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Predictors of Clinical Outcomes of Pharmacomechanical Catheter-Directed Thrombolysis for Acute Iliofemoral Deep Vein Thrombosis – Analysis of a Multicenter Randomized Trial

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Abstract

Purpose: To determine if identifiable baseline patient characteristics predict who will benefit from pharmacomechanical catheter-directed thrombolysis (PCDT) of acute iliofemoral DVT.

Materials and Methods: In the ATTRACT multicenter randomized trial, 381 acute iliofemoral DVT patients received PCDT and anticoagulation or anticoagulation alone. Post-hoc regression analyses evaluated correlations between baseline factors and venous clinical outcomes over 24 months. Interaction terms were examined to evaluate for differential effects by treatment arm.

Results: Patients with clinically severe DVT (higher baseline Villalta score) experienced greater effects of PCDT in improving 24-month venous outcomes including moderate-or-severe post-thrombotic syndrome (PTS) (OR [95%CI] per unit increase in baseline Villalta score: PCDT 1.08 [1.01,1.15], Control 1.20 [1.12,1.29], p-interaction=0.03); PTS severity (between-arm differences in Villalta [p-interaction=0.004] and Venous Clinical Severity Scale [VCSS, p-interaction=0.002)] scores); and quality of life (between-arm difference in VEINES-QOL score, p-interaction=0.025). Patients with previous DVT had greater effects of PCDT on 24-month PTS severity than patients without previous DVT (mean [95%CI] between-arm difference in Villalta score: 4.2 [1.56,6.84] vs 0.9 [−0.44,2.26], p-interaction 0.03; VCSS score: 2.6 [0.94,4.21] vs 0.3 [−0.58,1.14], p-interaction=0.02). PCDT effects on some but not all outcomes were greater in patients presenting

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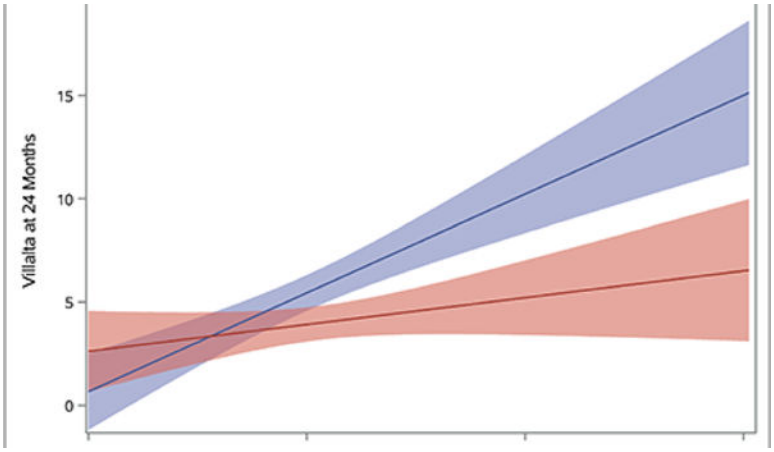
with left-sided DVT (Villalta PTS severity, p-interaction 0.04; venous ulcer, p-interaction 0.0499) or a non-compressible popliteal vein (PTS, p-interaction 0.02). PCDT effects did not vary by sex, race, ethnicity, BMI, symptom duration, hypertension, diabetes, or hypercholesterolemia.

Conclusion: In patients with acute iliofemoral DVT, greater presenting clinical severity (higher baseline Villalta score) and a history of previous DVT predict enhanced benefits from PCDT.

Graphical Abstract



Introduction

Patients with acute iliofemoral deep vein thrombosis (DVT) frequently develop the post-thrombotic syndrome (PTS) (1). Catheter-directed thrombolysis (CDT, image-guided intra-thrombus fibrinolytic drug administration) and pharmacomechanical CDT (PCDT, includes mechanical thrombectomy devices) have been used to treat iliofemoral DVT for many years (2). In the iliofemoral DVT subgroup of the Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) Trial, PCDT led to thrombus reduction and restoration of venous patency in most treated patients, but did not reduce the occurrence of PTS over 24 months (3). PCDT did improve important secondary outcomes but the average size of these benefits and the associated improvements in health-related quality of life (QOL) were modest (4). As the trial also observed increased major bleeding in PCDT recipients, it is likely that PCDT is an optimal first-line treatment for some, but not all, iliofemoral DVT patients (5).

Published reports from ATTRACT have evaluated correlations of a limited number of pre-specified baseline factors with PCDT treatment effects, with a central focus upon the study's primary outcome (cumulative occurrence of PTS over 24 months) (3–5). However, additional data elements were collected at study entry to characterize the study population including demographic factors, co-morbidities, and characteristics of the index DVT. Key secondary outcomes that appeared to be favorably influenced by PCDT included the severity of PTS, the occurrence of moderate-or-severe PTS, and venous disease-specific QOL (3–5). This study describes a post-hoc exploratory analysis aimed at identifying additional baseline predictors of PCDT treatment effect upon 24-month outcomes in patients with acute iliofemoral DVT.

Materials and Methods

Study Design, Patients, and Treatments

This study is a post-hoc analysis of the iliofemoral DVT subgroup of the ATTRACT trial, a Phase III, multicenter, open-label, assessor-blinded, randomized controlled trial. All patients provided written informed consent. The study was approved by the institutional review boards of all clinical centers (Appendix E1). The population, methods, and main outcomes of ATTRACT and its iliofemoral DVT subgroup have been previously described (3–5). Briefly, patients with acute symptomatic proximal DVT were randomly assigned to receive, or not receive, PCDT for initial DVT treatment at 56 U.S. clinical centers. Randomization was stratified by clinical center and by whether there was involvement of the iliac or common femoral vein (iliofemoral DVT), or not (femoral-popliteal DVT), at baseline. All study patients were to receive anticoagulant therapy and elastic compression stockings (BSN Medical); in addition, patients in the PCDT Arm underwent PCDT at a median of one day post-randomization. PCDT involved the intra-thrombus delivery of recombinant tissue plasminogen activator (rt-PA, alteplase, Activase ®, Genentech, South San Francisco, CA) by board-certified physicians using one of several methods, after which they used catheter aspiration, mechanical thrombectomy, balloon maceration, and/or stent placement to restore venous patency (5).

This analysis includes 381 ATTRACT patients with acute iliofemoral DVT who actually received their study-assigned treatment within 7 days (per-protocol study population) (Figure 1).

Baseline Characteristics

Previous publications have summarized subgroup analyses for 11 categorically expressed baseline factors that were pre-specified in the study's statistical analysis plan (3–5). This post hoc analysis considers a more detailed set of potential PCDT effect predictors collected at baseline including demographic characteristics (sex, continuous age, race, Hispanic/Latino ethnicity), medical history (hypertension, diabetes, hypercholesterolemia, previous DVT, continuous body-mass index [BMI]), and index DVT features (right or left leg, provoked or unprovoked, popliteal vein compressibility, continuous DVT symptom duration, continuous Villalta clinical severity scores). For some factors, categories that did not constitute at least 10% of the population were combined with an adjacent category for analysis (Appendix E2). The distributions of baseline factors were well-balanced between the two treatment groups (Table 1).

Clinical Outcomes

Patient outcomes were assessed at 6, 12, 18, and 24 months after randomization by blinded clinician examiners. PTS was evaluated with the Villalta Scale, in which 5 patient-reported symptoms (pain, cramps, heaviness, pruritus, paresthesia) and 6 clinician-observed signs (edema, skin induration, hyperpigmentation, venous ectasia, redness, pain on calf compression) are scored 0–3 and summed together (6). PTS was also assessed using the modified Venous Clinical Severity Scale (VCSS) in which 9 items (8 signs, 1 symptom) are scored 0–3 and summed together (7).

