Journal club

"Getting the clot out" – has the ATTRACT trial truly failed?

One of the most important complications after proximal deep-vein thrombosis (DVT) is the post-thrombotic syndrome (PTS) leading to chronic limb pain, swelling, venous claudication or leg ulcers. Half of the patients with ilio-femoral thrombosis develop PTS [1]. Standard therapy is immediate therapeutic anticoagulant therapy after diagnosis of DVT. Anticoagulation and compression stockings are the mainstay to prevent PTS, venous insufficiency and relief the symptoms [2]. Additionally, guidelines as well as various randomized trials have suggested the "open vein hypothesis", indicating active removal of acute thrombus reducing development of PTS in these patients [3]. Several approaches to get the clot out are in use including pharmacomechanical catheter-directed local thrombolysis with or without active thrombus aspiration [4].

The ATTRACT trial is a multicentre phase III trial including 692 patients with acute proximal deep-vein thrombosis randomly assigned in a 1:1 ratio to the standard therapy group (anticoagulation alone) or the intervention group with anticoagulation plus pharmacomechanical thrombolysis [5]. Primary outcome was the cumulative occurrence of post-thrombotic syndrome after six and 24 months with the the Villalta Score and the Venous Clinical Severity Score [6, 7]. Secondary outcomes addressed safety, quality of life, severity of a PTS and cost-effectiveness. Of the 692 individuals recruited from December 2009 through December 2014, 337 were in the intervention group, 355 in the control group. In the intervention group, median days to stopping anticoagulant therapy was 211, compared to 231 in the control group, compression stocking use after 24 months for three or more days a week was comparable as well with 55% in both groups. The fibrinolyitic drug used was recombinant tissue plasminogen activator (r-tPA, Alteplase), in 82/336 (24%) patients, stents have been placed. After 24 months, there was no difference in both groups in the primary analysis, PTS developed in 157/336 (47%) in the intervention group and 171/355 (48%) in the control group respectively ($p = 0.56$). Moderate-to-severe PTS, defined as a Villalta score of 10 or higher, occurred in 18 vs. 24% with a significant benefit for patients treated by pharmacomechanical thrombolysis ($p = 0.04$) after 24 months. In visits at six, 12 and 18 months the Villalta score was significantly lower in the intervention group. The analysis of quality of life performed by the SF-36 questionnaire (generic Medical Outcomes Study 36-Item Short Form Health Survey) showed no significant difference in both groups, neither did the analysis of leg circumference after 10 and 30 days. In the short-term analysis of safety outcomes, more major bleeding in the intervention group (1.7%) than in the control group (0.3%) occurred. Recurrent venous thromboembolism occurred in 12 and 8% in the intervention group and the control group, respectively ($p = 0.09$).

Major limitations of the study might be an incomplete follow-up with missed visits especially in the control group, which is pointed out by the authors. The study also had limited power for subgroup analysis but there was a suggestion that younger patients, aged <65 years, were more likely to benefit from the intervention. The results of the ATTRACT trial also show a reduced severity of the PTS after pharmacomechanical thrombolysis which suggests that other subgroups may profit from an interventional treatment. The authors also did not differentiate between descending and ascending proximal deep vein thrombosis which have two different pathomechanisms and a different prognosis with standard therapy. In 43% of all patients in this trial, the popliteal vein was affected by thrombus. So, patients with ilio-femoral as well as femoropopliteal deep-vein thrombosis were included. During the last decade dedicated stents for venous interventions have been developed specifically addressing the requirements such as high flexibility and high radial force. These stents have not been used in the ATTRACT trial.

Despite the pure data with no significant difference between pharmacomechanical thrombolysis therapy and conventional standard therapy with anticoagulation, the ATTRACT trial may also show that pharmacomechanical catheter-directed thrombolysis should be performed only in a highly specific population, e.g., in young patients with a highly symptomatic descending proximal deep-vein thrombosis and a low risk for bleeding complications. Therefore more data of a more selective population needs to be collected to further confirm the hypothesis of "getting the clot out" as well as to reunite the two disagreeing camps of physicians who either prefer recanalization or stenting.

References

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