2020

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The version of record can be found here: https://doi.org/10.1016/j.jvsv.2019.03.023

Quality of life after pharmacomechanical catheter-directed thrombolysis for proximal deep vein thrombosis

Short title: Quality of life after endovascular thrombus removal

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Total word count of the manuscript, including the title page, abstract, text, references, tables, and figures legends: 8716

Word count for journal limit: 3495

Article Highlights

Type of Research: Analysis of a multicenter randomized trial

Key Findings: In this analysis of the ATTRACT Study, among patients with proximal DVT, pharmacomechanical catheter-directed thrombolysis (PCDT) with anticoagulation, compared with anticoagulation alone, had a beneficial effect on QOL during the first 6 months post-treatment (e.g. VEINES-QOL change scores were greater in PCDT vs. No PCDT from baseline to one month (difference 5.7; P=0.0006) and baseline to 6 months (5.1; P=0.0029). Further, among proximal DVT patients with iliofemoral DVT, this benefit was apparent over 24 months post-treatment.

Take Home Message: Patients with iliofemoral DVT have a worse long-term prognosis (poorer QOL) than patients with femoral-popliteal DVT. Early use of pharmacomechanical catheter-directed thrombolysis improves QOL in patients with acute iliofemoral DVT and may be reasonable to consider in selected patients who have severe symptoms, low bleeding risk, and a willingness to undergo a catheter-based procedure, after careful discussion of the benefits and risks.

Table of Contents Summary

In the ATTRACT randomized trial, among patients with proximal DVT, early use of pharmacomechanical catheter-directed thrombolysis had a beneficial effect on QOL during the first 6 months post-treatment. In proximal DVT patients with iliofemoral DVT, this QOL benefit was apparent over 24 months post-treatment.

Abstract

Background: After deep vein thrombosis (DVT), many patients have impaired quality of life (QOL). We aimed to assess if pharmacomechanical catheter-directed thrombolysis (PCDT) improves short-term or long-term QOL in patients with proximal DVT and if QOL is related to extent of DVT.

Methods: The ATTRACT Trial was an assessor-blinded randomized trial that compared PCDT with no PCDT in patients with DVT of the femoral, common femoral, or iliac veins. QOL was assessed at baseline and 1, 6, 12, 18 and 24 months using the VEINES-QOL/Sym disease-specific QOL measure and the SF-36 (PCS and MCS summary scores) general QOL measures. Change in QOL scores from baseline to assessment time were compared in the PCDT and No PCDT treatment groups overall, and in the iliofemoral DVT and femoral-popliteal DVT subgroups.

Results: 691 of 692 ATTRACT patients were analysed (mean age 53 years, 62% male, 57% iliofemoral DVT). VEINES-QOL change scores were greater (i.e. better) in PCDT vs. No PCDT from baseline to one month (difference 5.7; P=0.0006) and baseline to 6 months (5.1; P=0.0029), but not for other intervals. SF-36 PCS change scores were greater in PCDT vs. No PCDT from baseline to one month (difference 2.4; P=0.01), but not for other intervals. Among iliofemoral DVT patients, VEINES-QOL change scores from baseline to all assessments were greater in the PCDT vs. No PCDT group; this was statistically significant in the intention-to-treat analysis at 1 month (difference 10.0; P<0.0001) and 6 months (8.8; P<0.0001) and in the per-protocol analysis at 18 months (difference 5.8; P=0.0086) and 24 months (difference 6.6; P=0.0067). SF-36 PCS change scores were greater in PCDT vs. No PCDT from baseline to one month (difference 3.2;

P=0.0010), but not for other intervals. In contrast, in femoral-popliteal DVT patients, change scores from baseline to all assessments were similar in the PCDT and No PCDT groups.

Conclusions: Among patients with proximal DVT, PCDT leads to greater improvement in disease-specific QOL than No PCDT at 1 month and 6 months, but not later. In patients with iliofemoral DVT, PCDT led to greater improvement in disease-specific QOL over 24 months.

Clinical Trial Registration: www.clinicaltrials.gov; NCT00790335

Keywords: deep vein thrombosis, quality of life, randomized trial, proximal DVT, catheter-directed thrombolysis, iliofemoral DVT, femoral-popliteal DVT

Acknowledgements

The study's development and conduct were supported by the Society of Interventional Radiology Foundation. Dr. Kahn is a Tier 1 Canada Research Chair holder and is an investigator of the Canadian Institutes of Health Research-funded CanVECTOR Network. Dr. Kearon is supported by an Investigator Award from the Heart and Stroke Foundation of Canada and the Jack Hirsh Professorship in Thromboembolism. The authors wish to thank the entire network of investigators and study staff at the coordinating centers, core laboratories, and clinical centers (see Appendix B).

Sources of funding

The ATTRACT Trial was supported by grants from the National Heart, Lung, and Blood Institute (NHLBI) for the clinical coordinating center (U01-HL088476 to Washington University in St. Louis) and data coordinating center (U01-HL088118 to McMaster University, Hamilton, ON); the Washington University Center for Translational Therapies in Thrombosis, which is supported by a grant from the NHLBI (U54-HL112303); the Washington University Institute of Clinical and Translational Sciences, which is supported by a grant from the National Center for the Advancement of Translational Sciences (UL1-TR00044810); Boston Scientific; Covidien (now Medtronic); Genentech; the Society of Interventional Radiology Foundation; the Canada Research Chairs Program (Tier 1 support to Dr. Kahn); the CanVECTOR Network (funded by Canadian Institutes of Health Research CDT-142654, to Dr. Kahn); the Heart and Stroke Foundation of Canada (Investigator Award to Dr. Kearon); and a Jack Hirsh Professorship in Thrombosis (to Dr. Kearon). BSN Medical donated the compression stockings.

Disclosures (in order of authorship)

Susan R. Kahn: Advisory board fees from BMS Pfizer, Sanofi, and Aspen.

Jim A. Julian: None.

Clive Kearon: None.

Chu-Shu Gu: None.

David J. Cohen: Grant support from Abbott Vascular and Boston Scientific; consulting fees, Cardinal Health; grant support and consulting fees, Medtronic.

Elizabeth A. Magnuson: None.

Anthony J. Comerota: Consulting fees from Medtronic.

Samuel Z. Goldhaber: Grant support from BiO2 Medical; grant support and consulting fees, Boehringer Ingelheim, BMS, Daiichi Sankyo, Janssen, Portola, Bayer, and BTG/Ekos.

Michael R. Jaff: Holds equity in Embolitech and Venarum; uncompensated advisor, Boston Scientific, Cordis Corporation, and Medtronic; consultant, Volcano/Phillips.

Mahmood K. Razavi: Consulting fees from Abbott, Boston Scientific, Medtronic, Veniti, and Volcano/Phillips

Andrei L. Kindzelski: None.

Joseph Schneider: None.

Paul Kim: None.

Rabih Chaer: Speaker, Boston Scientific; medical advisory board, Abbott.

Akhilesh Sista: Unrestricted research grant to NYU, Penumbra, Inc.; Unpaid scientific advisory board member, Thrombolex.

Robert McLafferty: DSMB member for clinical trial, Veniti.

John A. Kaufman: Medical Advisory Board, Argon Medical; Consultant, Novate; Medical Advisory Board and Ownership Interest, Bio2 Medical; Ownership Interest, Veniti; Consultant, Cook Medical.

Brandt Wible: Amirsys-Elsevier for work performed on STATdx, RADPrimer, and the textbook Diagnostic Imaging: Interventional Procedures, 2nd edition.

Morey Blinder: Honoraria from Janssen Pharmaceuticals.

Suresh Vedantham: Grant support from Cook Medical.

INTRODUCTION

Despite treatment with anticoagulation and compression stockings, 30-50% of patients with proximal deep vein thrombosis (DVT) develop the post-thrombotic syndrome (PTS), a chronic, burdensome complication.[1, 2] PTS is characterised by limb pain, heaviness, swelling and skin changes, including, in severe cases, venous ulceration. Greater recognition of PTS, with an increased focus on using patient reported outcome measures to assess the impact of illness, has highlighted the importance of studying health-related quality of life (QOL) in patients with DVT.

QOL is impaired in the acute phase of DVT[3, 4], and development of PTS reduces QOL in the months to years following DVT.[5] In the Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis (ATTRACT) Trial, we showed that pharmacomechanical catheter-directed thrombolysis (PCDT) did not reduce the occurrence of PTS during 24 months follow-up but reduced the severity of PTS and accelerated resolution of acute symptoms.[6] In the current analysis, we assessed the effect of PCDT on short-term and long-term QOL in all patients in ATTRACT and in predefined subgroups with (iliofemoral DVT) or without (femoral-popliteal DVT) involvement of the iliac or common femoral vein, and assessed if this effect differed over time.

METHODS

The ATTRACT Trial was an NHLBI (NIH)-sponsored, randomized controlled trial conducted at 56 U.S. clinical centers.[6, 7] Patients with symptomatic proximal DVT of the femoral, common femoral, or iliac vein were potentially eligible. Patients were excluded if they were younger than 16 or older than 75 years; were pregnant; or had symptoms for more than 14 days, high bleeding risk, active cancer, established PTS, or ipsilateral DVT in the prior 2 years.

Patients were randomly assigned to receive PCDT (PCDT group) or not receive PCDT (No PCDT group). Randomization was stratified by clinical center and by whether there was involvement of the common femoral or iliac vein ("iliofemoral DVT"), or not ("femoral-popliteal DVT"), as per societal reporting guidelines [8, 9]. Patients in both treatment groups received initial and long-term anticoagulation as recommended in published guidelines[10, 11], and were provided with knee-high, 30-40 mmHg elastic compression stockings (initially at the 10-day follow-up visit, with replacement every 6 months). The stockings were sized-to-fit and their daily use was encouraged by study personnel at each follow-up visit throughout the 24 months. PCDT was performed consistent with published guidelines.[12]

Patients were assessed at baseline and 1 month (±7 days), 6 months (±1 month), 12 months (±1 month), 18 months (±1 month), and 24 months (±2 months) post-randomization. PTS, the primary outcome of the ATTRACT Trial, was defined as a Villalta score of 5 or higher or an ulcer in the leg with the index DVT, any time between 6 and 24 months.[13, 14] Full eligibility criteria, study investigators, study sites and detailed description of PCDT methods are provided in the primary publication.[6] The study was approved by the institutional review boards at all participating centers, and all patients provided informed consent.

Quality of life assessments

Validated, self-administered instruments were used to measure venous disease-specific and general QOL. Venous disease-specific QOL was measured using the Venous Insufficiency Epidemiological and Economic Study Quality of Life (VEINES-QOL/Sym), a patient self-assessment questionnaire.[15] The instrument consists of 25 items that measure venous symptoms (heavy legs, aching legs, swelling, night cramps, heat or burning sensation, restless legs, throbbing, itching, tingling, intensity of leg pain), limitations in daily activities due to venous

disease, psychological impact of venous disease, and change over the past year. Responses are rated on 2-point to 7-point Likert scales of intensity, frequency, or agreement. The VEINES/Sym is a validated subscale of the VEINES instrument (10 of the 25 items) that measures venous symptoms. The VEINES-QOL/Sym has undergone comprehensive and rigorous psychometric evaluation and is acceptable, reliable, valid, and responsive for use as a patient-reported measure of outcome in studies of chronic venous disease, including PTS and DVT.[15, 16] General QOL was measured using the Medical Outcomes Study Short-Form Health Survey-36, Version 2 (SF-36v2), a validated, widely-used instrument.[17, 18] The SF-36 has been used in other DVT studies to assess general QOL.[5, 19-21] For all measures, lower scores indicate poorer QOL.

Administration of QOL instruments

The VEINES-QOL/Sym and SF-36 were combined into a single questionnaire document that took approximately 15-20 minutes for most patients to complete. Following a standard orientation, the patient filled in the questionnaire in a quiet office. The research nurse then checked for missing data and, without coercion, encouraged the patient to respond to all items. The nurse administering the questionnaire was blinded to the patient's treatment allocation.

Scoring of QOL instruments

For the SF-36, an established computer scoring algorithm [22, 23] was used to generate summary scores for the Physical (PCS) and Mental (MCS) Component Scales (which reflect physical and mental health status, respectively). For VEINES-QOL, the intrinsic scoring method recently proposed by Bland[24] was used, as the original "relative" scoring method[15] has the disadvantage of always producing the same mean and standard deviation and, thus, cannot be used to study changes over time and to compare findings in different studies. Summary scores were computed for VEINES-QOL (impact of venous disease on QOL) and VEINES-Sym

(venous symptom severity).

For SF-36 PCS and MCS, a change of 4 points is considered a minimal clinically important difference.[25] For VEINES-QOL and VEINES-Sym scored using the intrinsic method, the minimal clinically important difference is uncertain, but is thought to be about 4 to 6 points, which is similar or a bit larger than for the original relative scoring method[16].

Sample size and power

The total sample size required for the ATTRACT Trial's primary outcome of PTS was 692 patients.[6] For secondary outcomes including QOL scores, this sample size provided approximately 88% power to detect an effect size of 0.25 with continuous outcomes. An effect size of 0.25 translates into ability to detect a difference between groups of 1.25 points in the VEINES-QOL and VEINES-Sym and 2.5 points in the SF-36 PCS and MCS.

Statistical analysis

QOL analyses were performed using both modified intention-to-treat (ITT) and per-protocol analysis sets. The modified ITT analysis set consisted of all patients randomized except for those who did not have DVT at enrollment. The per-protocol analysis set excluded randomized patients who, within 7 days post-randomization, were assigned to receive PCDT but did not undergo the procedure, or who were assigned to No PCDT but underwent PCDT.

Group means and standard errors of the VEINES-QOL, VEINES-Sym, SF-36 PCS and MCS scores, and the mean differences and 95% confidence intervals (CIs) between treatment arms at each assessment were calculated. The repeated QOL scores over time (i.e. at baseline, 1, 6, 12, 18, 24 months) were analyzed with growth curve mixed models using piecewise-linear regression.[26] The models took into account the correlation between the repeated observations. Models included both fixed effects: the pre-specified baseline factors (treatment, center, extent of

DVT, sex), and continuous covariates (age at randomization, body mass index [BMI], and Villalta score); and random effects (actual visit dates, patient). Interaction terms (treatment x time for each visit) were assessed in each model, and a best-fit model was determined by removing non-significant ($p>0.05$) interaction terms. Change in QOL scores from baseline to 24 months, the pre-specified primary QOL outcome, were compared between treatment arms using estimates derived from the final growth curve models.