Categorical clinical outcomes in this analysis were the cumulative occurrence over 24 months of: any PTS (Villalta ≥5 or an ulcer), moderate-or-severe PTS (Villalta ≥10 or an ulcer), severe PTS (Villalta ≥15 or an ulcer), and venous ulcer. Continuous clinical outcomes included PTS severity at 24 months as measured by the Villalta score (range, 0–33) and modified VCSS score (range, 0–27); for both scales, higher scores indicate more severe PTS (6,7). Patient-reported venous disease-specific QOL at 24 months was assessed using the Venous Insufficiency Epidemiologic and Economic Quality of Life Survey (baseline-adjusted VEINES-QOL and VEINES-Sym subscores, reflecting venous QOL and venous symptoms, respectively) (4,8).

Statistical Analysis

Descriptive statistics were used to summarize baseline patient characteristics. Continuous data were summarized using mean (standard deviation [SD]) and median (inter-quartile range [IQR]). Categorical variables were summarized as proportions. Kruskal-Wallis, Chi-Square, and Fisher's Exact Tests (when appropriate) were performed to evaluate for associations of baseline variables with treatment response outcomes. Logistic regression was used to assess associations between independent variables and four binary outcomes (PTS, moderate-or-severe PTS, severe PTS, venous ulcer). Linear regression models were used to identify associations between baseline variables and four continuous outcomes at 24 months: Villalta, VCSS, VEINES-QOL, and VEINES-Sym scores. Each model examined the interaction term between the treatment assignment and baseline variables to assess whether there was a differential treatment effect for each level of the baseline variables. The odds ratios (OR) and their 95% confidence intervals (95%CI) were reported for logistic regression models. Model estimates, standard error, and mean differences were reported for linear regression models. To visualize the associations between treatment assignment and four continuous baseline variables of interest (Villalta score, DVT symptom duration, patient age, BMI), plots depicting the predicted probabilities of PTS and moderate-or-severe PTS as a function of the continuous baseline variables, with 95%CIs, were created for each treatment group based on the logistic regression model. Plots were also created to depict the mean scores at 24 months on the continuous outcome measures, with 95%CIs, as a function of the same four continuous baseline variables of interest.

A two-sided P value < 0.05 was considered statistically significant for these exploratory analyses. Analyses were conducted in SAS version 9.4 (SAS, Cary, NC).

Results

Demographical Factors

Patient sex, race (white versus non-white), and ethnicity (Hispanic/Latino versus not) were not associated with differential effects of PCDT upon binary (Figure 2, Appendix E3) or continuous (Figure 3, Appendix E4) outcomes. Younger patients receiving PCDT had nominally lower odds of developing moderate-or-severe PTS over 24 months, but this finding was not statistically significant (OR [95% CI] per 5-year increase in age: PCDT 1.20 [1.05, 1.40], Control 1.03 [0.91, 1.15], p-interaction=0.08). Predicted probability plots from this model (Figure 4, Appendices E5-E8) suggest that PCDT may be more likely

to reduce moderate-or-severe PTS relative to Control treatment in younger patients up to approximately 650 years of age (Figure 4C).

Medical History and Co-Morbidities

Patients with previous DVT experienced a greater effect of PCDT upon 24-month PTS severity than patients with no previous DVT (mean [95% CI] PCDT-Control difference in Villalta score 4.2 [1.56, 6.84] points versus 0.9 [−0.44, 2.26] points, p-interaction=0.03) (Figure 3A); and VCSS score (2.6 [0.94, 4.21] points versus 0.3 [−0.58, 1.14] points, p-interaction=0.02) (Figure 3B). PCDT's effects upon binary outcomes (Figure 2) and QOL (Appendix E4) were nominally greater in patients with previous DVT compared to no previous DVT, but these findings were not statistically significant.

The impact of baseline continuous variables on PCDT effects on continuous outcomes are presented in Figure 5 and Appendices E9-E17. Continuous BMI was not a statistically significant predictor of PCDT treatment effect in the overall model (moderate-or-severe PTS: OR [95% CI] per 5-unit increase in BMI: PCDT 1.14 [0.90, 1.44], Control 1.31 [1.08, 1.59], p-interaction=0.36). Predicted probability plots from this model depict a gradual divergence of the PCDT and Control curves for moderate-or-severe PTS as the BMI increased (Figure 4D). The effect of PCDT appears prominent for patients with a very high BMI (moderate-or-severe PTS in patients with BMI > 40 kg/m^2: OR 0.23 [0.07, 0.75]), but the 95% confidence intervals overlap with those for patients with BMI < 40 kg/m^2 (OR 0.71 [0.41, 1.21]), perhaps reflecting the fact that these estimates are based on very small numbers of patients who had a BMI of that magnitude. BMI did not exert significant effects on between-arm differences in Villalta, VCSS, and VEINES-QOL scores (Appendices E15-E17) (). Pooled across treatment arms, patients with elevated BMI did have increased odds of developing moderate-or-severe PTS (p=0.006).

A history of hypertension, diabetes, or hypercholesterolemia did not show a differential effect by treatment arm on clinical outcomes (Figures 2–3, Appendices E3-E4).

Characteristics of Presenting DVT Episode

A patient's presenting DVT clinical severity was a key predictor of the effects of PCDT upon 24-month clinical outcomes in this analysis of iliofemoral DVT patients. Adjusted for treatment assignment, as the baseline Villalta score increased, the occurrence of PTS increased (p<0.0001 in logistic interaction model). Use of PCDT was associated with lower odds of moderate-or-severe PTS in patients with higher baseline Villalta scores (OR [95% CI] per unit increase in baseline Villalta score: PCDT 1.08 [1.01, 1.15], Control 1.20 [1.12, 1.29], p-interaction=0.03). This effect was also nominally apparent for PTS but was not statistical significant (OR [95% CI] per unit increase in baseline Villalta score: PCDT 1.06 [1.01, 1.13], Control 1.14 [1.07, 1.21], p-interaction=0.11). Predicted probability plots from the models suggest that relative to Control, PCDT is most likely to reduce moderate-or-severe PTS in patients with a baseline Villalta score that exceeds 10 (Figure 4A).

As the baseline Villalta score increased, the benefits of PCDT upon PTS severity and venous QOL also increased. For patients with a baseline Villalta score > 10, the mean 24-month Villalta (p-interaction=0.004) (Figure 5A) and VCSS (p-interaction=0.002) (Figure

5B) scores were lower in the PCDT Arm compared with the Control Arm, and the mean VEINES-QOL (p-interaction=0.025) (Figure 5C) and VEINES-Sym (p-interaction=0.02) scores were higher for PCDT compared with Control, with 95% confidence intervals that did not overlap.

DVT symptom duration did not predict the effects of PCDT on 24-month occurrences of PTS (OR [95% CI] per additional day of symptoms: PCDT 1.04 [0.96, 1.11], Control 1.00 [0.94, 1.06], p-interaction=0.46) or moderate-or-severe PTS (p-interaction=0.52), or on between-arm differences in 24-month Villalta or VCSS scores. Although gradual divergence of PCDT and Control curves for VEINES-QOL and VEINES-Sym is apparent as symptom duration increases, the 95% CIs around these curves overlapped at all symptom durations (Appendices E9-E11).

For all outcomes assessed over 24 months, PCDT was nominally more effective in patients with left leg DVT than right leg DVT, but the differences only reached statistical significance for PTS severity (mean [95% CI] PCDT-Control difference in Villalta score: left DVT 2.60 [1.04, 4.12] points, right DVT 0.01 [−1.96, 1.98] points; p-interaction=0.04) (Figure 3A) and venous ulcer (left leg: PCDT 2.4% versus Control 7.4%; right leg: PCDT 9.0% versus Control 4.3%; p-interaction=0.049) (Appendix E3). Similarly, patients with a non-compressible popliteal vein appeared to have nominally more favorable outcomes with PCDT than patients with a compressible popliteal vein, but significance was only seen for PTS: (compressible: PCDT 64% versus Control 37%; non-compressible: PCDT 47% versus Control 54%, p-interaction=0.02) (Figures 2–3). The presence of provoking risk factors at the time of the index DVT did not show a differential effect by treatment arm upon clinical outcomes (Figures 2–3).

