

Three-dimensional computed tomography venogram enables accurate diagnosis and treatment of patients presenting with symptomatic chronic iliofemoral venous obstruction

Arjun Jayaraj, MD, and Seshadri Raju, MD, Jackson, Miss

ABSTRACT

Objective: The last several years has witnessed an increase in the diagnosis and treatment of chronic iliofemoral venous obstructive lesions. Although intravascular ultrasound (IVUS) examination has become the gold standard in the management of chronic iliofemoral venous obstruction (CIVO), it is an invasive technique. To ascertain the usefulness of noninvasive imaging technology in diagnosing and treating CIVO in symptomatic patients, we compared three-dimensional (3D) reconstructions from computed tomography venogram (CTV) with IVUS examination.

Methods: Twenty-two continuous patients who underwent IVUS interrogation during intervention for CIVO formed the study cohort. Patients who had stenting performed in the setting of chronic total occlusion of the iliofemoral segment or acute iliofemoral deep venous thrombosis were excluded. All patients underwent CTV as part of their standard preoperative work up. Minimal (smallest) luminal areas of the common iliac vein (CIV), external iliac vein (EIV), common femoral vein (CFV) and the inflow channel (segment caudal to the CFV) were obtained from 3D CTV and IVUS. Centerline length measurements were obtained from 3D CTV to estimate the length of the venous stents necessary; the inflow channel luminal area was used to predict the required stent diameter. Pearson correlation was used to evaluate the association between the luminal areas obtained from the two techniques. Agreement was ascertained by use of Bland-Altman limits of agreement. Sensitivity, specificity, positive predictive value, negative predictive value and accuracy of 3D CTV in predicting luminal areas was also determined. Predicted stent diameters and lengths were compared against actual stent diameters and lengths used.

Results: Pearson correlation statistic for luminal areas between 3D CTV and IVUS for the CIV was 0.89 ($P < .01$), for EIV was 0.77 ($P < .01$), and for CFV was 0.69 ($P < .01$). The correlation statistic for the inflow channel luminal area was 0.90 ($P < .01$). The sensitivity of 3D CTV in diagnosing CIVO in the CIV, EIV, and CFV were 100%, 100% and 80%, respectively. The specificity was 67%, 57%, and 86%, respectively, in the CIV, EIV, and CFV segments. The positive predictive value of 3D CTV in determining CIVO in the CIV, EIV, and CFV segments was 89%, 83%, and 92%, and the negative predictive value was 100%, 100%, and 67%, respectively. The overall accuracy was 91%, 86%, and 82% in the CIV, EIV, and CFV segments. Thus, 3D CTV is able to predict stent length within 9.5 mm of the actual stent length used. With respect to stent diameter, 3D CTV was able to predict within 2 mm of the actual stent diameter used 91% (20/22) and within 4 mm of the actual stent diameter used 100% (22/22) of the time.

Conclusions: From a diagnostic standpoint 3D CTV does well with an overall accuracy ranging from 82% in the CFV to 91% in the CIV in predicting CIVO. It is also able to accurately predict venous stent diameter and lengths required, rendering it a good tool in the diagnosis and treatment of symptomatic CIVO. (*J Vasc Surg: Venous and Lym Dis* 2021;9:73-80.)

Keywords: Computerized tomography venogram; Chronic iliofemoral venous obstruction; Iliac vein stenting; May Thurner syndrome; Post thrombotic syndrome

The last two decades have witnessed a great increase in the use of iliac vein stenting for chronic obstructive lesions in symptomatic patients.¹⁻¹⁰ Intravascular ultrasound (IVUS) examination has been established as the gold standard for confirmation of diagnosis and treatment in such patients.¹¹⁻¹³ However, IVUS examination is

invasive and cannot be used as the initial mode of testing for chronic iliofemoral venous obstruction (CIVO). Duplex ultrasound (DUS) examination is the most often used screening tool to make a diagnosis of CIVO. The shortcomings of DUS examination include an inability to accurately visualize the iliac venous segment owing to the depth or tortuosity of the vessel or owing to acoustic shadowing. A computed tomography venogram (CTV) is able to overcome problems associated with DUS examination. This study endeavors to explore the ability of three-dimensional (3D) CTV in diagnosing CIVO by comparing it to IVUS examination by evaluating the minimal (smallest) luminal areas obtained in common femoral, external iliac and common iliac veins in both studies. Such comparative data is lacking. A recent study compared CTV with IVUS, but used vein diameters for the comparison.¹⁴ However, luminal areas can be

From The RANE Center for Venous & Lymphatic Diseases, St. Dominic Hospital. Author conflict of interest: none.