Sensitivity analyses for the VEINES (QOL and Sym) and SF-36 (PCS and MCS) outcomes used multiple imputation for missing baseline covariates and missing summary scores (except for deceased subjects), and the modelling structure described above. Missing data were assumed to be missing-at-random. The following auxiliary variables assisted in the imputation phase: for VEINES QOL/Sym scores, age, sex, BMI, extent of DVT and all available VEINES-QOL/Sym scores from previous visits; and for SF-36 MCS/PCS scores, age, sex, race, BMI, and all available SF-36 scores from previous visits. Imputation was performed separately within each treatment arm.

Analyses for the change scores, similar to the above, were reported for the iliofemoral DVT and femoral-popliteal DVT subgroups. The growth curve mixed models were expanded to assess the treatment x time interactions within the extent of DVT subgroups (i.e. treatment x time x extent) using the data from all patients. Plots of the response trajectories (from baseline to 24 months) of the model-fitted VEINES-QOL change scores within each of the four groups defined by treatment (PCDT, No PCDT) and highest extent of DVT (iliofemoral, femoral-popliteal) were developed using locally-weighted scatterplot smoothing (LOESS), a non-parametric smoothing technique.[27]

Finally, forest plots were created to display model-fitted baseline-to-24-month change

scores for PCDT vs. No PCDT within pre-specified subgroups defined by baseline age (<65, ≥65), sex, race (white, non-white), BMI (<25, 25-29, ≥30), DVT symptom duration pre-enrolment (<1 week, ≥1 week), DVT extent, and Villalta severity score (<5 points, 5-9, 10-14, ≥15). Linear regression models for the change scores were used to assess differential treatment effects within subgroups (i.e. subgroup x treatment interactions). Change scores using the growth-curve model-fitted estimates (with and without multiple imputation) were analyzed separately.

To account for the multiplicity of comparisons between treatment arms, statistical significance was declared only when P-values were less than 0.01. Statistical analyses were performed using SAS version 9.4 and the R version 3.5 programming language.

RESULTS

Between December 2009 and December 2014, 692 patients were randomized (337 to PCDT, 355 to No PCDT) and were followed for 2 years (Figure 1). One patient assigned to the PCDT group was found not to have a qualifying DVT and, therefore, was excluded from all analyses, leaving 691 patients in the modified ITT analysis set. Within 7 days of randomization, a further 11 patients who were assigned to receive PCDT but did not have PCDT, and 5 patients who were assigned to No PCDT but had PCDT were excluded from the per-protocol analysis (675 patients in per-protocol analysis set).

Baseline characteristics of the patients were similar in the PCDT and No PCDT groups (Table 1). Overall, median age was 53 years, 62% of patients were male, 78% were white, and median BMI was 31 kg/m^2. The qualifying DVT was iliofemoral in 57% of patients and femoral-popliteal in 43% of patients.

Quality of life

Detailed summaries of the raw QOL scores over time are presented in the Supplement (Tables A-I). The numbers of patients who completed QOL assessments at each visit are shown in Table J. In this section, we provide results for the change in QOL scores from baseline to each assessment time.

All Patients

In the modified ITT analysis set, model-fitted VEINES-QOL change scores from baseline to 24 months (primary outcome) was an average of 3.9 points higher in PCDT than No PCDT patients (P=0.04; Table 2). Difference in change scores in favor of PCDT achieved statistical significance at 1 month (5.7; P=0.0006) and at 6 months (5.1; P=0.0029), but not at 12 months and at 18 months (Table 2).

For the VEINES symptom subscale (VEINES-Sym), there was a suggestion that the model-fitted change scores were greater in PCDT vs. No PCDT from baseline to 6 months (difference 4.3; P=0.045) but not at any other change interval (Table 2).

For SF-36 PCS, the model-fitted change score was greater in PCDT than No PCDT patients at 1 month (difference 2.4; P=0.012) but not at any other change interval. For SF-36 MCS, there were no differences between PCDT and No PCDT in model-fitted change scores at any assessment (Table 2).

Results were similar in sensitivity analyses with models using multiple imputation (Tables 2), and when analyzed using the per-protocol analysis set (Supplement; Tables D and E).

Subgroup Analysis

Forest plots of differences in model-fitted baseline-to-24-month VEINES-QOL change scores between PCDT and No PCDT patients according to subgroups are shown in Figure 2. For

the change in QOL scores (VEINES-QOL, VEINES-Sym, SF-36 MCS, SF-36 PCS) from baseline to 24 months, none of the pre-specified subgroups, including for the iliofemoral vs. femoral-popliteal subgroups, showed statistically different ($p<0.05$) treatment effects. As a sensitivity analysis, we repeated the subgroup analysis using the change scores calculated from the raw data and the imputation-enhanced model-fitted estimates; none of these data sets showed any statistically significant subgroup effects.

Iliofemoral DVT Subgroup

In the modified ITT analysis set, model-fitted VEINES-QOL change scores from baseline to all assessment times were greater in the PCDT group. Compared to the differences at 1 month (difference 10.0; P<0.0001) and at 6 months (difference 8.8; P<0.0001), the differences in favor of PCDT were about half as large at 12 months (difference 4.3; P=0.046), 18 months (difference 4.9; P=0.024), and at 24 months (difference 5.5; P=0.023). For VEINES-Sym, results were similar to those of VEINES-QOL (Table 3).

For SF-36 PCS, model-fitted change scores at 1 month were greater in the PCDT group (difference 3.2; P=0.0010), but change scores from baseline to other assessment times, including 24 months, did not differ (Table 3). For SF-36 MCS, there were no differences between PCDT and No PCDT in model-fitted change in scores from baseline to any assessment, including 24 months (Table 3).

Results were substantively similar in the sensitivity analyses with models using multiple imputation (Tables 3). When analyzed using the per-protocol analysis set (Supplement; Tables F and G), the above noted differences between PCDT and no PCDT were greater, particularly for change in VEINES-QOL scores from baseline to 18 months (difference 5.8; P=0.0086) and baseline to 24 months (difference 6.6; P=0.0067) (Table F).

Femoral-popliteal DVT Subgroup

VEINES-QOL, VEINES-Sym, SF-36 PCS and SF-36 MCS change scores from baseline to each assessment were similar in the PCDT and No PCDT groups (Table 4). Results were similar in sensitivity analyses with models using multiple imputation and when analyzed using the per-protocol analysis set (Supplement; Tables H and I).

Trajectories of the VEINES-QOL scores in Iliofemoral and Femoral-popliteal DVT Subgroups

Figure 3 shows LOESS-smoothed estimates of the model predicted VEINES-QOL change scores from baseline to each assessment in the four groups defined by treatment (PCDT, No PCDT) and extent of DVT (iliofemoral, femoral-popliteal). All groups showed substantial improvement in VEINES-QOL change scores during follow-up. The change in the PCDT iliofemoral subgroup was greater than in the No PCDT iliofemoral subgroup, particularly during the first 6 months. The change in PCDT and No PCDT femoral-popliteal groups were similar at all time points.

Interpretation of the growth curve model QOL results

In addition to evaluating QOL improvement with PCDT from baseline to individual timepoints through 2 years, our analysis sought to determine the pattern of change over time. With the inclusion of the extent of DVT subgroups in the growth curve model, we observed that the improvement in VEINES-QOL/Sym and SF-36 PCS QOL with PCDT was statistically significantly greater in the iliofemoral DVT group compared with the femoral-popliteal DVT group during the first month post-randomization, but not during the intervals from 1 to 6 months, 6 to 12 months, 12 to 18 months, or 18 to 24 months (Supplement, Appendix A). The incremental changes in VEINES-QOL scores between assessments are shown in Figure 4. For all

four groups, there are substantial QOL incremental improvements from baseline to 1 month, and from 1 month to 6 months, but not beyond that. For patients with iliofemoral DVT, the largest interval improvement occurs in PCDT vs. No PCDT patients from baseline to 1 month. However, for the between-visit intervals beyond 1 month, differences in the degree of QOL change between treatment arms are not apparent. For femoral-popliteal DVT patients, the treatment differences were negligible for all incremental changes.

DISCUSSION

In our original publication describing the main results of the ATTRACT Trial, we evaluated QOL scores at two time-points (baseline and 24 months post-randomization) in the overall study population, and reported no difference in the degree of change in QOL between patients who were assigned, versus not assigned, to PCDT. In the current, more detailed analysis of QOL outcomes in the ATTRACT Trial, we used more sophisticated analytic methods that allowed us to more fully utilize all available data from all follow-up assessments, enabling us to assess time-dependent patterns of QOL change during different time periods within the 24 months of study follow-up.

We report four main findings. First, regardless of treatment group, venous disease-specific QOL and general QOL improved markedly during the 24 months after diagnosis of proximal DVT, with most of this improvement occurring during the first 6 months after diagnosis. Second, patients with iliofemoral DVT had poorer QOL scores over the 24 months of follow-up than patients with femoral-popliteal DVT. Third, in the total study population, patients in the PCDT group had greater improvement in venous disease-specific QOL during the first 1 month and 6 months after randomization compared with the No PCDT group, but this benefit

was no longer apparent by 12, 18 or 24 months, and there was no difference in the extent of improvement with PCDT in overall physical or mental general QOL at any time point. Fourth, the greater improvement in disease-specific QOL with PCDT during the first 6 months was only observed in patients who had iliofemoral DVT, and not in patients with femoral-popliteal DVT. Our results also suggest that in patients with iliofemoral DVT, but not those with femoral-popliteal DVT, disease-specific QOL change scores were also better with PCDT at 12, 18, and 24 months. In patients with iliofemoral DVT, the improvement in disease-specific QOL with PCDT vs. No PCDT was large enough to be considered clinically important during the first 6 months, but of uncertain clinical importance subsequently.

Our observation that general and venous disease-specific QOL improves over 24 months after DVT and that most of this improvement occurs in the first 6 months after DVT is consistent with previous reports by our group[5, 21] and by the CAVENT (Catheter-Directed Venous Thrombolysis in Acute Iliofemoral Vein Thrombosis) trial investigators [28].

We found that patients with iliofemoral DVT have worse QOL than patients with femoral-popliteal DVT, which is consistent with previous observations that QOL is poorer after proximal DVT than after isolated distal DVT [5], and that PTS is more common and more severe after iliofemoral DVT than after femoral-popliteal or more distal DVT.[29, 30]

Why might PCDT have improved venous QOL even though it did not prevent PTS? First, most of the improvement in QOL was in the first 6 months and the ATTRACT trial did find that PCDT reduced clot burden and reduced early leg pain and swelling to a greater extent than No PCDT, and was associated with a reduced point prevalence of PTS at the 6-month visit (but not thereafter)[6]. Second, although PCDT did not prevent PTS it did reduce its severity, and less severe PTS is likely to be associated with improved QOL. Third, although both measures ask

about leg pain, heaviness, cramping, itching, and pins and needles sensation, the VEINES-QOL instrument used to measure venous QOL may have captured different clinical characteristics than the Villalta scale used to measure PTS. We did not utilize a self-reported QOL measure as the study's primary outcome because of the possibility of response bias that could stem from patients' knowledge of their treatment allocation in this open-label study. Further work to compare the performance and correlation of these and other outcome measures would be of interest.

Strengths of our study include that we assessed both disease-specific and general QOL repeatedly during 24 months using validated measures. Although patients and healthcare providers were not blinded to treatment, bias was minimized by having central randomization, allocation concealment, blinded outcome assessment, and comparable use of anticoagulants and compression stockings during follow-up in both groups. Our modelling techniques enabled us to use all of the data during follow-up, to assess if effects on QOL differed over time, and to adjust for baseline factors that may influence QOL. Consistency of findings in sensitivity analysis that used multiple imputation to address missing data and in per-protocol analyses increase confidence in the validity of our findings. Stratification of randomization by whether the iliofemoral outflow tract was involved, which is known to influence the risk of PTS and its severity, supports separate reporting of findings in the iliofemoral and femoral-popliteal subgroups, as recommended by societal consensus guidelines.[8, 9]

Our study also has limitations. During the ATTRACT Trial, a number of measures were taken to ensure that patients attended follow-up visits, including electronic reminders to study sites of upcoming patient visits, and routine education of study teams on best practices for patient retention at investigator meetings, teleconferences, and via electronic communications. In some

instances, patients who had moved out of town were permitted to be seen at different study sites. Nevertheless, we had missing QOL responses primarily due to missed visits, which increased over time and were greater in the No PCDT group, for reasons that are unclear. However, as noted in the preceding paragraph, sensitivity analyses suggest that our findings are robust. We also acknowledge that our analysis has limited power to detect differences in treatment effects between subgroups and, particularly, within each of the femoral-popliteal and iliofemoral subgroups.

In conclusion, PCDT leads to better disease-specific QOL at 1 month and 6 months in patients with iliofemoral DVT, but not in patients with femoral-popliteal DVT. PCDT also appears to lead to greater improvement in disease-specific QOL over 24 months in patients with iliofemoral DVT.

