized that using lower kilovoltage CTV could improve the contrast of thrombus to vein even in a clinical context. Therefore, the aim of this study was to evaluate the utility of low kilovoltage CTV in the detection of DVT in the lower limbs.

2. Materials and methods

2.1. Subjects

Our institutional review board approved this retrospective study; the need for obtaining informed patient consent was waived. CTV was performed in a total of 1186 patients to exclude DVT,

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Department of Radiology, Asahikawa Medical University, Asahikawa, Hokkaido, Japan.

* Correspondence: Tomoaki Sasaki, Department of Radiology, Asahikawa Medical University, 2-1-1-1 Midorigaoka-higashi, Asahikawa, Hokkaido 078-8510, Japan (e-mail: tomoaki3est@gmail.com).

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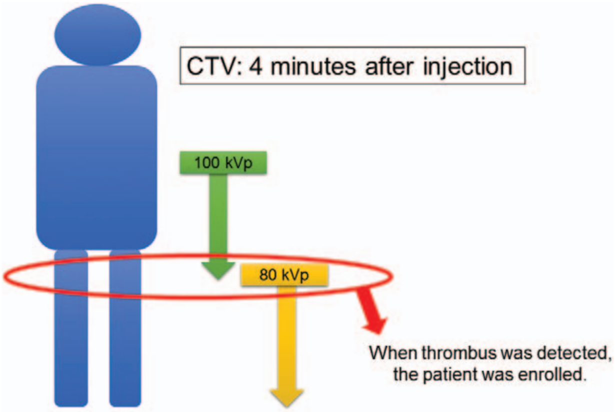

Figure 1. Scan protocol for computed tomographic venography (CTV). Initially, CTV was obtained at 100 kVp from the liver in the direction of the lower limbs. At the femur level, the tube voltage was immediately switched from 100 to 80 kVp to scan the lower regions. Nineteen patients with venous thrombi at the femur level were enrolled in the study.

in addition to the primary purpose, between April 2015 and June 2016 (Fig. 1). We identified 87 patients with DVT from the picture archiving and communication system. Nineteen patients (mean age ± standard deviation [SD]: 61.7 ± 8.5 years, range: 45–78 years) who had venous thrombi at the femoral vein in both 100 and 80 kVp settings of CTV were then enrolled in the study (Table 1). None of the candidates had metallic implants in the lower limbs. All thrombosis cases were confirmed using US examination or direct venography. Two cases involved several thrombi in the bilateral femoral veins; therefore, in total, we assessed 21 thrombi in 19 patients.

2.2. Computed tomography examination

All CTV studies were performed with a 256-row detector CT scanner (Revolution CT, GE Healthcare, Milwaukee, WI). CTV data were acquired after an intravenous bolus injection of 521 to 600 mg I/kg of non-ionic iodinated contrast material (Omnipaque, Daiichi Sankyo Ltd., Tokyo, Japan). All CTV images were obtained using automatic current modulation and were reconstructed with 30% adaptive statistical iterative reconstruction-V (GE Healthcare). We obtained CTV using 100 or 80 kVp 4 minutes after the start of the injection. The tube voltage of the venous phase images was switched from 100 to 80 kVp at the femoral level to avoid degradation of image quality in the pelvis and to increase vein contrast in the lower limbs. The time lag of switching tube voltage was a few seconds.

2.3. Evaluation of CT values of thrombi and veins

Two radiologists (11 years and 5 years of experience, respectively) placed a circular region-of-interest (ROI) to measure CT density and SDs of the thrombus and vein, in 100- and 80-kVp images. First, the CT values obtained by each reader were evaluated to assess interobserver reliability, and mean values were calculated. Second, the mean values of the thrombus, vein, and the ratio of the thrombus to vein, and contrast-to-noise ratio (CNR) in each kilovoltage image were compared.

The CNR was calculated using the following formula:

$$\mathrm{CNR} = \frac{(\mathrm{CT\ vein} - \mathrm{CT\ thrombus})}{\mathrm{SD}}$$

where CT vein and CT thrombus represented the CT value of the vein and thrombus, respectively. Third, the CT dose index (CTDI), an indicator of radiation exposure, was compared with 100 and 80-kVp images.

Table 1

Patient demographics.