Additional material for this article may be found online at www.jvsvenous.org. Correspondence: Arjun Jayaraj, MD, The RANE Center, 971 Lakeland Dr, Ste 401, Jackson, MS 39216 (e-mail: jayaraj.arjun2015@gmail.com).

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computed more easily with minimal error compared with observer estimation of minimal diameter. Additionally, this study explores the effectiveness of 3D CTV in predicting stent sizing, both luminal caliber and stent length(s).

METHODS

Study design. This single-center retrospective analyzed prospectively collected data on 22 continuous patients who underwent CTV for initial assessment and IVUS interrogation for confirmation of diagnosis of CIVO. Patients who had stenting performed in the setting of chronic total occlusion of the iliofemoral segment or acute iliofemoral deep venous thrombosis were excluded. Patient consent was obtained for the study, as was hospital institutional review board approval.

Setting. The center is a tertiary center for management of venous and lymphatic disorders.

Participants. Patients presenting with chronic disabling symptoms suggestive of CIVO including swelling, pain, heaviness, tiredness, hyperpigmentation, and/or lipodermatosclerosis who had failed conservative therapy including use of compression stockings (or intolerant to them) formed the study cohort. Patients who had chronic total occlusions or those who presented with acute iliofemoral deep venous thrombosis were excluded.

CTV. CTV was performed using the 128 slice Siemens scanner (Siemens Healthineers, Erlangen, Germany) using the Stanford protocol. 5mm slices were obtained and evaluated using 3D reconstruction (Fig 1). The minimal (smallest) luminal areas of the common iliac, external iliac and common femoral veins were evaluated (Fig 2) by circumference tracing using M2S software (M2S Inc, West Lebanon, NH). The minimal luminal area just below the anticipated caudal landing zone of the stent but above the femoral venous confluence was termed as the inflow channel luminal area. This inflow channel luminal area was used to determine the stent diameter for the caudal (CFV/EIV) stent (Table) with a 2-mm addition to the diameter of the cranial (CIV/EIV) stent to allow for adequate upscaling.¹⁵⁻¹⁷ Based on this criterion, the smallest stent size that was used in the common femoral vein was 14 mm and in the common iliac vein was 16 mm. Center line lengths (lengths obtained along the central axis of the vessel generated by use of 3D reconstruction software) were computed from the landing zone cranial to iliocaaval junction (approximately 10 mm cranial) to the caudal landing zone in the external iliac or common femoral vein (Fig 3). This was used to predict stent lengths for Wallstents (Boston Scientific, Marlborough, Mass) allowing for adequate overlap between stents.

ARTICLE HIGHLIGHTS

- **Type of Research:** Single-center, retrospective analysis of prospectively collected data
- **Key Findings:** In 22 patients, three-dimensional computed tomography venogram was able to diagnose chronic iliofemoral venous obstruction with an overall accuracy of 91%, 86% and 82% in the common iliac, external iliac, common femoral veins segments, respectively, when compared with intravascular ultrasound examination. It was also adept at predicting both the stent diameter and length(s) that was necessary to correct the obstruction.
- **Take Home Message:** Three-dimensional computed tomography venogram enabled accurate diagnosis and treatment of chronic iliofemoral venous obstruction.

