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INTERVENTIONAL RADIOLOGY

CT IVC venogram: normalized quantitative criteria for patency and thrombosis

Marina Mityul[1] · David J. Kim[1] · Amber Salter[2] · Motoyo Yano[1]

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Abstract

Purpose Establish normal attenuation ratios for vein to artery on CT IVC venogram and determine a vascular attenuation ratio diagnostic of thrombus.

Methods This retrospective, HIPAA-compliant study included 56 CT IVC venograms. Images were reviewed for the presence of femoral vein or IVC thrombus. Attenuation ratios for each vein and its corresponding artery were calculated by two observers and averaged in four venous stations (right and left femoral veins, and IVC at the confluence of the iliac veins and at the left renal vein). The reference standard for the absence of thrombus was clinical follow-up and for the presence of thrombus it was thrombectomy or catheter venogram. Receiver operating characteristic (ROC) analysis was performed using ratios from one venous station and threshold for thrombus was determined using the Youden's index.

Results 36 of 56 CTs demonstrated no thrombus. 20 CTs demonstrated thrombus, confirmed in eight patients. For CTs with no thrombus, median ratios among the venous stations ranged from 0.89 (IQR 0.83–0.93) to 0.91 (IQR 0.86–0.94). ROC analysis of ratios from a single representative station (left femoral vein, $n=4$ confirmed clots) demonstrated an area under the curve (AUC) of 0.994 ($p=0.001$) and a threshold of 0.67 for diagnosing thrombus [sensitivity 100% (95% CI 39.76–100%), specificity 97.5% (86.84–99.94%)].

Conclusion The normal attenuation ratio of vein to artery in the absence of venous thrombus on a 3-min delay CT IVC venogram is approximately 0.91. A ratio less than 0.67 is highly suggestive of thrombus.

Keywords Inferior vena cava · Femoral vein · Thrombosis

Introduction

Deep venous thrombosis (DVT) in the inferior vena cava (IVC) is considered an under-recognized diagnosis estimated to occur in up to 4% of patients with lower extremity DVT [1]. Acute pulmonary embolism (PE) is estimated to occur in 12% of patients with thrombosis of the IVC [2] but chronic sequelae of DVT, known collectively as post thrombotic syndrome, is thought to affect the majority of patients with IVC thrombosis [1]. IVC thrombosis is a challenging clinical diagnosis to consider, especially given its non-specific and variable clinical presentation [1, 3] which may or may not elicit dedicated imaging investigation.

Ultrasonography is the first-line imaging examination for detection of lower extremity DVT [4, 5]. However, diagnosis of DVT in the iliofemoral veins and IVC is limited with ultrasonography, and often necessitates the use of contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) for evaluation of the full extent of thrombus [6]. Thrombus in the iliofemoral veins and IVC is important to identify because in addition to anticoagulation, thrombus in these locations may be treated with endovascular or surgical procedures [1].

The presence of deep venous thrombosis on CT can usually be diagnosed qualitatively. These features include low-attenuation filling defect, vascular expansion, and perivenous stranding [7–9]. The most commonly published CT IVC venogram protocol prescribes the acquisition of images 3 min after injection of intravenous contrast [10–19].

✉ Motoyo Yano
myano@wustl.edu

[1] Mallinckrodt Institute of Radiology, Washington University School of Medicine, Campus Box 8131, 510 S. Kingshighway Blvd, St Louis, MO 63110, USA

[2] Division of Biostatistics, Washington University School of Medicine, Campus Box 8067, 660 Euclid Ave., St Louis, MO 63110-1093, USA

With this delay, the contrast bolus injected in an upper extremity vein becomes diluted with unopacified blood in both the peripheral arterial and venous circulation before returning to the femoral veins, iliac veins, and IVC [8]. The 3-min delay allows equilibration and improves homogeneity of the venous blood pool, but also results in lower intravascular contrast density [20] than visceral veins on a standard portal venous phase CT. To the radiologist accustomed to identifying thrombus in the portal venous phase of contrast (such as portal vein thrombus), the prospect of identifying or ruling out the presence of thrombus in diffusely hypodense "washed out"-appearing IVC and iliofemoral veins may seem challenging and diagnostic confidence may potentially be diminished. The purpose of this retrospective study is to establish normal attenuation ratios for vein to artery on CT IVC venogram and determine a vascular attenuation ratio diagnostic of thrombus.