Table 1. Demographic and Clinical Characteristics at Baseline

	PCDT n = 336	**No PCDT** n = 355	**Total** N = 691
Age, years: *median (IQR)*	52 (41, 62)	53 (43, 62)	53 (42, 62)
Male: *n (%)*	205 (61)	221 (62)	426 (62)
Race: *n (%)*			
White	265 (79)	276 (78)	541 (78)
Black/African-American	61 (18)	62 (17)	123 (18)
Other	10 (3)	17 (5)	27 (31)
Weight, kg: *median (IQR)*	95 (81, 111)	92 (79, 110)	93 (80, 110)
Body mass index, kg/m^2: *median (IQR)*	31 (27, 36)	30 (26, 35)	31 (27, 35)
DVT characteristics: *n (%)*			
Left leg with index DVT	207 (62)	218 (61)	425 (62)
Extends into common femoral and/or iliac vein	195 (58)	196 (55)	391 (57)
Previous DVT or PE	83 (25)	87 (25)	170 (25)
Previous ipsilateral DVT	5 (1)	14 (4)	19 (3)
DVT risk factors: *n (%)******			
Major surgery	27 (8)	34 (10)	61 (9)
Hospitalization	26 (8)	38 (11)	64 (9)
Plaster cast immobilization	8 (2)	9 (3)	17 (2)
Childbirth	3 (1)	5 (1)	8 (1)
Outpatient when DVT diagnosed: *n (%)*	268 (80)	300 (85)	568 (82)
DVT symptom duration (prior to randomization), days: *median (IQR)*	6 (4, 10)	6 (4, 9)	6 (4, 10)

* Patients may contribute to more than one category

IQR, inter-quartile range; DVT, deep vein thrombosis; PE, pulmonary embolism

Notes for Tables 2-4

* statistical comparison using an unpaired t-test (based on the raw data)

† statistical comparison using a Wald test using a growth curve model with piece-wise linear regression over time adjusted for stratification factors: extent of DVT (iliofemoral vs. femoral-popliteal) and center, and baseline covariates: age, sex, BMI, Villalta score.

VEINES-QOL score (0-100 range) – higher is better; SF-36 major scales (0-100 range): physical component score (PCS) and mental component score (MCS) – higher is better; a 4-point difference is considered to be clinically meaningful

‡ Auxiliary variables used in multiple imputation (MI): for SF-36 (MCS and PCS), age (continuous), sex, race, BMI (continuous) and all available SF-36 scores from previous visits; for VEINES-QOL, age (continuous), sex, BMI, extent of index DVT and all available VEINES scores from previous visits

SE, standard error; Est, estimate; 95% CI, 95% confidence interval

Table 2. All Patients: Change in Disease-specific and General QOL according to Treatment

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-QOL:											
Baseline to 1 month:											
Raw data*	314	14.2	1.4	314	8.5	1.2	5.7	1.8	2.1	9.3	**0.0021**
Model fitted†		14.7	1.3		9.0	1.3	5.7	1.7	2.5	9.0	**0.0006**
Model fitted using MI‡		14.9	1.3		8.9	1.3	6.0	1.7	2.7	9.3	**0.0003**
Baseline to 6 months:											
Raw data*	287	26.0	1.6	277	21.3	1.5	4.7	2.1	0.5	8.9	0.03
Model fitted†		26.5	1.3		21.5	1.3	5.1	1.7	1.7	8.4	**0.0029**
Model fitted using MI‡		27.1	1.3		21.6	1.3	5.5	1.6	2.3	8.7	**0.0008**
Baseline to 12 months:											
Raw data*	267	26.0	1.6	252	25.1	1.6	0.9	2.2	-3.5	5.3	0.70
Model fitted†		26.8	1.3		25.3	1.4	1.5	1.7	-1.8	4.8	0.38
Model fitted using MI‡		27.2	1.3		25.7	1.3	1.5	1.7	-1.8	4.7	0.37
Baseline to 18 months:											
Raw data*	244	27.2	1.8	220	25.5	1.7	1.7	2.5	-3.1	6.6	0.48
Model fitted†		27.4	1.3		24.7	1.3	2.7	1.7	-0.6	5.9	0.11
Model fitted using MI‡		28.1	1.3		25.3	1.3	2.7	1.6	-0.5	5.9	0.10
Baseline to 24 months:											
Raw data*	249	27.4	1.7	227	24.1	1.8	3.3	2.5	-1.6	8.2	0.18
Model fitted†		28.1	1.5		24.2	1.5	3.9	1.9	0.1	7.6	0.04
Model fitted using MI‡		28.9	1.6		25.0	1.5	3.9	2.0	0.1	7.8	0.04
VEINES-Sym:											
Baseline to 1 month:											
Raw data*	311	12.1	1.5	314	8.8	1.3	3.3	2.0	-0.6	7.1	0.10
Model fitted†		12.9	1.5		9.6	1.5	3.3	2.1	-0.8	7.4	0.11
Model fitted using MI‡		13.1	1.5		9.3	1.5	3.8	2.1	-0.4	8.0	0.08
Baseline to 6 months:											
Raw data*	285	20.2	1.6	277	16.2	1.5	4.0	2.2	-0.3	8.3	0.07
Model fitted†		21.1	1.5		16.8	1.5	4.3	2.1	0.1	8.4	0.04
Model fitted using MI‡		21.5	1.5		16.8	1.5	4.7	2.2	0.4	9.1	0.03
Baseline to 12 months:											
Raw data*	266	18.1	1.6	252	18.1	1.6	0.0	2.3	-4.5	4.5	0.99
Model fitted†		19.1	1.5		18.2	1.5	0.9	2.1	-3.3	5.1	0.68
Model fitted using MI‡		19.2	1.5		18.4	1.5	0.8	2.2	-3.5	5.1	0.72
Baseline to 18 months:											
Raw data*	243	19.3	1.8	220	18.1	1.8	1.2	2.6	-3.9	6.2	0.65
Model fitted†		20.2	1.5		18.2	1.5	2.0	2.1	-2.2	6.1	0.35
Model fitted using MI‡		20.6	1.5		18.7	1.5	2.0	2.1	-2.1	6.1	0.34
Baseline to 24 months:											
Raw data*	248	20.7	1.7	227	18.2	1.7	2.5	2.4	-2.2	7.1	0.30
Model fitted†		21.2	1.6		18.2	1.7	3.0	2.3	-1.5	7.6	0.19
Model fitted using MI‡		22.1	1.7		18.9	1.6	3.2	2.3	-1.3	7.7	0.16

Table 2. All Patients: Change in Disease-specific and General QOL according to Treatment

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 PCS:											
Baseline to 1 month:											
Raw data*	313	7.2	0.6	314	4.9	0.6	2.3	0.9	0.6	4.0	**0.0077**
Model fitted†		7.4	0.7		5.1	0.7	2.4	0.9	0.5	4.2	0.01
Model fitted using MI‡		7.6	0.7		5.0	0.7	2.6	1.0	0.7	4.4	**0.0072**
Baseline to 6 months:											
Raw data*	287	10.9	0.8	277	9.5	0.7	1.4	1.1	-0.7	3.5	0.19
Model fitted†		11.5	0.7		9.7	0.7	1.8	0.9	0.0	3.6	0.05
Model fitted using MI‡		11.8	0.7		9.6	0.7	2.2	1.0	0.3	4.1	0.02
Baseline to 12 months:											
Raw data*	266	11.6	0.8	252	10.4	0.8	1.2	1.1	-1.0	3.4	0.27
Model fitted†		11.5	0.7		10.0	0.7	1.5	0.9	-0.3	3.4	0.10
Model fitted using MI‡		11.8	0.7		10.0	0.7	1.8	0.9	-0.1	3.6	0.06
Baseline to 18 months:											
Raw data*	242	11.9	0.8	220	11.6	0.9	0.3	1.2	-2.1	2.6	0.83
Model fitted†		11.6	0.7		10.3	0.7	1.3	1.0	-0.7	3.3	0.21
Model fitted using MI‡		11.9	0.7		10.5	0.7	1.3	1.0	-0.6	3.3	0.18
Baseline to 24 months:											
Raw data*	248	11.7	0.9	227	11.0	0.9	0.6	1.2	-1.8	3.0	0.62
Model fitted†		11.7	0.8		10.7	0.8	1.0	1.1	-1.2	3.3	0.37
Model fitted using MI‡		11.9	0.8		11.0	0.8	0.9	1.1	-1.3	3.1	0.42
SF-36 MCS:											
Baseline to 1 month:											
Raw data*	314	-0.2	0.7	314	-0.5	0.6	0.3	0.9	-1.5	2.2	0.71
Model fitted†		0.3	0.1		0.4	0.1	-0.1	0.1	-0.3	0.1	0.42
Model fitted using MI‡		0.3	0.1		0.5	0.1	-0.2	0.1	-0.4	0.0	0.11
Baseline to 6 months:											
Raw data*	287	1.8	0.7	277	1.6	0.8	0.2	1.1	-1.9	2.2	0.88
Model fitted†		1.8	0.5		2.4	0.5	-0.6	0.7	-1.9	0.8	0.42
Model fitted using MI‡		1.8	0.5		2.9	0.5	-1.1	0.7	-2.4	0.3	0.11
Baseline to 12 months:											
Raw data*	267	1.8	0.8	252	1.7	0.8	0.1	1.1	-2.1	2.3	0.93
Model fitted†	.	2.2	0.4		2.8	0.5	-0.6	0.6	-1.7	0.5	0.30
Model fitted using MI‡	.	2.3	0.5		3.3	0.5	-1.0	0.6	-2.1	0.1	0.08
Baseline to 18 months:											
Raw data*	243	2.0	0.9	220	2.2	0.8	-0.2	1.2	-2.6	2.2	0.87
Model fitted†		2.5	0.5		3.2	0.5	-0.6	0.6	-1.8	0.5	0.29
Model fitted using MI‡		2.7	0.5		3.6	0.5	-1.0	0.6	-2.2	0.2	0.11
Baseline to 24 months:											
Raw data*	249	2.9	0.8	227	3.0	0.8	-0.1	1.1	-2.3	2.1	0.94
Model fitted†		2.9	0.6		3.6	0.6	-0.7	0.7	-2.1	0.8	0.36
Model fitted using MI‡		3.1	0.6		4.0	0.6	-0.9	0.7	-2.4	0.6	0.22

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Table 3. Iliofemoral DVT Subgroup: Change in Disease-specific and General QOL according to Treatment

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-QOL:											
Baseline to 1 month:											
Raw data*	180	15.5	1.7	169	5.3	1.8	10.2	2.5	5.3	15.1	**<0.0001**
Model fitted†		16.1	1.6		6.1	1.7	10.0	2.2	5.7	14.2	**<0.0001**
Model fitted using MI‡		16.0	1.7		6.0	1.7	10.1	2.1	5.9	14.3	**<0.0001**
Baseline to 6 months:											
Raw data*	168	27.1	2.0	144	18.4	2.1	8.7	2.9	2.9	14.5	**0.0032**
Model fitted†		27.7	1.7		18.8	1.8	8.8	2.2	4.5	13.2	**<0.0001**
Model fitted using MI‡		28.1	1.7		18.9	1.7	9.2	2.1	5.0	13.3	**<0.0001**
Baseline to 12 months:											
Raw data*	153	26.8	2.2	133	24.4	2.2	2.4	3.1	-3.8	8.6	0.44
Model fitted†		27.7	1.7		23.3	1.8	4.3	2.2	0.1	8.6	0.05
Model fitted using MI‡		27.9	1.7		23.5	1.7	4.4	2.1	0.3	8.5	0.04
Baseline to 18 months:											
Raw data*	139	28.3	2.4	122	25.8	2.4	2.4	3.4	-4.2	9.0	0.47
Model fitted†		28.1	1.7		23.2	1.8	4.9	2.2	0.6	9.1	0.02
Model fitted using MI‡		28.6	1.8		23.4	1.7	5.2	2.2	0.9	9.5	0.02
Baseline to 24 months:											
Raw data*	141	28.3	2.3	128	23.3	2.6	5.0	3.4	-1.8	11.8	0.15
Model fitted†		28.5	1.9		23.0	2.0	5.5	2.4	0.8	10.2	0.02
Model fitted using MI‡		29.4	2.0		23.4	1.9	6.0	2.5	1.0	11.0	0.02
VEINES-Sym:											
Baseline to 1 month:											
Raw data*	177	12.7	1.9	169	5.7	1.9	7.1	2.7	1.7	12.4	**0.0094**
Model fitted†		13.6	1.7		6.6	1.8	7.1	2.2	2.7	11.4	**0.0015**
Model fitted using MI‡		13.6	1.7		6.5	1.8	7.0	2.3	2.6	11.5	**0.0020**
Baseline to 6 months:											
Raw data*	166	20.1	2.1	144	13.6	2.1	6.5	3.0	0.7	12.4	0.03
Model fitted†		21.8	1.8		13.9	1.8	7.9	2.2	3.5	12.3	**0.0004**
Model fitted using MI‡		22.0	1.8		14.2	1.9	7.9	2.3	3.3	12.5	**0.0008**
Baseline to 12 months:											
Raw data*	152	18.2	2.2	133	17.1	2.3	1.1	3.2	-5.2	7.3	0.74
Model fitted†		19.7	1.7		15.8	1.8	4.0	2.2	-0.3	8.3	0.07
Model fitted using MI‡		19.7	1.7		16.1	1.9	3.7	2.3	-0.8	8.2	0.11
Baseline to 18 months:											
Raw data*	138	20.2	2.4	122	18.3	2.5	1.9	3.5	-4.9	8.7	0.58
Model fitted†		20.7	1.7		16.0	1.8	4.7	2.2	0.5	8.9	0.03
Model fitted using MI‡		21.2	1.7		16.5	1.9	4.7	2.2	0.3	9.0	0.04
Baseline to 24 months:											
Raw data*	140	20.8	2.2	128	17.2	2.4	3.6	3.3	-2.8	10.1	0.27
Model fitted†		21.6	1.9		16.2	1.9	5.4	2.4	0.7	10.1	0.02
Model fitted using MI‡		22.7	1.9		17.0	2.0	5.6	2.4	0.8	10.4	0.02

Table 3. Iliofemoral DVT Subgroup: Change in Disease-specific and General QOL according to Treatment