Discussion

This analysis of the ATTRACT Trial found that in patients with acute iliofemoral DVT, (a) higher presenting clinical severity (baseline Villalta score) predicts greater benefits of PCDT (versus anticoagulation alone) upon PTS severity, moderate-or-severe PTS, and venous QOL over 24 months; (b) a history of previous DVT predicts greater PCDT effects in reducing 24-month PTS severity; (c) patients with left-sided DVT or a non-compressible popliteal vein at baseline may experience stronger PCDT effects on some 24-month outcomes, but these findings were not compelling in magnitude or consistency; and (d) PCDT treatment effects did not differ based on sex, race, Hispanic/Latino ethnicity, continuous BMI, continuous symptom duration (within trial parameters), hypertension, diabetes, hypercholesterolemia, or provoked DVT.

Although some societal guidelines now suggest use of CDT/PCDT for selected patients with acute iliofemoral DVT, evidence linking discernible baseline patient characteristics to the treatment effects of endovascular therapies has not been available to guide such decisions (9,10). In the randomized Catheter-Directed Venous Thrombolysis (CAVENT) Trial, baseline factors including symptom duration (≤21 days), thrombus extent, and side of DVT did not influence thrombolysis grade, residual thrombus score, patency, or PTS (11,12). Late patency was more frequent in women but PTS was similar for men and

women. Left leg DVT predicted lower 24-month Villalta scores than right leg DVT, but PTS occurrence was similar in both legs. The randomized CAVA Trial, which studied ultrasound-assisted CDT for acute iliofemoral DVT, was unable to identify baseline modifiers of the treatment effects of the intervention (13).

A pre-specified subgroup analysis of ATTRACT found PCDT to lead to a higher PTS occurrence over 2 years in proximal DVT patients ≥ 65 years of age, compared with younger patients (p-interaction=0.04); age ≥ 65 years also predicted major bleeding ($p<0.0001$) (5,14). In the trial's iliofemoral DVT subgroup, PCDT reduced the occurrence of moderate-or-severe PTS over 2 years in patients < 65 years old (PCDT 16% versus Control 30%) compared with patients ≥ 65 years old (PCDT 28% versus Control 19%) (p-interaction=0.04) (3). Hence, it has been noted that patient age is relevant to factor into PCDT treatment decisions. That conclusion is supported to some extent here by the predicted probability plots which suggest that moderate-or-severe PTS is less frequent in PCDT-treated patients up to around 65 years of age. However, viewed as a continuous variable, age was not a statistically significant predictor of PCDT effect in this study, perhaps partly due to the limited number of very young patients in the analysis.

In this analysis, a history of previous DVT predicted a stronger effect of PCDT upon PTS severity. In theory, this finding could be explained by (a) a greater ability of anticoagulation alone to permit restoration of a normal venous system in limbs with only acute thrombus (no previous event); and/or (b) a greater likelihood that patients with previous DVT had chronic venous abnormalities (compression, residual thrombus) that were addressed via adjunctive endovascular therapy during PCDT. Similarly, patients with a compressible popliteal vein may respond well to anticoagulation alone, and treatment of iliac vein compression in patients with left leg DVT could account for the finding of greater PCDT benefit in some analyses.

Randomized trials of CDT/PCDT have limited enrollment to patients with symptom duration ≤ 14–21 days. In a venogram analysis of ATTRACT PCDT recipients, patients randomized within 7 days of symptom onset had a higher rate of complete lysis (35% versus 23%, p-interaction=0.04) and nominally greater thrombus removal (88% versus 82%, $p=0.06$) than patients randomized 7–14 days after symptom onset (15). However, complete lysis did not lead to reduced PTS and the effect of PCDT on PTS prevention did not differ between these two groups. The current study, which analyzed symptom duration as a continuous variable, also does not suggest a major effect on clinical outcomes that would argue for expedited conduct of PCDT.

The current analysis identified greater presenting DVT severity (higher baseline Villalta score) as a key predictor of enhanced PCDT effect in improving 24-month venous outcomes. Patients with a baseline Villalta score >10 experienced very high rates of moderate-or-severe PTS. In these patients, PCDT reduces the probability of developing moderate-or-severe PTS by over one-third, with the projected effect increasing as the baseline clinical severity increases. These effects were also visualized in consistently larger differences between the PCDT and Control Arms in PTS severity scores and QOL in patients with severe clinical presentations.

The Villalta Scale was originally developed as a tool to identify and quantify PTS, and is endorsed for this purpose by the International Society of Hemostasis and Thrombosis (6). In ATTRACT, the Villalta scale was also used to grade the clinical severity of DVT in the acute phase. The correlations identified in this analysis suggest that using the Villalta Scale at the time of DVT diagnosis may help in stratifying a patient's risk of developing clinically important PTS and in predicting the effects of more aggressive treatment.

The current analysis has several limitations. In ATTRACT, benefits of PCDT upon PTS severity and venous QOL were mainly apparent in the iliofemoral DVT subgroup. Stratification of randomization by baseline thrombus extent enhanced the study's ability to evaluate PCDT treatment effects within each anatomic subgroup. For these reasons, the current analysis was limited to the iliofemoral subgroup; however, this reduced the sample size and statistical power. The study was not able to analyze genetic determinants or other biomarkers that might predict PCDT effects. Because this study was intended as an exploratory analysis that would transparently present the observed outcomes against the baseline factors, subgrouping of continuous scale data by arbitrarily selected threshold cut-points was not performed, and a P-value threshold of 0.05 was used for statistical significance. The predicted probability plots should be interpreted with care since for any variable, the number of patients at each point on the spectrum varied, precluding robust statistical comparisons. For these reasons, prospective confirmation of these findings in additional studies would be desirable.

In conclusion, in patients with acute iliofemoral DVT, PCDT is more effective in improving 24-month venous outcome in patients with more severe baseline clinical presentation or a history of previous DVT. Left-sided DVT and a non-compressible popliteal vein may also connote a greater likelihood to benefit from PCDT, but these apparent relationships are less conclusive since they were only seen for some outcomes evaluated. The findings of this analysis may help to inform the design of future studies evaluating new or existing thrombus removal strategies.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Research Highlights

- A post-hoc analysis of the iliofemoral DVT subgroup of the ATTRACT multicenter randomized trial was performed to identify baseline predictors of treatment effect of pharmacomechanical catheter-directed thrombolysis (PCDT) upon primary and secondary venous outcomes over 24 months.
- Patients with higher baseline Villalta score experienced greater effects of PCDT in reducing post-thrombotic syndrome (PTS) severity, reducing the occurrence of moderate-or-severe PTS, and improving venous health-related quality of life over 24 months.
- Patients with previous DVT also had greater effects of PCDT on 24-month PTS severity (mean PCDT-Control difference in Villalta score was 3.3 points, p-interaction=0.03; mean PCDT- Control difference in VCSS score was 2.3 points, p-interaction=0.02).

