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Letter to the Editors-in-Chief

Suitability for catheter-directed thrombolysis in patients with acute lower extremity deep vein thrombosis according to various international consensus guidelines

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1. Introduction

Patients with iliofemoral deep vein thrombosis (DVT) have the highest risk of a post-thrombotic syndrome (PTS), and spontaneous recanalization is frequently incomplete in these patients with conservative treatment [1]. Early thrombus removal aims to prevent PTS by restoring venous patency and preserve valve function [2]. Among the different treatment options, catheter-based thrombus removal therapies (CBTR) have the most favorable risk–benefit ratio and are the recommended treatment strategy in selected patients with proximal DVT according to the latest international consensus guidelines [2–6]. Catheter-directed thrombolysis (CDT) or percutaneous mechanical thrombectomy alone or with additional CDT, also known as pharmacomechanical thrombectomy, are the CBTR techniques most frequently used nowadays [7].

Several studies have reported on short-term success of CBTR concerning thrombus load reduction, but high-quality studies with relevant clinical outcomes such as PTS, DVT recurrence or quality of life are still sparse [7]. In the Norwegian CaVenT trial, patients with acute DVT localized in the upper half of the thigh or more proximal treated with additional CDT had a significant reduction in the absolute PTS risk of 15% after 2 years and 28% after 5 years compared to patients treated with conservative therapy alone [1,8]. However, the recently published ATTRACT study, the largest randomized controlled trial comparing different CTBR therapies with conservative treatment in nearly 700 patients with acute proximal DVT, did not show any reduction in the incidence of PTS over a follow-up of 2 years, but only a reduction of PTS severity [9].

Because PTS develops several months or years after initial DVT diagnosis, awareness of PTS among the emergency physicians dealing with acute DVT might be low. Furthermore, there is currently no consensus among the different medical societies on which patient should be offered CDT, and selection criteria vary considerably between the different guidelines [2–6].

This study aims to evaluate and compare the proportion of patients with confirmed lower extremity DVT suitable for CDT according to the most recent international consensus guidelines.

2. Methods

We performed a post-hoc analysis of a prospectively collected database on consecutive patients older than 18 years of age with objectively confirmed acute lower extremity DVT by duplex sonography in a tertiary teaching hospital in Switzerland from January 2014 to December 2015. Thrombosis extension was defined according to the lower extremity thrombosis classification (LET) [10] (see Fig. 1). Proximal DVT was defined as LET class II, III and IV.

We selected the five most established international guidelines on CBTR for DVT (Table S1 in Supplementary Appendix): a) Scientific statement for the management of iliofemoral DVT from the American Heart Association (AHA-IFDVT) [3]; b) Clinical practice guidelines from the Society for Vascular Surgery and the American Venous Forum (SVS-AVF) [4]; c) Quality improvement guidelines for the treatment of lower extremity DVT from the Society of Interventional Radiology and Cardiovascular and Interventional Radiology Society of Europe Standards of Practice Committees (SIR-CIRSE) [6]; d) Scientific statement for the management of PTS from the American Heart Association (AHA-PTS) [2]; e) 10th Guideline and expert panel report on the antithrombotic therapy for venous thromboembolism from the American College of Chest Physicians (ACCP10) [5]. For patients fulfilling the anatomic inclusion criteria for catheter-based treatment according to the different guidelines, retrospective chart review to assess the complete inclusion and exclusion criteria was performed. Life expectancy was considered < 1 year for patients with a metastatic cancer, and institutionalized patients were considered as having a bad functional status. The bleeding risk was considered low if no absolute contraindication was present. The study was conducted according to local institutional review board regulations.

Primary endpoint was the proportion of patients with acute lower extremity DVT who were considered suitable for CDT according to each consensus guideline, defined as conformity with all recommendations (inclusion criteria) in the absence of absolute contraindications. Secondary endpoints were the proportion of patients with acute proximal DVT considered suitable for CDT, the proportion of patients considered suitable for