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 PCS:											
Baseline to 1 month:											
Raw data*	180	8.2	0.8	169	3.6	0.9	4.6	1.2	2.2	7.0	**0.0002**
Model fitted†		7.7	0.8		4.5	0.8	3.2	1.0	1.3	5.1	**0.0010**
Model fitted using MI‡		7.8	0.8		4.5	0.8	3.3	1.0	1.4	5.2	**0.0007**
Baseline to 6 months:											
Raw data*	168	11.0	1.0	144	8.1	1.1	2.9	1.5	0.0	5.8	0.05
Model fitted†		11.3	0.8		9.3	0.8	1.9	1.0	0.0	3.9	0.05
Model fitted using MI‡		11.7	0.8		9.3	0.8	2.4	1.0	0.4	4.4	0.02
Baseline to 12 months:											
Raw data*	153	11.4	1.1	133	10.4	1.2	1.0	1.6	-2.2	4.3	0.53
Model fitted†		11.1	0.8		10.0	0.8	1.1	1.0	-0.8	3.0	0.25
Model fitted using MI‡		11.5	0.8		10.1	0.8	1.4	0.9	-0.4	3.3	0.13
Baseline to 18 months:											
Raw data*	138	11.5	1.2	122	11.9	1.3	-0.4	1.7	-3.8	2.9	0.81
Model fitted†		11.0	0.8		10.7	0.9	0.3	1.0	-1.7	2.2	0.78
Model fitted using MI‡		11.3	0.8		10.9	0.9	0.5	1.0	-1.5	2.4	0.64
Baseline to 24 months:											
Raw data*	141	11.2	1.2	128	11.2	1.3	0.0	1.8	-3.5	3.4	0.99
Model fitted†	.	10.8	0.9		11.4	0.9	-0.5	1.1	-2.7	1.7	0.63
Model fitted using MI‡	.	11.2	0.9		11.7	1.0	-0.5	1.1	-2.7	1.7	0.66
SF-36 MCS:											
Baseline to 1 month:											
Raw data*	180	0.1	0.9	169	0.3	1.0	-0.1	1.3	-2.7	2.5	0.93
Model fitted†		0.3	0.1		0.4	0.1	-0.1	0.1	-0.3	0.2	0.56
Model fitted using MI‡		0.3	0.1		0.5	0.1	-0.2	0.1	-0.4	0.1	0.21
Baseline to 6 months:											
Raw data*	168	1.9	0.9	144	3.1	1.1	-1.2	1.5	-4.0	1.7	0.43
Model fitted†		1.8	0.6		2.2	0.6	-0.5	0.8	-2.0	1.1	0.56
Model fitted using MI‡		1.8	0.6		2.8	0.6	-0.9	0.8	-2.4	0.5	0.21
Baseline to 12 months:											
Raw data*	153	1.9	1.0	133	3.4	1.2	-1.5	1.6	-4.6	1.6	0.34
Model fitted†		2.1	0.5		2.6	0.5	-0.5	0.7	-1.9	0.8	0.41
Model fitted using MI‡		2.2	0.5		3.2	0.5	-0.9	0.6	-2.2	0.3	0.15
Baseline to 18 months:											
Raw data*	138	1.5	1.2	122	3.4	1.2	-1.8	1.7	-5.2	1.5	0.27
Model fitted†		2.4	0.5		3.1	0.5	-0.6	0.6	-1.9	0.6	0.33
Model fitted using MI‡		2.6	0.5		3.5	0.5	-0.9	0.6	-2.2	0.3	0.16
Baseline to 24 months:											
Raw data*	141	3.7	1.1	128	3.9	1.2	-0.2	1.6	-3.3	2.9	0.88
Model fitted†		2.8	0.6		3.5	0.6	-0.7	0.7	-2.2	0.7	0.32
Model fitted using MI‡		3.0	0.6		3.9	0.6	-0.9	0.7	-2.4	0.6	0.23

Table 4. Femoral-popliteal DVT Subgroup: Change in Disease-specific and General QOL according to Treatment

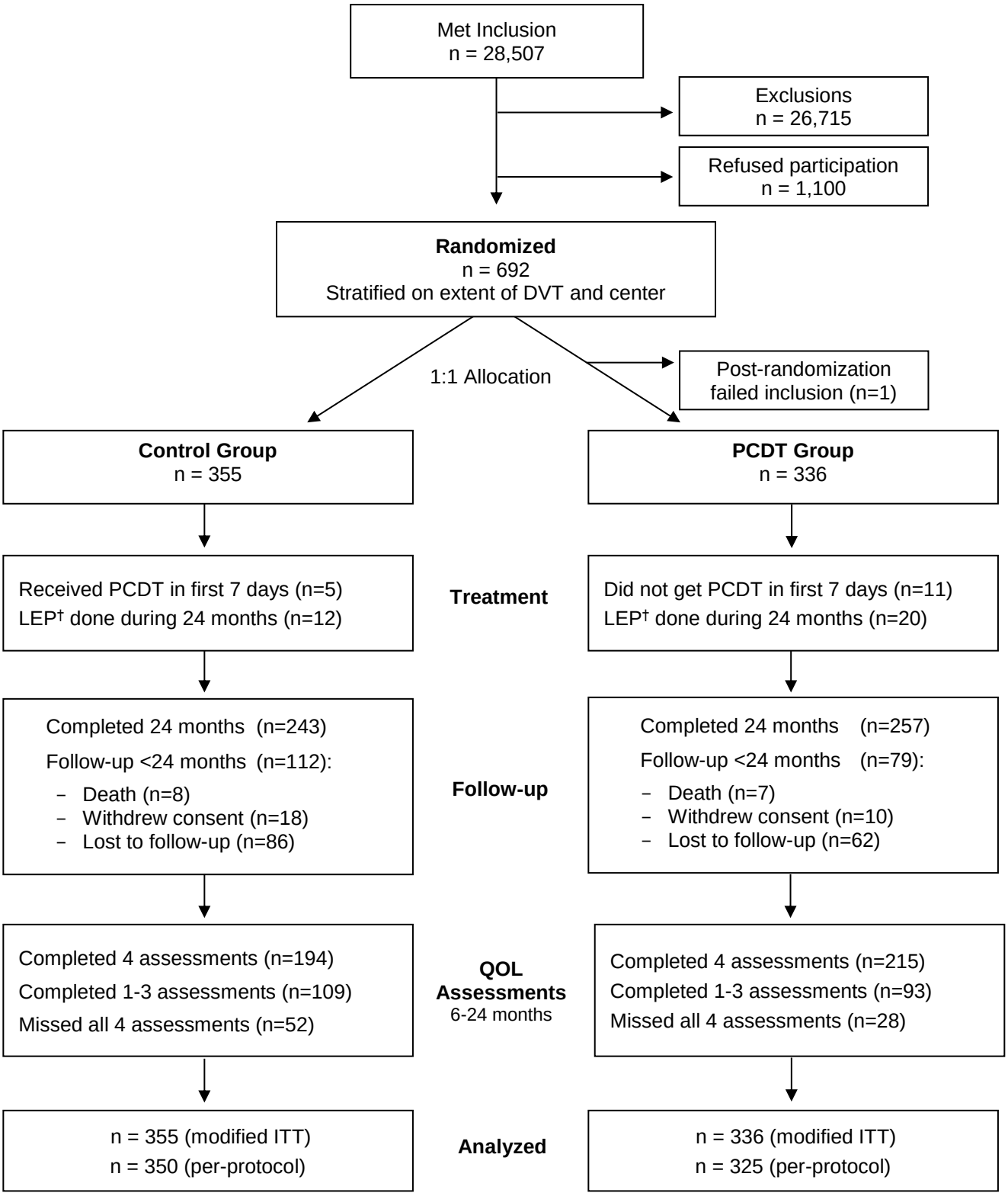
Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-QOL:											
Baseline to 1 month:											
Raw data*	134	12.4	2.2	145	12.3	1.6	0.1	2.7	-5.2	5.4	0.97
Model fitted†		13.0	1.9		12.5	1.8	0.5	2.4	-4.2	5.2	0.83
Model fitted using MI‡		13.5	1.9		12.6	1.8	0.9	2.5	-3.9	5.7	0.71
Baseline to 6 months:											
Raw data*	119	24.4	2.4	133	24.3	2.0	0.0	3.1	-6.1	6.1	0.75
Model fitted†		25.0	1.9		24.4	1.9	0.6	2.4	-4.1	5.4	0.32
Model fitted using MI‡		25.8	1.9		24.8	1.9	1.0	2.4	-3.6	5.7	0.28
Baseline to 12 months:											
Raw data*	114	24.9	2.4	119	25.9	2.1	-1.0	3.2	-7.3	5.3	0.83
Model fitted†		25.5	1.9		27.9	1.9	-2.4	2.4	-7.0	2.3	0.90
Model fitted using MI‡		26.1	1.9		28.6	1.9	-2.5	2.3	-7.1	2.1	0.82
Baseline to 18 months:											
Raw data*	105	25.8	2.7	98	25.0	2.5	0.8	3.7	-6.5	8.1	0.99
Model fitted†		26.5	2.0		26.8	1.9	-0.3	2.4	-5.0	4.5	0.79
Model fitted using MI‡		27.2	2.0		27.7	1.9	-0.6	2.4	-5.3	4.2	0.67
Baseline to 24 months:											
Raw data*	108	26.3	2.6	99	25.2	2.3	1.1	3.5	-5.8	8.1	0.75
Model fitted†		27.4	2.2		25.7	2.1	1.8	2.7	-3.5	7.1	0.51
Model fitted using MI‡		28.3	2.2		26.9	2.2	1.4	2.8	-4.1	6.9	0.61
VEINES-Sym:											
Baseline to 1 month:											
Raw data*	134	11.2	2.3	145	12.5	1.8	-1.3	2.9	-6.9	4.4	0.66
Model fitted†		12.4	2.0		12.7	1.9	-0.3	2.5	-5.1	4.5	0.91
Model fitted using MI‡		12.8	2.0		12.4	1.9	0.4	2.5	-4.5	5.4	0.86
Baseline to 6 months:											
Raw data*	119	20.3	2.4	133	19.1	2.2	1.2	3.3	-5.2	7.7	0.70
Model fitted†		20.8	2.0		19.6	1.9	1.1	2.4	-3.7	5.9	0.65
Model fitted using MI‡		21.2	2.0		19.6	1.9	1.7	2.5	-3.2	6.6	0.50
Baseline to 12 months:											
Raw data*	114	18.0	2.4	119	19.2	2.3	-1.2	3.3	-7.6	5.3	0.72
Model fitted†		18.9	2.0		20.9	1.9	-2.1	2.4	-6.8	2.6	0.39
Model fitted using MI‡		18.9	2.0		20.9	1.9	-2.1	2.3	-6.6	2.5	0.38
Baseline to 18 months:											
Raw data*	105	18.0	2.8	98	17.9	2.7	0.1	3.8	-7.5	7.7	0.97
Model fitted†		20.0	2.0		20.6	2.0	-0.7	2.4	-5.4	4.1	0.79
Model fitted using MI‡		20.3	2.0		20.9	1.9	-0.6	2.3	-5.1	3.9	0.79
Baseline to 24 months:											
Raw data*	108	20.4	2.7	99	19.5	2.1	0.9	3.5	-5.9	7.7	0.78
Model fitted†		21.1	2.2		20.3	2.1	0.8	2.7	-4.5	6.1	0.78
Model fitted using MI‡		21.7	2.1		20.8	2.1	0.9	2.6	-4.3	6.0	0.74

Table 4. Femoral-popliteal DVT Subgroup: Change in Disease-specific and General QOL according to Treatment

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 PCS:											
Baseline to 1 month:											
Raw data*	133	5.9	1.0	145	6.4	0.8	-0.5	1.2	-2.9	2.0	0.70
Model fitted†		6.3	0.9		6.6	0.8	-0.3	1.1	-2.4	1.8	0.77
Model fitted using MI‡		6.4	0.9		6.4	0.9	0.0	1.1	-2.2	2.1	0.97
Baseline to 6 months:											
Raw data*	119	10.7	1.2	133	11.0	1.0	-0.3	1.5	-3.3	2.7	0.86
Model fitted†		10.4	0.9		11.0	0.9	-0.6	1.1	-2.7	1.5	0.59
Model fitted using MI‡		10.8	0.9		10.7	0.9	0.0	1.1	-2.1	2.1	0.98
Baseline to 12 months:											
Raw data*	113	12.0	1.1	119	10.5	1.0	1.5	1.5	-1.4	4.5	0.31
Model fitted†		10.9	0.9		11.0	0.9	-0.2	1.1	-2.2	1.9	0.88
Model fitted using MI‡		11.1	0.9		10.9	0.8	0.2	1.0	-1.8	2.2	0.85
Baseline to 18 months:											
Raw data*	104	12.4	1.2	98	11.2	1.2	1.2	1.7	-2.2	4.5	0.50
Model fitted†		11.3	0.9		11.1	0.9	0.3	1.1	-1.9	2.5	0.82
Model fitted using MI‡		11.5	0.9		11.1	0.9	0.4	1.1	-1.7	2.5	0.73
Baseline to 24 months:											
Raw data*	107	12.3	1.2	99	10.9	1.2	1.4	1.7	-2.0	4.8	0.41
Model fitted†		11.8	1.0		11.1	1.0	0.7	1.3	-1.8	3.2	0.59
Model fitted using MI‡		11.8	1.0		11.3	1.0	0.5	1.2	-1.9	2.9	0.66
SF-36 MCS:											
Baseline to 1 month:											
Raw data*	134	-0.6	1.0	145	-1.4	0.8	0.8	1.3	-1.7	3.4	0.53
Model fitted†		0.3	0.1		0.4	0.1	-0.1	0.1	-0.3	0.2	0.56
Model fitted using MI‡		0.3	0.1		0.5	0.1	-0.2	0.1	-0.4	0.1	0.21
Baseline to 6 months:											
Raw data*	119	1.5	1.1	133	0.0	1.0	1.5	1.5	-1.5	4.6	0.33
Model fitted†		1.8	0.6		2.2	0.6	-0.5	0.8	-2.0	1.1	0.56
Model fitted using MI‡		1.8	0.6		2.8	0.6	-0.9	0.8	-2.4	0.5	0.21
Baseline to 12 months:											
Raw data*	114	1.6	1.3	119	-0.2	1.0	1.9	1.6	-1.3	5.1	0.26
Model fitted†		2.1	0.5		2.6	0.5	-0.5	0.7	-1.9	0.8	0.41
Model fitted using MI‡		2.2	0.5		3.2	0.5	-0.9	0.6	-2.2	0.3	0.15
Baseline to 18 months:											
Raw data*	105	2.6	1.2	98	0.7	1.1	1.9	1.7	-1.4	5.2	0.26
Model fitted†		2.4	0.5		3.1	0.5	-0.6	0.6	-1.9	0.6	0.33
Model fitted using MI‡		2.6	0.5		3.5	0.5	-0.9	0.6	-2.2	0.3	0.16
Baseline to 24 months:											
Raw data*	108	1.8	1.1	99	1.8	1.2	0.1	1.6	-3.1	3.3	0.95
Model fitted†		2.8	0.6		3.5	0.6	-0.7	0.7	-2.2	0.7	0.32
Model fitted using MI‡		3.0	0.6		3.9	0.6	-0.9	0.7	-2.4	0.6	0.23

1

Figure 1: CONSORT diagram for participants in QOL analyses



† LEP denotes late endovascular procedure.