Materials and methods

Informed consent was waived for this IRB-approved, retrospective, single-institution, HIPAA-complaint study. The Montage radiology report database system was used to query for CT examinations performed according to IVC venogram protocol from 2011 to 2017. This identified 58 unique patients. CT examinations were performed on a 64 or 128 detector row Siemens CT with reference kV of 120 and mAs of 180 using automatic tube current modulation and tube voltage adjustment. Images were acquired from the diaphragm to lesser trochanters and reconstructed with slice thickness of 2 mm and reconstruction increment of 1 mm. All patients received 125 mL of Optiray® 350 (ioversol injection 74%) intravenous contrast at a rate of 4 mL/s and were imaged at a fixed delay of 3 min post-contrast. The reported technique of the examination was interrogated for protocol deviations, and any examinations with images acquired outside of 180 s ± 30 s were excluded (Fig. 1).

Image analysis

Four venous stations were interrogated with Hounsfield unit (HU) attenuation measurements. The largest possible circular regions of interest (ROI) were placed within the confines of the vein and corresponding artery on the same image in confirmed cases of patency. In cases of non-occlusive venous thrombus, the largest possible ROI was placed on the visually suspected thrombus within the vein. These four vascular pairs consisted of (1) right common femoral vein and right common femoral artery, (2) left common femoral vein and left common femoral artery, (3) IVC and aorta at the level of the iliac vein confluence, and (4) IVC and aorta at the level of the left renal vein. The vein-to-artery attenuation ratio was calculated for each venous station. Before measurements were performed, all observers completed a training session to standardize measurement methods. Two observers (third year radiology residents) independently measured the attenuation within the vein and artery on CTs in which no thrombus was detected. A third observer (attending radiologist with 5 years of subspecialty experience) measured attenuation ratios on CT examinations in which thrombus was present, in the same four stations.