Demographics	*N* = 19
Age	61.7 ± 8.5 y
Height	161.3 ± 5.3 cm
Weight	58.2 ± 9.5 kg

2.4. Subjective evaluation for detecting thrombi

We qualitatively analyzed the detection of thrombi in the veins in each kilovoltage image. All images were randomly interpreted by an additional 2 radiologists (Reader 1 and 2), each with 6 years of experience, who were blinded to the scan parameters and clinical states. Image interpretation was performed using commercial software (ShadeQuest, Yokogawa Solutions, Tokyo, Japan). We used a 5-point visual scoring system: 1, unable to evaluate due to noise or artifacts; 2, equivocal venous thrombus; 3, possible venous thrombus; 4, probable venous thrombus; and 5, definite venous thrombus. Mean scores from the 2 readers for each kilovoltage image were compared.

2.5. Statistical analysis

All statistical analyses were performed using a commercially available software program (Statistical Package for the Social Sciences, version 22 for Windows, SPSS Inc., Chicago, IL). Interobserver assessment of the quantitative analysis between the 2 readers was evaluated using intraclass correlation coefficients. Furthermore, interobserver reliability for the subjective evaluation was analyzed using weighted kappa tests. Comparisons of mean CT number, SDs, and CNRs of thrombus and vein, and CTDI in each kilovoltage image were assessed using a paired *t*-test. Comparison of the 5-point score was evaluated using the Wilcoxon signed-rank test. A P-value $<.05$ was considered statistically significant.

3. Results

3.1. Interobserver agreement for quantitative and qualitative analyses

The intraclass correlation coefficients between the 2 readers ranged from 0.65 to 0.90, indicating good interobserver reliability. The weighted kappa value between the 2 readers for the qualitative analysis was 0.66, and indicated substantial interobserver agreement.

3.2. Evaluation for CT value of thrombi and veins

Venous density on 100-kVp images (mean ± SD: 122 ± 23 HU, 95% confidence interval [CI]: 111–133 Hounsfield unit [HU]) was significantly lower than that on 80-kVp images (136 ± 24 HU, 95% CI: 125–147 HU, $P < .001$). There was no significant difference in thrombi between 100-kVp images (55 ± 14 HU, 95% CI: 49–61 HU) and 80-kVp images (57 ± 16, 95% CI: 50–64

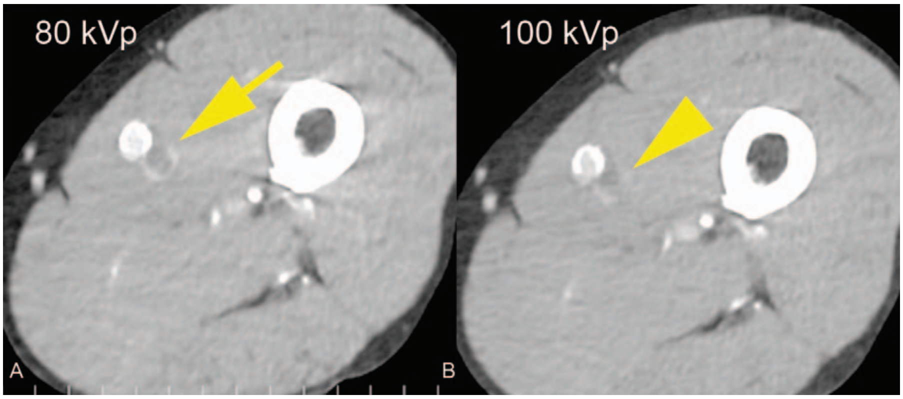

Figure 2. A 60-year-old man with a thrombus in the left femoral vein. The contrast of the thrombus to the vein in the left femoral vein was better in (A) the 80 kVp image (arrow) than in the (B) 100 kVp image (arrowhead) due to the increased venous density surrounding the thrombus.

HU, $P=.168$). The thrombus to vein ratio on 100-kVp images (0.47 ± 0.20, 95% CI: 0.39–0.56) was significantly higher than that on 80-kVp images (0.44 ± 0.16, 95% CI: 0.37–0.51, $P=.048$). The SDs of thrombus and vein did not show significant differences between 100-kVp images (9.0 ± 1.5 HU and 9.7 ± 2.9 HU, respectively) and 80-kVp images (10.3 ± 3.2 HU and 10.9 ± 3.7 HU, $P=.107$ and $P=.135$, respectively). The CNR at 100 kVp was lower than that at 80 kVp, but there was no significant difference among them (7.24 ± 3.12, 95% CI: 5.82–8.67, 7.68 ± 3.43, 95% CI: 6.12–9.24, respectively, $P=.381$). The CTDI in the 100-kVp images (6.36 ± 2.27 mGy) was significantly lower than that in the 80-kVp images (2.06 ± 0.66 mGy, $P<.001$).