Figure 2: VEINES-QOL model-fitted change scores (Baseline to 24 months) treatment effects within subgroups. SE, standard error; CI, confidence interval

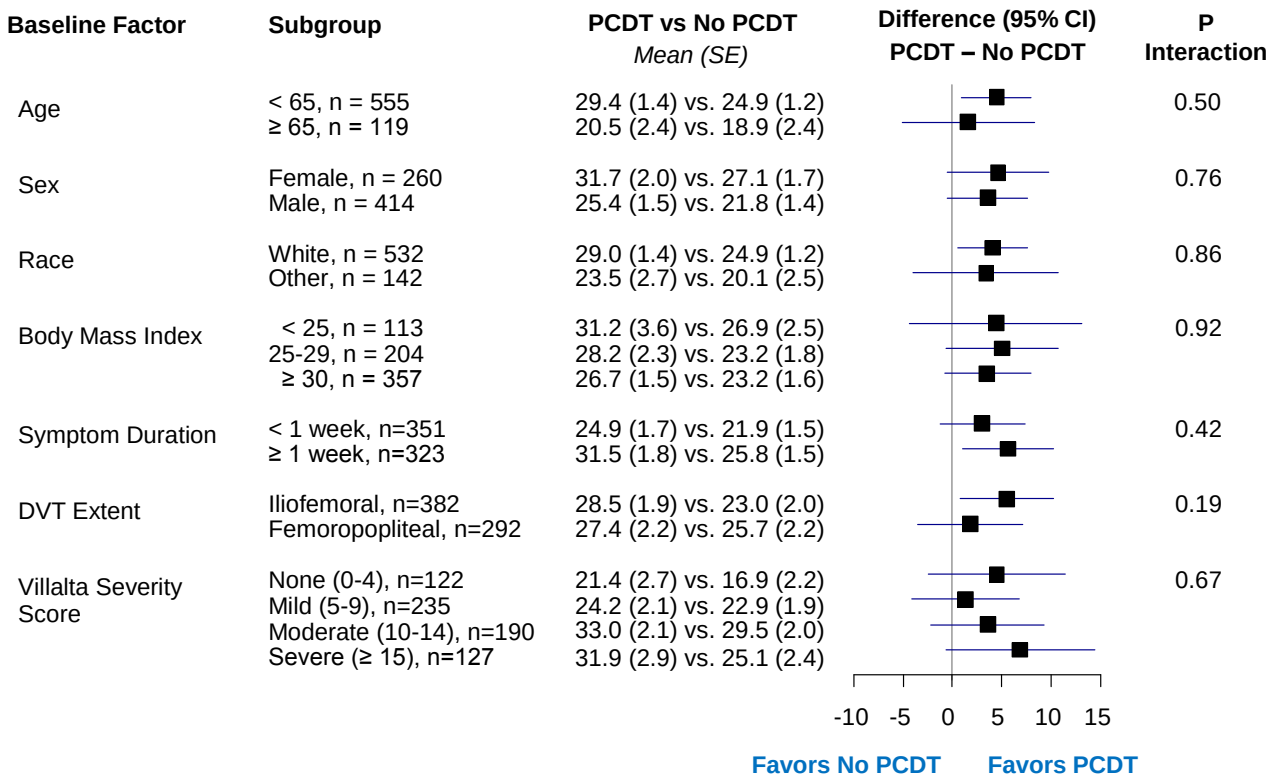


Figure 3: LOESS-smoothed estimates of the model-predicted VEINES-QOL mean change-from-baseline scores at each assessment for the 4 groups defined by extent of DVT and treatment arm. IF, iliofemoral DVT; FP, isolated femoral-popliteal DVT

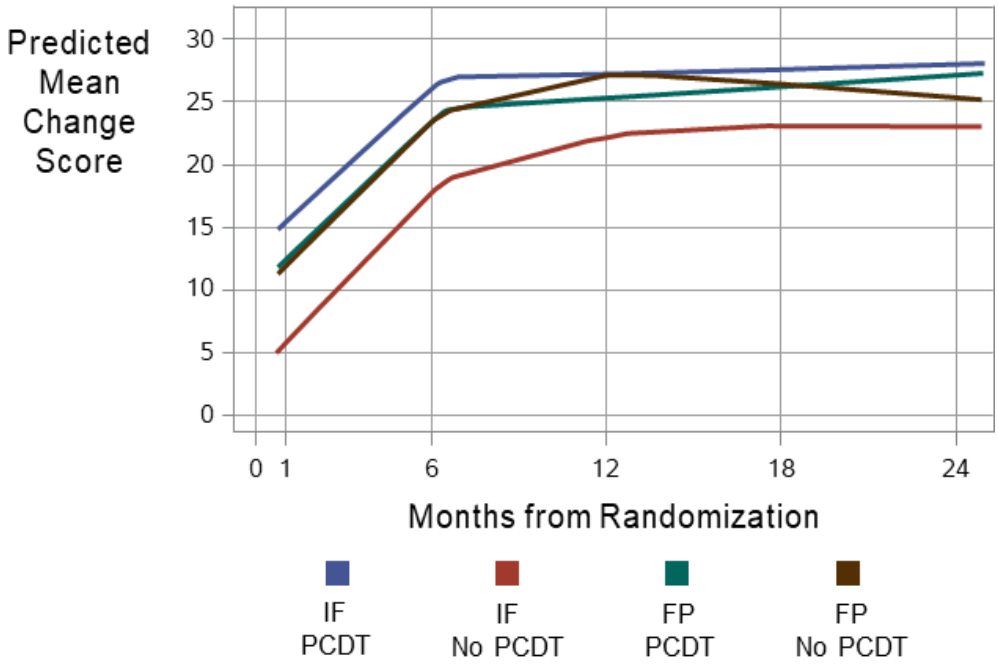
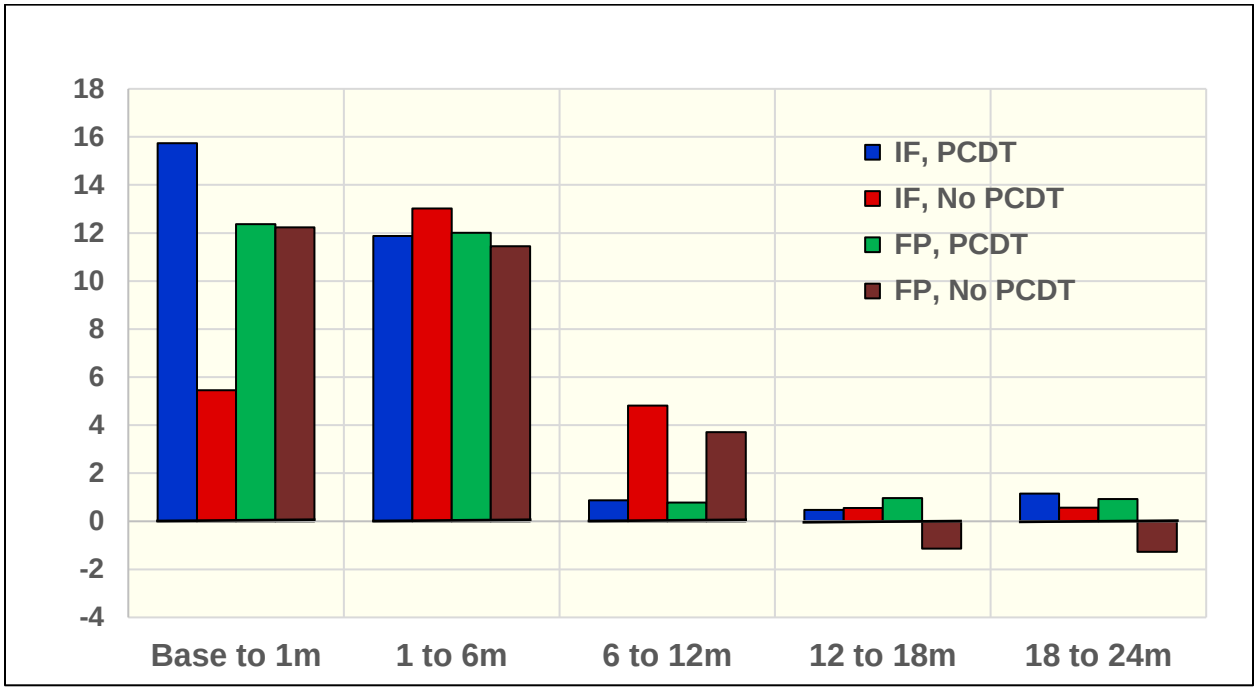


Figure 4. VEINES-QOL Incremental Change by Group (Model-fitted Estimates). IF, iliofemoral DVT; FP, isolated femoral-popliteal DVT



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Supplementary Materials

Tables A-C: Modified ITT set

Table A. All Patients: Disease-specific and general QOL mean scores at each assessment point, according to treatment and treatment difference

Table B. Iliofemoral DVT Subgroup: Disease-specific and general QOL mean scores at each assessment point, according to treatment and treatment difference

Table C. Femoral-popliteal DVT Subgroup: Disease-specific and general QOL mean scores at each assessment point, according to treatment and treatment difference

Footnotes for Supplementary Tables A-C

VEINES-QOL score (0-100 range) – higher is better; SF-36 major scales: physical component score (PCS) and mental component score (MCS) (0-100 range) – higher is better, with a difference of 4 points considered clinically meaningful

SE, standard error; Est, estimate; CI, confidence interval

Tables D-I: Per Protocol Analysis Set

Table D. All Patients: Disease-specific QOL (VEINES-QOL, VEINES-Sym) results according to treatment

Table E. All Patients: General QOL (SF-36 PCS and MCS) according to treatment

Table F. Iliofemoral DVT subgroup: Disease-specific QOL (VEINES QOL, VEINES-Sym) results according to treatment

Table G. Iliofemoral DVT subgroup: General QOL (SF-36 PCS and MCS) results according to treatment

Table H. Femoral-popliteal DVT subgroup: Disease-specific QOL (VEINES-QOL, VEINES-Sym) results according to treatment

Table I. Femoral-popliteal DVT subgroup: General QOL (SF-36 PCS and MCS) results according to treatment

Footnotes for Supplementary Tables D-I

* statistical comparison using an unpaired t-test (based on the raw data)

† statistical comparison using a Wald test using a growth curve model with piece-wise linear regression over time adjusted for stratification factors: extent of DVT (iliofemoral vs. femoropopliteal) and center, and baseline covariates: age, sex, BMI, Villalta score.

VEINES-QOL score (0-100 range) – higher is better; SF-36 major scales: physical component score (PCS) and mental component score (MCS) – higher is better, with a difference of 4 points considered clinically meaningful

‡ Auxiliary variables used in multiple imputation: for SF-36 (MCS and PCS), age (continuous), sex, race, BMI (continuous) and all available SF-36 scores from previous visits; for VEINES-QOL, age (continuous), sex, BMI, extent of index DVT and all available VEINES scores from previous visits

MI, multiple imputation; SE, standard error; Est, estimate; CI, confidence interval

Table J. Missing QOL Assessments by Visit and Treatment

Appendix

Appendix A. Interaction terms involving time, treatment and extent of DVT in the growth curve models

Appendix B. ATTRACT Study Leadership and Investigators

Table A. All Patients: Disease-specific and general QOL mean scores at each assessment point, according to treatment and treatment difference

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT			
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*	
VEINES-QOL:										
At Baseline	329	50.3	1.3	347	51.4	1.3	-1.1	1.8	-4.7	2.5
At 1 month	318	64.9	1.4	320	60.3	1.4	4.6	1.9	0.8	8.5
At 6 months	290	77.0	1.4	282	73.1	1.4	3.9	2.0	0.1	7.8
At 12 months	270	77.8	1.4	256	77.7	1.4	0.1	2.0	-3.8	4.1
At 18 months	245	78.9	1.5	222	78.8	1.5	0.1	2.1	-4.0	4.3
At 24 months	250	80.3	1.3	230	77.9	1.5	2.4	2.0	-1.5	6.3
VEINES-Sym:										
At Baseline	327	56.7	1.4	347	56.7	1.4	0.0	1.9	-3.8	3.8
At 1 month	317	69.5	1.4	320	66.3	1.4	3.2	2.0	-0.6	7.0
At 6 months	290	77.8	1.3	282	73.7	1.5	4.1	2.0	0.2	7.9
At 12 months	270	76.5	1.4	256	76.4	1.4	0.1	2.0	-3.9	4.0
At 18 months	245	77.3	1.5	222	76.6	1.6	0.7	2.2	-3.6	5.1
At 24 months	250	79.9	1.3	230	77.4	1.5	2.5	2.0	-1.4	6.3
SF-36 PCS:										
At Baseline	328	35.7	0.6	347	37.1	0.6	-1.4	0.9	-3.1	0.3
At 1 month	318	42.9	0.6	320	41.9	0.6	1.0	0.9	-0.7	2.7
At 6 months	290	47.1	0.7	282	46.3	0.7	0.8	0.9	-1.0	2.7
At 12 months	270	48.0	0.7	256	47.5	0.7	0.5	1.0	-1.4	2.4
At 18 months	244	47.9	0.7	222	48.7	0.7	-0.8	1.0	-2.8	1.2
At 24 months	250	48.1	0.7	230	48.4	0.7	-0.4	1.0	-2.3	1.6
SF-36 MCS:										
At Baseline	329	48.2	0.7	347	48.4	0.7	-0.1	1.0	-2.1	1.9
At 1 month	318	48.2	0.7	320	48.4	0.7	-0.2	1.0	-2.1	1.7
At 6 months	290	50.1	0.7	282	51.2	0.6	-1.2	0.9	-3.0	0.7
At 12 months	270	50.4	0.7	256	51.8	0.7	-1.4	1.0	-3.3	0.6
At 18 months	244	50.9	0.7	222	52.7	0.6	-1.8	1.0	-3.7	0.1
At 24 months	250	52.1	0.6	230	53.2	0.6	-1.1	0.9	-2.8	0.5