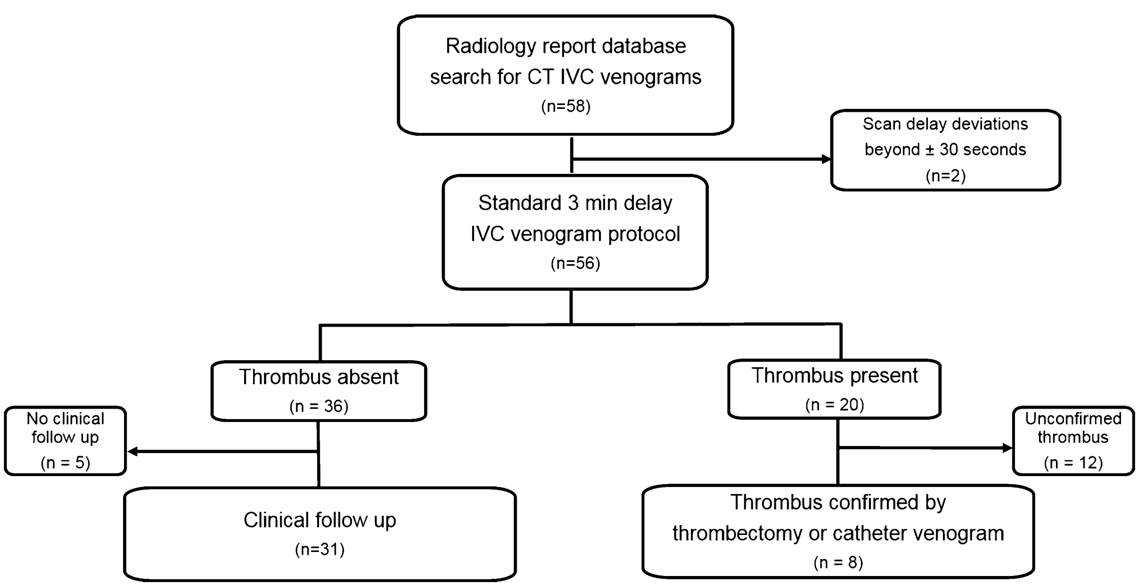

Fig. 1 Schema for study population

Reference standard for presence or absence of thrombus

The electronic medical record was interrogated for clinical, imaging, or procedural follow-up after IVC venogram protocol CT. The reference standard for absence of thrombus in the pelvic veins and IVC consisted of clinical follow-up notes and absence of other imaging studies suggesting DVT or PE. Clinical follow-up notes documented the absence of lower extremity edema on physical exam and did not contain concern for DVT. If clinical follow-up of > 1 day was not available, the patient was excluded. The reference standard for presence of thrombus on CT IVC venogram was either surgical thrombectomy or conventional catheter venogram. If this was not performed, the patient was excluded.

Statistical analysis

Normal vascular attenuation ratios for patients with no thrombus on CT IVC venogram were obtained after averaging the ratios obtained by 2 observers. The distribution of ratios were expressed as median, range, and interquartile range (IQR). Intraclass correlation coefficients (ICC) were calculated for the ratios obtained at 4 venous stations. ICC values of 0.5 to 0.75 were considered moderate agreement, 0.75 to 0.90 were considered good agreement, and greater than 0.90 were excellent agreement. A receiver operating characteristic (ROC) analysis was conducted to examine vascular attenuation ratios which predicted the presence of thrombus using logistic regression and the optimal cutoff was determined using the Youden's index. Due to dependency between venous stations within a patient, ROC analysis was performed for a single representative venous station (left common femoral vein for all patients). Statistical analyses were performed in SAS, version 9.4.

Results

Normal vein-to-artery attenuation ratios

Two of the 58 CTs found in the institutional radiology report database were excluded, as the scan delay was beyond 180 s ± 30 s (Fig. 1). 53 CTs were scanned with a 180-s delay, one with a 150-s delay, and two with a 210-s delay. Of the 56 CT examinations, 36 CTs demonstrated no evidence of thrombus, and clinical follow-up was available for 31 of these patients; these patients were included for analysis. In the available follow-up period [median 147 days (IQR 35–547 days), range 2–1449 days], interrogation of the electronic medical record did not reveal suggestion of a missed diagnosis of pelvic deep vein, IVC thrombus, or PE by follow-up imaging or in clinical notes documenting a physical exam.

The median attenuation ratio of vein to artery in the 4 venous stations (right and left CFV, and IVC at confluence and at the level of the left renal vein) ranged from 0.89 (IQR 0.82–0.92) to 0.91 (IQR 0.84–0.95) in patients with clinical follow-up confirming no thrombus in the iliac veins and IVC (Table 1; Fig. 2a). The ICC for HU values measured in these arteries and veins ranged from 0.91 to 0.98 [IVC at the confluence of the iliac veins: 0.91 (95% CI 0.83–0.95); IVC at level of left renal vein: 0.98 (95% CI 0.96–0.99); right common femoral artery: 0.98 (95% CI 0.96–0.99); aorta at the level of the left renal vein: 0.98 (95% CI 0.96–0.99)].

Vein-to-artery attenuation ratios diagnostic of thrombus

There were 20 CTs with thrombus qualitatively detected in the iliac veins or IVC in the radiology report, but only 8 of these patients went on to surgical thrombectomy or catheter venogram, and therefore had confirmed thrombus (Fig. 1). ROC analysis of the left CFV was performed to determine threshold vascular attenuation ratios for the presence of thrombus (Fig. 3). This analysis included 4 left CFVs with confirmed thrombus (Fig. 2b) and 35 left CFVs with no thrombus, established either via clinical follow-up or surgery/catheter venogram. The AUC was 0.994 (95% CI 0.97 to 1.01), $p = 0.0013$. The Youden's index gives a threshold ratio of less than 0.67 as diagnostic of thrombus [sensitivity 100% (95% CI 39.76–100%); specificity 97.5% (86.84–99.94%)].