3.3. *Subjective evaluation of thrombus*

Both readers observed venous thrombosis in both low kilovoltage settings. The mean score of the 2 radiologists was 4.45 and 4.76 on the 100 and 80 kVp images, respectively. The 5-point score on 80-kVp images was significantly higher than that on 100-kVp images ($P=.016$, Fig. 2).

4. Discussion

This study assessed the ability of low kilovoltage CTV to detect DVT in the lower limbs. Venous density was significantly higher on 80-kVp images than on 100-kVp images; however, thrombotic density was not significantly higher. Therefore, thrombus to vein ratios were significantly lower on the 80-kVp images than on the 100-kVp images, which could emphasize the contrast of thrombi in the veins on 80-kVp images. Image noise and CNR at 80 kVp tended to be higher than at 100 kVp, although there was no significant difference between the 100 and 80-kVp images. Subjective evaluation indicated that the 80-kVp images provided a better contrast of thrombi in veins for interpretation. Consequently, the 80 kVp setting would be superior for the detection of DVT in the lower limbs with radiation exposure.

Our study directly demonstrated an increased contrast of thrombi to veins on CTV, in a low kilovoltage setting. Most similar studies have revealed only increased venous contrast in each low kilovoltage image.[7,8,10,13–16] Cho et al[11] presented higher contrast of the thrombi to veins at 100 kVp than at 120 kVp. Thrombotic density did not increase, even in a low kilovoltage setting, which could contribute to the improved contrast of thrombi to veins, resulting in a higher detection rate. Since Cho et al evaluated different groups of patients, their thrombotic composition might not conform. However, our data revealed that by enrolling patients with same thrombotic composition, we could observe that the thrombi did not increase in density even in low kilovoltage (80 kVp) images, when compared with DVT in 100 kVp images. Our data indicated that both a constant density of DVT and an increased density of veins can generate better contrast in low kilovoltage CTV. We speculate that this is due to the difference in atomic number between iodine (atomic number 53 being the main component of the contrast material), and iron (atomic number 26 being the main component of hemoglobin and thrombi), which emphasizes the contrast of CT density on low kilovoltage images. The photoelectric effect contributes markedly to increasing CT density in diagnostic x-ray energies: in particular, under low kilovoltage settings, iodine attenuation increases due to the k-edge of iodine.[18–21] Furthermore, the incidence of the photoelectric effect is proportional to the fifth power of the atomic number and inversely proportional to the 3.5th power of photon energy.[18,19] Therefore, lower kilovoltage images provide better iodine enhancement in the veins than thrombi.

There are several limitations of this study. First, it was a retrospective study and involved a small sample size. Second, this study was not able to exclude a slight scan time lag between 100 and 80 kVp images. Rapid scanning using advanced CT in the venous phase could minimize the scan time lag when switching from 100 to 80 kVp. Previous studies have scanned CTV 3 minutes after starting contrast material injection.[11,20,22] Yankelevitz et al[23] demonstrated that venous density would gradually continue to decrease after the broad peak enhancement around 3 minutes after the injection of contrast material in the femoral veins. Therefore, venous density in the latter CTV scan performed a few seconds later due to the switching time lags should be lower than or at least equal to that in the former CTV scan. Moreover, the thrombus to venous ratio in the latter scan should be increased. Our data, which represent the opposite results, that is, a decreased thrombus to venous ratio, could not have been affected by the time lag. Third, we did not include patients with metallic implants in the lower limbs. The number of elderly patients receiving artificial hip or knee joint replacement surgery is increasing, and the presence of metallic substances makes it difficult to evaluate the veins surrounding the metal. Indeed, further evaluation is needed in patients with metallic implants in the lower limbs. However, lower tube voltage may be useful in assessing veins below the knee level, which are unaffected by metallic artifacts from artificial hip or knee joint replacements and in which the diagnostic accuracy of US is occasionally unreliable.[3,5]

In conclusion, lower kilovoltage CTV significantly improved thrombotic and venous ratios in the lower limbs, with reduction of radiation exposure. Therefore, DVT detection ability may be enhanced in lower kilovoltage CTV. Based on our findings, we suggest the use of low kilovoltage images for DVT detection in the lower limbs, as distally as possible. In future, it might also be possible to reduce the dose of iodine-containing contrast material for CTV in DVT.

References

[1] Huisman MV, Klok FA. Current challenges in diagnostic imaging of venous thromboembolism. Blood 2015;126:2376–82.

[2] Konstantinides SV, Torbicki A, Agnelli G, et al. 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. Eur Heart J 2014;35:3033–69. 3069a–3069k.