Table B. Iliofemoral DVT Subgroup: Disease-specific and general QOL mean scores at each assessment point, according to treatment and treatment difference

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT			
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*	
VEINES-QOL:										
At Baseline	193	48.0	1.7	190	49.2	1.7	-1.2	2.4	-6.0	3.5
At 1 month	181	63.5	1.8	173	55.1	1.9	8.4	2.6	3.3	13.6
At 6 months	169	76.4	1.9	147	68.6	2.0	7.9	2.8	2.4	13.3
At 12 months	154	76.2	2.0	135	75.1	2.0	1.1	2.8	-4.5	6.6
At 18 months	139	77.5	1.9	123	76.4	2.1	1.1	2.9	-4.5	6.7
At 24 months	141	78.7	1.8	129	75.2	2.1	3.5	2.8	-2.0	9.0
VEINES-Sym:										
At Baseline	191	55.6	1.7	190	56.0	1.9	-0.4	2.6	-5.4	4.6
At 1 month	180	68.8	1.8	173	62.6	2.0	6.2	2.7	0.9	11.5
At 6 months	169	77.5	1.8	147	70.7	2.1	6.7	2.7	1.3	12.1
At 12 months	154	75.2	1.9	135	74.8	2.1	0.4	2.8	-5.2	5.9
At 18 months	139	77.0	1.9	123	75.0	2.3	1.9	3.0	-3.9	7.8
At 24 months	141	79.1	1.7	129	75.3	2.1	3.8	2.7	-1.6	9.1
SF-36 PCS:										
At Baseline	193	34.8	0.9	190	36.5	0.8	-1.7	1.2	-4.0	0.6
At 1 month	181	42.9	0.8	173	40.2	0.8	2.7	1.2	0.4	4.9
At 6 months	169	46.4	0.9	147	44.7	1.0	1.6	1.3	-0.9	4.2
At 12 months	154	47.0	0.9	135	46.9	0.9	0.0	1.3	-2.6	2.6
At 18 months	138	46.8	1.0	123	48.1	1.0	-1.3	1.4	-4.1	1.4
At 24 months	141	46.6	1.0	129	48.2	0.9	-1.6	1.4	-4.2	1.1
SF-36 MCS:										
At Baseline	193	47.1	0.9	190	45.7	1.0	1.4	1.4	-1.3	4.1
At 1 month	181	47.2	1.0	173	46.2	1.0	1.1	1.4	-1.7	3.8
At 6 months	169	49.3	0.9	147	50.0	1.0	-0.7	1.3	-3.4	1.9
At 12 months	154	49.1	1.0	135	50.9	1.0	-1.8	1.4	-4.5	1.0
At 18 months	138	49.2	1.0	123	51.0	1.0	-1.8	1.4	-4.6	1.0
At 24 months	141	51.3	0.9	129	51.7	0.9	-0.4	1.3	-2.9	2.1

Table C. Femoral-popliteal DVT Subgroup: Disease-specific and general QOL mean scores at each assessment point, according to treatment and treatment difference

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT			
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*	
VEINES-QOL:										
At Baseline	136	53.5	2.0	157	54.1	1.9	-0.5	2.8	-6.0	5.0
At 1 month	137	66.8	2.1	147	66.4	1.9	0.3	2.8	-5.2	5.8
At 6 months	121	77.8	2.0	135	78.0	1.8	-0.1	2.7	-5.4	5.2
At 12 months	116	80.0	2.0	121	80.6	2.0	-0.6	2.8	-6.2	5.0
At 18 months	106	80.8	2.2	99	81.8	2.1	-1.0	3.1	-7.0	5.1
At 24 months	109	82.4	1.9	101	81.4	1.9	1.0	2.7	-4.4	6.4
VEINES-Sym:										
At Baseline	136	58.3	2.1	157	57.7	2.0	0.7	3.0	-5.2	6.5
At 1 month	137	70.3	2.1	147	70.5	1.9	-0.2	2.8	-5.7	5.3
At 6 months	121	78.2	2.0	135	77.0	2.0	1.2	2.8	-4.3	6.8
At 12 months	116	78.1	2.1	121	78.1	2.0	0.0	2.9	-5.6	5.6
At 18 months	106	77.7	2.4	99	78.5	2.3	-0.8	3.3	-7.3	5.7
At 24 months	109	80.9	2.0	101	80.1	2.0	0.8	2.9	-4.9	6.4
SF-36 PCS:										
At Baseline	135	37.0	0.9	157	37.8	0.9	-0.8	1.3	-3.4	1.7
At 1 month	137	43.0	1.0	147	44.0	0.9	-1.0	1.3	-3.6	1.7
At 6 months	121	48.2	1.0	135	48.0	1.0	0.2	1.4	-2.5	2.9
At 12 months	116	49.3	0.9	121	48.1	1.0	1.3	1.4	-1.5	4.0
At 18 months	106	49.4	1.0	99	49.5	1.1	-0.1	1.5	-3.0	2.9
At 24 months	109	49.9	0.9	101	48.8	1.1	1.1	1.4	-1.6	3.9
SF-36 MCS:										
At Baseline	136	49.8	1.1	157	51.6	0.9	-1.8	1.4	-4.6	1.1
At 1 month	137	49.5	1.0	147	51.0	0.8	-1.6	1.3	-4.2	1.0
At 6 months	121	51.2	1.0	135	52.6	0.8	-1.4	1.3	-3.9	1.2
At 12 months	116	52.1	1.0	121	52.8	0.9	-0.7	1.4	-3.4	2.0
At 18 months	106	53.1	1.0	99	54.8	0.8	-1.7	1.3	-4.2	0.8
At 24 months	109	53.0	0.8	101	55.1	0.7	-2.1	1.1	-4.2	0.1

Table D. All patients: Disease-specific QOL (VEINES-QOL, VEINES-Sym) results according to treatment: Per Protocol Analysis Set

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-QOL:											
At Baseline	319	50.3	1.3	342	51.4	1.3	-1.1	1.9	-4.8	2.5	
At 30 days	309	65.1	1.4	316	60.4	1.4	4.7	2.0	0.8	8.6	
At 6 months	281	77.0	1.4	280	73.0	1.4	4.0	2.0	0.1	7.9	
At 12 months	262	77.9	1.5	253	77.7	1.4	0.3	2.0	-3.8	4.3	
At 18 months	237	79.1	1.5	219	78.6	1.5	0.5	2.1	-3.7	4.7	
At 24 months	243	80.6	1.3	227	77.8	1.5	2.9	2.0	-1.1	6.8	
Change baseline to 30 days											
Raw data*	305	14.4	1.4	310	8.5	1.2	5.9	1.9	2.2	9.5	**0.0017**
Model-fitted†		15.0	1.3		9.0	1.3	6.0	1.7	2.7	9.3	**0.0004**
Model-fitted using MI‡		15.3	1.3		8.8	1.3	6.5	1.7	3.2	9.9	**0.0001**
Change baseline to 6 months											
Raw data*	278	26.0	1.6	275	21.2	1.5	4.8	2.2	0.5	9.0	0.03
Model-fitted†		26.6	1.3		21.4	1.3	5.1	1.7	1.8	8.5	**0.0029**
Model-fitted using MI‡		27.2	1.4		21.4	1.4	5.8	1.8	2.3	9.3	**0.0013**
Change baseline to 12 months											
Raw data*	259	26.2	1.7	249	25.1	1.6	1.1	2.3	-3.4	5.6	0.64
Model-fitted†		27.0	1.4		25.2	1.4	1.8	1.7	-1.6	5.1	0.31
Model-fitted using MI‡		27.4	1.4		25.7	1.4	1.7	1.8	-1.8	5.3	0.33
Change baseline to 18 months											
Raw data*	236	27.6	1.8	217	25.3	1.7	2.3	2.5	-2.6	7.2	0.36
Model-fitted†		27.7	1.3		24.6	1.4	3.1	1.7	-0.2	6.4	0.06
Model-fitted using MI‡		28.4	1.3		25.2	1.4	3.2	1.7	-0.2	6.6	0.06
Change baseline to 24 months											
Raw data*	242	27.8	1.8	224	23.9	1.8	3.9	2.5	-1.0	8.9	0.12
Model-fitted†		28.4	1.5		24.0	1.5	4.5	1.9	0.7	8.3	0.02
Model-fitted using MI‡		29.4	1.5		24.7	1.6	4.7	2.0	0.8	8.6	0.02

Table D, continued

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-Sym:											
At Baseline	317	56.8	1.4	342	56.6	1.4	0.2	2.0	-3.7	4.1	
At 30 days	308	69.7	1.4	316	66.2	1.4	3.5	2.0	-0.4	7.4	
At 6 months	281	77.6	1.4	280	73.6	1.5	4.0	2.0	0.1	7.9	
At 12 months	262	76.5	1.4	253	76.3	1.5	0.1	2.0	-3.9	4.1	
At 18 months	237	77.3	1.5	219	76.4	1.6	0.9	2.2	-3.5	5.4	
At 24 months	243	79.9	1.3	227	77.2	1.5	2.7	2.0	-1.2	6.6	
Change baseline to 30 days											
Raw data*	302	12.3	1.5	310	8.8	1.4	3.5	2.0	-0.4	7.4	0.08
Model-fitted†		13.1	1.5		9.7	1.5	3.5	2.1	-0.7	7.6	0.10
Model-fitted using MI‡		13.3	1.6		9.3	1.5	4.0	2.1	-0.2	8.2	0.06
Change baseline to 6 months											
Raw data*	276	20.1	1.6	275	16.2	1.5	3.9	2.2	-0.5	8.2	0.08
Model-fitted†		20.9	1.5		16.9	1.5	4.0	2.2	-0.3	8.2	0.07
Model-fitted using MI‡		21.3	1.6		16.6	1.5	4.7	2.3	0.3	9.1	0.04
Change baseline to 12 months											
Raw data*	258	18.1	1.7	249	18.1	1.6	0.0	2.3	-4.6	4.5	0.99
Model-fitted†		19.0	1.5		18.3	1.5	0.7	2.2	-3.6	5.0	0.75
Model-fitted using MI‡		19.2	1.6		18.4	1.6	0.8	2.2	-3.4	5.0	0.71
Change baseline to 18 months											
Raw data*	235	19.3	1.8	217	18.0	1.9	1.3	2.6	-3.8	6.5	0.62
Model-fitted†		20.1	1.5		18.3	1.5	1.8	2.1	-2.3	6.0	0.39
Model-fitted using MI‡		20.6	1.5		18.4	1.5	2.2	2.1	-1.9	6.3	0.29
Change baseline to 24 months											
Raw data*	241	20.7	1.7	224	18.1	1.7	2.6	2.4	-2.2	7.3	0.29
Model-fitted†		21.2	1.7		18.2	1.7	3.0	2.4	-1.6	7.6	0.21
Model-fitted using MI‡		22.1	1.7		18.5	1.6	3.6	2.3	-0.9	8.2	0.12

Table E. All patients: General QOL (SF-36 PCS and MCS) results according to treatment
Per Protocol Analysis Set

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 PCS:											
At Baseline	318	35.6	0.6	342	37.1	0.6	-1.5	0.9	-3.2	0.2	
At 30 days	309	42.9	0.6	316	42.0	0.6	0.9	0.9	-0.9	2.6	
At 6 months	281	47.0	0.7	280	46.3	0.7	0.7	1.0	-1.2	2.6	
At 12 months	262	47.9	0.7	253	47.5	0.7	0.4	1.0	-1.5	2.3	
At 18 months	236	48.0	0.7	219	48.7	0.7	-0.7	1.0	-2.7	1.4	
At 24 months	243	48.2	0.7	227	48.4	0.7	-0.2	1.0	-2.1	1.8	
Change baseline to 30 days											
Raw data*	304	7.3	0.6	310	4.9	0.6	2.3	0.9	0.6	4.1	**0.0083**
Model-fitted†		7.5	0.7		5.1	0.7	2.3	1.0	0.5	4.2	0.01
Model-fitted using MI‡		7.6	0.7		5.0	0.7	2.6	1.0	0.7	4.5	**0.0080**
Change baseline to 6 months											
Raw data*	278	10.8	0.8	275	9.5	0.7	1.4	1.1	-0.8	3.5	0.21
Model-fitted†		11.4	0.7		9.7	0.7	1.7	1.0	-0.1	3.6	0.07
Model-fitted using MI‡		11.7	0.7		9.6	0.7	2.1	1.0	0.2	4.0	0.03
Change baseline to 12 months											
Raw data*	258	11.7	0.8	249	10.4	0.8	1.3	1.1	-1.0	3.5	0.27
Model-fitted†		11.6	0.7		10.0	0.7	1.6	1.0	-0.3	3.4	0.10
Model-fitted using MI‡		11.9	0.7		10.1	0.7	1.8	1.0	-0.1	3.6	0.06
Change baseline to 18 months											
Raw data*	234	12.1	0.9	217	11.5	0.9	0.6	1.2	-1.8	3.0	0.62
Model-fitted†		11.7	0.7		10.3	0.7	1.4	1.0	-0.6	3.4	0.17
Model-fitted using MI‡		12.0	0.7		10.6	0.7	1.5	1.0	-0.5	3.4	0.14
Change baseline to 24 months											
Raw data*	241	11.9	0.9	224	10.9	0.9	1.0	1.3	-1.5	3.4	0.44
Model-fitted†		11.9	0.8		10.6	0.8	1.3	1.2	-1.0	3.5	0.28
Model-fitted using MI‡		12.2	0.8		11.0	0.8	1.2	1.1	-1.0	3.3	0.30