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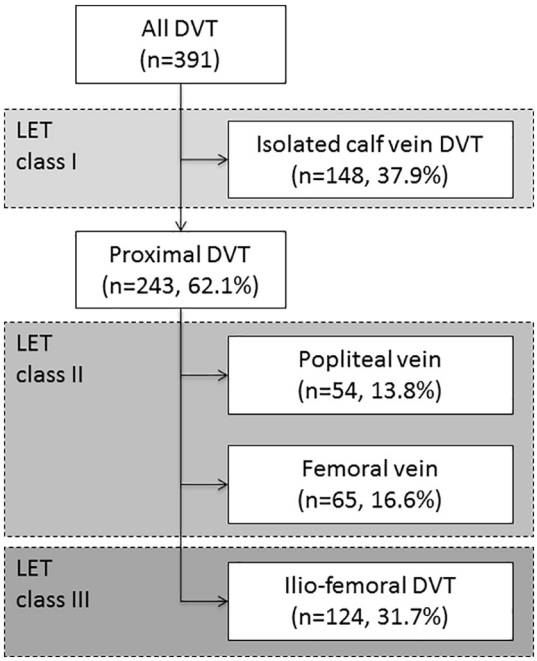

Fig. 1. Frequency of DVT according to the LET classification [10].
Definition: LET class I includes isolated calf vein thrombosis, LET class II thrombus extension up to the popliteal and/or femoral vein, LET class III iliofemoral DVT defined as thrombosis of the common femoral and/or the iliac veins, and LET class IV for thrombosis extension into the inferior vena cava.
Abbreviations: DVT, deep vein thrombosis; LET, lower extremity thrombosis classification.

CDT without any relative contraindication, and the description of the different contraindications. Cochran's Q test was used to compare the primary endpoint for each guideline, with pairwise comparisons using the McNemar test with Bonferroni correction in case of rejection of the null hypothesis of proportion equality.

3. Results

A total of 391 patients (51% women) with a mean age of 61.3 ± 19.4 years (median 64 years, range 18–101 years) were included. Of the 243 (62.1%) patients with proximal DVT, 124 (51%) were iliofemoral DVT (LET class III, Fig. 1). Patients with LET class III were older (67.7 ± 19.4 years) than patients with LET class I (57.0 ± 19.7 years) or II (59.9 ± 17.4 years, $P < 0.01$ for both comparisons).

3.1. Suitability for catheter-based early thrombus removal

The primary endpoint of suitability for CDT was around 11% for the AHA-IFDVT, the AHA-PTS and the ACCP10 guidelines, with a significantly higher proportion for the SIR-CIRSE guidelines (22.5%) and a significantly lower proportion for the SVS-AVF guidelines (6.1%; $P < 0.001$ for both compared with the other guidelines, Table 1). Absolute contraindications were more frequent for the SVS-AVF guidelines (17.7%, $P < 0.001$ compared to the other guidelines). The most frequent absolute contraindications were thrombocytopenia (n = 10), intracranial neoplasia (n = 5) and suspected or confirmed septic thrombus (n = 5).

4. Discussion

The key finding of the present study is that suitability for CDT for the treatment of acute lower extremity DVT is highly variably between the most respected international consensus guidelines on the management of DVT [2–6]. Especially the important difference in suitability between the radiological and the surgical guidelines might have an important impact on health-care facilities and costs.

Despite the lack of high-quality evidence supporting the use of CDT, a recent analysis of the Nationwide Inpatient Sample database including > 90,000 hospitalized patients with the principal discharge diagnosis of proximal DVT showed that the rate of CDT nearly tripled from 2.3% in 2005 to 5.9% in 2010 in the United States [11]. The same database showed that CDT was associated with increased length of stay and hospital charges, higher rate of pulmonary embolism and bleeding complications, and the rate of in-hospital mortality and intracranial bleedings was higher in low-compared to high-volume institutions [11,12]. According to our study, even a higher percentage of patients with lower extremity DVT would be suitable for CDT. Suitability for CDT ranged from 6.1% and 9.9% for the SVS-AVF guidelines to 22.5% and 36.2% for the SIR-CIRSE guidelines for all and proximal DVT, respectively. In a similar study by Nghiem et al. including 208 cases of acute occlusive lower extremity DVT, 25.1% of patients with a proximal DVT were considered suitable for CBTR according to selection criteria based on the ACCP guidelines and the ATTRACT protocol [13]. These important differences between the guidelines, with nearly 4 times more patients suitable for the SIR-CIRSE guidelines compared to the SVS-AVF guidelines, have an important impact on healthcare facilities and hospital costs [11].

It is interesting to note that the suitability rate was highly depending on the medical speciality. The surgical guidelines from the SVS-AVF were much more restrictive than the interventional radiology guidelines from the SIR-CIRSE, and medical guidelines from the AHA and the ACCP were in between. All guidelines only included patients with iliofemoral DVT (LET III), except for the SIR-CIRSE guidelines, which also included proximal femoral DVT. Furthermore, symptom duration of up to 28 days was allowed in the SIR-CIRSE guidelines, while for most of the other guidelines the