Applying a threshold of 0.67 to the 3 other venous stations shows that 6 of 7 venous stations with thrombus demonstrated an attenuation ratio less than 0.67 (Fig. 4). 114 of 117 venous stations without thrombus showed an attenuation ratio greater than 0.67. The three stations without thrombus in which the attenuation ratio was less than 0.67 occurred in a single patient.

Table 1 Vein-to-artery attenuation ratios in four venous stations in the 31 patients with confirmed absence of thrombus

Venous station	Median	Min	25th percentile	75th percentile	Max
Right common femoral vein	0.91	0.66	0.84	0.95	1.1
Left common femoral vein	0.91	0.68	0.84	0.93	1.2
IVC confluence of common iliac veins	0.91	0.59	0.86	0.94	0.97
IVC at left renal vein	0.89	0.57	0.82	0.92	0.96

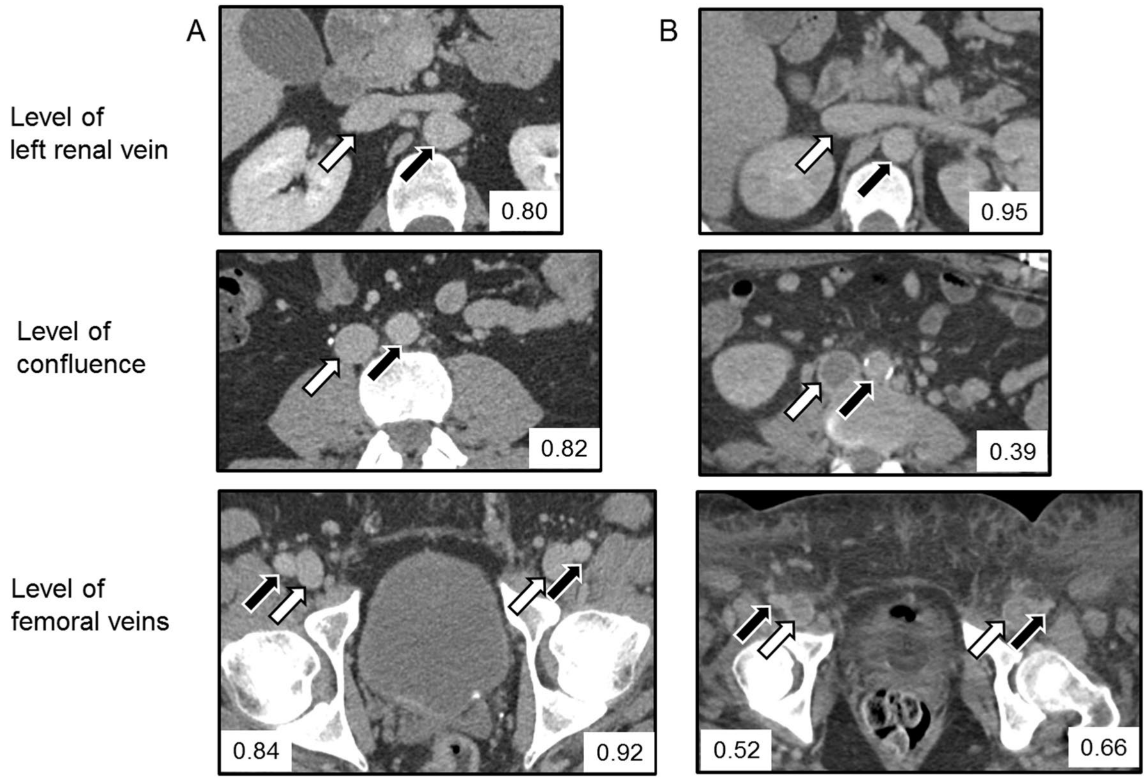

Fig. 2 CT IVC venogram images of the IVC at the level of the left renal vein and confluence of right and left common iliac veins, as well as the level of the femoral veins (rows as labeled on the left). **a** A 47-year-old man status post recent spinal surgery with lower extremity edema. No thrombus is identified within the veins. **b** A 42-year-old woman with prior abdominal surgery, known DVT, and PE status post IVC filter placement has thrombus in the IVC at the level of