Table E, continued

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 MCS:											
At Baseline	319	48.2	0.7	342	48.4	0.7	-0.2	1.0	-2.2	1.9	
At 30 days	309	48.3	0.7	316	48.4	0.7	0.0	1.0	-2.0	1.9	
At 6 months	281	50.1	0.7	280	51.2	0.7	-1.1	1.0	-3.0	0.8	
At 12 months	262	50.6	0.7	253	51.8	0.7	-1.2	1.0	-3.1	0.8	
At 18 months	236	51.1	0.7	219	52.7	0.7	-1.6	1.0	-3.5	0.3	
At 24 months	243	52.3	0.6	227	53.2	0.6	-0.9	0.9	-2.6	0.8	
Change baseline to 30 days											
Raw data*	305	0.0	0.7	310	-0.6	0.7	0.5	1.0	-1.3	2.4	0.57
Model-fitted†		0.3	0.1		0.4	0.1	-0.1	0.1	-0.3	0.1	0.44
Model-fitted using MI‡		0.3	0.1		0.5	0.1	-0.2	0.1	-0.4	0.0	0.11
Change baseline to 6 months											
Raw data*	278	1.8	0.7	275	1.6	0.8	0.2	1.1	-1.9	2.3	0.84
Model-fitted†		1.8	0.5		2.3	0.5	-0.5	0.7	-1.9	0.8	0.44
Model-fitted using MI‡		1.8	0.6		2.9	0.5	-1.2	0.7	-2.6	0.3	0.11
Change baseline to 12 months											
Raw data*	259	1.9	0.8	249	1.6	0.8	0.3	1.1	-1.9	2.5	0.78
Model-fitted†	.	2.2	0.5		2.7	0.5	-0.5	0.6	-1.7	0.6	0.37
Model-fitted using MI‡	.	2.2	0.5		3.3	0.5	-1.0	0.6	-2.2	0.1	0.09
Change baseline to 18 months											
Raw data*	235	2.2	0.9	217	2.1	0.8	0.1	1.2	-2.3	2.4	0.96
Model-fitted†		2.6	0.5		3.1	0.5	-0.5	0.6	-1.7	0.7	0.39
Model-fitted using MI‡		2.7	0.5		3.6	0.5	-0.9	0.6	-2.1	0.3	0.13
Change baseline to 24 months											
Raw data*	242	3.1	0.8	224	2.9	0.9	0.2	1.1	-2.1	2.4	0.88
Model-fitted†		3.1	0.6		3.5	0.6	-0.5	0.7	-1.9	0.9	0.50
Model-fitted using MI‡		3.2	0.6		3.9	0.6	-0.8	0.7	-2.2	0.6	0.28

Table F. Iliofemoral DVT Subgroup: Disease-specific QOL (VEINES QOL, VEINES-Sym) results according to treatment: Per Protocol Analysis Set

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-QOL:											
At Baseline	188	48.1	1.7	186	49.2	1.8	-1.1	2.5	-6.0	3.7	
At 30 days	177	64.0	1.9	170	55.1	1.9	8.9	2.7	3.6	14.1	
At 6 months	165	76.6	1.9	146	68.4	2.1	8.2	2.8	2.8	13.7	
At 12 months	151	76.6	2.0	133	75.1	2.0	1.5	2.8	-4.0	7.1	
At 18 months	135	78.1	1.9	121	76.0	2.1	2.1	2.9	-3.5	7.8	
At 24 months	138	79.4	1.8	127	74.8	2.2	4.6	2.8	-0.9	10.1	
Change baseline to 30 days											
Raw data*	176	16.0	1.8	166	5.2	1.8	10.8	2.5	5.8	15.7	**<0.0001**
Model-fitted†		16.6	1.7		6.1	1.7	10.5	2.2	6.2	14.8	**<0.0001**
Model-fitted using MI‡		16.6	1.7		5.8	1.7	10.8	2.2	6.5	15.1	**<0.0001**
Change baseline to 6 months											
Raw data*	164	27.3	2.1	143	18.3	2.1	9.1	3.0	3.2	14.9	**0.0024**
Model-fitted†		27.9	1.7		18.7	1.8	9.2	2.2	4.8	13.6	**<0.0001**
Model-fitted using MI‡		28.4	1.8		18.6	1.8	9.8	2.2	5.4	14.2	**<0.0001**
Change baseline to 12 months											
Raw data*	150	27.2	2.2	131	24.3	2.3	2.9	3.2	-3.3	9.2	0.36
Model-fitted†		28.1	1.7		23.1	1.8	4.9	2.2	0.6	9.3	0.03
Model-fitted using MI‡		28.5	1.7		23.3	1.8	5.2	2.2	0.8	9.5	0.02
Change baseline to 18 months											
Raw data*	135	28.9	2.4	120	25.4	2.4	3.5	3.4	-3.2	10.2	0.30
Model-fitted†		28.6	1.7		22.9	1.8	5.8	2.2	1.5	10.1	**0.0086**
Model-fitted using MI‡		29.4	1.7		23.2	1.8	6.3	2.2	1.9	10.6	**0.0046**
Change baseline to 24 months											
Raw data*	138	28.9	2.3	126	22.8	2.6	6.1	3.5	-0.8	12.9	0.08
Model-fitted†		29.2	1.9		22.6	2.0	6.6	2.4	1.8	11.3	**0.0067**
Model-fitted using MI‡		30.4	1.9		23.0	2.0	7.4	2.5	2.6	12.2	**0.0027**

Table F, continued

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-Sym:											
At Baseline	186	55.7	1.8	186	55.8	1.9	-0.1	2.6	-5.2	5.1	
At 30 days	176	69.3	1.9	170	62.5	2.0	6.8	2.7	1.5	12.2	
At 6 months	165	77.4	1.8	146	70.6	2.1	6.8	2.8	1.4	12.3	
At 12 months	151	75.3	1.9	133	74.7	2.1	0.6	2.8	-5.0	6.2	
At 18 months	135	77.3	2.0	121	74.7	2.3	2.6	3.0	-3.4	8.5	
At 24 months	138	79.5	1.7	127	75.0	2.2	4.6	2.7	-0.8	9.9	
Change baseline to 30 days											
Raw data*	173	13.2	1.9	166	5.5	2.0	7.6	2.7	2.2	13.0	**0.0057**
Model-fitted†		14.1	1.8		6.4	1.8	7.7	2.3	3.2	12.1	**0.0007**
Model-fitted using MI‡		13.9	1.8		6.2	1.8	7.7	2.2	3.3	12.0	**0.0006**
Change baseline to 6 months											
Raw data*	162	20.0	2.1	143	13.4	2.1	6.6	3.0	0.6	12.5	0.03
Model-fitted†		21.8	1.8		13.8	1.8	8.1	2.3	3.6	12.5	**0.0004**
Model-fitted using MI‡		22.0	1.8		13.7	1.8	8.4	2.3	3.8	13.0	**0.0004**
Change baseline to 12 months											
Raw data*	149	18.2	2.2	131	17.0	2.3	1.2	3.2	-5.1	7.5	0.71
Model-fitted†		20.0	1.8		15.6	1.8	4.4	2.2	0.0	8.8	0.05
Model-fitted using MI‡		20.0	1.8		15.7	1.8	4.3	2.1	0.1	8.5	0.04
Change baseline to 18 months											
Raw data*	134	20.4	2.4	120	18.0	2.6	2.5	3.5	-4.5	9.4	0.49
Model-fitted†		21.0	1.7		15.8	1.8	5.3	2.2	0.9	9.6	0.02
Model-fitted using MI‡		21.5	1.8		15.9	1.8	5.6	2.1	1.5	9.7	**0.0081**
Change baseline to 24 months											
Raw data*	137	21.1	2.2	126	16.9	2.5	4.2	3.3	-2.4	10.7	0.21
Model-fitted†		22.1	1.9		15.9	2.0	6.1	2.4	1.4	10.9	0.01
Model-fitted using MI‡		23.1	1.9		16.2	2.0	6.9	2.5	2.1	11.7	**0.0051**

Table G. Iliofemoral DVT Subgroup: General QOL (SF-36 PCS and MCS) results according to treatment: Per Protocol Analysis Set

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 PCS:											
At Baseline	188	34.9	0.9	186	36.5	0.8	-1.7	1.2	-4.0	0.7	
At 30 days	177	43.0	0.8	170	40.3	0.8	2.7	1.2	0.4	5.0	
At 6 months	165	46.4	0.9	146	44.7	1.0	1.7	1.3	-0.8	4.3	
At 12 months	151	47.1	0.9	133	47.0	0.9	0.1	1.3	-2.5	2.7	
At 18 months	134	47.0	1.0	121	48.0	1.0	-1.0	1.4	-3.7	1.8	
At 24 months	138	47.0	1.0	127	48.0	0.9	-1.0	1.4	-3.7	1.6	
Change baseline to 30 days											
Raw data*	176	8.3	0.8	166	3.6	0.9	4.7	1.2	2.3	7.1	**0.0002**
Model-fitted†		7.8	0.8		4.5	0.8	3.3	1.0	1.4	5.2	**0.0009**
Model-fitted using MI‡		7.8	0.8		4.5	0.8	3.3	1.0	1.4	5.2	**0.0006**
Change baseline to 6 months											
Raw data*	164	11.0	1.0	143	8.1	1.1	3.0	1.5	0.0	5.9	0.05
Model-fitted†		11.3	0.8		9.4	0.8	1.9	1.0	0.0	3.9	0.05
Model-fitted using MI‡		11.7	0.8		9.3	0.8	2.3	1.0	0.4	4.3	0.02
Change baseline to 12 months											
Raw data*	150	11.5	1.1	131	10.4	1.2	1.1	1.7	-2.2	4.4	0.51
Model-fitted†		11.2	0.8		10.0	0.8	1.3	1.0	-0.6	3.2	0.19
Model-fitted using MI‡		11.6	0.8		10.1	0.8	1.5	0.9	-0.3	3.3	0.10
Change baseline to 18 months											
Raw data*	134	11.7	1.2	120	11.7	1.3	0.0	1.7	-3.4	3.4	0.99
Model-fitted†		11.2	0.8		10.6	0.9	0.6	1.0	-1.4	2.6	0.54
Model-fitted using MI‡		11.6	0.8		10.9	0.8	0.7	0.9	-1.1	2.6	0.45
Change baseline to 24 months											
Raw data*	138	11.5	1.2	126	11.0	1.3	0.5	1.8	-2.9	4.0	0.76
Model-fitted†		11.1	0.9		11.2	0.9	-0.1	1.1	-2.3	2.2	0.96
Model-fitted using MI‡		11.5	0.9		11.6	0.9	-0.1	1.1	-2.2	2.0	0.93

Table G, continued

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 MCS:											
At Baseline	188	47.0	1.0	186	45.7	1.0	1.3	1.4	-1.5	4.0	
At 30 days	177	47.4	1.0	170	46.1	1.0	1.4	1.4	-1.4	4.1	
At 6 months	165	49.4	0.9	146	50.0	1.0	-0.6	1.4	-3.3	2.1	
At 12 months	151	49.5	1.0	133	50.8	1.0	-1.4	1.4	-4.1	1.4	
At 18 months	134	49.7	1.0	121	50.9	1.0	-1.2	1.4	-4.0	1.5	
At 24 months	138	51.7	0.9	127	51.7	0.9	0.1	1.2	-2.4	2.5	
Change baseline to 30 days											
Raw data*	176	0.4	0.9	166	0.1	1.0	0.3	1.3	-2.4	3.0	0.82
Model-fitted†		0.3	0.1		0.4	0.1	-0.1	0.1	-0.3	0.2	0.60
Model-fitted using MI‡		0.3	0.1		0.5	0.1	-0.2	0.1	-0.4	0.1	0.20
Change baseline to 6 months											
Raw data*	164	2.1	0.9	143	3.0	1.1	-0.9	1.5	-3.8	2.0	0.53
Model-fitted†		1.8	0.6		2.2	0.6	-0.4	0.8	-2.0	1.1	0.60
Model-fitted using MI‡		1.8	0.6		2.8	0.6	-1.0	0.8	-2.6	0.6	0.20
Change baseline to 12 months											
Raw data*	150	2.3	1.0	131	3.3	1.2	-0.9	1.5	-4.0	2.1	0.55
Model-fitted†		2.2	0.5		2.6	0.5	-0.4	0.7	-1.8	0.9	0.51
Model-fitted using MI‡		2.2	0.5		3.2	0.5	-0.9	0.7	-2.2	0.4	0.16
Change baseline to 18 months											
Raw data*	134	2.1	1.2	120	3.2	1.2	-1.2	1.7	-4.5	2.2	0.49
Model-fitted†		2.6	0.5		3.1	0.5	-0.5	0.6	-1.8	0.8	0.46
Model-fitted using MI‡		2.7	0.5		3.5	0.5	-0.8	0.6	-2.1	0.4	0.19
Change baseline to 24 months											
Raw data*	138	4.1	1.0	126	3.8	1.2	0.3	1.6	-2.8	3.5	0.83
Model-fitted†		3.0	0.6		3.5	0.6	-0.5	0.7	-1.9	0.9	0.48
Model-fitted using MI‡		3.1	0.6		3.9	0.6	-0.7	0.7	-2.2	0.7	0.30

Table H. Femoral-popliteal DVT Subgroup: Disease-specific QOL (VEINES-QOL, VEINES-Sym) results according to treatment: Per Protocol Analysis Set