IVUS examination. IVUS was performed for confirmation of diagnosis through use of the Visions PV .035 catheter (Phillips Volcano, San Diego, Calif) after access was obtained in the mid-thigh femoral vein under ultrasound guidance. This process enabled an accurate assessment of the cranial femoral vein and above. Although an initial and completion venograms were performed when there was no contraindication, the findings on the uniplanar venogram were not used to confirm diagnosis or for determining stent configuration. This was all done through use of IVUS examination. The catheter has a 90-cm length and affords a 60-mm maximum imaging diameter. Minimal luminal areas of the common iliac, external iliac and common femoral veins of the involved extremity were measured using IVUS planimetry (Supplementary Fig, online only). A minimal luminal area of less than 200 mm², 150 mm², and 125 mm² for the common iliac, external iliac and common femoral veins were considered abnormal,¹⁸ warranting treatment in the symptomatic patient. These numbers were used as the cut-off points for defining abnormal vs normal luminal areas in the study. The minimal luminal area just below the anticipated caudal landing zone of the stent but above the femoral venous confluence was termed as the inflow channel luminal area. Stent diameter determination was carried out using this inflow channel luminal area as noted elsewhere in this article. With regard to determining the stent length, the IVUS catheter has radiopaque markings that can be used to determine stent length once the tip is placed in the appropriate cranial landing zone. For the purposes of this study, stent lengths were measured from intraoperative images after stent deployment and angioplasty, thereby factoring in loss of length from foreshortening and overlap.

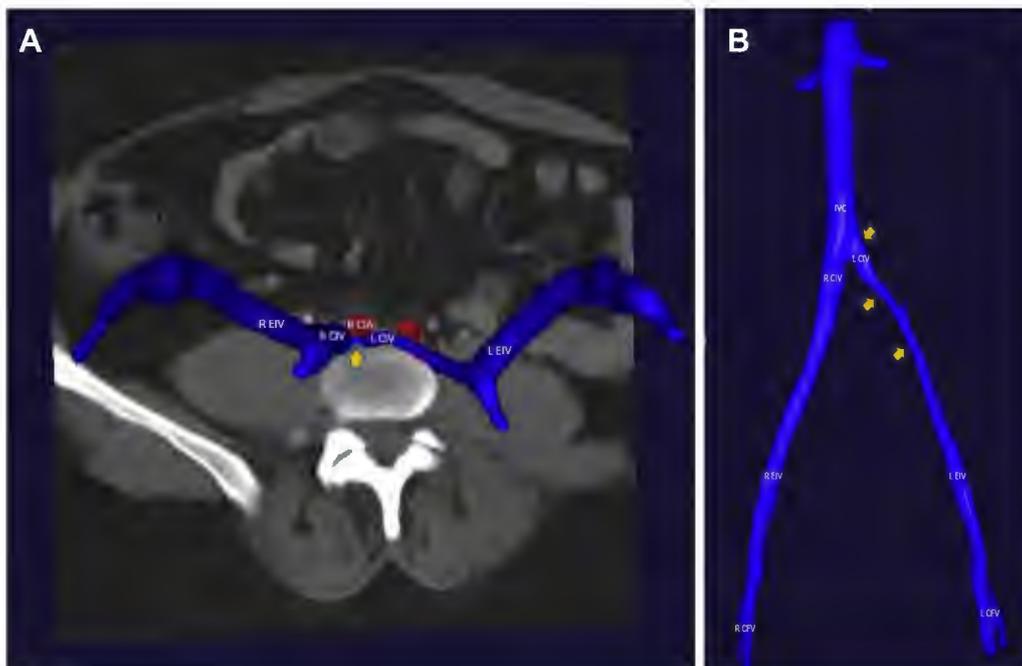


Fig 1. Three-dimensional (3D) computed tomography venogram (CTV) reconstructions in the axial (A) and coronal (B) views demonstrating severe left iliofemoral venous obstruction. Orange arrows point to areas of obstruction. IVC, Inferior vena cava; CIV, common iliac vein; EIV, external iliac vein; CFV, common femoral vein; CIA, common iliac artery; R, right; L, left.