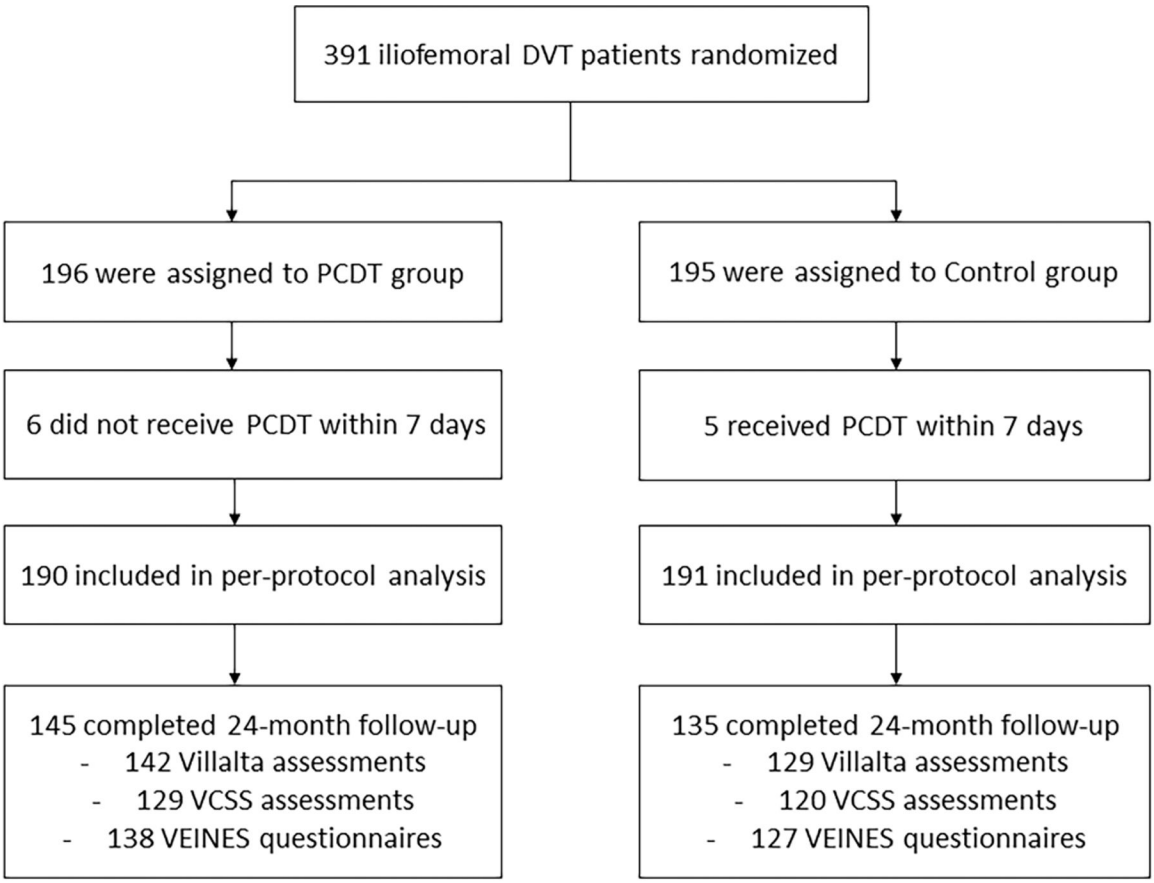


Figure 1 - Patient Flow (CONSORT) Diagram
Patient flow and outcome data in the ATTRACT Trial (per-protocol analysis population).

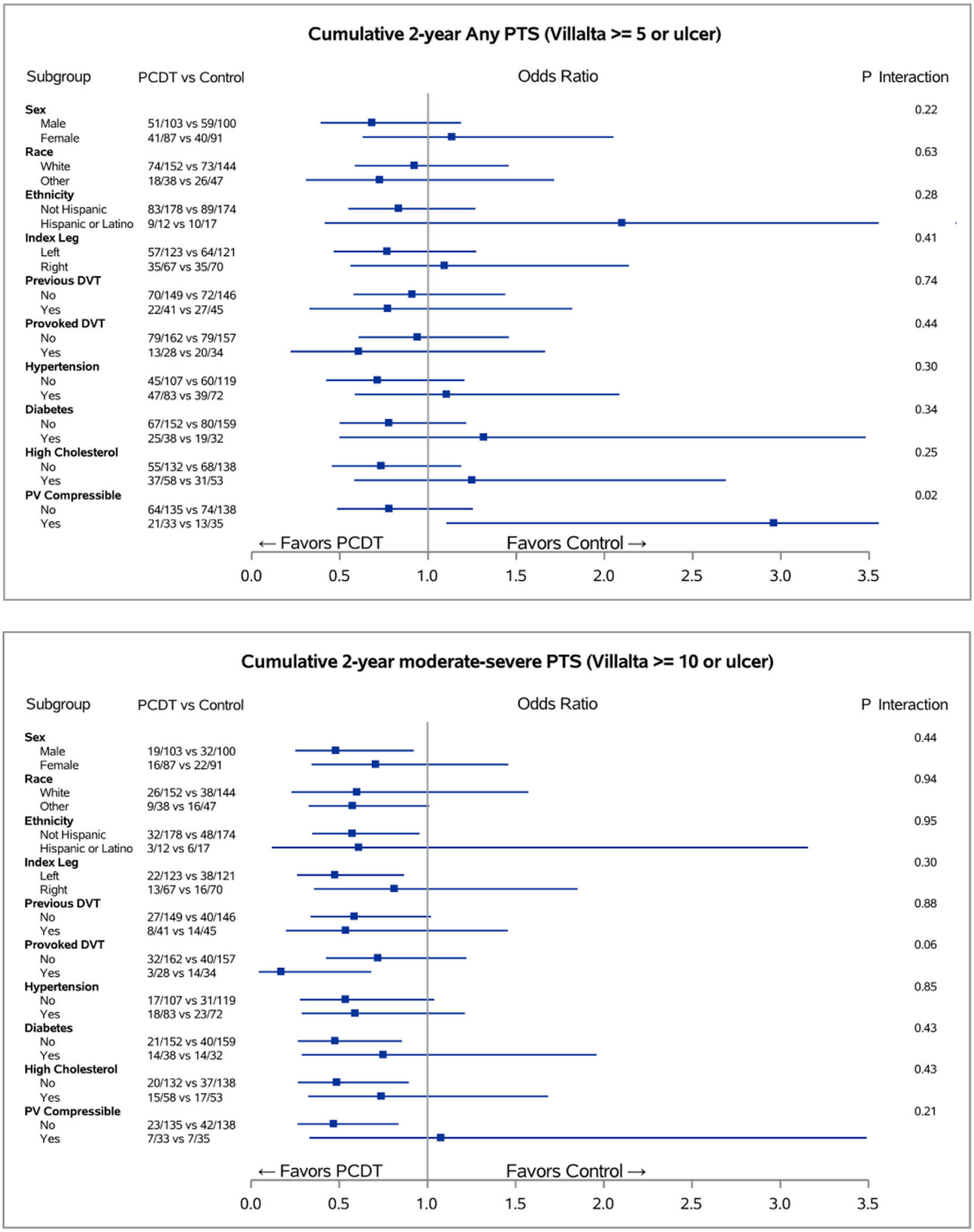


Figure 2 –. Baseline Predictors of PCDT Effect on 24-Month Binary Venous Outcomes

Forest plots of odds ratios for the 24-month cumulative occurrences of PTS (A) and moderate-or-severe PTS (B), in subgroups of ATTRACT patients with acute iliofemoral DVT for each level of baseline factors. The horizontal lines represent 95% confidence intervals (CIs).