the confluence of the iliac veins and in the bilateral femoral veins. There is no thrombus at the level of the left renal vein. White arrows are directed at the veins, and black arrows are directed at the corresponding arteries. The value in the lower corner of the images is the vascular attenuation ratio at the corresponding level and side

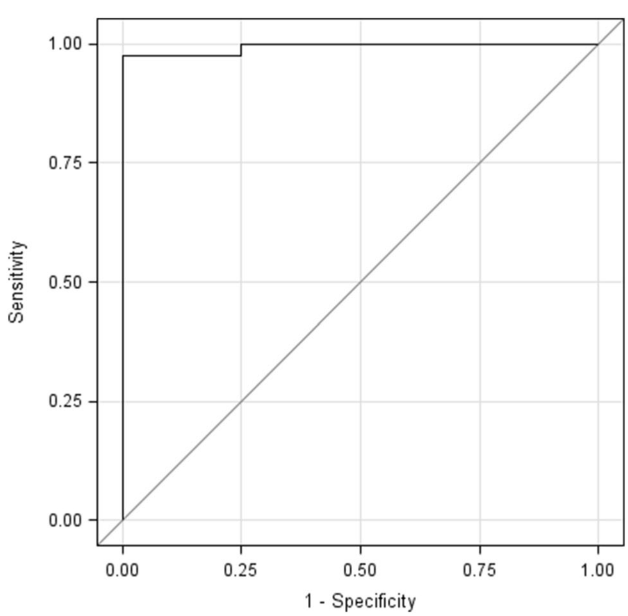

Fig. 3 ROC curve for the diagnosis of venous thrombus using vein-to-artery attenuation ratios in one of the eight venous stations; in this case, the left common femoral vein. AUC is 0.99, $p = 0.001$

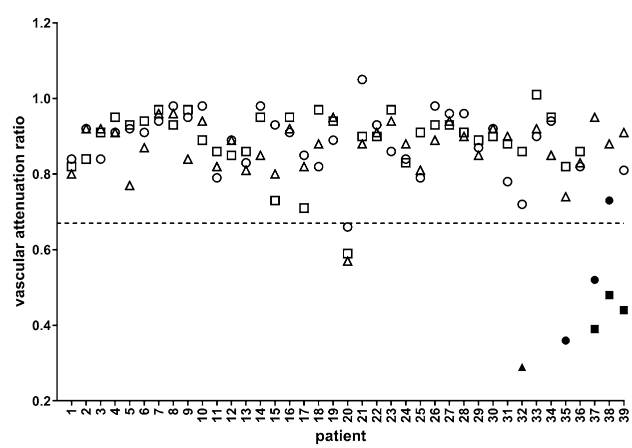

Fig. 4 Scatterplot for vascular attenuation ratio in three venous stations for all patients with confirmed presence or absence of thrombus. Patients 1 through 31 represent those without thrombus and patients 32 through 39 represent those with thrombus. Each venous station is represented by a shape; open shapes correspond to veins with no thrombus and solid shapes correspond to veins with thrombus. Circles represent the right common femoral vein, squares represent the IVC at the confluence of the iliac veins, and triangles represent the IVC at the level of the left renal vein. A dotted reference line is provided at a vascular attenuation ratio of 0.67