Stent technique. Stenting was carried out using a composite stent configuration with a Wallstent body and a Z stent top. The diameter of the Wallstents used ranged from 14 to 24 mm, whereas that for the Z stent (Cook Medical, Bloomington, Ind) ranged from 20 to 30 mm. Stenting merited coverage of all areas of obstruction with adequate overlap (approximately 2-3 cm) between stents to ensure adequate inflow and outflow and to prevent shelving. In this regard, extension into the inferior

vena cava was typically up to 10 mm for the Wallstent and about 20 mm for the Z stent and caudal nondiseased venous segment with good inflow was used as the caudal landing zone. The details of this technique have been described previously.¹⁹

Perioperative care. Patients were typically admitted for overnight observation to ensure adequate pain control in the immediate postoperative period. Antithrombotic

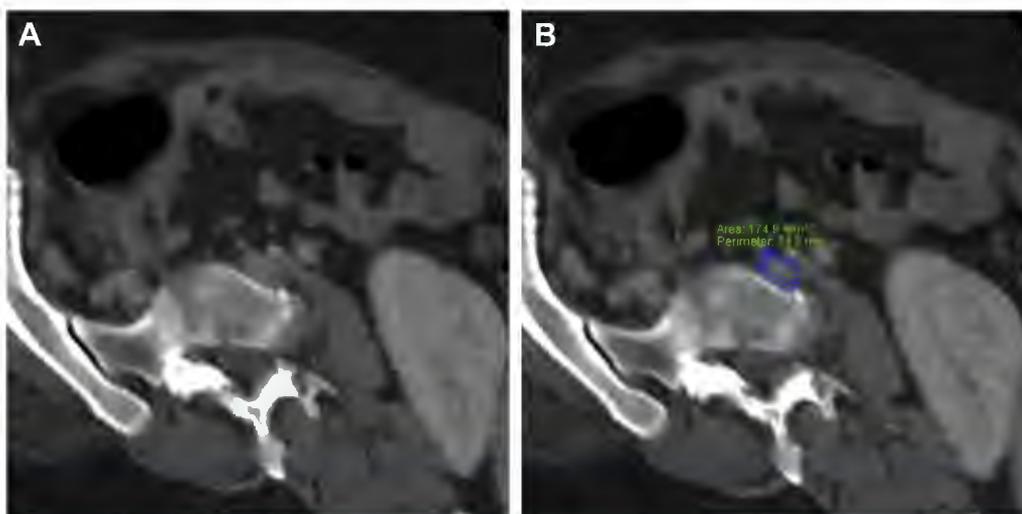


Fig 2. Three-dimensional (3D) computed tomography venogram (CTV) before (A) and after (B) circumferential tracing to determine the narrowest luminal area of the left common iliac vein. Here the luminal area is 175 mm².

Table. Inflow channel minimal luminal area derived caudal Wallstent diameter

Inflow channel minimal luminal area, mm ²	Caudal/cranial Wallstent diameter, mm
<125	14/16
125-149	16/18
150-199	18/20
200-249	20/22
250-299	22/24
>300	24/24

therapy was started in the perioperative period and continued for at least for 6 months post operatively. Pre-operatively, this included bivalirudin 75 mg and prophylactic enoxaparin (30-40 mg subcutaneously). In the postoperative setting, therapeutic enoxaparin (1 mg/kg/dose subcutaneously every 12 hours) was continued while in the hospital. After discharge, the antithrombotic therapy consisted of a combination of anticoagulation (direct oral anticoagulant or warfarin), cilostazol, and aspirin 81 mg as long as no contraindications existed for their use. An extended duration of anticoagulation was pursued in patients with thrombophilia or those who developed stent complications (severe/rapidly progressive in-