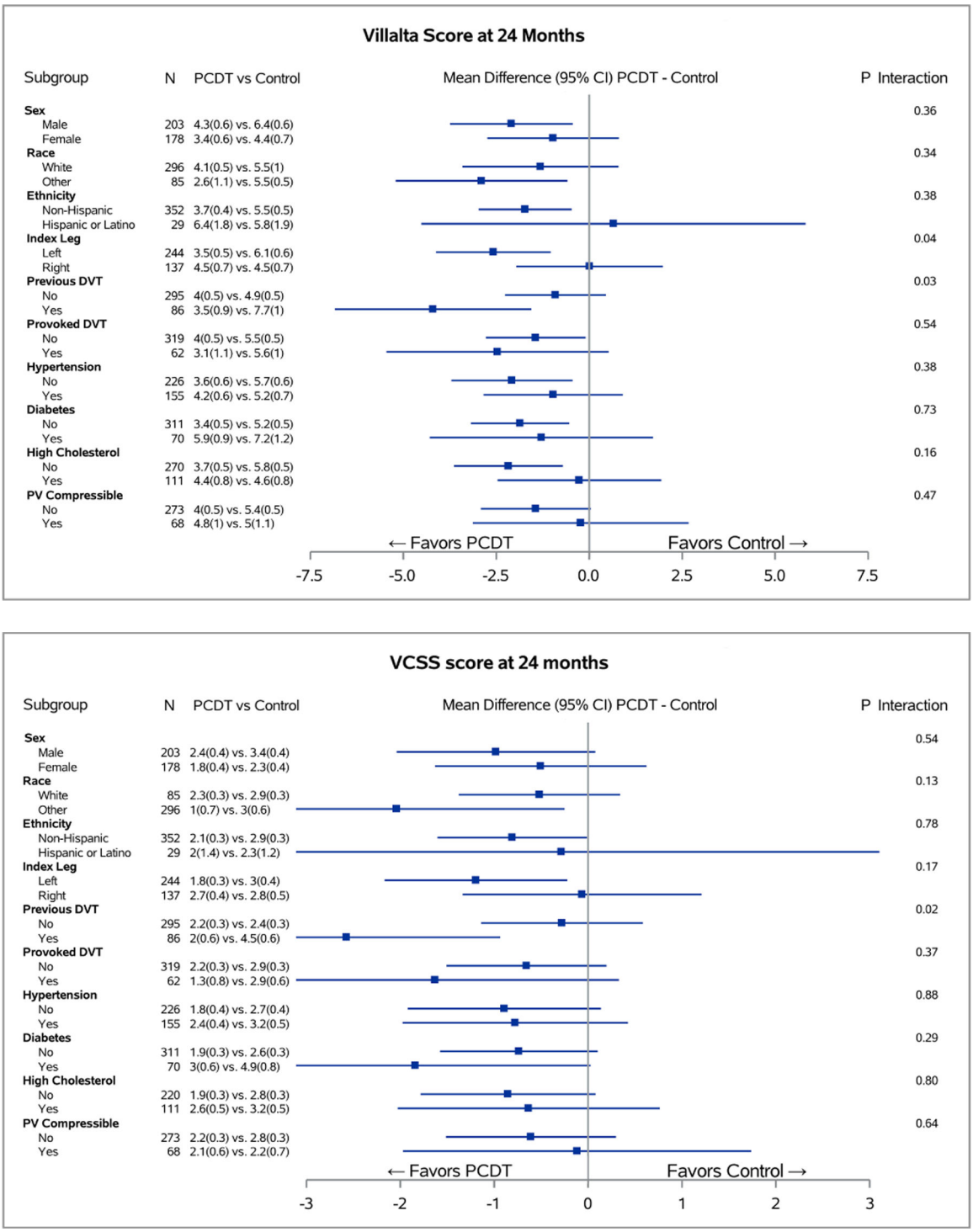
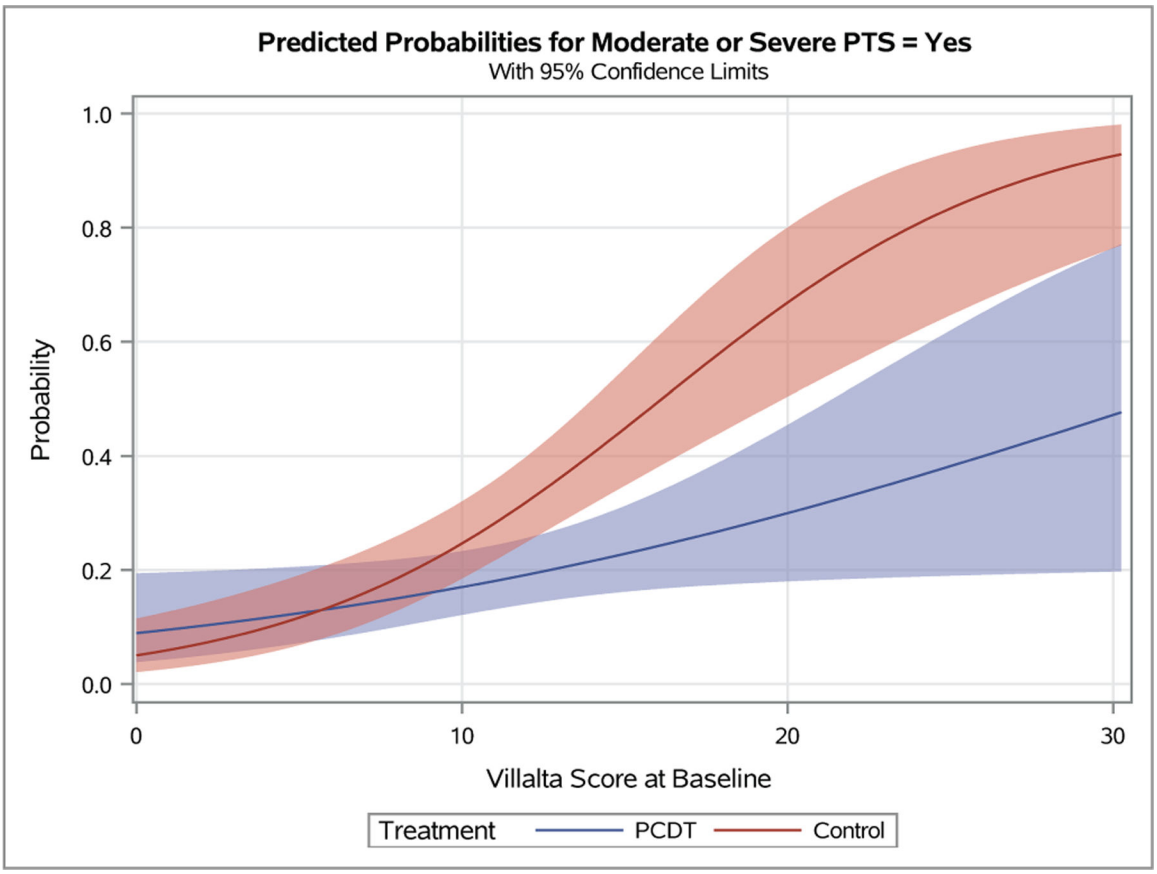