[3] Bates SM, Jaeschke R, Stevens SM, et al. Diagnosis of DVT: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest 2012;141(Suppl):e351S–418S.

[4] Subramaniam RM, Heath R, Chou T, et al. Deep venous thrombosis: withholding anticoagulation therapy after negative complete lower limb US findings. Radiology 2005;237:348–52.

[5] Huisman MV, Klok FA. Diagnostic management of acute deep vein thrombosis and pulmonary embolism. J Thromb Haemost 2013; 11:412–22.

[6] Stein PD, Fowler SE, Goodman LR, et al. Multidetector computed tomography for acute pulmonary embolism. N Engl J Med 2006;354: 2317–27.

[7] Oda S, Utsunomiya D, Funama Y, et al. Evaluation of deep vein thrombosis with reduced radiation and contrast material dose at computed tomography venography. Circ J 2012;76:2614–22.

[8] Fujikawa A, Matsuoka S, Kuramochi K, et al. Vascular enhancement and image quality of CT venography: comparison of standard and low kilovoltage settings. AJR Am J Roentgenol 2011;197:838–43.

[9] Pontana F, Pagniez J, Duhamel A, et al. Reduced-dose low-voltage chest CT angiography with Sinogram-affirmed iterative reconstruction versus standard-dose filtered back projection. Radiology 2013;267:609–18.

[10] Kim JH, Choo KS, Moon TY, et al. Comparison of the image qualities of filtered back-projection, adaptive statistical iterative reconstruction, and model-based iterative reconstruction for CT venography at 80 kVp. Eur Radiol 2016;26:2055–63.

[11] Cho ES, Chung JJ, Kim S, et al. CT venography for deep vein thrombosis using a low tube voltage (100 kVp) setting could increase venous enhancement and reduce the amount of administered iodine. Korean J Radiol 2013;14:183–93.

[12] Kulkarni NM, Sahani DV, Desai GS, et al. Indirect computed tomography venography of the lower extremities using single-source dual-energy computed tomography: advantage of low-kiloelectron volt monochromatic images. J Vasc Interv Radiol 2012;23:879–86.

[13] Cho ES, Kim JH, Kim S, et al. Computed tomographic venography for varicose veins of the lower extremities: prospective comparison of 80-kVp and conventional 120-kVp protocols. J Comput Assist Tomogr 2012;36:583–90.

[14] Park CK, Choo KS, Jeon UB, et al. Image quality and radiation dose of 128-slice dual-source CT venography using low kilovoltage combined with high-pitch scanning and automatic tube current modulation. Int J Cardiovasc Imaging 2013;29(Suppl):47–51.

[15] Schindera ST, Winklehner A, Alkadhi H, et al. Effect of automatic tube voltage selection on image quality and radiation dose in abdominal CT angiography of various body sizes: a phantom study. Clin Radiol 2013;68:e79–86.

[16] Ichikawa S, Ichikawa T, Motosugi U, et al. Computed tomography (CT) venography with dual-energy CT: low tube voltage and dose reduction of contrast medium for detection of deep vein thrombosis. J Comput Assist Tomogr 2014;38:797–801.

[17] Bongers MN, Schabel C, Krauss B, et al. Noise-optimized virtual monoenergetic images and iodine maps for the detection of venous thrombosis in second-generation dual-energy CT (DECT): an ex vivo phantom study. Eur Radiol 2015;25:1655–64.

[18] Alpen EL. Chapter 4 - Interaction of radiation with matter. Radiation Biophysics (Second ed.) 1998;Academic Press, San Diego:50–77.

[19] Nishio T. Nagata Y. Physics. Stereotactic Body Radiation Therapy: Principles and Practices Springer Japan, Tokyo:2015;27–43.

[20] Oda S, Utsunomiya D, Awai K, et al. Indirect computed tomography venography with a low-tube-voltage technique: reduction in the radiation and contrast material dose–a prospective randomized study. J Comput Assist Tomogr 2011;35:631–6.

[21] Schueller-Weidekamm C, Schaefer-Prokop CM, Weber M, et al. CT angiography of pulmonary arteries to detect pulmonary embolism: improvement of vascular enhancement with low kilovoltage settings. Radiology 2006;241:899–907.

[22] Kalva SP, Jagannathan JP, Hahn PF, et al. Venous thromboembolism: indirect CT venography during CT pulmonary angiography–should the pelvis be imaged? Radiology 2008;246:605–11.

[23] Yankelevitz DF, Gamsu G, Shah A, et al. Optimization of combined CT pulmonary angiography with lower extremity CT venography. AJR Am J Roentgenol 2000;174:67–9.