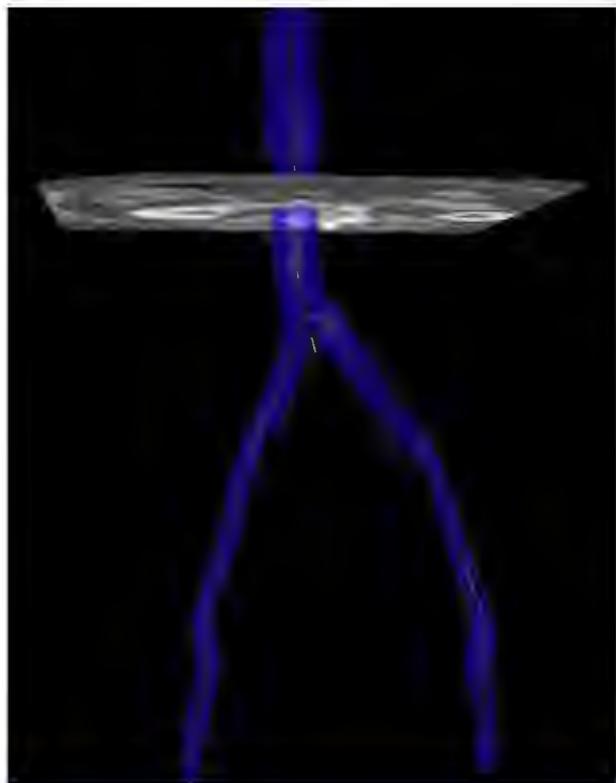


Fig 3. Three-dimensional (3D) reconstruction using M2S software with centerline display of the entire femoro-iliocaval system on both sides with a single caval axial computed tomography (CT) image. The centerline enables computation of relevant lengths.

stent restenosis or occlusion) after discontinuation of anticoagulation. Aspirin 81 was typically continued life-long. Additionally, after the intervention patients received a pair each of compression wraps and graduated compression stockings (20-30 mm Hg) with the recommendation to be worn regularly. Follow-up from an imaging standpoint included DUS examination that was done on day 1, at 2 and 4 weeks, at 3 months and 6 months, at 1 year, and yearly thereafter if patients remained asymptomatic without any evidence of stent malfunction. Clinic visits started at 6 weeks after the procedure and at every DUS appointment subsequently.

Statistical analysis. All statistical analysis was performed using SPSS statistics version 26 (IBM Corp, Armonk, NY). The correlation between 3D CTV and IVUS examination obtained luminal areas was appraised using Pearson correlation. Bland-Altman analysis was used to evaluate agreement between measurements obtained by 3D CTV and IVUS examination. This process was undertaken after confirming normal distribution of the differences between luminal areas obtained by the two methods. Additionally, diagnostic analysis was carried out by determining sensitivity, specificity, positive predictive value, negative predictive value, and accuracy. Stent diameters and lengths as predicted by 3D CTV were compared with actual stent diameters and lengths used. A *P* value of .05 or less was considered significant.

RESULTS

Of the 22 patients, there were 15 women and 7 men. The mean age was 60 ± 12.3 years. The mean BMI was 38.0 ± 6.6 . The symptomatic lower limb was the right one in 9 patients and left in 13 patients. Fifteen patients had post thrombotic syndrome, and seven had non-thrombotic iliac vein lesions. With regard to CEAP scores, although there were no CEAP 0-2 patients, there was 1 (4%) C3 patient, 16 (73%) C4 patients, 2 (9%) C5 patients, and 3 (14%) C6 patients.

Clinical improvement after the intervention. After stenting, there was clinical improvement in the entire cohort as evidenced by improvement in the mean VCSS score at 12 months from a baseline of 6.0 ± 0.9 to 3.6 ± 0.6 ($P = .04$). The mean visual analog pain score (on a scale of 0 [no pain] to 10 [worst possible pain]) improved from 6.6 ± 0.8 to 2.7 ± 0.9 ($P = .008$) over the same time frame.

Correlation between 3D CTV and IVUS obtained luminal areas. Pearson correlation statistic for luminal areas of the common iliac vein between CTV and IVUS was 0.89 ($P < .01$). The statistic for the external iliac vein was 0.77 ($P < .01$) and for the common femoral vein was 0.69 ($P < .01$). The correlation statistic for the inflow channel luminal area was 0.90 ($P < .01$).