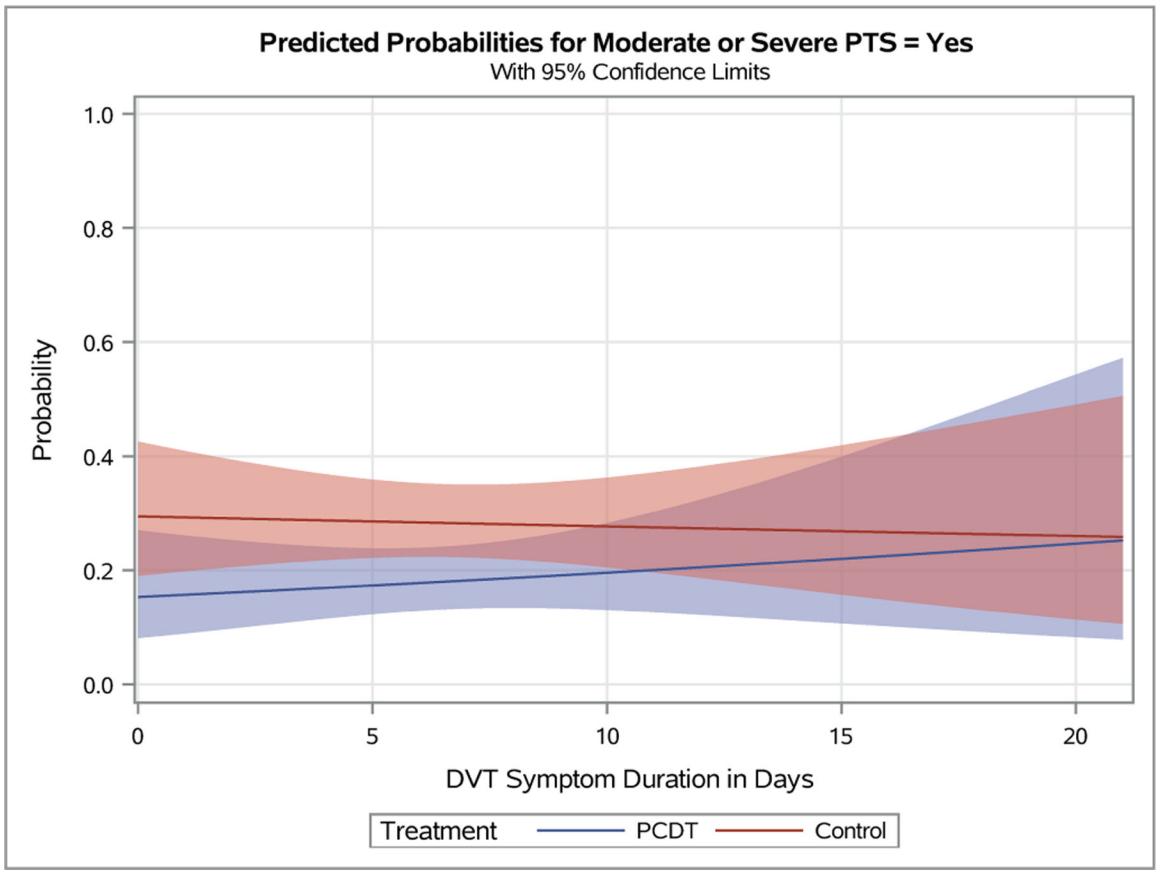
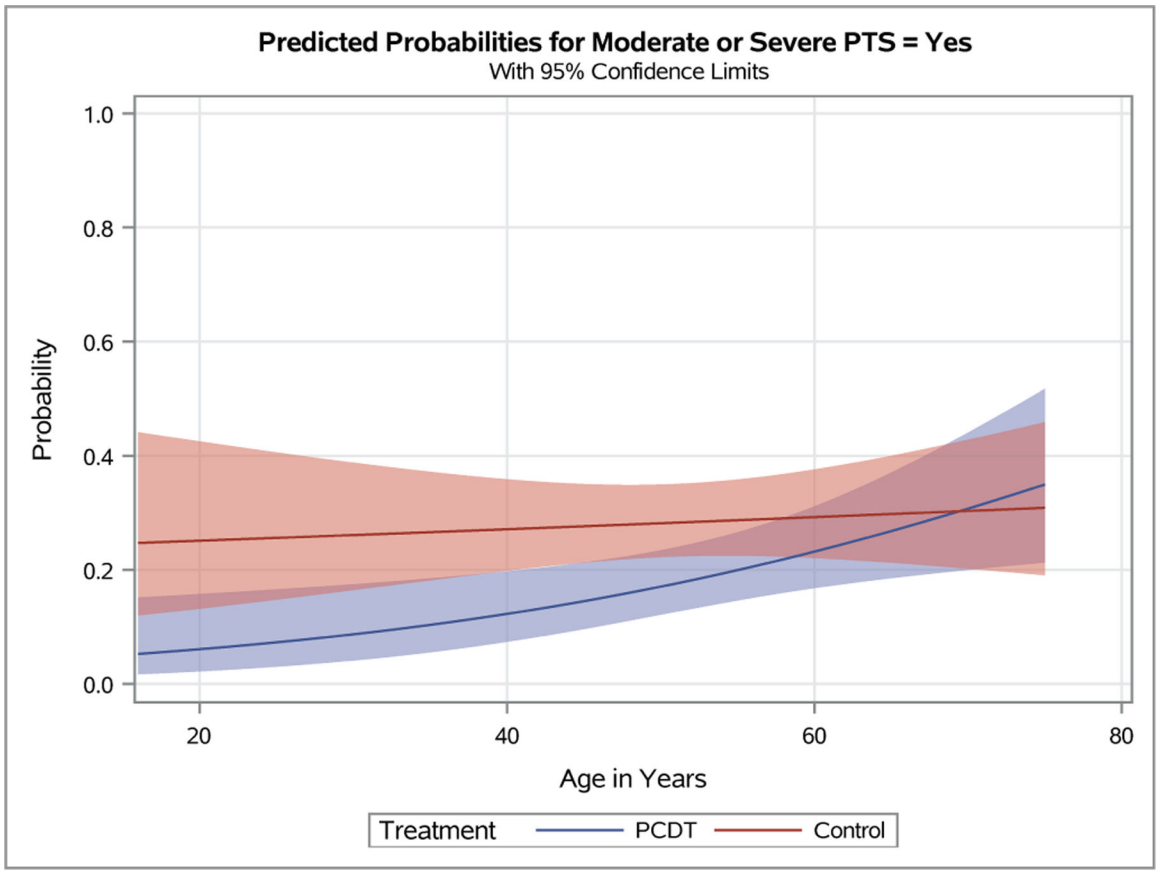