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-QOL:											
At Baseline	131	53.4	2.0	156	54.0	1.9	-0.6	2.8	-6.2	4.9	
At 30 days	132	66.6	2.1	146	66.5	1.9	0.1	2.8	-5.5	5.6	
At 6 months	116	77.4	2.0	134	78.0	1.9	-0.6	2.7	-6.0	4.8	
At 12 months	111	79.7	2.1	120	80.6	2.0	-0.9	2.9	-6.6	4.9	
At 18 months	102	80.4	2.3	98	81.8	2.2	-1.4	3.2	-7.6	4.8	
At 24 months	105	82.2	2.0	100	81.5	1.9	0.7	2.8	-4.8	6.2	
Change baseline to 30 days											
Raw data*	129	12.3	2.3	144	12.4	1.6	-0.1	2.7	-5.5	5.3	0.97
Model-fitted†		13.0	1.9		12.6	1.8	0.5	2.4	-4.3	5.3	0.85
Model-fitted using MI‡		13.6	2.0		12.5	1.9	1.1	2.5	-3.8	6.0	0.67
Change baseline to 6 months											
Raw data*	114	24.1	2.5	132	24.4	2.0	-0.3	3.1	-6.5	5.8	0.91
Model-fitted†		24.7	2.0		24.4	1.9	0.3	2.4	-4.5	5.1	0.90
Model-fitted using MI‡		25.6	2.0		24.7	1.9	0.9	2.5	-4.1	5.8	0.73
Change baseline to 12 months											
Raw data*	109	24.7	2.5	118	26.0	2.1	-1.3	3.3	-7.7	5.2	0.70
Model-fitted†		25.4	2.0		28.0	1.9	-2.6	2.4	-7.4	2.1	0.28
Model-fitted using MI‡		25.8	2.0		28.7	1.9	-2.8	2.4	-7.6	1.9	0.24
Change baseline to 18 months											
Raw data*	101	25.8	2.8	97	25.1	2.5	0.7	3.8	-6.7	8.1	0.85
Model-fitted†		26.4	2.0		26.8	1.9	-0.5	2.5	-5.3	4.3	0.85
Model-fitted using MI‡		27.0	2.0		27.8	2.0	-0.8	2.4	-5.6	4.0	0.75
Change baseline to 24 months											
Raw data*	104	26.4	2.7	98	25.2	2.4	1.2	3.6	-6.0	8.3	0.75
Model-fitted†		27.4	2.2		25.7	2.2	1.7	2.7	-3.7	7.1	0.54
Model-fitted using MI‡		28.1	2.3		26.8	2.3	1.3	2.8	-4.1	6.7	0.64

Table H, continued

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
VEINES-Sym:											
At Baseline	131	58.2	2.2	156	57.5	2.1	0.7	3.0	-5.2	6.6	
At 30 days	132	70.2	2.1	146	70.5	1.9	-0.3	2.8	-5.8	5.3	
At 6 months	116	78.0	2.0	134	77.0	2.0	1.0	2.9	-4.7	6.6	
At 12 months	111	78.0	2.1	120	78.2	2.0	-0.1	2.9	-5.9	5.6	
At 18 months	102	77.4	2.5	98	78.5	2.3	-1.1	3.4	-7.8	5.5	
At 24 months	105	80.5	2.1	100	80.1	2.1	0.4	2.9	-5.4	6.1	
Change baseline to 30 days											
Raw data*	129	11.2	2.3	144	12.6	1.8	-1.4	2.9	-7.2	4.3	0.63
Model-fitted†		12.7	2.0		12.8	1.9	0.0	2.5	-4.9	4.9	0.99
Model-fitted using MI‡		13.2	2.1		12.4	2.0	0.8	2.5	-4.2	5.7	0.76
Change baseline to 6 months											
Raw data*	114	20.2	2.5	132	19.2	2.2	1.0	3.3	-5.6	7.5	0.77
Model-fitted†		20.5	2.0		19.7	2.0	0.8	2.5	-4.0	5.7	0.73
Model-fitted using MI‡		21.1	2.1		19.5	2.0	1.7	2.5	-3.3	6.7	0.51
Change baseline to 12 months											
Raw data*	109	17.9	2.5	118	19.4	2.3	-1.4	3.4	-8.1	5.2	0.67
Model-fitted†		18.7	2.0		21.0	2.0	-2.3	2.4	-7.1	2.5	0.35
Model-fitted using MI‡		18.8	2.0		21.0	2.0	-2.2	2.5	-7.1	2.7	0.39
Change baseline to 18 months											
Raw data*	101	17.9	2.8	97	18.1	2.7	-0.2	3.9	-7.9	7.5	0.96
Model-fitted†		19.8	2.0		20.7	2.0	-0.9	2.5	-5.7	3.9	0.71
Model-fitted using MI‡		20.2	2.0		20.8	2.0	-0.6	2.5	-5.5	4.2	0.80
Change baseline to 24 months											
Raw data*	104	20.1	2.7	98	19.7	2.2	0.5	3.5	-6.4	7.4	0.89
Model-fitted†		20.9	2.2		20.4	2.2	0.5	2.8	-4.9	5.9	0.86
Model-fitted using MI‡		21.5	2.2		20.6	2.2	0.9	2.7	-4.5	6.3	0.74

Table I. Femoral-popliteal DVT Subgroup: General QOL (SF-36 PCS and MCS) results according to treatment: Per Protocol Analysis Set

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 PCS:											
At Baseline	130	36.7	0.9	156	37.8	0.9	-1.1	1.3	-3.6	1.5	
At 30 days	132	42.7	1.0	146	44.0	0.9	-1.3	1.3	-3.9	1.4	
At 6 months	116	47.8	1.0	134	48.0	1.0	-0.2	1.4	-3.0	2.5	
At 12 months	111	49.0	1.0	120	48.0	1.0	1.0	1.4	-1.8	3.8	
At 18 months	102	49.3	1.1	98	49.5	1.1	-0.2	1.5	-3.2	2.8	
At 24 months	105	49.8	0.9	100	48.8	1.1	1.0	1.4	-1.8	3.8	
Change baseline to 30 days											
Raw data*	128	5.8	1.0	144	6.4	0.8	-0.6	1.3	-3.1	1.9	0.65
Model-fitted†		6.2	0.9		6.7	0.9	-0.5	1.1	-2.6	1.7	0.67
Model-fitted using MI‡		6.3	0.9		6.5	0.9	-0.2	1.1	-2.4	2.0	0.84
Change baseline to 6 months											
Raw data*	114	10.6	1.2	132	11.0	1.0	-0.4	1.6	-3.5	2.6	0.78
Model-fitted†		10.2	0.9		11.0	0.9	-0.9	1.1	-3.0	1.3	0.44
Model-fitted using MI‡		10.5	0.9		10.9	0.9	-0.3	1.1	-2.5	1.9	0.77
Change baseline to 12 months											
Raw data*	108	11.9	1.1	118	10.5	1.0	1.5	1.5	-1.5	4.5	0.33
Model-fitted†		10.7	0.9		11.0	0.9	-0.4	1.1	-2.5	1.7	0.74
Model-fitted using MI‡		11.0	0.9		11.1	0.9	-0.1	1.0	-2.1	2.0	0.95
Change baseline to 18 months											
Raw data*	100	12.6	1.2	97	11.2	1.2	1.4	1.7	-2.0	4.8	0.42
Model-fitted†		11.2	1.0		11.1	0.9	0.1	1.1	-2.1	2.4	0.91
Model-fitted using MI‡		11.4	1.0		11.2	0.9	0.2	1.1	-1.9	2.3	0.86
Change baseline to 24 months											
Raw data*	103	12.4	1.3	98	10.8	1.2	1.6	1.8	-1.9	5.0	0.38
Model-fitted†		11.7	1.1		11.1	1.0	0.6	1.3	-1.9	3.1	0.62
Model-fitted using MI‡		11.9	1.1		11.4	1.0	0.4	1.2	-1.9	2.8	0.71

Table I, continued

Outcome Measure	PCDT			No PCDT			PCDT – No PCDT Difference				
	n	*Mean*	*SE*	*n*	*Mean*	*SE*	*Est.*	*SE*	*95% CI*		*p*
SF-36 MCS:											
At Baseline	131	50.0	1.1	156	51.6	0.9	-1.6	1.5	-4.5	1.3	
At 30 days	132	49.5	1.1	146	51.0	0.9	-1.5	1.4	-4.2	1.2	
At 6 months	116	51.2	1.0	134	52.6	0.8	-1.3	1.3	-3.9	1.2	
At 12 months	111	52.1	1.1	120	52.8	0.9	-0.7	1.4	-3.5	2.1	
At 18 months	102	52.9	1.0	98	54.8	0.8	-1.9	1.3	-4.4	0.6	
At 24 months	105	53.0	0.9	100	55.1	0.7	-2.1	1.1	-4.3	0.1	
Change baseline to 30 days											
Raw data*	129	-0.6	1.1	144	-1.4	0.8	0.7	1.3	-1.9	3.3	0.59
Model-fitted†		0.3	0.1		0.4	0.1	-0.1	0.1	-0.3	0.2	0.60
Model-fitted using MI‡		0.3	0.1		0.5	0.1	-0.2	0.1	-0.4	0.1	0.20
Change baseline to 6 months											
Raw data*	114	1.4	1.2	132	0.0	1.1	1.4	1.6	-1.7	4.5	0.39
Model-fitted†		1.8	0.6		2.2	0.6	-0.4	0.8	-2.0	1.1	0.60
Model-fitted using MI‡		1.8	0.6		2.8	0.6	-1.0	0.8	-2.6	0.6	0.20
Change baseline to 12 months											
Raw data*	109	1.4	1.3	118	-0.2	1.0	1.6	1.7	-1.6	4.9	0.33
Model-fitted†		2.2	0.5		2.6	0.5	-0.4	0.7	-1.8	0.9	0.51
Model-fitted using MI‡		2.2	0.5		3.2	0.5	-0.9	0.7	-2.2	0.4	0.16
Change baseline to 18 months											
Raw data*	101	2.3	1.3	97	0.7	1.1	1.6	1.7	-1.8	4.9	0.36
Model-fitted†		2.6	0.5		3.1	0.5	-0.5	0.6	-1.8	0.8	0.46
Model-fitted using MI‡		2.7	0.5		3.5	0.5	-0.8	0.6	-2.1	0.4	0.19
Change baseline to 24 months											
Raw data*	104	1.7	1.1	98	1.8	1.2	-0.1	1.6	-3.3	3.1	0.95
Model-fitted†		3.0	0.6		3.5	0.6	-0.5	0.7	-1.9	0.9	0.48
Model-fitted using MI‡		3.1	0.6		3.9	0.6	-0.7	0.7	-2.2	0.7	0.30

Table J. Missing QOL Assessments by Visit and Treatment

Visit	PCDT		No PCDT		All	
	n	%	*n*	%	*n*	%
Baseline	7	2%	8	2%	15	2%
1 month	18	5%	35	10%	53	8%
6 months	46	14%	73	21%	119	17%
12 months	66	20%	99	28%	165	24%
18 months	91	27%	133	37%	224	32%
24 months	86	26%	125	35%	211	31%
All Missed	**314**		**473**		**787**	

Appendix A

Interaction terms involving time, treatment and extent of DVT in the growth curve models

For each QOL outcome, interaction terms between treatment and time (one term at each assessment time: baseline, 1, 6, 12, 18 and 24 months) were included in the final growth curve model if they maintained statistical significance at the 0.05 level. Thus, when treatment-specific slopes differed significantly from each other within an assessment interval, the interaction term was retained in the model.

For the VEINES-QOL/Sym outcomes, the interaction terms at baseline, 1, 6 and 12 months were retained, suggesting different rates of change in QOL in the two treatment arms during the interval starting at each of these assessment times. For SF-36 PCS, the terms at baseline, 1 and 6 months remained, indicating a similar effect during these intervals. For SF-36 MCS, only the terms at baseline and 6 months remained in the model, suggesting only one change in slope at 6 months.

For the models which included interaction terms for the two extent subgroups (iliofemoral, femoral-popliteal), the two-factor treatment x time and three-factor treatment x time x extent interactions were assessed concurrently.

For the VEINES-QOL/Sym outcomes, the treatment x time terms at baseline, 1, 6 and 12 months were retained (as above), but only the treatment x time x extent terms at baseline and 1 month remained in the model, suggesting that the larger QOL improvement in the PCDT arm compared with the No PCDT arm, was apparent only for those with iliofemoral DVT and only during the first month post-randomization. Similarly, for SF-36 PCS, the treatment x time terms at baseline, 1 and 6 months were retained (as above), while only the treatment x time x extent terms at baseline and 1 month remained in the model. For the SF-36 MCS, only the treatment x time interactions at baseline and 6 months remained in the model (as above) since none of the three-factor interactions were significant.

Collectively, these observations suggest that the effect of improved VEINES-QOL/Sym and SF-36 PCS QOL with PCDT in the iliofemoral DVT group was statistically different from the effect in the femoral-popliteal DVT group over the first month post-randomization, but not during subsequent time intervals. There were no subgroup differences at any time for the SF-36 MCS.

Appendix B: ATTRACT Study Leadership and Investigators

Steering Committee

Samuel Z. Goldhaber, MD **(Chair)**	Harvard Medical School
David J. Cohen, MD, MSc	St. Luke's Mid America Heart Institute
Anthony J. Comerota, MD	Inova Heart and Vascular Institute, Inova Alexandria Hospital, Alexandria, VA
Heather L. Gornik, MD, MHS, RVT	Cleveland Clinic Heart & Vascular Institute
Michael R. Jaff, DO	Harvard Medical School
Jim Julian, MMath	McMaster University
Susan R. Kahn, MD, MSc	McGill University, Jewish General Hospital
Clive Kearon, MB, PhD	McMaster University
Stephen Kee, MD	UCLA Medical Center *(SIR Foundation representative)*
Andrei L. Kindzelski, MD, PhD	National Heart, Lung, and Blood Institute
Lawrence Lewis, MD	Washington University in St. Louis
Elizabeth Magnuson, ScD	St. Luke's Mid America Heart Institute
Mahmood K. Razavi, MD	St. Joseph's Vascular Institute
Timothy P. Murphy, MD	Brown University
Suresh Vedantham, MD	Washington University in St. Louis *(Principal Investigator)*

Clinical Coordinating Center

Mallinckrodt Institute of Radiology, Washington University in St. Louis, United States

Data Coordinating Center

Ontario Clinical Oncology Group, McMaster University, Hamilton, Canada

Health Economic Core Laboratory

Mid America Heart Institute, St. Luke's Hospital, Kansas City, United States

Vascular Ultrasound Core Laboratory

VasCore, Massachusetts General Hospital, Boston, United States

ATTRACT Clinical Centers: Site Investigators

Adventist Midwest Health: Michael Sichlau – site PI, Athanasios Vlahos, Steven Smith, Quinn Thalheimer, Nisha Singh, Rekha Harting, John Gocke, Scott Guth, Neel Shah

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