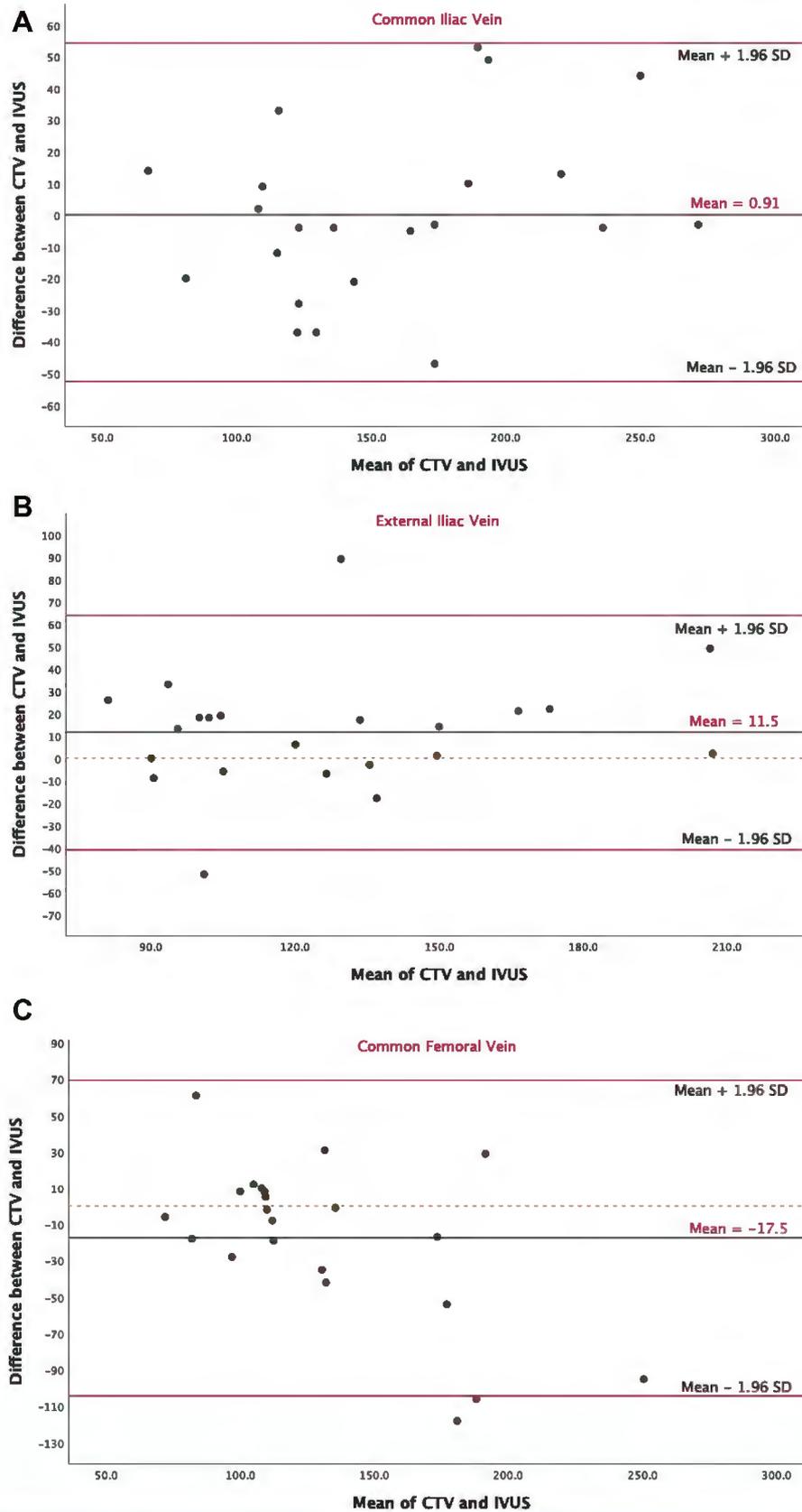


Fig 4. **A**, Bland-Altman plot for agreement interval between the intravascular ultrasound (IVUS) luminal areas and Three-dimensional (3D) computed tomography venogram (CTV) luminal areas for the common iliac vein. **B**, Bland-Altman plot for agreement interval between IVUS luminal areas and three-dimensional (3D) CTV luminal areas for the external iliac vein. **C**, Bland-Altman plot for agreement interval between IVUS luminal areas and 3D CTV luminal areas for the common femoral vein.

Agreement between 3D CTV and IVUS obtained luminal areas. Bland-Altman plots were computed to evaluate agreement between the luminal areas obtained by the two techniques. These are depicted in Fig 4, A-C. The mean of the differences between measurements obtained by 3D CTV and IVUS examination of the common iliac vein was 0.9 mm². For the external iliac vein, the mean of the differences was 11.5 mm², and for the common femoral vein was -17.5 mm². These numbers are suggestive of 3D CTV underestimating the luminal areas in the common and external iliac veins and overestimating the luminal area in the common femoral vein.