Figure 3 –. Baseline Predictors of PCDT Effect on 24-Month Continuous Venous Outcomes

Associations of binary baseline factors with 24-month Villalta (A) and Venous Clinical Severity Scale (B) scores in subgroups of ATTRACT patients with acute iliofemoral DVT for each level of baseline factors. The horizontal lines represent 95% confidence intervals (CIs).







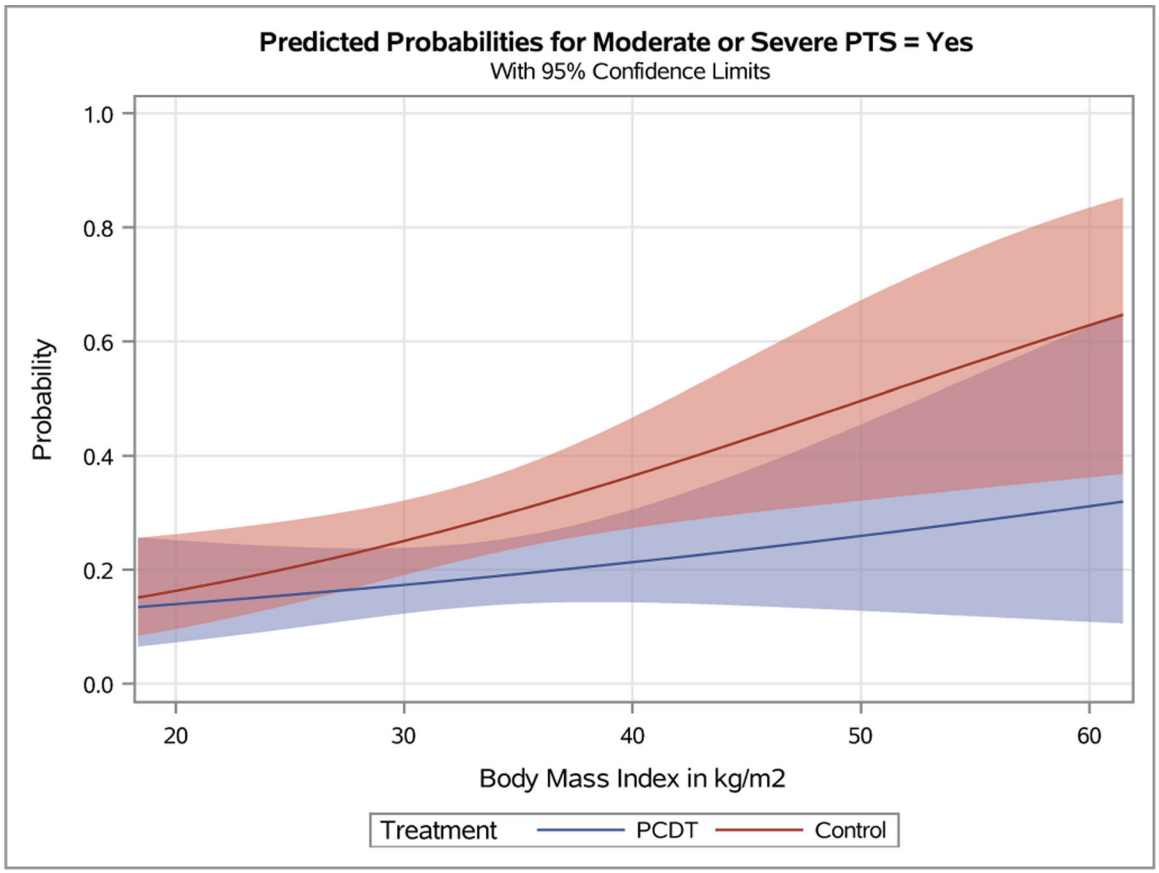
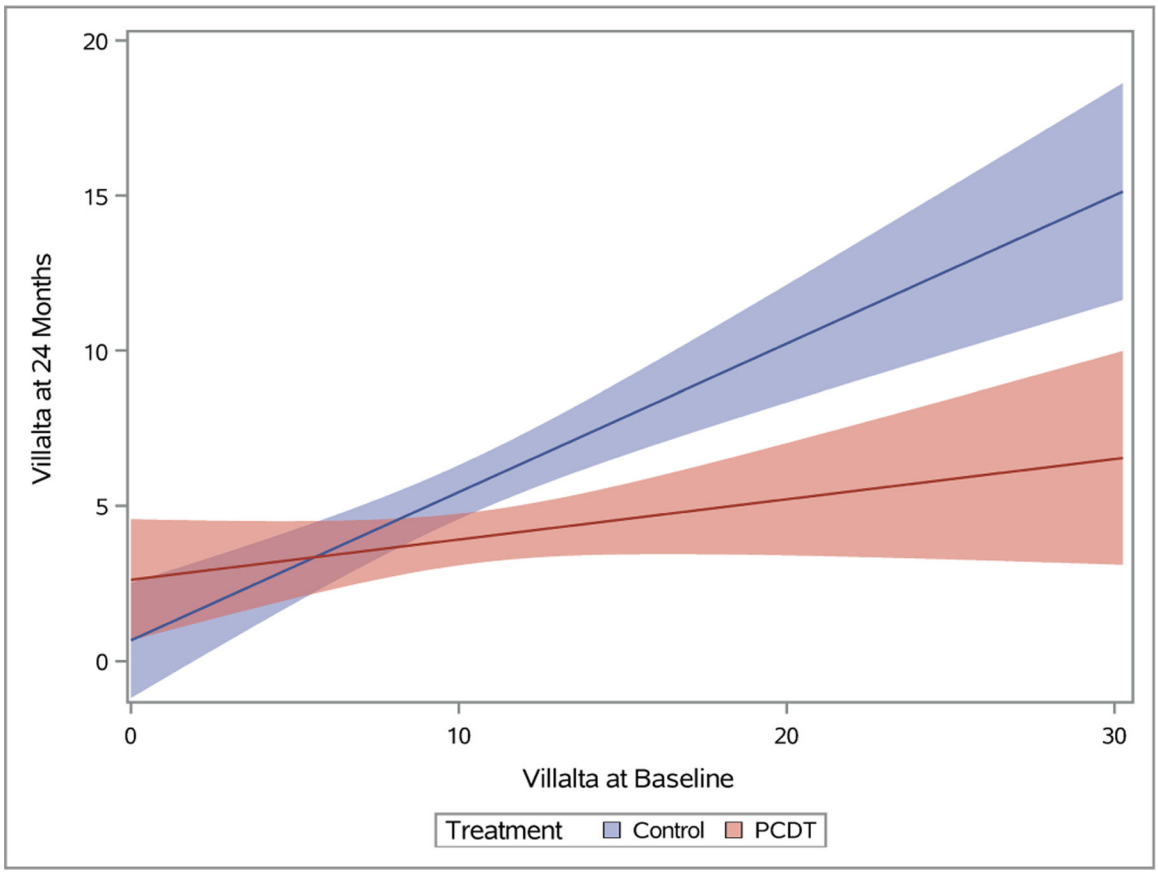
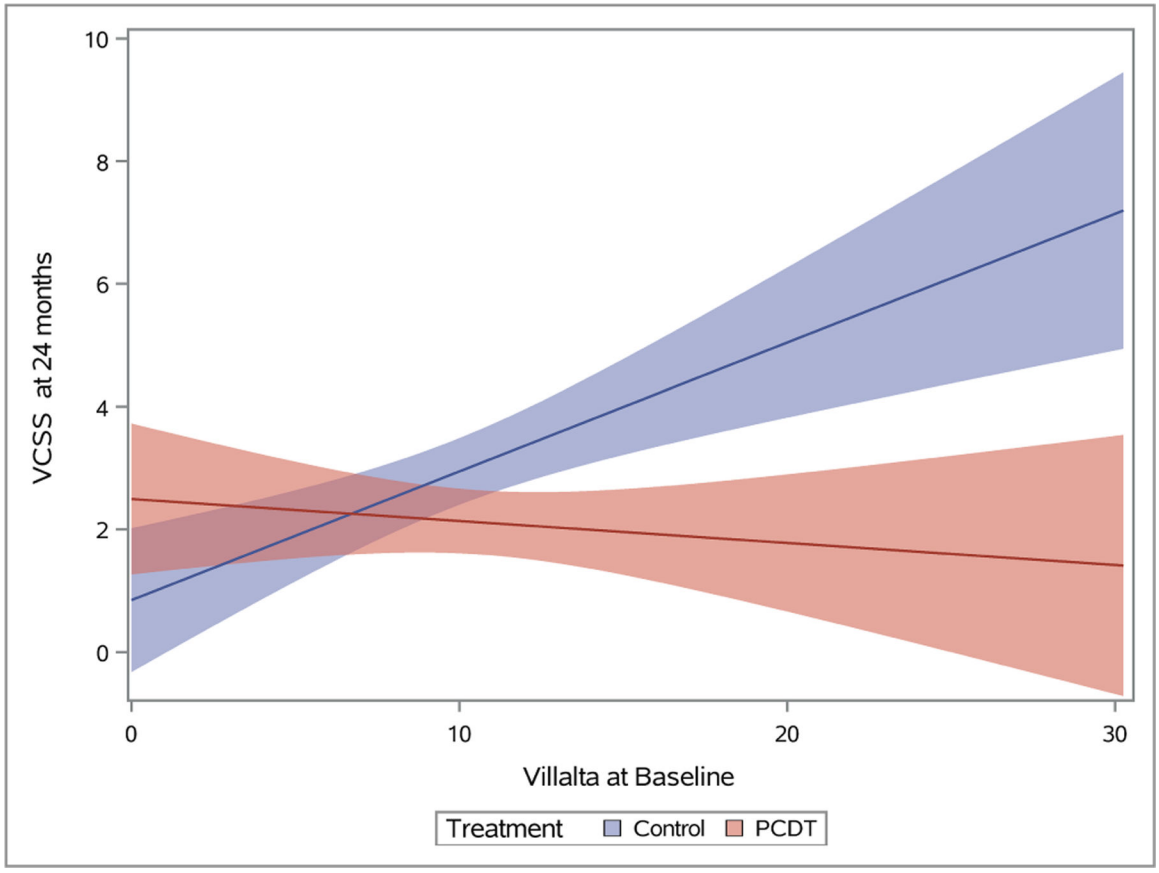


Figure 4 –. Predicted Probabilities of Venous Outcomes by Continuous Baseline Factors

Plots depicting the predicted probabilities of moderate-or-severe PTS in patients with increasing baseline Villalta score (A), symptom duration (B), patient age (C), and body-mass index (D). The light red and blue colored bands represent the 95% confidence intervals (CIs) around the estimates for each respective treatment arm; the dark red/purple bands represent areas of overlap between the 95% CIs for the two treatment arms.