Discussion

We have demonstrated that in the absence of venous thrombus, the normal vein-to-artery enhancement ratio is approximately 0.9 within the femoral veins as well as IVC when scanned 3 min after the administration of IV contrast. Our vascular attenuation ratios in the IVC and pelvic veins are difficult to compare to prior studies as only absolute attenuation values have previously been reported in this phase of contrast [10, 20]. However, when comparing absolute measurements within the vein and adjacent artery from published figures, the ratio appears similar to our results. The use of vein-to-artery attenuation ratios may potentially be more applicable than absolute HU in the diagnosis of pelvic and IVC thrombosis as it represents an internally controlled value which may allow for differences in contrast agent and in patient factors such as cardiac output. Knowledge of this internally normalized attenuation ratio could bolter diagnostic confidence for the interpreting radiologist who infrequently encounters these examinations.

As multiple vascular attenuation ratios in a single patient constitutes clustered data [21], our statistical analysis utilized a single representative vascular station in the determination of an attenuation threshold. While it is difficult to apply statistical methods to evaluate the attenuation ratios obtained in the other vascular stations, it appears that a vascular attenuation ratio of less than 0.67 has a high sensitivity and specificity for the presence of thrombus in our population. Prior studies have evaluated qualitative features in the diagnosis of deep venous thrombosis, such as the presence of a low-attenuation filling defect, vascular expansion, venous wall enhancement, perivenous fat stranding, and opacification of collateral veins [7, 8, 22]. These qualitative features are certainly less laborious and more practical to utilize than quantitative features, but in cases of uncertainty, about either the presence of thrombus or the quality of vascular opacification, the vascular attenuation ratio could prove helpful. These measurements appear to be reproducible, as evidenced by our high interobserver reliability, similar to other studies reporting vascular attenuation [7].

There are several limitations to this study. First, the retrospective nature of this study may introduce bias. Second, the number of IVC venograms available for analysis ($n = 58$) was very small, especially considering our 1400-bed tertiary referral center. Our study population was further decreased by excluding patients without clinical follow-up ($n = 5$) and thrombectomy/catheter venography ($n = 12$). These reference standards constitute our third limitation. We acknowledge that clinical follow-up is not the best reference standard for true absence of DVT, as we may have missed cases of asymptomatic DVT, but this is the best available reference standard in the retrospective setting. An ideal study design would be prospective data collection with all patients undergoing catheter venography or contrast-enhanced MR venography after CT IVC venogram. However, a prospective study which includes confirmatory correlative exams such as these would potentially increase the risk of harm and lengthen hospital stay in many patients already hospitalized for other acute illness and would definitely be costly. Therefore, in the retrospective setting, excluding patients without clinical follow-up and catheter venography/thrombectomy, is perhaps as close to ideal as can be designed, and serves to increase confidence in the validity of this quantitative data compared to not excluding these patients. Fourth, qualitative data were not formally collected and analyzed with the quantitative data, but our goal was to solely analyze quantitative data.

Despite the small sample size and further limitations imposed by dependency of data collected within the same patient (i.e., only a single venous station could be analyzed), we obtained statistically significant results. The normal attenuation ratio of vein to artery in the femoral veins and IVC is approximately 0.9, and this appears to be reproducible between venous stations and observers, as evidenced by similar ratios with narrow IQR and high ICC with narrow 95% CI, respectively. An attenuation value of less than 0.67 distinguishes thrombus from patent vein in our population. This would need to be validated in a separate, larger patient population, which also includes data on cardiac output, to ensure that the ratio remains valid for differing contrast agents. The challenge may arise from the infrequency with which this scanning protocol is utilized. Quantitative, normalized data from CT IVC venogram in conjunction with qualitative findings described elsewhere may bolster diagnostic confidence by the interpreting radiologist.

Conclusion

The normal vein-to-artery attenuation ratio in femoral veins and IVC on CT IVC venogram performed 3-min post-contrast is approximately 0.9. A vascular attenuation ratio of less than 0.67 is supportive of the presence of venous thrombus.

Compliance with ethical standards

Ethical approval **IRB statement**: The Institutional Review Board of Washington University School of Medicine approved this study (IRB # 201801002).

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