Diagnostic accuracy of 3D CTV in predicting CIVO. The sensitivity of 3D CTV in diagnosing CIVO in the CIV, EIV, and CFV was 100%, 100%, and 80%, respectively. The specificity was 67%, 57%, and 86%, respectively, in the CIV, EIV, and CFV segments. The positive predictive value in the CIV, EIV, and CFV segments was 89%, 83%, and 92%, whereas the negative predictive value was 100%, 100%, and 67%, respectively. The overall accuracy was 91%, 86%, and 82% in the CIV, EIV, and CFV segments, respectively.

Prediction of stent characteristics by 3D CTV. The 3D CTV was able to predict stent length within a median -9.5mm of the actual stent length used (Supplementary Table, online only). In essence, the 3D CTV tended to underpredict the stent length required. With respect to stent diameter, 3D CTV was able to predict within 2 mm of the actual stent diameter used 91% (20/22) of the time and within 4 mm of the actual stent diameter used 100% (22/22) of the time.

DISCUSSION

DUS examination is generally used as the first-line screening tool for CIVO in most practices because of its availability and cost effectiveness as a diagnostic tool. However, DUS examination is at times unable to visualize the iliac segments owing to the depth of the vessel and/or acoustic shadowing. It also has a limited ability to help with operative planning. These factors highlight the need for another diagnostic tool to be able to accurately diagnose CIVO and potentially help with treatment planning; 3D CTV has the potential to fill this gap.

Diagnostic capability of 3D CTV in detecting CIVO. Unlike DUS examination, CTV is able to visualize and discern individual segments of the iliofemoral territory. The use of 3D reconstruction further amplifies this effect. Because IVUS luminal areas are what are used in our practice for diagnosis of CIVO, we felt that it would be best to use luminal areas derived from circumference tracing around the centerline on the 3D reconstruction for comparison (Fig 2). This process was done using M2Ssoftware. From a correlation standpoint, there is good to excellent statistically significant correlation between luminal areas obtained via 3D CTV to those obtained via IVUS. This

correlation is highest in the common iliac vein (0.89) and lowest in the common femoral vein (0.69).

However, such correlation alone is not enough, because it cannot assess the relationship between the differences. Such study of the differences between measurements is possible through Bland-Altman analysis. The latter found that the mean of the differences between luminal area measurements obtained by 3D CTV and IVUS of the common iliac vein was only 0.9 mm². This difference denotes excellent agreement between the two studies for the common iliac vein. Agreement was also noted for luminal area measurements in the external iliac vein where the mean of the differences was 11.5 mm². Such a positive difference denotes that the CTV underestimates the luminal area in the EIV by 11.5 mm². This difference represents 7.7% of the normal luminal area for the EIV, which is 150 mm². With regard to the common femoral vein, the mean of the differences was -17.5 mm². Here the 3D CTV overestimates the IVUS measurements by 17.5 mm². This difference represents approximately 14% of the normal luminal area of the common femoral vein (125 mm²). Overall, there is good agreement between the differences of the luminal areas obtained by the two techniques (0%-14% of normal luminal area), with the agreement being highest in the CIV and lowest in the CFV.

With regard to the diagnostic accuracy of the 3D CTV, the sensitivity of 3D CTV in diagnosing CIVO in the CIV, EIV, and CFV were found to be 100%, 100%, and 80%. This excellent sensitivity reflects the ability of 3D CTV to identify CIVO in patients who have CIVO rendering it a good screening tool. The specificity of 3D CTV in diagnosing CIVO was noted to be 67%, 57%, and 86%, respectively, in the CIV, EIV, and CFV segments. The test also had excellent predictive values, with the positive predictive value in the CIV, EIV, and CFV segments noted to be 89%, 83%, and 92%. The negative predictive values were determined to be 100%, 100%, and 67%, respectively, in the CIV, EIV, and CFV segments. The overall accuracy was 91%, 86%, and 82% in the CIV, EIV, and CFV segments. These results support the diagnostic capabilities of 3D CTV in identifying patients with CIVO.