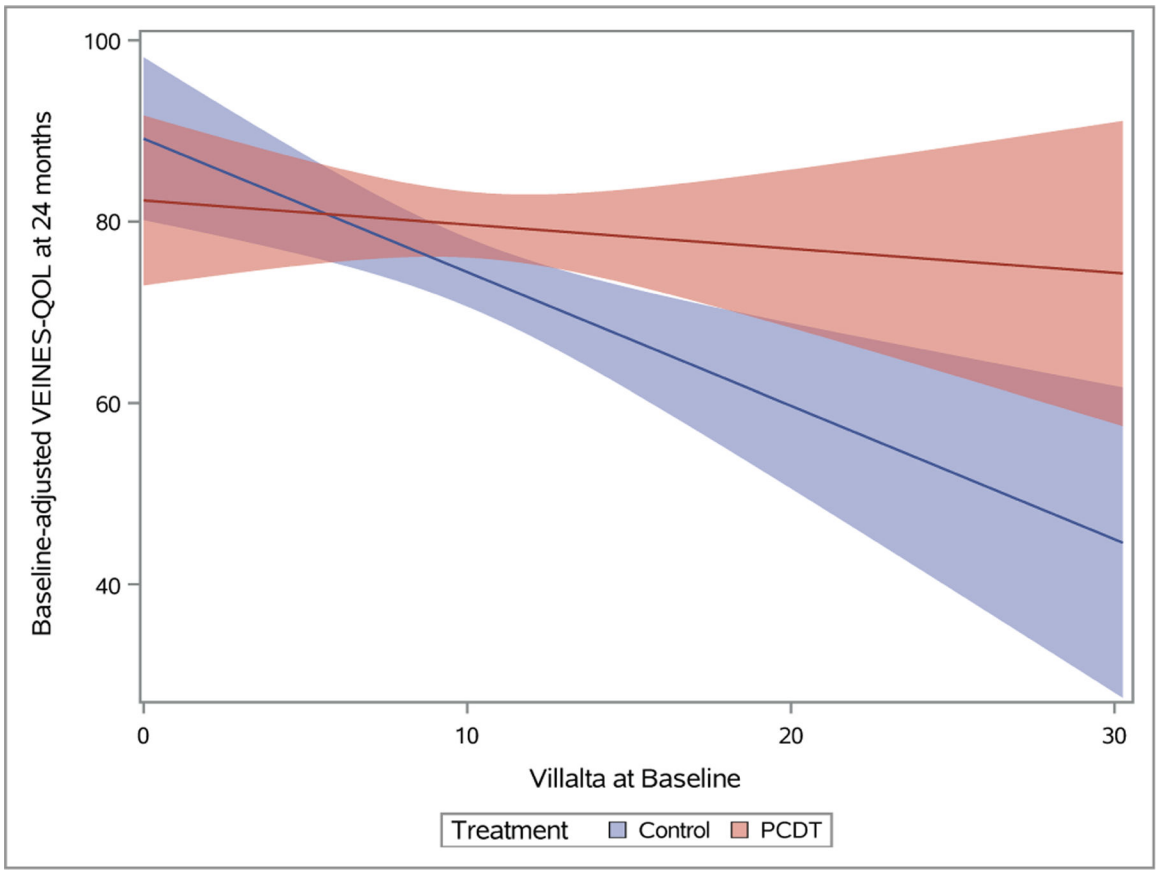


Figure 5 –. Association of Continuous Baseline Factors with 24-Month Venous Outcomes

Plots depicting predicted mean scores for the Villalta (A), Venous Clinical Severity Scale (B), and baseline-adjusted VEINES-QOL (C) scores at 24 months as a function of increasing continuous baseline Villalta score. The light red and blue colored bands represent the 95% confidence intervals (CIs) around the estimates for each respective treatment arm; the dark red/purple bands represent areas of overlap between the 95% CIs for the two treatment arms.

TABLE 1 –

Distribution of Baseline Variables

Factor	Overall (N=381)	PCDT Arm (N=190)	Control Arm (N=191)	P Value
Age (years)	51.0 [39.0,62.0]	51.0 [38.0,62.0]	52.0 [42.0,61.0]	0.65 [a]
Sex				0.72 [b]
Male	203 (53.3%)	103 (54.2%)	100 (52.4%)	
Female	178 (46.7%)	87 (45.8%)	91 (47.6%)	
Race				0.28 [b]
White	296 (77.7%)	152 (80.0%)	144 (75.4%)	
Other	85 (22.3%)	38 (20.0%)	47 (24.6%)	
Ethnicity				0.34 [b]
Not Hispanic or Latino	352 (92.4%)	178 (93.7%)	174 (91.1%)	
Hispanic or Latino	29 (7.6%)	12 (6.3%)	17 (8.9%)	
BMI (kg/m2)	30.8 [27.0,36.7]	30.9 [27.6,36.9]	30.8 [25.5,36.4]	0.26 [a]
Index Leg				0.78 [b]
Left	244 (64.0%)	123 (64.7%)	121 (63.4%)	
Right	137 (36.0%)	67 (35.3%)	70 (36.6%)	
Previous DVT				0.64 [b]
No	295 (77.4%)	149 (78.4%)	146 (76.4%)	
Yes	86 (22.6%)	41 (21.6%)	45 (23.6%)	
Provoked DVT				0.42 [b]
No	319 (83.7%)	162 (85.3%)	157 (82.2%)	
Yes	62 (16.3%)	28 (14.7%)	34 (17.8%)	
Hypertension				0.23 [b]
No	226 (59.3%)	107 (56.3%)	119 (62.3%)	
Yes	155 (40.7%)	83 (43.7%)	72 (37.7%)	
Diabetes				0.41 [b]
No	311 (81.6%)	152 (80.0%)	159 (83.2%)	
Yes	70 (18.4%)	38 (20.0%)	32 (16.8%)	
High Cholesterol				0.55 [b]
No	270 (70.9%)	132 (69.5%)	138 (72.3%)	
Yes	111 (29.1%)	58 (30.5%)	53 (27.7%)	

Factor	Overall (N=381)	PCDT Arm (N=190)	Control Arm (N=191)	P Value
PV Compressible				0.89 [b]
No	273 (80.1%)	135 (80.4%)	138 (79.8%)	
Yes	68 (19.9%)	33 (19.6%)	35 (20.2%)	
Total Villalta Score	10.0 [6.0,14.0]	10.0 [7.0,14.0]	9.6 [6.0,14.0]	0.23[a]
Symptom Duration (days)	6.0 [3.0,9.0]	6.0 [3.0,9.0]	6.0 [3.0,9.0]	0.42 [a]

PCDT = pharmacomechanical catheter-directed thrombolysis

DVT = deep vein thrombosis

PV = popliteal vein

BMI = body-mass index

[a] = Kruskal-Wallis test

[b] = Pearson's Chi-square test