The future of iliofemoral deep vein thrombosis treatment

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In the last decade, pharmacomechanical thrombectomy for iliofemoral deep venous thrombosis (DVT) has become increasingly popular. The results from several case series demonstrated good results with improved vein patency, quality of life (QOL), and clinical scores.[1-3] In addition the publication of the 5-year outcomes of the Catheter-directed Venous Thrombolysis (CaVenT) trial had suggested the potential for long-term improvement in post-thrombotic syndrome (PTS) for patients undergoing intervention with an absolute risk reduction for developing a PTS of 15% after 2 years and 28% after 5 years.[4,5]

The recently published data from the Acute Venous Thrombosis: Thrombus Removal With Adjunctive Catheter-Directed Thrombolysis (ATTRACT) trial[6] did not confirm the benefit for the patients 2 years after pharmacomechanical thrombectomy, which is in contrast with the CaVenT study. If the CAtheter Versus Anticoagulation Alone (CAVA) trial, to be published soon, is also unable to objectify the benefit regarding prevention of PTS 1 year after ultrasound accelerated catheter-directed thrombolysis using the EKOS system, the conclusion from the medical community could be to abandon these invasive treatments to prevent PTS based on the results of these later trials. This step, however, would be an error and the publication of the QOL outcomes from the ATTRACT trial by Kahn et al[7] supports this notion.

There have been a number of criticisms of the ATTRACT study that have addressed the principle concerns that the inclusion of femoropopliteal DVT in addition to the more extensive iliofemoral DVTs has diluted the potential outcomes. This was supported by the publication of the subgroup analysis by Comerota et al[8] and is further enhanced by the findings of the QOL analysis presented by Kahn et al.[7] In simple terms, patients with iliofemoral DVT have worse outcomes if treated with an oral anticoagulant alone, and the potential for benefit from treatment is likely to be greater.

The analysis by Kahn et al[7] indicates that patients with iliofemoral DVT have a sustained improvement in QOL out to 24 months if treated and is significant at every follow-up point. This improvement in QOL is an important finding because the similar comparison in the CaVenT trial failed to show this benefit. Clearly the use of a disease-specific QOL tool may explain some of this benefit, but the findings again serve to highlight that the focus for treatment should legitimately continue to be on the iliofemoral segment. To compare all future publications related to these treatments, we should standardize the diagnosis, as for example proposed by Strijkers et al,[9] using the lower extremity thrombosis classification (LET classification). Only common femoral, iliac, and inferior vena cava thromboses should be considered for this treatment and these are LET 3 and 4 scores. The benefit may be even greater, if we analyze the potential screening bias that existed in the ATTRACT trial. For every 50 patients screened only one was enrolled. The balance failed either owing to age or comorbidities such as cancer that excluded the patients (ie, screen failures). This ratio is not the experience of most centers and the possible conclusion is that many patients with severe DVT were not considered for the study and treated. These patients are potentially likely to have demonstrated an even greater benefit.

The complexity of running trials in multiple centers has compounded interpretation of the results for the ATTRACT trial, and likely will be the same for the CAVA trial. It is well-recognized that expert centers are likely to get better outcomes and the results of treatment are directly related to the quality of the intervention. Poor treatment vs best medical therapy results in predictable outcomes. In the ATTRACT trial no patency data are presented beyond the initial procedure—although a small subgroup will be analyzed—and its therefore difficult to know if the vein was patent in the long term. In the CAVA study, these long-term outcomes have been tracked, which may help in clarifying the importance of a patent vein at follow-up to the ultimate success of intervention. It is vital to compare successful (is patent) procedures vs nonsuccessful procedures. When successful procedures do show a clinically significant benefit, we should not abandon this treatment but improve the treatment with better tools and techniques to increase the success rate and lower the complication rate. Improvements such as purely mechanical tools that takes out the clot in less than 1 hour in a day care procedure of course with, if necessary, stenting of an underlying

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mechanical outflow obstruction as a cause for the DVT, may decrease both bleeding risk and the cost of these procedures.

Ultimately the publication of further outcomes from the initial ATTRACT study has allowed some clarity of treatment strategies to be formed. Patients with femoropopliteal disease (LET 1 and 2) alone should not currently be treated, but those with extension into the iliofemoral segment (LET 3 and 4) are likely to benefit.

The continued uncertainty of the outcomes of the study are driven in principle by the ongoing difficulty of agreeing and establishing unequivocal classification and outcome measures that are broadly agreed on by the community to be appropriate for DVT.

We have not settled on a standard definition of proximal/distal DVT, which is now outdated and is reflected by the ATTRACT results. Proposals such as the LET score, which classifies DVT into three groups, have not yet been applied widely despite offering the benefit of a clearer anatomical division and improved patient selection.

The Villalta score has been widely criticized—it is a very sensitive but not very specific score—and its application as a binary measure has been heavily criticized. Despite this no consensus has been reached on what an alternative score should be. The Venous Clinical Severity Score was used in the Comerota paper and suggests that, if this had been the outcome measure for the ATTRACT trial, it would have demonstrated a positive result. This is further compounded by the absence of a clear score for Venous Claudication in any of the outcome measures but specifically the Villalta scale.[10] Better and more robust clinical outcome measure could influence the trial results significantly.

In conclusion, the ongoing publication of results from the ATTRACT study—first the Comerota subgroup analysis and now the QOL outcomes from Kahn et al[7]—continues to support the arguments for treating iliofemoral (LET 3 and 4) disease. Let us take arms against the clot and by treating end the suffering of patients with PTS.

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