Usefulness of 3D CTV in operative planning. Among the key characteristics of iliac vein stenting are determining adequate cranial/caudal landing zones, ideal stent diameter, and suitable stent length to cover all areas of obstruction. The ability of 3D CTV to determine with good accuracy the area of maximal obstruction in the CIV and CFV enable prediction of cranial and caudal landing zones. With regard to the determination of stent diameter, the inflow channel luminal area is what is used to predict stent size on IVUS examination (Table). The excellent correlation between CTV and IVUS examination determined inflow channel luminal areas,

substantiates the ability of the 3D CTV to predict stent diameter. In fact, 3D CTV was able to predict within 2 mm of the actual Wallstent diameter used 91% (20/22) of the time and within 4 mm of the actual Wallstent diameter used 100% (22/22) of the time. With regard to determination of stent length, 3D CTV was able to predict stent length within a median of -9.5 mm of the actual stent length used ([Supplementary Table](#), online only). In essence, 3D CTV tended to underpredict the stent length required by less than 1 cm.

These findings reflect the ability of 3D CTV to not only diagnose CIVO lesions with good accuracy, but also to help with operative planning by determining landing zones, stent diameters, and stent lengths. Although IVUS examination remains the current gold standard, the use of 3D CTV in patients presenting with symptoms suggestive of CIVO can help to establish the diagnosis and aid in treatment planning. The hydration status of patients undergoing cross-sectional imaging studies and intervention has been brought up as a shortcoming. At our institution, CT scans with contrast are performed only if the patient has a serum creatinine of less than 1.5. Additionally, given that our patients get hydrated before both CT scanning and the intervention, and the issue of dehydration is less likely to impact the diagnosis. Cost, need for contrast agent, and radiation exposure, however, have to be borne in mind before the use of this study. Nevertheless, in patients who are already undergoing CTV as part of their preoperative planning, addition of 3D reconstruction can provide the interventionalist with much-needed data to aid in diagnosis and treatment. The CTV can also provide additional information regarding intraabdominal and pelvic pathology as a cause for iliac vein obstruction. A positive 3D CTV in the symptomatic patient with a high suspicion for CIVO needs to be confirmed by IVUS interrogation with ilio-caval stenting dictated by results of the IVUS study.

Limitations of this study include the small sample size and the inherent retrospective nature of the study. These 3D reconstructions require dedicated software, which can be expensive, depending on use. Practices that use the software for planning aortic interventions will find additional use of such software in the diagnosis and treatment of obstructive iliofemoral venous lesions.

CONCLUSIONS

From a diagnostic standpoint, 3D CTV does well with an overall accuracy ranging from 82% in the CFV going up to 91% in the CIV in predicting CIVO. It is also able to accurately predict venous stent diameter and lengths required rendering thereby rendering it a good tool both in the diagnosis and treatment of symptomatic CIVO. However, obvious drawbacks including radiation exposure and need for contrast agents have to be considered before its use.

AUTHOR CONTRIBUTIONS

Conception and design: AJ
Analysis and interpretation: AJ, SR
Data collection: AJ
Writing the article: AJ
Critical revision of the article: AJ, SR
Final approval of the article: AJ, SR
Statistical analysis: AJ
Obtained funding: Not applicable
Overall responsibility: AJ

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Additional material for this article may be found online at www.jvsvenous.org.



Supplementary Fig (online only). Intravascular ultrasound (IVUS) determination of the right common iliac vein luminal area in a study patient. The minimal luminal area of the common iliac vein (CIV) here is 102 mm². *Dia*, Diameter; *Max*, maximum; *Min*, minimum.

Supplementary Table (online only). Stent length prediction for 22 patients using three-dimensional (3D) computed tomography venogram (CTV)

Patient	Actual stent length, mm	3D CTV predicted, mm	Difference, mm
1	127	111	-16
2	128	120	-8
3	80	125	45
4	86	105	19
5	189	178	-11
6	130	136	6
7	210	196	-14
8	126	133	7
9	110	92	-18
10	80	63	-17
11	115	98	-17
12	92	129	37
13	70	75	5
14	140	139	-1
15	102	110	8
16	93	119	26
17	130	117	-13
18	130	82	-48
19	125	101	-24
20	134	104	-30
21	130	104	-26
22	124	195	71
Median			-9.5

Median of the difference between the 3D CTV predicted lengths and the actual lengths of the stents used are noted.